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Protocol and Statistical Analysis Plan for a Comparative Interrupted Time Series Evaluation of the Impact of Deemed Consent for Organ Donation Legislative Reform in Nova Scotia, Canada

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Abstract. The Canadian province of Nova Scotia recently became the first North American jurisdiction to implement deemed consent for deceased organ donation as part of a comprehensive legislative reform of their donation and transplantation system. This study will examine the performance metrics and effectiveness of this policy in comparison with other Canadian provinces via a natural experiment evaluation.We will use a cross-sectional controlled interrupted time series quasi-experimental design. Our primary outcome will be consent for deceased donation as confirmed at the time of eligibility (prior registered intent to donate will be noted but not be considered positive unless affirmed at the time of eligibility). Secondary outcomes will include identification and referral of patients who are potential donors, rates of family override of previously registered intent to donate, and donation and transplantation rates per million population. Data will be collected from potential donor audits in Nova Scotia and 3 control provinces (provinces in Canada without deemed consent policies). Study outcomes will be compared in Nova Scotia relative to control provinces in the 3 y before and 3 y after the implementation of legislative reform. These provinces were selected as having systems resembling those of Nova Scotia but without deemed consent.Using controlled interrupted time series methodology compared with other Canadian provinces with otherwise similar systems, we aim to isolate the impact of the deemed consent aspect of legislative reform in Nova Scotia using a robust natural experiment evaluation design as much as possible. Careful selection of outcome measures will allow donation and transplantation stakeholders to properly evaluate if similar reforms should be considered in their jurisdictions.

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After years of relatively stagnant donation rates—16.8–26.5 (mean 20.7) per million population between 2010 and 2019[1]—the province of Nova Scotia, Canada, passed the Human Organ and Tissue Donation Act (HOTDA) in April of 2019, which came into effect in January 2021.[2] This multifaceted update of the legal framework for deceased donation and transplantation includes a deemed consent model, the first application of this model in any jurisdiction in North America. In a deemed consent model (also known as opt-out or presumed consent), competent adults are presumed to have consented to donation unless they have registered a decision to the contrary. In addition, the provincial government has committed to providing substantial resources to transform the deceased donation systems using established best practices, including donation physicians throughout the province, implementation of mandatory identification and referral, healthcare professional education, performance metric reviews, and public awareness campaigns.[3-5]

Historically, the impact of deemed consent has been inconsistent around the world. Deemed consent models have been incorporated into systems in several jurisdictions for decades and are components of some of the highest-performing donation systems in the world, including some with deceased donation rates >40 per million population.[6] However, the impact and effectiveness of deemed consent remain both poorly defined and controversial.[7-10] A report that analyzed data from 35 countries found no significant difference between the rates of donors with or without deemed consent.[8] Other studies have reported neutral and potentially negative impacts in the short term, particularly on living donor rates.[11,12] Complicating these analyses, consent model reform is typically introduced as part of a broad healthcare system transformation, making it difficult to determine the isolated impact of deemed consent. Finally, recent data from Wales, where a deemed consent model was implemented in 2015, demonstrated that a statistically significant increase in consent rates for deceased donation only occurred years after the transition.[13]

The present study aims to evaluate the impact of the legislation of deemed consent in Nova Scotia on quantitative metrics of donation system performance using interrupted time series methodology as a natural experiment evaluation. We hypothesize that we will observe a gradual increase in consent rates in Nova Scotia compared with similarly structured programs in other Canadian provinces without deemed consent. This work is part of the Legislative Evaluation: Assessment of Deceased Donation Reform (LEADDR) program of research described previously.[14]

PROTOCOL DESIGN AND METHODS

Objectives

The objective of this study is to evaluate changes in quantitative outcome measures of donation and transplantation system performance before and after implementation of the HOTDA-deemed consent model in Nova Scotia when compared with 3 other Canadian provinces that have explicit consent models in the context of a natural experiment evaluation of the deemed consent policy.

We will also evaluate whether other moments related to HOTDA implementation (eg, the announcement of the passage of the legislation) resulted in changes in system performance metrics.

Hypothesis

We hypothesize that the HOTDA legislation will increase measured performance metrics in Nova Scotia (intervention) compared with other Canadian provinces using explicit consent models (control provinces).

We also hypothesize that changes in these metrics within Nova Scotia will not be limited to the moment of HOTDA implementation but will also be observed at other moments, such as the announcement of the legislation or other unexpected moments of attention on deceased organ donation.

Study Steering Committee

A steering committee consisting of the authors of this article (S.B., S.D., J.D., D.H., C.I., K.K., N.L., S.L., K.T., G.T.M., A.V., H.V., and M.W.) has been convened to oversee this study. This committee is chaired by M.W. and co-chaired by K.K. and S.B. The composition of the committee was chosen to ensure content expertise from donation-focused physicians and researchers (S.B., S.D., K.K., and M.W.), transplantation-focused physicians and researchers (K.T. and A.V.), organ donation organization administration and data experts (D.H., C.I., N.L., and G.T.M.), methodologic experts (S.L. and C.K.), and patient partners (H.V.).

Study Design

This natural experiment evaluation will use a cross-sectional controlled interrupted time series (CITS) quasi-experimental design. In a CITS study, measurements of the outcome are taken repeatedly at equal intervals before and after the intervention for both the exposed and unexposed groups. A major strength of the CITS design is the ability to account for baseline trends, and it is among the strongest quasi-experimental approaches for evaluating the effect of an intervention. Although never perfectly matched, the control population can help to reduce additional confounding events or cointerventions.[15] This type of study design has been used previously to evaluate the implementation of health reform initiatives.[16,17] We will observe and compare the trend of outcomes over time in the intervention group (Nova Scotia) relative to the control group (British Columbia, Manitoba, and Ontario; not exposed to the deemed consent policy). For this study, the baseline rate of change of the previously mentioned outcomes will be established during a 3-y period before HOTDA implementation and continue for 3 y after implementation to capture delayed effects. The time of announcement and enactment will be the primary interruptions in the time series and comparisons will be made in Nova Scotia and the control provinces at time points before and after those events. We will also explore the impact of public relations campaigns, if applicable.

Because the data will be collected during a total period of up to 6 y (combined retrospective and prospective), we will also be able to observe other moments where the rate of change alters in the intervention and control provinces to adjust for naturally occurring changes over time. If we observe significant alterations in the rate of change in either Nova Scotia or the control provinces, we will explore any potential factors—such as unplanned media discussions of national donation stories—that could be correlated with the change in rates. This analysis will allow us to examine unexpected correlations with factors that could have influenced donation rates.

Study Setting

The study will be coordinated by Nova Scotia Health (NSH) in Halifax, Nova Scotia, with in-person and virtual participation from steering committee members across Canada. Data will be collected from each province's Potential Donor Audit (PDA) data. PDAs are the primary mechanism used by Organ Donation Organizations (ODOs) to measure performance in donation metrics, including potential donor identification and consent rates.[5,18,19] PDAs involve a retrospective review of all deaths in areas of the hospital that care for critically ill patients and have the capacity for invasive mechanical ventilation, such as intensive care units or emergency departments. The charts of these patients are reviewed to determine whether the patient met the criteria for referral to the organ donation organization and if that referral occurred by cross-referencing against actual referrals. PDAs also record the progress of referrals, including whether the patient's surrogate decision maker gave consent for donation and whether the patient became an actual donor. The metrics recorded in these PDAs are the same and will represent our primary and secondary outcomes as defined below. Data entry of PDAs is performed by various staff associated with organ donation associations, ranging from medical archivists to organ donation coordinators. The development and deployment of the Nova Scotia PDAs were detailed in a recent publication.[20]

The comparator provinces will be British Columbia, Manitoba, and Ontario. These provinces were chosen based on the similarity of their legislative and administrative practices to the Nova Scotia donation and transplantation system—excepting deemed consent—and the availability of their outcome data.

Ethics Approval and Potential Risks

Ethics approval has been obtained from the NSH research ethics board and will be sought in comparator provinces. The primary risk for this study is the breach of confidentiality of patient data. A secure research database will be created to house the data, and any patient-level data will be de-identified. Data will be transferred from the participating ODOs through secure email in CSV or Excel formats. All data will be stored on secure NSH servers that provide a high level of security and are routinely backed up. The research team will access no identifying information from the shared ODO clinical data.

Data Collection

We will request patient-level data from each province for the study period, including all fields from their provinces' PDAs. This data will be de-identified using study-identifying numbers before analysis. Besides the outcome data as defined below, we will collect the demographic and clinical data listed in Table 1. Each identified control province routinely performs PDAs and monitors data collection and validity.

If patient-level data are unavailable because of legislative or policy restrictions, we will request aggregate data on our primary and secondary outcomes. Aggregate data will be requested at quarterly intervals for each year of the study period.

Terminology and Definitions

Although there is variability in the preferred term in the donation literature and the wording of laws both within Canada and internationally,[18] we have chosen to refer to

TABLE 1.

Patient data to request from control provinces

Variable	Details
Age at death, y	Mean age of population and proportion of population in each age group: 0–1 y 1–18 y 19–34 y 35–44 y 45–54 y 55–64 y 65–74 y ≥75 y
Biologic sex	Proportion female
Postal code of residence	Proportion of population in each category[a] Small population centers, with a population between 1000 and 29 999 Medium population centers, with a population between 30 000 and 99 999 Large urban population centers, with a population of ≥100 000 or more. Rural
Type of unit or department where patient was hospitalized Emergency Department, Intensive Care Unit, Intermediate Care Unit	Frequency of patients in each unit/department
Details of death	
Cause of death (donor)	As defined in Nova Scotia PDAs[19]
Death determined by neurological vs circulatory criteria	Proportion of deaths determined by neurological criteria
Medically suitable for donation	Proportion of referred potential donors deemed suitable for donation

All data will be reported in aggregate format at quarterly intervals with population size reported for each interval if individual data are unavailable.

[a]A population center has a population of at least 1000 and a population density of ≥400 persons per square kilometer, based on population counts from the current Census of Population. All areas outside population centers are classified as rural areas.

PDA, Potential Donor Audit.

TABLE 2.

Definition of terms—clinical progression from potential to actual donor

Potential donor: a patient who meets the following organ donation referral criteria in the absence of exclusion criteria

Referral criteria (GIVE criteria retrospectively):

- G = grave prognosis, which, in the opinion of a physician, death is imminent
- I = injured brain or nonrecoverable injury or illness
- V = ventilated/circulatory support (invasive or noninvasive)
- E = end-of life care/withdrawal of life-sustaining therapy discussion is being planned

Exclusion criteria:

- Malignancy within 5 y (excluding primary central nervous system)
- CJD/rabies/West Nile Virus
- Prematurity, defined as <36 wk corrected gestational age

Referred potential donor: a potential donor who is referred to the organ donation program

Eligible donor: a potential donor who is not deemed medically unsuitable by the donor coordinator

Approached eligible donor: a potential donor whose SDM is approached or is approached themselves (in the case of a conscious competent donor) for consent to deceased donation

Consented donor: an approached eligible donor for whom legally valid consent was obtained for organ donation

Actual donor: a consented donor who had at least 1 organ recovered with the intent to transplant

CJD, Creutzfeldt-Jakob disease; SDM, substitute decision maker.

consent as opposed to authorization or affirmation because this is the term most widely used in Canada and the term that most easily encompasses practices related to both neurologic determinations of death and donation after circulatory death donation pathways.

Critical terms have been defined in the text of this article and in Table 2, including detailed definitions of all terms (eg, potential donor, eligible donor).

Outcomes

The primary outcome will be rates of consent to deceased organ donation given by substitute decision makers or the eligible patient themself at the time the patient is eligible for donation.

The consent rate will be defined numerically as the number of donors for whom consent to deceased donation is obtained divided by the number of approached eligible donors (expressed as a percentage). The numerator will be cases where consent was obtained for organ donation from either the substitute decision maker or the patient themselves after being approached by a representative of the ODO or medical treating team to discuss the possibility of donation according to local identification and referral practices. The denominator will be all patients approached for organ donation. Expressed consent in a registry—or lack of registered objection to deemed consent—will not be considered consent for donation unless confirmed at the moment of eligibility. Therefore, a patient who had registered consent before illness or injury but for whom consent was not given to proceed with donation after approach for donation when they were eligible would not be counted as positive consent. Cases where consent is given and withdrawn will be considered cases of nonconsent, and withdrawal will be recorded separately. Cases where consent is given but the patient is later deemed ineligible for medical or logistic reasons (including nonprogression to death in acceptable time frames for donation after circulatory death cases) or where no matched recipient is available for implantation of the donor's organs will be counted as positive consent.

For this study, deceased solid organ transplantation refers to heart, lung, liver, kidney, pancreas, pancreatic islet cells, or intestinal recovery transplantation. Consent for any other postmortem recovery of tissue or vascularized allografts (eg, face, hand) will be considered out of scope. Secondary outcomes are listed and defined in Table 3. Notably, living donation rates are being evaluated in a related project and were excluded as an outcome of this study.

DATA ANALYSIS

Controlled Interrupted Time Series

Each province will have aggregate quarterly outcomes for 3 y before and after the intervention (12 time points before and after the intervention), which puts us within the recommended number of data points for CITS analysis.[21] The a priori moments we will evaluate are the announcement in April 2019 and then the implementation of the legislation in January 2021.

Selection and Modeling of Control Group

We have 3 potential control provinces. These controls were selected because they did not experience a change in their donation consent model during the study period; data on the outcome of interest and donation system similarities are available. These similarities include legislation with a mandatory referral of potential deceased organ donors, audits of system performance, including missed donation opportunities, roles for donation-focused intensive care specialists, and participation in Canada-wide best practice development and implementation.[18,22,23] Because of the distance separating the intervention and control locations, no contamination effect is anticipated. The quality of the controls will be assessed by modeling the preintervention trend lines in the treatment and control groups.[24] All analyses will be supported by a biostatistician from NSH and performed using R and SAS.[25,26]

Descriptive Statistics

Baseline demographics, by province, will be represented in visuals and tabular format as descriptive statistics with categorical data summarized as frequencies and percentages and continuous data reported as means, medians, SDs, and interquartile ranges. Time series scatter plots will be created for

TABLE 3.

Secondary outcomes and analyses

	Patient-level outcome	Outcome analysis
Identification and referral	Documented referral of an eligible potential donor to the ODO	Number of patients referred to the ODO divided by the number of potential donors identified in the PDA (expressed as a percentage)
Family override of previous intent to donate	Family refusal to donate despite previous registration of intent to donate and/or a lack of a registered no in the case of Nova Scotia	Rate of family override is calculated as the number of instances of family override divided by the number of patients with registered intent to donate or a lack of a registered no in the case of Nova Scotia
Donor rates per million of the population	Number of actual donors in a province	Actual donors per million inhabitants in the province
Transplanted patients per million of the population	Number of patients receiving a transplanted organ from a deceased donor in a province	Number of people who received at least 1 organ transplantation from a deceased donor per million inhabitants in the province
Number of organs recovered per donor	The number of solid organs recovered from each actual donor	The median number of organs recovered per actual donor
Type of organs recovered for transplantation	Type of solid organs recovered for transplantation (eg, kidney, heart).	Median number of each type of organ recovered per actual donor
Donor conversion rate	Progression of an individual patient from an eligible donor to an actual donor	Number of actual donors divided by total number of eligible donors
Import and export activity	Not applicable	Number of organs from deceased donors imported and exported with the intent to transplant in and out of the reference province

ODO, Organ Donation Organization; PDA, Potential Donor Audit.

pretrend outcomes and covariates for the treated and control groups to explore underlying trends, seasonal patterns, and outliers.

Models

We will use a segmented regression model with variables that will allow for estimating both a level and trend change. To determine the most appropriate model, we will run several generalized linear models specifying various distributional families paired with compatible link functions, followed by an inspection of model output, Akaike's information criterion, and graphic displays. We suspect that a log-binomial or modified Poisson will be the most appropriate model for our primary outcome of consent rates (expressed as a percentage). An autoregressive (AR) serial covariance structure will also be considered to account for serial correlations. An extension of the Newey-West methodology for SEs will be used to adjust for any SE autocorrelation if present.[27] Augmented Dickey-Fuller test will be performed to test for nonstationarity. Diagnostic plots based on deviance residuals (deviance residuals versus time, partial autocorrelation function plots) will be used to investigate any anomalies in the data as well as residual correlation. Seasonality will be explored using periodic functions and a time-stratified model.[28]

Although ITS does not require a covariate balance between intervention and control series, a sensitivity analysis will be performed using a synthetic control method where nonexposed control units are reweighted.[29] An optimal weighting scheme is selected to maximize covariate imbalance. This will investigate how comparable the treated group is to the control group in terms of population subgroups and characteristics that may change differentially over time between the groups. Covariates to be potentially included are individual factors, such as biological sex, urban/rural address (4 categories defined by Statistics Canada), type of unit where patients were hospitalized, cause of death, and death determined by neurological as opposed to circulatory criteria. We will also consider population covariates such as the donation consent rate during the preintervention years, the preintervention percentage of the population in each age group (using Statistics Canada's classification structure), percentage of immigrants in the jurisdiction, percentage of population with a religious affiliation, and education attainment. Additionally, an uncontrolled ITS analysis of the intervention group will be performed to better understand the robustness and confidence of the CITS model.[30]

Additional Subgroup Analyses

Where possible, the primary and secondary outcomes will be stratified by patient demographic data (eg, age, mode of death, urban versus rural) and donation pathway (Donation after Death by Neurologic Criteria or after Death by Circulatory Criteria). We will also analyze the consent rates in patients who had previously registered intent to donate and for whom deemed consent *was* applied in Nova Scotia (eg, no registered intent, family unsure of wishes). We will focus more on effect estimates than statistical significance for these results, given the challenges around interaction tests generally having low power to detect differences in subgroup effects and the risk of falsely detecting differences because of multiple testing.[31] Collection of these data from comparator provinces will depend on the details of the data sharing agreement with each province (patient level versus aggregate data).

Threats to Validity and Robustness Checks

The announcement of the initiative was in April 2019 and the implementation was in January 2021, making this analysis susceptible to anticipatory effects (where knowledge of the impending intervention leads to a change in behavior different from what would otherwise have occurred). We will look for lead effects by "interrupting" the data at the time of implementation.

Spillover effects may also occur when aspects of the intervention spill over and affect the control group. The introduction of deemed consent in Nova Scotia was covered by several

news sources and widely discussed nationally. This may have prompted individuals in our control provinces to change their behavior regarding deemed consent. Most of the discussion took place at the time of announcement and not implementation; therefore, we will assess whether changes occurred in our control groups at the time of the announcement. If spillover effects are present, we will consider sensitivity analyses, which remove the time between the announcement and implementation from the pre-period.

Impact of COVID-19

The study period we have selected encompasses the entirety of the COVID-19 pandemic, which has been shown to have a variable impact on donation and transplant systems internationally.[32] Canadian Blood Services has closely tracked the relationship between COVID-19, the number of donors and transplants in Canadian provinces, and the time periods when programs were completely or partially closed because of the pandemic.[33] We will compare these data to our outcome data to see how they correlate. Depending on those results, we may consider removing outlier periods or exploring other options to account for this challenge.

DISCUSSION

The purpose of the LEADDR research program is to rigorously evaluate the impact of legislative strategies designed to improve donation and transplantation.[14] As the first North American jurisdiction to include deemed consent in its donation and transplantation system, there is widespread interest in the impact on Nova Scotia's performance. The proposed CITS is a key component of the LEADDR program to evaluate this novel natural experiment. This study will provide an evaluation of the measurable impact of implementation, including a comparison with similarly structured systems in the rest of Canada.

In designing this study, we carefully considered the question of what meaningful outcomes could be expected from legislative reform. Although the stated purpose of the HOTDA legislation is to increase transplantation activity, we considered simply looking at gross or adjusted donation and transplant rates per million population to be an inadequate outcome. Donation rates depend on the number of eligible donors in a given time frame, and implementing a novel consent model would have no anticipated effect on the rate of illness or injury that would lead people to become eligible donors. However, the consent model would be expected to influence the consent rate after the approach, which is why this is our primary outcome. By collecting secondary outcomes, such as identification and referral rates and the overall donation rates, we anticipate identifying what steps in the process of conversion from eligible to actual donor potential donors are most often lost. Doing so will allow stakeholders to accurately evaluate the legislative reform and direct resources efficiently to address system processes that require the most improvement.

In addition to careful outcome selection, another strength of this study is its robust interrupted time series methodology. Evaluation of medical system reform is fraught with the potential for confounders. Laws are not passed under experimentally controlled conditions, and teasing out the impact of the deemed consent aspect of HOTDA as opposed to the other aspects of the law, such as mandatory referral reform, will be difficult. Understanding those inherent limitations, this methodology will allow us to compare to Canadian provinces that have systems that are similar in terms of structure and function. All provinces collaborate with Canadian Blood Services, the national deceased donation coordinating body that creates leading practices and has multiple committees that allow for the exchange of practices and information between system clinicians and administrators. The systems also have several key components in common, such as mandatory referral, a donation to physicians, and a PDA. These provinces differ in other aspects—population, amount of donation, and transplantation funding—and none of them implemented a host of reforms that included aspects other than deemed consent during the study period. However, this is typical in donation system reform, where jurisdictions rarely enact consent model changes in isolation.[34] Absent a system that would enact stepwise reforms with ongoing comparisons to a matched control, we anticipate that our selection of otherwise similar provinces will allow for meaningful comparison.

The study will also have potential challenges related to data collection and comparison. We anticipate challenges related to the accuracy and availability of data from comparator provinces, including the logistics of obtaining data and any privacy concerns about sharing data between provinces. We may not be able to compare secondary outcomes related to intent to donate registration—necessary to calculate rates of family override of intent to donate—if data from the provincial organ donation organization are unavailable. Additionally, data collected from PDAs will come from multiple jurisdictions that created their PDAs independently and for quality assurance, not research purposes. As such, definitions regarding terms such as potential donors will vary slightly between provinces. We plan to engage the steering committee with their significant expertise in situations where we may be forced to determine whether definitions between provinces are comparable enough to permit comparison or if we should report outcomes if only some of the comparator provinces were able to provide data. As they are administrative databases in multiple provinces, it is also possible that data entry and validation practices will vary across provinces. However, these limitations represent the real-world limitations of analyzing clinic administrative data instead of prospective research databases. Finally, it is possible that trends unrelated to the consent model in the comparator provinces could impact our comparison. For example, the opiate overdose crisis has had a documented variable impact on donation rates across Canada, with British Columbia particularly affected.[35]

Ultimately, we anticipate that these results will be of broad interest as jurisdictions in Canada and North America consider if deemed consent should be integrated into their systems. These results will be disseminated in the form of technical reports for government and healthcare organizations, presentations, and prepared for academic publications. As this project is funded as part of a Health Canada initiative to improve the donation and transplantation system throughout Canada, and many of the steering committee members are key stakeholders in that system, we anticipate rapid dissemination and potential uptake of these findings within Canada. Further international dissemination will be performed through international academic societies, such as The Transplantation Society and the International Society of Organ Donation and Procurement.

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