A Retrospective Study on Potential Organ Donation and Transplantation Opportunities in Alberta Emergency Rooms and Intensive Care Units

by

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Abstract

Background: In patients with end stage organ failure, organ transplant is often the only life saving treatment. Unfortunately, worldwide, the number of organs needed for transplant far outnumber the number of organs available. This scarcity of organs has led to interest in methods of increasing organ donation (OD) globally, including identification and characterization of Potential Missed Donors (PMDs). Thus, we had three main aims in this retrospective, cross-sectional study: (1) Calculate the incidence of PMDs in Alberta in 2015, (2) Determine where potential donors are most likely to missed in terms of urban or rural hospital location as well as tertiary and non-tertiary centers, (3) to identify and describe common characteristics of PMDs as well as independent associations with PMD status.

Methods: We performed a retrospective chart audit of all deaths in Alberta, Canada that occurred between January 1, 2015 and December 31, 2015. In total, we collected information on 2682 deaths in Alberta from 16 hospitals. Univariate analysis was used to identify significant demographic and clinical differences between PMDs and Non-PMDs. Logistic regression was performed to identify significant independent association with categorization as a PMD.

Results: Of the 2682 deaths reviewed, 225 patients were identified as PMDs. Consequently, the incidence of PMD in Alberta in 2015 was 53.7 (95% CI 40.6, 70.5) per million population (pmp) in 2015. On average, PMDs were significantly younger than non-PMDs (47 years vs. 62 years, p=0.001) and were more likely to have a death diagnosis of anoxic encephalopathy (49% vs. 39%, p=0.04). PMDs, on average, also had a significantly lower Glasgow Coma Score (GCS)

compared to Non-PMDs (3.69 (1.65) vs. 4.36 (2.05), p=0.001). More non-PMDs than PMDs died in an urban tertiary ICU (p=0.04). However, more PMDs than non-PMDs died in an urban non-tertiary ICU. Multivariable analysis revealed independent associations with both younger age (Odds ratio (OR)=0.96, 95% CI (0.94, 0.97), p=0.001) and lower GCS (OR=0.87, 95% CI (0.76, 0.10), p=0.04). Independent association with tertiary hospital of death was marginally significant (OR=0.59, 95% CI (0.33, 1.07), p=0.08).

Conclusions: There is a large cohort of potential donors currently being missed in Alberta hospitals. Better identification in this group could lead to higher donor yield. Younger patients with a GCS lower than 4 presenting in urban, non-tertiary ICUs, are most likely to be PMDs and future efforts and resources should be focused on early identification of patients meeting these criteria.

Preface

This thesis is an original work by Amanda N. Ewasiuk. No part of this thesis has been previously published.

Dedication

I dedicate this Master's thesis to my parents, Kimberly and Robert Ewasiuk, who have demonstrated and engrained within me the value of hard work, the necessity of faith and the importance of education throughout my childhood and continue to do so to this day.

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List of Abbreviations

AUROC	Area Under the Receiver Operating Characteristic
BMI	Body Mass Index
CBS	Canadian Blood Services
CI	Confidence Interval
CT	Computed Tomography
CVA	Cerebrovascular accident
DCD	Donation after Circulatory Death
ECD	Expanded Criteria Donor
EEG	Electroencephalography
ER	Emergency Room
FiO_2	Fraction of inspired oxygen
GCS	Glasgow Coma Score
HBV	Hepatitis B Virus
HCP	Health Care Provider
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HOPE	Human Organ Procurement and Exchange Program
ICH	Intracranial Hemorrhage
ICU	Intensive Care Unit
IQR	Interquartile Range
MAP	Mean Arterial Pressure
MD	Medical Doctor
ME	Medical Examiner
MRI	Magnetic Resonance Imaging
MV	Mechanical Ventilation
NDD	Neurologic Determination of Death

OD	Organ Donation
ODO	Organ Donation Organization
ONT	Spanish National Transplant Organization
OPTN	Organ Procurement and Transplantation Network
OR	Odds Ratio
PHS	Public Health Service
PMD	Potential Missed Donor
pmp	Per million population
RN	Registered Nurse
SAH	Subarachnoid Hemorrhage
SCD	Standard Criteria Donor
SD	Standard Deviation
SDM	Substitute Decision Maker
TBI	Traumatic Brain Injury
UNOS	United Network for Organ Sharing
UWDCD	University of Wisconsin Donation after Circulatory Death Evaluation Tool
WLST	Withdrawal of Life Sustaining Therapy

Chapter 1: Introduction

1.1 Statement of the Problem

Organ Donation (OD) and subsequent transplantation has become a viable and preferred treatment option for many patients with end-stage organ failure. While transplantation is often the only cure for failure of innate organs, there is a global shortage of organs available in comparison to those needed. In 2015, nearly 127 000 transplants were performed worldwide, accounting for less than 10% of the global need.[1] This shortage is costly at both the macro and micro levels for both healthcare systems, governments and patients alike. The greatest loss of this shortage is that of human life. According to the United Network for Organ Sharing (UNOS), over 7000 people died in the United States waiting for an organ in 2016.[2] Additionally, from a health care cost perspective, it is well known that patients requiring medical treatment for chronic organ failure over a long period of time carry a much greater cost burden to the health care system than those patients who receive an organ transplant.[3-6]

Given this shortage of available organs, health care professionals (HCPs) and other affected stakeholders are desperately seeking innovative methods for increasing both living and deceased OD. The gap in organ need and availability has been partially met through the re-emergence, yet somewhat slow acceptance amongst the medical community, of donation after circulatory death (DCD). In 2015, DCD accounted for nearly 17% of organ transplants worldwide and while DCD's utilization has increased in recent years, its potential continues to be plagued by legal and ethical criticism.[1,7,8] Additionally, many countries have subsidized programs to increase training for HCPs, from nurses to physicians, to be trained specifically in OD and transplantation processes.[9-11] From a public health perspective, many nations have now also invested in a variety of promotional and awareness campaigns in an effort to increase the general population's knowledge about OD and transplantation as well as registered consent.[12-15] While registered consent to OD has been popular in the recent past, specifically in North America, a debate on the effectiveness and use of opt in versus opt out systems has emerged.[16,17] However, there remains a lack of consensus on which system promotes a higher rate of OD, or if there is a difference between the two at all.[18]

A more recent strategy in an effort to increase OD is the characterization and subsequent identification of potential missed donors (PMD). While research in this realm is currently sparse, the ability to identify areas in the health care system where donors are missed would be beneficial for government in order to appropriately allocate funds to those areas greatest identified as missed opportunities. The characterization of PMDs may also hold the promise of increasing OD and consequently, significantly reduce health care costs, which as aforementioned would be beneficial to all stakeholders involved.

1.2 Objectives

The primary objectives of this research are as follows:

a) To determine the incidence of PMDs per million population (pmp) in Alberta from January 1 to December 31, 2015
b) To identify whether PMDs more commonly die in rural or urban hospitals and Intensive Care Units (ICU) or Emergency Rooms (ER)
c) To describe and characterize important clinical and demographic factors of non-PMDs and PMDs including the specific diagnosis of death, for example traumatic brain injury (TBI), cardiac arrest, anoxic brain injury, drug overdose

Chapter 2: Literature Review

2.1 Neurological Determination of Death (NDD) Donors

2.1.1 History and Definition of NDD

In 1968, a definition for irreversible coma was proposed by the Ad Hoc Committee of Harvard Medical School, providing the foundation for what is commonly known today as neurological death or brain death. The initial definition stated that unresponsiveness, lack of spontaneous movement and breathing, lack of neurological reflexes and lack of electroencephalogram (EEG) activity reported over a 24-hour period, constituted irreversible coma.[19] This definition, whose components are still largely used, led to a shift in OD practice from DCD to donation after neurological determination of death (NDD) thereafter. In Canada, the Neurocritical Care Group advocates the definition of brain death as the "irreversible loss of consciousness combined with irreversible loss of all brainstem functions including the capacity to breathe." [20]

2.1.2 Diagnosis of Neurological Death

NDD is adequately diagnosed solely according to clinical criteria in most cases. These clinical criteria include testing for absence of gag, vestibulocular, corneal and pupillary light reflexes, identification of etiology of death, confirmation of irreversible comatose state and apnea test[21]. During this evaluation it should be determined that there are no confounders to neurological death for example, hypothermia, described as a temperature of $\leq 34^0$C, or use of drugs known to alter neurologic function.[21] Finally, the patient should be re-evaluated by a qualified physician within the time requirement legislated locally, commonly 24 hours, if applicable. It should be noted that in Canada, it is legislated that two physicians must declare neurological brain death, however there is no legislation that this evaluation cannot be done at the same time.[21] Previously, in cases where brain death remained undeclared, patients were to undergo additional diagnostic tests including cerebral angiography or equivalent, EEG, magnetic resonance imaging (MRI) and/or computerized tomography (CT).[20] However, at present, recommended Canadian guidelines only support the use of ancillary testing in the form of either cerebral or radionucleotide angiography.[21]

2.1.3 Epidemiology of NDD Donors

Over the past several decades, NDD has been the preferred OD method and continues to be despite the re-emergence of DCD. In 2017, an audit of organ donors in Australia and New

Zealand found that the proportion of NDD donors had decreased from 95% in 2005 to 72% in 2014, representing a statistically significant decrease.[22] Alternatively, the number of NDD donors converted in Canada has remained relatively static, within the range of 12 to 14 donors pmp, since the beginning of the 21st century.[23] Kramer et al suggested in 2013 that this may due to a decreasing proportion of neurologic death over time with an odds ratio (OR) per year of 0.92 (p=0.01).[24]

Despite this stagnancy, the distribution of the etiology of death has shown remarkable re-configuration. Kramer et al demonstrated a statistically significant difference in the proportion of TBI donors between the periods of 2003-2005 (>30%) and 2012-2014.[23] Similar trends of decreasing TBI and increasing anoxic brain injury incidences were also reported in a study based at McGill Health Center in Montreal.[25] Additionally, a statistically significant increase in the proportion of patients diagnosed with an anoxic brain injury, which accounted for approximately 14% of NDD donors in 2003 compared with 80% in 2013, has been observed.[23,25] It should also be noted, that as seen in the general population, one study noted there is increasing prevalence of co-morbidities in the donor pool including body mass index (BMI) over 30, diabetes, hypertension, hyperlipidemia, coronary artery disease and smoking history.[25] Patients with certain comorbidities are often categorized as expanded criteria donors (ECDs) due to the increased risk of recipient graft dysfunction.[26] This should not be overlooked given the already large gap between organs available and increasing number of potential recipients.

2.2 Donation after Cardiocirculatory Death (DCD) Donors

2.2.1 History and Definition of DCD

Donation after cardiocirculatory death has faced renewed scrutiny in recent years due to its diverse ethical and legal ramifications.[27-30] While DCD was the initial form of OD, its use mainly ceased after the establishment of the definition of irreversible coma (neurological death) was brought forward by the Ad Hoc Committee of Harvard Medical School in 1968.[19] In order for DCD to proceed the patient must fulfill the cardiopulmonary criterion of death including irreversible cessation of circulation and respiration.[31] Today, DCD is described as the withdrawal of mechanical ventilation and vasoactive drugs, with observation of the patient until mechanical (no blood pressure) and electrical (asystole) cardiac standstill.

While protocols differ amongst hospitals and countries throughout the world, it is generally accepted that patients who have sustained irreversible brain damage, yet do not meet the definition of neurological brain death, are eligible to become a DCD donor if they die within 60 to 120 minutes of withdrawal of life-sustaining therapy (WLST).[31,32] The timing is dependent on both hospital specific protocol as well as accepted and/or viable organs. However, it is recommended that there is a 2 to 5 minute waiting period following cessation of cardiopulmonary function before organ procurement begins, so as to not violate the dead donor rule, which states that a person must be dead prior to organ retrieval and retrieval must not cause their death.[28,33]

2.2.2 Epidemiology of DCD Donors

Several studies in both the United States and Canada have found that the re-appearance of DCD has led to an overall increase in OD rates as well as DCD rates. In a retrospective study analyzing UNOS data, the DCD rate increased to nearly 15% of total donors in the decade when DCD was seemingly re-instituted.[34] Analysis of the UNOS database from 2001-2010, revealed that not only had deceased OD increased by nearly 20%, the percentage of DCD donors doubled in that timeframe.[35] In a similar analysis based on data from 2002 to 2014 in Ontario, Canada, an early proponent of DCD, it was also found that OD had increased within the timeframe, accompanied by a substantial increase in the number of DCD cases.[36]

2.3 Potential Donors

2.3.1 Proposed Definition and Prognostication Tool for Identification of Potential NDD Donors

In practice, it can be very difficult to predict which patients suffering from catastrophic brain injury are not only potentially eligible for OD, but also whether or not they will medically progress to a diagnosis of brain death, necessary in order for NDD donation to proceed. It has been suggested that one method of increasing the number of available organs is to retrospectively evaluate deaths to determine potential donors that may have been missed, defining their characteristics and educating HCPs on some of the habitual qualities of potential donors in hope of increasing awareness of those most likely to be converted.[37]

In 2010, de Groot and colleagues in Europe proposed the following definition of imminent brain death in order to facilitate the identification of potential donors: “A mechanically ventilated,

deeply comatose patient, admitted to an ICU, with irreversible catastrophic brain damage of known origin (e.g. TBI, subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH)).[37] A condition of imminent brain death requires either a Glasgow Coma Score (GCS) of 3 and the progressive absence of at least three out of six brainstem reflexes, or a FOUR score of $E_0M_0B_0R_0$."[37] This definition was intended to be a prognostic tool to assist in actively determining the likelihood of brain death and subsequent donation. Its additional purpose was for it to be used retrospectively in order to identify those deaths which could have led to potential OD and could then be computed into a meaningful PMD rate, available for comparison with other countries as well as for directing public health efforts. Imminent death is defined similarly by the Organ Procurement and Transplantation Network (OPTN); however, it does not include GCS as a component. Applying de Groot's proposed definition retrospectively in 2013, one Canadian study found and incidence between 3.3 and 7.5 for NDD abdominal organ donors and between 0.5 and 2.7 for NDD lung donors pmp were missed between 2008 and 2010.[38] The study also reported that only half of patient deaths audited had 3 or more brain reflexes tested and recorded, which is problematic in terms of harnessing the imminent brain death tool's full intended use. However, it also suggests that the number of potential donors missed pmp may underestimate the actual number of donors missed in the study.

2.3.2 Prognostication Tool for Identification of Potential DCD Donors

As previously mentioned, most DCD policies only permit donation of DCD donors if they die within 60 to 120 minutes of WLST. Due to the time sensitivity of DCD, countless potential donors are not procured if they do not die within the strict time requirements. This has led to a call for identification of associated and predictive factors of death in potential DCD donors. Rabinstein et al created a prognostic tool aimed at critical care physicians, to be used at the bedside, which they call the DCD-N score.[32] The score is comprised of four factors including absent cough reflex, absent corneal reflex, extensor or absent motor response to pain and oxygenation index, which involves the fraction of inspired oxygen (FiO_2) mean airway pressure (MAP) and partial pressure of oxygen in arterial blood (PaO_2). Evaluation of the tool showed that each of the aforementioned factors were significantly associated with death within 60 minutes of WLST.[32]

More recently in 2017, a multicenter, prospective Chinese study compared the performance of a new prognostic tool called the C-DCD-Nomogram to the other three published diagnostic DCD tools including Rabinstein's DCD-N score, the University of Wisconsin Donation after Cardiac Death (UWDCD) and the UNOS criteria.[39] Xu et al report that the UWDCD and utilization of UNOS criteria are very poor predictors of DCD death requirements and while the DCD-N score performed quite well (c-statistic 0.73) in predicting death within 120 minutes of WLST, it was less effective at predicting death within 30, 60 and 240 minutes of WLST.[39] Alternatively, the C-DCD-Nomogram had a c-statistic of 0.86 when predicting death within 120 minutes of WLST. It was also the best performing model compared to all those aforementioned in predicting death 30, 60 and 240 minutes following WLST.[39]

2.4 Strategies for Increasing OD

2.4.1 Expanded Criteria Donors

Expanded Criteria Donors (ECD) are loosely defined as those individuals who are not considered an ideal candidate for OD due to one or more pre-existing factors but are considered eligible donors under less restrictive criteria for the purpose of increasing the number of available organs for transplantation. To date, there is no universally accepted criteria for ECD. However, in 2002 UNOS in the United States created a working definition for kidney ECD as follows "any braindead donor ≥60 years, or 50 to 59 years with two or more of: a history of hypertension, pre-terminal serum creatinine ≥1.5 mg/dL (133 μmol/L), or death due to stroke," which has become more widely accepted.[40] There has been some hesitation regarding the use of ECD as some studies have found statistically significant differences in the survival rates between kidney ECD and standard criteria donor (SCD), with ECD having less favorable survival outcomes.[41,42] In contrast, others have found long term survival to be similar between kidney ECD and SCD and attribute much of its increased donation success to utilization of ECDs.[43] Furthermore, expanded criteria donation has been shown to decrease health care costs. The use of ECD in kidney transplantation has emerged as a more cost-effective treatment option compared to prolonged dialysis.[41] A study done by Young et al found that patients receiving an ECD kidney spent approximately five months less on dialysis prior to transplant than their non-ECD counterparts.[41] This is an important finding given that patients on prolonged dialysis have an increased risk of complication and are more costly to the health care system.[3]

Unfortunately, there is little agreement on what should compose appropriate ECD criteria for each area of transplantation. Despite this lack of consensus on all criteria, it is generally accepted that older age should not exclude an individual from becoming an organ donor. Interestingly, Young and colleagues also found that 80% of ECD were classified as such due to their old age at death.[41] This finding would suggest that there is little if anything physiologically wrong with the ECD organs of interest other than older age. ECD classified as such due to their older age have also been accepted in the lung transplantation domain. In fact, one study found no statistical survival difference at 5 years post-transplant between those patients receiving lungs from donors younger than 60 years old compared to those 60 years and older.[44] These results are encouraging for the transplant community, desperately looking for effective ways to increase the number of available transplantable organs. One variation of the age criterion of ECD has been the utilization of older donors only for older recipients. Use of this strategy, referred to as age matching, has shown promise in many hospital programs with optimal post-liver transplant survival rates.[45]

While older age garners much attention for its potential to boost OD numbers, the transplant community continues to look for other potential factors that may be exploited for this purpose. This discussion has also lead to the idea that each transplantable organ should have its own ECD criteria.[42] For example, one study suggested that sex (female), cause of death (cerebrovascular accident (CVA)), elevated sodium level, prolonged cold ischemic time and elevated gamma glutamyl transferase were acceptable factors that could potentially be included in liver ECD criteria. However, it should be noted that each of the aforementioned factors were associated with lower graft survival rates at 3 months post-transplant.[46]

2.4.2 Opt in (Explicit) and Opt Out (Presumed) Consent Systems

While Canada continues to utilize an explicit consent approach, the opt out system is gaining popularity with many countries switching to this method.[47] The presumed consent model operates under the assumption that all members of the population consent to organ donation unless they intentionally opt out.[48] There have been several studies which have found an association between the presumed consent system and increased deceased OD rates.[17] It has been suggested that the opt out system is responsible for increased donation for several reasons including creation of societal perception that consent to OD is the norm not the exception.[48]

Additionally, it has been noted that opt out systems encourage individuals to actively evaluate their views on OD and motivates them to follow up with action (ie. opt out) should they choose. In an opt in system, it is more likely that only those individuals who are strong in their conviction to become a donor will follow through with the act of registration.[48] Consequently, there is presumably a cohort of potential donors who agree with OD and are willing to participate but have not registered and therefore may not be identified should the opportunity present itself.

Those opposed to the opt out system have suggested that the model's only purpose is to increase the number of available organs, regardless of an individual's consent thereby violating their human rights, by considering their body and/or organs as functional pieces that can be removed and used to better the life of the whole population.[49] Others have also raised issue with the fact that this system diminishes the "gift of life" principle which OD was founded on, instead making it a process of supply and demand. The opt out system also creates increased potential for exploitation of both those with mental disabilities and children. Others worry about the issue of organ ownership which is inevitably brought forward as a direct result of the presumed consent system. This argument asks when one owns their organs, when their ownership ends and how ownership is then transferred.[49]

While controversy persists regarding which consent model is superior, the debate has fortunately stimulated more research regarding each system which has arguably found more similarities than differences between the two processes. In 2017, Rosenblum and colleagues discovered that countries which employed opt out systems still actively searched for denial of consent prior to proceeding with OD and often the final decision was left to next of kin. Rosenblum et al referred to this as a soft opt out system.[50] In fact, only Belgium, Finland and Sweden employ opt out systems which proceed with OD if the deceased wishes were known,, regardless of objection by next of kin.[50]

2.4.2.1 Canada: An Opt In System

Despite recent debate regarding the benefits and detriments of both opt in (explicit) and opt out (presumed) systems and their potential influences on OD rates emerging globally, Canada continues to operate under an opt in system.[48] In this explicit consent model, individuals register their intention to donate and are encouraged to discuss their wishes with their families to ease the burden of decision should it arise unexpectedly which is most commonly the case. While Canada

as a country universally employs an opt in system, it is the responsibility of each provincial/territorial government to establish a registration process amenable to their population. This has led to variability in how Canadians in different provinces and territories identify themselves as a potential donor.

In Alberta, individuals are asked about their intention to donate each time they commence or renew a driver's licence. If their intention to donate is declared, a sticker identifying them as such is placed on their licence and their assent is then entered into an Alberta electronic organ donor registry available to Organ Procurement Organizations (OPO). Alternatively, Albertans can also directly register their consent to donate through an online registry which is then available to HCPs as needed. In contrast, the other Canadian provinces use health care cards in favor of driver licences and/or an online registry in tandem in order to register consent. Residents of these provinces can call their local health authority or fill out a form indicating their intent to donate. A sticker is then placed on the individual's health care card or they are issued a new card indicating their intention to donate. It should be noted that through their OD and transplantation resources, each province highlights the importance of each person discussing their intention to donate or lack thereof with their family. This is an extremely important component, as it has been commonly noted in the literature that families are more likely to opt out, if an organ donation discussion has not taken place prior to a catastrophic event leading to OD.[51]

2.4.3 Organization of Hospital Care

Traditionally in Canada, major tertiary hospitals with intensive care and surgical units are able to offer both OD and transplantation services. When a potential OD is identified by NDD or DCD criteria the OPO is notified and begins an OD work up including diagnostic tests such as bronchoscopy, echocardiogram, biopsy, and laboratory blood work within the ICU, working with the ICU team. If the OD is identified in a smaller community hospital or a center without transplant capabilities they are transferred to a larger center appropriately. Once consent is given, studies are completed and recipients are identified, the viable organs are recovered and are allocated depending on the transplant list. This process may result in organs being allocated within the same hospital as organ recovery or hospitals across the country in which case, organs may travel hours by ground and/or plane.

In the United States Midwest, an innovative project is underway in which one hospital is exclusively responsible for OD and its associated processes.[52] Following the declaration of brain death at the presenting hospital and contingent on consent, organ donors are transferred to the organ donation hospital for work up, management and eventual procurement. The specialized hospital, which opened in 2008, has unlimited access to both laboratory services as well as diagnostic tests from CT to bronchoscopy, cardiac catheterization procedures and a dedicated operating room for organ procurement.[52] The eight years of available data show that on average, the hospital recovers nearly 30% more organs per donor overall than the national average. This includes an ECD recovery rate 18% higher than the national average, which is significant given the call to increase the donor pool by utilizing this cohort of potential donors.[52] Doyle et al also found that the facility discarded significantly less organs, which may be attributed to a more thorough work up by transplant specialists in all areas of practice from registered nurses, transplant surgeons and experienced transplant radiologists and pathologists.[52] It should also be noted that the entire OD takes significantly less time, which may ease the donor family's bereavement. Finally, from a cost savings perspective, OD at this specialized hospital costs under $14 000 compared to the OD process at a standard hospital which averages $33 000.[52]

2.5 A Brief Case Study: The Spanish Model

In the 1980s, after the World Health Assembly identified a disproportionation in the number of organs needed compared to the number of those available for transplant, member countries were urged to strengthen their specific OD and transplantation processes, specifically with respect to deceased donors.[53] In response to this plea and in anticipation of a more formal call, Spain created the Spanish National Transplant Organization (ONT), responsible for overseeing all donation and transplantation activities.[53] Three decades later, Spain is the world's leader in organ donation with 40 deceased donors pmp reached in 2015.[53] To date, much of Spain's success in OD practice is attributed to the ONT's conception and implementation of the Spanish Model of Organ Donation and Transplantation. The Spanish Model includes many important components, which other countries continue to strive for including involvement and commitment to OD at the national, regional and hospital levels, ongoing surveillance for potential donors through internal and external audits, dedicated physician transplant coordinators and focused organ donor

identification, as well as detailed education on OD and procurement practices to all involved medical personnel.[53]

While the Spanish Model is one which has been templated in other countries due to its success, the ONT has continued to strive to increase deceased OD. This has been partially perpetuated by trends also seen in other westernized countries such as Canada and the United States of decreased death rates due to traffic accidents and increased death rates due to CVA, consequently decreasing the number of potential organ donors. The ONT's response to these emerging trends was to implement a new initiative known as the 40 Donors Per Million Population Plan in 2008. Continuing the country's ingenuity in OD and transplantation, the plan has three main objectives: to increase awareness and referral of potential donors to the ICU for elective, non-therapeutic care in anticipation of donation, development of protocol related to DCD and increased acceptance of nonstandard risk donors and ECD.[53]

2.6 Deceased OD in Canada

While awareness and general acceptance of OD has increased amongst the Canadian population over the last several decades, the demand for transplantable organs continues to be substantially higher than the number of those available. In 2016, 4541 Canadians needed an organ transplant, with only 2930 people in that cohort receiving the necessitated organ(s).[54] Unfortunately, due to this discrepancy, in 2016 alone 409 patients withdrew from the transplant list because they became too ill and 260 people died on the transplant waiting list. To put this in perspective of those listed 14% became to sick to transplant or died while waiting, and approximately 21% of those listed were still in need of transplant by the end of 2016.[54] Interestingly, OD and transplantation rates are not consistent throughout Canada. While Canadian Blood Services (CBS) was tasked by the federal government to develop and implement a specific Organ Donation and Transplantation Program in 2008 to increase productivity, Canada continues to lag behind the developed world's leaders in this area.

2.6.1 Provincial and Territorial Variation in NDD and DCD rates

Across the country, provinces and territories vary in both their donation and transplant rates as well as their specific policies. In 2016, nearly half of deceased donations in Canada occurred in Ontario, 243 NDD donors and 108 DCD donors respectively. Quebec was also a large contributor, as an additional 20% of NDD and DCD donations, 140 and 30 respectively,

occurred in that province. It is hard to ignore that nearly 70% of deceased organ donors came from only 2 of the 13 Canadian provinces and territories. British Colombia and Alberta were also significant contributors to NDD donation, with 75 and 63 donors, coming from each province respectively. DCD was less common in both provinces, with 22 and 7 DCD donors each in 2016. The remaining NDD and DCD organ donors came from Saskatchewan, 13 and 1, Manitoba, 13 and 3 and the Atlantic provinces, 37 and 3, respectively.

It has been suggested that some of the variation in OD rates across the country are at least, in part, due to the difference in DCD acceptance, implementation and practice across the country.[55] From this perspective, it is not surprising that Ontario and Quebec, who were first to perform DCD in 2006 have consistently contributed the most NDD and DCD donors over the past decade.[54] BC and Northern Alberta were also swift in their implementation of DCD programs in 2008 and 2009 respectively. It should be noted that the four aforementioned provinces are the biggest in Canada from a population perspective. Nova Scotia also started its DCD program in 2006 and while the number of crude donors it contributes seems relatively small due to its small population, it held Canada's leading deceased donation rate pmp in 2015.[56]

2.6.2 Provincial and Territorial Variation in Conversion Rates

As expected, conversion rates also vary widely across the country. Conversion rate is defined as the number of potential organ donors that go on to become actual organ donors.[57] Canada's estimated potential donor rate from the period of 2008 to 2012 was 87 potential donors pmp with a conversion rate of 16%.[57] The provinces with the highest conversion rates were Quebec (21%), Nova Scotia (18%) and Ontario (16%). Interestingly, these provinces did not have the highest potential donor rates. In western and central Canada, including British Colombia (14%), Alberta (11%), Saskatchewan (10%) and Manitoba (10%) conversion rates were significantly lower.[57]

2.7 Deceased OD in Alberta

2.7.1 Legislation

As the demand for transplantable organs continues to rise, HCPs, governments, health care systems and other crucial stakeholders have created and invested in countless initiatives and legislation in an attempt to increase OD. In 2013, the Alberta government passed Bill 207, the Human Tissue and Organ Donation Amendment Act.[58] The purpose of this legislation was to

increase public awareness, acceptance and commitment to OD, as well as reform certain health care system practices in order to better identify potential organ donors. Bill 207 mandated the creation of the Human Organ and Tissue Donation Registry, an opportunity for individuals to register consent to donate their organs in a centralized system. One of the intended reverberations of the registry's creation was to encourage a public discussion of OD as well as to facilitate conversations amongst families, friends and loved ones about their views regarding donation, along with their intention or lack thereof to donate.

Bill 207 also aimed to implement concrete methods for health care professionals to identify potential organ donors in a systematic way. This new regulation required that physicians identify and document each patient's eligibility for OD prior to WLST in the medical record and to refer those eligible for OD to the organ procurement agency for assessment. Finally, it became the joint responsibility of the OD agency and/or the physician to seek consent from the patient's family or substitute decision maker (SDM). The spirit of this legislation largely echoes the sentiment of existing practices of some of the world's leaders in OD.

Chapter 3: Methods

3.1 Study Design

This is a retrospective study involving data collected from a government-initiated chart review of all deaths occurring between January 1, 2015 and December 31, 2015 in Albertan ICUs and ERs. The purpose of analysis is to differentiate those classified as PMDs from those classified as non-donors in the specified cohort.

3.2 Study Population

In total, the study cohort included 2682 patients who died in 16 hospitals province-wide in 2015. Note that age was not an exclusionary criterion in this study.

3.3 Definition of PMD and Clinical Eligibility

In this study a PMD was defined as a person who died in hospital, was clinically eligible for OD but whose family was not approached regarding OD per documentation in the patient's medical record upon retrospective review. Clinical eligibility was defined as a person who suffered severe brain damage leading to subsequent brain death or circulatory death, was mechanically ventilated near or at the time of death and had no medical contraindications to OD.

3.4 Data Collection

In Alberta, the Human Organ Procurement and Exchange Program (HOPE) is responsible for managing all OD activities. The HOPE Program has two branches: (1) Northern branch, based in Edmonton, is responsible for any centres north of Red Deer and, (2) Southern branch, based in Calgary, is responsible for any centres South of Red Deer. Both branches have highly specialized Registered Nurses (RN) dedicated to the organization of all OD and transplant activities, known as HOPE Program Coordinators. The HOPE Coordinators were responsible for collecting data from both electronic and physical patient charts from hospitals with five or more deaths in 2015 and which had an Emergency Department, ICU and/or ventilation capability.

3.4.1 Partial Chart Review

Demographic information was collected for each of the 2682 patients who died in 2015. This information included sex, hospital of death, hospital of referral (if applicable), date and time of admission and death, location and age at death. Additionally, capture of relevant clinical information included means by which death was determined and the diagnosis related to death.

3.4.2 Eligibility for Full Chart Review

Eligibility for full chart review was dependent on death diagnosis. The following categorizations of death diagnosis did not lead to a full chart review: cardiac arrest or other non-neurological, as diagnosis precluded them from becoming an organ donor. A death diagnosis of cardiac arrest, described those patients who died in the ER, were asystolic or had pulseless electrical activity (PEA) or suffered from v-tachycardia or fibrillation. Other non-neurological death diagnosis examples include metastatic cancer and septic shock. All other death diagnoses proceeded to full chart review.

3.4.2.1 Variables Collected during Full Chart Review

For those deaths qualifying for full chart review more detailed demographic and clinical information was collected. Clinically significant variables collected related to death diagnosis included use of mechanical ventilation, performance and outcome of neurological reflexes, presence of respiration, performance and outcome of apnea test, presence of motor response and eye opening and GCS.

Variables related to WLST included: rationale and documentation of WLST, decision and time of WLST, WLST action, documentation of patient's known wishes regarding OD, documentation of OPO contact, documentation of whether or not the family was approached regarding OD and if so which HCP approached them and when, which family members were present during the OD discussion, and reason for decline (if applicable).

3.5 Statistical Analysis

All statistical analysis was computed using STATA 14.2 (Stata Corp LLC, College Station, Texas, USA, 2018).

3.5.1 Descriptive Statistics

The majority of the variables of interest in this study were categorical in nature and are appropriately presented as counts and proportions. Normally distributed continuous variables are presented as means and standard deviations (SD). Non-normally distributed continuous variables are presented as medians and interquartile ranges (IQR).

3.5.2 Univariate Analysis

Univariate analysis was conducted to evaluate possible differences between PMDs and non-PMDs. Categorical variables were compared using a chi-squared test. Alternatively, if one of the two categories of interest had 5 or less observations, a two-sided Fisher's Exact Test was used. A student's t-test was utilized for parametric, continuous variables. For non-parametric, continuous variables a Mann-Whitney test was employed. A p-value of ≤ 0.05 (95% Confidence Interval (CI)) was considered statistically significant in this analysis.

3.5.3 Multivariate Analysis

Binary logistic regression was performed to identify independent associations with PMD status. Odds Ratio and 95% CI were reported for each covariate. Model performance was evaluated using Area Under Receiver Operating Characteristic Curve (AUROC) and is presented with corresponding c-statistic.

Chapter 4: Results

4.1 Patient Flow through the Alberta Healthcare System

Figure 4-1 illustrates how patients moved through the healthcare system. All 2682 patients in this study died in urban hospitals. Approximately 45% patients were referred to a non-tertiary hospital and 55% were referred to a tertiary center. Referrals occurred from rural to urban hospitals and between urban hospitals, for example from an urban non-tertiary center to an urban tertiary center. In both tertiary (n=1020) and non-tertiary (n=723) centers, most patients died in the ICU. Approximately 40% of patients in non-tertiary hospitals and 30% of patients in tertiary hospitals died in the ER. The remaining patients died on general wards or in transit (other).

The retrospective chart review was most commonly stopped if the patient death occurred in the ICU. Audit was stopped due to either non-resuscitated cardiac arrest or other non-neurological diagnosis as previously described. The audit was stopped most frequently due to non-resuscitated cardiac arrest in the ER for both tertiary (n=416) and non-tertiary (n=450) hospitals. In contrast, audit stopped most frequently in the ICU due to other non-neurological diagnoses in both tertiary (n=573) and non-tertiary (n=457) hospitals. In total, partial audit was completed for 1237 patients with a death diagnosis described as other non-neurological and 945 patients with a death diagnosis of non-resuscitated cardiac arrest.

4.2 Significant Demographic and Clinical Factors in PMDs and Non-PMDs

A summary of the univariate analysis of the demographic differences between PMDs and non-PMDs is presented in Table 4-1. PMDs were on average, younger than non-PMDs (46.7 (20.4) vs. 61.7 (21.1) years, p=0.001). There were more males than females represented in both the PMD and non-PMD groups (59% vs. 61% male, p=0.6). As expected, the majority of the audited population were adults aged 18 years and older. However, nearly one in ten PMDs and one in twenty non-PMDs were pediatric patients less than 18 years old (9.4% vs. 6.1%, p=0.2).

The majority of the audited population originated from within the province of Alberta, but 10 cases were referred from outside the province or outside the country. Approximately 17% of non-PMDs compared to 12% of PMDs were initially admitted to an urban center and then transferred to a second urban center, where they died (p=0.08). Approximately 15% of both PMDs and non-PMDs were initially admitted to a rural hospital and transferred to an urban

hospital afterwards where they went on to die (p=0.7). Referring hospital was not documented in more PMD records than in non-PMD records (3.6% vs. 0.4%, p=0.02). PMDs were far more likely to die in the ICU (90%) than in the ER (10%). More non-PMDs than PMDs died in an urban tertiary ICU, which was statistically significant (65.3% vs. 55.8%, p=0.04). However, more PMDs than non-PMDs died in an urban non-tertiary ICU (33.9% vs. 20.4%, p=0.001). There was no significant difference in the proportion of PMDs and non-PMDs dying in a tertiary or non-tertiary setting.

Cardiocirculatory criteria was used to determine death in 94% of non-PMDs compared to 81% of PMDs (p=0.001). However, neurologic clinical criteria or a combination of neurologic clinical criteria and neurologic ancillary testing was more likely to be used in death determination of PMDs than non-PMDs (8.5% vs. 1.8%, p=0.001 and 5.8% vs. 1.3%, p=0.01, respectively).

Diagnoses of TBI, subarachnoid hemorrhage, non-cerebral sepsis, cancer were similar among PMDs and non-PMDs. Anoxic encephalopathy, comprised of those dying from hanging, asphyxia, carbon monoxide poisoning and most commonly cardiac arrest, was more often diagnosed in PMDs than non-PMDs (49.1% vs. 39.5%, p=0.04). Contrarily, those suffering from hemorrhagic or ischemic stroke were more commonly non-PMDs. Interestingly, PMDs were more likely to have a drug overdose diagnosis compared to non-PMDs (p=0.07).

4.3 Significant Differences in Medical Assessments between PMDs and Non-PMDs

Table 4-2 provides a summary of the univariate analysis of medical assessments relevant to OD, including neurological reflexes and frequency of medical interventions. Nearly all PMDs in comparison to approximately three quarters of Non-PMDs were mechanically ventilated, which was statistically significant (p=0.001). There were no survivors amongst PMDs greater than 24 hours after discontinuation of mechanical ventilation. When compared to Non-PMDs, PMDs were more likely to have absent spontaneous respiration (29.60% vs. 13.67%, p=0.001) and were more likely to be apneic (11.66% vs. 2.16%, p=0. 001).

Nearly 70% of PMDs had absent pupillary light reflexes in both left and right eyes compared to 51% of non-PMDs (p=0.001). Each of the five remaining neurologic reflexes were also more likely to be absent in PMDs than in non-PMDs including corneal reflex (43.50% vs. 28.06%, p=0.003), oculocephalic reflex (OC) (31.84% vs. 16.55%, p=0.001), vestibulo-ocular (Doll's eye

or VO) reflex (19.28% vs 10.07%, p=0.019), gag reflex (40.36% vs. 30.22%, p=0.051) and cough reflex (27.80% vs. 17.27%, p=0.022). Out of 224 PMDs, 90 had three or more absent cranial reflexes compared to only 37 of 228 non-PMDs (p=0.001).

Based on the medical assessments completed, the likelihood of neither right or left PLR being tested was more common amongst PMDs than non-PMDs (68.7% vs. 50.8%, p=0.001). The likelihood of both right and left PLR being tested was also less common in PMDs compared to Non-PMDs (28.4% vs. 45.3%, p=0.002). Documentation of corneal reflex and gag reflex were only recorded in approximately 50% of both PMDs and non-PMDs records. Lack of documented testing of OC reflex was noted in 65.9% of PMD and 78.4% of non-PMD cases, which represented a statistically significant difference (p=0.01). Documentation of VO reflex was the least likely to be tested of all reflexes, with lack of documentation reported in 78.9% of PMD cases and 86.3% of non-PMD cases (p=0.07).

In addition to differences in neurologic reflexes, several motor responses to stimulation were also significantly different amongst PMDs and non-PMDs. Lack of any motor response was most commonly reported and was more likely to occur amongst PMDs compared to non-PMDs (51.6% vs. 37.4%, p=0.01). The second most common response to stimulation was extensor posturing, which was also more frequent in PMDs in comparison to non-PMDs (19.3% vs. 10.8%, p=0.03). Contrarily, flexor posturing (10.8% vs. 4.9%, p=0.04) and withdrawal responses (18.7% vs. 7.2%, p=0.001) to stimuli were more commonly observed in non-PMDs compared to PMDs. Spontaneous eye opening was also more common amongst non-PMDs than PMDs (12.2% vs. 6.3%, p=0.05). Finally, on average, Glasgow Coma Score (GCS) was higher in non-PMDs compared to PMDs (4.36 (2.05) vs. 3.69 (1.65), p=0. 001), indicating that PMDs were more comatose.

4.4 Significant Differences in WLST Processes between PMDs and Non-PMDs

Summary of univariate analysis of variables involved in the decision and action of WLST between PMDs and non-PMDs is provided in Table 4-3. There was no difference between the two groups with respect to whether or not the WLST decision was or was not documented. However, it should be noted that 12.1% of PMDs and 9.4% of non-PMDs, did not have this WLST information within their medical record at all. Brain death as the primary reason for WLST was more common amongst PMDs than non-PMDs (4.9% vs. 0.7%, p=0.03). There were

three primary methods of WLST action, which were categorized as primarily discontinuation of mechanical ventilation without extubation, primarily extubation and primarily discontinuation of hemodynamic support. There were no statistically significant differences in the aforementioned categories amongst the two groups of interest. The most common mode of WLST was extubation which occurred in 81.2% of PMDs and 86.3% of non-PMDs.

The ODO was only contacted in 0.9% of PMD cases, compared to 12.9% of non-PMD cases, which was statistically significant (p=0.001). Lack of documentation in this category was inconsequential. There were several reasons why the ODO was not contacted in the case of PMDs, the most common being that DCD was not available at the time of the audit in southern Alberta hospitals. More than 1 in 5 PMDs were not referred to the ODO due to family or Substitute Decision Maker (SDM) declining OD. Other less common reasons that PMDs were not referred to the ODO included medical instability (1.8%), Medical Examiner (ME) decline (1.4%) and MD decline (0.5%). The most common reason the ODO was not contacted in the case of non-PMDs, was lack of medical suitability for OD (45.3%). An extension of this category are those patients who did not meet institutional criteria for DCD donation, which represented 1.4% of the cohort. Other less common reasons for not contacting the ODO in non-PMDs included, family or SDM declining OD (5.04%), the patient themselves declining OD (0.7%) and the patient dying prior to WLST (1.4%).

4.5 Significant Differences in the OD Family Discussion and Consent Process in PMDs and Non-PMDs

Table 4-4 provides a summary and description of the univariate analysis involving the OD consent process including patient's known wishes regarding OD, documented reasons for not approaching the family and alternatively if the family was approached, who was involved in the OD family discussion. In nearly 20% of both PMDs and non-PMDs the family was approached regarding the possibility of OD. Conversely, approximately 51% of PMD and 60% of non-PMD families were not documented as being approached at all. Additionally, 29.60% of PMDs compared to nearly 21% of non-PMDs had no documentation regarding whether a family discussion had or had not taken place (p=0.046).

Overs 96% of PMDs and non-PMDs did not have their intentions regarding OD documented in the registry. The patient's wishes were communicated by their family in only 0.45% and 0.72%

of PMDs and non-PMDs cases. Of those categorized as PMDs only 1 patient (0.45%) had known wishes of not wanting to participate in OD, while 2.88% of those classified as Non-PMDs intended to donate but were not eligible to do so.

Of those families approached, there were no statistically significant differences in which family members were a part of the OD discussion in either PMDs nor non-PMDs. Parents were most commonly involved in family discussions regarding OD for both PMDs and non-PMDs (35.29% vs. 47.83%, p=0.279). Other family members commonly included in OD discussions for both PMDs and Non-PMDs included children (25.49% vs. 26.09%), siblings (31.37% vs. 13.04%), spouses (33.33% vs. 30.43%) and extended family which we categorized as grandparents, aunts, uncles and friends (39.22% vs. 34.78%). In nearly 50% of family discussions involving PMDs and 35% of those involving Non-PMDs, two or more of the aforementioned family members or groups of family members were involved.

4.6 Significant Time Differences in Patient Flow through the Healthcare System in PMDs and Non-PMDs

Univariate analysis of patient time flow through the healthcare system is summarized in Table 4-5 for both PMDs and non-PMDs. None of the five calculated time differences evaluated were normally distributed and therefore the median and interquartile range are reported. The median time from initial admission to hospital to the time of admission to the hospital of death was 4.1 hours (2.6-11) for PMDs and 6.6 hours (4.0-32.1) for non-PMDs (p=0.1). Non-PMDs spent more time in hospital overall, defined as the time from admission to the referring hospital to the time of death, in comparison to PMDs (4.5 days (2.0-11.6) vs. 4.0 days (1.5-8.9), p=0.2), although the difference was not statistically significant. Furthermore, time from admission to hospital of death to time of death was longer in non-PMDs than in PMDs (3.3 days (1.0-7.8) vs. 2.3 days (0.9 vs. 5.0), p=0.06), approaching borderline statistical significance.

Two additional important clinical time differences were also evaluated. The time from when WLST decision was made to the time of WLST action was longer in PMDs compared to non-PMDs (3.9 hours (0.8-14.6) vs. 1.8 hours (0.4-12.8), p=0.08). The time from admission to hospital of death to the time the decision to WLST was made was fairly short and similar amongst PMDs and non-PMDs (2.6 hours (1.1-5.8) vs. 2.6 hours (1.0-5.4), p=1.0).

4.7 Incidence of PMDs in Alberta in 2015

Out of the 2682 deaths audited in this study, 225 were identified as PMDs and were subsequently considered cases in the numerator of the incidence rate equation. In the first quarter of 2015, Alberta's total population was 4 177 527 and in the first quarter of 2016 the population was reported to be 4 206 927. To calculate the incidence rate, an average of the aforementioned populations was calculated and became the denominator of the incidence rate. A 95% CI was generated using the Poisson distribution. The study data revealed that in 2015, there were 53.7 (95% CI 40.6, 70.5) PMDs pmp in Alberta.

4.8 Independent Associations with PMD Status

A logistic regression model, presented in Table 4-6, was constructed in order to evaluate possible independent associations with categorization as a PMD. The final model included age at death, GCS and tertiary hospital of death. After adjusting for other covariates, younger age and lower GCS were independently associated with becoming a PMD. Tertiary death hospital was not independently associated with PMD status (p=0.08), after adjusting for covariates. However, there was a trend towards statistical significance. Performance of the model was evaluated using an AUROC curve. The final model had a c-statistic of 0.758.

4.9 Data Validity

Internal validity of data was seen in several locations. For example, there were no PMDs identified as having died greater than 24 hours after discontinuation of mechanical ventilation (MV). This is important, as organs are not viable for donation greater than 2 hours after WLST.

Figure 4-1 Patient Flow by Hospital and Location of Eventual Death, Eligibility for OD (Audit Continued) and Exclusion (Audit Stopped) including death diagnosis

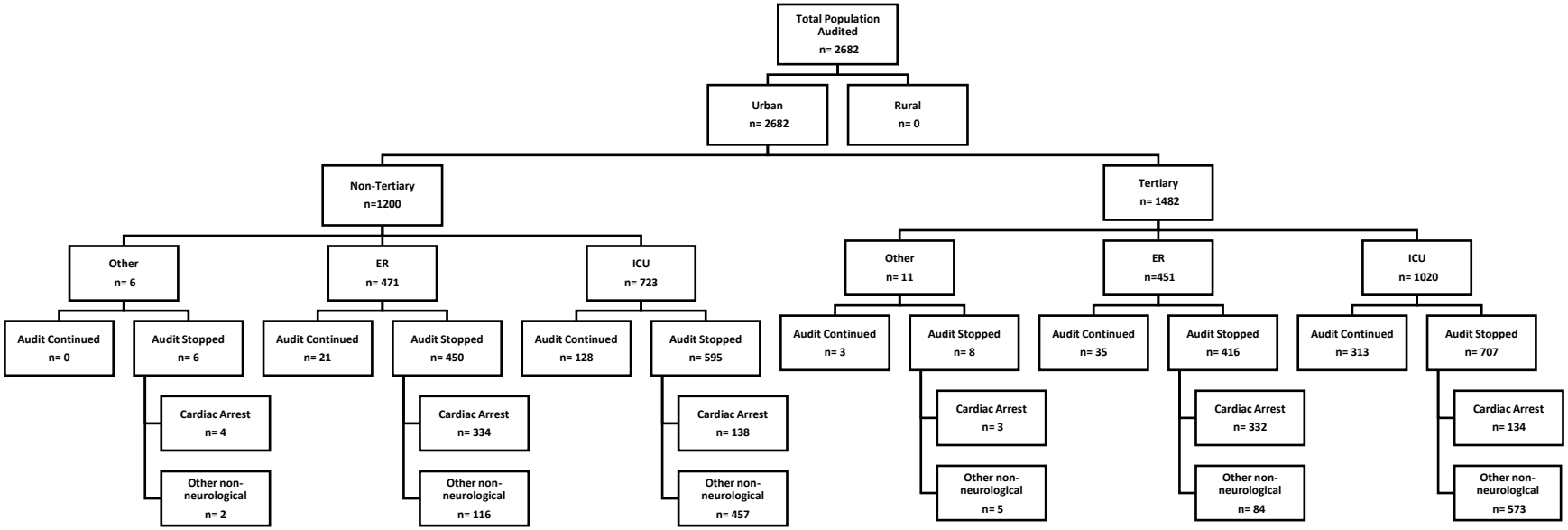


Figure 4-2 Histogram of Age at Death by Non-PMD (0) and PMD (1)

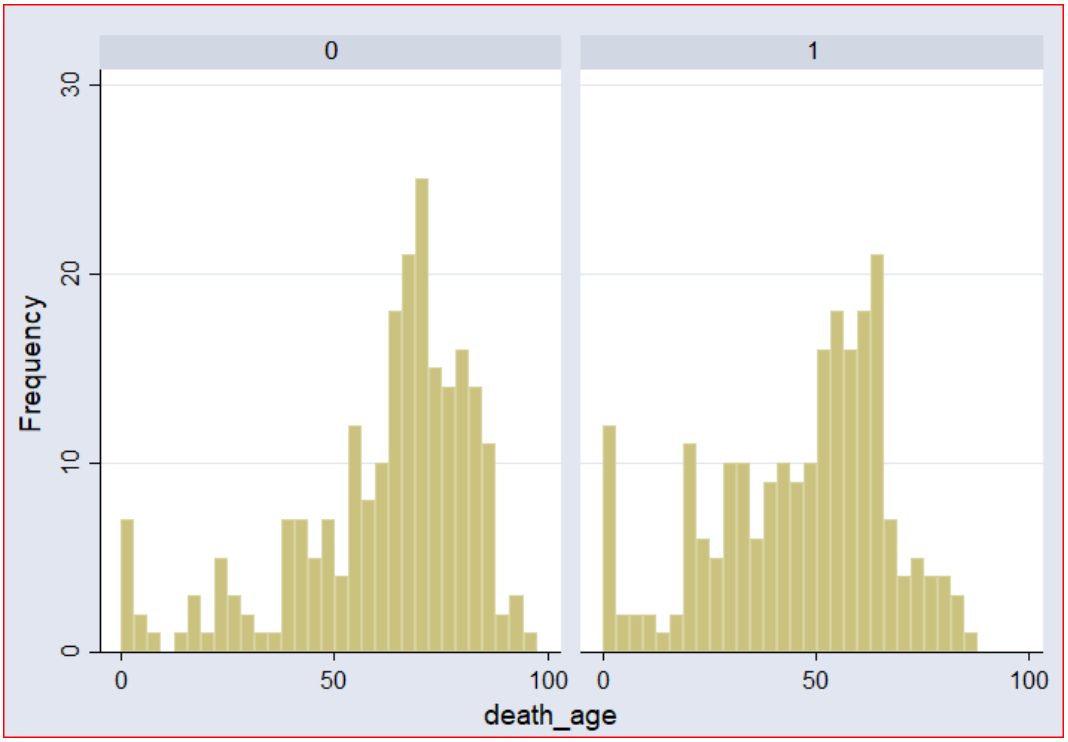


Figure 4-3 Histogram of GCS by Non-PMD (0) and PMD (1)

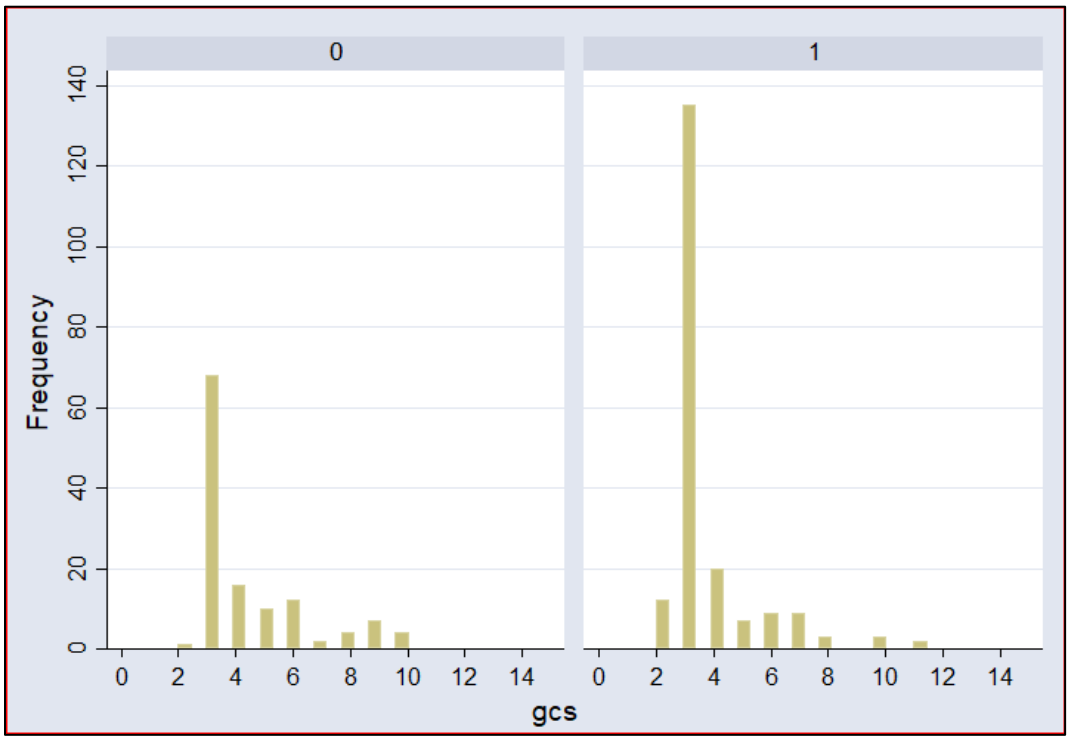


Table 4-1 Univariate Analysis of Demographic and Clinical Factors in PMDs and Non-PMDs

	Total Population Audited	n	Potential Donor	n	Not Potential Donor	p-value
Age						
	451	225	46.7 (20.4)	227	61.7 (21.1)	0.001
Male						
	452	224	132 (58.9%)	228	140 (61.4%)	0.6
Pediatric						
	452	224	21 (9.4%)	228	14 (6.1%)	0.2
Referring Hospital						
Urban	452	224	27 (12.1%)	228	41 (17.1%)	0.08
Rural	452	224	35 (15.6%)	228	33 (14.5%)	0.7
Out of Province	452	224	3 (1.3%)	228	5 (2.2%)	0.7
Out of Country	452	224	0 (0%)	228	2 (0.9%)	0.5
Not Applicable	452	224	151 (67.4%)	228	146 (64.0%)	0.5
Not documented	452	224	8 (3.6%)	228	1 (0.4%)	0.02
Hospital Site of Death						
Urban tertiary ER	449	224	16 (7.1%)	225	19 (8.4%)	0.6
Urban tertiary ICU	449	224	125 (55.8%)	225	147 (65.3%)	0.04
Urban non-tertiary ER	449	224	7 (3.1%)	225	13 (5.8%)	0.2
Urban non-tertiary ICU	449	224	76 (33.9%)	225	46 (20.4%)	0.001
Death Determination						
Cardiocirculatory Criteria	452	224	183 (81.7%)	228	215 (94.3%)	0.001
Neurologic ancillary testing	452	224	9 (4.0%)	228	6 (2.6%)	0.4
Neurologic clinical criteria	452	224	19 (8.5%)	228	4 (1.8%)	0.001
Neurologic clinical criteria and ancillary testing	452	224	13 (5.8%)	228	3 (1.3%)	0.01
Death Diagnosis						
Anoxic encephalopathy	452	224	110 (49.1%)	228	90 (39.5%)	0.04
Ischemic Stroke[1]	452	224	17 (7.6%)	228	29 (12.7%)	0.07
Hemorrhagic Stroke[2]	452	224	25 (11.2%)	228	46 (20.2%)	0.01
Subarachnoid hemorrhage	452	224	14 (6.3%)	228	9 (4.0%)	0.4
TBI	452	224	34 (15.2%)	228	28 (12.3%)	0.4
Drug Overdose	452	224	11 (4.9%)	228	4 (1.8%)	0.07
Non-cerebral sepsis	452	224	1 (0.5%)	228	2 (0.9%)	1
Meningitis/ Encephalitis	452	224	5 (2.2%)	228	3 (1.3%)	0.5
Cancer[3]	452	224	0 (0%)	228	1 (0.4%)	1
Brain tumor	452	224	1 (0.5%)	228	5 (2.2%)	0.2
Other neurological	452	224	2 (0.9%)	228	8 (3.5%)	0.1
Other cardiac	452	224	3 (1.3%)	228	1 (0.4%)	0.4
Other non-neurological and non-cardiac	452	224	1 (0.5%)	228	2 (0.9%)	1.000

[1] Ischemic stroke includes death diagnoses of infarction and cerebrovascular accident
[2] Hemorrhagic stroke includes intracranial, brainstem, intracerebral, intraventricular and cerebral hemorrhage
[3] Excludes brain cancer

Table 4-2 Univariate Analysis of Factors used in Brain Death Prognostication in PMDs and Non-PMDs

	Total Population Audited	n	Potential Donor	n	Not Potential Donor	p-value
Use of Mechanical Ventilation (MV)						
Yes	452	224	223 (99.6%)	228	172 (75.4%)	0.001
No	452	224	1 (0.5%)	228	38 (16.7%)	0.001
>24 hours from discontinuation of MV to time of death	452	224	0 (0%)	228	18 (7.9%)	0.01
Pupillary Light Reflex (Right)						
Absent	362	223	144 (64.6%)	139	69 (49.6%)	0.01
Present	362	223	59 (26.5%)	139	60 (43.2%)	0.001
Unable to Test	362	223	1 (0.5%)	139	1 (0.7%)	1
Not documented	362	223	19 (8.5%)	139	9 (6.5%)	0.5
Pupillary Light Reflex (Left)						
Absent	362	223	140 (62.8%)	139	67 (48.2%)	0.01
Present	362	223	61 (27.4%)	139	62 (44.6%)	0.001
Unable to Test	362	223	1 (0.5%)	139	0 (0%)	1
Not documented	362	223	21 (9.4%)	139	10 (7.2%)	0.5
Pupillary Light Reflex (Both)						
Neither Left or Right present	329	201	138 (68.7%)	128	65 (50.8%)	0.001
One of Left or Right present	329	201	6 (3.0%)	128	5 (3.9%)	0.7
Both Left and Right present	329	201	57 (28.4%)	128	58 (45.3%)	0.002
Corneal Reflex						
Absent	362	223	97 (43.5%)	139	39 (28.1%)	0.003
Present	362	223	20 (9.0%)	139	25 (18.0%)	0.01
Unable to Test	362	223	2 (0.9%)	139	2 (1.4%)	0.6
Not documented	362	223	104 (46.6%)	139	73 (52.5%)	0.3
OC Reflex						
Absent	362	223	71 (31.8%)	139	23 (16.6%)	0.001
Present	362	223	4 (1.8%)	139	6 (4.3%)	0.2
Unable to Test	362	223	1 (0.5%)	139	1 (0.7%)	1
Not documented	362	223	147 (65.9%)	139	109 (78.4%)	0.01
VO Reflex						
Absent	362	223	43 (19.3%)	139	14 (10.17%)	0.02
Present	362	223	2 (0.9%)	139	4 (2.9%)	0.2
Unable to Test	362	223	2 (0.9%)	139	1 (0.7%)	1.000
Not documented	362	223	176 (78.9%)	139	120 (86.3%)	0.08
Gag Reflex						
Absent	362	223	90 (40.7%)	139	42 (30.2%)	0.05
Present	362	223	15 (6.7%)	139	18 (13.0%)	0.05
Unable to Test	362	223	1 (0.5%)	139	3 (2.2%)	0.2
Not documented	362	223	117 (52.5%)	139	76 (54.68%)	0.7
Cough Reflex						
Absent	362	223	62 (27.8%)	139	24 (17.3%)	0.02
Present	362	223	24 (10.8%)	139	24 (17.3%)	0.08
Unable to Test	362	223	2 (0.9%)	139	1 (0.7%)	1
Not documented	362	223	135 (60.5%)	139	90 (64.8%)	0.4

	Total Population Audited	**n**	**Potential Donor**	**n**	**Not Potential Donor**	**p-value**
Three or more Absent Cranial Nerve Reflexes						
Yes	452	224	90 (40.2%)	228	37 (16.2%)	0.001
Spontaneous Respiration						
Absent	362	223	66 (29.6%)	139	19 (13.7%)	0.001
Present	362	223	91 (40.8%)	139	98 (70.5%)	0.001
Unable to Test	362	223	2 (0.9%)	139	0 (0%)	0.5
Not documented	362	223	64 (28.7%)	139	22 (15.8%)	0.01
Apnea Test						
Apneic	362	223	26 (11.7%)	139	3 (2.2%)	0.001
Not Apneic	362	223	22 (9.9%)	139	17 (12.2%)	0.5
Aborted	362	223	1 (05.0%)	139	0 (0%)	1
Unable to Test	362	223	5 (2.2%)	139	4 (2.9%)	0.7
Not Documented	362	223	169 (75.8%)	139	115 (82.7%)	0.1
Best Motor Response to stimulation within 24 hours						
None	362	223	115 (51.6%)	139	52 (37.4%)	0.01
Extensor Posturing	362	223	43 (19.3%)	139	15 (10.8%)	0.03
Flexor Posturing	362	223	11 (4.9%)	139	15 (10.8%)	0.04
Following Commands	362	223	11 (4.9%)	139	5 (3.6%)	0.6
Localization	362	223	10 (4.5%)	139	13 (9.4%)	0.07
Withdrawal Response	362	223	16 (7.2%)	139	26 (18.7%)	0.001
Not documented	362	223	17 (7.6%)	139	11 (7.9%)	0.9
Eye opening						
None	362	223	178 (79.8%)	139	99 (71.2%)	0.06
Spontaneous	362	223	14 (6.3%)	139	17 (12.2%)	0.05
To Pain	362	223	16 (7.2%)	139	11 (7.9%)	0.8
To Voice	362	223	2 (0.9%)	139	5 (3.6%)	0.1
Not documented	362	223	13 (5.8%)	139	7 (5.0%)	0.7
Glasgow Coma Score (GCS)						
	324	200	3.69 (1.65)	124	4.36 (2.05)	0.001

Table 4-3 Univariate Analysis of Factors involved in WLST decision and action in PMDs and Non-PMDs

	Total Population Audited	n	Potential Donor	n	Not Potential Donor	p-value
WLST decision documented						
Yes	362	223	196 (87.9%)	139	126 (90.7%)	0.4
No	362	223	13 (5.8%)	139	6 (4.3%)	0.5
Not applicable	362	223	14 (6.3%)	139	7 (5.0%)	0.6
Primary Reason for WLST intervention based on Neurological Criteria						
Brain Dead	362	223	11 (4.9%)	139	1 (0.7%)	0.03
Not Brain Dead	362	223	189 (84.8%)	139	126 (90.7%)	0.1
Not applicable	362	223	14 (6.3%)	139	8 (5.8%)	0.8
Not documented	362	223	9 (4.0%)	139	4 (2.9%)	0.8
Primary Reason for WLST based on Patient Stability						
Supportable	362	223	193 (86.6%)	139	125 (89.93%)	0.338
Not Supportable	362	223	7 (3.1%)	139	2 (1.4%)	0.4
Not applicable	362	223	14 (6.3%)	139	8 (5.8%)	0.8
Not documented	362	223	9 (4.0%)	139	4 (2.9%)	0.8
WLST Action						
Primarily Discontinuation of Mechanical Ventilation	326	197	32 (16.2%)	129	16 (12.4%)	0.3
Primarily Extubation	326	197	160 (81.2%)	129	109 (84.5%)	0.5
Primarily Discontinuation of Hemodynamic Support	326	197	5 (2.5%)	129	4 (3.1%)	0.7
ODO Contacted						
Yes	362	223	2 (0.9%)	139	18 (13.0%)	0.001
No	362	223	219 (98.2%)	139	120 (86.3%)	0.001
Not documented	362	223	2 (0.9%)	139	1 (0.7%)	1
Reason ODO not contacted						
Not documented	362	223	98 (44.0%)	139	29 (20.9%)	0.001
DCD not available	362	223	60 (26.9%)	139	13 (9.4%)	0.001
Medically unsuitable	362	223	6 (2.7%)[1]	139	63 (45.3%)	0.001
Not applicable	362	223	6 (2.7%)	139	22 (15.8%)	0.001
Family or SDM declined	362	223	45 (20.2%)	139	7 (5.0%)	0.001
Patient unstable	362	223	4 (1.8%)	139	0 (0%)	0.3
Medical Examiner declined	362	223	3 (1.4%)	139	0 (0%)	0.3
MD Declined	362	223	1 (0.5%)	139	0 (0%)	1
Didn't meet institutional criteria for DCD	362	223	0 (0%)	139	2 (1.4%)	0.1
Patient declined	362	223	0 (0%)	139	1 (0.7%)	0.4
Patient died prior to WLST	362	223	0 (0%)	139	2 (1.4%)	0.1

	Total Population Audited	n	Potential Donor	n	Not Potential Donor	p-value
Reason ODO not contacted based on organ condition						
Medically suitable	362	223	28 (12.6%)	139	0 (0%)	0.001
Unsupportable	362	223	4 (1.8%)	139	2 (1.4%)	1
Medically Unsuitable: Organs suitable but patient died >2hrs after	362	223	30 (13.5%)	139	7 (5.0%)	0.01
Medically Unsuitable: Organs not suitable due to age, organ condition	362	223	10 (4.5%)[1]	139	73 (52.5%)	0.001
Organs declined (Family, SDM, MD, ME)	362	223	47 (21.1%)	139	6 (4.3%)	0.001
Not applicable	362	223	6 (2.7%)	139	22 (15.8%)	0.001
Not documented	362	223	98 (44.0%)	139	29 (20.9%)	0.001
Medical Examiner approval						
Yes	362	223	6 (2.7%)	139	8 (5.8%)	0.1
No	362	223	47 (21.1%)	139	19 (13.7%)	0.08
Not documented	362	223	170 (76.2%)	139	112 (80.6%)	0.3

[1]Patients miscoded into these categories

Table 4-4 Univariate Analysis of Family Discussion and Consent Process regarding OD in PMDs and Non-PMDs

	Total Population Audited	n	Potential Donor	n	Not Potential Donor	p-value
Family Approached regarding OD						
Yes	362	223	43 (19.3%)	139	27 (19.4%)	0.9
No	362	223	114 (51.1%)	139	84 (60.4%)	0.08
Not documented	362	223	66 (29.6%)	139	28 (20.1%)	0.05
Patients Documented Wishes Regarding OD						
None documented	362	223	221 (99.1%)	139	134 (96.4%)	0.1
Family Discussion	362	223	1 (0.5%)	139	1 (0.7%)	1.000
Did not want to donate	362	223	1 (0.5%)	139	0 (0%)	1.000
Intended to donate	362	223	0 (0%)	139	4 (2.9%)	0.02
Reason Family Not Approached						
Medically Suitable	362	223	30 (13.5%)	139	3 (2.2%)[1]	0.001
Unsupportable[2]	362	223	5 (2.2%)	139	1 (0.7%)	0.4
Medically Unsuitable: Organs suitable but patient died >2hrs after	362	223	24 (10.8%)	139	35 (25.2%)	0.001
Medically Unsuitable: Organs not suitable due to age, organ condition	362	223	9 (4.0%)	139	41 (29.5%)	0.001
Organs declined (Family, SDM, MD, ME)	362	223	9 (4.0%)	139	2 (1.4%)	0.2
Not applicable	362	223	50 (22.4%)	139	40 (28.8%)	0.2
Not documented	362	223	96 (43.1%)	139	17 (12.2%)	0.001
Reason consent for OD was not Obtained						
Declined	362	223	23 (10.3%)	139	10 (7.2%)	0.3
Medically unsuitable	362	223	0 (0%)	139	7 (5.0%)	0.001
Unsupportable	362	223	0 (0%)	139	1 (0.7%)	0.4
Family not approached	362	223	2 (0.9%)	139	0 (0%)	0.5
Not applicable	362	223	150 (67.3%)	139	118 (84.9%)	0.001
Not documented	362	223	48 (21.5%)	139	3 (2.2%)	0.001
Which Family Members were present during OD discussion						
Parent	74	51	18 (35.3%)	23	11 (47.83%)	0.3
Child	74	51	13 (25.5%)	23	6 (26.09%)	1
Sibling	74	51	16 (31.4%)	23	3 (13.04%)	0.1
Spouse	74	51	17 (33.3%)	23	7 (30.43%)	0.8
Extended Family	74	51	20 (39.2%)	23	8 (34.78%)	0.7
Two or more of above	74	51	24 (47.1%)	23	8 (34.78%)	0.3
Consent Obtained						
Yes	362	223	0 (0%)	139	7 (5.0%)	0.001
No	362	223	220 (98.7%)	139	129 (92.8%)	0.01
Not documented	362	223	3 (1.4%)	139	3 (2.2%)	0.7

[1] Patients miscoded into these categories
[2]Defined as refractory hemodynamic shock or hypoxemia

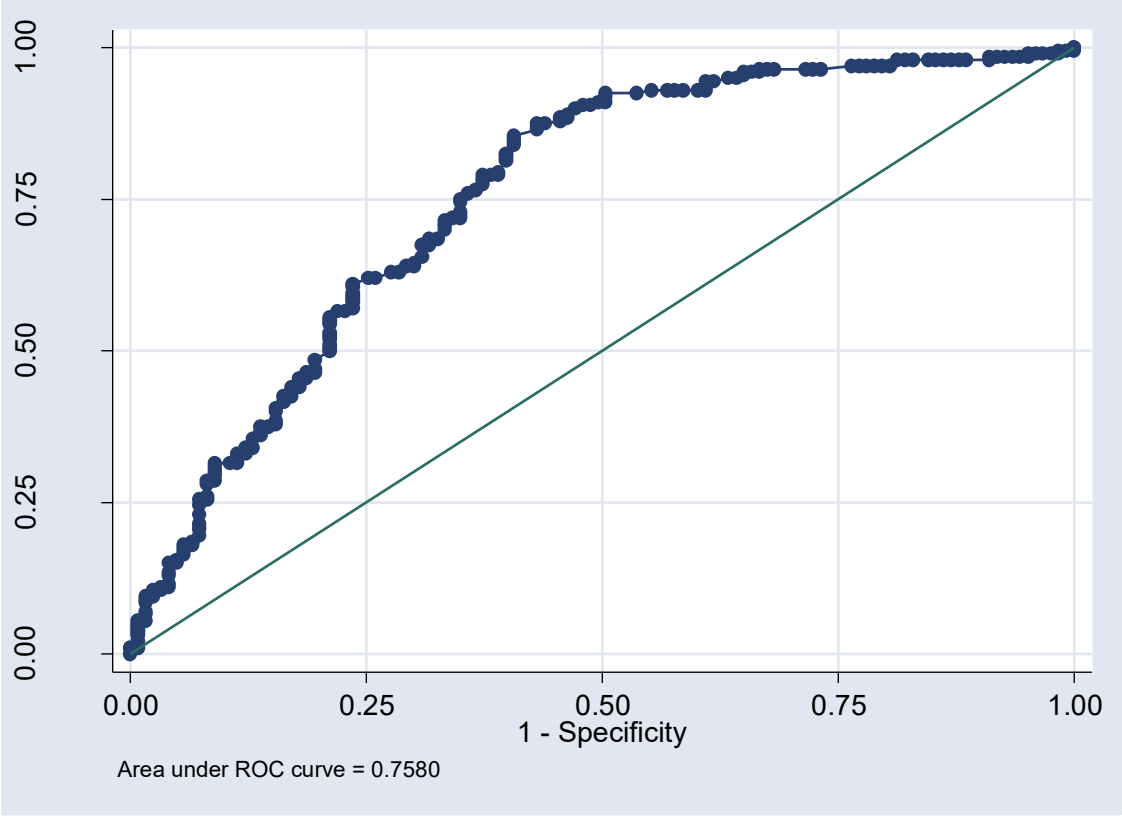
Table 4-5 Univariate Analysis of Clinically Significant Time Differences in PMDs and Non-PMDs

	Total Population Audited	**n**	**Potential Donor**	**n**	**Not Potential Donor**	**p-value**
Time from admission to referring hospital to time of admission to death hospital, in hours	134	62	4.1 (2.6-11.0)	72	6.6 (4.0-32.1)	0.01
Time from admission to referring hospital to time of death, in hours	134	62	95.8 (34.9- 212.3)	72	107.73 (48.4-277.1)	0.19
Time from admission to death hospital to time of death, in days	452	224	2.3 (0.9-5.0)	228	3.3 (1.0-7.8)	0.06
Time from WLST decision to time of WLST action, in hours	299	180	3.9 (0.8-14.6)	119	1.8 (0.4-12.8)	0.08
Time from admission to death hospital to WLST decision, in hours	297	177	2.6 (1.1-5.8)	120	2.6 (1.0-5.4)	0.95

Table 4-6 Logistic Regression Evaluating Independent Associations with PMD Status

Covariate	n	Unadjusted OR (95% CI)	p-value	n	Adjusted OR (95% CI)	p-value
Age at death	451	0.97 (0.96-0.98)	<0.001	323	0.96 (0.94-0.97)	<0.001
GCS	324	0.82 (0.72-0.93)	0.002	323	0.87 (0.76-0.99)	0.04
Tertiary Death Hospital	452	0.59 (0.40-0.89)	0.01	323	0.59 (0.33-1.07)	0.08

Figure 4-4 Area Under the Receiver Operating Characteristic (AUROC) Curve Evaluating Model Performance of Logistic Regression



Chapter 5: Discussion

5.1 Key Findings

5.1.1 Incidence of PMDs in Alberta in 2015

In our study, we identified the incidence of PMDs in 2015 to be 53.7 pmp (95% CI 40.6, 70.5). Interestingly, CBS reported the actual incidence of deceased OD nation wide to be 18 pmp in 2015.[56] In comparison, one study estimated Australia's incidence of PMDs to be 30 pmp.[59] Similarly research out of the United Kingdom has suggested their maximum potential NDD donation rate is 23.2 pmp.[60] While the incidence calculated in this study is significantly higher then those reported from Australia and the United Kingdom, it should be noted that these estimates relatively small compared to others. For example, in 2017, Spain became the first country worldwide to reach 40 donors pmp.[53] This provides evidence that the upper threshold of deceased donation has not been reached and our study in concert with these findings indicates that there is certainly room for growth and significant improvement. Additionally, in this context our results suggest that the incidence of deceased donation in Canada could see marked improvement if appropriate resources are allocated to the improvement of identification, referral and conversion of PMDs.

5.1.2 Independent Associations with PMD Status

In the present study we found that younger age and lower GCS were independently associated with PMD status, after adjusting for covariates. Per one-year increase in age, the odds of becoming a PMD decreased by 4%. This suggests that younger people have significantly higher odds of being missed as a potential donor than do older people. Given this information, HCPs should be attentive to this and ensure that younger people are very carefully screened for potentiality of OD. Additionally, per one unit increase in GCS, the odds of becoming a PMD decreased by 15%. We also noted that over 83% of PMD had a GCS less than or equal to 4. This is a significant finding as it has previously been suggested in the literature that screening for potential donors should be triggered with a GCS of less than or equal to 3.[61] Given our results we suggest a GCS of less than or equal to 4 be considered the threshold for future surveillance triggers. The independent association between urban tertiary hospital and PMD status was marginally significant (p=0.08) in the model after adjusting for covariates. This would indicate that dying in an urban non-tertiary hospital increased the odds of becoming a PMD by 69%. This

statistical trend towards significance should not be discounted and identifies an area where resources towards increasing donor identification would be most effective.

5.1.3 Importance of Improvement of Potential Donor Identification in Urban ICUs

Univariate analysis revealed that most potential donors, 125 of 225 patients in this study, were missed in urban tertiary ICUs. This is an interesting finding, as presumably, urban tertiary ICUs are most likely to have the appropriate infrastructure to identify, manage and convert donors, with access to donation and transplant experts, surgical suites and surgical personnel. This idea is reinforced by a Canadian cohort study which found that actual OD was four times as likely to occur in transplant hospitals with a designated transplant service than in large general hospitals without a specific transplant unit.[62] We speculate that many donors are missed or may be purposely overlooked in the urban tertiary ICU setting as patient volume is often high in terms of HCP to patient ratio and OD is taxing on hospital resources from a cost, personnel and space (ie, ICU beds and surgical suite) perspective. This is not a new idea, as one Dutch study reported that 10% of physicians surveyed did not pursue an OD discussion with family or SDM because they were too busy.[63] It has also been previously reported that a substantial proportion of ICU physicians favor admission and treatment of individual critically ill patients with poor prognosis who are unlikely to benefit from aggressive care over management of donors with the potential to benefit several patients waiting for transplant.[64]

From a healthcare cost and resource distribution perspective the most substantial opportunity for gain in increasing identification of missed donors are within urban non-tertiary ICUs. With 76 of 225 potential donors missed in this setting in 2015, there may be greater opportunity for improvement in this area. It should also be noted that more PMDs than non-PMDs died in an urban non-tertiary ICU, whereas less PMDs than non-PMDs died in urban tertiary ICUs. This would indicate that identification of donors is better in tertiary ICUs, or there is a referral bias of PMDs to tertiary ICUs, though we suspect the latter is unlikely. Improving identification of donors in non-tertiary hospitals may include more substantial OD training and education of all HCPs involved from physicians to registered nurses. Support for this strategy is advocated by previous findings from one Polish study which reported that physicians practising in areas with low donation rates were less confident and less likely to diagnosis brain death than those physicians practicing in places with high donation rates.[65] This is significant as lack of

declaration of brain death automatically precludes NDD donation. Another American cross-sectional study surveyed medical residents and fellows at a large transplant center and report that knowledge regarding guidelines for potential donor management and knowledge of OD in general was significantly lacking.[66]

In order to reduce the number of PMDs, many hospitals have also instituted specific OD units and/or physician and nurse donation specialists within their centers. For example, in one Quebec hospital, a specialized OD and procurement unit was developed within the center's existing ICU structure.[67] This ensured 24-hour access to specialized OD physicians and nurses as well as unlimited access to both ICU beds for management as well as operating rooms for procurement. This OD unit was able to transplant a remarkable 124.6 people per million which was substantially greater than the nearly 54 people per million transplanted in all of Quebec over the same period of time.[67] In hospitals where an OD unit is not necessarily possible, it has been brought forward that potential organ donors can be identified and managed by specialists in the ICU setting, as critical care principles also apply to organ donor management and lead to increases organ yield.[68] In Canada, it is recognized that donation physicians are invaluable resources that educate, support and implement OD practices and they have been instituted throughout the country.[56] Based on our findings, it would appear that donation physicians may be optimally placed in urban non-tertiary ICUs to have the greatest effect.

5.1.4 Emergence of Changing Potential Donor Pool Demographic

As shown in many recent North American studies, the demographic of the potential donor pool has changed significantly in recent years. In our study, death diagnosis of anoxic encephalopathy had the highest incidence amongst PMDs, with nearly 50% of this group succumbing due to same. This is consistent with a recent cohort study performed in southern Alberta which showed anoxic brain injury had increased from 14-37% in 2000 to 46-80% by 2014.[23] Additionally, our study found that 15% of PMDs died of TBI which is also congruent with Kramer's study, where they found TBI decreased from >30% in the early 2000s to 6-23% in the period from 2012 to 2014.[23] From a public health perspective this is reinforced by the current aging structure of the Canadian population. With life expectancy rising and an increasingly large cohort of Canadians reaching both elderly and middle age, anoxic encephalopathy from cardiac arrest is more likely than in the past. Our findings suggest that patients with a diagnosis of anoxic

encephalopathy should not be discounted as potential organ donors and this is an area where identification and consent of donors could be improved moving forward.

Our study also found a statistically significant difference in the number of patients suffering from a death diagnosis of drug overdose, accounting for 4.91% of PMDs and 1.75% of Non-PMDs. This is a very significant finding due to the emergence of the opioid crisis in recent years and suggests there may be a knowledge gap or unconscious bias against drug and overdose related deaths and their viability for OD amongst HCPs. Another explanation could be that overdose death are more likely to die from cardiac arrest, making them more suitable as a PMD that other non-neurological forms of death with preclude them from OD. One American study, highlighted the increasing incidence of this category, reporting that the number of drug overdoses leading to OD increased from 138 in 2003 to 625 in 2014, a marked 350%.[69] The study also found that utilization of livers from organ donors who suffered a drug overdose led to increased graft survival in comparison to donors with a diagnosis of cardiovascular disease.[69] Despite positive outcomes, HCPs and recipients alike are hesitant to accept organs from these donors, often classified by Public Health Service (PHS) "increased risk." However, Goldberg and colleagues note that while this terminology is being applied to organ donors suffering from drug overdose, in reality the term is used to describe those with risk factors associated with increased risk of Human Immunodeficiency Virus (HIV), Hepatitis C (HCV) and Hepatitis B (HBV), few of which ever lead to disease transmission.[69]

5.1.5 Importance of Reinforcing Legislated Documentation in Alberta

Despite provincial legislation implemented in Alberta in 2013, requiring determination of OD eligibility prior to WLST and documentation of same, our study found that there continues to be lack of documentation in the patient record.[58] Of all charts undergoing full audit, a combined 11% irrespective of PMD status did not have this information recorded anywhere in the medical record, two years following Bill 207's implementation. This finding is very concerning from a patient care and quality assurance perspective. Accountability of this documentation lies mainly with physicians who as a professional group are largely autonomous. Therefore, the use of retrospective chart audits, likely remains the most effective method for identifying lack of adherence to this component of Bill 207 and for evaluating future progress as well as assessing the need for further intervention moving forward.

Another component of the Human Tissue and Organ Donation Act necessitates the referral of all eligible patients for review to the designated ODO.[58] In our study, referral should not have occurred in any PMD by definition. It should be noted that our data revealed that 1% of PMDs were referred to the ODO and missed on other grounds. Nonetheless, non-compliance to this particular element of the Bill is problematic as it identifies a large systematic gap in the process of identification of potential donors. Lack of referral to the ODO may be perpetuated for several reasons including lack of knowledge of physicians on OD eligibility, lack of willingness to seek advice from ODO personnel, and personal bias in the way of negative view of OD and/or it's associated practices. It could be argued that each of the aforementioned plausible causes for lack of referral could be positively influenced by increased OD education.

The last HCP-related responsibility outlined in Bill 207 is seeking consent for OD from the family or SDM of the potential donor.[58] It is the noted that seeking consent is considered the joint responsibility of both treating physicians and the ODO. Our study revealed that consent for OD was sought in just under 20% of both PMD and Non-PMD cases. Again, this reveals a significant departure from best practice which may be perpetuated by lack of referral to the ODO in the first place. The attitude, preference and practice of the treating physician are likely the most influential factors in seeking consent as their decisions determine whether or not the ODO becomes involved and if so at what point in the treatment process.

5.1.6 Importance of Public Awareness of Alberta Donor Registry

Bill 207 also called for the implementation of OD registration infrastructure in the form of a donor registration system allowing the public to document their informed consent online or when renewing their driver's licence.[58] Through the present chart audit, we discovered that nearly 98% of PMDs and non-PMDs did not have their consent registered in the online donor registry. Lack of the donor registry's impact in this study is consistent with a report published by CBS that showed two years after commencing in 2014, only 7% of Albertans were registered as organ donors.[56] Willingness to register to donate in Alberta pales in comparison to eastern Canadian provinces like Nova Scotia, Quebec and Ontario whose OD registration totals 52%, 32% and 29% of their respective provincial populations.[56] In 2012, Rosenblum and colleagues reported that only 12% of the Canadian population had registered their intent to donate.[50] This accounted

for less than half the proportion of other developed countries such as New Zealand (51%), the United States (39%) and Australia (32%).[50]

CBS has reported awareness of a growing desire for a consistent, nationwide OD registry in preference to the current system which differs provincially.[56] Other countries have encouraged OD consent registration by giving priority to registered donors and families on the transplant list should the need arise and by mandating that all citizens declare their OD intention at the time of driver's licence issuance.[50] While Canada remains a collection of provincially run opt in systems, public health awareness campaigns may be warranted in an effort increase in OD registration. One randomized study underway in Ontario, is studying the effectiveness of education of OD registration at family physicians' offices and its plausibility in promoting awareness and subsequent OD registration through the online registry.[70]

5.1.7 The Impact of the Family and SDM in the Decision to Donate

It is well documented in the literature that a potential organ donor's family is the most influential component of the OD decision and is an area of focus in the effort to increase donation rates. In this study we found that 10.31% and 7.19% of PMD and non-PMDs families, respectfully, refused OD consent. The presented findings may represent an underestimation of the actual refusal rate, due to the lack of documentation and inaccurate coding in this category, however they still represent a significant cohort. In a retrospective study of neuro-ICUs in Denmark, Thybo et al found that lack of consent by the potential donor's family occurred in over 40% of cases.[71] With so many useful organs not being utilized, many in the transplant field have identified factors which seem to guide family decisions. Consistent influential factors which are well documented in the literature include understanding of brain death, known wishes and previous discussion regarding OD with the deceased, previous knowledge of OD through public health initiatives and professionalism and care shown by the treating HCPs involved in both end of life care, as well as OD consultation.[72-75] Collectively with our findings, as well as other literature suggest resources be allocated towards public health campaigns aimed at the public as well as further education of HCPs regarding donation and best practice when approaching families, in an effort to reduce high refusal rates.

Through the chart audit, we were also able to ascertain which family members were approached as part of the OD discussion. We were surprised to find that there was no one predominant class

of next of kin approached for consent. Parents, spouses, children, siblings, and extended family were all commonly a part of these discussions if not a combination of two or more of the aforementioned groups. This is an important finding for targeting public health campaigns regarding donor registry and OD, as it highlights the importance of ensuring that all members of an individual's family are aware of stance or intention with respect to OD. In a qualitative study of families who had been approached regarding OD of a loved one without registered donation wishes, de Groot et al found that rationale for refusal was often that the deceased wishes regarding OD were unknown and the family did not speak openly about OD in general.[74] In one UK study, Morgan et al also found that even when the potential donor was registered to donate, over a 3 year period, the deceased's family overrode their consent.[76] These findings highlight the importance of reminding the public through educational campaigns to discuss their wishes with all members of their family, so that their intentions are well known and there is no undue pressure or resistance from any members.

5.2 Limitations of the Study

While this study certainly presents several important and applicable clinical findings, the results should be considered within the following limitations. This study is both cross-sectional and retrospective in nature which introduces potential bias, specifically selection and information bias. Additionally, the definition of a PMD in this study is pragmatic and this audit was deliberately designed to be over-sensitive in order to avoid missing any potential donors over the course of the audit. Classification of PMD outcome in the current study was assigned by specialized HOPE RN coordinators, who were instructed to err on the side of inclusion in terms of their assignment of PMD, which may have led to additional bias and over-estimation of the true number of PMDs. Verification of PMD plausibility is currently being validated by MD donation specialists for quality assurance purposes. This study did reveal many areas for improvement in terms of documentation within the medical record. Consequently, as demonstrated in statistical analysis, there is a significant amount of missing data which could lead to misrepresentation of the actual clinical picture.

5.3 Future Directions

As previously mentioned, the literature currently available in the area of identifying PMDs as a method of increasing deceased donation is relatively sparse and has only recently emerged. With

Canada's modest deceased donation rates, there is much ground to be gained by undertaking further audits in each province to evaluate areas where potential donors may be missed and how corrective steps might be implemented in an effort to prevent these oversights. Compilation of complete provincial findings would be useful in identifying areas where national health care resources in terms of funds and personnel would be best utilized, for example in non-tertiary urban hospitals, on public awareness campaigns and on additional physician and HCP OD training and education. Additionally, while in this study we were able to identify several independent associations with PMD status, further work is required to recognize other potential associations, including physiological state (ie. laboratory values, co-morbidities) of the potential donor for a more clear and complete clinical picture. Finally, this study was a retrospective chart review and as such had a significant number of missing values, in part due to lack of documentation. In this respect, a prospective study design would enable more consistent, complete and potentially more accurate data and should be utilized moving forward.

Chapter 6: Conclusion

In this retrospective, cross-sectional study of all deaths occurring in Alberta ERs and ICUs, we determined that the incidence of PMDs was 53.7 (95% CI 40.6, 70.5) pmp in 2015. This suggests that there is an unexploited cohort, which could provide a substantial number of viable organs, to help address the consistent shortage of organs needed. Younger age and lower GCS, were found to be independently associated with PMD status after adjusting for covariates. Tertiary hospital was marginally significant in the logistic regression model. Therefore, we suggest that allocation of resources would be best utilized to improve identification and consent of patients under 70 years of age with a GCS of less than 4 admitted to urban non-tertiary ICUs. With funds allocated to the aforementioned demographic and investment in additional research to identify further factors associated with PMDs, increased deceased donation rates could be observed nationwide.

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Appendix

ALBERTA ORGAN AND TISSUE DONATION AGENCY

STANDARD OPERATING PROCEDURE
CHART REVIEW METHODOLOGY
ALBERTA POTENTIAL DONOR AUDIT

This information supplements the Training Manual developed for the Alberta Potential Donor Audit

May 2016

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Objective

The Alberta Organ and Tissue Donation Agency has received approval from Alberta Health Services (AHS) and Covenant Health to allow AHS chart reviewers to collect data on patient deaths in their hospitals.

The purpose of this data collection is to establish an accurate measure of potential organ donors across the province and organ utilization. Data will inform if and where potential donors are missed and will enable evidence–informed initiatives to minimize missed opportunities.

Data will inform discussions focused to potential donor identification methods or areas for other improvements in the organ donation process.

Data collection will consider only solid organ donation from deceased donors. It will focus on donation potential for "Donation after Cardiocirculatory Death" (DCD) as well as "Donation after Neurological Determination of Death" (NDD).

An audit of tissue donors will be completed in a subsequent phase of the Alberta Potential Donor Audit.

In-Scope Hospitals

The hospitals with ventilation capacity where the potential donor audit will be conducted are:

- Calgary Zone
  - Alberta Children's Hospital
  - Foothills Medical Centre
  - Peter Lougheed Centre
  - Rockyview General Hospital
  - South Health Campus

- Edmonton Zone
  - Royal Alexandra Hospital
  - Stollery Children's Hospital
  - Sturgeon Community Hospital
  - University of Alberta Hospital

- Regional Hospitals
  - Red Deer Regional Hospital (Central)
  - Northern Lights Regional Health Centre (North)*
  - Queen Elizabeth II Hospital (North)

- Chinook Regional Hospital (South)
- Medicine Hat Regional Hospital (South)

- Covenant Health Hospitals
  - Grey Nuns Community Hospital
  - Misericordia Community Hospital

*Due to the wildfire issues experienced by Fort McMurray, we will determine when the reviews of charts at this location will occur depending on the hospital's ability to enable this activity and other logistics.

Charts for Review

Data will be extracted from hospital charts by trained Chart Reviewers. All in-hospital deaths from January 1, 2015 to December 31, 2015 will be reviewed.

1. Hospital chart of deceased patients

- All patient deaths in in-scope hospital units with ventilation capacity will be reviewed
- Request and obtain a list of charts for all patient deaths in all ventilated units. This list will include
  - Deaths in Emergency Departments
  - Deaths in ICUs
- Request the entire hospital chart including nursing notes and diagnostic reports such as blood work and imaging reports
- Some data may require access to the Organ Donation Organization (ODO) chart
- Some data may require access to the eCritical and/or Metavision system

2. Health charts: Electronic and hard copies

- All deaths in the specified time period are reviewed. There is no patient age restriction
- Create and submit a record for chart being reviewed using the Alberta Potential Donor Audit web data form
- For missing charts please notify the Health Information Management (HIM) professional, Project Manager and Project Administrator upon completion of the facility's chart reviews and entry into the database

Reviewers' Responsibilities: Preparation for Chart Review

1. The Chart Reviewer will
    - Request and obtain a list of deaths from AHS HIM and Covenant Health HIM
    - Request the charts to be pulled from the relevant site's HIM depending on the amount of time the Chart Reviewer has available to conduct reviews
    - Access the Alberta Potential Donor Audit web data form by logging into AOTDR at https://iam1.health.alberta.ca/otdr/home
    - All chart review data are to be entered using the Alberta Potential Donor Audit web data form

2. Items to bring to the Chart Review
    - Post-it notes for flagging specific sections of chart
    - List of deaths to review

3. At the end of each chart review session, complete the Data Submission Form, recording the Chart Reviewer, Facility, Date of Review, and Number of Charts Reviewed. HIM will provide the number of total charts to be reviewed at each hospital

Chart Review Requirements

A FULL REVIEW OF THE CHART IS REQUIRED IF

The patient is ventilated within 24 hours of death and there is no exclusion diagnosis or condition as indicated in the Alberta Potential Donor Audit tool

A FULL REVIEW OF THE CHART IS NOT REQUIRED IF

The patient was not ventilated within 24 hours of death
or
If an exclusion diagnosis or disease is documented in the patient's health records

In instances where the full chart review is not required, complete the data elements up to the point at which the audit is stopped. The audit can be stopped if indicated in these data elements:

- Diagnosis directly related to death
- Mechanical ventilation
- Exclusions

If the audit is stopped, complete the "Outcome" field and save the record as complete.

Note that each field with a down arrow means there is a drop down menu. This applies to dates and fields with checklists. You will find options such as "Not documented" and "Not applicable" in the drop down menu where appropriate.

Data Elements and Sources

Administrative Information

Administrative information is required for each record.

Item	Data Source	Data Entry
Reviewer name	Reviewer	Enter the reviewer's first initial and last name
Date of review	Calendar date	Document the date the chart was reviewed ***YYYY/MM/DD*** *Example 2016-02-01*

Patient Information

Patient Information is collected from **ALL** charts. All of the patient information should be on the demographics sheet.

Item	Data Source	Data Entry
Patient last name	Admitting form Hospital card stamp	Enter the patient's last name
Patient first name	Admitting form Hospital card stamp	Enter the patient's first name
Postal code	Admitting form Hospital card stamp	Enter the postal code of the patient's home address If the postal code is not available, select "Not documented"
PHN (or MRN)	Admitting form Hospital card stamp SCM	Enter the PHN If the PHN is not available, enter the MRN The PHN (or MRN) will be used to identify the record in the database and will not be editable after it is entered

Institution

Institution information is collected from **ALL** charts.

Item	Data Source	Data Entry
Referring hospital	Admitting form ER record	Enter hospital that referred the patient. The field is free text as the referring hospital is not restricted to the in-scope hospitals

	EMS record Physician notes Nursing Notes SCM Netcare	Select "Not documented" or "Not applicable" if appropriate Please do not use abbreviations
Date and time admitted to referring hospital	Admitting form Hospital card stamp Admission triage form SCM Netcare	Document date and time the patient was admitted to the referring hospital ***YYYY/MM/DD HH:MM*** Select "Not documented" or "Not applicable" if appropriate
Hospital where death occurred	Brain death form Death certificate Discharge summary Physician notes ER record SCM Netcare	Enter the hospital where death occurred. Use the drop down list to select the hospital where the death occurred
Date and time admitted to hospital where death occurred	Admitting form Hospital card stamp Physician notes Nursing notes SCM Netcare	Document date and time patient admitted to the hospital where death occurred ***YYYY/MM/DD HH:MM*** Select "Not documented" if appropriate
Location	Discharge summary Physician notes Demographics sheet SCM Netcare	Enter the ward where the patient died. Use the drop down list to select the location If the location is not listed, select "Other" and enter the location

Patient Demographics

Patient demographic information is collected from **ALL** charts. Note the exceptions for the Ethnicity and Religion elements.

Item	Data Source	Data Entry
Date of birth	Hospital card stamp Discharge summary ER record EMS record Demographics sheet SCM Netcare Physician notes Nursing notes	Document the date the patient was born ***YYYY/MM/DD*** If the date is not known, select "Please enter an approximated date" using estimated year, month as 01 and day as 01. Use physician or nursing notes that refer to "this 30 year old woman" for example to estimate the year Select "Not documented" if appropriate
Age at death		Automatically calculated based on date and time of death and date of birth
Sex	Discharge summary ER record EMS record Admission form	Enter "M" for male Enter "F" for female
Ethnicity	Admitting form ER record EMS record Physician notes Nursing notes	Enter the ethnicity of the patient. Use the drop down list to select the ethnicity. If not documented select "Not documented" Enter ethnicity information only if it is apparent—do not spend time searching through the chart to find ethnicity
Religion	Admitting form ER record EMS record Physician notes Nursing notes	Enter the religion of the patient. Use the drop down list to select the religion. If not documented select "Not documented" Enter the religion information only if it is apparent—do not spend time searching through the chart to find religion

Clinical Picture

To donate organs at death, the patient must have a perfusable cardiac rhythm and be intubated and ventilated within 24 hours of death. This section provides data

about the potential for both DCD and NDD. Patients who die within two hours of withdrawal of ventilation may be eligible for DCD.

Depending on the death determination, some subsequent fields will not be applicable. In those instances, the drop down menu includes a "Not applicable" option.

Ventilation is defined as breathing via electronically powered device or by manual bagging.

Item	Data Source	Data Entry
Date and time of death	Death Certificate Brain Death Form Physician notes Nursing notes SCM Netcare	Document date and time of patient's death ***YYYY/MM/DD HH:MM***
Death determination	Death Certificate Brain Death Form Physician notes Nursing notes SCM Netcare	Enter the criteria used for death determination. Use the drop down list to select the appropriate response. Note there is no option for "Not documented"
Diagnosis directly related to death	Discharge summary Death Certificate Brain Death Form Physician notes Nursing notes SCM Netcare	Enter the diagnosis directly related to death. Use the drop down list to select the appropriate response If the response selected indicates the audit is stopped, complete the "Outcome" field and save as complete

Item	Data Source	Data Entry
Mechanical ventilation	ER record EMS record Physician notes Nursing notes Respiratory therapist record Discharge summary eCritical/Metavision SCM Netcare	Was the patient ventilated within 24 hours of death? Use the drop down list to select the appropriate response If the patient was **not ventilated** or there is no documentation of ventilation in the patient's record the audit is stopped. Complete the "Outcome" field and save as complete If there is documentation of ventilation but the patient was **not ventilated in the 24 hours** before death the audit is stopped. Complete the "Outcome" field and save as complete
Exclusions	Discharge summary Coding summary Physician notes ER record EMS record Death certificate Lab reports SCM Netcare	Did the donor have any disease or diagnosis which is an automatic exclusion for organ donation? Select from the drop down list to identify any diagnosis If **yes** to any of the exclusions, the audit is stopped. Complete the "Outcome" field and save as complete If there are no exclusions, select "No exclusions"
2nd neuro test date and time	Brain death form Physician notes eCritical/Metavision SCM Netcare	Document date and time of 2nd neurologic test for brain death ***YYYY/MM/DD HH:MM*** Select "Not documented" or "Not applicable" if appropriate
Brainstem reflex within 24 hrs of WLST intervention or last documented	ED record Discharge summary Coding summary Physician notes Brain death form Radiologic reports eCritical/Metavision SCM Netcare	Document indications of brainstem reflex within 24 hrs of Withdrawal of Life Sustaining Therapy (WLST) using the drop down list to select the appropriate response Complete review for each reflex Note the drop down menu for Apnea test has different response options

Item	Data Source	Data Entry
Date and time last brainstem reflex prior to WLST	Physician notes Nursing notes Brain death form eCritical/Metavision SCM Netcare	Document date and time of last brainstem reflex prior to WLST ***YYYY/MM/DD HH:MM*** Select "Not documented" if appropriate
Best motor response to stimulation within 24 hours of WLST	Physician notes Nursing notes Brain death form Discharge summary eCritical/Metavision SCM Netcare	Detail the best motor response to stimulation within 24 hours of WLST. Use the drop down list to select the appropriate response. If the information is not found, select "Not documented"
Eye opening	Physician notes Nurses notes Brain death form Discharge summary eCritical/Metavision SCM Netcare	Was there eye opening within 24 hours of WLST? Use the drop down list to select the appropriate response Select "Not documented" if appropriate
Date and time best motor response to stimulus prior to WLST	Physician notes Nursing notes Brain death form eCritical/Metavision SCM Netcare	Document the date and time of best motor response to stimulus prior to WLST ***YYYY/MM/DD HH:MM*** Select "Not documented" if appropriate
Glasgow Coma Score	Physician notes Nurses notes Brain death form Discharge summary eCritical/Metavision SCM Netcare	Enter the last Glasgow Coma Score prior to death. Enter the actual score Select "Not documented" if appropriate

Item	Data Source	Data Entry
WLST decision documented	Physician notes Nursing notes Brain death form Discharge summary eCritical/Metavision SCM Netcare	Was the decision to WLST documented? Enter "Yes" or "No" or "Not applicable"
Primary reason for WLST interventions	Physician notes Nursing notes Brain death form SCM Netcare	Enter the **primary** reason for WLST intervention. Use the drop down list to select the appropriate response. If "Other" is selected, enter the reason Select "Not documented" or "Not applicable" if appropriate
WLST decision documentation date and time	Physician notes Nursing notes Brain death form	Document the date and time of the decision to WLST ***YYYY/MM/DD HH:MM*** Select "Not documented" or "Not applicable" if appropriate
WLST action	Physician notes Nursing notes Brain death form Discharge summary eCritical/Metavision	What actions were taken in the WLST? Use drop down list and check all the responses that apply Select "Not documented" or "Not applicable" if appropriate
Date and time of WLST Action	Physician notes Nursing notes Brain death form Discharge summary eCritical/Metavision	Document date and time of WLST ***YYYY/MM/DD HH:MM*** Select "Not documented" or "Not applicable" if appropriate

Approach and Consent

In addition to consent rates, data collected in this section provides information on the identity and profession of the healthcare professional discussing organ donation with the family as well as reasons consent is refused or withdrawn. Data will also document discussions and communications relating to the donation process and outcomes of the donation opportunity.

Item	Data Source	Data Entry
ODO contacted	ED Record Discharge summary Coding summary Physician notes Nursing notes ODO Database/chart	Was the donation program contacted about the impending or actual death? Select the appropriate response from the drop down list Select "Not documented" if appropriate
Reason ODO not contacted	ED Record Discharge summary Coding summary Physician notes Nursing notes	Enter the reason the ODO was not contacted. Use the drop down list to select the most appropriate response Select "Not documented" or "Not applicable" if appropriate
Donor documented choices	ED Record Discharge summary Coding summary Physician notes Nursing notes	Were the patient's donation wishes documented? Use the drop down list to select the most appropriate response Select "Not documented" if appropriate
Approached family for OD	ED Record Discharge summary Coding summary Physician notes Nursing notes	Was the patient's family approached about donating organs? Enter "Yes" or "No" or "Not documented"
Approached date and time	Physician notes Nursing notes Consent form	Document date and time the family was approached about organ donation ***YYYY/MM/DD HH:MM*** Select "Not documented" or "Not applicable" if appropriate

Item	Data Source	Data Entry
Who approached family	Physician notes Nursing notes Consent form	Enter who approached the family to discuss donation. Use the drop down list and check all that apply Team approach means a minimum of two people Select "Not documented" or "Not applicable" if appropriate
Who was approached	Physician notes Nursing notes Consent form	Enter the relationship of the person who was approached. Use the drop down list and check all that apply. If "Other" is selected, enter the relationship Select "Not documented" or "Not applicable" if appropriate
Reason for non-approach	Physician notes Nursing notes Consent form	Enter the reason the family was not approached for organ donation. Use the drop down list and select the most appropriate response. If "Other" is selected, enter the reason Select "Not documented" or "Not applicable" if appropriate
Consent obtained	Physician notes Nursing notes Consent form	Was consent for organ donation obtained? Enter "Yes" or "No" or "Not documented" or "Not applicable"
Consent date and time	Physician notes Nursing notes Consent form	Document the date and time the family consented to organ donation ***YYYY/MM/DD HH:MM*** Select "Not documented" or "Not applicable" if appropriate
Reasons for non-consent	Physician notes Nursing notes Consent form	Enter the reason the family did not consent to organ donation. Use the drop down list to select the most appropriate response. If "Other" is selected, enter the reason Select "Not documented" or "Not applicable" if appropriate
Consent withdrawn	Physician notes Nursing notes Consent form ODO Database/chart	Use the drop down list to record whether the family consented to organ donation and then subsequently withdrew their consent Select "Not documented" or "Not applicable" if appropriate
Item	**Data Source**	**Data Entry**
Consent withdrawn date and time	Physician notes Nursing notes	Document the date and time when the family withdrew their consent ***YYYY/MM/DD HH:MM***

	Consent form ODO Database/chart	Select "Not documented" or "Not applicable" if appropriate
Reasons consent withdrawn	Physician notes Nursing notes Consent form ODO Database/chart	Enter the reason the family withdrew consent. Use the drop down list to select the most appropriate response. If "Other" is selected, enter the reason Select "Not documented" or "Not applicable" if appropriate
Medical examiner approval received	ED Record Discharge summary Coding summary Physician notes Nursing notes ODO Database/chart	Was medical examiner approval for organ donation required? Enter "Yes" or "No" or "Not documented"
Donor brought to OR for procurement	Physician notes Nursing notes OR record ODO Database/chart	Was the patient brought to the operating room for organ procurement? Enter "Yes" or "No" or "Not documented"
Brought to OR for procurement date and time	Physician notes Nursing notes OR record ODO Database/chart	Document the date and time when the donor was taken to the operating room for organ procurement ***YYYY/MM/DD HH:MM*** Select "Not documented" or "Not applicable" if appropriate
Reasons not brought to OR for procurement	Physician notes Nursing notes OR record ODO Database/chart	If the patient was not taken to the OR, use the drop down list to select the most appropriate response. If "Other" was selected, enter the reason Select "Not documented" or "Not applicable" if appropriate
Organs procured	Physician notes Nursing notes OR record ODO chart	Document each of the organs procured. Use the drop down list and check all that apply Select "Not documented" or "Not applicable" if appropriate

Item	Data Source	Data Entry
Organs transplanted	OR record ODO chart	Document which organs were transplanted. Use the drop down list and check all that apply Select "Not documented" or "Not applicable" if appropriate
Reasons organs not procured/not transplanted	OR record ODO chart	If the patient's organs were not procured and not transplanted, use the drop down list to indicate the reason. If "Other" is selected, enter the reason Select "Not documented" or "Not applicable" if appropriate
Outcome	Physician notes Nursing notes ODO chart	Document the outcome. Use the drop down list to select the most appropriate response. If physician review is required to determine the outcome, save the record for review (pending)

Outcome Definitions

Actual donor NDD: NDD donor with at least one solid organ or part of it successfully transplanted into a donor recipient

Actual donor DCD: DCD donor with at least one solid organ or part of it successfully transplanted into a donor recipient

Not accepted NDD: Patient met all brain death criteria, legal consent was obtained, and no organs were accepted by the transplant team for various reasons including positive serology, poor organ function, abnormal physiology, decline on visualization

Not accepted DCD: Patient determined to be a suitable candidate for DCD donation but declined by the transplant team for various reasons including age, medical history, blood type, size

Did not progress NDD: Patient showed signs of progression to brain death and discussion was initiated regarding donation but the patient did not fully progress to meet all brain death criteria prior to expiration

Did not progress DCD: Patient was identified as a potential DCD donor, legal consent was obtained but the patient did not arrest in a suitable time frame for donation to occur

Medically unsuitable (rejected): Patient met any of the following exclusionary conditions: Confirmed HIV infection, confirmed West Nile Virus, Active (within 5 years) Hematologic malignancy, Active (within 5 years) Non-CNS malignancy; Active (within 5 years) metastatic malignancy

Potential missed donor: Patient died in hospital, was clinically eligible to be an organ donor but there was no documentation that family was approached regarding organ donation. To be clinically eligible, the patient died after experiencing severe brain damage (leading to brain or cardiocirculatory death), was mechanically ventilated at or near time of death, and had no medical contraindications to donation