ORGAN DONATION AFTER DEATH BY CIRCULATORY CRITERIA

ORGAN DONATION AFTER DEATH DETERMINATION BY CIRCULATORY CRITERIA: EVALUATION OF TWO CONTROVERSIAL PRACTICES

By KIMIA HONARMAND, MSc, MD, FRCPC

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Lay Abstract

Organs that are donated and transplanted from deceased individuals save thousands of lives every year. Some organs are donated after death by circulatory criteria (i.e., after the heart has stopped beating). We evaluated two controversial practices in organ donation after death is determined by circulatory criteria: (1) giving heparin, a blood thinner, just before death, and (2) heart donation after death is determined by circulatory criteria. In *Project 1,* our review of existing literature showed broad differences in heparin use around the time of death and heparin had no benefits on liver transplant outcomes. In *Project 2,* we found that healthcare providers and members of the public supported heart donation after death is determined by circulatory criteria but expressed concerns that are important to consider when establishing heart donation programs. Our approach of using multiple methods to evaluate practices in organ donation can serve as one model for evaluating other controversial practices in organ donation.

Abstract

Background

Organ donation may occur after death determination by neurological criteria or by circulatory criteria (DCC). This thesis evaluates two controversial practices specific to DCC: (1) antemortem heparin administration to DCC donors with the aim of improving organ function, and (2) cardiac donation after DCC, which has not yet been adopted in Canada.

Objectives

(1) Describe antemortem heparin practices in DCC and explore its effects on transplant outcomes.

(2) Describe the opinions, concerns, and insights of Canadian healthcare providers and the public regarding cardiac DCC.

Methods

Project 1: Systematic review and meta-regression analysis of published studies examining antemortem heparin in DCC donation.

Projects 2 and 3: A qualitative interview study to evaluate the perspectives of healthcare providers and a mixed methods study involving focus groups with members of the Canadian public.

Results

Project 1: We found broad variability in the dosing and timing of heparin administration in DCC. While there were no clinical trials, meta-regression analysis detected no benefit to antemortem heparin in liver transplantation.

Projects 2 and 3: Among healthcare providers, we found broad support for cardiac DCC but concerns about potential lack of support by the public. Among members of the public, we found majority support for cardiac DCC with priorities including respect for the wishes of dying individuals and ensuring that they are treated with dignity.

Conclusions

While preliminary results failed to demonstrate the benefit of antemortem heparin administration to DCC donors, high-quality clinical trials are needed to better evaluate the risks and benefits. Regarding cardiac DCC, despite healthcare providers' concerns about lack of public support, most public stakeholders engaged in our study were supportive. The multi-modal approach of this thesis may serve as a model for evaluating other controversial practices in deceased organ donation.

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List of Abbreviations and Symbols

DCC: Death determination by circulatory criteria

SDM: Substitute decision maker

DCDD: Donation after circulatory death determination

DPP: Direct Procurement and Perfusion

NRP: Normothermic Regional Perfusion

COVID-19: Coronavirus Disease 2019

Declaration of Academic Achievement

I declare this thesis to be my own work. I am the primary author of all chapters included in this thesis, responsible for project conceptualization and design, data collection, data analyses, data interpretation, and manuscript preparation. The contributions of co-authors vary for each of the studies and include conceptualization and study design, data collection, data analysis, data interpretation, and manuscript revision. The following individuals contributed to various aspects of the projects: Dr. Maureen O. Meade, Dr. Gordon Guyatt, Dr. Bram Rochwerg, Dr. Emilie Belley-Cote, Dr. Ian M. Ball, Dr. Jeanna Parsons Leigh, Dr. Aimee Sarti, Dr. John Basmaji, Dr. Marat Slessarev, Dr. Frederick D'Aragon, Dr. Dr. Fayez Alshamsi, Michaël Chassé, Dr. Farid Foroutan, Ms. Alla Lansavitchene, Ms. Danielle LeBlanc, Ms. Sydni Paleczny, Dr. Graham Mclure, Dr. Markus Selzner, Dr. Alp Sener, Dr. Sam Shemie, Mr. Robert Sibbald, and Dr. Matthew J. Weiss.

Chapter 1. Introduction

1.1 Background

1.1.1 Deceased Organ Donation & Transplantation

Organ transplantation is considered definitive treatment for patients with end-stage organ failure (Grinyo, 2013). A deceased organ donor can potentially donate up to eight organs, including heart, lungs, liver, pancreas, kidneys, and small bowel, if the function of the organ is deemed to be adequate for transplantation. However, demand far exceeds the supply of available organs (Lewis, Koukoura, Tsianos, et al., 2021.

1.1.2 Death Declaration in the Context of Organ Donation

Based on Canadian evidence-based guidelines (Shemie, Wilson, Hornby, et al., 2023), in deceased organ donation, organ retrieval for transplantation can only occur after death has been declared. This foundational principle, often referred to as the 'Dead Donor Rule', purports that death must occur prior to organ retrieval (Truog & Robinson, 2003). In patients receiving organ support (i.e., mechanical ventilation), there are two distinct approaches to determining that death has occurred: (1) Death determination by neurological criteria (formerly known as neurological determination of death) and (2) death determination by circulatory criteria (DCC; previously known as circulatory determination of death).

Organ Donation After Death Determination by Neurological Criteria

In donation after death determination by neurologic criteria, a patient with catastrophic brain injury who is maintained on organ support (e.g., invasive mechanical ventilation) but has no clinical or imaging evidence of brain activity is determined to be dead by two physicians (Shemie et al., 2023). If organ donation is believed to have been consistent

with the patient's prior wishes, their substitute decision maker (SDM) may consent to the patient being assessed for possible organ donation while the patient is still on organ support. In this scenario, the patient's cardiac activity and circulation to organs other than the brain is maintained during the organ assessment and subsequent organ retrieval processes (Shemie et al., 2023). Any organ (e.g., heart, lungs, liver, pancreas, kidneys, small bowel) and tissue can be retrieved from donors for the purposes of transplantation, if it is deemed to have adequate function.

Organ Donation After Death Determination by Circulatory Criteria

Although most deceased organ donation involves donors who have been determined to be dead based on neurological criteria, DCC is an alternative source of organs in circumstances where a patient does not meet death determination by neurologic criteria but there the prognosis for meaningful recovery, as judged by an informed family, is grim. DCC is considered in patients receiving organ support (i.e., invasive mechanical ventilation) for whom a decision is made by their SDM, in discussion with the patient's healthcare team, to withdraw life-support and allow the patient to die from their underlying illness or injury (Shemie, Baker, Knoll, et al., 2006). If organ donation is believed to have been consistent with the patient's prior expressed wish, the SDM may decide to allow the patient to be assessed for possible organ donation prior to the withdrawal of life-sustaining measures (Shemie et al., 2006). If the patient is deemed to be eligible for organ donation, the healthcare team proceeds with withdrawal of life-sustaining measures. After the patient passes, and usually after a 5-minute observation period to ensure the absence of circulation, two physicians will determine death by circulatory criteria (Shemie et al., 2006). Only then, will organ retrieval take place in the operating room.

According to Canadian Blood Services, DCC has the greatest potential for increasing the deceased organ donor pool (Canadian Blood Services, 2015). Currently in Canada, all

organs except the heart, can be retrieved from DCC donors for the purposes of transplantation. To date, no cardiac donation after DCC has taken place in Canada, although this procedure has been performed in other countries (Messer et al., 2020; Chew et al., 2019; Hoffman et al., 2021; Miñambres et al., 2021). Adoption of DCC in many countries has substantially increased the supply of transplantable organs globally (Canadian Blood Services, 2015; DSA Data on Donation and Transplantation, 2017; NHS Blood and Transplant, 2017).

1.1.3 Inconsistent Terminologies in Deceased Organ Donation

There are historical variations in the terminologies around death determination in the context of organ donation. A recent Canadian Clinical Practice Guideline (Shemie et al., 2023) has established standardized terminology, including death determination by circulatory criteria or DCC, that will be used in most of this dissertation. Alternative terms for DCC include Donation after circulatory death determination (DCDD; a term which is used in the published study in Chapter 2), donation after circulatory death, cardiac death, circulatory death, cardio-circulatory death, non-heart beating donation (Thuong, Ruiz, Evrard, et al., 2016).

1.1.4 Controversial Practices in DCC as Threats to the Organ Donation System

Success of any organ donation system relies on the altruistic motives of public (e.g., registration for organ donation after death) and the potential donor's SDM agreeing to proceed with organ assessment and retrieval. Any factors that decrease trust in the organ donation system may pose threats to organ donation. As such, it is paramount to engage stakeholders, including healthcare providers, the general public, and donor families, in discourse around existing or emerging organ donation practices and protocols (Escoto, Issa, Cayouette, et al., 2023).

Stakeholder engagement in the topic of organ donation is challenging due to the limited knowledge of some healthcare workers and the general public about the intricacies and complexities of various donation protocols. This necessitates education prior to discussing stakeholder perspectives. In addition, perspectives about complex issues such as organ donation, occur on a continuum and are rarely binary. As such, multi-method studies are best suited to evaluate perspectives around such complex topics (Morgan, 1996).

1.2 Overview of Thesis Projects

The projects described in this thesis evaluate two controversial donation DCC protocols: (1) the administration of high-dose intravenous heparin during the antemortem period in donation after DCC, and (2) cardiac donation after DCC. The thesis objectives include:

Antemortem heparin administration in DCC organ donors (Chapter 2):

- To describe the breadth of practices regarding antemortem heparin administration to DCC organ donors as reported in existing studies.
- To explore the effects of antemortem heparin administration on transplant outcomes based on existing studies.

Cardiac donation after DCC (Chapters 3-5):

- To understand the opinions, concerns, and insights of healthcare workers and the general public in Canada regarding cardiac DCC protocols.
- To identify barriers and facilitators for implementing cardiac DCC protocols in Canada.
- To establish strategies to facilitate implementation of cardiac DCC in a manner that is consistent with Canadians' values.

1.3 Organization of the Thesis

Chapter 1 presented an introduction to the content and structure of this thesis;

Chapter 2 focuses on the first project, related to the antemortem administration of intravenous heparin in DCC, and culminates with the already published first paper;

Chapter 3 introduces the second and substantially larger project, which was related to cardiac donation after DCC, and culminates in the already published second paper of this thesis: the protocol for the two projects described in Chapter 4 and 5;

Chapter 4 presents the manuscript for a qualitative study of healthcare providers' perspectives about cardiac donation after DCC which has been prepared for submission at the time of the submission of this thesis;

Chapter 5 presents the manuscript for a mixed methods study of the Canadian public's perspectives about cardiac donation after DCC which has been prepared for submission at the time of the submission of this thesis;

Chapter 6 provides a general discussion of these works, with conclusions for future directions.

Chapter 2. Heparin in Donation After Death Determination by Circulatory Criteria

2.1 Preamble

2.1.1 Antemortem heparin administration in DCC

A key concern about organ retrieval in the context of DCC is the potential for formation of microthrombi (small blood clots) within organs during the peri-mortem low-flow and post-mortem no-flow states prior to organ retrieval, which may decrease successful transplantation (Algahim & Love, 2015). This concern is unique to DCC (since circulation after death determination by neurologic criteria persists until the moment of organ retrieval) and has been the impetus for the administration of high-dose intravenous heparin around the time of withdrawal of life-support in potential DCC donors at many centres.

Heparin, also known as unfractionated heparin, is an anticoagulant medication that binds to and activates antithrombin III, which in turn inactivates thrombin and factor Xa in the coagulation pathway, reducing the risk of thrombus (clot) formation in the blood (Schwartz, 1990). When used in DCC donors, heparin is administered intravenously at doses as high as 1000 units/ kilogram or 50,000 units in some studies (Kollmann et al., 2018; De Vera et al., 2009) around the time of withdrawal of life-support. It is hypothesized that for heparin to have any potential benefit on organs, it must be administered while there is still cardiac activity that can circulate the drug to the organs; as such, heparin is often administered prior to cessation of cardiac activity and determination of death.

2.1.2 Ethical concerns about antemortem heparin administration in DCC

Antemortem interventions in the context of organ donation has raised ethical concerns. Administering an intervention for the sole purposes of *potentially* preserving organs for donation, without any direct benefit to the health or comfort of the dying individual, has been

questioned (Motta, 2005; Brierley & Shaw, 2016; Truog & Robsinson, 2003; Rady et al., 2008). This concern is unique to DCC donation since most interventions aiming to preserve organ function in donors declared dead by neurologic criteria are administered *after* death has already been determined. The ethical discussions of peri-mortem interventions are being conducted without robust empirical evidence evaluating the actual benefits and harms (Shemie et al., 2006).

2.1.3 Objectives

The project described in Chapter 2 is a systematic review and meta-regression analysis, aiming to:

1. Describe the breadth of practices regarding antemortem heparin administration to DCC organ donors as reported in published studies across all countries.
2. Explore the reported effects of antemortem heparin administration on transplant outcomes based on existing studies.

Chapter 2 has been previously published (Honarmand et al. Transplantation 2021; 105(12):e337-e346. doi: 10.1097/TP.0000000000003793.).

2.2 Antemortem Heparin in Organ Donation after Circulatory Death Determination (DCDD): A Systematic Review of the Literature

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Title: Antemortem heparin in organ donation after circulatory death determination (DCDD): a systematic review of the literature

Authors:
Kimia Honarmand MD MSc[1], Fayez Alshamsi MD[2], Farid Foroutan PhD[3], Bram Rochwerg MD MSc[4,5], Emilie Belley-Cote MD PhD[4,5,6,7], Graham Mclure MD MSc[5], Frederick D'Aragon MD MSc[8], Ian M. Ball MD MSc[1,9], Alp Sener MD PhD[10], Markus Selzner MD[11], Gordon Guyatt MD MSc[5,12], Maureen O. Meade MD MSc[4,5]

Affiliations:
1 Division of Critical Care, Department of Medicine, Western University, London, Canada
2 Department of Internal Medicine, College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates.
3 Ted Rogers Centre for Heart Research, Peter Munk Cardiac Center, Toronto, Canada
4 Division of Critical Care, Department of Medicine, McMaster University
5 Department of Health Research Methods, Evidence, and Impact (HEI), McMaster University, Hamilton, Canada
6 Division of Cardiology, Department of Medicine, McMaster University
7 Population Health Research Institute, Hamilton, Canada
8 Department of Anesthesiology, Université de Sherbrooke, Quebec, Canada
9 Department of Epidemiology and Biostatistics, Western University, London, Canada
10 Department of Surgery and Microbiology and Immunology, Schulich School of Medicine & Dentistry, Western University, London, Canada
11 Multi-Organ Transplant Program, Department of Surgery, Toronto General Hospital, Toronto, Canada
12 Department of Medicine, McMaster University, Hamilton, Canada

Corresponding Author
Kimia Honarmand MD MSc
Critical Care Western, Department of Medicine, Western University
London Health Sciences Centre, 800 Commissioners Rd E, London Canada N6A 5W9
kimia.honarmand@medportal.ca

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Abbreviations

DCDD, donation after circulatory death

DGF, delayed graft function

MAP, mean arterial pressure

NDD, neurological determination of death

RCT, randomized controlled trials

ABSTRACT

Donation after circulatory death determination (DCDD) frequently involves antemortem heparin administration to mitigate peri-arrest microvascular thrombosis**.** We systematically reviewed the literature to: (1) describe heparin administration practices, and (2) explore the effects on transplant outcomes. We searched MEDLINE and EMBASE for studies reporting DCDD heparin practices including use, dosage, and timing (Objective 1). To explore associations between antemortem heparin and transplant outcomes (Objective 2), we (i) summarized within-study comparisons and (ii) used meta-regression analyses to examine associations between proportions of donors that received heparin and transplant outcomes. We assessed risk of bias using the Newcastle Ottawa Scale and applied the GRADE methodology to determine certainty in the evidence. For Objective 1, among 55 eligible studies, 48 reported heparin administration to at least some donors (range: 15.8% to 100%) at variable doses (up to 1000 units/kg) and times relative to withdrawal of life sustaining therapy. For Objective 2, seven studies that directly compared liver transplants with and without antemortem heparin reported lower rates of primary nonfunction, hepatic artery thrombosis, graft failure at 5 years, or recipient mortality (low certainty of evidence). In contrast, meta-regression analysis of 32 liver transplant studies detected no associations between the proportion of donors that received heparin and rates of early allograft dysfunction, primary nonfunction, hepatic artery thrombosis, biliary ischemia, graft failure, re-transplantation, or patient survival (very low certainty of evidence). In conclusion, antemortem heparin practices vary substantially with an uncertain effect on transplant outcomes. Given the controversies surrounding antemortem heparin, clinical trials may be warranted.

INTRODUCTION

The persistent and high global demand for transplantable organs from deceased donors includes over 113,000 candidates on transplant waiting lists in the United States [1], over 4,000 in Canada [2] and over 6,000 in the United Kingdom [3].

Although the majority of organs are donated after a neurologic determination of death (NDD), donation after circulatory determination of death (DCDD) contributes to a substantial and rising proportion of organs donated globally, accounting for 17% of transplants in the United States in 2016 [1], 29% of deceased donations in Canada in 2018 [2], and 39% of deceased donations in the United Kingdom in 2017-2018 [3].

Theoretical concerns suggest that, in DCDD, formation of microthrombi and clots within organs during the low-flow or no-flow state prior to organ recovery may have deleterious effects on transplant function and longevity. This concern has, at some centers, motivated the antemortem administration of intravenous heparin [4]. In addition to its known anticoagulant properties, animal studies suggest that antemortem heparin decreases graft endothelial damage, increases antiplatelet activity, preserves nitric oxide activity, and inhibits of leukocyte adhesion [5-7].

For intravenous heparin to reach the organs intended for donation, it must be administered prior to the cessation of circulation. However, antemortem treatments for dying patients who will not derive any direct health benefits remain controversial [8-9]. Consequently, some clinicians are reluctant to administer heparin prior to determination of death, despite requests from transplant teams [10]. This is particularly an issue when the potential donor's condition could be exacerbated and therefore death hastened by the administration of high dose heparin prior to death (i.e., intracranial or pulmonary hemorrhage).

Recommendations regarding antemortem heparin administration vary substantially across jurisdictions and among donor management guidelines. American guidelines suggest

following local policies and procedures [11], while antemortem interventions including heparin are strictly prohibited in some other countries including the United Kingdom [12]. Canadian guidelines provide no recommendation regarding antemortem heparin and identified this issue as an important research priority [13].

The clinical benefits of antemortem heparin on graft and recipient outcomes remain unclear. We launched this systematic review with two objectives:

1. To describe the breadth of reported practices regarding antemortem heparin administration to DCDD organ donors.
2. To explore the effects of antemortem heparin administration on transplant outcomes.

METHODS

Eligibility Criteria, Search Strategy & Study Selection

With the support of a librarian, we searched Ovid Medline and EMBASE to identify English-language articles (from database inception until July 2020) including the search terms 'human' and 'donation after circulatory death', 'transplant outcomes', and other synonymous terms (**SDC, Methods**). 'Heparin' and related terms were not required components in this step because we anticipated that heparin therapy would not be the primary focus of most reports relevant to this review. We assessed for heparin and related terms during full-text review.

We sought randomized controlled trials (RCTs) or observational studies of DCDD transplants that (1) reported whether or not antemortem heparin was administered, or (2) explored the effects of antemortem heparin on any transplant outcome. We excluded studies with fewer than 10 donors, studies of islet cell or cardiac transplantation, uncontrolled DCDD, and studies with outdated practices in organ donation (i.e., post-mortem chest compressions prior to organ recovery).

Three reviewers (KH, FA, FF) screened titles and abstracts independently and in duplicate to identify articles describing DCDD transplants, then reviewed articles in full to identify those that met the inclusion criteria (including whether or not antemortem heparin administration was described). A fourth reviewer (MM) resolved conflicts. When two or more articles reported data from overlapping cohorts, we included the study with the largest sample size and supplemented information from the overlapping reports.

Data Extraction

One reviewer (KH) extracted the following elements: study design, number of study participants (organ donors and/or recipients); details about antemortem heparin administration (including proportion of donors receiving heparin, the dose or dose range, and timing of administration); recipient outcomes (including delayed graft function [DGF; for kidney transplants only], primary graft dysfunction, primary non-function, acute or chronic rejection, re-transplantation, graft and recipient survival); and organ-specific complications including, but not limited to, graft arterial or venous thrombosis. We recorded the frequency of each outcome as defined by each study.

Data Analysis

To describe the range of practices regarding antemortem heparin (Objective 1), we summarized the proportion of donors who received antemortem heparin, the dose or dose range of heparin administered, and the timing.

We planned a number of approaches to examine the effects of antemortem heparin on organ and recipient outcomes (Objective 2). First, we had planned to meta-analyze either observational or RCT data to generate pooled point estimates examining the effect of heparin on outcomes of interest; however, we identified no eligible RCTs. Although we did find

observational studies, we were unable to meta-analyze these as an insufficient number of studies included within-study comparisons of heparin as compared to no heparin administration. Finally, we planned between-study comparisons using random effects meta-regression analyses of studies that reported: (1) the proportion of donors who received antemortem heparin (independent variable) and (2) any graft or recipient outcomes that were reported in more than one study (dependent variable). We proceeded with meta-regression analyses only when there was variability in the proportion of donors that received heparin (i.e., when all studies report heparin administration to the same proportion of donors, meta-regression cannot be conducted due to lack of variability in the independent variable). We used STATA Version 15.1 [14] to conduct the meta-regression analyses.

Risk of Bias Assessment & Certainty of Evidence

For each study that contributed to Objective 2, assessing the effects of heparin on transplant outcomes, two reviewers independently assessed the risk of bias using the Newcastle Ottawa Scale (NOS) [15]. We then applied the GRADE framework to assess the certainty of the evidence (quality of evidence) for each transplant outcome [16-18]. The GRADE process offers a transparent structure for rating the certainty of the evidence and presenting evidence summaries. The certainty of evidence for each outcome is rated as high, moderate, low, or very low based on study design (RCTs starting as high certainty evidence, observational studies as low certainty), risk of bias of individual studies, consistency of results across studies, directness of the evidence, and precision of the results [16-18].

RESULTS

Objective 1: Description of Antemortem Heparin Practices

Study Selection

Among 4606 citations generated by the literature search, we included 55 studies reporting on distinct cohorts in analyses to describe the range of practices regarding antemortem heparin (**Figure 1**).

Overall Description of Antemortem Heparin Practices

Among the 55 studies reporting antemortem heparin administration practices, 33 administered heparin to *all* donors, 7 administered heparin to *some* donors (range: 16 to 96%), 8 did not report the proportion of donors that received heparin, and 7 did not administer heparin to *any* donors (**Table S1**). Among the 48 studies in which heparin was administered to at least some donors, 21 reported the dose. Eleven studies reported heparin doses in units (range: 5,000-50,000 International Units); 7 studies reported heparin doses in units/kg (range: 300-1000 International Units/kg); one administered heparin at 3 mg/ kg; another administered 10 mL of a heparin solution; and another reported two approaches (5000 International Units and 300 International Units/ kg) across two time points. Thirty-six studies reported the timing of antemortem heparin, which were primarily: before or around the time of withdrawal of life-sustaining measures (25 studies), after the withdrawal of life-sustaining measures (7 studies), and when mean arterial pressure (MAP) dropped to less than 50 mmHg (4 studies).

Table 1 summarizes heparin administration practices across studies involving liver [19-49], kidney [25,28,36,41,48,50-62], lung [25,48,61,63-68], pancreatic [69], simultaneous pancreas and kidney (SPK) [25,69-72], pancreas after kidney (PAK) [69], and simultaneous liver and kidney (SLK) [73] transplantation.

Objective 2: Assessment of the Effect of Antemortem Heparin on Transplant Outcomes

Study Selection

We found no randomized trials examining the role of antemortem heparin administration. Ten observational studies reported within-study comparisons of antemortem heparin versus no heparin on liver (7 studies) and kidney (3 studies) transplant outcomes and 32 additional studies of liver transplants did not report direct comparisons but met our criteria for between-study comparisons (i.e., they reported the proportion of donors that received heparin as well as recipient outcomes) using meta-regression analyses (**Figure 1**). Studies of kidney, lung and pancreas transplants were not amenable to meta-regression analyses due to an insufficient number of studies reporting the same transplant outcomes or insufficient variability in the proportion of donors receiving heparin.

Association between heparin use and outcomes – direct comparisons within studies

Seven studies that compared the outcomes of liver transplants from donors who received antemortem heparin to those who did not receive heparin found that antemortem heparin administration was not associated with liver discard rates (1 study [74]), post-transplant ischemic cholangiopathy (1 study [75]), biliary complications (1 study [76]), liver graft function (2 studies; defined by bilirubin level at 6 months in one [74] and undefined in one [77]),), and early (<3 months) or late transplant recipient mortality (1 study [76]). Conversely, heparin administration was associated with lower risk of primary nonfunction (1 study [74]) and hepatic artery thrombosis within 90 days of transplantation (1 study [78]), although no event rates were reported in this published abstract. Three studies found that antemortem heparin was associated with increased graft survival [74,79,80], while a fourth showed no effect [76]. **Table 2** shows the evidence summary for studies of liver transplants; for all outcomes evaluated, the certainty of evidence was rated as ‘very low’ or ‘low’ given that all studies were observational in design, and some were further rated down to ‘very low’ for imprecision.

Three studies that assessed heparin effects on kidney transplant outcomes found no

significant difference in kidney discard rates (1 study [81]), acute rejection (1 study [58]), primary nonfunction (1 study [81]), renal function as measured by the estimated glomerular filtration rate at one year (1 study [81]), graft survival (2 studies [58,81]), and transplant recipient mortality (1 study [81]). Two of these studies also reported no heparin effect on delayed graft function [58,81], whereas a third reported decreased rates of delayed graft function in the heparin group but did not report event rates. [82] **Table 3** shows the evidence summary for studies of kidney transplants; the certainty of evidence was rated as 'very low' for all outcomes that could be pooled (kidney discard rates, primary nonfunction, delayed graft function, and death censored graft failure). All were based on observational studies that were further rated down to 'very low' for imprecision.

Association between heparin use and outcomes – meta-regression analysis

Meta-regression analysis of 32 studies that reported DCDD liver transplants found no associations between the proportion of donors receiving antemortem heparin (ranging from 0 to 100% across studies) and the rates of early allograft dysfunction (7 studies including 677 patients; B = -0.203, 95% CI = -0.555 to 0.149; **Figure 2A** [29,44,68,77,83-85]), primary nonfunction (18 studies including 2316; B = 0.006, 95% CI = -0.085 to 0.098; **Figure 2B** [19,20,22,23,27,29,31,37,39,40,42,45,47,49,68,75,86,87], hepatic artery thrombosis (19 studies including 1603 patients; B = -0.012, 95% CI = -0.125 to 0.102; **Figure 2C** [19,20,22,23,27,29,31,37,39,47,49,68,75,83-86,88,89]), ischemic cholangiopathy/ biliary ischemia (17 studies including 1183 patients; B = 0.025, 95% CI = -0.161 to 0.211; **Figure 2D** [23,27,29,35,37,38,44,45,47,75,76,83,84,87,90-92], graft failure at 1 year (19 studies including 2462 patients; B = -0.034, 95% CI = -0.122 to 0.053; **Figure 2E** [27,29,31,37-40,42,43,45,47,68,90], re-transplantation (18 studies including 2395 patients; B = 0.041, 95% CI = -0.048 to 0.130; **Figure 2F** [19,20,23,27,31,35,37,38,40,42,45,49,68,84,86,89,91,93], and recipient mortality (18 studies including 2256 patients; B = 0.027, 95% CI = -0.063 to 0.118; **Figure 2G**

[20,23,27,29,31,37-40,43-45,47,49,68,87,93,94]. All results were judged to be very low certainty (observational studies rated down for imprecision) based on the GRADE framework (**Table 4**).

DISCUSSION

This systematic review aimed to describe antemortem heparin practices (Objective 1) and identify the effects of antemortem heparin therapy in DCDD on transplant outcomes (Objective 2). We identified substantial variability in approaches to antemortem heparin administration, ranging from centers that do not administer antemortem heparin to those that administer antemortem heparin to all donors. In addition, the dosage and timing of heparin administration varied across studies.

A previous systematic review examining the location of withdrawal of life-sustaining measures in liver donors also reported on the effect of antemortem heparin administration on transplant outcomes as a secondary objective [95]. Their findings suggested that antemortem heparin is associated with lower risk of primary non-function in DCDD versus NDD liver donation (6 studies that compared DCDD vs. NDD outcomes and another did not discuss antemortem heparin). Another meta-analysis of DCDD pancreatic transplantation found a higher thrombosis rate among recipients of DCDD donors who did not receive antemortem heparin (based on 4 studies) [96]. Finally, a meta-analysis of DCDD lung transplantation found no effect of heparin timing (before or after death determination) on subgroup analysis [97]. However, these prior meta-analyses compared heparin administration in DCDD to NDD transplant outcomes, rather than the effect of antemortem heparin vs. no heparin on DCDD transplants, precluding conclusions about the effect of antemortem heparin versus no heparin among DCDD donors [98].

In contrast, the current review more directly assesses effects of antemortem heparin on DCDD transplant outcomes. We found no RCTs. Among observational studies reporting on

liver transplant outcomes from donors who received antemortem heparin compared to those who did not (**Table 2**), we found low certainty evidence of reduced primary nonfunction and cumulative probability of graft failure at 5 years [74]. One study found reduced hepatic artery thrombosis associated with antemortem heparin use (low certainty) [78] and another reported reduced recipient mortality (very low certainty) [76]. There was no association between heparin administration and kidney transplant outcomes (very low certainty for all outcomes evaluated; **Table 3**). Finally, meta-regression analyses showed no significant association between the proportion of liver donors that received antemortem heparin and early allograft dysfunction, primary nonfunction, hepatic artery thrombosis, biliary ischemia, graft failure, re-transplantation, and recipient survival. The certainty in evidence was 'very low' for all outcomes due to imprecision (**Table 4; Figure 2**).

Strengths of this review include a comprehensive search, duplicate and independent citation screening, and inclusion of published abstracts. We employed meta-regression to assess the impact of heparin administration on outcomes and applied GRADE to report the overall certainty in the evidence for each outcome. This review is limited by the observational designs because many studies did not explore the effect of antemortem heparin administration as an explicit objective and reported a limited number of recipient outcomes. Furthermore, meta-regression analyses were limited to studies that reported the proportion of donors that received heparin and overlapping transplant outcomes in liver recipients leading to important imprecision.

The rationale for antemortem heparin therapy in DCDD donors is a possible reduction in microthrombosis, which could impair graft function or the healing and integrity of anastomoses. Findings from animal studies have been inconsistent, with some reporting potential improved lung [6,99,100] and liver [101] graft function with heparin administration and others reporting no effect on lung [102], liver [103], or DCDD heart [104] transplant function.

The findings of this review suggest that data supporting antemortem heparin administration is weak and inconsistent. Any presumed clinical benefits of antemortem heparin administration to DCDD donors must be weighed against ethical and pragmatic objections to this practice. Many deceased donors have sustained grave intracranial injuries that, in theory, could result in (or precipitate worsening of pre-existing) intracranial hemorrhage following heparin administration. Clinicians' ethical objections to the administration of heparin in the antemortem period and the lack of evidence for benefit may lead to variable practices in the dosing or timing of heparin administration and, in some cases, no heparin administration, which may lead transplant centers to reject organs that would otherwise be deemed acceptable for transplant and further reduce the number of organs offered to transplant waitlist patients.

The findings of this review suggest the desirability of more consistent reporting of antemortem heparin administration and other donor interventions in studies reporting transplant outcomes. The results highlight the need for rigorous RCTs examining the effect of antemortem heparin administration on transplant outcomes. There are several considerations in the design and planning of trials evaluating the effect of antemortem heparin in DCDD donors. Parallel group, randomized, controlled trials enrolling potential DCDD donors (of any organ) are ideally suited to answer questions about the efficacy and safety of intravenous heparin in DCDD donors. Placebo controlled trials are ideal, but in jurisdictions where heparin is part of current standard of care, these may not be feasible. Randomized trials that compare the dosing or the timing of heparin are likely to gain broader acceptance and, therefore feasibility. It will also be crucial to ensure the acceptance and collaboration of both donation centers and transplant programs throughout the study design and implementation, with input from the families of prior organ donors into issues of consent for donor participation.

CONCLUSION

This review found substantial variability in practices regarding the antemortem administration of heparin across studies and centres. While heparin administration to liver donors may decrease primary nonfunction, hepatic artery thrombosis, graft failure, and recipient mortality, these were based on low certainty of evidence and not supported by meta-regression findings. In light of current practice variability and controversies surrounding administration of antemortem heparin, RCTs examining the effects of antemortem heparin administration on transplant outcomes are needed.

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Table 1. Antemortem heparin administration practices across studies

Organ Transplanted	Number of Studies [Full articles/ Abstracts]	Number of studies that administered heparin to…			
		All donors	Some donors [range]	Unspecified proportion of donors	None of the donors
Liver	31 [27/ 4]	19	3 [86 to 96%]	5	**4**
Kidney	18 [16/ 2]	11	3 [16 to 94%]	3	**1**
Lung	9 [9/ 0]	5	2 [27 and 94%]	1	**1**
Pancreas	1	0	0	0	**1**
SPK	5	3	0	0	**2**
PAK	1	0	0	0	**1**
SLK	**1**	**0**	**0**	**1**	**0**

SPK: Simultaneous pancreas-kidney transplant; PAK: Pancreas transplant after kidney; SLK: Simultaneous liver kidney

Table 2. Evidence summary for observational studies comparing antemortem heparin to no antemortem heparin for liver donors

Certainty assessment						Summary of findings				
Nº of patients (Nº of studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Study event rates		Relative effect (95% CI)	Anticipated absolute effects		Certainty of evidence
						No heparin	With Heparin		No heparin	With heparin	
Liver discard rates[74]											
5495 (1 study)	not serious	not serious	not serious	serious [a]	none	180/589 (30.6%)	1511/4906 (30.8%)	**OR 1.01** (0.85 to 1.20)	No apparent effect		⊕◯◯◯ VERY LOW
Liver primary nonfunction[74]											

Table 2. Evidence summary for observational studies comparing antemortem heparin to no antemortem heparin for liver donors

Certainty assessment						Summary of findings					
Nº of patients (Nº of studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Study event rates		Relative effect (95% CI)	Anticipated absolute effects		Certainty of evidence
						No heparin	With Heparin		No heparin	With heparin	
3754 (1 study)	not serious	not serious	not serious	not serious	none	34/407 (8.4%)	142/3347 (4.2%)	**OR 0.51** (0.35 to 0.75)	84 per 1,000	**39 fewer per 1,000** (from 53 fewer to 20 fewer)	⊕⊕◯◯ LOW
Hepatic artery thrombosis - within 90 days of transplantation[78]											
6134 (1 study)	not serious	not serious	not serious	unknown event rates	none	In multivariable logistic regression analysis, antemortem heparin use was associated with lower risk of hepatic artery thrombosis among 6,134 liver recipients in whom the outcome was known.					⊕⊕◯◯ LOW

Table 2. Evidence summary for observational studies comparing antemortem heparin to no antemortem heparin for liver donors

Certainty assessment						Summary of findings					
Nº of patients (Nº of studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Study event rates		Relative effect (95% CI)	Anticipated absolute effects		Certainty of evidence
						No heparin	With Heparin		No heparin	With heparin	
Cumulative probability of liver graft failure at 5 years[74, i]											
3754 (1 study)	not serious	not serious	not serious	not serious	none	179/ 407 (44.0%)	1171/ 3347 (35.0%)	**OR 0.80** (0.66 to 0.96)	440 per 1,000	**54 fewer per 1,000** (from 98 fewer to 10 fewer)	⨁⨁◯◯ LOW
Recipient mortality[76, ii]											

Table 2. Evidence summary for observational studies comparing antemortem heparin to no antemortem heparin for liver donors

Certainty assessment						Summary of findings				
Nº of patients (Nº of studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Study event rates		Relative effect (95% CI)	Anticipated absolute effects		Certainty of evidence
						No heparin	With Heparin		No heparin	With heparin	
58 (1 study)	not serious	not serious	not serious	not serious	none	Not reported	Not reported	**RR 0.383** (0.16 to 0.90)	Not calculable		⊕⊕◯◯ LOW

CI: Confidence interval; **OR:** Odds ratio; **RR:** Risk Ratio; **HR:** Hazard Ratio

Explanations
a. Rated down for imprecision due to wide confidence interval.
b. Rated down for imprecision due to small sample size (failure to meet the optimal information size criterion).

i. Three other studies reported on graft failure outcomes but data could not be pooled as event rates were not reported: Detry et al. (*Transpl Int.* 2010;23[6]:611-618) reported no effect of antemortem heparin on graft failure (RR = 0.80, 95% CI, 0.60 to 1.069, p = 0.14) or death-censored graft failure (RR = 0.93, 95% CI, 0.69 to 1.26); Riddiough et al. (*Transplantation.* 2013;96[suppl. 10S]:S263) reported that not administering heparin was associated with increased risk of graft loss (p = 0.049); and DeRoover et al. (*Transpl Int.* 2011;24[suppl. 2]:84) reported that not administering heparin was associated with graft failure in univariate analysis (p < 0.05).

ii. The same study by Detry et al. (*Transpl Int.* 2010;23[6]:611-618) reported no effect of antemortem heparin on early death, defined as death less than 3 months post-transplant (RR = 0.51, 95% CI, 0.11 to 2.27, p = 0.338).

Table 3. Evidence summary for observational studies comparing antemortem heparin to no antemortem heparin for renal donors

Certainty assessment						Summary of findings					
						Study event rates (%)			Anticipated absolute effects		
Nº of patients (Nº of studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No heparin	With heparin	Relative effect (95% CI)	No heparin	With heparin	Certainty of evidence
Kidney discard rates[105]											
24861 (1 study)	not serious	not serious	not serious	serious [a]	None	480/2304 (20.8%)	4308/22557 (19.1%)	**OR 0.92** (0.83 to 1.02)	208 per 1,000	**No anticipated effect**	⊕◯◯◯ VERY LOW
Renal primary nonfunction[105]											
21550 (1 study)	not serious	not serious	not serious	serious [a]	None	62/1791 (3.5%)	553/19759 (2.8%)	**OR 0.81** (0.62 to 1.06)	35 per 1,000	**No anticipated effect**	⊕◯◯◯ VERY LOW
Delayed graft function[58,105,i]											

Table 3. Evidence summary for observational studies comparing antemortem heparin to no antemortem heparin for renal donors

Certainty assessment						Summary of findings					
						Study event rates (%)			Anticipated absolute effects		
Nº of patients (Nº of studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No heparin	With heparin	Relative effect (95% CI)	No heparin	With heparin	Certainty of evidence
21602 (2 studies)	not serious	not serious	not serous	serious [a]	None	755/1820 (41.5%)	7997/19782 (40.4%)	**OR 0.98** (0.89 to 1.07)	415 per 1,000	**No anticipated effect**	⊕◯◯◯ VERY LOW
Death censured graft failure - allograft nephrectomy, re-transplantation, or return to chronic dialysis[58]											
52 (1 study)	not serious	not serious	not serious	serious [a]	None	1/23 (4.3%)	2/29 (6.9%)	**OR 1.59** (0.14 to 18.61)	43 per 1,000	No anticipated effect	⊕◯◯◯ VERY LOW

CI: Confidence interval; **OR:** Odds ratio; **RR:** Risk Ratio; **HR:** Hazard Ratio

Explanation
a. Rated down for imprecision due to wide confidence interval.

i. A published abstract by Choubey et al. (*Am J Transplant.* 2020;20[suppl. 3]:40-41) reported on 22,241 DCDD renal transplants across 58 organ procurement organizations that were surveyed and found decreased odds of delayed graft function correlated with pre-mortem heparin use (OR = 0.41, p < 0.001; no other data reported to allow for pooling with findings of other studies).

Table 4. Evidence profile for studies of liver transplantation included in the meta-regression analysis

Certainty assessment							Effect Size		Certainty of evidence
№ of studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Beta co-efficient	95% CI	
Early liver allograft dysfunction									
7	677	not serious	not serious	not serious	serious [a]	none	-0.203	-0.555 to 0.149	⊕◯◯◯ VERY LOW
Liver primary nonfunction									
18	2316	not serious	not serious	not serious	serious [a]	none	0.006	-0.085 to 0.098	⊕◯◯◯ VERY LOW
Hepatic artery thrombosis									
19	1603	not serious	not serious	not serious	serious [a]	none	-0.012	-0.125 to 0.102	⊕◯◯◯ VERY LOW

Certainty assessment							Effect Size		Certainty of evidence
№ of studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Beta co-efficient	95% CI	
Biliary ischemia									
17	1183	not serious	not serious	not serious	serious [a]	none	0.025	-0.161 to 0.211	⊕◯◯◯ VERY LOW
Liver graft failure									
19	2462	not serious	not serious	not serious	serious [a]	none	-0.034	-0.122 to 0.053	⊕◯◯◯ VERY LOW
Re-transplantation									
18	2395	not serious	not serious	not serious	serious [a]	none	0.041	-0.048 to 0.130	⊕◯◯◯ VERY LOW
Recipient survival									

Certainty assessment							Effect Size		Certainty of evidence
№ of studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Beta co-efficient	95% CI	
18	2256	not serious	not serious	not serious	serious [a]	none	0.027	-0.063 to 0.118	⊕◯◯◯ VERY LOW

CI: Confidence interval

Explanations

a. Rated down for imprecision due to wide confidence intervals around the beta-intercept.

Figure legends

Figure 1. PRISMA Flow Diagram for Objective 1 [to describe antemortem heparin practices] and Objective 2 [to determine the effect of heparin on transplant outcomes].

Figure 2. Meta-regression analysis of the effect of heparin administration on liver transplant outcomes. **Independent variable:** Proportion of donors that received heparin in each study. **Dependent variables: 2**A. Early allograft dysfunction (EAD); **2B.** Primary nonfunction (PNF); **2C.** Hepatic artery thrombosis (HAT); **2D.** Ischemic cholangiopathy (IC); **2E.** Graft failure; **2F.** Re-transplantation; **2G.** Patient mortality.

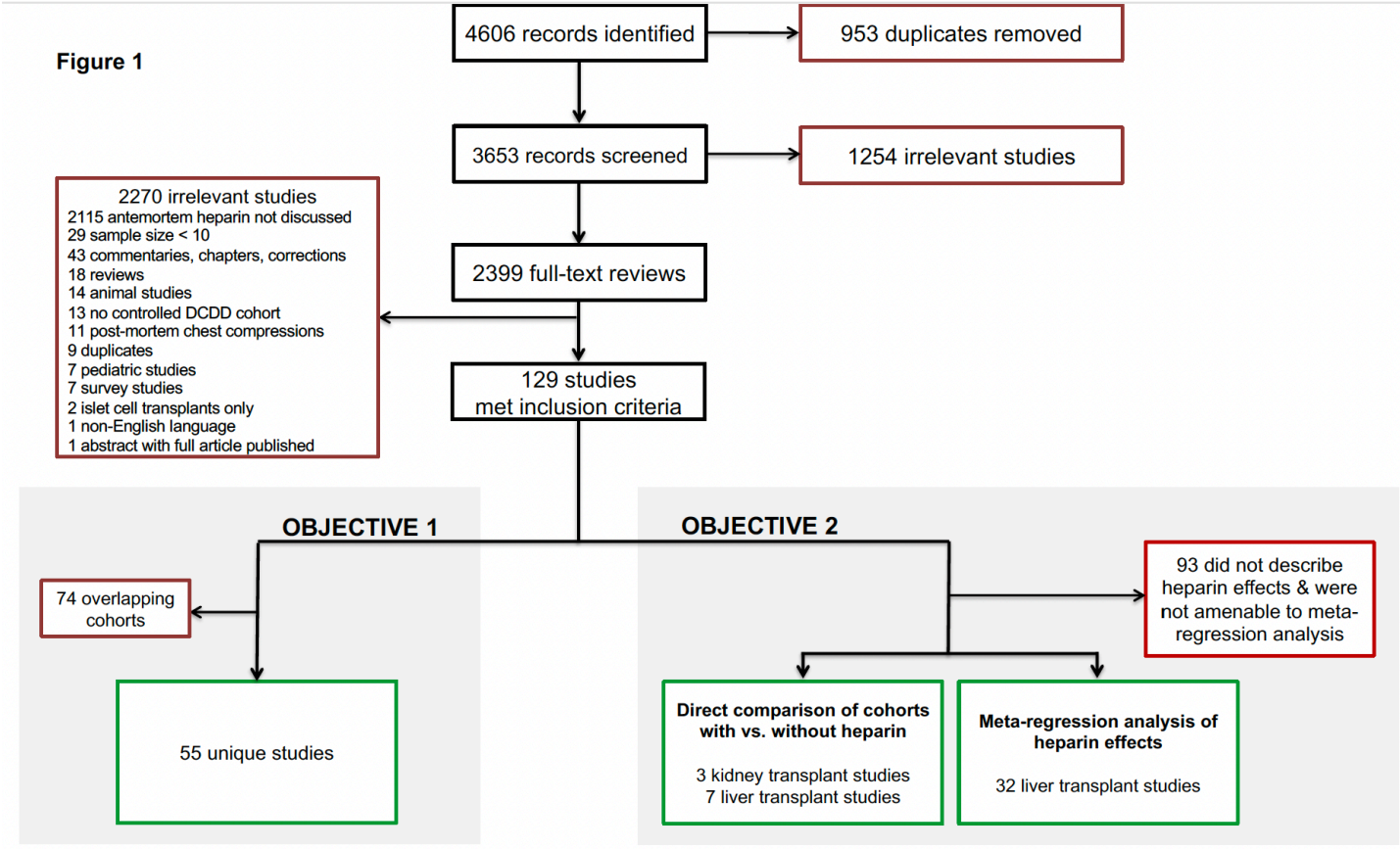

Figure 1. PRISMA Flow Diagram for Objective 1 [to describe antemortem heparin practices] and Objective 2 [to determine the effect of heparin on transplant outcomes].

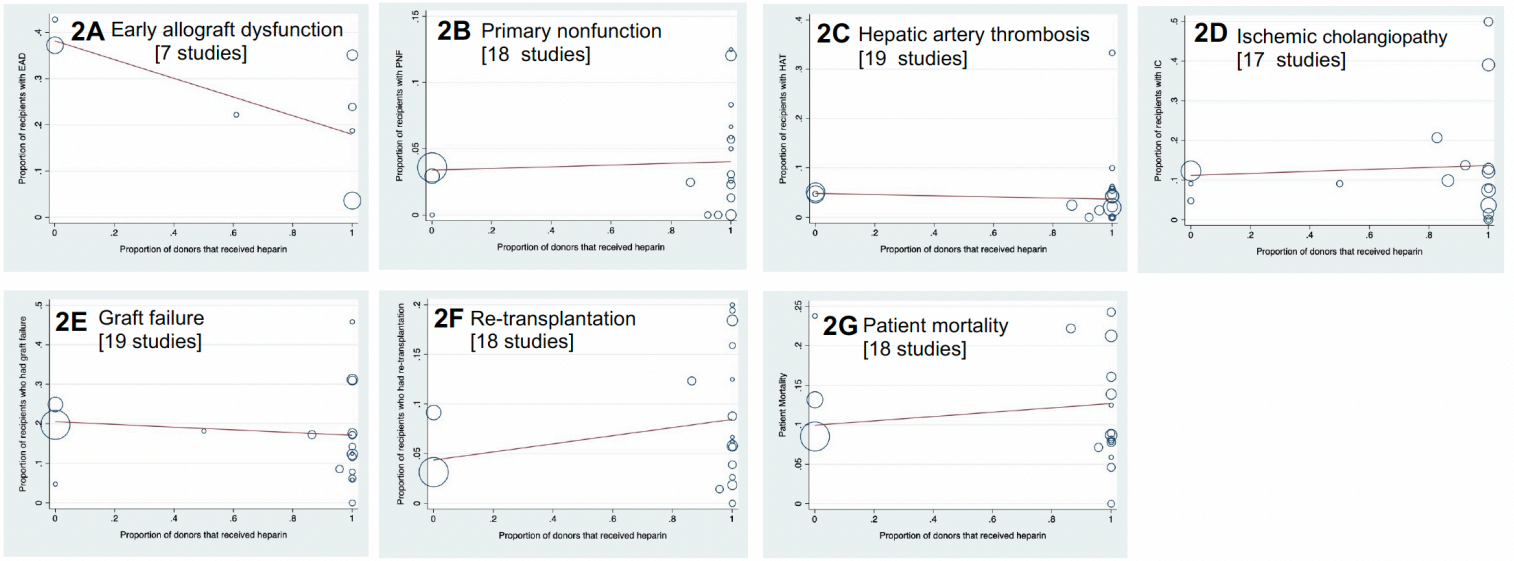

Figure 2

Figure 2. Meta-regression analysis of the effect of heparin administration on liver transplant outcomes. **Independent variable:** Proportion of donors that received heparin in each study. **Dependent variables: 2**A. Early allograft dysfunction (EAD); **2B.** Primary nonfunction (PNF); **2C.** Hepatic artery thrombosis (HAT); **2D.** Ischemic cholangiopathy (IC); **2E.** Graft failure; **2F.** Re-transplantation; **2G.** Patient mortality.

Supplemental Digital Content (SDC)

SDC, Methods. Systematic review search strategy.

Database: Ovid MEDLINE(R) ALL <1946 to July 3rd, 2020>

The same search strategy was used in EMBASE.

Search Strategy:

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1 exp Tissue Donors/ or exp "Tissue and Organ Procurement"/ (75984)
2 (donor$1 or donation$ or donate).mp. or ((tissue$ or organ$) adj3 (procurement$ or procured$ or harvest$ or sharing$)).tw,kw. (329157)
3 or/1-2 (332497)
4 Death, Sudden, Cardiac/ (14070)
5 ((cardiac$ or cardio$ or heart) adj3 (arrest$ or death$)).tw,kw. (80436)
6 ((cardio-circulat$ or cardiocirculat$ or circulat$) adj5 (cease$1 or death$)).tw,kw. (2055)
7 (non-heartbeating$ or non-heart-beating$ or nonheartbeat$).mp. or (without adj2 (heartbeat$ or heart-beat$)).tw,kw. (1356)
8 ((DCD or DCDs or NHBD or NHBDs) and (non-heartbeating$ or non-heart-beating$ or nonheartbeat$ or circulat$ or cardiac$ or cardio$ or death$)).tw,kw. (1362)
9 or/4-8 (89593)
10 3 and 9 (4276)
11 exp Heparin/ or (heparin$ or liquaemin$).mp. (101680)
12 exp anticoagulants/ or (anticoagul$ or anti-coagul$ or antithromb$ or anti-thromb$).tw. (257622)
13 or/11-12 (285850)
14 Graft Survival/ or Delayed Graft Function/ or ((graft$ or allograft$) adj2 (survival$ or function$ or dysfunction$)).tw,kw. (70187)
15 13 or 14 (355148)
16 3 and 9 and 15 (1511)
17 16 not (exp Animals/ not (Human/ and exp Animals/)) (1242)
18 (mice or rat or rats or cat$1 or cattle$1 or dog$1 or goat$1 or horse$1 or rabbit$1 or sheep$1 or swine$1 or pig$1 or canine$1 or feline$1 or porcine$ or calf).ti. (1687371)
19 17 not 18 (1222)
20 limit 19 to english language (1180)

Table S1. Description of heparin practices across centres/ studies

Primary study	Article Type	Country	Number of donors	Percentage of donors given heparin	Heparin dose	Heparin timing
Liver Donors						
Maheshwari, 2007[19]	Full Article	United States	20	100%	Not reported	Not reported
DeVera, 2009[20]	Full Article	United States	142	100%	50,000 units	Before extubation
Skaro, 2009[21]	Full Article	United States	32	Not reported	Not reported	According to hospital protocol
Yamamoto 2010[22]	Full Article	Sweden	24	100%	Not reported	In the operating room just before surgery
Hong, 2011[23]	Full Article	United States	81	86%	Not reported	Prior to WLST
Karp, 2011[24]	Full Article	United States	22	Not reported	Not reported	"According to hospital policy"
Bellingham, 2011[25]	Full Article	United States	Liver 87 Kidney 965[a] Lung 21[a] SPK 68 Pancreas 4	100%	10,000 - 30,000 units	While the patient was "fully supported"
Taner, 2012[26]	Full Article	United States	215	Not reported	"According to hospital policy"	"According to hospital policy"
Vanatta, 2013[27]	Full Article	United States	38	100%	Not reported	Before discontinuing ventilator & organ perfusion support
Oniscu, 2014[28]	Full Article	United Kingdom	Liver 11 Kidney 38[a]	0	Not applicable	Not applicable
Han, 2014[29]	Full Article	China	29	0	Not applicable	Not applicable
Abt, 2014[30]	Full Article	United States	110	100%	30,000 units	Before extubation
Detry, 2014[31]	Full Article	Belgium	70	96%	Not reported	Before WLST and cardiac arrest
Firl, 2015[32]	Full Article	United States	92	Not reported	Not reported	Prior to WLST
Halldorson 2015[33]	Full Article	United States	89	90%	Not reported	After extubation when MAP < 50 mmHg
Xia, 2015[34]	Full Article	China	127	100%	Not reported	Prior to WLST

Chirichella, 2016[35]	Full Article	United States	45	100%	30,000 units	Prior to extubation
Perez-Villares, 2017[36]	Full Article	Spain	Liver 28 Kidney 116[a] Lung 17[a] Pancreas 1	100%	500 - 600 units/ kg	Prior to WLST
Bohorquez, 2017[37]	Full Article	United States	138	100%	Early Era - 5000 units Late Era - 300 U/kg	Prior to withdrawal of ventilatory support
LaMattina, 2018[38]	Abstract	United States	108	100%	Not reported	Prior to extubation
Torabi, 2018[39]	Abstract	United States	17	100%	30,000 units	After extubation
Kollmann, 2018[40]	Full Article	Canada	77	100%	1,000 units/ kg	Prior to WLST
De Almeida, 2018[41]	Abstract	Spain	Liver 39 Kidney 74[a] Pancreas 1	100%	Not reported	Not reported
Farid, 2019[42]	Full Article	United Kingdom	1112	0	Not applicable	Not applicable
Mihaylov, 2019[43]	Full Article	USA	135	100%	300 units/ kg	At the time of withdrawal of life support
Ruiz, 2019[44]	Full Article	Spain	Liver 44 Liver-kidney 2[a]	100%	3 mg/ kg	After extubation
Tun-Abraham, 2019[45]	Full Article	Canada	70	100%	400 units/ kg	5 minutes before WLST
Crannell, 2020[46]	Abstract	United States	18	100%	Not reported	Prior to withdrawal of life support
Kramer, 2020[48]	Full Article	Canada	Liver 81 Kidney 321 Lung 50	Unspecified for liver donors[b]	Variable; not specified for liver donors[b]	Variable Based on O2 saturation < 70% or MAP < 50 or 60 mmHg[b]
Otero, 2020[47]	Full Article	Spain	65	100%	300 units/ kg	"Prior to cannulation"
vanLeeuwen, 2020[49]	Full Article	Netherlands	273	0	Not applicable	Not applicable
Kidney Donors						
Fujita, 1989[50]	Full article	Japan	61	100%	10 mL	Not reported
Casavilla, 1995[51]	Full article	United States	12	100%	30,000 units	Prior to laparotomy
Teraoka, 2001[52]	Full Article	Japan	759[a]	100%	10,000 - 20,000 units	Before cardiac standstill
Gok, 2003[53]	Full	United	36	100%	25,000 units	At time of

	Article	Kingdom & Netherlands				pronouncement of death
Ledinh, 2011[54]	Full Article	Belgium	59	Not reported	Not reported	Not reported
Farney, 2011[55]	Full Article	United States	134	100%	Not reported	Prior to WLST
Bellingham, 2011[25]	Full Article	United States	Liver 87 Kidney 965[a] Lung 21[a] SPK 68 Pancreas 4	100%	10,000 - 30,000 units	While the patient was "fully supported"
Hernandez-Alejandro, 2011[56]	Full Article	Canada	Liver 41[a] Kidney 128[a] Lungs 20[a]	Not reported	Not reported	Prior to declaration of death
Kute, 2013[57]	Full Article	India	33	100%	10,000 units	Not reported
Oniscu, 2014[28]	Full Article	United Kingdom	Liver 11 Kidney 38[a]	0	Not applicable	Not applicable
Kamal, 2015[58]	Full Article	United States	52	44%	Not reported	Not reported
Woodside, 2015[59]	Full Article	United States	19	15.8%	Not reported	Prior to withdrawal of life support
Allen, 2016[60]	Full Article	United States	566	100%	Not reported	Prior to extubation
Sidiropoulos 2016[61]	Full Article	Australia	Kidney 44 Lung 20	94%	Not reported	Following apnea and hypoxia but prior to loss of arterial line pulsatility
Perez-Villares, 2017[36]	Full Article	Spain	Liver 28 Kidney 116[a] Lung 17[a] Pancreas 1	100%	500 - 600 units/ kg	Prior to WLST
De Almeida, 2018[41]	Abstract	Spain	Liver 39[a] Kidney 74[a] Pancreas 1[a]	100%	Not reported	Not reported
Foss, 2019[62]	Abstract	Norway	18	100%	Not reported	At the time of WLST
Kramer, 2020[48]	Full Article	Canada	Liver 81 Kidney 321 Lung 50	Unspecified for kidney donors[b]	Variable; not specified for kidney donors[b]	Variable Based on O2 saturation < 70% or MAP < 50 or 60 mmHg[b]
Lung Donors						
VanDeWauwer, 2010[63]	Full Article	Netherlands	35	0	Not applicable	Not applicable
Bellingham,	Full	United States	Liver 87	100%	10,000 - 30,000	While the patient was

2011[25]	Article		Kidney 965[a] Lung 21[a] SPK 68 Pancreas 4		units	"fully supported"
Levvey, 2012 [64]	Full Article	Australia	174	27%	Not reported	Not reported
Machuca, 2015 [65]	Full Article	Canada	55	100%	"At least 300 units/ kg"	Five minutes before WLST
Sidiropoulos 2016 [61]	Full Article	Australia	Kidney 44 Lung 20	94%	Not reported	Following apnea & hypoxia, prior to loss of arterial line pulsatility
Costa, 2018[66]	Full Article	United States	45	100%	30,000 units	Five minutes before WLST
Inci, 2018[67]	Full Article	Switzerland	21	100%	5,000 units	When MAP < 50 mmHg
Minambres, 2020[68]	Full Article	Spain	Liver 16 Lung 21[a]	100%	500-600 units/ kg	Prior to withdrawal of life support
Kramer, 2020[48]	Full Article	Canada	Liver 81 Kidney 321 Lung 50	Unspecified for lung donors[b]	Variable; not specified for lung donors[b]	Variable Based on O2 saturation < 70% or MAP < 50 or 60 mmHg[b]
Pancreas & Simultaneous Multi-organ Transplants						
Fernandez, 2005[70]	Full Article	United States	SPK 37	100%	Not reported	Prior to cessation of ventilator support
Bellingham, 2011[25]	Full Article	United States	Liver 87 Kidney 965[a] Lung 21[a] SPK 68 Pancreas 4	100%	10,000 - 30,000 units	While the patient was "fully supported"
Muthusamy, 2012[69]	Full Article	United Kingdom	Pancreas 26 SPK 79 PAK 29	0	Not applicable	Not applicable
Wadei, 2014[73]	Full Article	United States	SLK 12	Not reported	Not reported	At the time of WLST
Kopp, 2018[72]	Full Article	Netherlands	SPK 20 PAK 1	0	Not applicable	Not applicable
Romano 2019[71]	Full Article	Sweden	SPK 21	100%	Not reported	Not reported

MAP: Mean arterial pressure; WSLT: Withdrawal of life support; SPK: Simultaneous pancreas-kidney transplant; PAK: Pancreas transplant after kidney; SLK: Simultaneous liver kidney

[a] Number of allografts (rather than number of donors).

i. Sample size reflects number of transplants (allografts) rather than donors.
ii. Kramer et al., 2020. Of all DCDD potential organ donors. 82% received heparin [not specified by organ]. The dose of heparin was < 300 units/ kg in 41.8%, => 300 units/ kg in 58.2% among 237 potential donors. Timing of heparin administration was based on hypoxemia (oxygen saturation < 70%) in 59% of potential donors and hypotension (MAP < 60 or < 50 mmHg) in 39%

Chapter 3. Cardiac Donation After Death Determination by Circulatory Criteria

3.1 Preamble

3.1.1 Cardiac donation After death determination by circulatory criteria

While most cardiac transplantation occurs from donors who are declared dead by neurologic criteria, there are two protocols that allow for cardiac donation from DCC donors, including Direct Procurement and Perfusion (DPP) and Normothermic Regional Perfusion (NRP; White, Messer, Large, et al., 2018). Briefly, in DPP, following death determination, the sternum is opened, and the heart is retrieved, placed in a perfusion device that restores its activity, and is then transferred to the location of the recipient for transplantation (White et al., 2018). In NRP, after death is determined and the sternum is opened, the arteries supplying the brain are surgically interrupted, then thoraco-abdominal circulation is restored, before in-situ cardiac assessment and finally retrieval, transportation, and transplantation (White et al., 2018).

3.1.2 The fall & resurgence of cardiac DCC

Cardiac DCC is not new. The first hearts transplant, performed by Christiaan Bernard in 1968, was retrieved from a “non-heart beating” (i.e., DCC) donor (Barnard et al., 1967). Subsequently, with the rise in donation after death determination by neurologic criteria, cardiac DCC was largely abandoned until its recent resurgence nearly 40 years later which started when Boucek and colleagues reported three pediatric cases of cardiac DCC in the United States between 2004 to 2007 (Boucek et al., 2008). This report was met with renewed ethical controversies (Veatch, 2008; Bernat, 2008) and the practice was yet again halted. Briefly, ethical debates include the argument that if the determination of death by circulatory criteria necessitates the cessation of cardiac activity, its resumption following death in NRP invalidates the diagnosis

of death (Veatch, 2008; Joffe, 2011; Tibballs & Bhatia, 2015), and any organ retrieval in this context may be in violation of the 'Dead Donor Rule'. The existing ethical debates are ongoing but have been largely devoid of discussions about the perspectives of some key stakeholders, including healthcare providers and the public.

3.1.3 State of cardiac DCC implementation in Canada

While there is great interest in implementing cardiac DCC in Canada, the procedure has not been adopted in this country to date. In 2018, a Canadian consensus building process that consisted of a multidisciplinary panel of Canadian stakeholders was convened to evaluate the medical, legal, and ethical aspects of cardiac DCC and pave the way towards its implementation in Canada. The group identified several priorities that warrant inquiry, including the evaluation of public and healthcare provider understanding of DCC in general, the role for further public consultation, and further qualitative research to better understand the perspectives of donor families (Shemie et al., 2021).

3.1.4 A Program of Research

The projects described in Section 3.2 and Chapters 4 and 5 of this thesis are part of a larger program of research aiming to evaluate the acceptability of cardiac donation after DCC among Canada's healthcare workers and the public. Previously, we performed a scoping review (Ball et al., 2019) and two national surveys to evaluate the perspectives of Canadian healthcare providers (Honarmand et al, 2020a) and members of the general public (Honarmand et al., 2020b) about cardiac donation after DCC and its implementation in Canada.

Summary of Previous Projects

Scoping review of the literature

In a scoping review of the literature, we identified no studies that evaluated the perspectives of healthcare providers, the public, or organ donor families about cardiac DCC (Ball et al., 2019; Appendix A).

Survey of Canadian healthcare providers

In a nationwide survey of 391 Canadian healthcare providers who manage organ donors and/ or those who manage transplant recipients, we found that 92.3 percent of respondents believed that the DPP protocol is acceptable, and 87.3 percent supported its implementation in Canada. We also found that 78.4 percent of respondents believed that NRP is acceptable, and 70.6 percent supported its implementation in Canada (Honarmand et al., 2020a; Appendix B). Healthcare providers endorsed several concerns and perceived barrier regarding cardiac DCC, including: the ethics of cardiac DCC, particularly for NRP, concerns about the quality of the heart retrieved from DCC donors, the potentially high resource requirements, and an important minority endorsed concerns that cardiac DCC would have a negative impact on other transplantable organs being retrieved simultaneously from the same donor, particularly in DPP. In open-ended questions, respondents expressed concerns that the public will not understand nor accept cardiac donation after DCC, concerns about resumption of cardiac activity after death determination, including potential repercussion of brain activity, and the potential invasiveness of the NRP protocol.

Survey of Canadian public

In a nationwide survey of a representative sample of 1,001 members of the Canadian public, 84.2 percent of respondents indicated that they would agree to donate their heart using DPP and 73.7 percent would support its implementation in Canada. We also found that 77.8 percent would agree to donate their heart using NRP and 65.4 percent would support its implementation in Canada (Honarmand et al., 2020b; Appendix C). In open-ended responses, some respondents indicated concerns about the possibility of restoration of consciousness if cardiac activity within the donor's body in NRP led to brain activity, and others expressed general 'discomfort' with the 'invasiveness' of the NRP protocol.

3.1.5 Rationale & Objectives

While these national surveys identified that most healthcare providers and the public support cardiac donation after DCC, there remains gaps in knowledge about the concerns of both groups about cardiac DCC and the perceived facilitators and barriers to its implementation in Canada. The subsequent chapters describe three manuscripts:

Section 3.2. Description of project protocol

Chapter 4. A qualitative study evaluating healthcare providers' perspectives on cardiac DCC

Chapter 5. A mixed methods study evaluating the public's perspectives on cardiac DCC

3.2 Cardiac donation after circulatory determination of death: Protocol for a mixed-methods study of healthcare provider and public perceptions in Canada

Full citation:

Honarmand K, Ball IM, Weiss MJ, Slessarev M, Sibbald R, Sarti A, Meade MO, D'Aragon F, Chasse M, Basmaji J, Parsons Leigh J. Cardiac donation after circulatory determination of death: Protocol for a mixed methods study of healthcare provider and public perceptions in Canada. BMJ Open 2020; 10(7): e0033932. doi: 10.1136/bmjopen-2019-033932.

Title: Cardiac donation after circulatory determination of death: Protocol for a mixed methods study of healthcare provider and public perceptions in Canada

Authors:
Honarmand Kimia MD MSc[1]; Ball Ian M MD MSc[2]; Weiss Matthew J MD[3]; Slessarev Marat MD[1]; Sibbald Robert MSc[4]; Sarti Aimee MD MEd[5]; Meade Maureen O MD MSc[6]; D'Aragon Frederick MD MSc[7]; Chasse Michael MD PhD[8]; Basmaji John MD[1]; Parsons Leigh Jeanna PhD[9]

Affiliations:
1. Division of Critical Care, Department of Medicine Western University, London, Ontario, Canada
2. Department of Epidemiology and Biostatistics, Western University, London, Ontario, Canada
3. CHU de Québec – Université Laval Research Center, Population Health and Optimal Health Practices Research Unit, Trauma-Emergency-Critical Care Medicine, Université Laval, Québec, Québec; Transplant Québec, Montréal, Québec; Canadian Donation and Transplant Research Program, Ottawa, Ontario, Canada
4. Department of Family Medicine, Western University, and London Health Sciences Centre
5. Department of Critical Care, The Ottawa Hospital, Ottawa, Ontario, Canada
6. Department of Medicine, Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada
7. Department of Anesthesiology, Universite de Sherbrooke, Sherbrooke, Quebec, Canada; Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Quebec, Canada
8. University of Montreal Research Center, Innovation Hub and Department of Medicine (Critical Care), Montreal, Québec, Canada
9. School of Health Administration, Faculty of Health, Dalhousie University, Halifax, Nova Scotia, Canada and Department of Critical Care Medicine, Cummings School of Medicine, University of Calgary, Calgary, Alberta, Canada

Corresponding Author
Dr Kimia Honarmand MD MSc FRCPC
Department of Medicine, Western University
London Health Sciences Centre, Victoria Hospital
800 Commissioners Road East, London ON N6A 5W9
Phone: (519) 685-8500 Ext. 71513
Fax: (905) 685-8089
Email: kimia.honarmand@medportal.ca

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ABSTRACT

Introduction

Cardiac transplantation remains the best treatment for patients with end-stage heart disease that is refractory to medical or device therapies, however, a major challenge for heart transplantation is the persistent discrepancy between the number of patients on waiting lists and the number of available hearts. While other countries (e.g., United Kingdom, Australia, and Belgium) have explored and implemented alternative models of transplantation such as cardiac donation after circulatory determination of death (DCDD) to alleviate transplantation wait times, ethical concerns have hindered implementation in some countries. This study aims to explore the attitudes and opinions of healthcare providers and the public about cardiac DCDD in order to identify and describe opportunities and challenges in ensuring that proposed cardiac DCDD procedures in Canada are consistent with Canadian values and ethical norms.

Methods and analysis

This study will include two parts that will be conducted concurrently. *Part 1* is a qualitative study consisting of semi-structured interviews with Canadian healthcare providers who routinely care for organ donors and/ or transplant recipients to describe their perceptions about cardiac DCDD. *Part 2* is a convergent parallel mixed methods design consisting of a series of focus groups and follow-up surveys with members of the Canadian general public to describe their perceptions about cardiac DCDD.

Ethics and dissemination

This study has been approved by the Research Ethics Board at Western University. The findings

will be presented at regional and national conferences and reported in peer-reviewed publications.

Keywords: cardiac donation, cardiac transplantation, organ donation, donation after circulatory determination of death, mixed methods research, healthcare professional perceptions, public perceptions

STRENGTHS AND LIMITATIONS

- This study will utilize qualitative and mixed methods approaches to describe the perceptions of Canadian healthcare providers and the general public towards cardiac DCDD.
- An in depth description of the perceptions of Canadian healthcare providers towards cardiac DCDD using a mixed methods approach and identification of facilitators and barriers along with potential solutions.
- Generation of a rich, in-depth description of the attitudes, opinions, and concerns of the Canadian public regarding cardiac DCDD and its implementation in Canada using a mixed methods approach.
- The findings of this study will inform the development of a framework to facilitate implementation of cardiac DCDD programs across the country.
- It is not within the scope of this project to provide an in depth comparison of the opinions and concerns of important specific sub-groups within the general Canadian population (ex. First Nations persons, recent immigrants, or specific religious groups).

INTRODUCTION

Cardiac Donation & Transplantation

While the majority of organ donors donate after neurological determination of death (NDD; also referred to as 'brain death'), a growing number of organ donors follow the donation after circulatory determination of death (DCDD) pathway.[1-3]. Patients in the DCDD group usually suffer critical illness and a decision is made between the healthcare team and substitute decision makers to withdraw life-sustaining therapy and allow natural death. One key difference between these pathways is that while the heart continues to beat and organs remain perfused from the moment of NDD to organ recovery, the DCDD pathway includes a period of hypoxia followed by circulatory arrest prior to death determination (after a 5-minute 'no-touch' period) and recovery. DCDD accounts for the largest increase in the number of donated organs in Canada and is believed to have the most potential for further increasing the multi-organ donor pool.[4]

While it is technically possible to retrieve all organs from DCDD donors that can be retrieved from NDD donors (heart, lungs, kidneys, liver, pancreas), in most countries, cardiac donation has been limited to NDD donors. But the number of patients on cardiac transplant waitlists exceeds the number of available NDD heart donors. In 2018, 157 patients were on the heart transplant waitlist in Canada[1] and 3753 patients were on the heart transplant waitlist in the United States[2]. During the same year, 9 patients died before receiving a heart transplant in Canada[1] and 345 patients died while waiting for a heart transplant in the United States[2]. Recent successes in cardiac DCDD programs in the United Kingdom,[5] Australia,[6], and Belgium[7] have led to calls for widespread implementation of such a program in other centres across the world.

Cardiac DCDD Protocols

Current cardiac DCDD programs have employed two alternative surgical procedures for retrieving hearts from DCDD donors: Direct Procurement and Perfusion (DPP) and Normothermic Regional Perfusion (NRP).[8] In DPP, after withdrawal of life-sustaining therapy and declaration of death by circulatory criteria, the donor's sternum is opened, and the heart is surgically removed and placed into an *ex-situ* perfusion device (a heart machine), where a pulsatile pump restores cardiac activity to maintain perfusion during transport. The transplant team then transports the beating heart to the location of the recipient for transplantation. In NRP, after the same process of withdrawal of life-sustaining therapy and declaration of death by circulatory criteria, the donor's sternum is opened, and the central vessels are cannulated. Then, an extracorporeal device is used to restore thoraco-abdominal perfusion. This process will allow for circulation of the donor's blood to the thoracic and abdominal organs. To safeguard against restoring perfusion of the brain, vessels that supply the brain are surgically interrupted to prevent circulation of blood to the brain while circulation to the target organs is restored. With NRP, donor cardiac activity is restored prior to surgical removal of the heart, thus permitting *in-situ* assessment of cardiac function.[8]

Widespread implementation of cardiac DCDD has been slowed partly by questions surrounding the ethics of resuming cardiac activity after declaration of death by circulatory criteria. It has been argued that if the diagnosis of death by circulatory criteria necessitates the irreversible cessation of cardiac activity, its restoration violates the dead donor rule, which states that organ recovery can only occur after death.[9-11]

NRP is possibly more controversial than DPP because it involves restoration of circulation *within the donor body* after surgically interrupting the cerebral vasculature to ensure that circulatory flow

to the brain is not restored. In some jurisdictions, such as Australia, where the definition of death is based on permanent cessation of systemic circulation, its restoration within the donor body would violate such a definition.[12] Furthermore, there are concerns about the restoration of cerebral blood flow when thoraco-abdominal circulation is restored within the donor body.[10] There is no consensus on the best methods to ensure that surgical techniques are effective in preventing restoration of any cerebral perfusion nor what amount, if any, such flow would violate the dead donor rule.

Although these ethical considerations have been previously debated within organ donation and transplant communities, these discussions have been largely devoid of any consideration for stakeholder perceptions.[13] Given any policy change would impact an entire population, and there is no ethical certainty about the practice of cardiac DCDD, it is important to gauge stakeholder perceptions towards cardiac DCDD and its implementation in Canada.

Stakeholder Perceptions Towards Cardiac DCDD

We conducted a scoping review of the literature exploring the attitudes and opinions of stakeholders (healthcare professionals, donor families, transplant recipients, or the general public) on cardiac DCDD and identified no studies in which the attitudes and opinions of stakeholders about cardiac DCDD was described.[13]

To address this critical knowledge gap, we conducted two national web-based surveys to explore stakeholder perceptions about cardiac DCDD.[14,15] Among 398 healthcare providers, 92% believe that the DPP approach (in which the heart is retrieved and placed in a pefusion device) to

cardiac DCDD is acceptable and 87% support its implementation in Canada. Similarly, 78% believe that the NRP approach (in which circulation to thoraco-abdominal regions is re-started within the donor's body prior to heart retrieval) to cardiac DCDD is acceptable and 71% support its implementation in Canada. Participants agreed that there are concerns related to ethical considerations, resource requirements, the quality of the donated heart, and the potential for negative impact on other organs being recovered for transplantation.[14]

Among 1,001 members of the Canadian public, 84% believe that the DPP approach to cardiac DCDD is acceptable and 74% support its implementation in Canada. Similarly, 78% of Canadians believe that the NRP approach to cardiac DCDD is acceptable and 65% support its implementation in Canada.[15]

Despite this high level of acceptance, open-ended survey responses revealed several areas of concern among the Canadian public that recurred in our thematic analysis. There were concerns around:

- The certainty of death determination: *"I am concerned that people may not actually be dead."*
- The restoration of thoraco-abdominal circulation in NRP: *"[I am] uncomfortable with restarting heart within body. If this is possible then why not just treat patient?"*
- The possibility of brain reperfusion in NRP: "*What if blood made it through and the brain awoke?",* and *"it would be fine if the brain is not reactivated.",* and

- The ligation of the central vessels to prevent cerebral perfusion: *"The proposed procedure of tying off the vessels to the brain …seem[s] quite invasive and family/decision makers may not approve."*

These concerns, if not addressed during the implementation of cardiac DCDD programs in Canada, could erode public trust in deceased organ donation with potentially negative effects on consent rates and future organ donation research. Similarly, the ethical and practical concerns expressed by the majority of healthcare providers across various groups suggest that the acceptance for cardiac DCDD in Canada is far from settled among healthcare providers in Canada.

The findings of these surveys have been influential in shaping further discourse and research about the acceptability of cardiac DCDD among healthcare providers and the Canadian public. However, survey methodology does not permit the assessment of respondents' comprehension of complex topics and does not allow for in-depth probing or follow-up inquiries to understand respondent thought processes. Qualitative and mixed methods approaches are far better suited to elucidate a rich, in-depth description of the perceptions of Canadians.

Objectives

The proposed study is part of a program of research (depicted in Figure 1) that aims to develop a framework for the implementation of cardiac DCDD programs across Canada that are acceptable to, and consistent with, the values of Canadians. Building on the results of our national survey, we will conduct a study that prioritizes engagement and promotes bilateral dialogue between the organ donation and transplantation communities and the general public in Canada. The specific

objectives of this study are to:

(1) Describe the attitudes, opinions, and concerns of Canadian healthcare providers involved in the management of organ donors and/ or transplant recipients on cardiac DCDD and to identify facilitators and barriers to widespread implementation of such programs in Canada, and

(2) Describe the attitudes, opinions, and concerns of the Canadian general public on cardiac DCDD and its implementation in Canada.

METHODS & ANALYSIS

Study Design

The purpose of this study is to describe the perspectives of Canadians regarding cardiac DCDD by utilizing a mixed methods approach which involves the merging of both qualitative and quantitative data[16] (Figure 2). In *Part 1,* we will conduct a qualitative study to describe the perspectives of Canadian healthcare providers towards cardiac DCDD through semi-structured interviews. In *Part 2*, we will conduct a concurrent mixed methods study[16] to describe the perceptions of the Canadian general public using focus groups followed by a survey of focus group participants to contextualize the qualitative data collected as part of the focus groups in terms of participants' individual perspectives towards cardiac DCDD protocols.

Patient and Public Involvement

Public advisors (members of the Canadian public without medical training) reviewed the protocol for this study and participated in the development and refinement of the educational material that will be used for the focus groups with members of the general public and video clip development.

Part 1: Semi-structured Interviews with Healthcare Providers

Sampling & Recruitment

We will conduct approximately 50 individual semi-structured interviews with the following groups of healthcare providers who routinely care for organ donors and/or transplant recipients: (1) transplant physicians and surgeons (transplant cardiologists: n=5-10, transplant cardiac surgeons: n=5-10; thoracic/ abdominal transplant surgeons: n=5-10), (2) organ donation physicians (critical care physicians who are specially trained as organ donation experts; n=5-10), (3) donation coordinators (critical care nurses who are specialty trained to discuss organ donation with patients' substitute decision makers and help to coordinate all activities related to the donation process; n=5-7) (4) critical care physicians (who manage the care of deceased or dying potential organ donors in the ICU but who are not designated as donation physicians; n = 5-10), (5) ICU nurses (n=5-7), (6) transplant coordinators (nurses who assist in the retrieval of organs in the operating room; n=5-7), (7) perfusionists (n=5-7), and (8) cardiac anesthetists (n=5-7).

We will purposefully recruit healthcare providers through their respective institutions/ departments in a manner that ensures adequate representation of demographic factors including sex/ gender and geographical region to maximize the diversity of perspectives captured. Although we plan to conduct approximately 50 interviews across all professional groups, data analysis will be conducted on an ongoing basis and we are prepared to conduct additional interviews until thematic saturation has been achieved.[17]

Interview Guide

We developed an interview guide consisting of prompting, probing, and follow-up questions to guide the interview process. These questions are based on themes that emerged from our scoping review[13] and our national survey of healthcare providers[14,15] about concerns, expected barriers, and facilitators to cardiac DCDD. We also tailored interview themes, questions, and language for specific participant groups; for example, adding technical questions about surgery for interviews with transplant surgeons. Prior to launching the interviews, experts in organ donation and transplantation reviewed the interview guide content, and clarity, providing feedback for final revisions. The interview guide is provided in Supplementary Material A.

Procedures

Interviews will use web-based video conferencing platforms (e.g., Skype, Zoom). Prior to launching the interviews, will conduct five pilot interviews with healthcare providers across Canada to further assess and refine the interview guide. The findings of the pilot interviews will be incorporated into the overall study findings. At the start of each interview, participants will read a concise and pretested summary of cardiac donation in the context of circulatory death. Thereafter, the interviewer (KH) will present specific questions, elicit open-ended responses, and ask follow-up questions to further explore all statements. Each interview will last 30 to 45 minutes.

Data Analysis

All interviews will be audio-recorded, transcribed verbatim by a professional transcriptionist, and reviewed for accuracy by one investigator. Two investigators will undertake thematic analysis[18] by independently conducting line-by-line coding of the transcripts and formulating provisional

codes and themes, which will be refined through weekly meetings. This process will generate themes and subthemes that describe participants' attitudes, opinions, and concerns related to cardiac DCDD protocols as well as facilitators and barriers to their implementation in Canada. The findings will be contextualized based on the professional characteristics and geographical location of participants.

Part 2: Focus groups with members of the general public

Sampling & Recruitment

We plan to conduct 12 focus groups, each consisting of 6 to 8 Canadians residing in four major cities (Montreal, Quebec; Toronto, Ontario; Calgary, Alberta; and Vancouver, British Columbia). We will purposefully sample members of the general public, aiming to achieve a representative sample from each province with respect to gender, age groups, ethnicity, and religious affiliation.

A professional recruitment agency/ company will recruit participants through advertisements and by telephoning potential participants from a database of panelists. Participants will be eligible to partake in the study if they are 18 years of age or older, currently living in Canada, fluent in spoken English (or French in Quebec), and able and willing to provide written informed consent to participate in the study. Participants will receive a financial incentive for their participation.

Data analysis will be ongoing and we will be prepared to conduct additional focus groups until thematic saturation has been achieved.[17]

Focus Group Educational Content & Discussion Guide

We developed a series of educational content to provide participants with basic information on the following topics: (1) cardiac transplantation, (2) non-cardiac DCDD, (3) cardiac DCDD using the DPP protocol (in which the heart is retrieved and placed in a perfusion device), and (4) cardiac DCDD using the NRP protocol (in which circulation to thoraco-abdominal regions is re-started within the donor's body prior to heart retrieval). The development of the educational series was informed by a review of the existing literature on cardiac DCDD protocols and ethical challenges.

The educational content has been rigorously pre-tested among healthcare professionals with content or process expertise to ensure accuracy and comprehensiveness. It has also been pre-tested with 18 community advisors (members of the Canadian public with no medical expertise) to ensure that the content is coherent and understandable for the lay public. In addition, we conducted cognitive interviews with three members of the Canadian public to ensure that the content is comprehensible.

The educational content will be pre-recorded into a small series of brief video clips, which will be presented to participants during focus groups. Video motion graphics will be used to demonstrate the procedures involved in DPP and NRP using animated illustrations. All investigators will be consulted in the production of the videos at all stages of development to ensure that they accurately reflect the processes and procedures that they are intended to portray. We will also consult with community advisors during the early stages of video development through to video editing to ensure that the videos are comprehensible to the lay public. Closed captioning will be provided.

The video clips will be pilot tested prior to the start of the study.

The educational video clips will be presented to participants during the focus groups. This will ensure consistency in content presentation across various focus groups (and avoids portrayal of any biases by the facilitator) and may enhance participant engagement. In addition, such animations were preferred over 'real-life' portrayals of the procedures by members of the general public whom we consulted as part of our national survey studies, with the latter deemed to be potentially uncomfortable to view for some members of the general public. Related questions (prompts, probing, and follow-up) will be used to further explore the rationale for participants' perspectives, generating a richer depth of discussion among participants regarding the facilitators and barriers of cardiac DCDD acceptability. These questions have been adapted from our national survey and expanded to delve more deeply into the attitudes, perceptions, and concerns expressed by respondents, particularly in free-text comment sections of the survey. The focus group discussion guide is presented is Supplementary Material B.

Study Setting

Focus groups will take place in person at specialized facilities in four Canadian provinces (British Columbia, Alberta, Ontario, and Quebec). These provinces were targeted for study recruitment due to their high volumes of cardiac transplants and readiness for implementation of cardiac DCDD programs.

Procedures

One investigator with training in focus group methodology (KH) and a research associate will

facilitate the focus groups in consultation from experts in qualitative research methodologies (JPL, AS). Focus group methodology is ideally suited to achieve our objectives because it provides a deeper level of insight and understanding of a phenomenon by encouraging debate and discussion on a topic not previously familiar to participants.[19]

Prior to launching the focus groups, we will conduct two pilot sessions each with 3 to 5 Canadians residing in Ontario. This step will allow us to further assess and refine the educational video clips and the focus group discussion guide to ensure that both are clear, concise and appropriate for use in a focus group format.

To allow for a description of the study sample, participants will first be asked to complete a brief survey consisting of 12 Likert-like items where we will collect the demographic characteristics of participants and their previous experiences and self-rated knowledge about organ donation (Supplementary Material C).

Focus groups will be facilitated using the Focus Group Discussion Guide (Supplementary Material B). During the focus group, the facilitator will present each of the educational video clips during and encourage participants to share their perceptions and feelings towards each donation protocol in an unstructured manner whenever possible. The facilitator will also ask a series of open-ended prompting, probing, and follow-up questions as appropriate to help stimulate a rich discussion and debate among participants (Supplementary Material C).

At the conclusion of each focus group, participants will be asked to complete a brief survey

consisting of 11 Likert-type items that covered the same themes as the focus group discussion guide. Items will explore overall acceptance, willingness to consent for self, and willingness to consent on behalf of a family member to non-cardiac DCDD, cardiac DCDD using the DPP protocol, and cardiac DCDD using the NRP protocol. Each item will be followed by an opportunity to provide free-text comments to explain responses (Supplementary Material D).

Data Analysis

All focus group discussions will be audio-recorded, transcribed verbatim by a professional transcriptionist, and reviewed for accuracy by one investigator. Two investigators will undertake thematic analysis[18] according to the procedures described previously. This process will generate the themes and subthemes that describe the public's attitude towards DCDD in general as well as cardiac DCDD protocols.

For the quantitative (survey) data, we will use descriptive statistics to summarize the demographic characteristics of participants and their perceptions towards DCDD in general as well as cardiac DCDD protocols. We will not conduct inferential statistics given that responses to surveys are intended to elucidate the perceptions of participants after the discussion in which they participated as well as any comments they wish to share confidentially and are not intended to draw any conclusions regarding the attitudes of Canadians in general, a topic that has already been explored in our large-scale national survey study. The findings of the thematic analysis of qualitative data will be contextualized based on participants' demographic characteristics and their survey responses.

Data Integration

We will report the findings of the proposed study independently as well as conduct data integration to include findings from various phases of this program of research. The findings from the interviews with healthcare providers will be integrated with those of the published healthcare provider survey[14] to describe healthcare provider perceptions and identify the facilitators and barriers (along with potential solutions) to the implementation of cardiac DCDD programs at centres across the country, contextualized based on participants' professional roles and geographical region within Canada. The findings from the focus groups with members of the Canadian public will be integrated with those of the published Canadian public survey[15] to describe public perceptions on various aspects of cardiac DCDD, contextualized based on participants' demographic characteristics and attitudes towards cardiac DCDD protocols as identified by the follow-up surveys. Data from all four studies of this program of research, (the two proposed studies and the two published national surveys,[14,15] will be synthesized to provide a framework that will inform the development of a comprehensive description of stakeholder perceptions, perceived facilitators, and perceived barriers along with any potential solutions that arise from this work.

Validity & Methodological Rigor

Several strategies will be used across all stages of this study to enhance the validity, methodological rigor, and trustworthiness of the findings of this study according to the approach described by Krefting.[20] To optimize the credibility of findings, the researchers who will conduct interviews and focus groups and participate in data analysis will engage in reflexive journaling during the study to document and assess their own perspectives that may influence the

research process. To further enhance, triangulation will be achieved using two data sources (healthcare providers and the general public) and various data collection methods (interviews with healthcare providers, focus groups with the general public, and follow-up surveys of the focus group participants). Furthermore, the researchers will discuss emerging insights and perspectives with co-investigators and other colleagues as a form of peer debriefing aimed at enhancing credibility.

To enhance transferability, we will provide a thick description of participants and by use of purposive sampling. Dependability will be enhanced by step-wise replication during data analysis by enlisting two members of the research team to participate in coding of a sample of transcripts to identify initial codes that emerge from the data and to develop consensus around the code definitions. Finally, confirmability will be enhanced by the maintenance of a comprehensive audit trail to memorialize all study processes from study design to data analysis to integration, as well as reflexivity and triangulation as previously described. All qualitative findings will be reported in accordance with the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist.[21]

ETHICS & DISSEMINATION

We have obtained approval from the Research Ethics Board (REB) at Western University (WesternREM) for both components of this study (ID numbers 113807 and 113808). All participants will be asked to provide written informed consent to participate in the study. All participants will be asked to provide written informed consent prior to participating in the study.

The findings of both studies will be provided to Canadian Blood Services (the national organization that oversees organ donation activity in Canada), presented at regional and national meetings and conferences, and prepared as at least two manuscripts for publication in peer-reviewed journals.

Relevance of Findings

There is a discrepancy between the number of available donor hearts and the number of patients on heart transplant waitlists. Widespread implementation of cardiac DCDD in Canada has the potential to improve outcomes for patients on the heart transplant waitlist and reduce the heart transplant waitlist by increasing the number of available donor hearts. Implementation of any cardiac DCDD program requires rigorous planning and examination of its acceptability including stakeholder perceptions, and a comprehensive approach to identifying facilitators that can be capitalized and barriers that may be faced along with exploration of possible solutions to the latter. The proposed studies are part of a program of research that is the most comprehensive approach in engaging with healthcare providers and the general public regarding any protocol in organ donation and transplantation.

Engagement of the surgical and medical transplant community is of particular interest given their insights into the acceptability of DCDD heart retrieval from the perspective of those who care for recipients, their perceptions of the impact of such practice on non-heart organs, and possible technical and pragmatic facilitators and barriers that may be faced if DCDD donors were to also become heart donors. Engagement of members of the general public is paramount to identifying any specific areas of concern regarding cardiac DCDD protocols, devising appropriate ways to

address any misconceptions and knowledge gaps among the public, and ensuring that steps towards this process are consistent with Canadian values. Direct, multi-faceted dialogue in a focus group setting is the ideal setting for exploring the Canadian public's perceptions of the complex issues surrounding the ethics of cardiac DCDD programs. We will develop a comprehensive description of the perceptions of the Canadian public on cardiac DCDD, the important contextual factors that influence those perceptions, and the opportunities and challenges its implementation may bring from the perspectives of the public. This will provide a practical and well-informed framework that integrates the opportunities as well as expected challenges, which will in turn guide the design and development of cardiac DCDD programs in Canada.

Together, these findings will provide researchers, providers, and decision makers at national and provincial levels with vital information to launch well-informed cardiac DCDD programs that are consistent with Canadian values based on comprehensive public and provider consultation. Moreover, while the focus of this research is on cardiac DCDD, our model of public and provider engagement may be applied to current and future practice changes and new innovations in organ donation and transplantation. Equipped with the findings of this work, the organ donation and transplant communities will be able to ensure that our cardiac DCDD programs are conducted in a manner that is acceptable to Canadians and maintains trust in the organ donation system.

Author Contributions

KH, IB, and JPL contributed to the conception and design of this study with input from all other authors, developed the instruments that will be used in the conduct of the proposed study, and drafted the manuscript. MJW, MS, RB, AS, MOM, FD, MC, and JB contributed to the refinement of the study design and all study instruments, and provided revisions to this manuscript.

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Competing Interest Statement

The authors report no conflicts of interest.

Ethics approval and consent to participate

Both components of this study have been approved by the Research Ethics Board at Western University.

FIGURE LEGENDS

Figure 1. Overview of the overall program of research describing stakeholder perceptions towards cardiac donation after circulatory determination of death.

Figure 2. Overview of the procedures and products of the proposed study.

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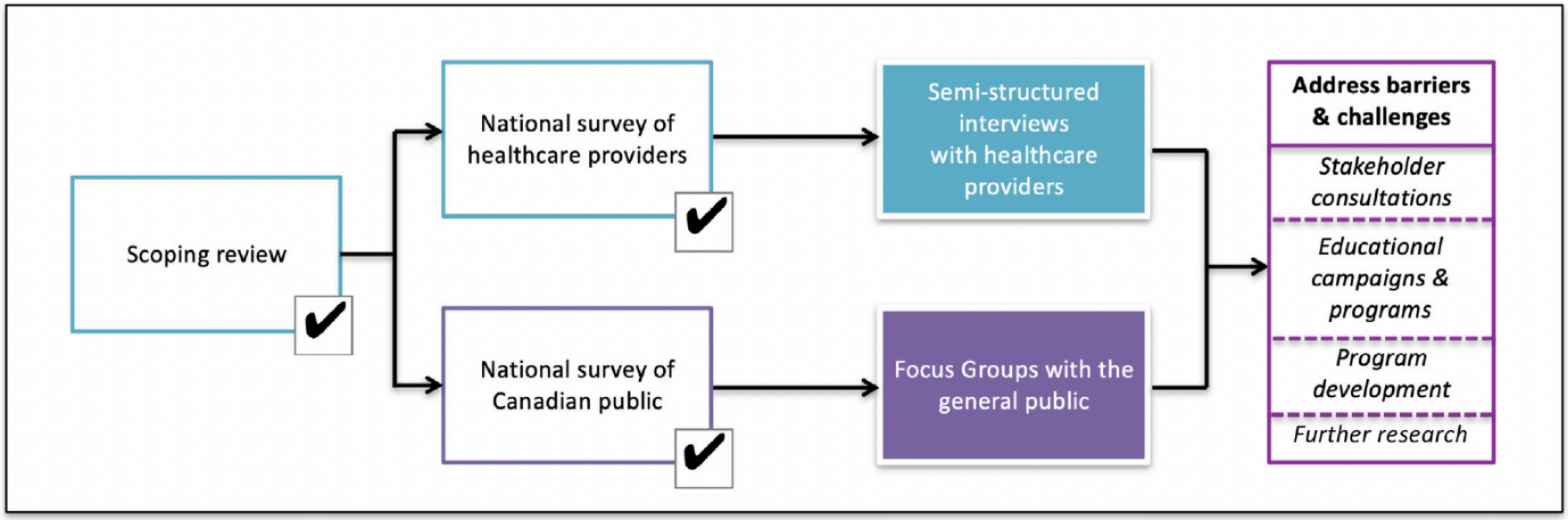

Figure 1 Overview of the overall programme of research describing stakeholder perceptions towards cardiac donation after circulatory determination of death.

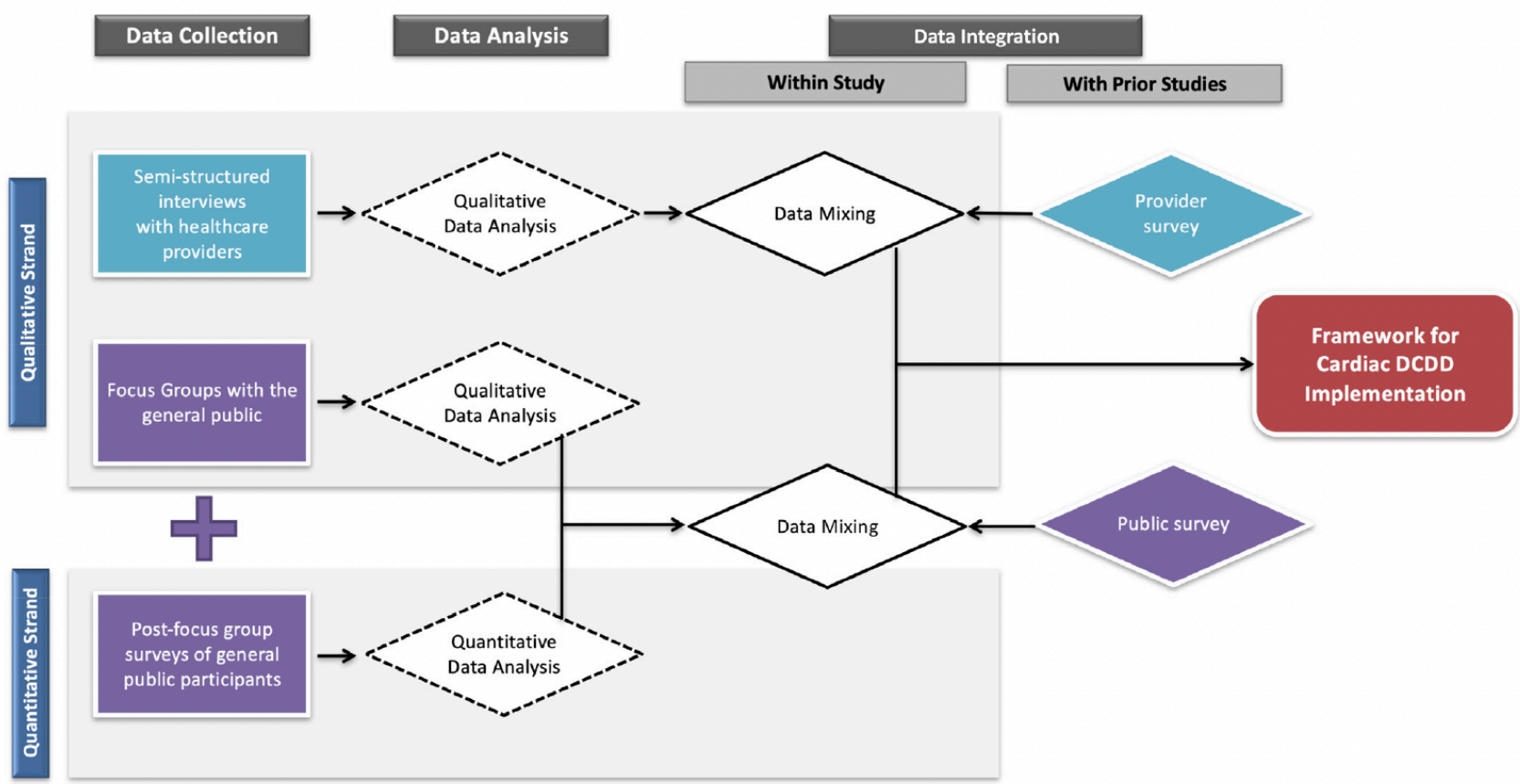

Figure 2 Overview of the procedures and products of the proposed study. DCDD, donation after circulatory determination of death.

Supplementary Material A - Interview Guide

PART I – DCDD in general

1. *Have you ever been involved in a DCD case before?*
    a. *If so, what was your involvement?*
2. *Do you believe that it is acceptable for a healthcare team to retrieve the liver, kidney, and/ or other non-heart organs of a donor after circulatory determination of death?*
3. *Do you have any concerns about the donation of organs after circulatory determination of death?*
    a. *If so, what are the concerns?*
4. *Additional topics for follow-up questions:*
    a. *How do you feel about organ donation in the context of medical assistance in dying (MAiD)?*

PART II – CARDIAC DCDD

1. *Before reviewing the pre-written material, had you heard of cardiac DCDD before?*
    a. *If so, how did you hear about it?*
        i. *Colleagues? Conferences? Television?*

PART III – DPP

1. *What is your understanding of DPP?*
2. *What do you think about recovery/ retrieval of the heart of a donor after circulatory death using the DPP approach?*
    a. *Do you think this is different from recovery/ retrieval of non-heart organs after circulatory determination of death? How so?*
3. *Would you support implementation of the DPP approach?*
    a. *In Canada?*
    b. *At your hospital?*
        i. *Why or why not?*
4. *Do you have any concerns about the donation the heart using the DPP approach?*
    a. *What could be done differently to decrease your concern?*
5. *Additional topics for follow-up questions:*
    a. *How do you feel about DPP in the context of medical assistance in dying (MAiD)?*
    b. *Issues related to determination of death*
        i. *Some have questioned whether the donor can really be dead if the heart can be restarted at all. How do you feel about this?*

PART IV – NRP

1. *What is your understanding of NRP?*
2. *What do you think about recovery/ retrieval of the heart of a donor after circulatory determination of death using the NRP approach?*
    a. *Do you think this is different from recovery/ retrieval of non-heart organs after circulatory determination of death or the NRP approach? How so?*
3. *Would you support implementation of the NRP approach?*
    a. *In Canada?*
    b. *At your hospital?*
        i. *Why or why not?*
4. *Do you have any concerns about the donation of the heart using the NRP approach?*
    a. *What could be done differently to decrease your concern?*
    b. *Approach #2 or NRP involves clamping vessels that go to the brain in order to prevent blood flow to the brain while restarting blood flow to the organs in the chest and abdomen. Do you have any concerns regarding this particular component of the NRP approach to heart donation?*
        i. *What specifically is concerning to you about this procedure?*
        ii. *What do you think you need to know or see to lessen your concerns? What level of evidence? What type of evidence?*
            1. *ie, animal studies showing absence of blood flow*
5. *Relative to the DPP approach, what are your thoughts on the NRP approach?*
6. *Additional topics for follow-up questions:*
    a. *How do you feel about NRP in the context of medical assistance in dying (MAiD)?*
    b. *Issues related to determination of death*
        i. *How do you understand & define death?*
        ii. *Does the heart have special significance/ meaning to you? To members of the public?*
        iii. *Some have questioned whether the donor can really be considered dead if the circulation/ heartbeat is restarted within the donor's body. How do you feel about this?*
        iv. *Do you have any concerns about blood flow reaching the brain during this procedure? What if there was no blood flow to the brain? What if there was some blood flow to the brain? What if we didn't know whether there is any blood flow to the brain?*

PART V – PUBLIC PERCEPTIONS

1. *What do you think the public's perception will be regarding cardiac donation after circulatory determination of death?*
    a. *Non-cardiac DCD vs. DPP vs. NRP approaches.*

PART VI – IMPLEMENTATION & BARRIERS/ SOLUTIONS

1. *What do you think about the implementation of DPP in Canada?*
   a. *Do you foresee any concerns or barriers in the implementation of DPP in Canada? How about locally?*
      (a) Potential topics
      - *Resource limitations*
      - *Ethical considerations*
      - *Public acceptability*
      - *Donor family acceptability*
      - *Quality of recovered heart*
      - *Effect of other transplantable organs*
      - *Providers who choose not to participate in DCDD protocols (should they be permitted? How can this be addressed?)*

      (i) How do you think this barrier should be addressed?
2. *What do you think about the implementation of NRP in Canada?*
   a. *Do you foresee any concerns or barriers in the implementation of NRP in Canada? How about locally?*
      - *Potential topics: As above*

      (i) How do you think this barrier should be addressed?

3. What would you advise policymakers on next steps when it comes to cardiac DCDD?

4. Generally, who should lead the way towards implementation of cardiac DCDD in Canada

a) Role of CBS? Provincial ODOs? Individual centres? Federal / provincial governments?

b) What supports should be provided to centres contemplating implementation of cardiac DCDD programs?

5. What do you think about the role of research in the field of cardiac DCDD?

   c. *What are the research priorities in this area?*
   d. *What, if any, research do you think would be important to conduct in the field of cardiac DCDD after it has been implemented in Canada?*
   e. *What's the most pressing research question in this area?*

6. Additional topics for follow-up questions:

f. From your perspective, is there something unique to your province that should be taken into consideration if/when DCD heart is considered for implementation there?

Supplementary Material B - Focus Group Discussion Guide.

PART I QUESTIONS: DCDD IN GENERAL

1. *What do you think about the recovery of liver, kidney, and/ or other non-heart organs after circulatory/ heart death?*
    a. *[if undecided] What additional information would help you make a decision?*
2. *What do you think about the fact that the donor heart stops when the donor dies, and the heart is then removed and re-started outside the donor body and later transplanted into a recipient?*
3. *Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using this approach, if being an organ donor was consistent with their wishes and values?*
    a. *Why?*
    b. *Why not?*
    c. *[if undecided] What additional information would help you make a decision?*
4. *Would you be okay with your family member consenting to donating your liver, kidney, and/ or other non-heart organs after circulatory death (where the heart stops)?*
    a. *Why?*
    b. *Why not?*
    c. *[if undecided] What additional information would help you make a decision?*
5. *If you were asked, would you consent to the donation of the liver, kidney, and/ or other non-heart organs of a family member after circulatory death (where the heart stops), if you knew that being an organ donor was in keeping with their wishes and values?*
    a. *Why?*
    b. *Why not?*
    c. *[if undecided] What additional information would help you make a decision?*
6. *Do you have any concerns about the donation of organs after circulatory/ heart death?*
7. *Additional topics for follow-up questions:*
    a. *[After a very brief explanation of Medical Assistance in Dying] How do you feel about organ donation in the context of medical assistance in dying (MAiD)?*

PART II QUESTIONS: DPP APPROACH

1. *What do you think about this approach to heart donation?*
2. *Do you find heart donation using this approach to be the same or different than the donation of other organs (like liver, kidneys, etc) as was previously described? How so?*
3. *Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using the DPP approach, if being an organ donor was consistent with their wishes and values?*
    a. *Why?*
    b. *Why not?*

c. *[if undecided] What additional information would help you make a decision?*

4. Would you be okay with your family member consenting to donating your heart after circulatory death (where the heart stops) using the DPP approach?

a. Why?

b. Why not?

c. [if undecided] What additional information would help you make a decision?

5. If you were asked, would you consent to the donation of the heart of a family member after circulatory death (where the heart stops) using the DPP approach, if you knew that being an organ donor was in keeping with their wishes and values?

a. *Why?*
b. *Why not?*
c. *[if undecided] What additional information would help you make a decision?*

6. Do you have any concerns about the donation the heart using this approach?

7. In this approach, the heart is removed from the body and its activity is restarted inside a storage device. What are your thoughts on this?

8. Additional topics for follow-up questions:
a. *How do you feel about DPP in the context of medical assistance in dying (MAiD)?*
b. *Issues related to definition of death*
    i. *Some have questioned whether the donor can really be dead if the heart can be restarted at all. How do you feel about this?*

PART III QUESTIONS: NRP APPROACH

1. What do you think about this approach to heart donation?

2. Do you think heart donation using this approach is different than the donation of other organs (like liver, kidneys, etc) as was previously described? How so?

3. Do you think this approach is different than the first approach (DPP) discussed earlier? If so, how?

4. *Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using the NRP approach, if being an organ donor was consistent with their wishes and values?*
    a. *Why?*
    b. *Why not?*
    c. *[if undecided] What additional information would help you make a decision?*
5. *What concerns do you have about the donation of the heart using the NRP approach?*
6. *Would you be okay with your family member consenting to donating your heart after circulatory death (where the heart stops) using the NRP approach?*
    a. *Why?*
    b. *Why not?*
    c. *[if undecided] What additional information would help you make a decision?*
7. *If you were asked, would you consent to the donation of the heart of a family member after circulatory death (where the heart stops) using the NRP approach, if you knew that being an organ donor was in keeping with their wishes and values?*
    a. *Why?*
    b. *Why not?*
    c. *[if undecided] What additional information would help you make a decision?*
8. *Do you have any concerns about the donation the heart using this approach?*
9. *What do you think about the ligation/ tying off of blood vessels that supply the brain? Does this concern you?*
    a. *What if there is a small chance of a small amount of blood getting to the brain… does this change what you think about this approach?*
10. *Additional topics for follow-up questions:*
    a. *How do you feel about NRP in the context of medical assistance in dying (MAiD)?*
    b. *Issues related to definition of death*
        i. *How do you understand & define death?*
        ii. *Does the heart have special significance/ meaning to you? To members of the public?*
        iii. *Some have questioned whether the donor can really be considered dead if the circulation/ heartbeat is restarted within the donor's body. How do you feel about this?*

iv. *Do you have any concerns about blood flow reaching the brain during this procedure? What if there was no blood flow to the brain? What if there was some blood flow to the brain? What if we didn't know whether there is any blood flow to the brain?*

PART IV QUESTIONS: IMPLEMENTATION

1. Compared with heart donation after brain death, do you think that heart donation after circulatory/ heart death more concerning, less concerning, or no difference in level of concern?

2. What do you think about the DPP approach being done in Canada if it leads to more patients receiving a heart transplant sooner?

   b. *Why?*
   c. *Why not?*
   d. *[if undecided] What additional information would help you make a decision?*

3. *What do you think about the NRP approach being done in Canada if it leads to more patients receiving a heart transplant sooner?*
   a. *Why?*
   b. *Why not?*
   c. *[if undecided] What additional information would help you make a decision?*
4. *Are there any other comments or questions regarding this topic?*
5. *If your family member was at a hospital that does not allow for these protocols to be implemented, how would you feel about the possibility of having them transferred before death to a centre where these protocols can take place?*

Supplementary Material C – Pre-focus Group Baseline Questionnaire ID: _____

Please respond to the following questions. Do not write your name on this page.

1. **Age: _____**

2. **Gender: _____**

3. Highest level of education
   - □ Some high school, no diploma
   - □ High school degree or equivalent
   - □ Vocational or technical school
   - □ Some college, no degree
   - □ College or associate degree
   - □ Bachelor's degree (e.g., BA, BS)
   - □ Master's degree (e.g., MA, MS, MEd)
   - □ Professional degree (e.g., MD, DDS)
   - □ Doctorate degree (e.g., PhD, EdD)
   - □ Other [please specify]: _____

4. **Occupation: _____**

5. **Ethnicity: _____**

6. **Religious affiliation: _____**

7. **Residency in Canada**
   - □ I was born outside of Canada and immigrated to Canada at the age of _____ year(s) old
   - □ I was born in Canada and both of my parents were born outside of Canada
   - □ I was born in Canada and one of my parents was born in Canada and my other parent was born outside of Canada
   - □ I was born in Canada and both of my parents were born in Canada
   - □ Other [describe here if needed]:
     _____

8. **Which of the following statements applies to you:**
   - □ I am a registered organ donor.
   - □ I am not a registered organ donor.
   - □ I am unsure as to whether I have registered to be an organ donor.

9. **What personal experience(s), if any, do you have with organ donation? [Please select all that apply]**

   - □ I have donated an organ to someone I know
   - □ I have been an organ recipient
   - □ My family member, relative, or friend has donated an organ
   - □ My family member, relative, or friend has been an organ recipient
   - □ I have no personal experience with organ donation
   - □ Other [please specify]: _____

10. In general, how knowledgeable would you say you are on the topic of organ donation?

- □ I have no knowledge about this topic
- □ I have limited knowledge about this topic
- □ I have some knowledge about this topic
- □ I am very knowledgeable about this topic
- □ I consider myself an expert on this topic

Supplementary Material D – Post-focus Group Survey of Perceptions

ID: _____

Please respond to the following questions regarding the various organ donation protocols we discussed today. Do not write your name on this page.

Non-cardiac DCDD

1. Do you believe that it is acceptable for a healthcare team to retrieve the liver, kidney, and/ or other non-heart organs of a donor after circulatory death (where the heart stops), if being an organ donor was consistent with their wishes and values?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

2. Would you be okay with your family member consenting to donating your liver, kidney, and/ or other non-heart organs after circulatory death (where the heart stops)?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

3. If you were asked, would you consent to the donation of the liver, kidney, and/ or other non-heart organs of a family member after circulatory death (where the heart stops), if I knew that being an organ donor was in keeping with their wishes and values?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

DPP approach to cardiac DCDD

4. Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using the DPP approach, if being an organ donor was consistent with their wishes and values?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

5. Would you be okay with your family member consenting to donating your heart after circulatory death (where the heart stops) using the DPP approach?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

6. If you were asked, would you consent to the donation of the heart of a family member after circulatory death (where the heart stops) using the DPP approach, if you knew that being an organ donor was in keeping with their wishes and values?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

NRP Approach to cardiac DCDD

7. Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using the NRP approach, if being an organ donor was consistent with their wishes and values?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

8. Would you be okay with your family member consenting to donating your heart after circulatory death (where the heart stops) using the NRP approach?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

9. If you were asked, would you consent to the donation of the heart of a family member after circulatory death (where the heart stops) using the NRP approach, if you knew that being an organ donor was in keeping with their wishes and values?

   Strongly Disagree Disagree Undecided Agree Strongly Agree

Chapter 4. Healthcare Providers' Perceptions on Cardiac Donation After Death by Circulatory Criteria: A Qualitative Study

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Healthcare providers' perceptions on cardiac donation after death by circulatory criteria: A qualitative study

Short Title: HCP perceptions on cardiac donation after circulatory death

Kimia Honarmand MD, MSc[1], Ian Ball MD, MSc[2,3], Maureen O. Meade MD, MSc[4,5], Aimee Sarti MD[6,7], Danielle LeBlanc[2], John Basmaji MD[2], Emilie P Belley-Cote MD, PhD[4,5,8], Michaël Chassé MD, PhD[9], Fred D'Aragon MD, PhD[10,11], Gordon Guyatt MD, MSc[5] , Bram Rochwerg MD, MSc[4,5], Sam Shemie MD[12,13], Robert Sibbald MSc[14], Marat Slessarev MD, PhD[2,15], Mathew J. Weiss MD[16,17], Jeanna Parsons Leigh, PhD[18]

Affiliations

1 Division of Critical Care, Department of Medicine, Mackenzie Health, Vaughan, ON, Canada
2 Department of Medicine, Western University, London, ON, Canada
3 Department of Epidemiology and Biostatistics, Western University, London, ON, Canada
4 Department of Medicine, McMaster University, Hamilton, ON, Canada
5 Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada
6 University of Ottawa, Ottawa, ON, Canada
7 The Ottawa Hospital, Ottawa, ON, Canada
8 Population Health Research Institute, McMaster University, Hamilton, ON, Canada
9 Université de Montréal, Montreal, QC, Canada
10 Department of Anesthesiology, Universite de Sherbrooke Faculte de Medecine et des Sciences de la Sante, Sherbrooke, QC, Canada
11 Centre de Recherche du CHUS, Sherbrooke, QC, Canada
12 McGill University, Montreal, QC, Canada
13 Canadian Blood Services, Ottawa, ON, Canada
14 Department of Family Medicine, Western University, London, ON, Canada
15 Ontario Health, Trillium Gift of Life Network, Toronto, ON, Canada
16 Transplant Québec, Montréal, QC, Canada
17 Division of Critical Care, Department of Pediatrics, Centre Mère-Enfant Soleil du CHU de Québec, Québec, Canada
18 Faculty of Health, Dalhousie University, Halifax, NS, Canada

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Corresponding Author:
Kimia Honarmand, MD, MSc
kimia.honarmand@mackenziehealth.ca

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ABSTRACT

Background

Cardiac donation after death determination by circulatory criteria (DCC) can be performed using either (i) direct procurement and perfusion (DPP) of ex-situ organs or (ii) normothermic regional perfusion (NRP). Neither of these methods are currently performed in Canada. Implementing these protocols represents an opportunity to reduce the cardiac transplant waitlist in Canada but both present ethical challenges that warrant further exploration.

Methods

We performed a qualitative description interview study of 75 healthcare providers who care for organ donors (n=51) and/ or transplant recipients (n=24) in Canada to elucidate their perspectives and insights into cardiac DCC and its implementation in Canada.

Results

We found that the broad support and interest to implement cardiac DCC among the cohort of healthcare providers interviewed was tempered by their anticipation that other healthcare providers, donor families, and the public would be less supportive. Donor clinicians were particularly concerned about potential erosion in public trust in the organ donation system as a whole. Participants identified opportunities to address anticipated challenges, including strategies for education and communication around cardiac DCC, staged/ gradual introduction of cardiac DCC protocols, and the option for stakeholders (healthcare providers, donor families, potential transplant recipients) to opt out of participation in cardiac DCC protocols.

Conclusions

In this qualitative description study of healthcare providers across Canada, we found broad support for cardiac DCC, but several challenges with the implementation of cardiac DCC

protocols in Canada, particularly concerns of non-support by other stakeholders. Participants also identified opportunities to address anticipated barriers.

Introduction

Most modern cardiac transplantations stem from donors declared dead by neurological criteria (DNC). Cardiac donation after death determination by circulatory criteria (DCC) represents a re-emerging opportunity for heart transplantation, thus far performed in the United Kingdom,[1] Australia,[2] the United States,[3] and Spain,[4] with the potential, if implemented in Canada, to markedly reduce the cardiac transplant waitlist.

There are two distinct surgical approaches for retrieving hearts from DCC donors: direct procurement and perfusion (DPP) and normothermic regional perfusion (NRP).[5] Both procedures begin with a decision to donate organs, based on discussion between the donor's family, healthcare team, and organ donation professionals. This is followed by withdrawal of life-sustaining measures, cessation of cardiac activity, death declaration by two physicians after a mandatory 5-minute "hands-off" waiting period.[5] At this point, the two procedures for retrieving hearts diverge. In DPP, the sternum is opened, and the heart is retrieved and placed in an ex-situ perfusion device where cardiac activity is restored during transport of the heart to the recipient. In NRP, the central vasculature is cannulated, the deceased donor is placed on an extracorporeal support, followed by restoration of thoracoabdominal circulation and cardiac activity. Once cardiac activity resumes, surgeons retrieve the heart for transport to the recipient.[5] Importantly, in NRP, prior to central cannulation, the blood vessels that supply the brain are surgically interrupted to safeguard against the restoration of brain perfusion when thoracoabdominal circulation is restored.[5]

There is great interest in implementing cardiac DCC in Canada.[6] Ensuring lasting success of

cardiac DCC programs and maintaining trust in organ donation requires understanding perspectives of stakeholders and exploring facilitators and barriers to implementation. There are concerns regarding acceptability of these procedures among Canadians, particularly with respect to NRP in which the surgical interruption of cerebrovascular supply and restoration of thoraco-abdominal circulation in a deceased donor may lead to ethical concerns, particularly the potential for cerebral blood in NRP. These concerns prompted our broader program of research, including a national web-based survey of Canadian healthcare workers, in which most participants endorsed ethical and practical concerns about implementing these protocols in Canada. These findings highlighted a need for deeper understanding of stakeholder concerns, best addressed by rich, in-depth qualitative data. In this qualitative interview study, we describe the perceptions, concerns, and ideas regarding cardiac DCC from Canadian healthcare providers who care for organ donors and/or transplant recipients.

Methods

Study design

We conducted a qualitative description study[7] to elucidate the perspectives of Canadian healthcare providers regarding cardiac DCC. Western University's Research Ethics board approved the study (#113808). We published the detailed study protocol.[8] **Appendix 1** presents the Consolidated criteria for reporting qualitative research (COREQ) checklist.

Sampling & Recruitment

We purposively recruited clinicians who routinely care for organ donors (donor clinicians) and transplant recipients (transplant healthcare providers) through their institutional email addresses

in a manner that maximized geographic diversity and conducted 75 interviews to achieve thematic saturation.[9] The published study protocol details the recruitment process.[8] We informed participants of the study topic and objectives. Participation was voluntary; we did not record the characteristics of those who chose not to participate.

Interview guide

The study team, who have expertise in organ donation and/or transplantation, developed an interview guide based on themes that emerged from a prior scoping review[10] and the national survey of healthcare providers[11] (**Appendix 2**). We tailored interview themes, questions and language for specific participant groups; for example, adding technical questions regarding surgery for interviews with transplant surgeons. We pretested the interview guide with experts in cardiac donation and transplantation and pilot-tested it with five participants to examine clarity and ease of use and refined the interview guide based on these interviews.

Procedures

We provided participants with a pretested summary of DPP and NRP, then conducted interviews via web-based video conference or telephone. Two female interviewers (an intensivist-researcher [KH] and a PhD research associate) with training in qualitative research conducted the interviews in English, each lasting between 25-70 minutes. Some participants may have been previously familiar with one of the interviewers (KH) through involvement within the academic community. Participants who were less familiar with cardiac DCC protocols tended to have longer interview times than those with more expertise.

Data analysis

All interviews were audio-recorded, transcribed verbatim, checked for accuracy, and uploaded to MAXQDA qualitative data management software. Two researchers (KH and DL) conducted thematic content analysis[12] through line-by-line coding of the transcripts, formulating a series of provisional codes that were refined through monthly meetings. The two researchers independently and later conjointly identified relationships between the codes and derived a series of themes and subthemes that emerged from the data. We ensured methodological rigour,[13,14] as described in the study protocol.[8] This qualitative work is not designed to make statistical inferences or conduct comparative statistics. As such, we reported the findings in categories/ themes rather than numerically.

Results

Participant Characteristics

Table 1 summarizes the characteristics of the 75 healthcare provider participants. Participants were well-represented across Canadian regions and duration of professional practice. Participants included those who care for organ donors ('donor clinicians'; n=51) and transplant recipients ('transplant clinicians'; n=24; Table 1). Figure 1 presents an overview of the 6 themes and their subthemes.

Support & Acceptance for Cardiac DCC

Overall, 72 of 75 participants (96.0%) supported the DPP protocol (94.1% donor clinicians and all transplant clinicians) and 61 (81.3%) supported NRP (78.4% donor clinicians and 87.5%

transplant clinicians (**Appendix 3**). Many participants viewed donation as a highly valued gift and felt that cardiac DCC with either protocol would lead to more donation, thereby honouring patients' wishes to donate organs. Some who expressed concern for possible collateral blood flow to the brain during NRP nevertheless articulated similar sentiments. Some participants also noted that the improved opportunity to donate the heart will help donor families with the grieving process (**Appendix 4**).

Participants who supported DPP considered this protocol to be a natural extension of existing DCC practices and some described similarities between the DPP protocol and existing practices using ex-vivo lung perfusion. Some participants felt that DPP is unlikely to adversely impact other transplantable organs (**Appendix 4).**

Many participants indicated no personal concerns regarding the resumption of donor circulation with the NRP protocol. They noted a 'less rushed' retrieval procedure with NRP, ability to assess heart quality pre-retrieval, reduced ischemic time and lower risk of cardiac injury which may lead to better graft quality. Some supported NRP because it parallels donation after DNC due to the procedural interruption of blood flow to the brain before resumption of circulation in the chest and abdomen (**Appendix 4**). Some participants, particularly non-cardiac transplant clinicians, indicated the potential for beneficial effects on other transplantable organs (i.e., abdominal organs and lungs), "*because you are cutting down that warm ischemic time.*" (Non-heart Transplant Physician-04: 112).

For many participants, support for cardiac DCC protocols was conditional on the following

additional factors, including support ***if***:

1. Heart function is *superior* using NRP compared to DPP.
2. The donor does not regain "consciousness" or "awareness" after the resumption of thoraco-abdominal circulation.
3. Research on the expected amount of brain perfusion after resumption of thoraco-abdominal circulation found either *no* brain perfusion for some participants, or no more than minimal brain perfusion for other participants.

Concerns & Hesitations

All participants either expressed or endorsed (when specifically asked) at least some concerns about cardiac DCC protocols, either (1) their own concerns (**Table 2**), or (2) concerns about others' non-support/ objections (**Appendix 5**).

Participants' Own Concerns & Hesitations

Frequent concerns about DPP included heart quality and the inability to assess heart function after a relatively prolonged warm ischemic time. Participants with concerns about DPP cited superior cardiac and non-cardiac graft function and potentially better recipient outcomes (as perceived by participants), as well as the high costs of DPP, particularly the cost of the extracorporeal perfusion device. Other participants, particularly non-cardiac transplant clinicians, worried about the impact of the protocol on the quality of other transplantable organs (**Table 2**), due to the delays in retrieving other organs after the heart is retrieved with the potential for increased warm ischemic time for other organs.

Some non-cardiac transplant surgeons expressed concerns regarding the potential increase in warm ischemic time during the cannulation process for NRP. Several participants, particularly ICU clinicians, described NRP as "invasive" (**Table 2**). Conversely, some participants pointed out that the additional processes are likely no more invasive than the sternotomy that is required for thoraco-abdominal organ donation. Some participants, particularly donor clinicians (i.e., ICU clinicians, donation physicians) expressed discomfort with the resumption of cardiac activity within the donor's body, while many expressed uncertainty/concerns about cerebral blood flow despite the surgical interruption of the vessels supplying the brain, either due to inadequate surgical technique or through collateral vasculature. Conversely, some participants questioned the necessity of this aspect of the procedure, suggesting that there is 'weak reasoning' for this. Others described general feelings of repugnance (e.g., "*Frankensteinish*"), felt that "*it is crossing the lines*", and used terms like "*strange*", "*surprising*", and "*archaic*" to describe this aspect of the procedure (**Table 2**).

Participants' Anticipated Non-support from 'Other' Key Stakeholders

Many participants anticipated that others (i.e., healthcare providers, donor families, and the public), would not support cardiac DCC protocols (**Appendix 4**). This concern was endorsed as a key barrier to the NRP protocol by nearly all respondents; many expressed support for this protocol themselves but had concerns that others would not be supportive. Among health care providers, sources of non-support might include general non-support of DCC donation and peri-mortem interventions in general, and specifically, for DPP: Ethical objections, general discomfort with the procedure, cultural and religious reasons, confusion around restarting activity of a 'dead' heart, and misinformation. For NRP specifically, participants cited potential

discomfort with resumption of cardiac activity within the donor's body and ligation of blood vessels that supply the brain, and concerns about possible residual blood flow to the brain. Some acknowledged that for DPP, such objections would reflect a small minority of healthcare providers. Concerns about the reactions of donor families were primarily related to NRP and included: lack of comprehension of how the heart can be donated after DCC, potential for additional stress or potential to overwhelm donor families provided with information about NRP, discomfort with resumption of cardiac function within the donor's body, and the perceived invasiveness of the procedure. Perceived public concerns mirrored those expressed in relation to other healthcare providers for both protocols. Here also, most believed that the public would strongly prefer DPP over the NRP (**Appendix 5**).

Respondents were concerned that the potential lack of public support and negative media/press, particularly related to NRP, may jeopardize trust in the organ donation system as a whole (Table 2): *"… The public trust that comes if it goes well or it goes poorly doesn't stay within the [hospital name] catchment area, right? It goes all across Canada." (*Non-heart Transplant Physician-04: 124).

Logistical Barriers

Participants identified logistical barriers to the successful implementation of DCC Heart in Canada, including the cost of the ex-vivo organ perfusion device in DPP, personnel barriers including the availability of transplant surgeons and perfusionists particularly in smaller transplant programs, limited knowledge/ expertise among providers, and limited availability of organ retrieval teams during efforts to avoid having to transport the patient to a larger transplant

centre for organ retrieval, particularly across distant geographical locations across Canada. Other logistical barriers included additional complexity of the technology/ machinery required, limitations in ICU beds, and operating room time.

Facilitators & Strategies

Existing Facilitators

Participants maintained that members of the Canadian public have trust in medical professionals and are generally highly supportive of organ donation, which will facilitate implementation of re-emerging organ donation opportunities. Participants also proposed success in existing programs, including ex-vivo programs for other organs (i.e., lungs) and cardiac DCC success in other countries, that may portend the likely success of cardiac DCC in Canada. Some participants held that the rise in acceptance of medical assistance in dying (MAiD) in Canada may foreshadow response to cardiac DCC over time. Others held that MAiD provides opportunity for first-person consent to organ donation, which may be an avenue to overcome some of the initial hesitations towards cardiac DCC (**Appendix 6**).

Proposed Strategies

Participants advocated that healthcare providers, donor families, the general public, and leading organ donation bodies be proactively engaged in cardiac DCC implementation. Some had concerns that the level of stakeholder engagement required has yet to be achieved. Others compared cardiac DCC implementation to early days of organ donation in Canada and proposed a similar approach to stakeholder engagement: ***"****So, and I remember when… they got the consensus in Canada, setting up for [DNC] … it was multidisciplinary and spiritual people,*

spiritual leaders were at the table too. And I think that this might be the time to sort of… do exactly the same thing again." (ODC-02: 430-431).

Table 3 summarizes the proposed strategies for education of healthcare providers and for public outreach to increase uptake of cardiac DCC. Table 3 also summarizes participants' proposed strategies to facilitate communication with donor families, including:

- Participants were divided on the level of details we should provide for donor families, between "complete transparency" about the details versus the belief that providing technical/ surgical details would be a disservice for grieving families and that communication should focus on the dying/deceased loved one. To balance these conflicting views, many participants proposed inquiring the level of detail the donor family prefers and tailoring the conversation accordingly.
- Establish appropriate language used to describe cardiac DCC protocols, particularly around NRP, to ensure transparency while minimizing the amount of potential distress on families.
- Normalize cardiac DCC; avoid presenting as a different decision than the decision to donate other organs.

Many participants advocated a staged and stepwise introduction of these re-emerging organ retrieval approaches (**Appendix 6**) including implementation of abdominal regional perfusion as a first step towards NRP implementation, staged approach involving the introduction of DPP before considering NRP because *"… it's probably the easiest to explain to the community, to explain to families." (*Transplant Cardiologist-05: 62-63), initiation at a few, select centres "*that would be poised for success… then it should expand to other centres in a serial fashion.*" (ICU

MD-06: 69), and implementation in the context of a collaborative research program.

Participants proposed an opt-out option to address concerns related to non-support by some healthcare providers. Some felt that this was a more effective strategy in addressing clinician concerns regarding cardiac DCC than attempting to "convince them". However, one donation coordinator raised the concern that if the group of clinicians choosing to opt out is large, *"... that puts a lot of pressure on the people who are willing to carry through."* (ODC-02: 410-411). Some donation coordinators agreed with a separate opt-out option for donor families specific to cardiac DCC and advocated for a "second approach" (family being approached a second time after initial consent to organ donation in general to obtain consent specific to cardiac DCC. (**Appendix 6; Figure 2**).

Proposed Research Priorities

Participants identified priorities for the research/ scientific community, including (1) efficacy of the procedures/ recipient outcomes, (2) impact of cardiac DCC on the organ donation system, (3) acceptability of cardiac DCC protocols by stakeholders, (4) readiness of the healthcare system to implement cardiac DCC, and (5) research specific to NRP and death definition/ determination (**Appendix 7**).

Discussion

In this qualitative description study of 75 healthcare providers across Canada, we found broad support for cardiac DCC. ***They expressed several concerns and hesitations, primarily related to their perception of non-support by other stakeholders*** and identified opportunities to address

potential challenges. Many participants viewed DPP as a "natural extension" of existing DCC organ donation practices and some viewed NRP akin to the existing practice of cardiac donation in DNC. Support for cardiac DCC protocols centered around honoring the wish to donate organs and facilitating the grieving process for donor families as reported in previous studies.[15,16] Consistent with prior studies of DCC in general[16], participants' *own* concerns about DPP were primarily pragmatic including graft quality and potential negative effect on other transplantable organs (**Table 2**). Participants expressed concerns about cardiac DCC primarily related to perceived non-support of cardiac DCC by *others* (i.e., other clinicians, the public, and donor families), and fears that non-support may propagate mistrust in and adversely impact existing organ donation procedures (**Appendix 5**), a view that was most poignant among donation clinicians. Some participants felt that non-support for DCC in general may be a barrier to acceptance of cardiac DCC, particularly the DPP protocol. This is consistent with a survey in which over half of Canadian healthcare workers who did not support DPP were also unsupportive of non-cardiac DCC in general.[11]

A survey of Canadian healthcare providers found that 78% of respondents found the NRP approach to be acceptable.[11] Although most participants in this study also supported NRP, there was great ambivalence and hesitations, primarily related to the perceived invasiveness and imagery evoked by the procedure. The restoration of cardiac activity within the donor's body and ligation of the blood vessels led to 'pause' for many participants (for reasons outlined in **Table 2**). Participants were primarily concerned that *others* would find NRP to be overly 'invasive' to the donor's body and expressed terms like "*Frankenstein-ish*" to describe the procedure. Indeed, in a web-based survey of the Canadian public, we previously reported that whereas 74% of

respondents supported DPP, support for NRP was only 65%.[17] Many reported that their support for NRP is contingent upon evidence showing that heart graft function was *superior* to the DPP approach and that the risk of cerebral perfusion was minimal or none.

Organ donation consent discussion can be a source of distress for donor families,[18] highlighting the need to develop standardized, family-focused communication strategies addressing organ donation. Recent initiatives have focused on developing more family-centered strategies for communicating with donor families.[19–21] Participants in our study identified several proposed strategies for communicating with donor families about cardiac DCC (**Table 3**), which may form a blueprint for developing a standardized approach to introducing cardiac DCC protocols in a manner that mitigates distress for donor families. Participants also advocated for proactive public engagement and transparency, normalizing the procedures, framing them as a positive development in the medical field, and identifying and utilizing consistent language to describe the procedures (**Table 3; Figure 2**). They emphasized opportunities to harness existing facilitators including public trust in the medical profession and public awareness of organ donation. Indeed, one study reported broad support for organ donation in the context of MAiD.[22] These strategies can inform national public awareness campaigns to garner acceptance for cardiac DCC. Recommendations for implementation included various forms of staged introduction of cardiac DCC protocols, such as starting with non-cardiac (i.e., abdominal) regional perfusion (as has been previously suggested[23]), starting with the DPP protocol, or starting at select centers under the umbrella of a well-planned research program. Participants also advocated for variable levels of choice for opting out of participation in cardiac DCC as a means to improve acceptability (**Table 3; Figure 2**).

This study has several limitations. Healthcare providers who are more supportive of organ donation may be more likely to participate, leading to selection bias. Some participant groups had more expertise in the topic (e.g., cardiac transplant surgeons) compared to others (e.g.,, many ICU clinicians without prior exposure to the topic). Nonetheless, the variable expertise levels also yielded more diverse perspectives and insights. Furthermore, we did not include the perspectives of healthcare providers in the Canadian territories, who should be included in future evaluations of this topic. Study strengths include use of rigorous methodology in the development of study protocols and the interview guide and thematic content analysis, inclusion of a large sample of healthcare providers with representation from diverse professions across most Canadian regions, and pre-interview education provided to participants, ensuring that they were familiar with the protocols prior to the interview.

Conclusion

In this in-depth description of the perspectives of Canadian healthcare workers, we found strong support to implement cardiac DCC in Canada and identified opportunities to address barriers in a manner that is informed by frontline stakeholders directly. These findings contribute to the limited literature on the perspectives of stakeholders regarding cardiac DCC. This program of research also provides a model for the stakeholder engagement that can be applied to emerging donation and transplantation innovations.

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Table 1. Summary of participant characteristics

Sample characteristics (N=75)											
Characteristics	Total (N=75)	Cardiac surgeon (N=5)	Donation physician (N=11)	ICU MD (N=10)	ICU RN (N=15)	Donation coordinator (N=10)	Perfusionist (N=5)	Transplant cardiologist (N=8)	Other transplant physician (N=5)	Other transplant surgeon (N=5)	Recovery coordinator (N=1)
Regions (N [%])											
Western	35 (46.7)	2 (40)	6 (54.5)	3 (30)	7 (46.7)	6 (60)	2 (40)	3 (37.5)	3 (60)	3 (60)	0 (0)
Ontario	22 (29.3)	3 (60)	2 (18.2)	4 (40)	5 (33.3)	1 (10)	3 (60)	2 (25)	0 (0)	1 (20)	1 (100)
Quebec	12 (16)	0 (0)	2 (18.2)	2 (20)	0 (0)	3 (30)	0 (0)	2 (25)	2 (40)	1 (20)	0 (0)
Atlantic	6 (8)	0 (0)	1 (9.1)	1 (10)	3 (20)	0 (0)	0 (0)	1 (12.5)	0 (0)	0 (0)	0 (0)
Gender (N [%])											
Male	38 (50.7)	5 (100)	9 (81.8)	7 (70)	1 (6.7)	1 (10)	1 (20)	5 (62.5)	3 (60)	5 (100)	1 (100)
Female	37 (49.3)	0 (0)	2 (18.2)	3 (30)	14 (93.3)	9 (90)	4 (80)	3 (37.5)	2 (40)	0 (0)	0 (0)
Years of experience Mean (SD)											
<1	1 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
1-5	13 (17.3)	0 (0)	3 (27.3)	4 (40)	0 (0)	3 (30)	2 (40)	1 (12.5)	0 (0)	0 (0)	0 (0)
6-10	21 (13)	1 (20)	5 (45.5)	1 (10)	4 (26.7)	3 (30)	1 (20)	3 (37.5)	0 (0)	2 (40)	1 (100)
11-15	13 (17.3)	1 (20)	1 (9.1)	2 (20)	3 (20)	2 (20)	0 (0)	1 (12.5)	2 (40)	1 (20)	0 (0)
16+	27 (36)	3 (60)	2 (18.2)	3 (30)	8 (53.3)	1 (10)	2 (40)	3 (37.5)	3 (60)	2 (40)	0 (0)
Support for… (N [%])											
DPP	72 (96)	5 (100)	11 (100)	9 (90)	15 (100)	9 (90)	4 (80)	8 (100)	5 (100)	5 (100)	1 (100)

NRP*	61 (81.3)	5 (100)	9 (81.8)	8 (80)	14 (93.3)	6 (60)	3 (60)	6 (75)	4 (80)	5 (100)	1 (100)

*Support for NRP was frequently conditional upon research initiatives (e.g., absence of collateral flow, better outcomes than DPP, etc.) and support from the Canadian public.

Table 2. Participants' *OWN* concerns and hesitations about cardiac DCC

Themes	Illustrative Quotes
Direct Procurement & Perfusion (DPP)	
Concerns about heart quality & recipient outcomes	*"There is no question that uh there's going to there's more of an ischemic hit on the heart when you are forced to take it out without re-perfusion in an ischemic situation that until you can get it on a pump… Now how that plays out clinically remains to be seen… it wouldn't be a surprise at all if the primary graft dysfunction rate was worse."* Cardiac Surgeon-01: 31 *"So with [DPP], I'd be concerned that that's too much time without blood flow, that it would compromise the integrity of the cardiac tissue… I'd be concerned about the integrity for sure."* ICU RN-08: 165
Potential impact of procedure on other transplantable organs	*"… then when they do their harvest because the [DCC], the harvest is much more I wouldn't say rushed, but you know, cuts and things like they might be worried that they might damage the lungs when they're doing the heart because it's uh gonna impact the easily the lungs. Let's say if they made a mistake and damage the lungs during the procurement, those are concerns that I have. So I don't think I have any ethical concerns with a per se but I do have some technical concerns with how it's done, and how it would impact my lungs that we would procure at the same time."* Non-heart Transplant Surgeon-01: 97 *"… if the if the declaration of death occurs at time zero, and then it's the cardiac team that comes first. And they take, let's say, a minute or two to remove the heart, and then the abdominal team comes in. So we're losing (time), if we cannot do it at the same time, then there is a significant risk that the period of warm ischemia will be longer for the abdominal organs and as far as the liver is concerned, this is an issue."* Non-heart Transplant Physician-03: 86-87 *"Well, I guess it just seems to me like there's a lot more steps for things to go wrong than to jeopardize the the big picture of all of all the organs not just the heart."* Non-heart Transplant Surgeon-04: 162-163
Normothermic Regional Perfusion (NRP)	
Perception of invasiveness of the procedure	*"… If I had a loved one who was in the situation, I would just feel like oh my God, that's just I just can't. They've been through this horrific, horrific process in the ICU, we're deciding that they're, you know, not going to survive and, and now they're gonna have to go through this really kind of invasive thing at the end of their life or after*

	they've died. I don't know how I feel about that. Um that just it just seems like a lot." ICU MD-08: 199 *"There has to be a more academic word than icky but it is kind gives you the "ew" feeling that it's quite invasive. I know it is all invasive, I know taking the heart out and giving it to someone else is invasive but this seems like an extra step of aggressiveness on that donating body. I do not know, that's how I feel."* ICU RN-04: 81
Concerns about reanimation of the heart within the donor's body	*"It's hard to explain. But for me and my comfort level, I'm still I'm open to [DCC], taking the heart out of the chest. It's a little harder pill to swallow, maybe just from an emotional standpoint to see a heart beating in a chest in a patient that's connected to a circuit, it's harder to establish that they are truly dead. We know they're dead, but it's hard to wrap your, your mind around it, if that makes sense."* Perfusionists-03: 128 *"… Once they're dead, we should not be recirculating blood for any reason. Like it just there's that's the whole point of being dead within that individual is that their heart has stopped, there's going to be no reperfusion within the cavity, within the body for anything, and I think it's - I just think that, you know, restarting it and having perfusion everywhere but the head just seems very um artificial and that we've it's losing the respect of the of the body."* ODC-04: 102-103
Discomfort with ligation of blood vessels to the brain	*"It seems to me it is something that we are doing largely to make ourselves feel better, when in reality, we may not. We can't...I think it is just something that we are doing to...it is...it is utilitarian to me in a way."* Donation MD-10: 196 *"It seems to me it is something that we are doing largely to make ourselves feel better, when in reality, we may not."* Donation MD-10 *"… there is a bit of an ick factor. It does seem a bit gruesome… Ah, well, they said, "Oh my god, like, what are you actually doing? Like this person is dead and you're stopping blood flow in the brain, but they're actually dead. So like, why are you doing this?"* Non-heart Transplant Physician-02: 198-199
Concerns about possible residual blood flow to the brain	*"If there is a lot of blood flow [to the brain], it would definitely give me pause. And I would probably be concerned that that person was no longer... not deceased if there was sufficient blood flow to their brain that would allow for some level of brain functioning."*

	Non-heart Transplant Physician-04: 108 *"… There's a ethical issue for that. Because the brain can start to have function back and maybe the patient would feel something or suffer from that, compared to a normal [DCC] donation."* Transplant Cardiologist-08: 67-68 *"That's a huge ethical hard line… So now you've re-established flow to the brain. But when you think about it, logically, and at its core, that brain is still brain dead. And now you have a true DBD donor on the table. So even if you re-established flow, after five minutes of having no brain flow, that brain is all intense, like, for all intents and purposes, is dead. Um so even after you've established blood flow, you now have a DBD donor. Basically… converted a [DCC] to a [DNC]. So, no, we don't want to see brain flow. Um but is it the worst thing in the world have brain flow when you look at the fundamentals of just brain death? Probably not. But ethically, it shouldn't happen."* Perfusionists-03: 167-168 *"And I don't know, is that something that's a bit like in in, in one of two ties, it's 100% this is going to tie it off? Okay then. But I would need to understand that better to know without stopping and doing testing to make sure there is no blood flow to the brain um without also if they did miss some blood flow when we did the testing and found blood flow, that would be very upsetting…"* ODC-01: 82
Propagation of mistrust in the organ donation system	*"I am worried for [NRP], that we may actually lose organ donation...organ donors in general who just say no to everything instead of at least some organs."* Non-heart Transplant Physician-05: 175-176 *"And I just did I see potential for for disaster. And I think that in a situation like that, if you were to implement a program with that thing, and there was a disaster, I think it could kill your entire [DCC] program."* ODC-05: 183 ***"…** The thing is, we're not going to have hearts to transplant in this method if we alienate our teams and our families because there are no transplants without donors."* ODC-08: 174-175 *"… if it's not rolled out properly, then it can be devastating in terms of the consequences."* Cardiac Surgeon-03: 170-171

Negative media/ press jeopardizing the organ donation system	*"… The last thing we would ever want if we started to see the heart program anywhere in Canada is for there to be a news story that highlights that we are doing maybe unethical or that this is not what what the donor would have wanted or their families would have wanted. Because I think a negative story like that could put the entire organ donation process under the microscope and can start raising doubts in donors, families and donors and people themselves as being potential organ donors. So, it has to be done correctly to avoid any negative PR and negative media attention."* Transplant Cardiologist-02: 35

Table 3. Proposed strategies for engaging & educating healthcare providers, donor families, & the public.

Themes	Illustrative Quotes
Healthcare Providers	
Education as a means to increase HCP acceptability of DCC Heart	*"… I think what would be beneficial, the most would probably be a video, like talking about the procedure, talking about why we're doing it, why this move to do it. You know, maybe highlighting some of the statistics about [it]… the last number of years, we had X number of patients that could have donated their heart and uh didn't because we don't do that in Canada… the amount of patients that could have benefited from that, like showing them what the outcome could have been if we had done this for years… because I think putting a number on it, even if it's just a speculative number… if they were able to see like quantitative benefits, um I think that would be really beneficial as well… also maybe some family interviews like of, of patients that could have received a heart but that ended up dying like their family saying how much of a difference that would have made to those, their life…"* ICU RN-08: 183
Education/ training around how to communicate with donor families about DCC Heart	*"We [nurses] are directly with families so if we have knowledge that we are able to support families better I think. And, we are more comfortable ourselves. We know what we are getting into, we know what is going on that sort of thing. So I think, yeah, the more information you can give us the better off we will be I think. That is my opinion."* ICU RN-01: 123
Practical education around antemortem care, intra-operative procedures, etc.	*"Well, I would be training on, on the device or the devices and whether it's the pump or the, the NRP pump. Um, just maybe going through the process, like watching videos on it just, just education. Knowing how it would change my role… going through the steps and, knowing what is expected of me."* Transplant coordinator-01: 135
Educational initiatives should be led by organ donation organizations	*"… then also having like, BC transplant involved and um they're really good specialists in those areas as well. So having maybe education sessions with them about the dialogue of at the bedside or sort of um what goes on during the whole process of transplant."* Perfusionists-01: 170
Learning from established cardiac DCC programs in other countries	*"Well, I think we need you need to talk to other centers that have moved ahead with this and see how they've handled it."* ODC-04: 158-159

	"So, [TGLN] has already sent a team about three years ago to England to learn from people who are already doing this. And so, it's probably actually cost more cost effective to bring some of the people from England who are already doing this to go from center to center in Canada, it wouldn't be a lot of centers, I mean, I'm guessing would be a handful or less of centers to do some of their first cases with them." ICU MD-02: 214-215
Donor Families	
Broad strategies relevant to organ donation in general	• Bedside healthcare providers/ donation staff should be transparent with donor families about organ donation processes. • Educational tools such as standardized video clips that describe the process of withdrawal of life-prolonging measures and organ donation to ensure consistent messaging. • Engagement of faith/ spiritual leaders.
Tailor the level of details/ information to each donor family preference	*"… I think like, honestly, I think we would almost have to ask families about how much they would want to know about what the preservation process and other things look like."* ICU MD-08: 95 *"… There are going to be families who want every little detail and other families are just gonna say like, nope, we are fine do whatever you want. So, I think... our intensivists and our donor providers, or care teams... need to be able to… approach it either way. … If we go in there with all or none with minimal information, this is not going to work."* ICU MD-09: 124
Establish appropriate & consistent language to describe cardiac DCC protocols	*"It's how it's framed, because if you're like, we're starting to heart and we're clamping off blood flow to the brain. People that don't have an understanding aren't going to receive that well. But if you say… 'your loved one has passed and we're, we're isolating the heart in order to be able to donate it to someone else'… The wording there is very different and you're not dishonest in either aspect."* Perfusionists\PER-01-MS: 94 *"… I think that would need to be still made into layman's terms, so they had a general sense of the procedure, what was being done. I think you start getting into terminology and medical terminology, I think we tend to lose our family members. I think they need it as simple down and easy."* ICU RN-10: 87
Normalize cardiac DCC protocols	*"I think you'd normalize it. You would talk about how any, any organ is possible for donation and if they are interested in being organ donors, they're not just interested in one organ."* ICU RN-04: 111 *"So… you meet families where they're at, and you listen to them… if we can make it all relevant and normalize it for them so that it fits into their worldview, then they're going to seriously consider donation."*

	ODC-02: 507
Present broad data/ statistical facts	*"… Probably for me maybe understanding the percentage of hearts that would be able to be used after being put on the machine so that when I am explaining it to the family I can give them that understanding of um you know, if you consent to the heart and we recover the heart, this is the percentage that it may not get transplanted or may get transplanted. I think that would be very helpful in explaining it to the families"* ODC-01: 100
General Public	
Stakeholder engagement and transparency	*"I think it needs to be something like this introduced with a lot of forethought and a lot of discussion and a lot of opportunity opportunities for question and answer and interchange back and forth. So that basically, hopefully everybody at the sites that start to become involved with this, understand had an opportunity to either opt in or opt out of the process and are supportive of the activities they're participating in."* Non-heart Transplant Surgeon-02: 89 *"… I'm not sure how carefully we've asked all the stakeholders because people may have harbor private views on this, this is not something they're comfortable with. It's just never floated to my attention."* Transplant Cardiologist-06: 107
Proactive public outreach/ education/ increasing public awareness	▪ *a priori* stakeholder engagement ▪ Being proactive & getting ahead of the 'story' (i.e., news) ▪ National public awareness campaign ▪ Increasing public discourse around organ donation ▪ Engaging younger population ▪ Framing the protocols as a positive development ▪ Normalizing the procedures ▪ Sharing stories and emphasizing positive outcomes of transplant recipients ▪ Having spokespersons in the community ▪ Engaging advocacy/ patient representative groups ▪ Correcting misconceptions ▪ Identifying appropriate/ consistent language to deliver the message in a transparent/ accurate way

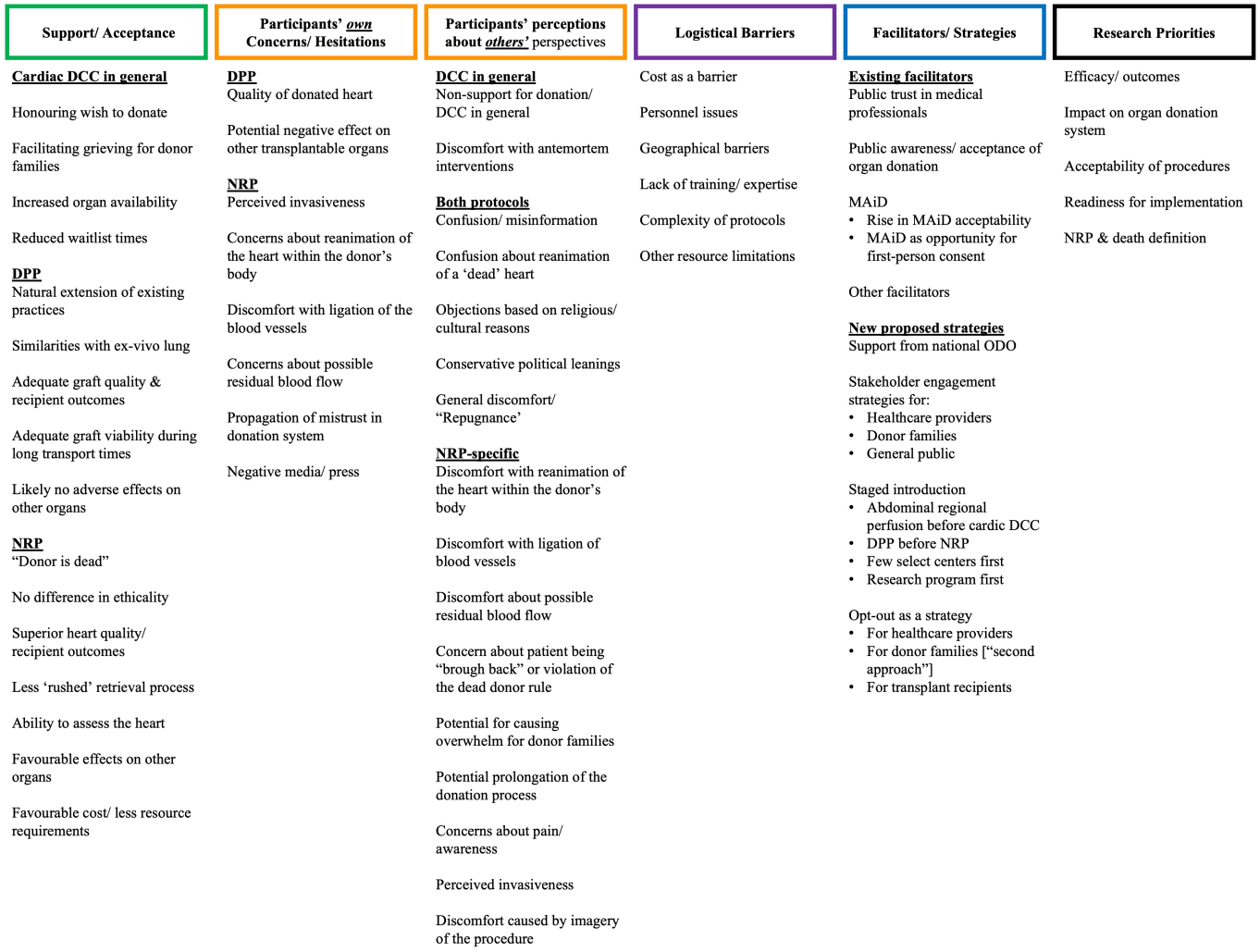
Figure Legends

Figure 1. Overview of themes & subthemes

Figure 2. Facilitators, concerns, & proposed strategies for the implementation of cardiac DCC in Canada

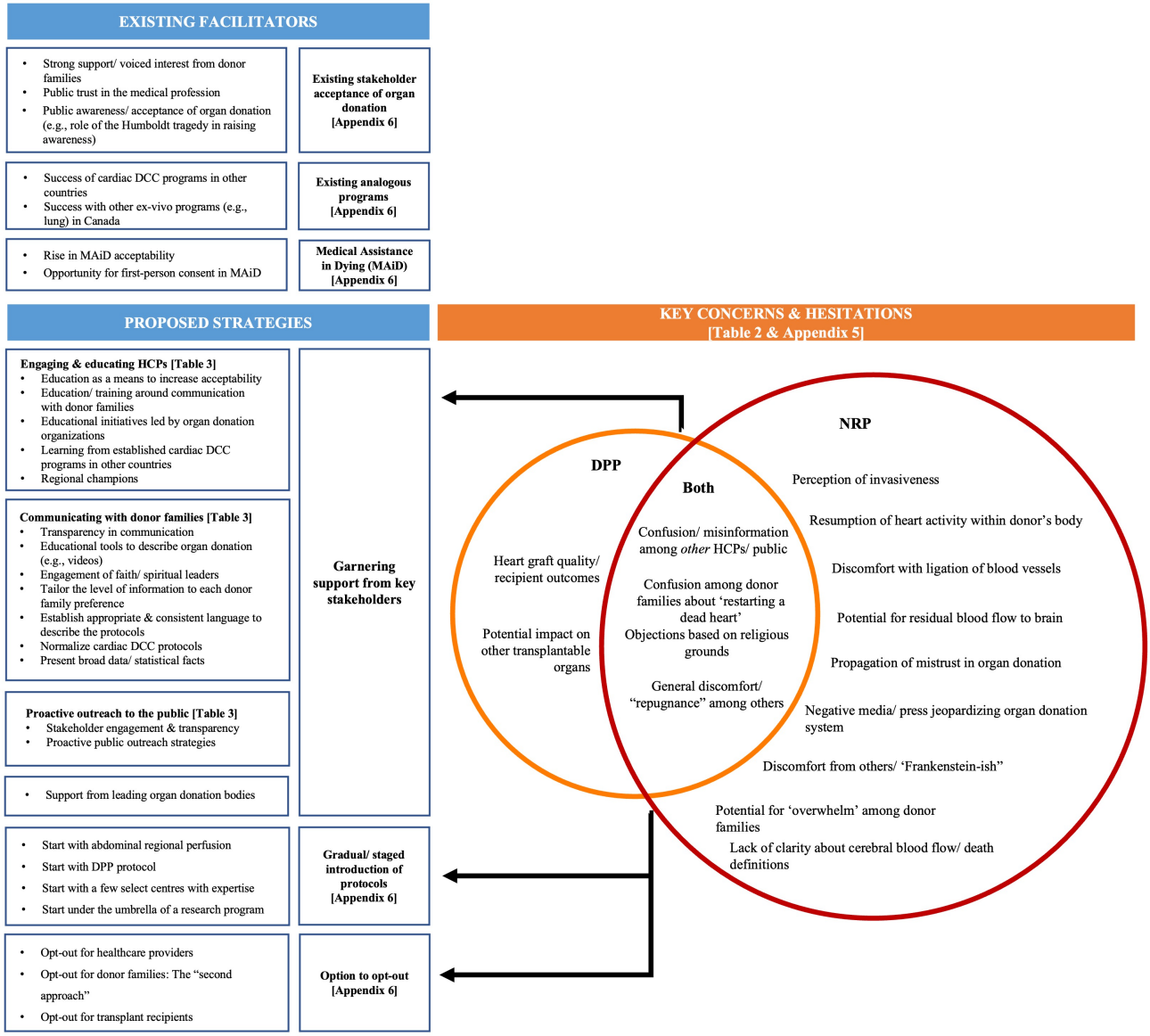
Figures

Figure 1. Overview of themes & subthemes



DCC: Death determination by circulatory criteria; DPP: Direct Procurement and Perfusion; NRP: Normothermic Regional Perfusion; MAiD: Medical Assistance in Dying; ODO: Organ Donation Organization

Figure 2. Facilitators, concerns, & proposed strategies for the implementation of cardiac DCC in Canada



DCC: Death by circulatory criteria; MAiD: Medical Assistance in Dying; HCPs: Healthcare providers; DPP: Direct procurement & perfusion; NRP: Normothermic regional perfusion

Appendices

Appendix 1. Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist.

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	**Page 5.**
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	**Page 5.**
3. Occupation	What was their occupation at the time of the study?	**Page 5.**
4. Gender	Was the researcher male or female?	**Page 5.**
5. Experience and training	What experience or training did the researcher have?	**Page 5.**
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	**Page 5.**
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	**Page 5.**
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	**Page 5.**
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	**Page 4.**
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	**Page 4.**
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	**Page 4.**
12. Sample size	How many participants were in the study?	**Page 4.**
13. Non-participation	How many people refused to participate or dropped out? Reasons?	**Page 5.**
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	**Page 5.**
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	**No.**
16. Description of sample	What are the important characteristics of the sample?	**Table 1.**

	e.g. demographic data, date	
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	**Appendix 2.**
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	**No.**
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	**Page 5.**
20. Field notes	Were field notes made during and/or after the interview or focus group?	**No.**
21. Duration	What was the duration of the interviews or focus group?	**Page 5.**
22. Data saturation	Was data saturation discussed?	**Page 4.**
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	**No.**
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	**Page 5.**
25. Description of the coding tree	Did authors provide a description of the coding tree?	**Figure 1.**
26. Derivation of themes	Were themes identified in advance or derived from the data?	**Page 5.**
27. Software	What software, if applicable, was used to manage the data?	**Page 5.**
28. Participant checking	Did participants provide feedback on the findings?	**No.**
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	**Included in all associated tables and appendices.**
30. Data and findings consistent	Was there consistency between the data presented and the findings?	**Yes.**
31. Clarity of major themes	Were major themes clearly presented in the findings?	**Yes.**
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	**Yes.**

Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Appendix 2. Summary of the interview guide.

	Topics covered in interviews
DCC non-heart organs	How many organ donation cases have you been involved in? How about DCC specifically? Do you believe that it is acceptable for a healthcare team to retrieve the liver, kidney, and/ or other non-heart organs of a donor after circulatory determination of death?
Cardiac DCC - general	Before reviewing the pre-written material, had you heard of cardiac DCC before? What did you know about it?
Direct procurement and perfusion (DPP)	What is your understanding of DPP? What do you think about recovery/ retrieval of the heart of a donor after circulatory death using the DPP approach? Do you have any concerns about the donation the heart using the DPP approach? Would you support implementation of the DPP approach?
Normothermic regional perfusion (NRP)	What is your understanding of NRP? What do you think about recovery/ retrieval of the heart of a donor after circulatory determination of death using the NRP approach? Do you have any concerns about the donation of the heart using the NRP approach? Would you support implementation of the NRP approach? Relative to the DPP approach, what are your thoughts on the NRP approach?
Public perception	What do you think the public's perception will be regarding cardiac donation after DCC?
Implementation (barriers and solutions)	What do you think about the implementation of DPP/NRP in Canada? Do you foresee any concerns or barriers in the implementation of DPP/NRP in Canada? How about locally? What would you advise policymakers on next steps when it comes to cardiac DCC? Generally, who should lead the way towards implementation of cardiac DCC in Canada? What do you think about the role of research in the field of cardiac DCC?

Appendix 3. Support for heart donation after circulatory determination of death [N(%)]

	DPP	**NRP***
	72 (96%)	61 (81.3%)
Profession		
Cardiac surgeon	5 (100%)	5 (100%)
Donation physician	11 (100%)	9 (81.8%)
Intensivist (ICU MD)	9 (90%)	8 (80%)
Registered Nurse		
Intensive care unit	13 (100%)	12 (92.3%)
Operating Room	2 (100%)	2 (100%)
Donation coordinator	9 (90%)	6 (60%)
Recovery coordinator	1 (100%)	1 (100%)
Perfusionist	4 (80%)	3 (60%)
Transplant cardiologist	8 (100%)	6 (75%)
Transplant physician (liver, kidney)	5 (100%)	4 (80%)
Transplant surgeon (lung liver, kidney, pancreas)	5 (100%)	5 (100%)

*Support was often conditional on research initiatives (e.g., absence of collateral flow, better outcomes than DPP, etc.) and support of the Canadian public.

Appendix 4. Reasons for support of Cardiac DCC protocols.

THEME	ILLUSTRATIVE QUOTE
SUPPORT DUE TO HONOURING THE WISH TO DONATE	
Honouring patients' wishes	*"… I kind of feel like if I'm honouring them and um ethically caring for them, but then also ethically caring for this heart that is being donated somewhere else, I feel like I'm doing my job."* OR RN-01: 95 *"So, it doesn't matter to me if it's their kidneys or their liver or their heart. They've chosen to give a gift. We have a responsibility to help that person give that gift."* Donation MD-09: 187-188 *"… ultimately, it's fulfilling the for the wishes of people who end up dying and their family members."* Transplant Cardiologist-02: 35 *"… that we are going to do everything we can to make sure that uh we're respecting their consents, their generous gift in this and, and being responsible with what they've given us, or the person who's waiting for it. And that, you know, we have a lot of things that we are able to do and we will do everything we can to make sure we're good stewards of what's been given to us."* ODC-07: 130-131 *"… I think for the most part, they'll understand that, you know, we treat the body with dignity, we ensure that, you know, whatever we can do to maximize the ability of the person to give the gift that they would like to give."* ICU RN-09: 59 *"This patient has already proven themselves to be deceased without life support, the family has already said, if he cannot live a meaningful quality life off life support, I want him to do the best possible uh to the possible best uh of his organs ability, I want him to save another life. That then becomes our ethical obligation."* ICU MD-05: 73
Honouring patients' wish to donate organs in the NRP protocol	*"At the same time however, [donor family members] are extremely disappointed if we don't use any of the organs because they're too damaged. And so wouldn't you want the organs to be as salvageable and as in good condition possible in order to be used down the road?"* Non-heart Transplant Surgeon-03: 210-211 *"Personally… I have more of an ethical issue if we do not offer this option to families and let them decide."*

	ICU RN-07: 104
Facilitating grieving for donor families	*"… I mean, especially with children, families are aware there is no more hope for their child and what they really want to do is something meaningful to come out of a terrible situation and that is where I feel like we should do our best to offer families everything we can to allow that to happen."* ICU RN-07: 152 *"… we make assumption that because they're the parent of a child who's dying, that we're gonna protect them, you know… (but) we're not protecting them. We're depriving them of opportunities that may be life saving for them in terms of their mental and emotional recovery from a from a terrible tragedy. It's not fair to treat them that way."* Transplant Cardiologist-03: 218-219 *"I have seen the benefits of offering organ donation to families. I truly believe in many cases it helps them grieve and so, again I am very supportive of organ donation."* ICU RN-07: 47 *"… that's cool. I didn't know that you could do that for human heart. Um and I mean, I think when people want to donate I think the more that… the patient can donate, you know, the better I think the family feels. Uh I think that's a really important outcome that that families, you know, feel like it's one small good in this terrible thing that's happened. Um so, you know, I thought that that was pretty uh, pretty interesting and pretty cool."* ICU MD-08: 70-71
SUPPORT DUE TO PRAGMATIC & OUTCOME-RELATED REASONS	
DCC HEART IN GENERAL	
Increased availability of viable donor hearts	*"…Listen, we have a huge problem getting hearts. So, there's no question we have to increase our pool of hearts. And I… would be very much in favour of using [DCC] hearts."* Transplant Cardiologist-04: 23 *"So every time I have to waste the heart, which is, I mean, it's so sad. I mean, so, so personally, myself, I'm in the front line, I see all the good heart going to the garbage, which is really bad. So this is where basically I mean, I'm struggling myself as researcher as well, having, you know, I've been doing research on how we can take these hearts…"* Transplant Cardiologist-08: 44

Reduced waitlist times	*"… I think once people understand that the list of people waiting for hearts is going to be helped, and the people that normally would have died waiting, could actually have another chance, I think there will be very little barriers, especially if it's proven to be safe…"* Perfusionist-05: 95 *"…I think um, could be kind of a game changer for a lot of patients waiting for hearts. Because I mean, I see a lot of people waiting for heart transplants with severe heart failure or other issues. And, you know, there's a lot of bridging methods that we can use to kind of get them there. But the number of organs is so small um that often they don't do very well waiting for very long. And so I think that that that could be a really big thing for those patients."* ICU RN-13: 219
DIRECT PROCUREMENT & PERFUSION	
Natural extension of existing DCC practices	*"… it's similar to the process of other organs. So, I don't think it would be something that would be too much of a challenge. And I don't think I don't think ethically it would make a difference considering where we're at now with the [DCC]."* ICU RN-11: 77 *"I think it is fine. I think… it is no different to me. I do not see any difference in that to other organs that are removed like lungs, kidney reperfusion. I think it is great."* Donation MD-04: 36 *"… what am I missing? Why would it be why would there be ethical issues? Is it the fact that - just because the hearts beating in a box somewhere outside the body?"* Cardiac Surgeon-04: 55
Similarities with ex-vivo lung	*"So that is very much like how we treat lungs when we, when we place them on an ex-vivo circuit so that I think people have had some time with and I think that is a viable option."* ICU RN-04: 55
Adequate heart quality and recipient outcomes	*"…But we know that sometimes prolonged time outside of the body between transplant for, you know, you could lose some viability, you could create a risk that have less success. And now we have an option to increase the possibility of greater success for the person receiving it. I think we have an ethical responsibility to do it if we can."* ODC-07: 75 *"From what I have heard and read it seems like it is actually an extremely um viable option to…it sounds good to me like, you know. A heart that is still beating I would assume would be better for a recipient then even a heart retrieved from a brain dead donor that is not beating for the hours before it goes in them right?…"* ICU RN-07: 37
Adequate graft viability during longer transport times	*"Yeah uh, listen, assuming that the device the profusion device is working well, and it gives us time to bring, you know, to get the device, the heart to where it has to go, I think it would be even better. It's going to be better than what we have done when we put the heart on ice."* Transplant Cardiologist-04: 71

	"…implementing something like DPP could, um you know, make more organs more viable for longer because the transport time for a lot of both organs could be huge." ICU RN-13: 239
Likely no adverse impacts on other transplantable organs	***"****Might add a little bit of time, but uh, you know, really didn't definitely didn't interfere with it with the kidneys. You know, we, we got to you know, I think once the once the flush has happened once the ice in there, everybody relaxes everybody chills…"* Non-heart Transplant Surgeon-04: 126-127 *"… The critical time point is the flush, and when we can put ice in the belly and that shouldn't be that shouldn't be much delay. It should be a minute or so now, not much more than that. So, I think I'm very supportive. I don't think there's a problem with that."* Non-heart Transplant Surgeon-05: 62-63 *"There usually there is there's usually more some delay when there are other organs uh and they're recovered before the kidneys, but I'm sure that we will be a learning curve and we will learn along the way. I don't expect a a negative impact, but it remains to be determined."* Non-heart Transplant Physician-01: 46-47
NORMOTHERMIC REGIONAL PERFUSION	
Consider the donor to be dead using current protocols for death declaration	*"… Once we said they're deceased, they're deceased. And then, you know, there may be some resuscitation… having 3 or 4 beats after this declaration, you know, resuscitation? I don't know. But I don't think there's enough that you'd have any awareness or any chance of recovery, so I wouldn't have any major ethical concerns with that."* Transplant Cardiologist-07: 133 *"…I wouldn't get hung up on it. I think if the way we declare death and um uh the margin of safety so high that I don't - you know in Canada and the centers that procure like this, our systems so well refined that I wouldn't make it obligatory myself. I'd be comfortable if the patient was in that process and then went uh asystolic for a certain period of time and then you just re-perfused um…"* Donation MD-05: 261
No differences in ethicality compared with the DPP protocol	***"****I don't think there's any difference whatsoever if you've got the same definition of death. Whether you reanimate the heart inside the body or on the back table, I think it's immaterial."* Non-heart Transplant Surgeon-02: 184-185
Superior heart quality and recipient outcomes	*"This improves the viability of the heart instead of you know, it's going to be 10 minutes or so while we're hooking it up to another machine. It certainly makes sense."* ICU RN-09: 89 *"My general thoughts are it seems like it would be better for the heart because there would be less ischemic time so I would be personally very comfortable with it…"*

	Donation MD-03: 35
Less 'rushed' retrieval process	*"...And so, for some cases, if you know that the team can't come out with time constrained, whereas if we could just do the withdraw and then have the patient in the OR, and we're perfusing the organs, then if the team, you know, is an hour, so delayed, that's not going to be a problem…"* ICU RN-09: 111 *"...Because you're re-perfusing everything so that you don't have this big rush, you don't have to, you know, get the organs out right to cool them down to put to limit the warm ischemia time and everything else because you're reperfusing not only the heart but the lungs, the liver, the kidneys, the pancreas, everything, everything…"* ODC-02: 323
Ability to assess the heart in-situ	*"...It's a better way of assessing the quality of the heart after you know, it's been um stopped for five minutes after you know death has been declared for five minutes or more, by the time it's restarted of course…"* Transplant Cardiologist-02: 35 *"...Because they're taking what we were just talking about testing that heart, and they're going to test it in the best way possible, which is in a human body. They're going to put that heart back into circulation um in a body, you know, it'll still be on a circuit for a little time just to give the heart some time to recover. And then they can come off their machine and see if the heart will keep beating, keep, you know, supplying flow..".* Perfusionist-03: 128
Reduced ischemic time	*"[NRP] would be faster than actually taking the heart out and putting it on the machine for re-perfusion. So, the warm ischemic time is actually shorter in NRP."* Cardiac Surgeon-02: 92 *"...one of the thoughts is that the NRP may minimize or even reverse some of the adverse impact of [DCC] or ischemic injury so that's the rationale behind its introduction…"* Non-heart Transplant Surgeon-02: 261
Favourable effects on other transplantable organs	"*We have great hopes it could significantly extend our ischemia time and increase a number of [DCC] grafts which we use. Currently very restrictive. We're very precise for half hour for the liver. And with the NRP I think we can extend to two hours and probably we could have many more organs. So I think the benefits for the recipients is huge.*" Non-heart Transplant Surgeon-05: 106-107
Favourable cost/ less resource requirements	*"...But you know it is true, if you exclude the box, then you can do NRP with existing resources. You know, the perfusion teams exist. The clamps they are going to use to either ligate or clamp the carotids exist. It is just a matter of using them…"* Donation MD-01: 40 *"On the flip side, normothermic regional perfusion, there's no real major an additional cost we have, you know, we use heart-lung machines every day, I think they only cost about $800 for a circuit, so not too expensive compared to a ex-vivo…"* Cardiac Surgeon-04: 171

Appendix 5. Participants' perceptions of the concerns of *OTHER* healthcare providers, donor families, and the Canadian public.

Themes	Illustrative Quotes		
	Other HCPs	**Donor families**	**General public**
Organ Donation in General			
Non-support of organ donation/ DCC in general	*"I think maybe certain physicians that already don't agree with [DCC] might have an issue with that… The physicians that I've encountered that have some kind of moral objection to [DCC], some of the comments I've heard is 'I don't like that we're just, you know, sitting around waiting for someone to die and then like, swoop in and take their organs'… So I think whether the heart is included or not, they're still going to be uncomfortable." (ODC-03: 137)*		*I can't think of any particular groups other than the people who are opposed to [DCC] in general. (ICU MD-02: 110-111)*
Discomfort with antemortem interventions in general	*"Some of our other physicians that have some issues with… pre-mortem procedures on a patient that's not going to help that patient, like it's all for the purposes of donation and transplantation but it actually has no benefit to that patient, and we have some physicians that are opposing that portion of [DCC]." (ODC-03: 137)*		
Direct Procurement & Perfusion (DPP)			
Confusion/ misinformation about the procedure	*"There's no question that it is going to create some concern and potentially confusion as with families, and also potentially with ICU staff and OR staff." (Non-heart Transplant Surgeon-02: 89)*		*"… The public would have a hard time dissecting it and understanding it and taking it, it probably just take it at face value [that] we are killing a patient to… obtain a heart, which isn't true." (Perfusionists\03: 91-92)*

Non-support among few/ "outliers"	*And I still don't understand why but like I say, there will always be outliers (Cardiac Surgeon-04: 87)*		*"I think you can always anticipate anytime something new happens, there will be some small, small group that will be perhaps… be vocal in some way." (Donation MD-08: 66)*
Confusion about reanimation of a 'dead' heart	*"The fact that you're taking a heart and restarting it and, you know, the whole idea of the circulatory death and… how can they be if you can restart and how can you say… I'm sure there will be some people who will be uncomfortable with it." (Donation MD-08: 46)*	*"I think it they are going to be some families… that are very concerned, because of course, they've been told in this situation with a [DCC] that it's donation after cardiac death. And there are clearly going to be some people confused by the idea that the heart is beating again. And yet they were told that that was the definition of death in their case." (Non-heart Transplant Surgeon-02: 89)*	*"I can imagine that people might say, well, if you can restart the heart inside the body, why couldn't you restart it in the body?" (ICU MD-07: 115)*
Objections based on religious or cultural reasons	*"I think it is more the medical people. Maybe the medical people who that who have some religious or other whatever ethical background that they have some sort of concern. Just in general, it is medical people, not necessarily the public." (Cardiac Surgeon-02: 51)*		*"Quebec, it's so multicultural… it's going to depend if you're going to have people saying 'yes' or if you're going to people saying 'no', if it's an immigrant family, depends what their what their backgrounds are going to be…" (Donation MD-08: 131)*
Conservative political leanings	*"I think again, it's… cultural, um religious and… value system… again, broadly based on a domains of, you know, small L liberal versus small C conservative um values." (Donation MD-05: 177)*		
Specific professional roles with concern	▪ ICU physicians/ nurses ▪ Donation physicians ▪ OR staff ▪ Healthcare aides		
General discomfort - "Repugnance"			*"I guess if a culture or religion has a belief that, you know, the beating of the heart is somehow intrinsic to life, um then sort of having the heart stopped and restarted might feel a little icky to them. I guess that's the best way I can put it is icky. (ICU MD-08: 82-83)*

Normothermic Regional Perfusion (NRP)			
Confusion/ misinformation about the procedure	*"I think with their concern, and this is just maybe my opinion, but with their concern, it's probably due to maybe a lack of um education or understanding surrounding the events that have already taken place, i.e. the patient is already dead." (Perfusionists-01: 116)*	*"I've had the family member go, 'you just killed them'. And I think that the clamping of the vessels, the explanation to it at first is gonna be like, you're just trying to make sure there was you're getting those organs, so there's no chance they're like "now you can't reanimate them now you can't bring them back." I have a concern or fear that there is going to be people that perceive it that way." (ODC-07: 179)*	*"I think you would have more um issues with the public having difficulty with it, difficulty with understanding what's going on and yeah. I think there there would be more ethical concerns with it." (ICU RN-01: 101)*
Objections based on religious or cultural reasons			*I think that there are some, you know, religious considerations for people that where the heart has special significance to them, that there will be difficulties. (ODC-05: 234-235)* *"And I can only relate like the Indian community, because I'm personally Indian… Like a lot of people think that your body's not going to be available for the funeral. So that's also a common misconception. So, if you're an organ donor, we can't have a funeral for you. And that's not the case at all." (Perfusionist-05: 314-315)*
Specific professional roles with concern	▪ ICU physicians/ nurses ▪ "Donation community" ▪ Operating Room staff ▪ Anaesthesiologists ▪ Healthcare aides		
General discomfort – "Frankenstein-ish"	*"I had a visceral reaction to the uh to sort of the modified ECMO and restarting the heart in the in the person's body. Uh even to other*	*"You know, they've just said goodbye to their loved one. And now their loved one is being used to um used - well, used as an incubator." (ICU RN\ICURN-11-SH: 127)*	*"I think some people would feel the same. Or think along the same lines as I do with this kind of being a bit, science fiction*

	people is spoken is a little Frankensteinish a little bit." (ODC-02: 239)	*"I do think it may be a little freaky for families to hear about." (Donation MD-07: 103)*	*[laughs]. Body snatcher type uh, type view. But not everybody." (ICU RN-11: 119) ethically I don't think there is really a huge difference between the two protocols. But optically, I can imagine that the second one would raise that repugnance meter a little bit more in people. (Recode\TxMD-04-AG RECODE: 76*
Others' concerns about reanimation of the heart within the donor's body	*"… It will be very hard for some health professionals, nursing etc. to know that we're reanimating the body." (ODC-05: 167)*	*"I just think that the families would have more of an issue with it being restarted inside the body than having it removed." (ICU RN-08: 167)*	*"So I don't know, but I anticipate, I guess I'm presuming that that uh they will bring up something with regards to restarting the heart in the body restarting circulation" (Non-heart Transplant Surgeon-04: 199)*
Others' discomfort with ligation of blood vessels to the brain	*"So I got a feeling the idea of clamping blood vessels to keep other things… yeah, there's going to be some people that are you gonna have some type of ethical argument to present." (ODC-07 : 219)*	*"I think with [NRP], there's a little bit more explaining to do. You open them up, you cut off blood supply to the brain and the legs, and then you restart blood supply. And then you look at everything and then you take everything out, you know, I think… I don't know if it's too much… if it might be too much for families to process." (ICU MD-08: 199)*	*"So that's what I'm not, I'm not totally sure. I don't think the public love the I would love the idea of uh you know tying off blood vessels to begin with." (Non-heart Transplant Physician-02: 339)*
Others' concerns about possible residual blood flow to the brain		*"It's just confusion of when is death actually going to happen. How is it that you're going to restart everything and then still say that they're dead?" (Perfusionist-05: 203)*	*"I think that people may have some issues with that like reperfusing the heart so it beats again even though you're tying off the brain… I think that the questions around how are you sure we're not perfusing the brain?" (ODC-09 : 18-19)*
Others' concerns about possible violation of the DDR/ concern of patient being brought "back to life"	*"So… the donation community would have a huge problem with it, you are violating the dead donor rule. Unless you reconcile a change or update your determination of death criteria." (Donation MD-04: 93)*	*"Maybe the second one? Um they might see as you know, if the heart can be revived inside of the body that they might see that as um, as, like a revival of the person. That may not necessarily be accurate, but I think that the perception is that that might be, I guess a continuation of life for that person." (ICU RN-13: 146-147)*	*"… I'm sure they're going to have concerns like, are they really dead?" (ODC-02: 335)*

Potential of causing 'overwhelm' among donor families		*"Would the families be receiving that type of information? I'm not really sure because if they were to receive how the organs are actually like explanted right now, like would they want to donate it's pretty horrific thing to, potentially, like picture your loved one going through?" (Perfusionist-01: 90)*	
Others' concerns about potential prolongation of the donation process		*"The point that families do change their minds is when it takes a long time for donation. So if you start telling them it's going to be like a day or 2 before the OR then some families say we've had enough and we're going to stop." (Donation MD-06:235)*	
Others' concerns about pain/ awareness		*"I think it also is potential for people to wonder about suffering. Right? There's always the discussions about does the brain die right away? You know, there's lots of those different studies… Do these people now need full anesthesia? I don't know. Right? What happens if there is an error in the OR and blood goes to the brain? What do you do?" (ODC-05: 171)*	*"And I'm sure they're going to concern like, are they really dead? I know and because the modified echoes - what about the brain, you know, that you're going to they're going to be aware." (ODC-02: 335)*
Others' perception of invasiveness of the procedure	*"… With the health professional and you know, even thinking about it, having this live discussion, I must say that it's more intrusive. Let's put it that way. It's more disturbing." (Non-heart Transplant Physician-03: 107)* *"I feel like they might feel like this is more uncomfortable, but I think it's it would probably be related again to that invasiveness, that happens." (ICU MD-08: 211)*	*"I don't know if it's too much for if it might be too much for families to process… They've been through this horrific, horrific process in the ICU, we're deciding that they're, you know, not going to survive and, and now they're gonna have to go through this really kind of invasive thing at the end of their life or after they've died." (ICU MD-08: 199)*	*"I think it would be very easy… for this to get very bad press and to become very problematic because it could used - it could be seen as very invasive." (ICU RN-04: 103)*

Others' discomfort caused by imagery of the procedure	*"It's a little harder pill to swallow, maybe just from an emotional standpoint to see a heart beating in a chest in a patient that's connected to a circuit, it's harder to establish that they are truly dead. We know they're dead, but it's hard to wrap your mind around it." (Perfusionist-03: 128)*	*"Like would the families be receiving that type of information?... It's pretty horrific thing to, potentially, picture your loved one going through." (Perfusionist-01: 90)*	*"If you are pro [donation], they don't necessarily want to know or aren't interested in what are the nitty gritty day-to-day pieces of it. I think if you told them what happened, most people who aren't in healthcare would be horrified." (ICU RN-04: 103)*

Appendix 6. Existing facilitators & proposed strategies for implementing cardiac DCC protocols as suggested by participants.

Themes	Illustrative Quotes
Existing Facilitators	
Existing stakeholder acceptance of organ donation as a facilitator	
Public trust in medical professionals as a facilitator	*"I think that part of the reason the public is so trusting of us, is because doctors are so conservative and so careful. And so, when I started this work, I thought the doctors were being ridiculous because they're the ones slowing this process down and public's ready. But now I've come around a little bit more and realize that it's important that the doctors are conservative and careful, because that's where the trust comes from."* ICU MD-02: 147
Public awareness and acceptance of organ donation as a facilitator	*"… We've seen the general culture of the public here with regards to transplantation… they are a lot more accepting a lot more pro-transplant, a lot more about organ donation and that for several reasons, and, you know, unfortunately, when one of those reasons was the Humboldt Broncos tragedy, and so everybody for that year was talking, everybody was registering everybody was… it definitely raised a lot of awareness as terrible as it was."* Non-heart Transplant Surgeon-04: 106-107
Success of analogous programs as facilitators	
Success with other ex-vivo programs as a facilitator	*"I do not see any difference with this...between this process and the fact of let's say harvesting lungs and putting them in an ex vivo machine or taking...taking the liver and the kidneys and doing the exact same thing with perfusion and keeping normothermia as opposed to put it on ice and rushing to the OR to transplant the organ to, to the receiver."* ICU MD\ICUMD-10-FL : 55
Success of cardiac DCC in other countries	*"And there is good data and it's done in a lot of patients in Spain in Britain. We won't be losing contact because we are hesitant while other centers in Europe are doing this routinely."* Other Tx Sx\TxOther-05-MS : 107
Medical Assistance in Dying (MAiD) as a facilitator	
Rise in MAiD acceptability as a facilitator	*"I think it is a bit like when MAiD became legal. I think some people transitioned to it in their minds very quickly and easily and I think other people struggled and I think there is a third group of people who are conscientious objectors who do not think this should be allowed and they just opt out and I think this will be the same. Like you will have people who are early adopters, you will have people who are a little slower who take more time to think about it and you will have people who will just say no and that's that."* ICU RN-04: 121

Opportunity for first-person consent in MAiD as a facilitator	*"… If stakeholders consider that we should implement cardiac [DCC] program, but we are struggling whether we should use DPP and/or NRP because of the fear of some physicians' reaction or the general public reaction, then… let's do the NRP approach in the context of MAiD just make sure crystal clear that the things that might be very tricky for some people… it has been addressed with the single most important person in the process...who is the donor essentially."* ICU MD-10: 166-167
Proposed Strategies	
Garnering Support from Stakeholders	
Engaging & educating healthcare providers	• Education as a means to increase HCP acceptability of DCC Heart • Education/ training around how to communicate with donor families about DCC Heart • Practical education around antemortem care, intra-operative procedures, etc. • Educational initiatives should be led by organ donation organizations • Learning from established cardiac DCC programs in other countries **See Table Provider Education for illustrative quotes.**
Communicating with donor families	• Broad strategies relevant to organ donation in general • Tailor the level of details/ information to each donor family preference • Establish appropriate & consistent language to describe cardiac DCC protocols • Normalize cardiac DCC protocols • Present broad data/ statistical facts **See Table Donor Family Communication for illustrative quotes.**
Proactive outreach to the general public	• Stakeholder engagement and transparency • Proactive public outreach/ education/ increasing public awareness **See Table Public Outreach for specific recommendations & illustrative quotes.**
Support from leading organ donation bodies	*"I think [CBS] definitely has a role to play because I think if they put out a statement saying that [DCC] heart is acceptable method of donation, would go a long way… It's basically to give the okay. … If the national leader in organ donation, giving the statement, I think the public, medical professions would be more at ease of letting individual programs deciding when and how they do it… without their blessing, I think people would be reluctant to go ahead."* Cardiac Surgeon-02: 269
Gradual/ staged introduction of protocols as a strategy	

Starting with Abdominal Regional Perfusion	*"… if we're going to be using such an approach, probably you would want to get some experience first with abdominal regional perfusion, and then potentially expand from there."* Non-heart Transplant Surgeon-02: 136-137
Starting with Cardiac Direct Procurement & Perfusion	*"… but we, you know, we have to move forward and using the ex-vivo approach is probably going to be the pragmatic way to go. And so, we'll get some experience with this and it's not a bad thing to be able to assess these hearts ex-vivo and how they perform and the beating heart mode, we just don't know that that's gonna be equivalent to an NRP mode."* Transplant Cardiologist-06: 27 *"I perceive approach number 1 [DPP] as being the first small step. And later on, you know, once people warm up to approach number 1, one could look into approach number 2, but I don't honestly think we can jump into approach number 2 from the get go here."* Non-heart Transplant Surgeon-04: 215 *"… I think the direct procurement could be taken up very quickly without much fuss. Um, I think the other option, there will be a lot of, a lot of discussion and a lot of debate and a lot of uh, a lot of… resistance and not all of our sites are on board with even [DCCs] yet. So, it's adding that component to it might just throw them over the edge."* ICU RN-11: 162-163
Starting with a few select centers	*"I think that we can become good at organ donation uh in these new forms and develop some mastery protocols and make it uh make it like uh part of our routine practice and iron out exactly what those routine practices are in highly specialized centres, um then we can roll it out. So, I think it should definitely be um only because of uh, I think that if you roll it everywhere, you are going to um…risk of having mistakes or problems is far higher is far higher."* ICU MD-01: 141 *"… I'm not suggesting that like every transplant center in the country start this I think, realistically, there's probably only three or four that would be ready to start this. Because you don't want to start this in 10 centers but I think there would be value in doing it in three or four rather than just one."* ICU MD-02: 215 *"it would need to be universally...protocols would need to be universally developed and I think if only one or two centres can do it, and help the others come up to speed that might be acceptable."* Donation MD-10-: 243-244
Starting under the umbrella of a research program	*"I think it would make sense for initial programs to be part of a research collaborative that is pan-Canadian that had ethics approval at 1 to 2 centres with shared approval, just like any other multisite study, I think that would make good sense because then you can say: look we have gone through the ethics and the ethics committees would push us to make sure that all of these questions around recipient consent would be part of it. Then we would also have a prospective*

	manner of collecting relevant data for future reporting as well as quality assurance. I think that is something that should be included in any rollout, and I think finding a motivated surgeon is also going to be a key aspect." Donation MD-01: 51
Option to opt-out as a strategy	
Opt-out for Healthcare Providers	*"… Irrespective of what the policy is, locally, provincially, nationally… we may run into situations where healthcare providers, like nurses, anesthesiologists, surgeons, may feel like ethically and morally they cannot participate in this… I think we just need to be aware of that… and ensure that there is an adequate team that's available that's willing to participate in these types of procedures."* Transplant Cardiologist-02: 94-99 *"… I really I imagine that there's going to be a pocket of physicians, yes, who are not going to be comfortable with that… So… we'd have to figure out a way like if someone is a treating physician is not comfortable with that, then we have to get somebody else in who is. Because I don't think that the treating physician should then say, well, this can't move forward because I'm not comfortable. If the family wants to do this… we have to find a way to do it."* ODC-02: 402-403
Opt-out for donor families: The "Second Approach"	*"I think I think we'd have to do our first approach like for [DCC]. And I think during the evaluation process, if we would see that the heart could be considered within maybe to do a secondary approach, saying… it's a very uncommon circumstance that we're in that… it's possible that we might be able to take the heart even though our hearts can stop your loved one has died. And I think it wouldn't be an approach to everybody."* ODC-08: 122-123 *"Maybe for our first couple of ones, kind of like when we first did our first face transplant here in Quebec, is that we did a secondary approach to the family… So, kind of testing out the waters, especially for the first couple of ones."* ODC-08: 111
Opt-out for transplant recipients	*"… Until it becomes um approved and not needed to be in a research scenario. And I think that patients should have the choice to opt in or opt out or having a consent process… around accepting this type of donor, but once it becomes accepted as uh treatment as a donor option that is equivalent to the neurologic death, I don't um - I would have a lot of um concerns, leaving that decision to the recipient."* Transplant Cardiologist-05: 74-75

Appendix 7. Participants' perceptions about research priorities related to cardiac DCC.

Themes	Illustrative Quote
Research on protocol clinical efficacy & outcomes for transplant recipients	
Outcome data in countries where cardiac DCC is practiced	*"It would be cool to see what the evidence shows in these countries that do this. Like what are the outcomes like? How have the families recovered from this?"* ICU RN-01:127
Impact of warm ischemic time on heart quality	*"... It would be interesting to know if, you know, are we, there more potential for ischemia and fraction in the first method [DPP] versus the second method [NRP]."* ICU RN-02: 243
Outcomes of NRP relative to DPP	*"Research just exactly how effective either one of those methods is. What, you know, you do one method versus the other method when you're transplanting [the heart] into another person, what are the um what's the life expectancy with either one of those? Is one better than the other?"* ODC-09: 171
Impact of cardiac DCC on other transplantable organs	*"I would need to see more data to be honest. Like, I need to know what the impact would be, you know, what does it do to the warm/cold ischemia times? What does it do to DGF rates? What does it do to the rates of primary non-function? I actually don't know. But if it substantially increased our primary non-function rate, I think that that would be a big concern and problematic from our perspective"* Non-heart Transplant Physician-05: 172 *"Ideally, you should continue to collect that very same information and about all of the organs because, again, perfusing, the, the you know, keeping the heart perfused is going to keep the kidneys or livers etc perfused. So, will those recipients do better as well? And, you know, will we have the ability to, you know, instead of the patient only being able to donate two or three organs, now, we can get from five or six because we're able to perfuse them better."* ICU RN-09: 17
NRP impact on non-heart organ quality	*"Yeah, to me, the NRP makes more sense. Not necessarily for the heart, but for the other organs. And that too is another study that I think is really important. And there's some people in [my hospital] working on that just to see whether there's a an advantage to the abdominal organs uh from doing NRP..."* ICU MD-02: 106-107
Research on impact on the organ donation system	
Impact of cardiac DCC implementation (mainly NRP) on donation consent rates	*"...I don't think we need as much research on the on the actual biology as we do on social attitudes... the public. And I mean, I think we do need to understand it's, it's my number one concern is would this have a negative impact on uh on organ donation? And so I'd like to understand that in the Canadian public."* Non-heart Transplant Physician-02: 435

Impact of cardiac DCC protocols on supply of non-heart organs	*"Um there's obviously some signals in the literature that suggest that there may be a benefit to the other organs and that's something that needs to be considered globally as well"* ICU MD-06: 61
Impact of cardiac DCC on the heart transplant waitlist	*"Um but um, you know, the amount of patients that could have benefited from that, like showing them what the outcome could have been if we had done this for years."* ICU RN-08: 183 *"…you know, how many patients are waiting, the deaths that are happening and how this affects the numbers. So, I think it needs to be well you know it needs to be well documented how this is affecting our volume of activity."* Transplant Cardiologist-04: 284-285
Possibility that there is no need for more heart donors	*"So I would argue, is this whole exercise worth it because do we even need these hearts?"* TxOther-01-BL: 297 *"I don't know if there's a need for it. As there is, I mean, our heart lists, well, yes, there's still patients that will die on the waitlist, um we don't have like huge lists like we do for kidneys and livers and so like, are we able to get access to enough hearts for transplantation from brain dead donors?"* ODC-03: 272-273
Research on acceptability of cardiac DCC protocols	
Cardiac DCC acceptability by the public	*"…I don't think we need as much research on the on the actual biology as we do on social attitudes… the public. And I mean, I think we do need to understand it's, it's my number one concern is would this have a negative impact on uh on organ donation?"* Non-heart Transplant Physician-02: 434-435
Acceptability among waitlisted cardiac transplant patients	*"…the recipients is the most important as it should be. So I mean, that would probably be a good group to look at is the mean recipient programs and implanting programs and how they feel about this because they're going to be offered these hearts um and what that's going to mean for them or and depending on which way we do it?"* ODC-03: 341
Research on readiness of the healthcare system to implement cardiac DCC protocols	
Feasibility/logistics	*"What are the resources that are going to be required for that? Make sure those resources do not conflict with existing you know, live patient care processes"* ICU MD-09: 116 *"…Another priority maybe to look at what are … the small center who may be hosting the donor, what do they think about that? Um so, for example, the NRP if it requires uh basically a cardiac cardiac bypass machine to be able to do it, then many center may not have this…"*

	Transplant Cardiologist-05: 187
Cost-effectiveness studies	*"…Um, so I guess the question, you know, to me would be, the questions that would need to be answered, is, is this new protocols more expensive or less expensive?..."* Donation MD-07: 158 *"…if we implement these protocols, you know, what are the benefits to the Canadian taxpayer from such a proposal, which I imagine would be quite significant given the potential increase in heart transplantation that could occur, so those would be interesting things to look up."* Non-heart Transplant Physician-04: 128
Research on NRP & its implications for death definition/ determination	
Potential for cerebral perfusion	*"I think you really, you really need to prove above-board that there is no perfusion to the brain."* Donation MD-10: 172
Acceptability of low-flow cerebral perfusion among public and healthcare community	*"… I think that many people, you know, even if consciousness is very close to zero, um, but uh, but I think I would be most confident if I can reassure myself and my colleagues um that the risk is zero."* ICU MD-01: 107
Ascertaining no consciousness or pain in the donor during restoration of thoraco-abdominal blood flow	*"Um I think it raises the standard for what you have to demonstrate that there's no neurologic function residual, right?"* Transplant Cardiologist-06: 62-63 *"…It would be nice to know… to prove that restoring circulation, even to the brain provides no meaningful um return a function or return of sensation."* Transplant Cardiologist-06: 87

Chapter 5. Canadians' perceptions about heart donation after death by circulatory criteria: A mixed methods study

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Canadians' perceptions about heart donation after death by circulatory criteria: A mixed methods study

Short Title: Public views on heart donation after DCC

Kimia Honarmand MD, MSc[1], Ian Ball MD, MSc[2,3], Maureen O. Meade MD, MSc[4,5], Aimee J. Sarti MD[6,7], Sydni Paleczny BSc, MSc[8], Danielle LeBlanc BSc, MSc[2], John Basmaji MD[2], Emilie P Belley-Cote MD, PhD[4,5,9], Michaël Chassé MD, PhD[10], Fred D'Aragon MD, PhD[11,12], Gordon Guyatt MD, MSc[5], Bram Rochwerg MD, MSc[4,5], Sam Shemie MD[13,14], Robert Sibbald MSc[15], Marat Slessarev MD, PhD[2,16], Mathew J. Weiss MD[17,18], Jeanna Parsons Leigh, PhD[19]

Affiliations

19 Division of Critical Care, Department of Medicine, Mackenzie Health, Vaughan, ON, Canada
20 Department of Medicine, Western University, London, ON, Canada
21 Department of Epidemiology and Biostatistics, Western University, London, ON, Canada
22 Department of Medicine, McMaster University, Hamilton, ON, Canada
23 Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada
24 University of Ottawa, Ottawa, ON, Canada
25 The Ottawa Hospital, Ottawa, ON, Canada
26 Department of Critical Care, London Health Sciences Centre, London, ON, Canada
27 Population Health Research Institute, McMaster University, Hamilton, ON, Canada
28 Université de Montréal, Montreal, QC, Canada
29 Department of Anesthesiology, Universite de Sherbrooke Faculte de Medecine et des Sciences de la Sante, Sherbrooke, QC, Canada
30 Centre de Recherche du CHUS, Sherbrooke, QC, Canada
31 McGill University, Montreal, QC, Canada
32 Canadian Blood Services, Ottawa, ON, Canada
33 Department of Family Medicine, Western University, London, ON, Canada
34 Ontario Health, Trillium Gift of Life Network, Toronto, ON, Canada
35 Transplant Québec, Montréal, QC, Canada
36 Division of Critical Care, Department of Pediatrics, Centre Mère-Enfant Soleil du CHU de Québec, Québec, Canada
37 School of Health Administration, Faculty of Health, Dalhousie University, Halifax, NS, Canada

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Corresponding Author:
Kimia Honarmand, MD, MSc
kimia.honarmand@mackenziehealth.ca

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Implication Statement

Canadians support implementation of cardiac donation after death determination by circulatory criteria, but have several concerns, primarily related to the restoration of cardiac activity in normothermic regional perfusion. This study elucidates the hesitations and concerns of Canadians about cardiac DCC and identifies stakeholder-informed strategies to increase public support.

Abstract

Background

Cardiac donation after death determination by circulatory criteria (DCC) can be performed using either direct procurement and perfusion (DPP) or normothermic regional perfusion (NRP). These procedures have yet to be performed in Canada but if implemented, have the potential to reduce the cardiac transplant waitlist. We aimed to evaluate the perspectives of Canadians about cardiac DCC.

Methods

We performed a convergent design mixed methods study involving 21 focus groups and surveys of 109 adults in Canada on the topic of cardiac DCC.

Results

We found participants were broadly supportive of both cardiac DCC protocols. Principle concerns about DPP included relatively impaired heart quality, while concerns about NRP included the perception that the procedure may be invasive and may not be acceptable to other Canadians, including donor families. Participants who self-identified as second-generation immigrants were concerned about potential lack of support for cardiac DCC, especially NRP, by other Canadians. Participants suggested strategies to increase support for organ donation and cardiac DCC specifically, including mass media campaigns, educational initiatives, encouraging the public to discuss end-of-life wishes with family members, and enlisting primary care providers and community leaders to advance public knowledge and support.

Conclusions

In this mixed methods study of people living in Canada, we found broad support for cardiac DCC, with concerns primarily related to heart quality for DPP and perceived invasiveness for

NRP. Participants identified mass media campaigns, educational material, and engagement of primary care providers and community leaders as strategies to garner support for cardiac DCC.

Introduction

Cardiac donation in Canada is currently limited to the minority of patients who are determined to be dead in an intensive care unit according to neurological criteria for death. A growing body of evidence shows that hearts retrieved after death determination by circulatory criteria (DCC) have acceptable outcomes.[1-3] Cardiac DCC has not yet been performed in Canada; it stands to reason that if implemented, cardiac DCC could reduce the cardiac transplant waitlist.

Organ donation after DCC can occur only after a family and healthcare team decide to withdraw life-sustaining measures for a critically ill patient and subsequently, after obtaining consent for the patient to be considered for organ donation. Following a planned withdrawal of life-sustaining measures and eventual circulatory arrest, two physicians declare death after a 5-minute 'hands off' period.[4]

There are two possible surgical approaches for cardiac DCC: Direct Procurement and Perfusion (DPP) or Normothermic Regional Perfusion (NRP; Figure 1). In DPP, after death is determined by circulatory criteria, the sternum is opened, the heart is retrieved and placed into a perfusion device during transport to the location of the recipient.[4] In NRP, after death determination by circulatory criteria, the arteries that supply the cerebral vasculature are surgically interrupted and, subsequently, thoraco-abdominal circulation is mechanically restored *within the donor's body* by means of a mechanical device (i.e., cardiac bypass machine) prior to heart retrieval.[4]

Cardiac DCC is of great interest among the Canadian donation and transplantation communities,

but there are concerns about the acceptability of these procedures to the public.[5] In a national web-based survey of 1,001 Canadians, we previously found that 84% accepted DPP while 70 percent accepted NRP; leaving an important minority of respondents with reservations regarding the protocols.[6] Regardless of clinical potential, any successful donation program must proceed in a manner that is congruent with Canadian values. To address this need, we aimed to better elucidate the perspectives of the Canadian public about cardiac donation after DCC.

Methods

Study Design

We have previously published details of the study methodology.[7] Briefly, we performed a convergent design mixed-methods study consisting of focus groups with members of the Canadian public and surveys of the same individuals before and after the focus groups. In convergent mixed methods design, qualitative and quantitative data are collected concurrently and independently, first analyzed separately, and subsequently compared and combined to achieve a more complete understanding of a phenomenon.[8] **Appendix 1** presents the Consolidated criteria for reporting qualitative research (COREQ) checklist. Western University's Research Ethics Board approved this study (#113807). All participants provided informed consent before participation.

Recruitment

A professional recruitment company (Quality Response Incorporated, Toronto, Canada) purposively sampled target respondents from their database of public panellists to ensure representation of genders, age group, province, education level, ethnicity, and religious affiliation across Canada. We included individuals who were 18 years of age or older, currently living in

Canada, spoke English or French, and had at least a grade 12 education. We excluded those who considered themselves to be experts in organ donation/ transplantation, had medical training, or if they or any family member was employed by an organ donation organization. We did not record data on respondents who declined to participate in the study. Potential participants who were not comfortable discussing topics related to death and organ donation had the opportunity to decline to participate. We compensated participants $90 dollars. We planned to conduct up to 25 focus groups until we achieved thematic saturation.[9]

Educational Content

We contracted a professional media agency (Grumo Media, Vancouver, Canada) to assist us in developing a series of animated explainer videos, informed by a review of existing literature on cardiac DCC, to provide participants with basic information about cardiac transplantation, DCC, and cardiac donation after DCC (DPP and NRP). We presented the videos during focus groups. For example, to demonstrate NRP, an animation showed vessels being clamped to prevent circulation from reaching the brain, followed by restoration of the thoraco-abdominal circulation (**Appendix 2**).

Procedures

Pilot Testing: We conducted two pilot focus groups, each consisting of three to four members of the public in London, Canada to ensure that the educational video clips and focus group questions were clear and appropriate for a focus group format. We did not include the pilot focus groups in the final analysis.

Pre-focus group survey: Prior to the start of the focus group, we asked participants to complete an online survey (using REDCap®) consisting of demographic items, organ donation registration status, prior experiences with organ donation or transplantation, and self-rated knowledge about organ donation (**Appendix 3**).

Focus Groups: Focus groups took place over 60-minutes online using Cisco WEBEX for video conferencing facilitated by the Focus Group Discussion Guide (**Appendix 4**). One of two female interviewers (KH; critical care physician or a French-speaking research coordinator) with training in qualitative research and no pre-existing relationship with the participants moderated the discussions. An additional research associate (DL) was present during all focus groups. After presenting each video clip, the moderator responded to participants' questions and encouraged them to share their perspectives in an unstructured manner, followed by questions to help generate an in-depth discussion of the topics among participants. Two investigators (KH and DL) who later performed data analysis maintained a series of notes and memos about their interpretation of the data and potential personal biases as a form of reflexive journaling.

Post-focus group survey: After each focus group, participants completed an online survey to explore attitudes towards the topics that they discussed (**Appendix 5**).

Data Analysis

Focus Groups: We audio-recorded focus group discussions using Cisco WEBEX, transcribed verbatim, checked for accuracy, and uploaded to MAXQDA qualitative data management software. Two investigators (KH and DL) performed line-by-line coding of transcripts, formulated

of a series of codes, which they iteratively refined and merged into themes and subthemes through a series of meetings according to procedures that have been previously described.[8] As this qualitative data is not designed to support statistical inferences, we reported the findings in categories and themes rather than numerically.

Pre- and Post-surveys: We used descriptive statistics to summarize demographic characteristics and attitudes of participants. We did not use inferential statistics because responses to surveys are intended to elucidate the perceptions of participants after the focus groups and to solicit comments they wished to share confidentially. Therefore, findings of the post-surveys were not intended to draw conclusions regarding the attitudes of Canadians in general, a topic that has already been explored in our large-scale national survey.[6]

Data integration: We re-interpreted the qualitative data based on participants' province, organ donation registration status, and immigration status to identify patterns in perspectives by subgroup.

Results

Participants

We conducted 21 focus groups among 109 participants, whose characteristics are summarized in **Table 1**. Consistent with Canadians' geographical distribution, most participants resided in Ontario (n=35 [32%]) or Quebec (n=26 [24%]). Twenty-six participants (23%) were born outside of Canada, 31 (28%) were second-generation immigrants (one or both parents were born outside

of Canada; **Table 1**).

Figure 2 summarizes the themes and subthemes that emerged from the qualitative data. Most participants posed insightful clarification questions regarding the content they viewed in the explainer videos, suggesting that they were reflecting on the content they were learning before forming an opinion. Themes that emerged specifically from participants' questions and aspects that surprised participants are summarized in the appropriate sections below.

Questions About Organ Donation

After being presented with the general process of organ donation, participants expressed many questions, with themes generally focused on (1) organ donation registration processes (i.e., how to register to become an organ donor), (2) how organ donor eligibility is assessed/ how they are selected to optimize organ outcomes for recipients, and (3) the dying process in ICU and how death is determined.

Some participants were surprised and impressed with how the donation process occurs, particularly the short timelines to facilitate donation. Many participants were surprised, and some were disappointed at the low proportion of patients who die in hospital that are eligible for organ donation (presented as 1-2%). A few participants did not previously know that a patient must be deceased prior to organ retrieval, previously believing that organ donation could be the cause of death (**Appendix 6**).

Upon learning about family veto (the option for family members of a dying person to decline organ

donation irrespective of the patient's prior expressed wishes), many participants were surprised, and some disagreed with this, expressing that family veto disregards the patient's wishes and reduces the number of organs available for donation (**Appendix 6**).

Support for Cardiac DCC During Focus Groups

The most common question posed by participants was why this procedure is not currently performed in Canada, a sentiment raised in every focus group. Many were surprised at this, especially when informed that the protocols are performed in other countries, and were disappointed that Canada "is behind" in this regard.

Reasons for support for both DPP and NRP were similar and included: altruistic reasons (i.e., increased donor hearts will save more lives), respecting the donor/ family wishes to donate, trust in the healthcare professionals/ processes, pragmatic reasons (i.e., patient is already deceased, and post-death procedures are irrelevant; heart 'not wasted'), and a desire to see medical advancement (i.e., some were reassured that the protocols have already been implemented in other countries; **Appendix 7**).

Participants viewed DPP as similar to non-heart donation after DCC and many were "impressed" with the technology (i.e., the perfusion device). In support of NRP, a few participants commented on the additional time available to perform tests to ascertain heart graft quality before transplantation as well as the potential for cost savings. Some participants indicated conditional support for NRP, including (1) if more information were provided and (2) if outcomes were found to be superior to DPP (**Appendix 7**).

When asked specifically about their perspectives regarding the clamping of cerebral vessels that supply blood flow to the brain in NRP, participants were mostly comfortable with this, believing that it can reassure families of the absence of consciousness/ pain and that it helps to focus the blood flow to the organs that are candidates for transplantation.

Concerns About Cardiac DCC During Focus Groups

The most common concern about DPP was the quality of the donated heart (i.e., whether it would retain adequate function after transplantation). Participants expressed concern about the potential for organ loss and thus creating false hope for recipients, and some were concerned about the cost of the perfusion device (**Table 2; Figure 2**). Participants largely felt that DPP would be well-received by other Canadians, but some speculated about how the protocol would align with some cultural and religious beliefs (**Table 2; Figure 2**).

Participants were concerned about "too much being done to the donor's body" during NRP, which they deemed may be "too complicated" and "invasive". Several were concerned that the complexity of the protocol may put the donation "at risk" if the procedure "does not go well". For some participants, NRP evoked unsettling imagery, described as "creepy" or "Frankenstein-ish". Some felt that the idea of the donor's body being "used as a storage" contributed to their discomfort with the procedure. Some participants indicated that they would prefer not being told about the details of the procedure (**Table 2; Figure 2**). Many participants inquired about the rationale for clamping of the vessels that supply the brain and whether there is a possibility of brain activity despite this, with concerns about the donor "being brought back to life" or experiencing

consciousness or pain. Despite these expressed concerns, participants tended to accept the clamping of the vessels as an integral and "humane" part of the protocol (**Table 2; Figure 2**).

Some participants expressed concern for the reactions of donor families about this procedure, including the desire for the body to be returned to family in a timely manner. Participants believed that other members of the public may be concerned about NRP, including concerns of 'revival of the body' during the procedure, 'disturbing the dead', and non-support specifically from some religious or cultural groups (**Table 2; Figure 2**).

Perspectives Shared on the Post-Focus Group Surveys

On the post-focus group survey, 95% (n=104) of participants agreed or strongly agreed that donation after DCC in general is acceptable. The same 95% agreed or strongly agreed that cardiac donation after DCC using the DPP protocol is acceptable. The number decreased to 85% (n=93) for NRP acceptability (**Appendix 8**). In the post-focus group survey, one participant disagreed that DPP is acceptable, and four others indicated that they were "unsure but probably agree", with concerns expressed about quality of the donated heart. For NRP, three participants strongly disagreed, and three others were "unsure but probably disagreed" that NRP is acceptable. Among these participants, prominent concerns in open-ended questions included "too much is being done to the body" and concerns about "bringing the donor back to life".

Participant Characteristics and Views about Cardiac DCC

Participants from all provinces broadly supported DPP and NRP (**Figure 3**). Of the three participants that strongly disagreed that NRP is acceptable, and the 3 others that were 'unsure but

probably disagreed', all were either not registered or were unsure whether they were registered to be organ donors. The three participants who strongly disagreed with NRP questioned the ethics of the procedure and re-iterated that the procedure was "unsettling" in response to the survey's open-ended questions. All 6 agreed or strongly agreed that DPP is acceptable.

Figure 4 shows the acceptability of DPP and NRP by immigration status. Although there was broad support for DPP (**Figure 4A**) and NRP (**Figure 4B**), those who disagreed or strongly disagreed with DPP and NRP were all first-generation (i.e., born outside of Canada) or second-generation immigrants (i.e., born in Canada and at least one parent born outside Canada).

Based on the ***qualitative*** data, participants who were born in Canada and had at least one parent who was born outside of Canada (i.e., second-generation immigrants) expressed concern about non-support by *other* people for both DPP and NRP, referring to some religious or cultural groups whom they believed may object to cardiac DCC. As one participant indicated:

"Well, for my part, I'm Arab, and my parents, I know organ donation is difficult for them… I think that it might be more difficult for communities, it would be at the level of cultural and religious shocks. But I think that with discussions and the new generations, they will make sure that these two options there, they are not inhumane, and because they are there, they are scientifically proven to help. Then I don't really see why, after a good discussion, and show that we don't disrespect the remains, I don't see why we can't do it. So, I think it's a public information issue, that's really what's important… I would rather have someone from the community that speak for my community in a language they will understand, in a tongue they

will understand. Or either a doctor or health, who will tell the Arabs, OK, listen, here's where we're going. Then people do what they want… they're going to have the information."

- Second-generation immigrant

Proposed Strategies to Facilitate Cardiac Donation After DCC

When asked about what approaches they think would facilitate the implementation of cardiac donation after DCC in Canada, responses included (**Figure 2**):

(1) ***Approaches to increase the donor pool in general:*** (1) Opt-out system, (2) more options to register as an organ donor, (3) prohibit family-veto, (4) shorten the 5-minute hands off period during death determination.

(2) ***Stakeholder education methods:*** Mass media campaigns, education at the time of registration for donation, education provided by family practitioners, other healthcare providers, or community leaders, and education beginning with school-aged children.

(3) ***Stakeholder education topics:*** Educating the public about death criteria, encourage the public to discuss end-of-life wishes with family members, provide statistics and numbers to increase support for donation.

(4) ***General messaging proposal:*** Frame donation and cardiac donation after DCC as positive developments in the medical field and normalize the procedures.

(5) ***Compassionate communication with donor families***: Preparation of families for the discussion about cardiac donation after DCC, using clear and non-technical terminology in a compassionate way, and in some cases, avoid providing procedural details if not requested by some donor's families.

Discussion

In this mixed methods study, we confirmed strong support for cardiac donation after DCC among a diverse sample of the Canadian public. The most prominent theme was participants' surprise that cardiac DCC has not been implemented in Canada and concerns that Canada "is behind" other countries in implementing these advancements in cardiac donation.

Concerns about DPP were mostly related to the quality of the donated heart and perceived high cost of the perfusion device (although cost was not provided to participants). The imagery evoked by NRP caused hesitation around this protocol, with some finding it "unsettling" and "invasive". Some participants questioned whether the donor can still be considered deceased after the restoration of circulation in the thorax and abdomen, although some found this distinction (whether the donor is deceased or not) to be irrelevant to the overall goal of saving lives through organ donation. Some participants also felt that NRP would be less acceptable by *others*. Despite these expressed concerns, the majority still agreed or strongly agreed that NRP is acceptable when asked in the post-focus group survey.

We found no trends in level of support for either DPP or NRP protocols based on province of residence. Some participants who were second-generation immigrants expressed concerns about non-support by *others*. This may reflect their own anticipation of non-support by others, rather than reflecting the true perspectives of culturally diverse individuals. In addition, while some participants speculated that others might have religious objections, none expressed personally held objections based on religious grounds of their own. Indeed, the perspectives of individuals of

minority cultures and diverse religious affiliations are likely to be highly variable.[10-12]

These findings are consistent with the findings of a previous survey of Canadian public, with 84% finding DPP acceptable and 78% finding NRP acceptable.[6] The higher level of support in the current study among this smaller cohort of Canadians (95% for DPP and 85% for NRP on the post-focus group survey) suggests that the opportunity to learn about and discuss the procedures during focus groups may lead to increased acceptability.

In a parallel study of 75 healthcare providers across Canada, we found similarly high support for both cardiac DCC protocols, but much of healthcare providers' concerns related to their perception of non-support by other stakeholders, including the public.[13] The findings of this study suggest that those concerns are perhaps unfounded. These findings also suggest a need for a legal/ ethical framework to guide policy-making and multi-directional education to inform the public, but also to educate healthcare providers on public attitudes and perspectives.

Finally, participants in this study proposed various strategies to increase support for organ donation, including cardiac DCC. Interestingly, suggestions from the public were similar to those from donation/ transplantation experts in a parallel study[13] and can be considered in the implementation of cardiac DCC in Canada.

Historically, the Canadian organ donation and transplantation community has faced many challenges. We are now at a new frontier, with discomforts expressed around the eventual implementation of cardiac DCC protocols paralleling those faced during the implementation of

organ donation after death determination by neurological criteria in the late 1990s, followed by the implementation of organ donation after DCC in the early 2000s. While cardiac DCC may be viewed by some as a natural extension of existing organ donation practices, various stakeholders have raised concerns about various aspects of these protocols. In light of the momentum around cardiac DCC across many countries in an effort to augment cardiac transplant capabilities, Canada is likely to move forward with one or both cardiac DCC protocols in the near future. The impetus is on the donation and transplantation community to ensure that cardiac DCC implementation is done in a manner that is consistent with the perspectives and values of Canadians.

This study has several limitations. First, participants were informed of the topic prior to agreeing to participate. It is conceivable that those who were more supportive of organ donation were more likely to agree to participate, raising the possibility of selection bias. In addition, while we made efforts to present the procedures objectively, it is possible that participants felt pressure to express support the protocols due to any inadvertently transmitted bias in support of the cardiac DCC from the facilitators. Finally, some participants may have been influenced by the perspectives of other focus group participants. While this is an inherent risk of focus groups, nonetheless, focus group methodology is ideally suited to provide a deeper level of insight and understanding of complex phenomenon by encouraging debate and discussion on a topic not previously familiar to participants.[14] These limitations notwithstanding, this study is the most comprehensive evaluation of the perspectives of Canadians about cardiac donation after DCC and may pave the way towards its implementation in Canada.

Conclusions

We found that Canadians were highly supportive of both cardiac DCC protocols. This study provides rich data from a diverse group of Canadians about cardiac DCC and serves as one blueprint for implementation of cardiac DCC in a manner that is consistent with Canadians' values.

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Tables

Table 1. Characteristics of participants.

Characteristic	**N (%)**
Gender	
Female	54 (49.5%)
Male	55 (50.5%)
Age Groups	
18-24	13 (11.9%)
25-34	24 (22.0%)
35-44	27 (24.8%)
45-54	22 (20.2%)
55-64	20 (18.4%)
65+	3 (2.8%)
Highest level of education	
Completed high school	10
Some college/ university	21
Completed college/ university	66
Post-graduate education	12
City Type	
Urban	53
Suburban	56
Ethnicity	
Caucasian	33
African/ Black	7
Asian/ Chinese	5
South Asian	11
Southeast Asian	1
Latin American	2
West Indian	5
Canadian French/ American/ Canadian	23
Somalian	2
European	3
First Nations	5
West Asian/ Middle Eastern	5
Tibetan	1
Mixed Ethnicity	6
Religious affiliation	
Christian	57
Muslim	13
Jewish	2
Sikh	5
Hindu	1
Buddhist	7
Traditional (aboriginal) spirituality	4

Pagan/ Wiccan	1
Non-denominational	1
Mix	1
No religious affiliation	15
Prefer not to answer	2
Immigration Status	
Participant & parents born in Canada	49
Participant born in Canada, at least one parent born outside Canada	31
Participant born outside of Canada	
No Answer	27
	2
Registration as an organ donor	
Registered	39
Not registered	41
Unsure whether registered	28
No Answer	1
Personal experience with organ donation (family/ relative)	
Yes	21
No	87
Unclear	1
Donation knowledge	
No Knowledge	10
Limited Knowledge	60
Some Knowledge	35
Very Knowledgeable	3
No Response	1

Table 2. Concerns & Hesitations About Cardiac DCC

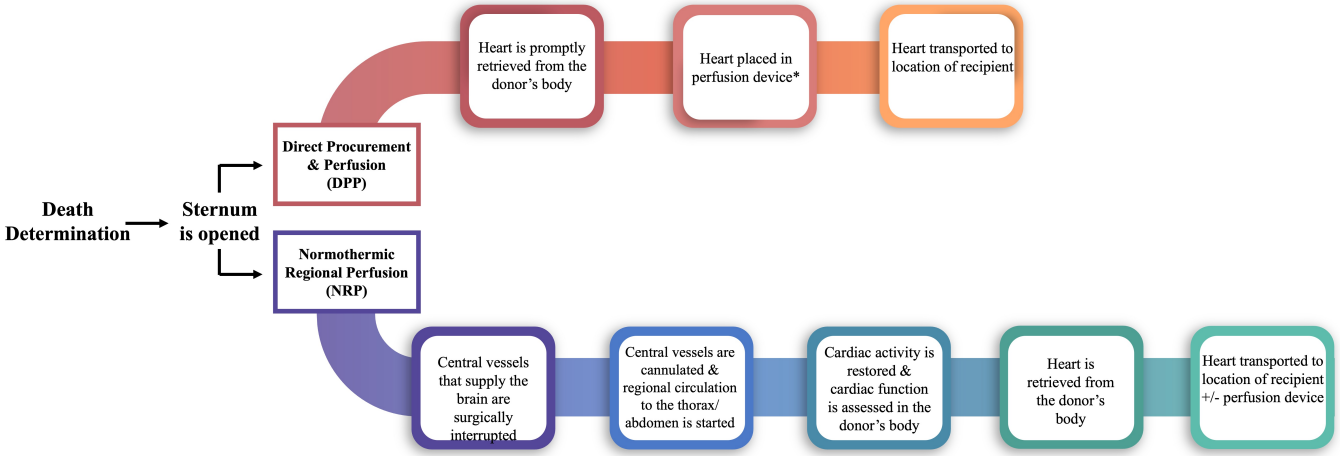
Themes	Illustrative Quotes
Direct Procurement & Perfusion	
Concern about quality of the heart	*"The first one I was very concerned about the viability of the heart once it went to the recipient."* (FG-08-BC, Pos. 106) *"I have questions about: how can we really know if the heart is still good? I can understand that we can restart it and he can start beating again, but how do we evaluate the damage that may have occurred during the time he was stopped?"* (FG-5F-QC, Pos. 109)
Transport process seems inhumane	*"… I am thinking like a limb of like meat, you know. Where you take the meat and you put it in the fridge… I am not against it. But it just seems very inhumane, a little bit, you know, inhumane just a little, but it is not… Because it is still, you know, this is somebody's heart, right? This is somebody who has lived, somebody who was loved. So, I do understand, and I do not have a problem with it being transported that way at all, but it just seems..."* (FG-12-MB, Pos. 107)
Concerns about complexity/ loss of heart	*"…It sounds like a complicated process with room for error. So I would be kind of interested to see what the success rate is for this procedure."* (FG-02-BC, Pos. 61) *"…I just do not feel like it being in a box controlled by, like different types of tubes, keeping your heart running is like, necessarily safe. I do not think it is kind of safe to do that."* (FG-11-ON, Pos. 125)
Concerns about getting donor's hopes up	*"I don't know if it can happen often, but I guess giving hope to someone and operating on them, then finally, the heart is unhealthy after two weeks. I don't know if it can happen often, I hope not."* (FG-5F-QC, Pos. 112) *"… I guess my only concern is, think about the, the heartache, no pun intended I guess, that the person would, would feel if they finally, you know, are on that waiting list for so long, they finally get that heart, they think everything is okay but they are not responding to it properly because this new method is being used, and there are some associated risks with it."* (FG-05-ON, Pos. 108)
Cost of procedure/ perfusion device	*"I am not too opposed to it. I just feel...the only thing I felt is that it probably would be costly."* (FG-11-ON, Pos. 84)
Perceived concerns by others: Religious or cultural groups	*"I mean, I imagine that maybe someone might have you know, like, you know, various religious concerns or belief concerns, but I see none from my perspective. I think that is...to be able to do that is fantastic."* (FG-12-MB, Pos. 105)
Normothermic Regional Perfusion	
Procedure too invasive/ complex/ too much being done to the body	*"What makes me uncomfortable is the body manipulation aspect that is more... it's for the respect for the body of our loved one or the person who died. There is an aspect of risk, I think, that is more present than the other method when talking about cutting the vessels so as not to fuel brain activity."* (FG-1F-QC, Pos. 143)

	"It's kind of...it is kind of a little too much. I feel like it would be hard to even watch. Although you are not there in the...in the room probably when this procedure is happening, but just the thinking about it, even watching this little commercial I had to like cover my eyes but that is...that is it for me." (FG-07-ON, Pos. 152)
Concerns about procedure putting donation at risk if it does not go well	*"But it's mostly the side that… do we put the donation at risk with this sort of way with the delay and the equipment."* (FG-1F-QC, Pos. 149)
Imagery: Creepy, Frankenstein-ish, unsettling	*"…the person is dying, and then you are almost kickstarting them up again. So just like in a science fiction kind of way It seems like even the heart in a box if you are just thinking about it, it does not...the picture is not...in your mind is not like, is not a nice visual to it…"* (FG-15-AB, Pos. 145) *"Essentially, yeah, it is kind of like you are doing like a Frankenstein operation on them, right? You are bringing it back to life, temporarily, but I see why you would do that to keep the organs functioning, but I can see the general public having some issues with that."* (FG-08-BC, Pos. 122) *"…my first thought is that it is intrusive and Frankensteinish."* (FG-07-ON, Pos. 172)
Concerns about revival of donor after withdrawal of life support	*"… the second procedure where they are actually reviving the heart within the body, so they have to clamp off those vessels, so, to me, if there.. was there a chance that you could have revived this person, but you were holding out, right, and that is, when you clamp the vessels, then that means if the blood was then flowing to the brain could this person have had a chance…"* (FG-04-AB, Pos. 109) *"You are taking them away. And then you are kind of bringing them back for that moment, even though they are not really back, the act is still there, I think."* (FG.01-ON, Pos. 194)
Concerns about donor experiencing consciousness/ pain	*"Could this cause the person to regain consciousness? For me there are ethical issues, I find, with this second method where I do not have the answers."* (FG-1F-QC, Pos. 206) *"These are really hard questions for me because I guess I have never really considered it before and when is someone considered deceased? And maybe if there is some brain activity, can they feel pain when, when they start, you know, cutting into to get the organs? They are kind of hard questions."* (FG-16-BC, Pos. 110)
Would not want to know the details	*"… maybe there are details like this we don't necessarily need to know. For the family just to know that at the last minute the medical team will make the best decision for the success of the transplant to another person."* (FG-1F-QC, Pos. 157) *"I definitely think if I was a family member of the donor, I would not want to know how it was being done. Now, now I know. Well, no, because it is not in Canada, but I would not want to know."* (FG-13-MT, Pos. 173)
Perceived concerns by others: Concerns about family feelings/ reactions	*"But I think it is one of those things that once you maybe tell the family, let's say they are not blocking it, let's say there is blood flow to the brain, I think it is trying to re explain that to a family member and they may get confused."* (FG-05-ON, Pos. 149)

	"If I put myself in the shoes of the family and loved ones who are there, death happens, the heart stops beating and in a short period of time it is restarted in the body of the person. It can be hard on the emotions of the family if they are around them, I can believe." (FG-1F-QC, Pos. 137)
Perceived concerns by others: Concerns that family may want the body back in a timely manner	*"I mean, the family usually wants the body back fairly quickly, so. Would this delay the receiving of the body?"* (FG-14-SK, Pos. 83) *"How long of a process would this be? Because I mean, families want to bury their loved one."* (FG-09-ON, Pos. 85)
Perceived concerns by others: Others may perceive the donor as having been revived	*"I think this procedure is more, I do not think this procedure would necessarily pass right away in Canada, just because it is so new and, and so many people are going to have that opinion that you just kind of revived the person."* (FG-03-ON, Pos. 189)
Perceived concerns by others: Others may feel this disturbs the dead	*"I could see some people maybe having a concern that, you know, it is one of these, you know, old concerns that we used to have from way...from the 19th century of disturbing the dead."* (FG-12-MB, Pos. 131) *"Well, I can understand why some people might refuse this procedure, because they could say: well, we use the body of the person I love, for example. It can be more difficult."* (FG-2F-QC, Pos. 213)
Perceived concerns by others: Religious/ cultural groups' concerns	*"Because yeah, like a lot of people are religious, and I am sure that would be a big problem for a lot of people."* (FG-03-ON, Pos. 109)

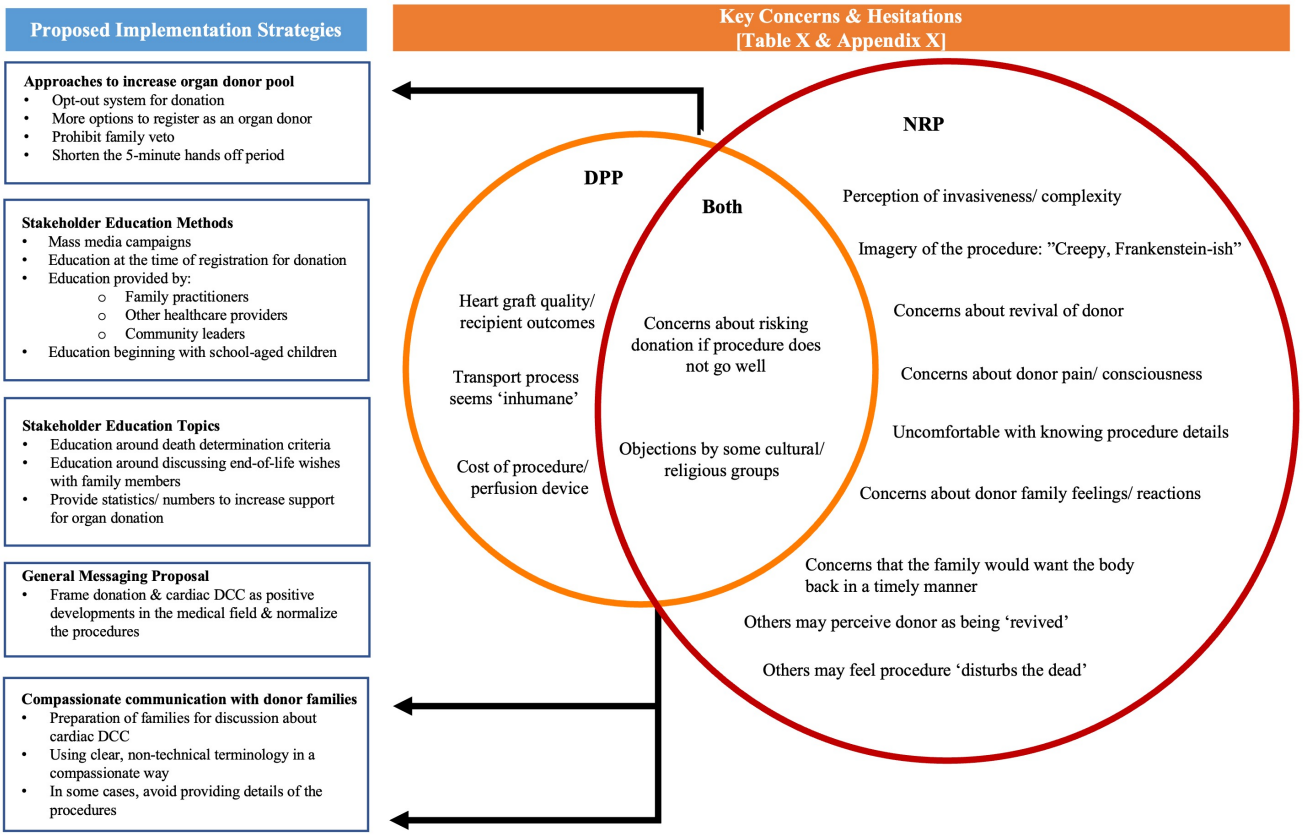
Figure Legends

Figure 1. Summary of cardiac DCC protocols



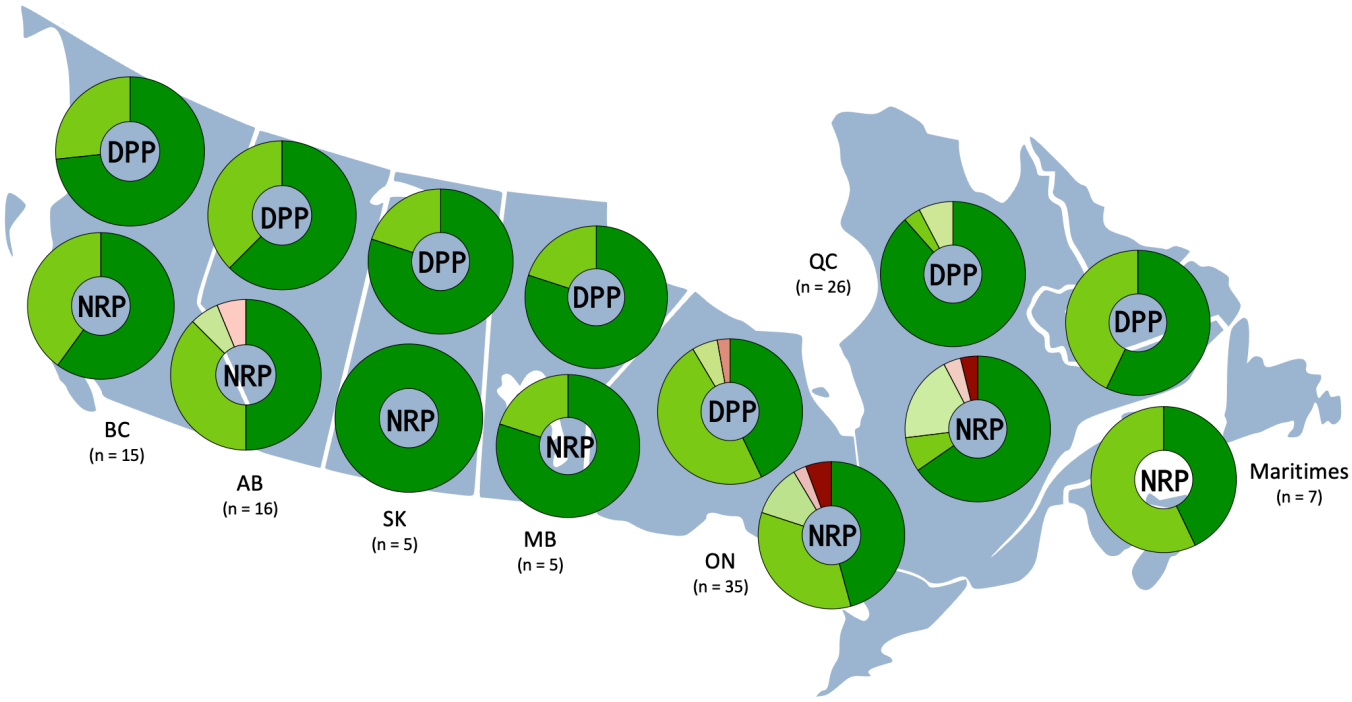
* A perfusion device is a self-contained system that supplies oxygenated blood to the heart, allowing it to resume contractions outside of the donor's body.

Figure 2. Themes & subthemes about cardiac donation and its implementation in Canada



DCC: Death by circulatory criteria; DPP: Direct procurement & perfusion; NRP: Normothermic regional perfusion

Figure 3. Perspectives about cardiac DCC by province of residence



DPP: Direct Procurement & Perfusion; NRP: Normothermic Regional Perfusion.

Figure 4A. Perspectives about DPP based on immigration status

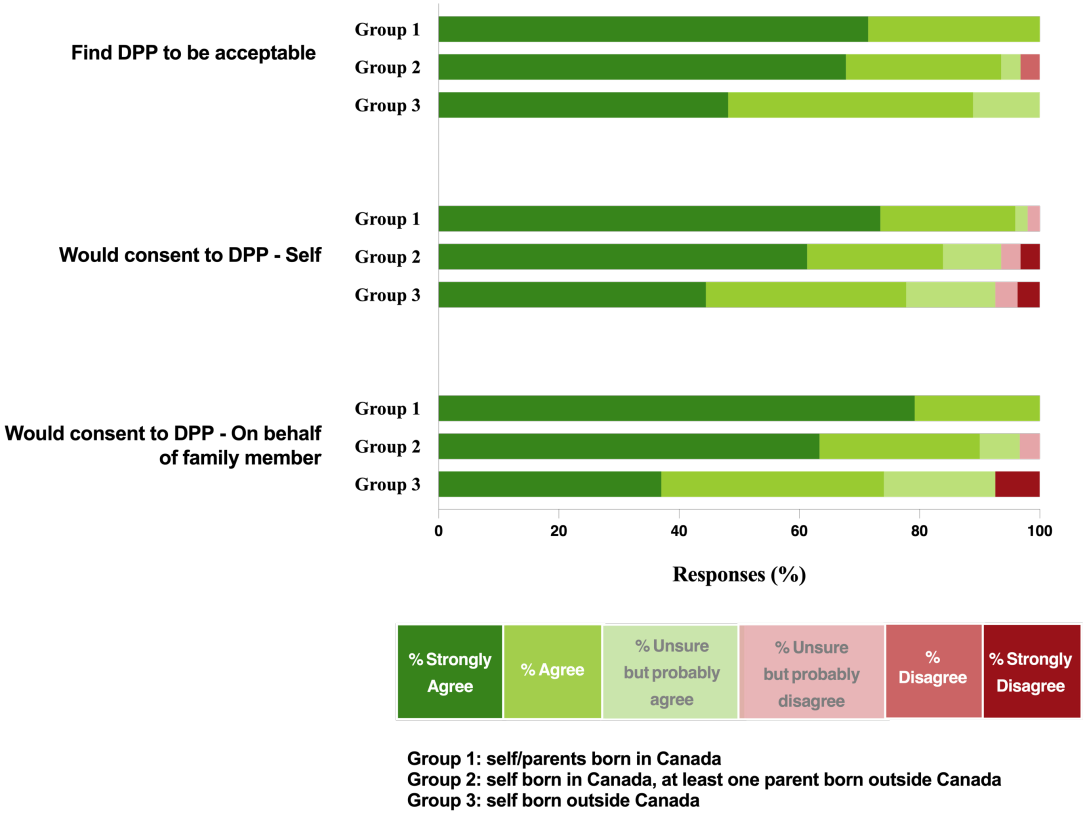
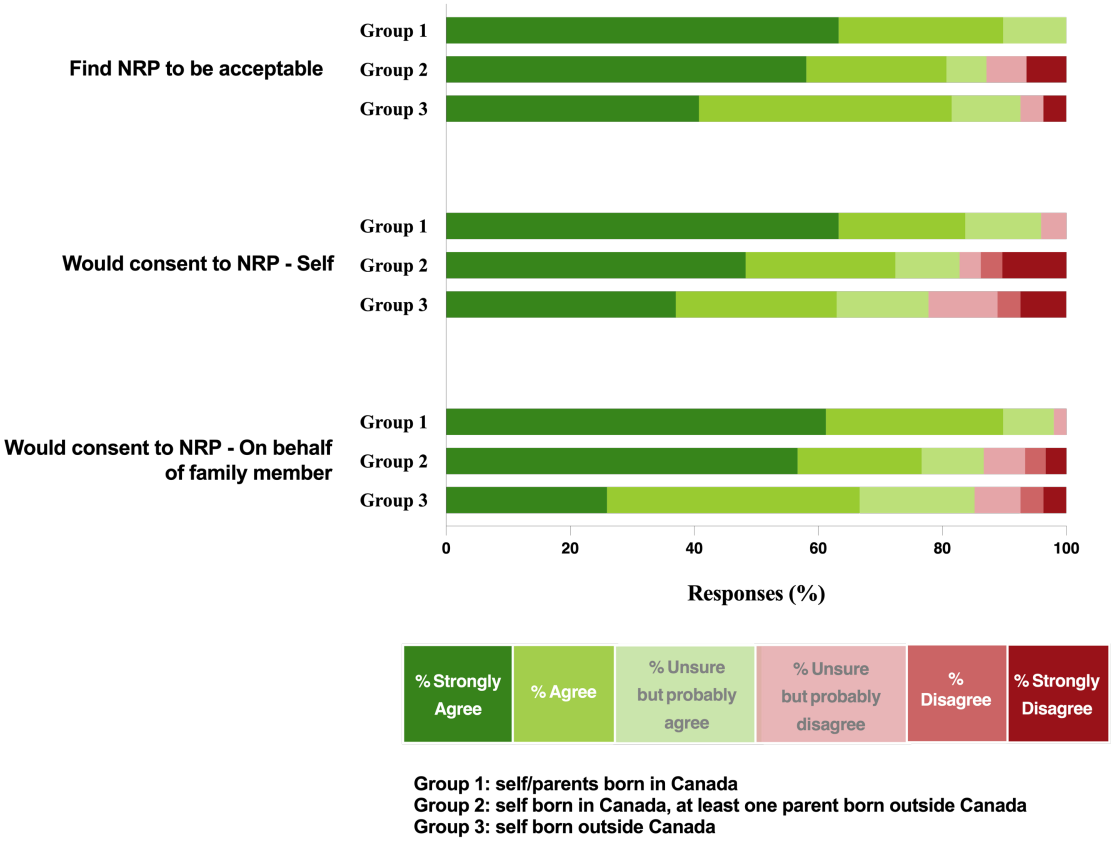


Figure 4B. Perspectives about NRP based on immigration status



Group 1: self/parents born in Canada
Group 2: self born in Canada, at least one parent born outside Canada
Group 3: self born outside Canada

Appendices

Appendix 1. Consolidated criteria for reporting qualitative research (COREQ) checklist

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	**Page 6.**
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	**Page 6.**
3. Occupation	What was their occupation at the time of the study?	**Page 6.**
4. Gender	Was the researcher male or female?	**Page 6.**
5. Experience and training	What experience or training did the researcher have?	**Page 6.**
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	**Page 6.**
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	**Research objectives only.**
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	**None.**

Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	**Page 5.**
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	**Page 5.**
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	**Page 5.**
12. Sample size	How many participants were in the study?	**Page 7, Table 1.**
13. Non-participation	How many people refused to participate or dropped out? Reasons?	**Page 5. Data not collected.**
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	**Page 6.**
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	**Page 6.**
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	**Table 1.**
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	**Appendices 3-5.**
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	**No.**
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	**Page 6.**
20. Field notes	Were field notes made during and/or after the interview or focus group?	**Page 6.**
21. Duration	What was the duration of the interviews or focus group?	**Page 6.**
22. Data saturation	Was data saturation discussed?	**Page 5.**
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	**No.**
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	**Pages 6-7.**
25. Description of the coding tree	Did authors provide a description of the coding tree?	**Figure 2 presents an overview of themes/ subthemes.**

26. Derivation of themes	Were themes identified in advance or derived from the data?	**Derived from the data. Page 7, Figure 2.**
27. Software	What software, if applicable, was used to manage the data?	**Pages 6-7.**
28. Participant checking	Did participants provide feedback on the findings?	**No.**
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	**Table 2, Appendices 6 and 7.**
30. Data and findings consistent	Was there consistency between the data presented and the findings?	**Yes.**
31. Clarity of major themes	Were major themes clearly presented in the findings?	**Yes. Pages 13-14, Figure 2.**
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	**Yes. Pages 8-9, Figure 2.**

Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Appendix 2. Explainer videos describing organ donation & cardiac DCC protocols

[Please refer to multimedia files]

Appendix 3. Pre-focus group survey

1. Age: _____

2. Gender: _____

3. Highest level of education

- □ Some high school, no diploma
- □ High school degree or equivalent
- □ Vocational or technical school
- □ Some college, no degree
- □ College or associate degree
- □ Bachelor's degree (e.g., BA, BS)
- □ Master's degree (e.g., MA, MS, MEd)
- □ Professional degree (e.g., MD, DDS)
- □ Doctorate degree (e.g., PhD, EdD)
- □ Other [please specify]: _____

4. Occupation: _____

5. Ethnicity: _____

6. Religious affiliation: _____

7. Residency in Canada

- □ I was born outside of Canada and immigrated to Canada in _____ (year)
- □ I was born in Canada and my parents were born outside of Canada
- □ I was born in Canada and my parents were born in Canada

8. What personal experience(s), if any, do you have with organ donation? [Please select all that apply]

- □ I have donated an organ to someone I know
- □ I have been an organ recipient
- □ My family member, relative, or friend has donated an organ
- □ My family member, relative, or friend has been an organ recipient
- □ I have no personal experience with organ donation
- □ Other [please specify]: _____

9. In general, how knowledgeable would you say you are on the topic of organ donation?

- □ I have no knowledge about this topic
- □ I have limited knowledge about this topic
- □ I have some knowledge about this topic
- □ I am very knowledgeable about this topic
- □ I consider myself an expert on this topic

Appendix 4. Focus Group Discussion Guide

Introduction [presented by moderator]

- Welcome statements
- Description of the purpose of the session
- Ground Rules

CLIP #1: DEATH DECLARATION + ORGAN DONATION AFTER DEATH BY CIRCULATORY CRITERIA

Part I Questions

1. What do you think about the recovery of liver, kidney, and/ or other non-heart organs after circulatory/ heart death?

a. *[if undecided] What additional information would help you make a decision?*

2. Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using this approach, if being an organ donor was consistent with their wishes and values?

a. *Why?*

b. *Why not?*

c. *[if undecided] What additional information would help you make a decision?*

3. Would you be okay with your family member consenting to donating your liver, kidney, and/ or other non-heart organs after circulatory/ heart death?

a. *Why?*
b. *Why not?*
c. *[if undecided] What additional information would help you make a decision?*

4. If you were asked, would you consent to the donation of the liver, kidney, and/ or other non-heart organs of a family member after circulatory death (where the heart stops), if I knew that being an organ donor was in keeping with their wishes and values?

a. *Why?*
b. *Why not?*
c. *[if undecided] What additional information would help you make a decision?*

6. *Do you have any concerns about the donation of organs after circulatory/ heart death?*

CLIP #2: HEART DONATION + DIRECT PROCUREMENT & PERFUSION

Part II Questions

1. What do you think about this approach to heart donation?

2. Do you find heart donation using this approach to be the same or different than the donation of other organs (like liver, kidneys, etc) as was previously described? How so?

3. Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using this approach, if being an organ donor was consistent with their wishes and values?

a. *Why?*
b. *Why not?*
c. *[if undecided] What additional information would help you make a decision?*

4. Would you be okay with your family member consenting to donating your heart after circulatory death (where the heart stops) using this approach?

a. *Why?*
b. *Why not?*
c. *[if undecided] What additional information would help you make a decision?*

5. If you were asked, would you consent to the donation of the heart of a family member after circulatory death (where the heart stops) using this approach, if you knew that being an organ donor was in keeping with their wishes and values?

a. *Why?*
b. *Why not?*
c. *[if undecided] What additional information would help you make a decision?*

6. Do you have any concerns about the donation the heart using this approach?

7. In this approach, the heart is removed from the body and its activity is restarted inside a storage device. What are your thoughts on this?

CLIP #3: NORMOTHERMIC REGIONAL PERFUSION

Part III Questions

1. What do you think about this approach to heart donation?

2. Do you think heart donation using this approach is different than the donation of other organs (like liver, kidneys, etc) as was previously described? How so?

3. Do you think this approach is different than the first approach (DPP) discussed earlier? If so, how?

4. Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using this approach, if being an organ donor was consistent with their wishes and values?

a. *Why?*
b. *Why not?*
c. *[if undecided] What additional information would help you make a decision?*

5. Would you be okay with your family member consenting to donating your heart after circulatory death (where the heart stops) using this approach?

a. *Why?*

b. *Why not?*

c. *[if undecided] What additional information would help you make a decision?*

6. If you were asked, would you consent to the donation of the heart of a family member after circulatory death (where the heart stops) using this approach, if you knew that being an organ donor was in keeping with their wishes and values?

a. *Why?*

b. *Why not?*

c. *[if undecided] What additional information would help you make a decision?*

7. *Do you have any concerns about the donation the heart using this approach?*
8. *What do you think about the ligation/ tying off of blood vessels that supply the brain? Does this concern you?*
   a. *What if there is a small chance of a small amount of blood getting to the brain… does this change what you think about this approach?*

Part IV - Final Questions

1. Compared with heart donation after brain death, do you think that heart donation after circulatory/ heart death more concerning, less concerning, or no difference in level of concern?

2. What do you think about the of the DPP approach being done in Canada if it led to more patients receiving a heart transplant sooner?

a. *Why?*
b. *Why not?*

c. *[if undecided] What additional information would help you make a decision?*

3. Would you support the NRP approach being done in Canada if it led to more patients receiving a heart transplant sooner?

a. *Why?*
b. *Why not?*
c. *[if undecided] What additional information would help you make a decision?*

Concluding Remarks [presented by moderator]

Appendix 5. Post-focus group survey

Please respond to the following questions regarding the various organ donation protocols we discussed today.

Response options for each question:

Strongly Disagree Disagree Unsure but Probably Disagree Unsure but Probably Agree Agree Strongly Agree

Non-cardiac DCC

1. Do you believe that it is acceptable for a healthcare team to retrieve the liver, kidney, and/ or other non-heart organs of a donor after circulatory death (where the heart stops), if being an organ donor was consistent with their wishes and values?
2. Would you be okay with your family member consenting to donating your liver, kidney, and/ or other non-heart organs after circulatory death (where the heart stops)?
3. If you were asked, would you consent to the donation of the liver, kidney, and/ or other non-heart organs of a family member after circulatory death (where the heart stops), if I knew that being an organ donor was in keeping with their wishes and values?

DPP approach to cardiac DCC

4. Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using the DPP approach, if being an organ donor was consistent with their wishes and values?
5. Would you be okay with your family member consenting to donating your heart after circulatory death (where the heart stops) using the DPP approach?
6. If you were asked, would you consent to the donation of the heart of a family member after circulatory death (where the heart stops) using the DPP approach, if you knew that being an organ donor was in keeping with their wishes and values?

NRP Approach to cardiac DCC

7. Do you believe that it is acceptable for a healthcare team to retrieve the heart of a donor after circulatory death (where the heart stops) using the NRP approach, if being an organ donor was consistent with their wishes and values?
8. Would you be okay with your family member consenting to donating your heart after circulatory death (where the heart stops) using the NRP approach?
9. If you were asked, would you consent to the donation of the heart of a family member after circulatory death (where the heart stops) using the NRP approach, if you knew that being an organ donor was in keeping with their wishes and values?

Additional questions about death determination were posed but not presented in the current study.

Appendix 6. Factors about organ donation that surprised participants

Themes	Illustrative Quotes
Surprised by how donation processes occurs	*"… Also that this is so cool that they can do that. I just...I never understood the nuts and bolts of how they do donations and it is so neat the way they can make this work."* (FG-14-SK, Pos. 127) *"This is new information for me. I have never been aware of how, like, I knew you could donate organs and such right. But I have never been aware of the criteria of like, how long you wait, you know what I mean? Like all those steps in the process, and that sort of thing. I mean, like, it is a pretty good process."* (FG-11-ON, Pos. 25)
Surprised by timing of donation processes	*"Well, I think I was aware of how it works in Canada, but I did not really think about how quickly it is, like how fast the transplant and the patient...like it all goes seems really fast. In the moment, I am sure it is not for the families, of course, but it seems really fast."* (FG-12-MB, Pos. 30) *"But to me, I was surprised that they would wait that long and risk losing organs as a result of that whole process."* (FG-10-AB, Pos. 70)
Surprised by low rate of donation (1-2% of hospitalized deaths)	*"But I didn't know, on the other hand, that it was just two patients, one to two patients out of a hundred, it surprised me as a statistic anyway, it's not much."* (FG-2F- QC, Pos. 16) *"I was also surprised it was only one or two out of 100. For some reason, I expected it to be higher than that."* (FG-09-ON, Pos. 21)
Previously believed that patient died due to organ donation (did not realize they must die first)	*"I thought it was interesting that they like...like unplug them off of the machines, and then they open them up and you know, just because I thought the organs would need the blood flowing in order to be viable organs. So you would almost think that they would be on all the machines while the procedures are happening."* (FG-05-ON, Pos. 60)
Surprised by family veto/ against family veto	*"When the person signs a paper, it is because at the time they signed it, they were aware of their decision. I do not understand why anyone then could end something they have decided. I think there's a gap in this point."* (FG-2F-QC, Pos. 104) *"Have there been any requests for changing that the fact that I sign my card then my family can decide otherwise. I mean, I sign it because it's my will."* (FG-4F-QC, Pos. 81) *"I have to go back to, I think it is best for people to declare their willingness to donate their organs in the first place rather than having family members make that decision for them."* (FG-02-BC, Pos. 160)
Surprised that heart can be donated after heart stops	*"… I did not know once like the heart has stopped beating, right, because then you are waiting five minutes before then they do the surgery to actually take out the heart. So, um, I did not know that, you know, it can actually be used as one of the organs that can be donated, so that is interesting to see that."* (FG-04-AB, Pos. 56)

Appendix 7. Support for cardiac DCC

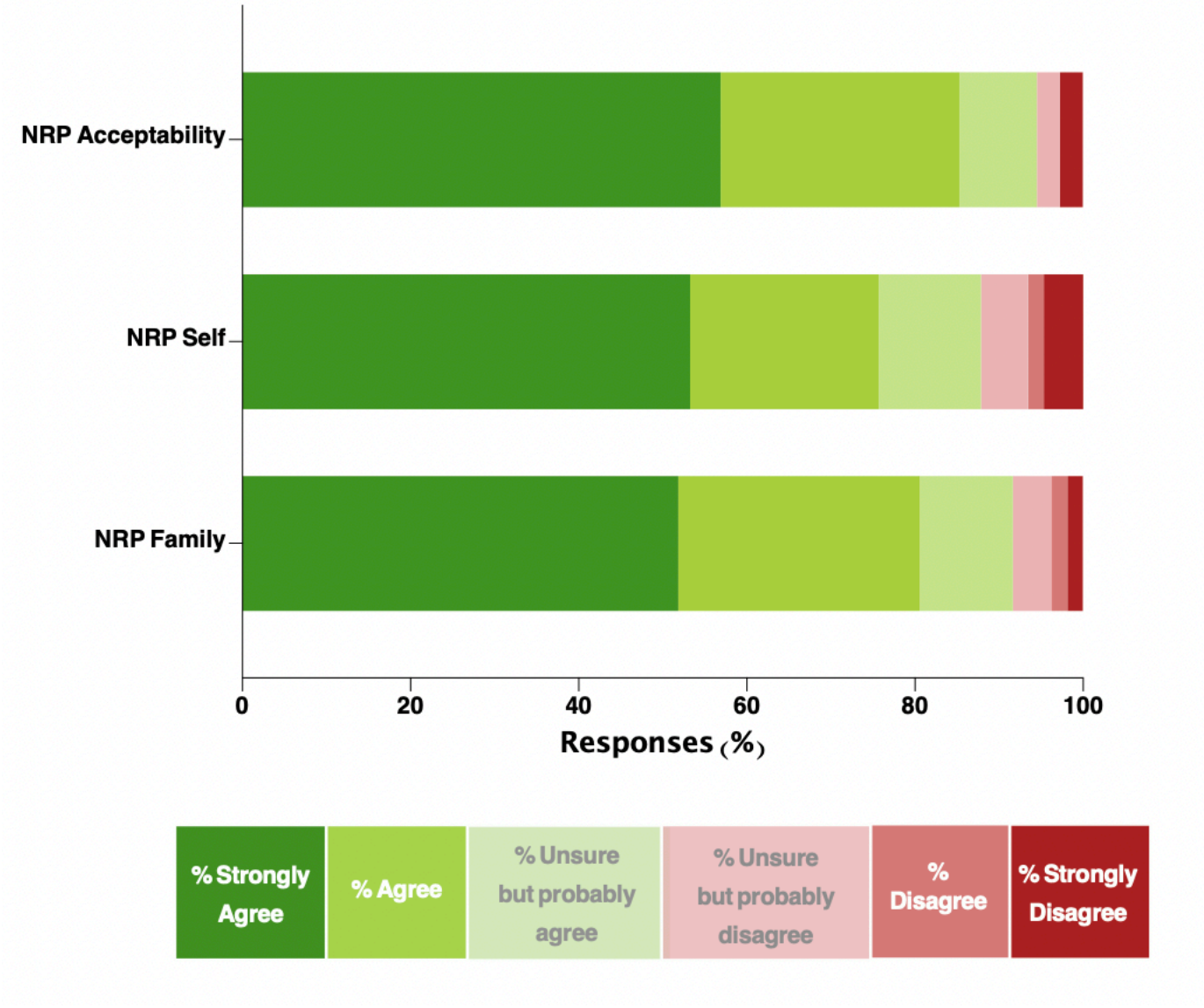
Themes	Illustrative Quotes
Organ Donation/ DCC in General	
General supportive statements related to organ donation	*"I think that is a good thing. For me, it doesn't make much difference, if I'm dead, I'm dead. It's for sure that it's up to my family to decide what's going to happen to me at the funeral and all that. But I tell myself if I can make a difference in someone else's life, for it's perfectly correct."* (FG-5F-QC, Pos. 49) *"I mean, at that point, why not just help someone else? You know, I think once you are in that state, you are sort of gone in a way as well. So, I mean, yeah, why not."* (FG-03-ON, Pos. 25)
Direct Procurement & Perfusion	
Surprised/ questioning why DPP has not been performed in Canada	*"The curiosity I have right now is what is holding it back? Like what seems to be the issue that does not allow it? You say other countries are doing it so it sounds like it is a procedure that is successful, but at the same time like something is holding it back here in Canada."* (FG-10-AB, Pos. 56) *"Well, if they practise it elsewhere and it works, why not do it here? Basically, the goal is to save as many lives as possible."* (FG-4F-QC, Pos. 135)
Supportive because it saves lives/ increases number of available donor hearts	*"… I think the more hearts that are available, the better. Actually, I am shocked that this has not already been implemented."* (FG-08-BC, Pos. 80) *"I do not see why we could not use the heart. I think if many more lives can be saved with a healthy heart and that healthy heart is available, it should be done."* (FG-03-ON, Pos. 76)
Natural extension of non-cardiac donation (similar to non-cardiac DCC)	*"It sounds like the exact same way of...the exact same process of, you know, harvesting all the other organs. So I do not know why they would not just do it as well."* (FG-03-ON, Pos. 111)
Impressed with/ supportive of perfusion device technology	*"That the machine kept it beating. I was just, wow, I was impressed by that. That is cool."* (FG-16-BC, Pos. 46) *"I mean, and they are able to do that with technology, that is pretty amazing. I do not really have any strong reactions to that other than that is just amazing that we are able to do it."* (FG-09-ON, Pos. 71) *"Personally, I think it's a really good approach. Then I find that it's really about leveraging scientific advances and be more up to date. Because if it's possible to do that, that's a good thing."* (FG-2F-Qc, Pos. 159)
Supportive because procedure is done in other countries	*"And I think it is great that we are trying to catch up on the times here, because if countries, other first world countries such as the UK are already practicing this, we do nothing but stand to benefit from it. You know, if the intent is already to donate the organs, why are we not doing that to our best ability?"* (FG-08-BC, Pos. 76)

Heart "not wasted"	*"I actually agree with the perspective of if there is a way to get a heart that we previously would not have been able to, then it is really just a win-win situation versus it just going to waste."* (FG-13-MT, Pos. 117) *"… There is not really anything to lose if someone is already declared dead and otherwise, if this was not practiced their heart would just, you know, go to waste per se."* (FG-02-BC, Pos. 71)
May help donor families with grieving process	*"I also think that the feedback from the close family would be positive… And to know that after their death, they have done this little act of kindness, and the family can get better."* (FG-1F-QC, Pos. 121)
Respects donor wishes	*"Well, the first thing that comes to mind for me is that, I mean, if that patient has already given the okay to donate, I do not really, like see the difference and if they are able to help someone, I think that is something that people would, you know, they would want."* (FG-15-AB, Pos. 54)
Reasons others would be supportive	*"I think my community would be supportive because it's to save lives and then it would be important."* (FG-4F-QC, Pos. 301)
Normothermic Regional Perfusion	
Surprised/ questioning why NRP has not been performed in Canada	*"My first thought is just why are they not doing this already? It seems to make a lot of sense."* (FG-12-MB, Pos. 117) *"It's fine! It should be. I think it's great that they use the heart to keep other organs alive. In any case, I think it's full of common sense there. I don't understand why doctors don't do that, especially in 2021."* (FG-2F-QC, Pos. 202)
Supportive because it saves lives/ increases number of available donor hearts	*"The body is just getting used to keep it healthier or...you know what I mean? It is keeping it better, so that it is a better match for that person who is going to receive it. I think if somebody wants to donate, they are going to be fine with whatever is going to make the donation process better."* (FG-10-AB, Pos. 103) *"… I would say I do not have a problem with the restarting in the body. Because it has been restarted for a particular purpose and is for...is to go forward, that someone else could benefit, that someone else could live from this restarting."* (FG-03-ON, Pos. 155)
Appears more efficient/ safer than DPP	*"I actually think that that is a much more efficient way of keeping the heart good than to take it out and then put it into a machine. And also, just strictly from an efficiency standpoint, because they are testing the heart before removing it, it actually allows them to see if they even want to remove it, or if they think it is going to be a viable transplant option. And so if they do not think it is going to be then they do not have to spend the time to take out a heart that is not even going to make it to a transplant."* (FG-12-MB, Pos. 129)

	"I think that there is more precaution that is taken, more steps are taken. Um, I feel more comfortable with this one than the prior one that you just showed." (FG-01-ON, Pos. 125)
Opportunity to perform tests to assess cardiac viability	*"I preferred the second method, because I thought keeping it in the body, it kept the other organs with a blood circulation. So we could also donate the other organs. It made it possible to do a test to really give a good heart to the patient."* (FG-4F-QC, Pos. 249) *"The blood vessels to the brain are clamped but they actually sit down and they do, do testing on the heart as opposed to remove it and then put it on a machine and to me, it sounds like they are crossing their fingers on the last one. This one seems that there is a lot of more due diligence."* (FG-01-ON, Pos. 128) *"The first one [DPP], I was very concerned about the viability of the heart once it went to the recipient. This way the heart is tested before it goes to recipient. That seems to me to be a more responsible way to do it."* (FG-08-BC, Pos. 106)
Supportive because donor is already deceased	*"… I think if you think about it logically, if the person is already dead, then you might as well save the organ to give it to somebody who is still alive."* (FG-12-MB, Pos. 119) *"… If there is no quality of life, and there is no hope for the person to come back, then I think that is completely fine."* (FG-03-ON, Pos. 167)
Trust the healthcare system/ believe checks & balances will be in place	*"I think if it is an irreversible condition just have faith in the presiding doctors that cannot reverse that level of consciousness that they are dead and then for that, when you sign your card, you do not put Asterix on what they can or cannot do, you have faith in the system."* (FG-04-AB, Pos. 167)
May be helpful for other organs	*"I think this approach is a lot more sound because all the organs are still receiving blood and they are functioning and that way the lifespan, and there will be less deterioration of the organs so when they have a little bit more time to test everything and make sure that it all works properly for the next recipient."* (FG-01-ON, Pos. 132) *"The fact that blood flow is started right away, I assume it also helps with blood flow to the other organs as well to give them even more time and also have the ability to have blood pumping to the other organs so that the other organs are also in a better condition when transplanted."* (FG-09-ON, Pos. 99)
Less cost than DPP	*"But I think it's a really good way to reduce the costs around that as well. It seems to me that a big machine that makes a heart beat [in DPP] it costs dearly."* (FG-2F-QC, Pos. 213) *"I think it is much better. And I am assuming, I mean, I am assuming like that the equipment used to kind of reanimate the heart and pump blood is probably much less expensive."* (FG-11-ON, Pos. 109)

Supportive ***IF*** recipient outcomes shown to be better than DPP	*"… I still have my reluctance about the second one. It depends on how much the percentage would be higher with the second procedure than the first."* (FG-3F-QC, Pos. 309) *"I think that if, if it is a better chance for the heart to be transported, then I think that that it is a good thing. They should do that for sure. Start doing it here."* (FG-03-ON, Pos. 117) *"I think, you know, if NRP had a higher success rate then I do think it is something that yeah, it might take a little bit of getting used to, but I think as it becomes mainstream medicine, yeah, I could be...I would be fine with it."* (FG-07-ON, Pos. 170)
Supportive of ligation/ clamping of the vessels that supply the brain in NRP	
Acceptable part of the procedure	*"They could clamp, they could do anything that they do as long as it works, and it is you know, then I am happy for it."* (FG-12-MB, Pos. 144).
Prevents donor from being revived	*"The fact that you have to block the circulation to the brain to make sure the person doesn't come back to life..."* (FG-1F-QC, Pos. 141) *"I see it basically as the clamping of the blood for the brain flow is more for the family than it is for the doctors. It is just so that the person has that belief that they are not going to come back or have anything…"* (FG-10-AB, Pos. 115)
Help to focus the blood flow to organs that are considered for transplant	*"Okay, so it is essentially an efficiency thing. Again, they are just trying to concentrate all the blood to the one area that they want to keep those organs good… I would say that is a very intelligent to do."* (FG-12-MB, Pos. 136)

Appendix 8. Perspectives about cardiac DCC for all participants



Chapter 6. Conclusions

6.1 Summary of Findings

In the systematic review of antemortem heparin in DCC (Chapter 2), our approach to addressing the paucity in clinical trials was to examine the current evidence base to describe practice variability in the use of antemortem heparin in DCC and meta-regression analysis to provide preliminary conclusions regarding the efficacy of antemortem heparin. Among observational studies, we found high variability in the frequency, dosing, and timing of antemortem heparin administration. Among studies that directly compared two cohorts (one that received heparin and one that did not), there was variability in the reported effects of antemortem heparin on graft survival. Finally, meta-regression analysis of DCC liver transplants showed no association between proportion of donors receiving heparin and transplant outcomes.

In Chapters 3 to 5, we describe two studies that evaluated the perspectives of Canada's healthcare providers caring for potential organ donors and/ or those caring for transplant recipients and members of the general public regarding cardiac DCC and its implementation in Canada. An overarching theme that emerged from both studies is the apparent discrepancy between the expectations of healthcare providers (i.e., concerns about non-support/ objections by the general public), that were not borne out when the perspectives of members of the general public were evaluated directly in focus groups. When it comes to cardiac DCC, the public's priorities are centered on preventing of suffering, dignified and humane treatment of the dying and deceased, and respecting their wishes at the end of life. In fact, the predominant queries and concerns of members of the public were related to why cardiac DCC protocols have yet to be

performed in Canada. The findings identify numerous opportunities to progress towards implementation of cardiac DCC programs in a manner that maintains public trust.

6.2 Methodological Challenges

Antemortem Heparin in Organ Donation After DCC

There were several methodological challenges related to the systematic review and meta-regression analysis of antemortem heparin practices in organ donation after DCC (Chapter 2). Meta-regression analysis suffers from the same inherent limitations as meta-analyses, including variability in the quality of included studies, clinical and statistical heterogeneity, and publication bias (Esterhuizen & Thabane, 2016). Meta-regression analysis has additional limitations, including ecological fallacy or regression bias (i.e., the logical fallacy that aggregate data between average patient characteristics and the pooled treatment effect reflect true associations between the individual patient-level treatment effect). This risk of this in our analysis is low, since this bias is common in analyses that aim to associate patient characteristics (e.g., age, gender, etc.) with treatment effects (Geissbühler et al., 2021). Another risk is overfitting (i.e., spurious associations between the covariate and treatment effect if the number of included studies is low; Geissbühler et al., 2021). In this study, we included 32 studies that reported DCC liver transplants and included only the proportion of donors that received heparin as a covariate. This exceeds the number recommended minimum number of studies per covariate, which varies from 5 (Geissbühler et al., 2021) to 10 (Higgins et al., 2019). While we identified several studies evaluating other organ transplant outcomes that reported the proportion of donors that received heparin and also reported transplant outcomes, we did not perform meta-regression analysis of these studies to avoid the risk of overfitting.

Cardiac Donation After DCC

Evaluating stakeholder perspectives (Chapters 3 to 5) presented several methodological challenges. The complexity of the procedures involved in cardiac DCC (particularly NRP), necessitated an approach to educating participants, particularly the general public. We therefore opted to develop the series of explainer videos that served to educate participants about the details of cardiac DCC protocols (**Appendix Multimedia file**). In addition, the initial study protocol entailed in-person focus groups with members of the public across four provinces (Quebec, Ontario, Alberta, and British Columbia), which represent provinces with the highest volume of deceased organ donation in Canada (Chapter 3; Honarmand et al., 2020c). Shortly before our first in-person focus group was scheduled to take place, the Coronavirus Disease 2019 (COVID-19) pandemic and resulting mandates for physical distancing curtailed this plan. To address this challenge, we opted to modify the study protocol to entail virtual focus groups using video conferencing. This allowed us to conduct focus groups involving members of the general public across all provinces in Canada, which in turn allowed for more generalizable findings. In recent years, virtual focus groups have provided invaluable opportunities to efficiently collect rich qualitative data, with reduced dropout rates and improved recruitment of participants that represent the diversity of the population from which they are recruited (Halliday et al., 2021). In the study involving the Canadian public, the inherent limitations of virtual focus groups (e.g., distractions in the participants' home environments, technical issues) were counterbalanced with the opportunity to expand our sample to include participants from all Canadian provinces and those residing outside of major cities.

6.3 Implications

It is important to ensure that implementation of new or revival of previously established innovations in organ donation are done in a manner that maintains the trust of stakeholders, including healthcare providers and the general public. The multi-method approaches described in this thesis may serve as one model for future evaluations of existing and re-emerging organ donation practices.

In Canada, explicit consent must be obtained from the potential donor's SDM to proceed with any antemortem procedures, including heparin administration (Shemie et al., 2017). When a potential donor's SDM consents to peri-mortem procedures such as heparin administration, they do so with the intent that the procedure may improve the chances of transplant success. From a societal perspective, there is potential risk of harm through loss of trust in the organ donation system as a whole. Specifically, loss of public trust in the organ donation system may lead to less willingness among individuals to register as an organ donor, which would adversely impact the organ donation system, and less willingness by families to consent to donation on behalf of their loved one. As such, the protocol warrants closer scrutiny to determine the veracity of claims about benefit. The findings of the systematic review and meta-regression analysis presented in Chapter 2 and ongoing debates around peri-mortem interventions in DCC support (1) more consistent reporting of heparin use and its effects in observational studies, and (2) the importance of high-quality clinical trials evaluating the efficacy and harms of antemortem heparin administration. Should our findings be confirmed in the setting of clinical trials, de-adoption of this practice may be warranted.

The findings of these studies suggest majority support for cardiac DCC protocols and identify facilitators and barriers to their implementation in Canada. Understanding perspectives and concerns about a complex topic like cardiac DCC is best achieved through rich qualitative data which provide an opportunity to converse in real-time with relevant stakeholders (Morgan, 1996). Our findings suggest that when it comes to organ donation practices, the priorities of the general public may be less centered on the specific protocols and procedures, and more focused on several widely held values and principles such as preventing the suffering in the dying, respecting the dignity of the dying and deceased, treating the deceased humanely, and respecting the wishes of the deceased individual. So long as the public trusts that their healthcare providers share these values and principles, many may leave decisions regarding the specific procedures and protocols in the hands of healthcare providers caring for dying patients.

6.4 Future Directions

The work in this thesis has identified important research priorities to advance the field of organ donation and transplantation. While antemortem heparin remains standard care in the management of DCC donors, its efficacy and optimal dosing and timing remain unclear. Future clinical trials are needed to evaluate the clinical benefits and harms of this practice, and to inform its optimal timing and dosing, which may lead to improved management of DCC donors.

With the renewed interest in cardiac DCC worldwide, many jurisdictions in Canada are planning to implement these protocols into their clinical practice. Implementation of cardiac DCC should be done in a rigorous manner, under the umbrella of a well-designed research program, with a view to the systematic collection of rigorous research data regarding the clinical outcomes associated with both cardiac DCC protocols, their impact on other transplantable

organs, and ongoing evaluation of stakeholder perspectives, including the experiences of deceased organ donors' families. The ideal approach towards optimizing deceased organ donation practices is one that incorporates evidence for clinical benefits and harms, as well as the perspectives of relevant stakeholders. While the topics explored in this thesis pertain to distinct practices in DCC, this overall body of work provides one approach to evaluating controversial practices in the field of organ donation and transplantation.

The following reference list includes those pertaining to thesis content that has not been previously published or prepared as a manuscript for submission. References for the studies presented in Chapters 2-5 are listed after their respective sections.

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APPENDICES

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