Organ Donation in Canada and Management of the Potential Organ Donor

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Declarations

I am the Hospital Donation Physician at Toronto General Hospital

Appointed (and funded) by Trillium Gift of Life Network

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Acknowledgements

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Toronto Western Hospital

Objectives – what I want to say

1. Review the current trends in organ donation in Canada and worldwide.
2. Characteristics of the potential donor for donation after cardiac death (DCD)
3. Clinical and ethical challenges of donor management
4. Withdrawal of life sustaining therapy in the ICU, in the context of DCD

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INTRODUCTION

Update on organ transplantation

University of Toronto

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Supply-Demand Problem

Worldwide:

- Approximately **120,000** organ transplants performed each year
- Kidney (70%), Liver (20%), Heart (5%), Lung (3%), and Pancreas (2%) of global activity
- Meets only **10%** of the World's transplant needs (WHO, 2016)

Canada:

- Over **4,500** people were waiting for organ transplants
- **2,903** organs were transplanted (CIHI, 2016)

Adam Smith's economic principles do not fully apply – if demand rises > supply:

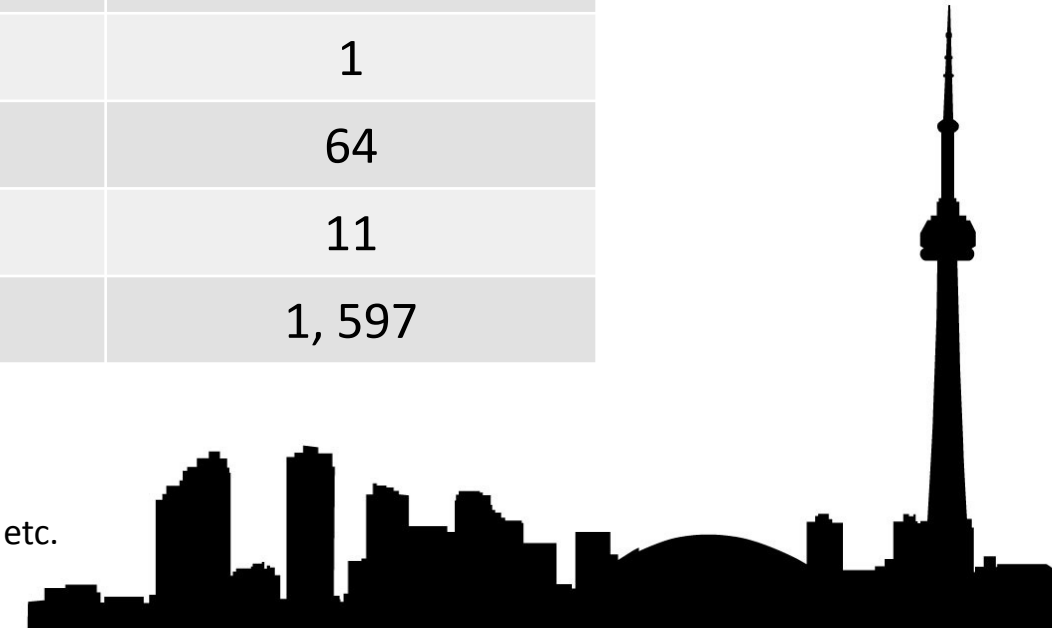
- **The price rises: 276 people died in Canada** waiting for a transplant
- If we cannot increase production/availability; to lower the price quality may fall

Ontario: Transplant Waiting List

Organ	March 31, 2017	March 31, 2016	March 31, 2015
Kidney	1, 120	1, 134	1, 146
Liver	237	221	214
Heart	45	56	67
Lung	62	64	81
Pancreas- Whole	16	16	13
Small Bowel	1	1	1
Kidney/ Pancreas	63	62	64
Multivisceral*	12	11	11
Total	1, 556	1, 565	1, 597

140 Died waiting

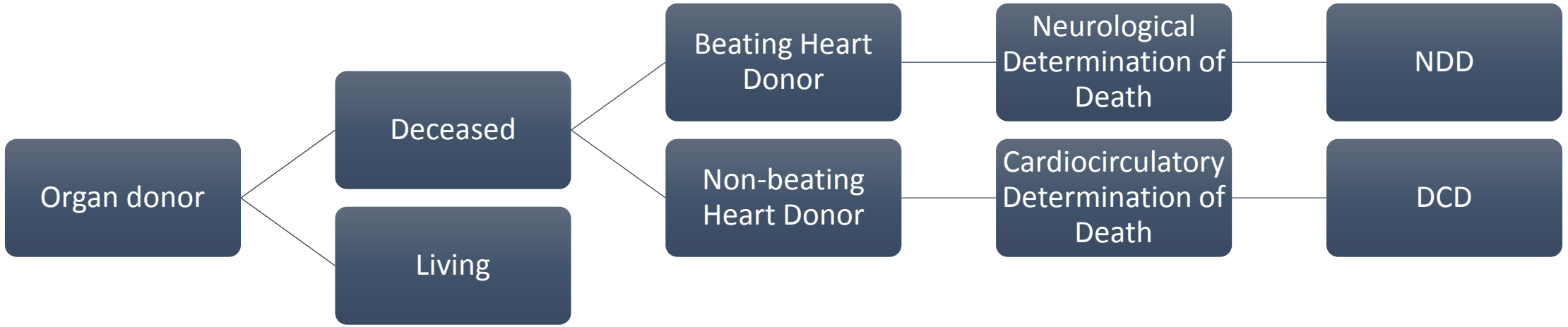
*Multivisceral i.e. liver/kidney, heart/lung, lung/ kidney, etc.



ORGAN SUPPLY

Update on organ transplantation

Organ donation



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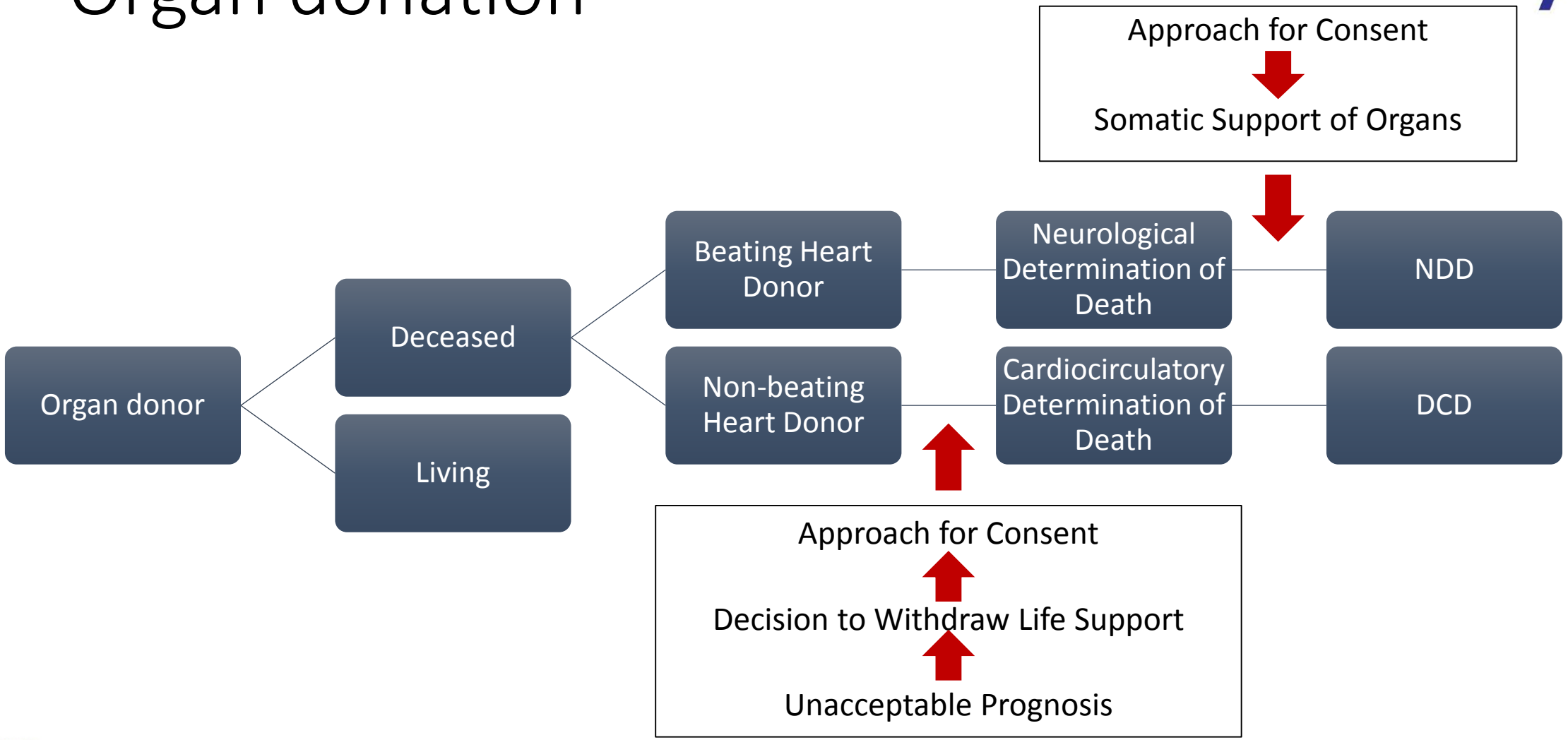
Organ donation



Terms and abbreviations

Non-heart beating organ donation (NHBD) – Maastrict 1995

Donation after cardiac death (DCD) – Paris 2013

Category I. Uncontrolled	*Found dead* IA. Out-of-hospital IB. In-hospital	*Sudden unexpected CA without any* attempt of resuscitation.
Category II. Uncontrolled	*Witnessed cardiac arrest* IIA. Out-of- hospital IIB. In-hospital	Sudden unexpected irreversible CA with *unsuccessful resuscitation*
Category III. Controlled	*Withdrawal of life-sustaining therapy*	Planned withdrawal of life-sustaining therapy, expected CA
Category IV. Uncontrolled Controlled	*Cardiac arrest while brain dead*	Sudden CA after brain death diagnosis during donor life-management but prior to planned organ recovery.

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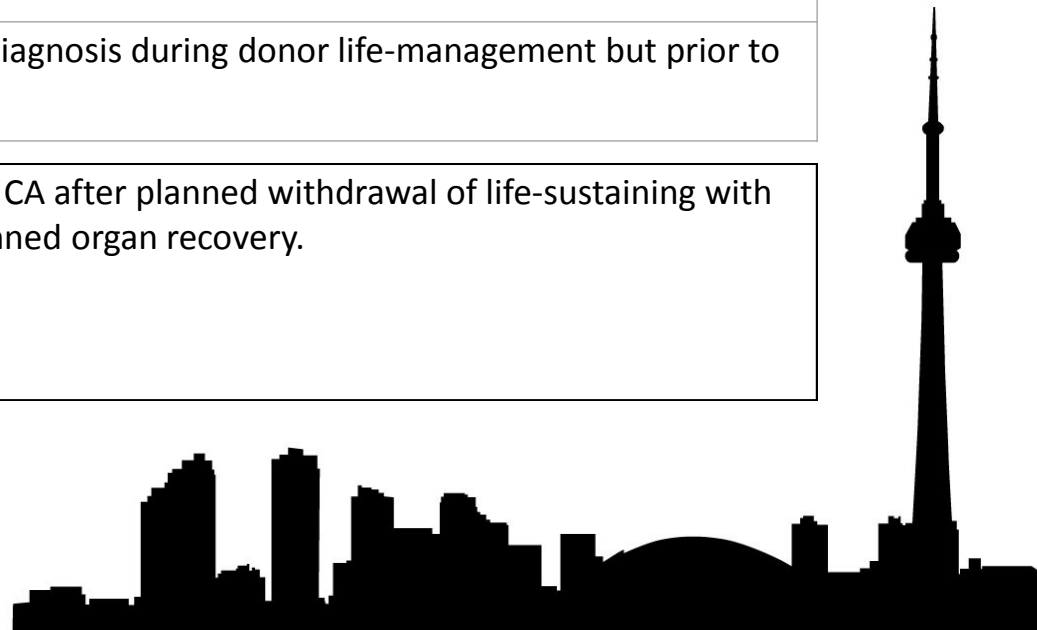
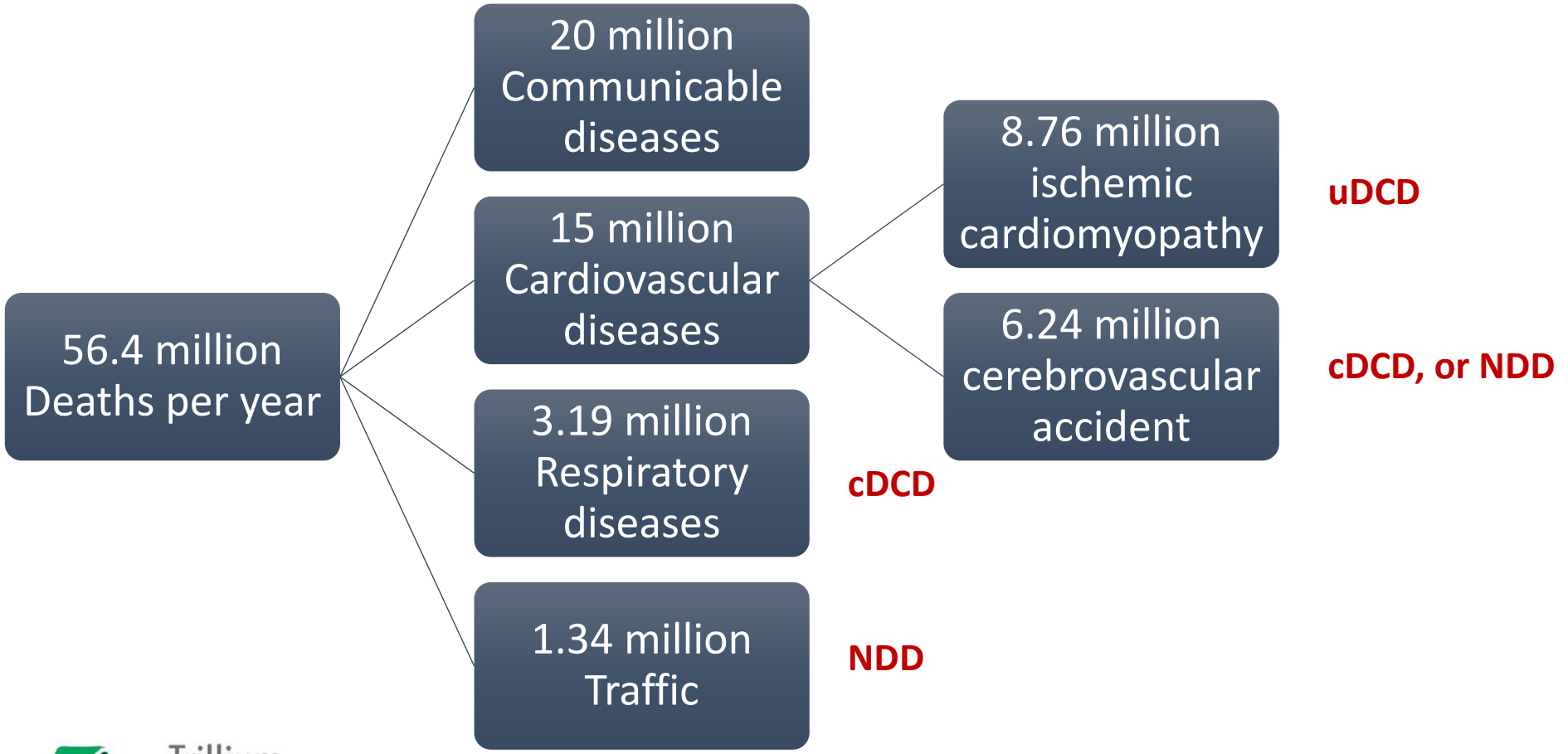
Category IV. Uncontrolled Controlled	*Cardiac arrest while brain dead*	Sudden CA after brain death diagnosis during donor life-management but prior to planned organ recovery.
Category V. Controlled	*Medical Assistance in Dying (Euthanasia)* VA. Medically assisted cardiocirculatory death in ICU or ward Controlled VB. Medically assisted cardiocirculatory death in OR Highly controlled	Expected CA after planned withdrawal of life-sustaining with prior planned organ recovery.



DCD – worldwide potential for donation



WHO – The top 10 causes of death - January 2017.

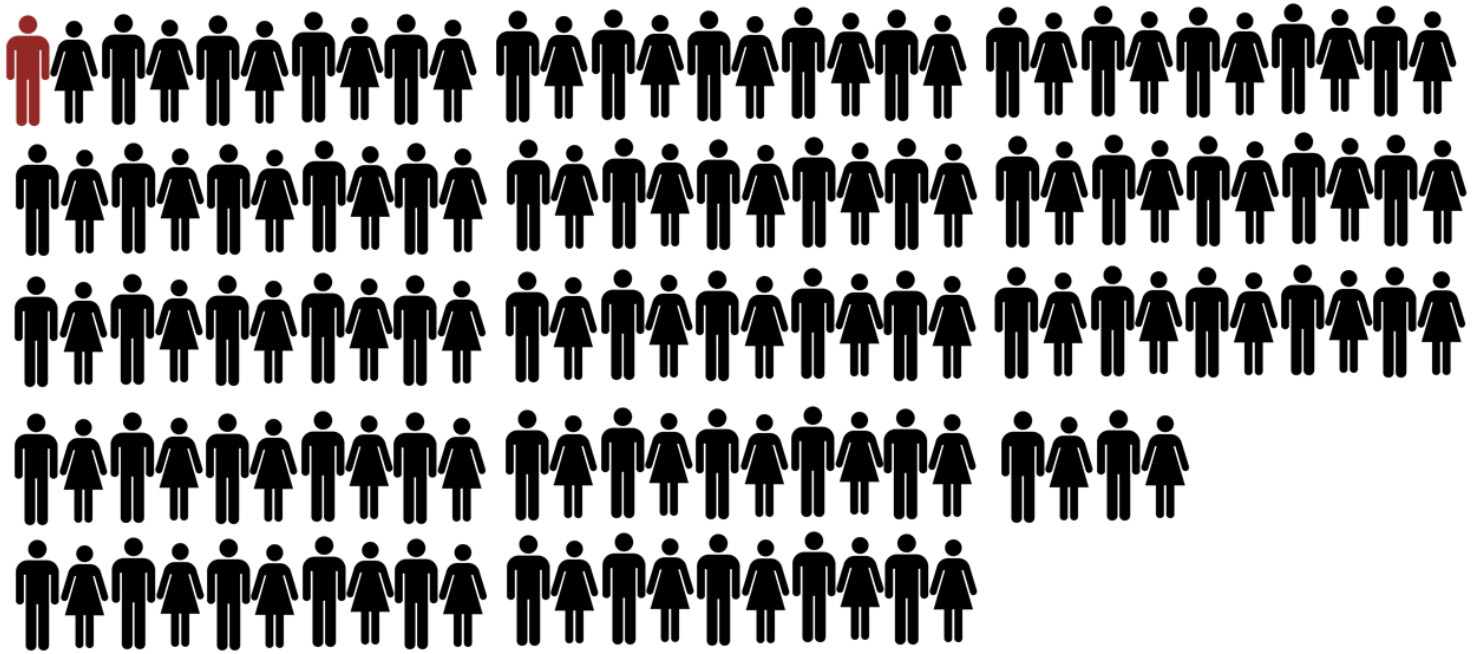
DCD – Canadian potential for donation

1:134

Canadian Death Ratio

35,848,600

Canadian Population



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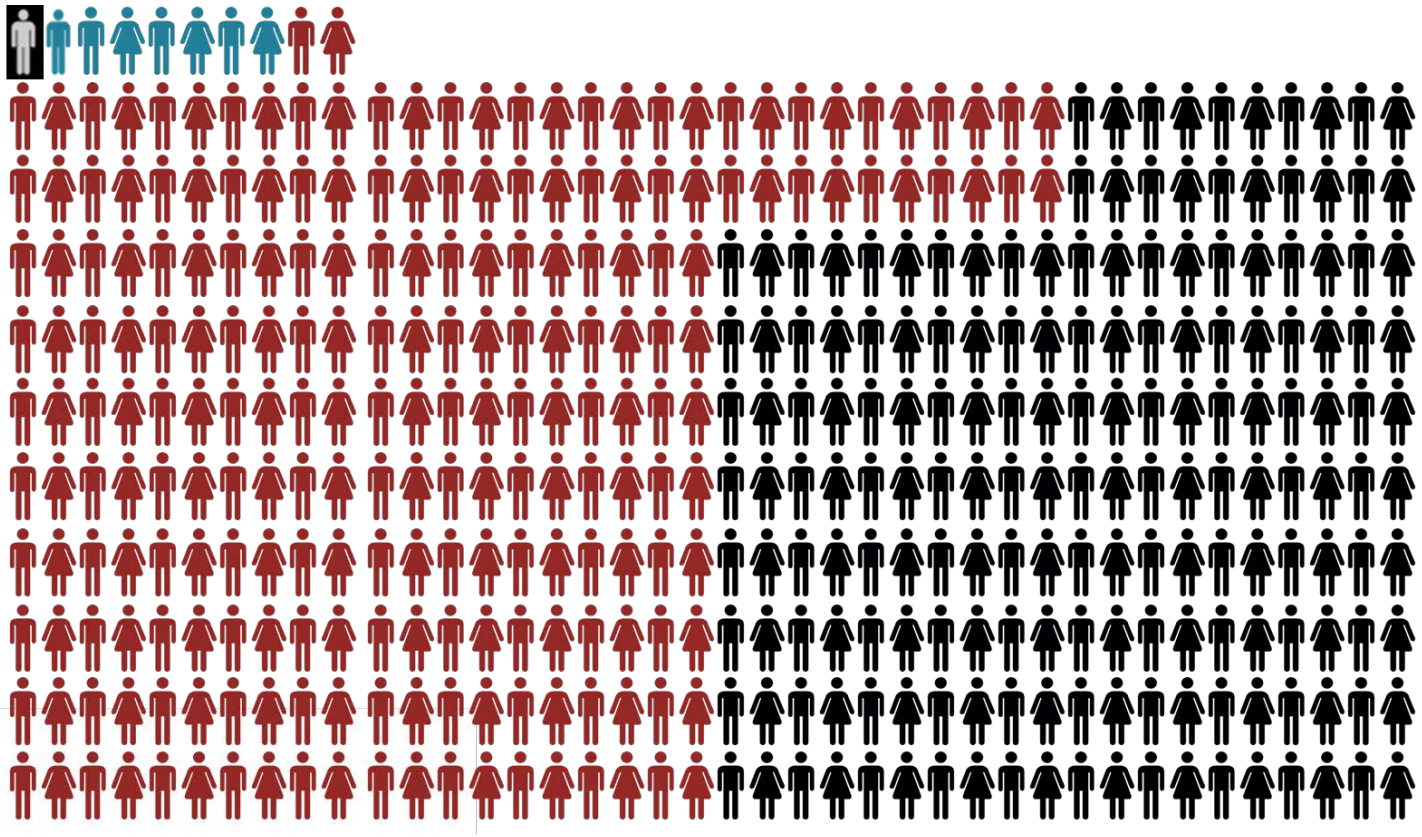
Deceased Donation is a Rare Gift



1 figure = 650.28 persons

~267,000
Deaths

~150,000
Hospital Deaths

5,236
*Potential Donors**

651
Utilized Donors

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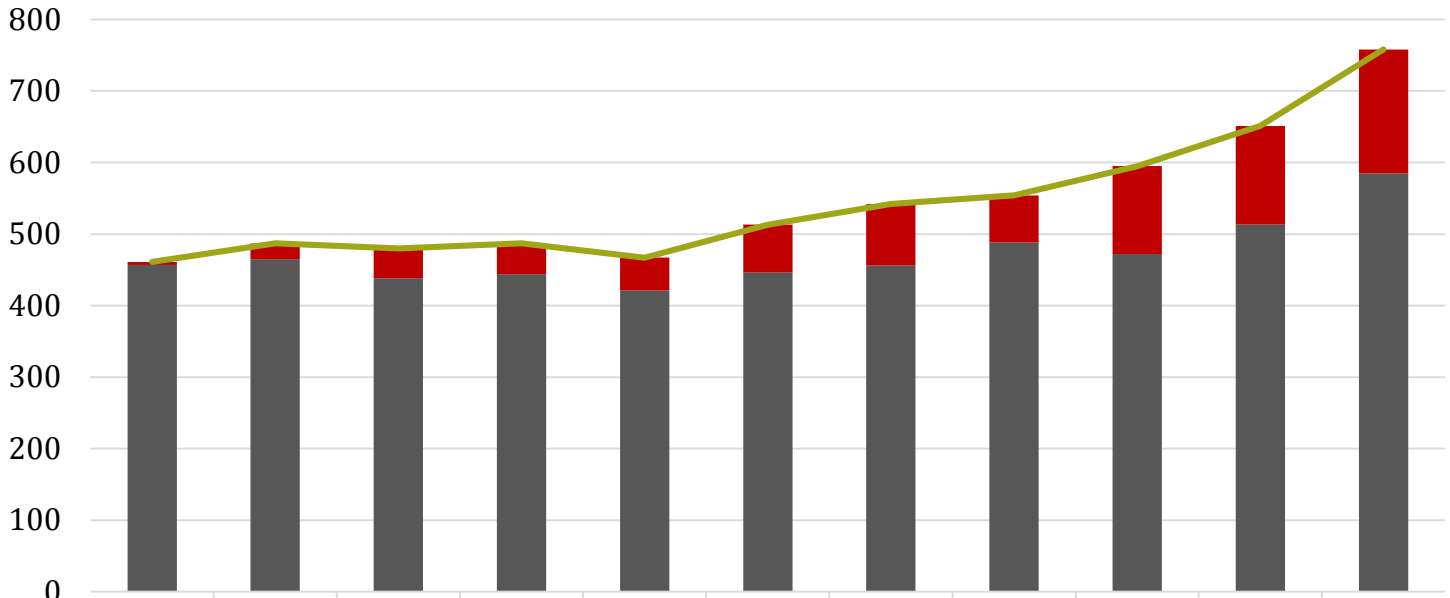
Deceased Donors in Canada 2006-2016



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
DCD	4	22	42	43	46	67	86	66	123	138	173
NDD	457	465	438	444	421	446	456	488	472	513	585
Total	461	487	480	487	467	513	542	554	595	651	758
% DCD	1%	5%	9%	9%	10%	13%	16%	12%	21%	21%	23%

64%

Increase in total deceased donors (2006-2016)

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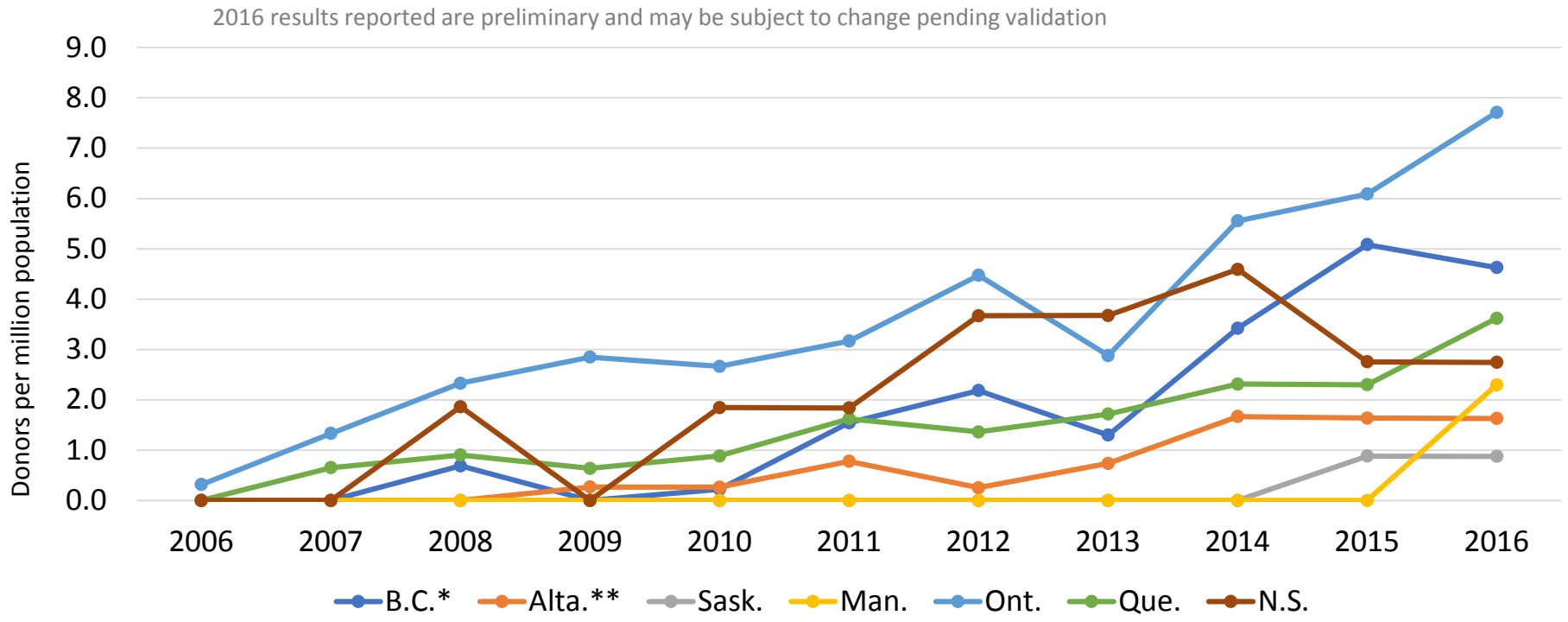
DCD Donors, 2006-2016



*Rates for BC - population of Yukon is included;
**Rates for Alberta - populations of NWT & Nunavut are included

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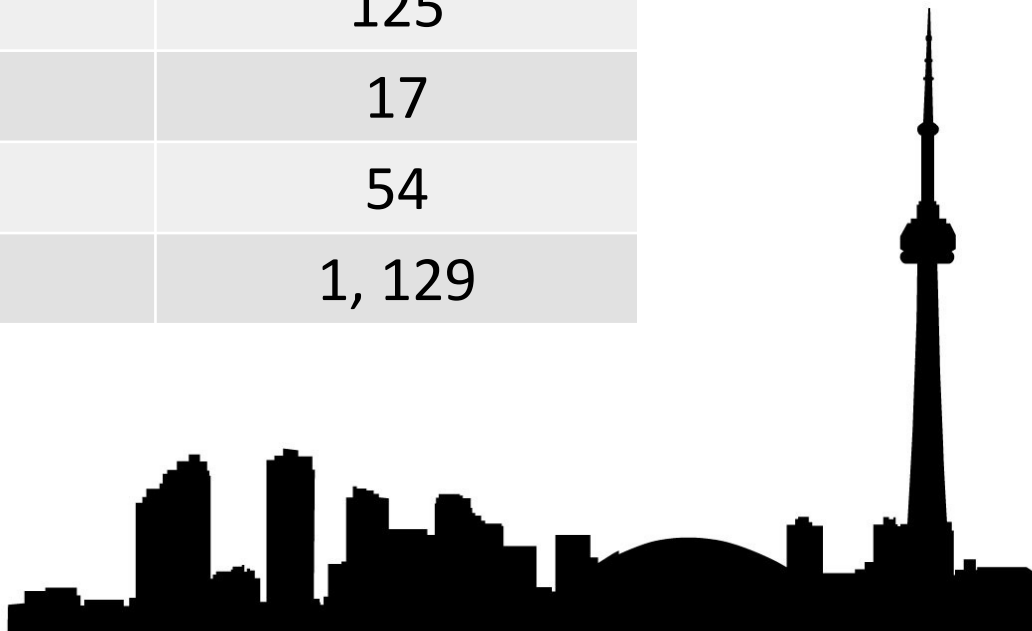
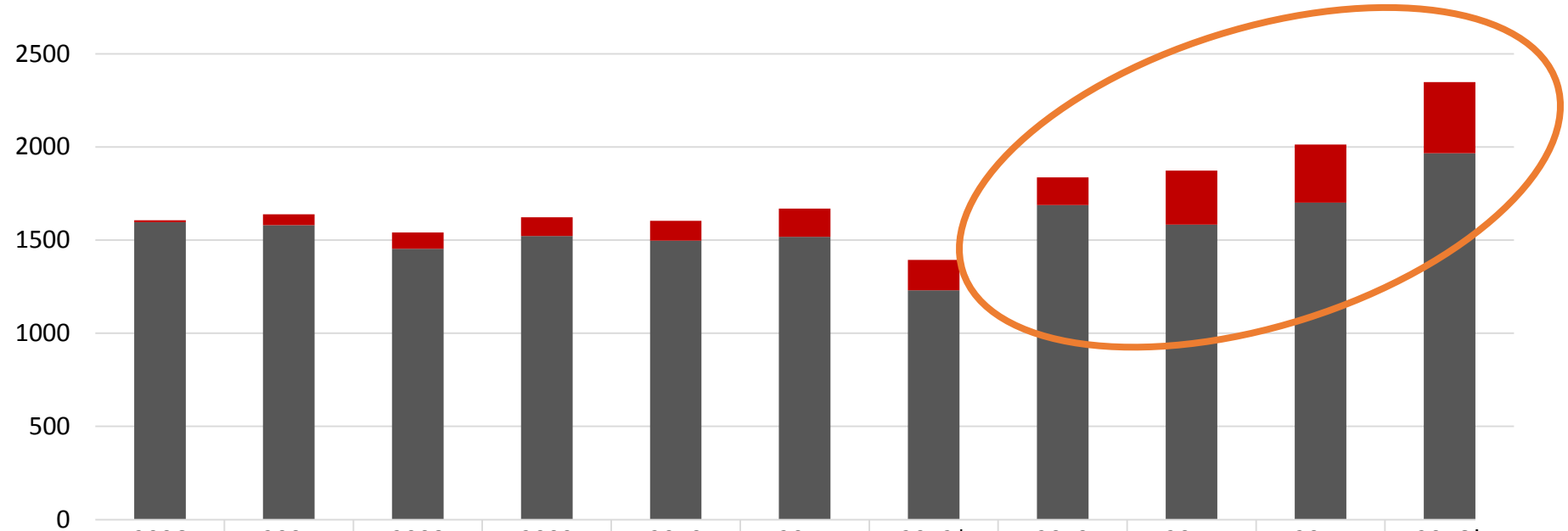
Ontario: Transplants from Deceased Donors*

Organ(s) Transplanted	2016/17	2015/16	2014/15
Kidney	500	416	383
Liver	209	189	194
Heart	89	83	78
Lung	149	128	125
Pancreas- Whole	22	22	17
Other	45	55	54
Total	1, 256	1, 174	1, 129

*Deceased donors include provincial and non-provincial donors



Organs Transplanted by Donor Type, 2006-2016



	2006	2007	2008	2009	2010	2011	2012*	2013	2014	2015	2016†
DCD	10	59	88	100	106	152	164	149	290	312	381
NDD	1596	1580	1453	1522	1498	1518	1230	1688	1584	1701	1967
Total	1606	1639	1541	1622	1604	1670	1394	1837	1874	2013	2348

* Missing Quebec data

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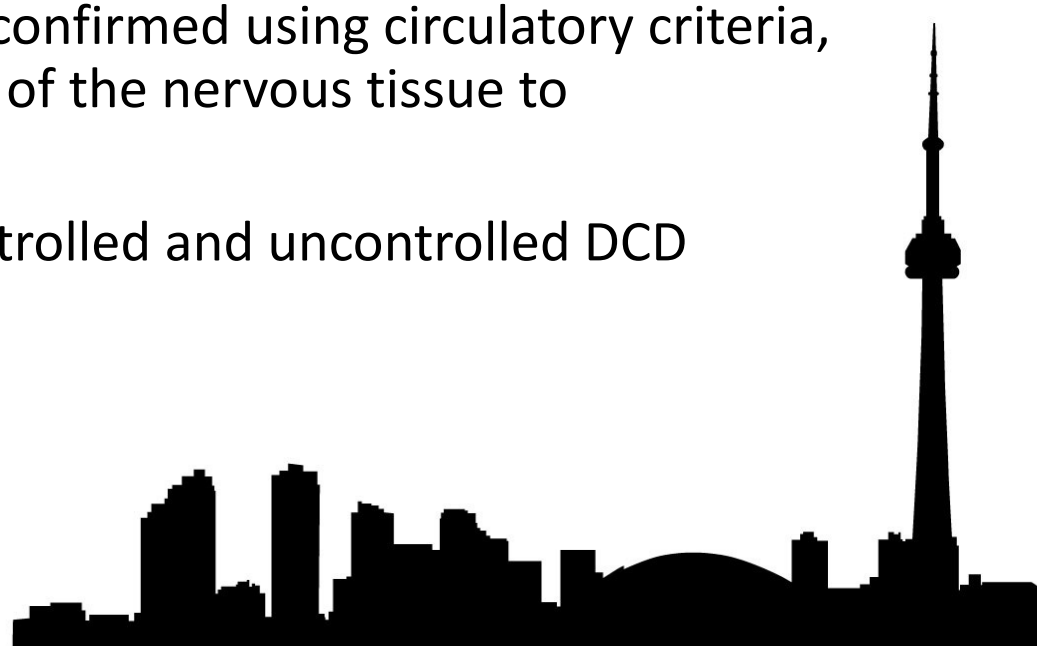
2016 results reported are preliminary and may be subject to change pending validation

Perceived Barriers to DCD Donation

- Temporal proximity and *perceived* conflict of interest and duty can be a source of distress
- The need to allow sufficient time to get patient wishes and allow organ procurement organisation (OPO) time to approach re: organ donation
- Discomfort or uncertainty at the clinical interface between end-of-life care and organ donation work up.
- Uncertainties around the time at which death can be confirmed using circulatory criteria, e.g. ROSC after asystole, and lingering responsiveness of the nervous tissue to restoration of cerebral blood flow.
- Concerns about the ethics and lawfulness of both controlled and uncontrolled DCD persist

Zellweger A et al. *Transplantation* 2017.



Ethical considerations

- Utilitarian justification
  - Violations of the dead donor rule, consent process, pre-mortem interventions are justified by the benefits to those awaiting organ transplants
- Abbreviated time to the declaration of death
  - 2-5 minute interval to the time the donor is declared dead, it is quite possible that portions of the brain (responsible for thoughts and emotions) have not yet ceased to function
- Surrogate consent
  - SDM or POA provide consent for a living individual for an intervention without benefit to that person
- Future considerations
  - Imminent death donation
  - MAID
  - Presumed consent (opt out vs. opt in)

APPROACHING THE FAMILY

Update on organ transplantation

We are not good at this!

Do you:

a. Negotiate a time for withdrawal of life support?

b. Make him a no-escalation/no CPR?

c. Ignore physiological goals now?

d. Ask family if he had ever discussed organ donation?

e. Give them time and space and circle back?

46 yr old male
GCS 4
Large supratentorial ICH
ICH Volume > 30 cc
Intraventricular hemorrhage

ICH Score predicted mortality = 97%

Neyricnk A. *Curr Opin Anaesthesiol* . 2013; 26: 382-390

Family override

- UK data suggests that family (SDM) override of first person consent occurs in approximately 11.7% of cases
- Factors associated with override:
  - Failure to involve organ donation specialist physician or nurse (OR 3.0)
  - Donation after cardiac death (DCD) (OR 2.7)
  - Black, Asian, or minority ethnicity family (OR 2.7)
- Stated reasons:
  - Length of time of donation process was too long (28%)
  - Didn't want further surgery (9.1%)
  - Patient had suffered enough (8.4%)
  - Family members divided over the decision (7.6%)

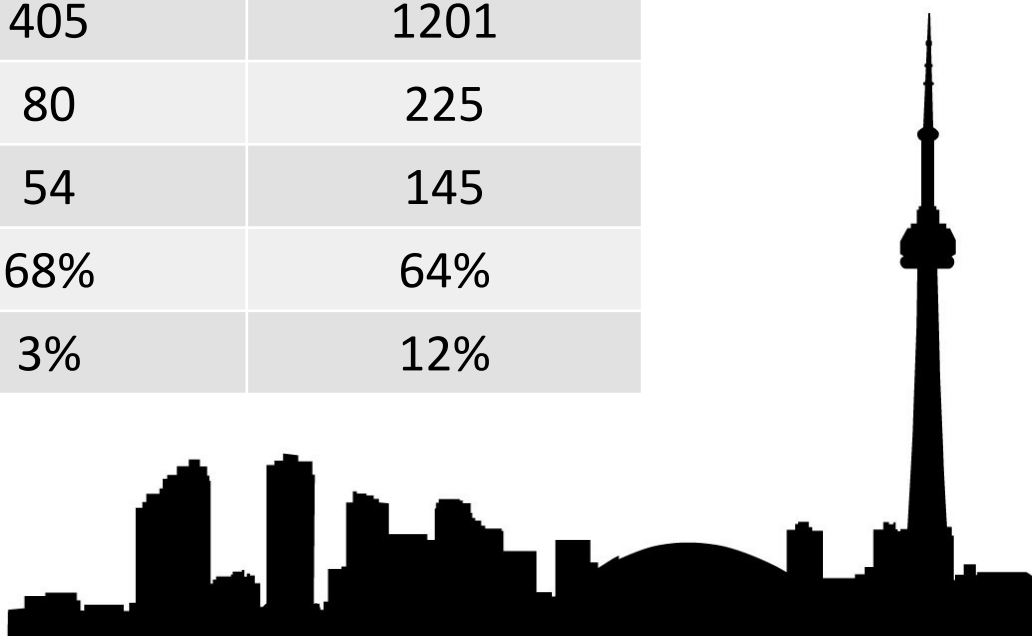
Morgan J, Hopkinson C, Hudson C, et al. *JICS* 2018; **19** (2): 101-106

Families Need Time to Consent

When WLST time has been set <6 hours from referral:

- Fewer families are approached about organ donation
- Fewer families consent to organ donation
- Fewer families uphold registered consent decisions

	WLST Not Discussed	WLST Time Set for Less Than 6 Hours	WLST Time Set for Greater Than 6 hours	WLST Time Unknown
Notifications	3399	1042	405	1201
Approaches	762	126	80	225
Consent	497	47	54	145
Consent Rate	65%	37%	68%	64%
Overturn Rate	13%	43%	3%	12%



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SUPPORTING DCD DONORS

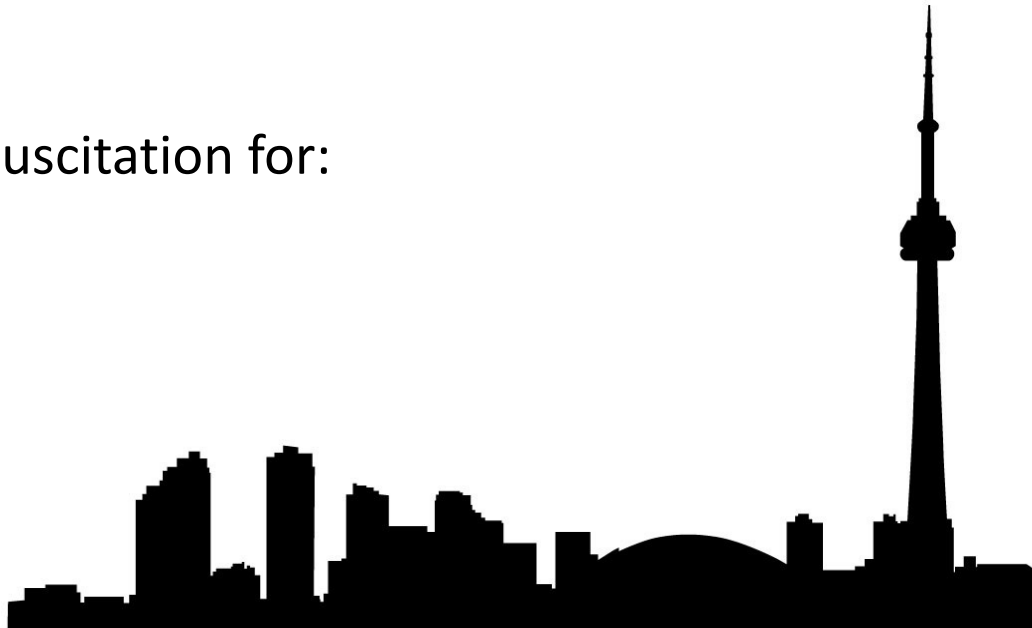
Update on organ transplantation

Support of the Consented DCD Donor

- Observational studies suggest that after consent for organ donation, up to 20% of organs may lose transplant potential due to suboptimal medical management.
- In 2015, the Society of Critical Care Medicine set out to develop evidence-based guidelines in donor management, but published, instead, consensus-based guidelines.
- Most guidelines and protocols worldwide centres on NDD donor management.

Within the context of patient-centered End of Life Care

1. Engage the organ donation organisation earlier
2. Don't write "no-escalation" orders
3. Allow for reasonable escalation of care / patient resuscitation for:
   - Hypotension
   - Ventilation parameters
   - Medications and fluids



Ante mortem ‘management’ of the donor

- In June 2008, nine donor management goals were prospectively implemented as a checklist and every donor after **neurologic determination of death** was managed to meet them.
- The donor management goals represented normal cardiovascular, pulmonary, renal, and endocrine end points
- If you met 7 of 9 Goals: OR **1.9** – of having 3+ organs transplanted

Original Investigation | PACIFIC COAST SURGICAL ASSOCIATION

The Impact of Meeting Donor Management Goals on the Number of Organs Transplanted per Expanded Criteria Donor

A Prospective Study From the UNOS Region 5 Donor Management Goals Workgroup

Madhukar S. Patel, MD, MBA, ScM; John Zatarain, MD; Salvador De La Cruz, MD; Mitchell B. Sally, MD; Tyler Ewing, BS; Megan Crutchfield, MPH; C. Kristian Enestvedt, MD; Darren J. Malinoski, MD

Table 1. United Network for Organ Sharing Region 5 Donor Management Goals

Donor Management Goal	Parameter
Mean arterial pressure, mm Hg	60-110
Central venous pressure, mm Hg	4-12
Ejection fraction, %	≥50
Low-dose vasopressors,[a] No. of agents	≤1
Arterial blood gas, pH	7.3-7.5
Pao_2:Fio_2 ratio	≥300
Serum sodium, mEq/L	≤155
Urine output, mL/kg/h over 4 h	≥0.5
Glucose, mg/dL	≤150

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Antemortem lung protection

- Compare conventional strategy and lung protective ventilation settings:
  - **VT 6-8 ml/Kg PBW**
  - **PEEP 8-10 cm H2O**
  - **CPAP for apnea**
  - **Closed circuit**
- Protective ventilation increases the number of lungs eligible and procured for transplant.
- No difference survival of recipients
- Data does not support extubation during WLST (and nor do our surgeons)

Effect of a Lung Protective Strategy for Organ Donors on Eligibility and Availability of Lungs for Transplantation
A Randomized Controlled Trial

Mascia et al. *JAMA*. 2010

Antemortem kidney protection

Donor risk factors:

- Hypernatremia (Na > 155 mmol/L) – considered to be independently associated with hepatic and renal dysfunction or graft loss after transplantation.

  Excessive sodium administration during resuscitation, or DI, may lead to accumulation of idiogenic osmoles in donor organs. Once transplanted, significant intracellular fluid shifts may occur into the graft.

- Donor age (>60 years)
- Warm ischemic time
- Cold ischemic time

Antemortem liver protection

- Review of 961 organ donors

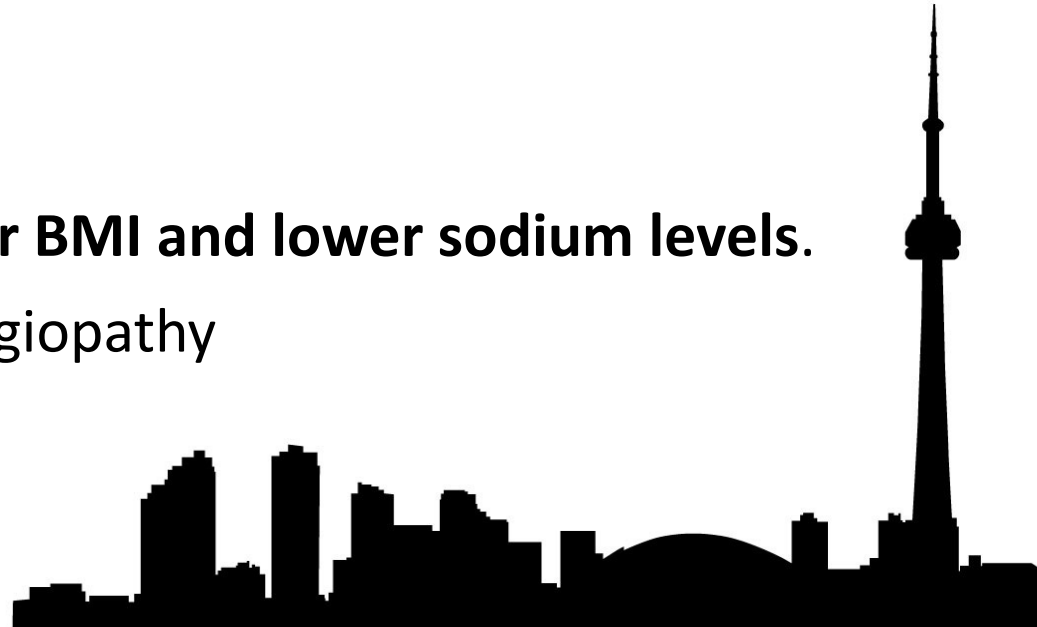
Variable	Odds Ratio for Liver Transplantation
donor BMI	0.94
male sex	1.89
glucose <150 mg/dL	1.97
Sodium at 12-18 hrs	0.95
lower dopamine dose	0.95
vasopressin use	1.95
ejection fraction >50%	1.77

Impact of Deceased Organ Donor Demographics and Critical Care End Points on Liver Transplantation and Graft Survival Rates

Matthew B Bloom, MD, FACS, Shariq Raza, MD, Akash Bhakta, BS, Tyler Ewing, BS, Madhukar Patel, MD, Eric J Ley, MD, FACS, Daniel R Margulies, MD, FACS, Ali Salim, MD, FACS, Darren Malinoski, MD, FACS

Bloom et al. *J Am Coll Surg*. 2015

- Increased graft survival was associated with **lower BMI and lower sodium levels**.
- tPA flushed liver grafts to reduce ischemic cholangiopathy



Antemortem heart protection

- Until recently, it has not been possible to assess either the severity or the reversibility of the ischemic injury which inevitably affects the heart in the DCD setting.
- The term “donation after cardiac death” has created a false impression that the heart “dies” during WLST, and that this is critical to the determination of death.
- The heart has stopped functioning but remains viable for a short period of time after death of the donor.
- Where it differs from other organs is in its greater susceptibility to the unavoidable warm ischemic injury that occurs during withdrawal of life support and during the interval between circulatory arrest and delivery of myocardial preservation solution.

Antemortem heparin

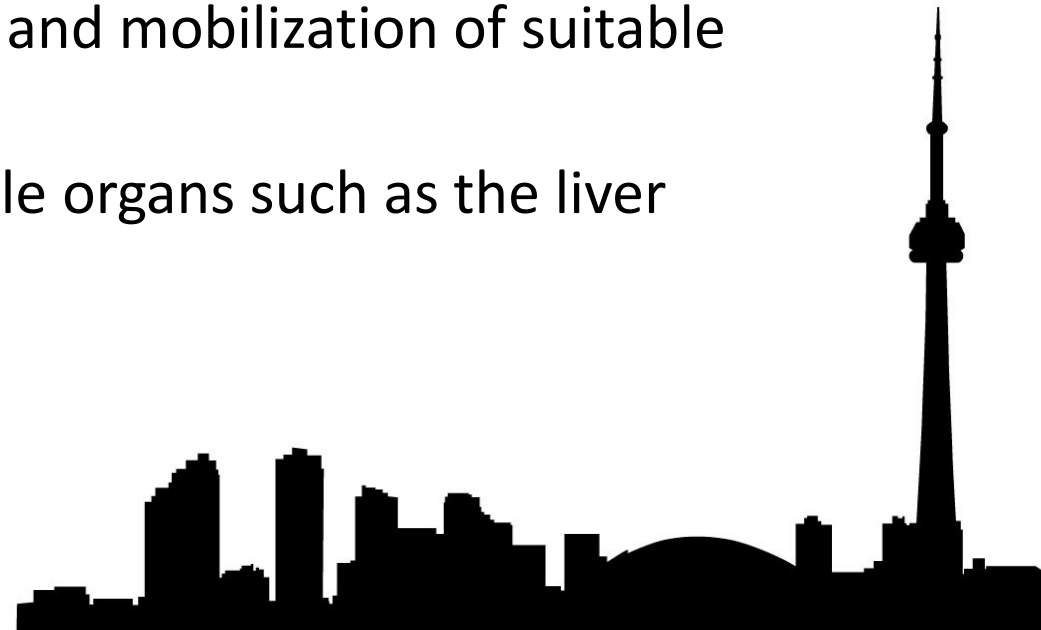
- **Liver Transplant:** Pre-mortem administration of heparin before WLST reduced incidence of primary non-function of the allograft from 11% to 3.4%.
- **Lung transplant:** Antemortem heparin in DCD, combined with retrograde and anterograde flushing, effectively removes thrombi that form during donation process
- **Pancreatic transplant:** DCD versus DBD pancreatic transplants, showed equivalent graft survival at 10 years; but the odds ratio of graft thrombosis was 1.67 times higher in the DCD cohort. This difference disappeared in patients whose donor had received heparin prior to withdrawal of life sustaining therapies
- **Kidney transplant:** It is recommended by the majority of organ procurement organizations, and has been shown to improve machine perfusion operation and its use may obviate the need for subsequent TPA or streptokinase for glomerular thrombi.

- **Ethical Aspects:** In the context of DCD there is no evidence that administering 20000 units of heparin (300mg/kg), at the time of withdrawal of life-sustaining therapy, hastens the patient's death"(16).

Neyricnk A, *et al. Curr Opin Anaesthesiol* 2013; **26**: 382-390
Cao Y *et al. Transplantation* 2016; **100**: 1513-1524

Optimisation of the DCD process

- Ante-mortem interventions (e.g. administration of heparin, steroids, and vasodilators)
- Consistent application of published schedules for the prompt identification of death
- Reducing the time interval between the diagnosis of death and organ retrieval (e.g. by withdrawing treatment in the operating theatre)
- Early tissue typing allowing prompt identification and mobilization of suitable recipients
- Post-mortem reperfusion of particularly vulnerable organs such as the liver



Postmortem reperfusion

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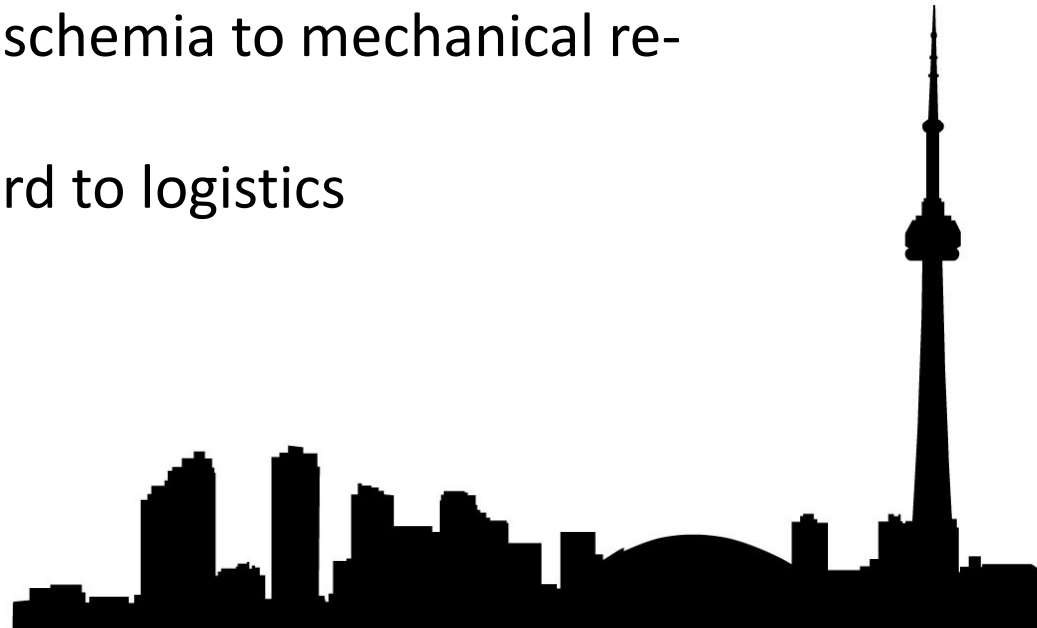
PREDICTING TIME TO DEATH

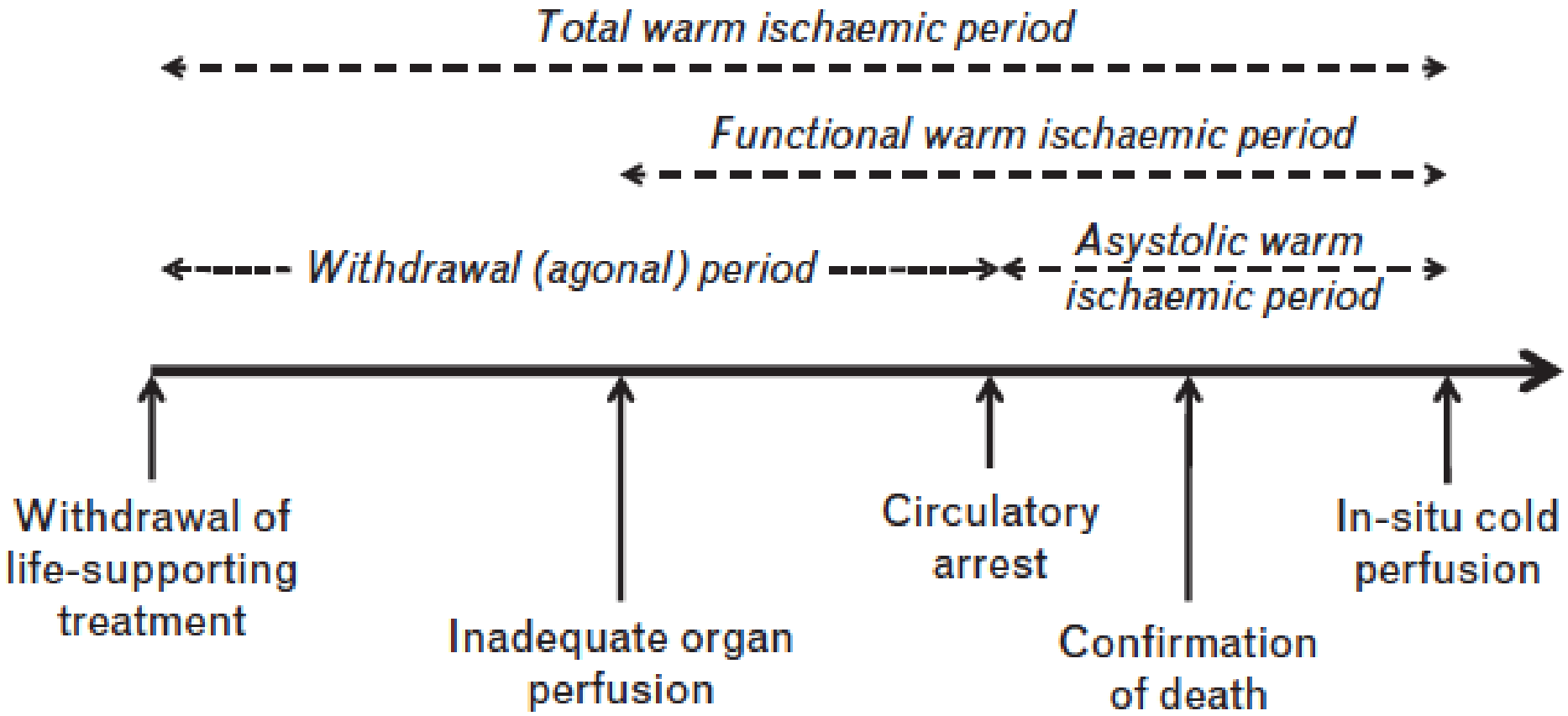
Update on organ transplantation

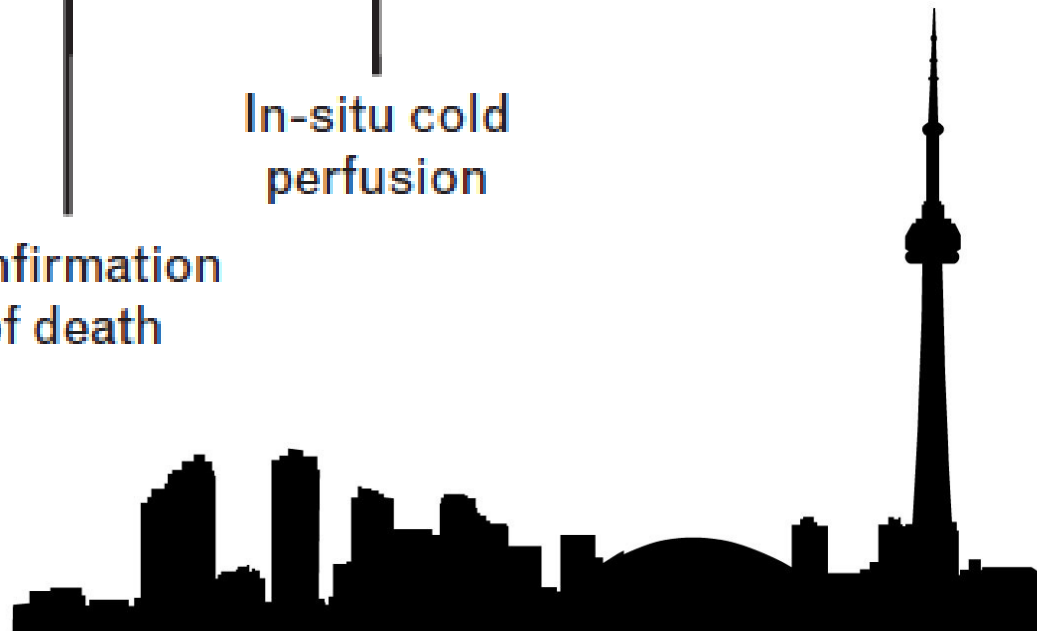
The biggest enemy – warm ischemic time

- Functional warm ischemia starts when:
  - systolic blood pressure <50 mm Hg
  - oxygen saturation <70%.
- Stand-down times from the onset of functional warm ischemia vary by organ:
  - Liver: 30 minutes
  - Pancreas: 30 minutes
  - Lungs: 60 minutes (onset of functional warm ischemia to mechanical re-inflation of lungs)
  - Kidney: 120 minutes - then reassess with regard to logistics



Warm ischemic time terminology

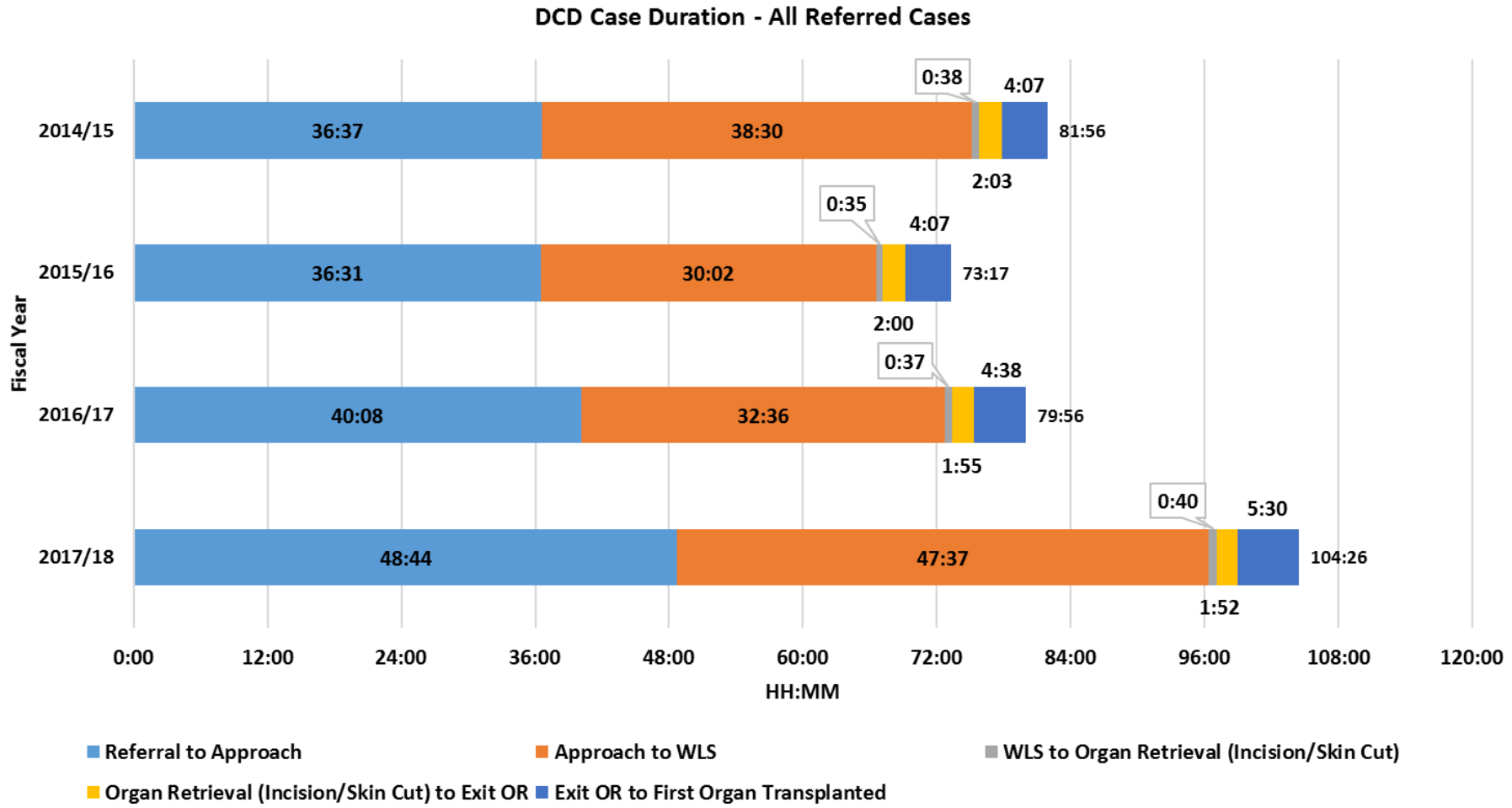




Predicting time to death after withdrawl

- Approximately 20–30 % of consented donors do not die within the time limits required to permit DCD, resulting in false expectations for families and consumption of hospital resources
- Currently existing prediction tools are not highly sensitive
- Consistent predictors of time to death that are recognised:
  - controlled ventilation
  - oxygenation
  - vasopressor use
  - Glasgow Coma Scale Score
  - brainstem reflexes.

Length of time for donation



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SUPPORTING YOURSELF

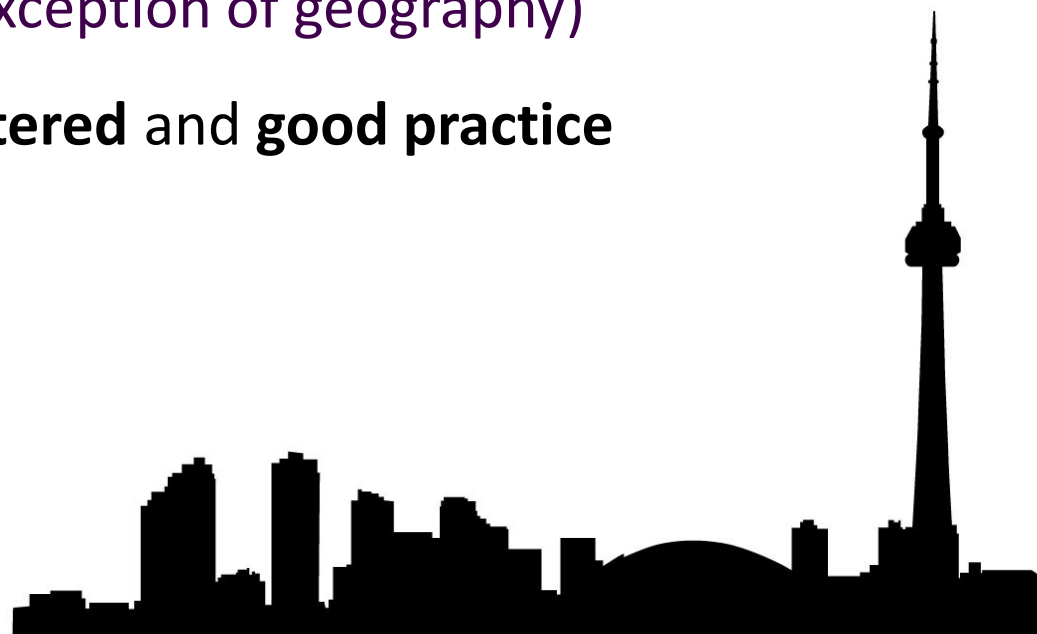
Update on organ transplantation

Importantly

Edge walking

Summary – what I wanted to say

1. Universally, early identification is critical.
2. Separate the discussion of WLST and Donation; separate team, separate time.
3. Allow for escalation of therapy until the approach is made.
4. Commence antemortem interventions only for the consented donor
5. Withdrawal as per the standard of care, (with exception of geography)
6. Including DCD in End of Life Care is **patient-centered** and **good practice**



Thank you

andrew.steel@uhn.ca

Your continued partnership in organ and tissue donation gives comfort to those grieving and hope to those still waiting.