ACCESS TO DEEP BRAIN STIMULATION IN CANADA

COMPREHENSIVE NEEDS ASSESSMENT FOR DEEP BRAIN STIMULATION IN CANADA, A HEALTH SERVICE RESEARCH PERSPECTIVE

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LAY ABSTRACT

Movement disorders are progressive, debilitating neurologic conditions that severely impact the quality, speed and fluency of movement as a result of basal ganglia dysfunction. Medical therapies remain the mainstay of treatment, however high quality evidence supports the use of deep brain stimulation (DBS) to relieve these symptoms in well-selected patients. Given the upfront cost of surgery associated with DBS, and the comprehensive evaluations at tertiary care centres (including a multidisciplinary team with neurologists, neurosurgeons, neuropsychologists, psychiatrists, and electrophysiologists), this is a limited resource, particularly in overburdened publicly funded healthcare systems.

There have been no previous attempts to comprehensively analyze access to DBS in Canada's public healthcare system through investigation of need for these services, matched access, and investigation of barriers to access.

This thesis comprises 5 chapters that inform this knowledge gap through the quadruple aim of health service research (patient perspective, health care provider perspective, cost, and population level data), aiming for equitable access to care in Canada.

Chapter 1 is an introduction providing the rationale for conducting each of the included studies.

Chapter 2 reports on an evaluation of cost, titled Economic Evaluations Comparing Deep Brain Stimulation to Best Medical Therapy for Movement Disorders: A Meta-Analysis.

Chapter 3 presents an evaluation of healthcare provider and patient perspective, titled Mixed Methods Survey of Stakeholders to Identify Barriers to Accessing Deep Brain Stimulation for Movement Disorders in Canada.

Chapter 4 is a retrospective cohort study providing population level data assessing patients who have received DBS in Canada, titled Canadian Access to Deep Brain Stimulation for Movement Disorders: A Nationwide Retrospective Study.

Finally, Chapter 5 discusses the conclusion, limitations, and implications of the research presented in this PhD thesis.

ABSTRACT

BACKGROUND:

The Canadian healthcare system is subject to national standards that may be challenging to meet, given the evolution and integration of technology in healthcare in disciplines like functional neurosurgery, utilizing therapies such as deep brain stimulation (DBS), whereby implanted devices have provided benefit for patients with movement disorders. A comprehensive assessment of the need for this service to match with the delivery of DBS has not been performed.

This thesis comprises a series of studies that aim to address this knowledge gap through the quadruple aim of health service research.

METHODS:

The first study is a systematic review and meta-analysis including economic evaluations comparing DBS for movement disorders with medical management only.
The second is a mixed methods survey of Canadian stakeholders for DBS.
The final study is a nationwide retrospective cohort study of DBS patients from 2019-2022 to determine factors that may influence access.

RESULTS:

Through analysis of 14 economic evaluations, DBS appears to be a cost-effective treatment when considered across the remaining lifespan of the patient with positive incremental net benefit for DBS with a mean difference of 40,504.81USD (95% CI 2,422.42; 78,587.19).

Additionally, 220 responses from all DBS stakeholder groups revealed that costs associated with travel, waitlists, lack of specific resources, poor understanding of movement disorders and DBS indications, and referral pathways were barriers to accessing DBS.

Finally, preliminary results identified 162 DBS patients. Potential factors that may increase access to DBS were indication (Parkinson's disease), higher socioeconomic status, and race.

CONCLUSIONS:

While DBS is a cost-effective therapy for patients with movement disorders, the current delivery of this service needs significant improvement. This includes improved education, streamlined referral pathways, and policy change at a governmental level, with further investigation to determine regions of the country where need for DBS far exceeds current access.

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Because of Mom and Dad; Thank you for teaching me to be whatever I want to be, and helping me become just that.

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CONTRIBUTIONS BY OTHERS

At the end of each chapter is a full account of authors' contributions.

PREFACE

The work in this dissertation is presented as a "sandwich thesis" that includes three manuscripts which have been published, accepted for publication, or prepared for submission. The manuscript in Chapter 2, Economic evaluations comparing deep brain stimulation to best medical therapy for movement disorders: A meta-analysis, was accepted for publication on August 28, 2023 to *Pharmacoeconomics*. The manuscript in Chapter 3, Mixed methods survey to identify barriers to accessing deep brain stimulation for movement disorders in Canada was submitted for publication on April 11, 2024 to *The Canadian Journal of Neurological Sciences*. The manuscript in Chapter 4, Canadian Access to Deep Brain Stimulation for Movement Disorders: A Nationwide Retrospective Study represents preliminary analyses for a multicentre retrospective cohort study in preparation for publication to The Canadian Journal of Neurological Sciences.

The systematic review and meta-analysis presented in Chapter 2 was completed under the supervision of Dr. Sunjay Sharma. I conceived of the idea for the study, developed the protocol and received feedback from the co-authors. I screened and abstracted data from studies along with a research team. I analysed the data and wrote the systematic review manuscript. I incorporated comments from co-authors and submitted the manuscript for publication. I responded to reviewer comments. I conceived of and conducted the work in Chapter 3 under the supervision of Dr. Sunjay Sharma and with the clinical and methodological input of an expert panel. I completed data analysis, drafted the manuscripts, incorporated feedback from the co-authors, and submitted the manuscript for publication. Chapter 4 is a multicentre retrospective cohort study being conducted under the supervision of Dr. Sunjay Sharma. I conceived of the

idea for the study, arranged collaboration with included sites, completed preliminary analyses, drafted the manuscript and incorporated feedback from co-authors.

The mixed methods survey presented in Chapter 3 in this dissertation was funded by the Regional Medical Associates of Hamilton.

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LIST OF ABBREVIATIONS

BMT Best medical therapy

ΔC Change in cost

CE Cost effectiveness

CHUM Centre Hospitalier de l'Universite de Montreal

CI Confidence interval

CPI Consumer price index

DBS Deep brain stimulation

ΔE Change in efficacy

ET Essential tremor

EQ-5D European Quality of Life five-dimension

GDP Gross domestic product

GPi Globus pallidus internus

HiREB Hamilton Integrated Research Ethics Board

H&Y Hoehn and Yahr Scale

ICER Incremental cost-effectiveness ratio

ICES Institute for Clinical Evaluative Sciences

ICU Intensive care unit

INB Incremental net benefit

NICE National Institute for Clinical Excellence

PD Parkinson's disease

PDQ-39 Parkinson's Disease Questionnaire-39

PPP Purchasing power parity

QALY Quality adjusted life years

QoL	Quality of life
SD	Standard deviation
STN	Subthalamic nucleus
UPDRS	Unified Parkinson's Disease Rating Scale
WTP	Willingness to Pay

CHAPTER 1: Introduction

1.1 Background

The Canadian healthcare system is a collection of provincial and territorial insurance plans subject to national standards set out by The Canada Health Act, established in 1984. These principles include comprehensiveness, public administration, accessibility, universality, and portability (1). While each of these stipulations are challenging to meet, access to care is particularly challenging in the Canadian context.

Access to healthcare is defined with respect to access to a service, provider, or institution, and therefore the ease with which individuals are able to utilize appropriate services in proportion to their needs (2,3). Equitable access to care is challenging in Canada, due to the unique geography of the country and its sparse population distribution. As a result, many Canadians in isolated regions of the country remain underserviced (4,5). As the complexity of healthcare delivery has evolved, concerns have grown about accessibility to critical healthcare services, particularly those requiring significant technological investment (6). Integration of technology in healthcare requires significant financial cost and expertise, limiting the ability of the Canadian healthcare system to provide such services in a widespread fashion. As such, these services are frequently centralized to larger centres in urban settings.

One example of the interface of medicine and technology is functional neurosurgery. A subspecialty of neurosurgery, its focus involves procedures to alleviate symptoms of a number of central nervous system disorders, and ultimately improve quality of life, through modulation of neurological circuits to modify the function of the nervous system. Procedures performed within the domain of functional neurosurgery involve the use of neurostimulators, ablative procedures,

intracranial monitoring, and implanted devices. While a number of central nervous system disorders can be treated within the domain of functional neurosurgery, movement disorders have remained a significant focus for therapies.

Movement disorders are a group of neurologic conditions that affect the speed, fluency, quality, and ease of movement (7). Examples of movement disorders commonly treated with functional neurosurgical procedures include Parkinson's disease, essential tremor, and dystonia. Deep brain stimulation (DBS) is a common therapeutic intervention with proven effectiveness. This surgical approach involves the surgical placement of microelectrodes deep within the brain to target specific nuclei associated with control of movement. Target sites commonly utilized for DBS include the ventral intermediate nucleus of the thalamus, globus pallidus internus, and subthalamic nucleus. Once leads are placed, high frequency electrical stimulation exerts functional deafferentation of the target structure that modulates cortical activity and influences involuntary aspects of movement and muscle tone, thereby improving efficiency of movement (7). This therapy has been effective in improving function for patients with movement disorders, reducing dependency on medications, and allows patients to avoid ablative surgical intervention.

Unfortunately, given the degree of expertise, specialized surgical equipment and staff including electrophysiologists, and cost of implantable devices, this treatment is only offered at a small number of large academic centres in Canada. Additionally, patient selection is a key factor in determining effectiveness of this therapy. As such, a rigorous assessment for candidacy is required, with experts in a number of disciplines. Movement disorder neurologists thoroughly assess patients symptoms and disease severity to determine the likelihood of success with DBS,

and optimize medical therapy. Comprehensive neuropsychological evaluation is required, as decline in cognitive functioning may occur in poorly selected patients that undergo DBS. Examples include impulsive behaviour, worsened speech articulation, and changes in mood (8–12), as well as speech fluency (13–29), and global cognitive deterioration (30,31). Medical optimization of comorbidities, concerns with neuroanaesthesia, physiotherapy, occupational therapy, and social work assessments are also utilized. These experts, along with functional neurosurgeons, review potential candidates as a multidisciplinary team. The specialized nature of such multidisciplinary teams further contributes to the centralization of this service to large academic centres in urban areas.

As the field of functional neurosurgery continues evolve and the population in Canada ages, it is essential to provide equitable access to DBS, a service that can profoundly improve quality of life for patients. Currently, gaps remain in our understanding of the prevalence of disease, burden of disability, access to care, or opportunities for alleviating suffering and reducing health care costs associated with conditions amenable to functional neurosurgical intervention.

Previously identified barriers to DBS for movement disorder indications include race (32–40), gender (33,35,38–41), socioeconomic status/insurance status (32,33,35,38,39,42,43), lack of referrals to tertiary centers/movement disorder clinics (44,45), and geographical distance from tertiary centers (46–49). The majority of studies have been conducted in the United States, however Honey *et al* provided a national snapshot of the geographic distribution of DBS services in Canada, revealing a clear disparity between provinces in terms of access (i.e. excellent access in Saskatchewan with extremely poor access in Newfoundland and Labrador). What this study

did not investigate was the patient need for these services to determine equitable access (50), Pooja *et al* investigated the demographics of patients treated with DBS in Edmonton, revealing that significant disparities in access exist based on gender and ethnicity (40), and Crispo *et al* completed a retrospective cohort study utilizing ICES data in Ontario, revealing that of 46,237 individuals with Parkinson's Disease, only 1.2% went on to receive DBS. They also highlighted that Northern Ontario residents were more likely than their Southern counterparts to receive DBS (AOR 2.23, 95%CI 1.15-4.34), and that neighbourhoods with the highest number of visible minorities were less likely to receive DBS, and that regular neurologist care, and use of multiple Parkinson's medications were positively associated with DBS (48). Again, this study did not investigate the need for this service. For example, they reported the proportion of patients going on to receive DBS without defining what an expected number should be.

There have been no previous attempts to comprehensively analyze access to DBS in Canada, through investigation of need for these services, matched access, and investigation of barriers for practitioners; the proposed study attempts to fill that gap in the literature. This study aims to thoroughly assess DBS across Canada to improve access through the Quadruple Aim of health service research, with the goal to achieve equitable access to DBS in Canada.

The 'Quadruple Aim' is an internationally-recognized framework focused on the design and delivery of an effective healthcare system. The four objectives of the Quadruple Aim are to improve the patient and caregiver experience, improve the health of populations, reduce the per capita cost of healthcare, and improve the work life of healthcare providers (51–54). Not only does this framework place focus on effectiveness of health systems, but equity of health services

(53). Through the lens of this framework, the current study aims to comprehensively analyze the need for DBS across Canada and determine if this need is being met through current access. Additionally, it aims to identify barriers to efficient access and means to address gaps in access to provide equitable access to this service for patients that may benefit from DBS. As such, the study seeks to assess DBS in Canada from the perspective of cost, population level data, patient and caregiver perspectives, and healthcare provider perspectives.

1.2 Cost

With advancing biomedical technology and an aging population, the Canadian healthcare system is faced with increasing demand in terms of financial cost, provincial healthcare programs have limited budgets with which to provide necessary services. Therefore, it is critical in health service research to determine the best use of these limited available funds to provide healthcare and promote health and wellbeing for the greatest number of Canadians. The underlying principle is maximizing value for money through allocative efficiency (i.e. setting priorities with the greatest impact).

Economic evaluations compare costs and effectiveness between therapeutic options, and provide critical insight for resource allocation, particularly within publicly funded healthcare systems. Full economic evaluations consider the health benefits of treatments under investigation, often measured in quality of life years (QALY) gained by a given therapy. QALY is a metric that measures both quality and quantity of life, and is accepted to include a number of domains of well-being, including activities of daily living, principal activities, health, outlook, support, and are generally patient reported. Cost per gain in QALY is used to compare therapies, with the

assumption tied to allocative efficiency that payers desire for their financial contributions to be put to work in maximizing health gain. If a treatment produces low levels of cost-effectiveness (i.e. high cost per QALY gained), a provider would not be allocatively efficient, as that financial resource could be better utilized elsewhere to achieve higher potential health gain. Cost-effectiveness analyses are particularly useful for the investigation of surgical interventions, which carry a significant up front cost and therefore are scrutinized by payers for the expense associated with surgery compared to medical therapy alone in cost analyses. Providing the context of cost-effectiveness over the duration of therapy (typically costs amortized over the remaining lifespan of the patient) can demonstrate the cost savings of such expensive interventions.

A number of economic evaluations have been conducted to determine the cost-effectiveness of DBS compared with best medical therapy alone, with previous systematic reviews summarizing available evidence for the use of DBS from a cost-effectiveness standpoint. However, previous literature has not provided meta-analysis of available economic evaluations comparing these therapeutic interventions.

Chapter 2 presents a systematic review and meta-analysis of available economic evaluations comparing DBS with best medical therapy alone.

We hypothesize that, when amortized over the duration of the patient's lifetime and in consideration of effectiveness in terms of quality of life for patients with movement disorders, that DBS is a cost-effective therapy. Additionally, we hypothesize that cost-effectiveness may

depend on factors such as diagnosis (i.e. Parkinson's disease vs. essential tremor), patient age (i.e. more cost-effective in younger patients), and healthcare system (i.e. single pay (public) systems vs. multi-payer (private) systems).

1.3 Perspectives of patients, caregivers, and healthcare providers

The equitable, effective provision of healthcare is contingent upon delivering services in a meaningful and effective manner that meets patients' needs and preferences. The concept of access to care considered through commonly utilized indicators often fails to reflect patient experience to provide a comprehensive picture (55). The inclusion of patient and caregiver perspective as a key component of the Quadruple Aim to deliver effective healthcare, given patients are frequently in contact with the healthcare system and therefore have expertise on barriers to access. Patients have a global perspective from primary to secondary healthcare and social care, that encompasses their personal needs for various services. Therefore, it is critical for decisionmakers and researchers to consider patients' perspective as to what access to care means (55).

The Quadruple Aim of health service research was initially developed as the Triple Aim – enhancing patient experience, improving population health, and reducing costs (56). It was an approach to optimizing health system performance, however in attempts to enact the Triple Aim in practice, healthcare providers reported increased stress and burnout as an increase in administrative demand occurred. As a result, work life dissatisfaction among healthcare providers threatened the patient centred approach that the Triple Aim promised. For this reason, a fourth component was proposed (52). Obtaining healthcare provider perspectives in health

systems research allows decisionmakers and investigators to streamline healthcare systems to better serve healthcare providers, thereby better serving patients. Healthcare providers develop an understanding of the barriers encountered in the delivery of health services, and can provide potential solutions to eliminate these barriers to accessing care.

To improve access to DBS in Canada, an understanding of barriers and facilitators to access is required. Both patients/caregivers and healthcare providers at every point of contact with the healthcare system along the referral pathway to DBS provide insight to eliminate these barriers and facilitate improved access across Canada.

An understanding of barriers alone cannot identify where to direct resources. To comprehensively assess access to DBS in Canada, an understanding of the need for this service is required. However, determining the prevalence of candidates for DBS is a challenging concept. The literature relies on retrospective data to determine a patient's ability to access functional neurosurgery, however this method is limited, in that patients have already overcome existing barriers to receive surgical intervention in many of these studies. Population-level data from databases such as the Canadian Institute for Health Information does not provide the granularity to assess operative candidacy, which requires clinical acumen. One previous international study surveyed neurosurgeons to estimate the proportion of patients with a number of neurologic diseases that warrant neurosurgical consultation or operative management. Investigators reported high concordance rates between clinicians regarding estimates (57), providing evidence of utility for utilizing expert opinion to estimate prevalence.

In the third chapter, utilizing mixed methods surveys of stakeholders for DBS along the patient care pathway (family physicians, neurologists, neurosurgeons, advocacy groups) and patients/caregivers, perspectives were elicited from healthcare providers and patients regarding barriers and facilitators to accessing DBS in Canada. Additionally, expert opinion was used to estimate the prevalence of candidates for DBS in Canada.

We hypothesize that the prevalence of candidates for DBS in Canada outweighs current access to the service, and that key barriers include distance of patient residence to a centre offering DBS therapy, and socioeconomic status, as previously demonstrated in the literature.

1.4 Population level data

The Quadruple Aim of health service research states that the delivery of efficient healthcare is contingent upon improving the health of populations. Organizations like the Ontario Ministry of Health and the Canadian Institute for Health Information that have adopted the Quadruple Aim have begun to consider factors like socioeconomic status, race, gender, and geography and how it contributes to equity in access (53,54). Through determining characteristics of individuals who have successfully met the outcome when it comes to accessing DBS, in that they have undergone this therapy, means to address disparities can be developed.

Although DBS is a mainstay of surgical treatment for movement disorders, access to the service is limited as a result of centralization to limited academic centres in larger cities (46–49). A number of socioeconomic and cultural differences have been demonstrated to negatively impact access to DBS, including race (32–35), gender (33,35,38–41), socioeconomic status

(32,33,35,38,39,42,43), and lack of referrals to tertiary centres with movement disorder clinics (44,45).

While the majority of studies on access to DBS have been conducted in the American healthcare system, a small number of Canadian studies have provided some understanding of barriers to access in Canada. In 2018, Honey *et al* utilized industry data to provide a national snapshot of the geographic distribution of DBS in Canada, revealing clear disparities in access between provinces. For example, investigators found excellent access to DBS in Saskatchewan and extremely poor access in Newfoundland and Labrador (50).

Since publication of the study by Honey *et al*, the Canadian healthcare system has continued to evolve. With the advent of the COVID-19 pandemic came unforeseen strain on the public healthcare system, resulting in significant delays in care. During the first 31 months after the first cases of COVID-19 were detected in North America in March 2020, resulting in cessation of elective surgical cases at nearly all Canadian institutions, approximately 937,000 (14%) fewer surgeries were performed than prior to the pandemic in 2019 (58). For patients living with movement disorders, care has been significantly impacted by the pandemic, with one Canadian study reporting patients with Parkinson's disease have experienced amplification of negative experiences in healthcare compared with prior to the pandemic (59).

Chapter 4 comprises a national, multicentre cohort study that aims to describe current access to DBS for movement disorders in Canada through retrospective data from each of the 15 Canadian centres offering this service. Additionally, it aims to compare current access to that reported by

Honey *et al* in 2018 to determine if improvements have been made in providing this therapy to patients who need it, particularly whether gaps in access identified by Honey *et al* have been addressed, and to determine the extent of the impact COVID-19 had on delivery of DBS nationally, in terms of decrease in number of cases and recovery of delivery throughout the pandemic. Finally, similar to Honey *et al*, the study aims to determine if factors such as gender, socioeconomic status, indication, or geographic location impact patients' ability to access DBS.

We hypothesize that, similar to results from Honey *et al*, patients who have undergone DBS are likely to have higher socioeconomic status than average and live closer to centres that provide DBS therapy. Additionally, we hypothesize that the COVID-19 pandemic was associated with a profound decrease in the number of DBS surgeries completed nationally, and that recovery to pre-pandemic numbers alone will not adequately address a backlog of surgical cases, as seen in other specialities.

1.5 Conclusion and future directions

Chapter 5 presents conclusions based on this thesis work, describes its limitations, and summarizes future research planned based on findings from this thesis.

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CHAPTER 2: Economic Evaluations Comparing Deep Brain Stimulation to Best Medical Therapy for Movement Disorders: A Meta-Analysis

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Economic Evaluations Comparing Deep Brain Stimulation to Best Medical Therapy for Movement Disorders: A Meta-Analysis

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Keywords:

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Key Points:

- Deep brain stimulation is cost-effective compared with best medical therapy in Parkinson's disease, when considered over longer time horizons.
- Inclusion of economic analyses conducted alongside clinical trials are needed to provide more robust data for economic evaluations to support decision making.
- Limited evidence exists in regard to economic evaluations for movement disorders other than Parkinson's disease.

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ABSTRACT

Background: Movement disorders (Parkinson's Disease, essential tremor, primary dystonia) are a debilitating group of conditions that are progressive in nature. The mainstay of treatment is best medical therapy (BMT), however a number of surgical therapies are available, including deep brain stimulation (DBS). Economic evaluations are an important aspect of evidence to inform decision makers regarding funding allocated to these therapies.

Objective:

This systematic review and meta-analysis evaluated the cost-effectiveness of DBS compared with BMT for movement disorder indications in the adult population.

Methods:

Ovid Medical Literature Analysis and Retrieval System Online, Embase, and Cochrane Central Register of Controlled Trials were queried. Only economic evaluations reporting incremental cost-effectiveness ratios for DBS vs. BMT for movement disorders were included. Studies were reviewed in duplicate for inclusion and data abstraction. Data was harmonized using Consumer Price Index (CPI) and Purchasing Power Parity (PPP) to standardize values to 2022 USD. For inclusion in meta-analyses, studies were required to have sufficient data available to calculate an estimate of the incremental net benefit. Meta-analyses of pooled incremental net benefit based on time horizon were performed. The study was registered at PROSPERO (CRD42022335436).

Results:

2,190 studies were reviewed, with 14 economic evaluations included following title/abstract and full-text review. Only studies considering Parkinson's Disease were available for meta-analysis. Quality of the identified studies was low, with moderate transferability to the American Healthcare System, and certainty of evidence was low. However, studies with longer time horizon (15 years to lifetime) were found to have significant positive incremental net benefit (indicating cost-effectiveness) for DBS with mean difference of 40,504.81USD (95% CI 2,422.42; 78,587.19).

Conclusion:

DBS was cost-effective for Parkinson's Disease when considered over course of the patient's remaining life after implantation.

1 INTRODUCTION

Movement disorders, including Parkinson Disease (PD), essential tremor, and primary dystonia, among others, are a group of conditions that impact the quality, along with speed and fluency of movement, resulting from basal ganglia dysfunction. The goal of treatment is to alleviate motor symptoms and in the case of PD, non-motor symptoms of the disease. While medical therapy remains standard first line treatment, high quality (level 1) evidence supports the use of deep brain stimulation (DBS) (1) in well selected patients resulting in significant symptomatic improvement. The most suitable candidates for DBS include patients with clear diagnosis of Parkinson's disease, essential tremor, or dystonia with motor fluctuations and/or dyskinesias that are not adequately controlled with optimized medical therapy. In Parkinson's disease specifically, patients should be responsive to levo-dopa therapy with normal cognitive, psychiatric, and behavioural status. Additionally, patients should have no significant co-morbidities, and ideal candidates are less than 70 years of age. Many patients with good response fall outside these ideals, and all patients should be evaluated with a multidisciplinary team including a neurologist, neurosurgeon, neuropsychologist and psychiatrist for consideration of therapy (2). Given the up front cost of surgery associated with DBS (approximately 37,000USD for surgical costs alone (3)), a number of economic evaluations have been conducted to attempt to determine the cost-effectiveness of this therapy, compared with best medical therapy (BMT).

Economic evaluations compare costs and effectiveness of novel therapies with standard treatments, and are critical in determining how health care resources should be allocated. Well conducted economic evaluations utilize quality of life years (QALY) as a measure of change in quantity and quality of life expected from a particular treatment. The difference a patient with

PD experiences before and after DBS, in terms of ability to interact with their family, participate in activities of daily living, and mobility, should be reflected in the positive change in health utility observed in economic evaluations. Utilities associated with surgical and medical complications should encompass potential need for re-operation, re-admission, antibiotic therapy for post-operative infection, or reduction in quality of life for long term complications such as post-operative hemorrhage. Economic evaluations then account for the potential time spent in any given health utility. For example, a patient with a short-term complication may have poorer quality of life, but for a brief period of time, compared with a patient with long term complication(s), that would reduce quality of life for perhaps the entire horizon of the study. As such, it is important that evaluations utilize in cases where at least one of the interventions has an impact over the patient's entire life. Additionally, longer duration time horizons provide a better picture for interventions that carry increased up front cost and risk of shorter term complications (i.e. surgical versus medical therapies), as the up front cost is balanced with sustained improvement over a longer period of time (4).

Previous systematic reviews have summarized literature findings of economic evaluations for PD (5–7), and movement disorders (8). Here we attempt to meta-analyze economic evaluations of DBS available in the literature.

Meta-analysis of economic evaluations is a relatively new concept, introduced by Crespo *et al*. (2014) (9). The idea is to calculate a tool, total incremental net benefit (TINB), of included studies through inverse variance weighting of incremental net benefits (INB), calculated from included studies. This validated tool allows simple determination of whether an intervention is

cost-effective (TINB>0). The premise of this methodology is that data is harmonized to a single currency through historical consumer price index (CPI) and purchasing power parity (PPP), which accounts for the economy of individual countries compared with the United States (the standard reference country for PPP), allowing some consideration for resources, infrastructure, and value of currency, as opposed to currency conversion alone. Market-based rates are more volatile than PPP, which is relatively stable over time (9). A number of factors can influence the INB of studies, including gross domestic product (GDP) of country of interest, patient factors (i.e. age, sex, comorbidities) in the source patient for models, as well as model lifetime (9–11). It is important to consider these factors when meta-analyzing these studies, as studies with one-year time horizons cannot be compared with those using lifetime horizons, for example, as the up-front cost associated with surgical intervention is dispersed over the total horizon time.

The objective of this review was to synthesize the TINB for DBS vs. BMT for movement disorders, to determine the cost-effectiveness of this intervention.

2 METHODS

This systematic review was registered with PROSPERO (ID:CRD42022335436) and conducted using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

2.1 Search Strategy and Screening

A search strategy (Appendix 1) was optimized with a medical librarian. Databases included Medline, Embase, and EBM Reviews Cochrane Central Register of Controlled Trials. Search

included inception through May 24, 2022. Search was repeated on March 12, 2023 to screen for additional studies.

Only cost-utility analyses were included. No limitation to year or language was imposed. Only original research articles were included. We included studies with patients (or base cases) aged 18 or older diagnosed with PD, essential tremor, or primary dystonia where BMT alone (defined as best available non-invasive pharmacotherapy) was compared with DBS (plus BMT). Studies were required to include ICER as a critically important outcome.

Studies were screened using Covidence (12), and screening, extraction, and quality assessment were performed in duplicate with consensus resolution of conflicts and a third author for conflict resolution.

Data was collected for patient (or base case) age, disease severity, time from diagnosis to surgical intervention, costs included in study, currency and year, discounting rate, perspective of analysis, effectiveness assessments, ICER, and results of sensitivity analyses.

For inclusion in meta-analyses, sufficient data was required to calculate the INB and its variance (cost and efficacy with variances either reported or sufficient data to estimate variance using Monte Carlo simulation).

2.2 Statistical Analyses

Data harmonization was performed using COMER framework (9). All currencies were first converted to the 2022 value for the currency reported in each individual study using the historical CPI of the country of study (13). Individual study currencies were then converted to 2022 US dollars (USD) by converting to purchasing power parity (PPP) using conversion rates from the International Monetary Fund (13). This was completed for incremental costs, thresholds, and ICERs for each study. After currency conversions for cost and threshold (K), the INB was estimated. See Appendix 2 for details of calculations.

INB was then pooled across studies, using a random-effects model, DerSimonian-Liard in all cases (15).

Heterogeneity was analyzed with holistic consideration of the Chi-squared, I^2 statistics (heterogeneity considered low, moderate, and high if the I^2 was <25%, 25-74%, or ≥75%, respectively). All analyses were performed using Stata software, version 17.0, and Microsoft Excel. Results were considered statistically significant for all analyses at $p<0.025$ (two-sided yielding significance of $p<0.05$).

Publication bias was assessed with funnel plots. Country income and disease severity, patient age, and time from diagnosis were assumed to potentially influence outcomes with expected bias against increased disease severity, delayed surgical intervention, and patient age. However, available data prevented us from conducting subgroup analyses testing these hypotheses. Subgroup analyses within time horizon were conducted for single vs. multi-payer health care system only. Sensitivity analyses were conducted by excluding outliers to reduce heterogeneity.

2.3 Quality Assessment

Quality Assessment was performed using the Consensus on Health Economics Criteria Checklist (CHEC)-extended checklist (16). Individual studies were reviewed for quality assessment by independent investigators (M.L., T.D.), and discussed for consensus.

An additional assessment of quality was performed considering common methodologic concerns with economic evaluations that is not addressed by the CHEC checklist. Each aspect was discussed among team members. These factors included model structure, model validity, estimation of costs, estimation of health state utility, and how these considerations and concerns contribute to heterogeneity in analyses.

2.3.1 Transferability

In economic evaluations, transferability is the extent to which results hold true for different populations and settings (17). Transferability of the studies included in the meta-analysis was assessed using a validated tool created by Welte *et al* (2004), which takes into consideration a number of important factors to determine whether comparison between the country of study and country of interest is reasonable. It also attempts to determine whether the cost effectiveness ratio in the country of interest would be higher, lower, or undetermined based on the transferability between the study and country of interest (18). See Table 1 for details of transferability assessment.

2.3.2 Certainty of Evidence

GRADE working group has provided recommendations for reporting in systematic reviews of economic evaluations. As such, we have followed these recommendations, identifying items of resource use that may differ between alternative management strategies that may be important to patients and decision makers, find evidence for these differences in resource use between comparisons, rating the confidence in estimates of effect, and valuation of resource use in terms of costs for our setting of interest (US) (30). These recommendations were included in our summary of findings table.

3 RESULTS

Of 1,872 studies, 14 met inclusion criteria (Figure 1) (3,31–43). Study characteristics are reported (Table 2).

Studies were published between 2001-2022. Mean age for base case in the analyses was 58.00 (3.83) for the eleven studies reporting this characteristic (mean age was not reported for 3/14 studies). Of the 14 included studies, only one investigated DBS versus BMT in dystonia (32), for this reason, it was not included in the meta-analysis, which ultimately included only patients with PD. Average duration of disease at time of surgery ranged from 7.3-16.9 years, although there was inconsistent reporting of patient characteristics among studies. All available patient characteristics are reported in Table 3.

No studies reported that DBS is not cost-effective when compared with BMT. However, one study did report that in the one year analysis, the intervention was not cost-effective, it did become cost effective with 5 year extrapolation, but again found reduced cost-effectiveness

when data was extrapolated to between 5 and 10 years (36). See hierarchical decision matrix for summary of cost-effectiveness decisions from included studies (Figure 2).

Meta-analyses included 11 studies for which INB and its variance could be calculated (see Table 4 and Appendix 2 for calculation details), and revealed cost effectiveness for longer time horizons (15 years to lifetime horizon) mean difference INB 40,504.81USD(95% CI 2,422.42; 78,587.19). For studies with a 1-3 year horizon, DBS was favoured but the mean INB difference did not reach statistical significance [13,684.07USD(95% CI -7,295.64; 34,663.77)]. For 5 year horizon studies, mean difference INB favoured BMT, but again, this difference was not statistically significant, mean difference INB -806.97USD(95% CI -27,000; 25,157.82). For studies with 10 year time horizon, again, BMT was favoured, but the difference was not statistically significant, mean difference INB -14,000USD(95% CI -45,000; 16,248.65). Studies with lifetime horizon alone favoured DBS, but not to a significant degree, mean difference INB 46,130.78USD(95% CI -5,855.99; 98,117.54). See forest plots for all primary horizon analyses (Figure 3).

Given limited studies available, subgroup analyses were not possible. A sensitivity analysis was performed, analyzing 15 years-lifetime studies with and without Tomaszewski *et al* (3), the only American study included from the perspective of a multi-payer system, and did not show any difference in cost effectiveness, mean difference INB 40,504.81USD(95% CI, 2.422.42; 78,587.19) for studies including all systems, vs. 54,549.85USD(95% CI, 17,207.52; 91,892.18) for analysis including only studies from countries with single payer healthcare systems (Appendix 3).

Given that McIntosh *et al* (36) was an outlier in the systematic review, in that it concluded DBS was not cost-effective at five and ten years, the 5-10 and 10 year time horizon analyses were repeated without this study. The analyses remained insignificant for both horizons with and without the study. For the 5-10 year horizon, with McIntosh, mean difference INB was -7,945.07USD(95% CI -34,000; 18,177.66) vs. 359.95USD(95% CI -117.61; 837.50) without. For 10 year horizons, with McIntosh, mean difference INB was 1,400USD(95% CI -45,000; 16,248.65) vs. 354.65 (95% CI -117.53; 826.82). See Appendix 4.

To minimize potential bias introduced by model-based evaluations, a sensitivity analysis was performed for the 1-3 year horizon, considering two study based evaluations, Valldeoriola *et al* (34) and Zhu *et al* (2014) (31), with and without the model-based evaluation Fann *et al* (2020) (39). Elimination of the model-based evaluation persistently favoured DBS over BMT with a pooled estimated INB to 22,171.79USD(95% CI -2,043.70; 46,387.29), however the heterogeneity of the analysis decreased considerably from I^2=99.63% to 77.69%. See Appendix 5.

No publication bias was identified for analyses, except for studies with 10 year horizon where publication bias favours BMT. Amongst studies with lifetime horizon, two identified outliers were balanced to neither favour BMT nor DBS (Figure 4).

A high degree of heterogeneity was observed among all analyses. Given the nature of data harmonization, this is to be expected to some extent. If a sufficient number of studies existed to

perform subgroup analyses for high, middle, and low income countries, this would limit the heterogeneity observed. It is important to note, however, that positive INB suggests economic efficacy of an intervention, regardless of its value. Therefore, the magnitude of the value for each study is less important. For this reason, it remains feasible to compare studies with lower INB to those with higher magnitude, accepting that the calculated I^2 will suggest high heterogeneity between studies.

3.1 Quality Assessment

CHEC assessment was conducted in duplicate, with a Cohen's kappa of 0.99 indicating near-excellent agreement between assessors. No formal cut-off has been established to determine low vs. high quality using this tool, however the majority of criteria were fulfilled for each included study. See Table 5 for details of quality assessment for individual studies.

In addition to the CHEC checklist, additional methodologic concerns related to heterogeneity among analyses were highlighted in Table 6. Ultimately, the high degree of heterogeneity within analyses limit certainty in effect estimates for all analyses, and limit the quality of evidence available for decision-makers.

3.2 Transferability

All but one study (3), was determined to have concerns with transferability. Most commonly, this was due to variations in discount rate[34,36–38,40,43], absolute and relative prices in health care, practice variation[34,36,37,39,40] (determined by time to surgery, which varied from 7.3 to 16.9 years among studies), disease incidence and prevalence (ranging from 0.8-6%), life

expectancy (ranging from 78.08 years in the China to 85.39 years in Hong Kong) (58), and health-status preferences (31,37,39,42,43). Productivity cost approach and productivity and work-loss time were not reported in any studies, and disease spread was not considered relevant for the current study. The study with most bias detected in transferability was Kawamoto (37), with the predicted direction being cost effectiveness ratios likely being predicted too high for the country of interest for direct transferability. The next least transferable studies were Dams (2013) (42), Eggington (40), McIntosh (36), and Fann (2020) (39). See Table 7 for full details of assessment.

4 DISCUSSION

In the same way that systematic reviews and meta-analyses of randomized controlled trials provide evidence for guidelines, meta-analyses of well-conducted economic evaluations based on large primary data sources should be taken into consideration in formation of guidelines and incorporation of newer or costly treatment strategies to ensure cost-effective care is provided to patients to maximize societal benefit.

In the case of DBS for movement disorder indications, there remains a paucity of high-quality economic evaluations to definitively make recommendations for cost-effectiveness, however the current study suggests that when an appropriate time horizon (i.e. lifetime) is considered for this intervention, it is a cost-effective treatment for PD.

Both the National Authority for Health (HAS) in France, NICE in England, and ICER in the United States recommend that economic evaluations analyze a time horizon appropriate for the

disease being studied, to account for all important differences in potential costs and benefits. Both organizations recommend lifetime horizons (59–62), with HAS specifying that lifetime horizons be selected if at least one of the interventions has an impact over the patient's entire life, in terms of cost, length of life, quality of life, morbidity, deficiencies, or incapacity. Shorter time horizons are only recommended when evaluating treatments where different costs and health outcomes are no longer observed beyond a certain period of time (62). In PD both DBS and BMT have implications for quality of life, morbidity, incapacity, and cost throughout the remainder of life, therefore, shorter time horizons would be inappropriate for evaluations of these therapies.

This review provides evidence that when the appropriate time horizon is considered, the upfront cost associated with surgery, as well as the costs associated with surgical complications or revisions for expected hardware replacement (IPG replacement) are significantly outweighed by the QALY benefit provided to patients undergoing therapy and reduced medication costs, when compared with costs of medications in BMT. The pooled INB for studies with longer time horizons (15 to lifetime) was estimated at 40,504.81USD(95%CI 2,422.42; 78.587.19), suggesting DBS is a favourable intervention from an economic efficacy standpoint, compared with BMT alone. Among economic analyses, it is important to consider that the magnitude of effect is more important than statistical significance, which can easily change based on a number of study factors. This further highlights the cost-effectiveness of DBS vs. BMT even in shorter term time-horizon studies. From a population standpoint, these potential cost savings may outweigh the high upfront cost of surgical intervention in patients with movement disorders.

Suboptimal transferability and the inclusion of model-based evaluations limits the degree of certainty in recommendations made by this review. Where limited economic evaluations exist alongside longitudinal studies with primary data, model-based evaluations often rely on the same data from larger trials. As such, data from the same populations may be utilized more than once in the pooled estimate. To improve upon economic evidence with respect to DBS vs BMT in movement disorders, conduction of economic evaluations routinely with longitudinal empiric studies is necessary to better inform healthcare systems with regard to appropriate allocation of resources for DBS. It is important to gain a better understanding as to whether the economic benefit modelled at longer time horizons is realistic. From an economic perspective, it is important to determine if patients sustain the benefit observed from DBS initially at 15-20 years out from surgery without significant complications, increase in medication use to similar doses as BMT patients at a similar timepoint in their disease course, or increased costs from other unexpected factors. Longitudinal studies of DBS vs BMT patients with well-conducted economic evaluations would answer these questions.

The highest quality study that was included was McIntosh *et al* (36). This study was conducted with the PD SURG trial, a randomized, open-label trial conducted at 13 neurosurgical centres in the UK, including 183 patients who underwent DBS with a further 183 allocated to receive BMT alone (48). Data for the economic evaluation was collected through the first year of randomization in the trial and extrapolated to 5 and 10 years. Life span of the DBS implant battery was estimated from trial data as a survival curve, and medication use was recorded at baseline, six months, and at 12-month follow up (36). The rigorous nature of this study, with multiple sensitivity analyses given assumptions in the model for extrapolation provide an

example of how economic evaluations should be conducted, however the short duration time horizon limits the value of this study in meta-analysis. It should be noted that this study is the only one revealing clear negative INB, and skews the analyses for 5 and 10 year time horizons. This is also evident in the funnel plot indicating publication bias for the 10 year analysis. Given there was a clear trend toward cost-effectiveness as time progressed in the model, it is likely that, had a lifetime time horizon been utilized in this model, it would have realized a positive INB as well. This, again, highlights the importance of using time horizons appropriate to the disease and treatments of interest.

Additionally, multiple model based evaluations utilizing data from the EARLYSTIM trial (63), bring into question the 15 year to lifetime horizon analysis, given two of the included studies utilized the same patient dataset (38,41). This is particularly concerning, as the 15 year to lifetime horizon analysis was the only significant pooled analysis in the present study. The number of patients included in each of these two studies differs, as well as costing (each study utilized costing from their respective country's systems). Finally, Fundament *et al* reports also utilizing the UK CPRD dataset (38). Although all data was not taken solely from the EARLYSTIM trial for both studies, conclusions regarding this particular meta-analysis should be approached with caution.

To have meaningful utilization of meta-analyses of economic evaluations, that create high quality, transferable results, a shift in perspective of empiric researchers must occur. High quality economic evaluations, with clearly described costs, efficacy in QALY as measured by a

consistent scale (EQ-5D is generally recommended (60–62)), and lifetime horizon should be conducted alongside empiric, prospective, comparative studies.

Even if these studies become readily available, applying them in complex healthcare contexts like those in North America remain challenging. For example, how do the results of studies transfer to Medicare/Medicaid patients vs. commercial insurance policy patients vs. private payer? Even in countries like Canada, with a single payer healthcare system, application remains complex, given health care is governed provincially, so application between provinces and territories can vary significantly. A thorough meta-analysis of high-quality economic evaluations would allow for subgroup analyses by such differences and would include transferability assessments to these various healthcare contexts.

Overall, the method outlined by the COMER group (9) to pool economic evaluations on an international scale through consideration of country income and resources, as opposed to only currency (through conversion using CPI and PPP Index), allows meta-analysis of all available evidence comparing two treatment strategies. The application of this strategy to neurosurgical evidence is an important step toward improved understanding of the true societal economic cost and benefit to make informed systems-level decisions in terms of improving funding and access to interventions with proven economic benefit.

In the context of DBS for movement disorders, while evidence has only been meta-analyzed for PD, this study concludes that DBS is a cost-effective intervention, compared with BMT, when considered over a patient's lifetime. Patients are expected to receive sustained QALY benefit

over the remainder of their lifetime, with reduced medication costs compared with BMT alone, that justifies the upfront costs associated with surgical assessment, surgical cost, cost of implants, hospital admission(s), and follow-up visits. A lifetime horizon also considers the cost(s) of complications and battery replacements, which balance with cost savings and QALY benefit over lifetime horizon as well. It should be considered, however, that longer time horizons are realized through modelling (given a lack of long-term data available for economic analyses). For interventions such as DBS, this is important, as the high up-front cost of surgery is balanced by QALY improvement over time. Given the QALY improvements are assumed based on modelling, carrying estimation error, it may not be entirely realistic to assume that these QALY effects are sustained for 15 years or longer. Limited longitudinal studies exist over periods of 8-16 years, and do suggest sustained improvements (64–78). Given DBS has been widely adopted since its approval from the Food and Drug Administration in 1997, there exists a population of patients for longitudinal studies of longer duration, with which parallel economic evaluations should be conducted.

4.1 Limitations

Meta-analysis of economic evaluations carries inherent limitations. For example, significant heterogeneity exists between evaluations. This can be caused by model type, perspective, population, country income, gross domestic product, and discounting. Utilization of CPI and PPP to account for the economic environment and year in which selected studies were conducted can help with some of these concerns, however these approaches carry some limitations as well. For example, price indices are calculated based on individual prices of selected commodities, as opposed to all commodities in every country considered (79). Insufficient evidence was available

in this study to allow for stratification by country income, study type, disease, and disease severity, as had been outlined in the analysis plan at the start of the study.

Beyond study specifics, characteristics of societies in the countries of study origin increase heterogeneity within the analysis as well. Willingness to pay differs between countries as a result of the value placed on health and well-being related to various cultures (25–29), and even amongst countries with similar income level, resources allocated to healthcare can differ significantly. Even within single countries, demographics and allocation of healthcare spending can differ between geographic regions. A transferability assessment is meant to account for this; however, some aspects of this assessment are difficult to thoroughly assess through consideration of individual studies and general country contexts.

Given the lack of available economic evaluations on the topic conducted parallel to longitudinal trials, model-based evaluations were included in the analysis. It is worth noting that longitudinal studies with durations of 15 years or greater are uncommon, and model based evaluations are a common means of estimating economic outcomes at these time points. Inclusion of models based on the same data sources in systematic review may infer double-counting of patient populations. For example, several studies utilizing models were based on efficacy and costs in the EARLYSTIM trial (63). Pooling of results from these model-based studies would consider the same efficacy multiple times in the analysis. The analysis where this seems most concerning is that considering the 15 years to lifetime time horizon.

Overall, heterogeneity among the analyses presented limits the certainty in effect estimates to a considerable degree.

Finally, although the goal of this study was to assess current evidence from economic evaluations comparing DBS vs. BMT for movement disorders, the only evidence available for meta-analysis was from studies of PD.

5 CONCLUSION

Our meta-analysis of available international economic evaluations assessing DBS vs. BMT for movement disorders suggest that when longer duration time horizons are considered, the upfront cost of DBS and any potential complications is outweighed by the quality of life benefit gained to patients with PD, in addition to decreased medication costs, compared with BMT alone. This provides further evidence favouring DBS over BMT in movement disorders, long considered to be an effective treatment, but limited in utilization by high costs, suggesting increased healthcare spending in upfront surgical costs may be balanced by long term quality of life benefits for these patients. It is important to consider that significant heterogeneity exists between included studies in terms of data sources, modeling structures, and estimated inputs. Therefore, further research is needed to corroborate findings.

We recommend any future longitudinal studies comparing these two treatments include an economic analysis component with longer time horizon to improve available evidence and allow for appropriate healthcare decision making. In an aging population, where healthcare spending continues to increase, these economic decisions will grow increasingly important. Therefore, the

academic community has a responsibility to ensure high quality economic evidence is available to inform decision makers regarding therapies that require additional upfront funding in order to make the most economically efficient decisions long term.

FIGURES

Figure 1: Adapted PRISMA flow diagram for included studies

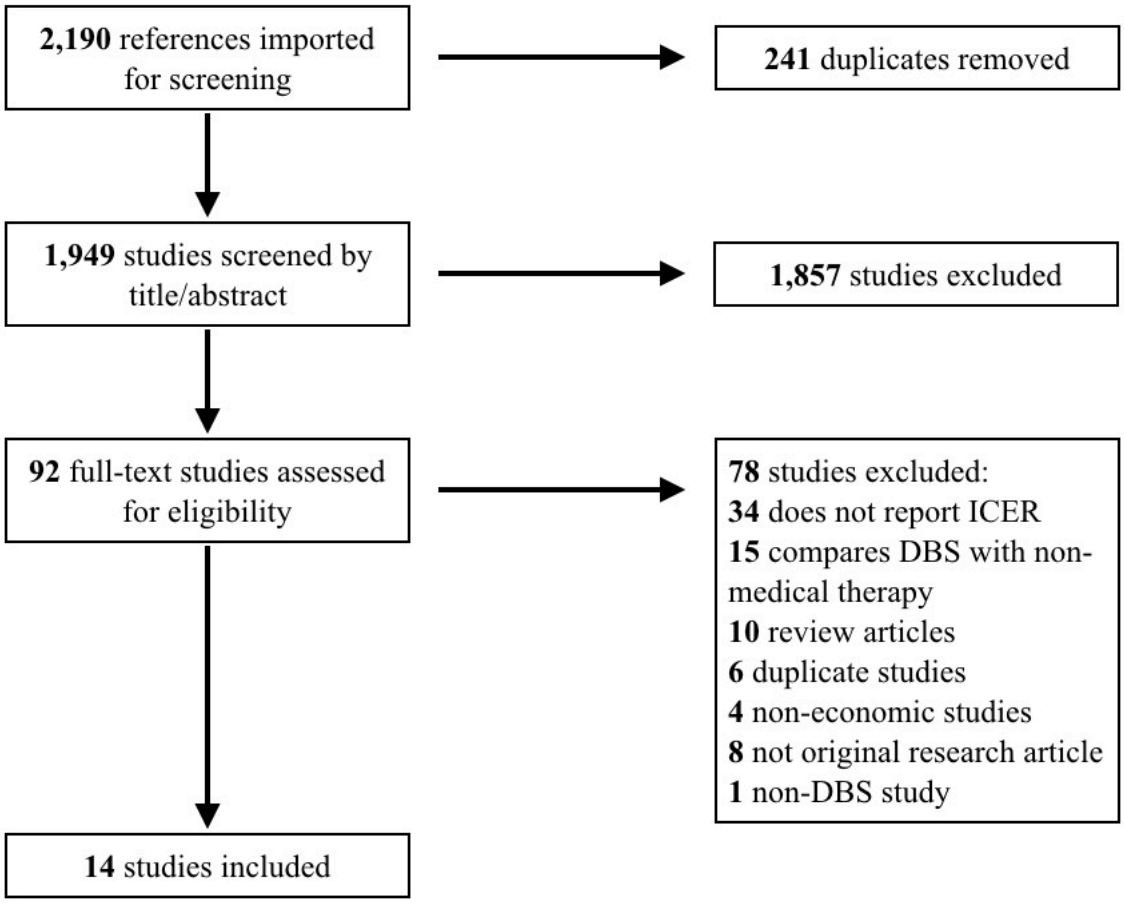


Figure 2: Hierarchical decision matrix representing conclusions of 14 included studies
Each of the included studies are placed in the matrix based on the overall recommendation for DBS vs. BMT for the individual study.
11/14 studies concluded that DBS was cost-effective compared with BMT [32–35,37–43], 2/14 concluded that further investigation is required [3,31], but that DBS is likely cost-effective compared with BMT, and 1/14 concluded that DBS is neutral in terms of cost-effectiveness compared with BMT [36].

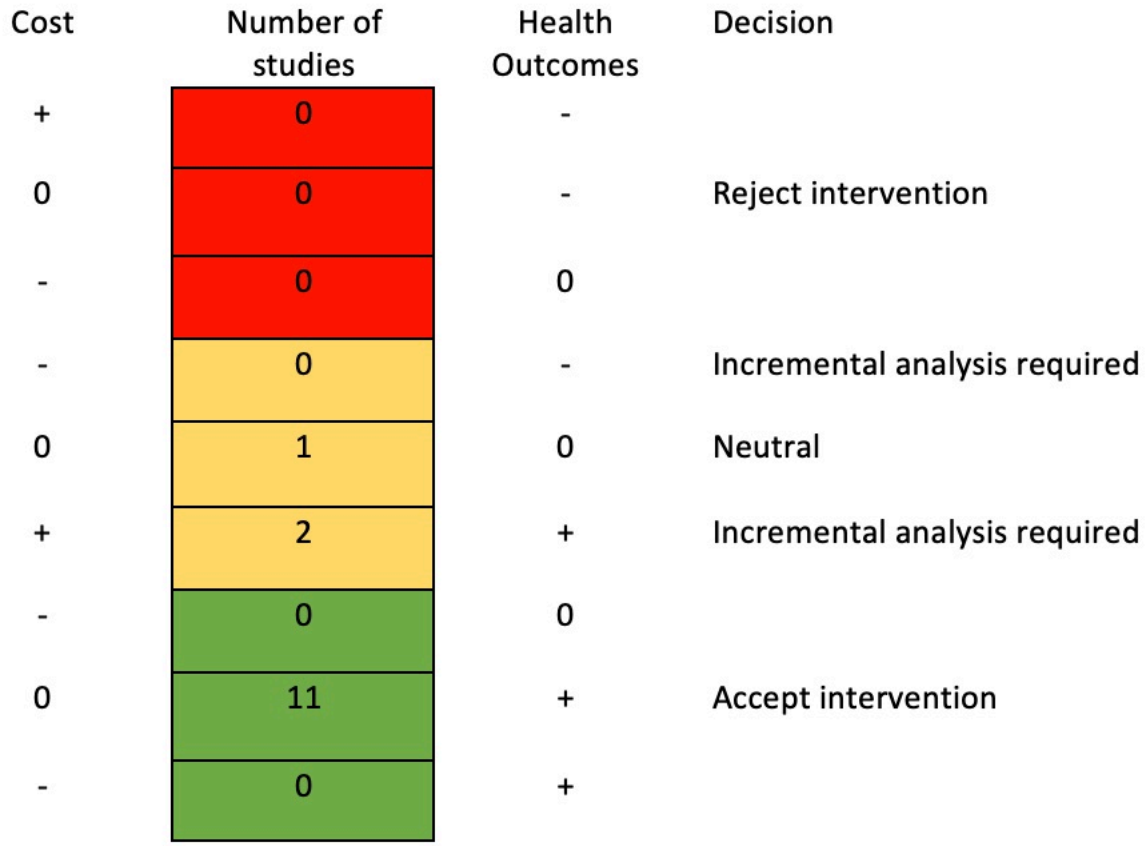


Figure 3: Forest Plots for Primary Analyses of Incremental Net Benefit: A) Studies with 1-3 year time horizon; B) Studies with 5 year time horizon; C) Studies with 10 year time horizon; D) Studies with lifetime horizon; E) Studies with 15 year-lifetime horizon. The effect size indicates the individual and summary mean INB differences and corresponding 95% confidence intervals.

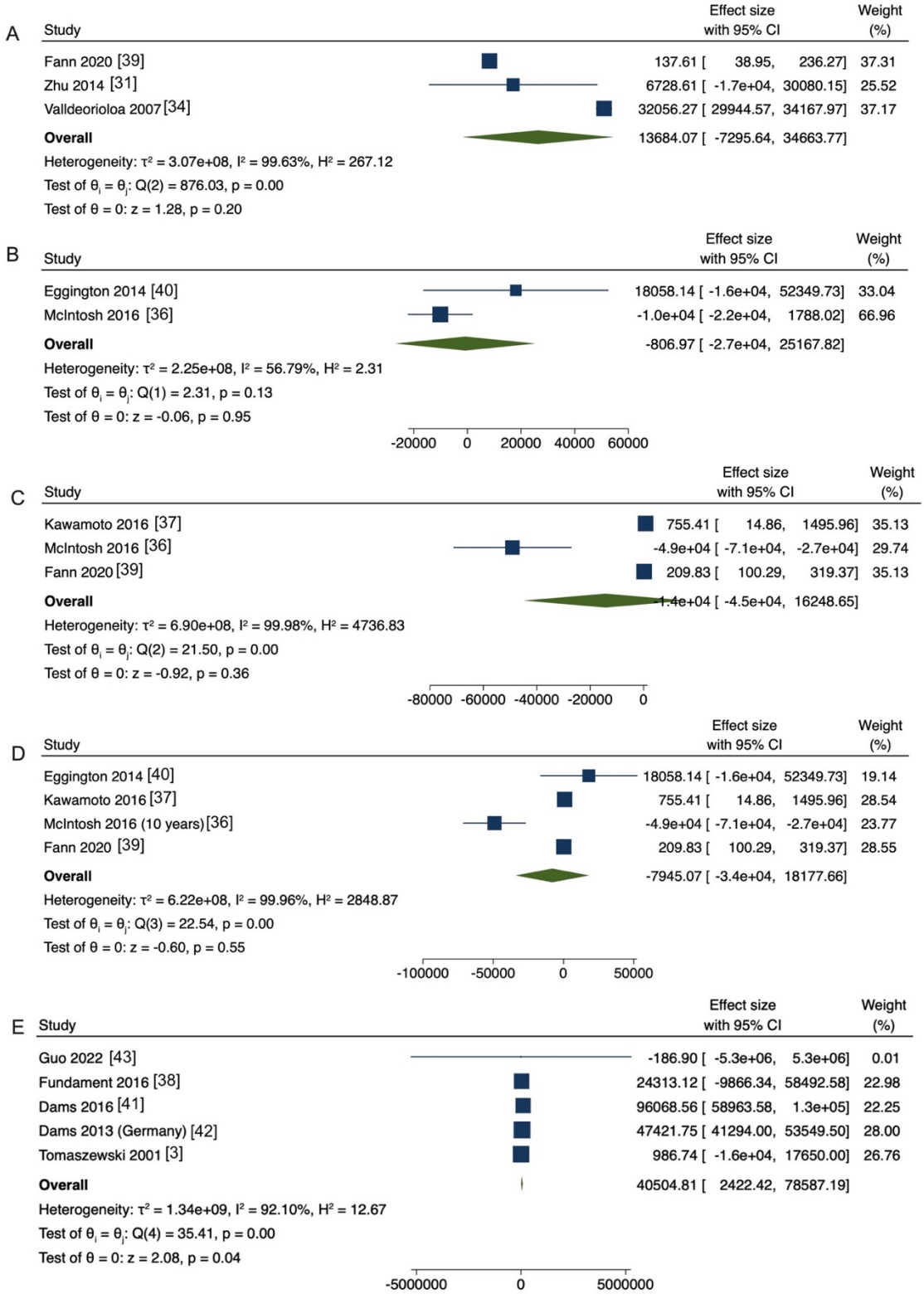
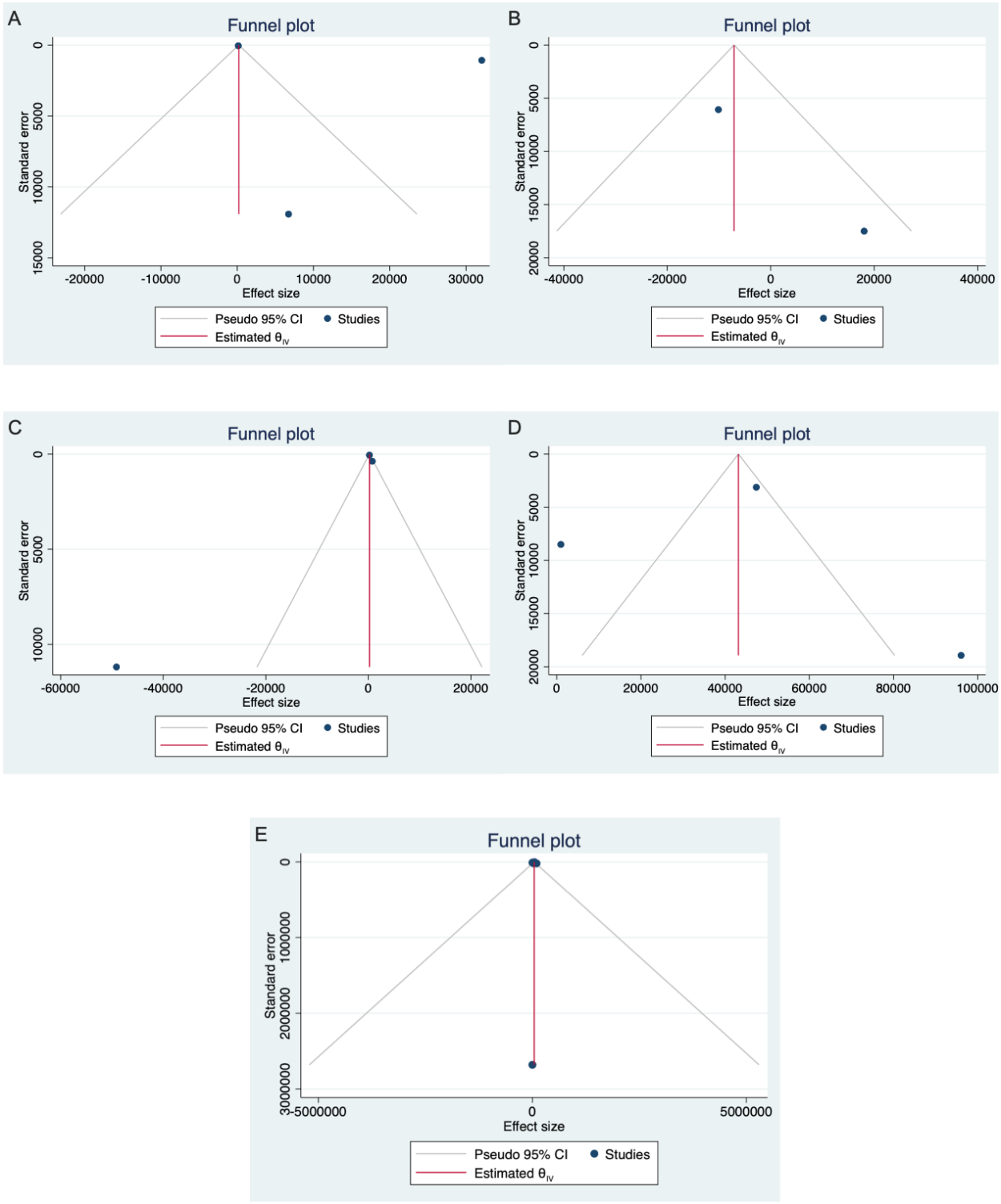


Figure 4: Funnel plots for primary analyses: A) Studies with 1-3 year time horizons; B) Studies with 5 year time horizon; C) Studies with 10 year time horizon; D) Studies with lifetime horizon; E) Studies with 15 year to lifetime horizon



TABLES

Table 1: Details of Transferability Assessment
QALYs=quality of life years; ICU=intensive care unit; DBS=deep brain stimulation; US=United States

Table 1 Details of transferability assessment

Transferability assessment component	Description and ideal for country of interest
Perspective	Healthcare decision maker perspective [18]
Discount rate	3% [18]
Medical cost approach	Method for estimating direct costs
	Can be through charges, fees, per diem costs, and market prices [17]
	Should include unit cost data most relevant to the decision maker, based on healthcare system data [18]
Productivity cost approach	Typically measured via the human-capital approach or the friction-cost method to determine loss of productivity from the disease being evaluated
	Individual loss of productivity should be measured as part of the QALYs [19]
Absolute and relative prices in healthcare	One study revealed a 1-day ICU admission in Italy was 2.5 times more costly as a gastroscopy, compared with Australia, where a 1-day ICU admission was six times more costly than a gastroscopy [20]
Practice variation	Hospitalization rates, duration of admission, dosage regimes, timing of interventions all vary greatly between countries
Technology availability	Lower number of magnetic resonance images per capita would lead to lower case numbers, in addition to a lack of DBS equipment and implants
Disease incidence and prevalence	0.3% for Parkinson's disease in the USA [21]
Case mix	Susceptibility to movement disorders depends on age and sex, or there is evidence that there are differences in care-seeking behaviors between Japan and the USA [22] that could lead to delay in care, causing a more severe case mix
Life expectancy	76.1 years in the USA [23]
Health status preferences	Preferences for different health states and trade-offs between lifetime and quality of life has been demonstrated to vary between countries
	Preferences have been shown to be similar between the Netherlands, Norway, Sweden, and the UK [24, 25], with significant differences between the Netherlands and Germany [26], Finland and the USA [27], and Japan and Western European countries [28]
Acceptance, compliance, and incentives to patients	Compliance with medication use, presence of direct monetary incentives for consumers in healthcare systems
Population productivity and work loss time	Can be measured using the friction method, or average number of work loss days as a result of the disease, which varies between countries
Disease spread	Not considered applicable, as movement disorders do not have an infectious component

DBS deep brain stimulation, *ICU* intensive care unit, *QALYs* quality-adjusted life-years

Table 2: Characteristics of 14 included studies Summary of Findings
*Study country used is Germany, as Finland and Spain were estimated in original study
ICER=incremental cost effectiveness ratio; USD=United States Dollar; GBP=Great Britain Pound; EUR=Euro; SEK=Swedish Krona; QALY= quality of life years; QoL=quality of life; DBS=deep brain stimulation; BMT=best medical therapy; EQ-5D=European Quality of Life five-dimension; UPDRS=Unified Parkinson's Disease Rating Scale; H&Y=Hoehn and Yahr Scale; PDQ-39=Parkinson's Disease Questionnaire-39; GPi=globus pallidus internus; STN=subthalamic nucleus; WTP=willingness to pay; NICE=National Institute for Clinical Excellence

Table 2 Characteristics of 14 included studies, summary of findings

Study	Country, healthcare system	Year Currency	Discount rate	Effectiveness data source	Cost data source	Horizon, cycles	Quality of life/severity assessment(s)	Patient population	ICER	Sensitivity analysis	Conclusion
Tomaszewski et al. [3] Parkinson's disease	USA, multi-payer	2000 US$	3%	Literature Review Utility Chrischilles et al. [43]	Operative costs estimated via expert opinion, Medicare reimbursements, hospital billing	Lifetime, 1-year cycles	From Chrischilles et al. [43]	Parkinson's disease	US$49,194/QALY gained	One way deterministic, no effect, greatest impact on ICER was QoL benefit from DBS	May be cost effective if QoL improves > 18% for DBS vs BMT
Yianni et al. [31] Dystonia	UK, single payer	2003 GBP	Not reported	Original pre-post study (26 patients)	Resource use data	Not reported	EQ-5D	Parkinson's disease with GPi stimulation	33,980 GBP/QALY gained WTP mean 291,231 (441,447), median 20,000 GBP; most common wage bracket < 5000 GBP (13/26 patients) Benefit (mean)-cost 259,289 GBP Benefit (median)-cost − 11,942	Not reported	Cost effective in terms of WTP in this study, but not when NICE recommendations considered

Table 2 (continued)

Study	Country, healthcare system	Year Currency	Discount rate	Effectiveness data source	Cost data source	Horizon, cycles	Quality of life/severity assessment(s)	Patient population	ICER	Sensitivity analysis	Conclusion
Valldeoriola et al. [33] Parkinson's disease	Spain, two-tier system	EUR	Not reported	Original prospective cohort study (14 DBS, 15 BMT patients)	Questionnaire to collect direct costs	1 year	UPDRSII, EQ-5D	Parkinson's disease with STN stimulation	34,389 EUR/QALY	Deterministic analyses, when BMT patients with prolonged hospitalization excluded ICER = 44,078/QALY, when continuous apomorphine BMT patients excluded ICER = 62,148/QALY	Cost effective
Dams et al, [41][a] Parkinson's disease	Germany, Finland, Spain, single payer	2010 EUR	3%	Data on disease progression from Marttila and Rinne [44] and validated with independent data set [45]	Billing department of University Hospital of Marburg	1, 2, 5, 10, 25 years and lifetime	UPDRSIII, H&Y, EQ-5D	Parkinson's disease (61 GPi stimulation, 138 STN stimulation, and 199 BMT patients)	ICUR 6700 EUR/QALY gained	Deterministic analyses, no effect. Model most sensitive to treatment effect of DBS, time until battery change, and discount rate	Range from cost effective to dominant

Table 2 (continued)

Study	Country, healthcare system	Year Currency	Discount rate	Effectiveness data source	Cost data source	Horizon, cycles	Quality of life/severity assessment(s)	Patient population	ICER	Sensitivity analysis	Conclusion
Eggington et al. [39] Parkinson's disease	UK, single payer	2011 GBP	3.5%	Deuschl et al. [46] RCT of DBS in Parkinson's	Deuschl et al. [46], Medtronic UK price list, UK tariffs, drug costs estimated from RCT plus data reported on drug therapy costs from PD SURG trial [47]	5 years, 6-month cycles	H&Y	Parkinson's disease (78 STN patients)	20,678 GBP/ QALY gained	One way sensitivity analyses, minimal effect	Cost effective
Zhu et al. [30] Parkinson's disease	Hong Kong, single payer	2010 Hong Kong dollars converted to US$	3%	Original prospective pre-post study	Hospital data	2 years, 1-year cycles	UPDRSIII, EQ-5D	Parkinson's (13 STN patients)	ICER of mobility (UPDRSIII) $364 for two years (range 260–467) ICER of QoL $24,868 for 2 years (range 5778–439.59) (by linear regression) ICER at 1 year UPDRS one point $926 $421 at 2 years ICER QoL $123,110 1 year (EQ5D) $62,846 for 2 years (ratio calculation by Drummond et al)	Not reported	Cost effective over time (not cost effective in first year of treatment, but cost effective in second year)

Table 2 (continued)

Study	Country, healthcare system	Year Currency	Discount rate	Effectiveness data source	Cost data source	Horizon, cycles	Quality of life/severity assessment(s)	Patient population	ICER	Sensitivity analysis	Conclusion
Walter et al. [32] Parkinson's disease	UK and Germany, single payer	GBP and EUR	3% and 3.5%	Transitional probabilities from Lowin et al. [48], Deuschl et al. [46], Tomaszewski et al. [3]	Resource data from Findley et al. [49]	Lifetime, 6-month cycles	H&Y, EQ-5D	Parkinson's disease (500 simulated patients in Monte Carlo)	Change in efficacy DBS: UK 2.75 QALY Germany 2.85 QALY BMT efficacy: UK 2.62 Germany 2.73 Change in cost DBS: UK 87,730.22 GBP Germany 105,737.08 EUR BMT: UK 76,793.49 GBP Germany 90,011.01 EUR	No sensitivity analyses performed for DBS vs BMT	Cost effective
Dams et al. [40] Parkinson's disease	Germany, single payer	2013 EUR	3%	EARLYSTIM RCT [50]	Tariffs	Lifetime	PDQ-39, EQ-5D	Parkinson's disease (111 DBS, 115 BMT)	Year 1: 3,135,600 EUR/QALY Year 5: 101,900 EUR/QALY Year 10: 51,400 EUR/QALY Lifetime 22,700 EUR/QALY Or 89 EUR/PDQ-39 point gained	One-way sensitivity analyses, no effect	Cost effective
Fundament et al. [37] Parkinson's disease	UK, single payer	GBP	3.5%	EARLYSTIM [50]	Hospital tariffs, British National Formulary for drug costs, and Personal Social Sciences Unit	15 years, 1-year cycles	UPDRSIII, PDQ-39, EQ-5D	Parkinson's disease (124 STN stimulation patients, 270 BMT patients)	19,887GBP/QALY gained	One-way and probabilistic analyses, no effect	Cost effective

Table 2 (continued)

Study	Country, healthcare system	Year Currency	Discount rate	Effectiveness data source	Cost data source	Horizon, cycles	Quality of life/severity assessment(s)	Patient population	ICER	Sensitivity analysis	Conclusion
Kawamoto et al. [36] Parkinson's disease	Japan, single payer	2015 Japanese Yen and US$	Not reported	Hudry et al. [51]	Hospital data, estimated that medical treatment costs following DBS would be approximately 20% lower, drug costs from Japanese Society of Neurology Guidelines. Yoritaka et al. to estimate costs of medical treatment	10 years, 6-month cycles	H&Y, EQ-5D	Parkinson's disease	3.1million yen/QALY gained (US$25,600/QALY)	On- way and probabilistic, additional scenarios of early-stage DBS showed ICERs of $70,200/QALY, intermediate of $27,200/QALY, and late-stage $27,000/QALY	Cost effective. More cost effective when performed in intermediate, rather than early or late stages of disease
McIntosh et al. [35] Parkinson's disease	UK, single payer	2010 GBP	3.5%	PD SURG [47]	UK reference costs and unit cost sources	1, 5, and 10 years (extrapolate from 1 year of study data)	H&Y, EQ-5D	Parkinson's disease (183 patients, pre-post)	Year 1: 458,528 Year 5: 45,180 (95% CI 19,499–225,287) Year 10: 70,537 (95% CI 34,191–371,22559)	Deterministic analyses increasing utility gain by 50%, decreasing surgical cost by 30%, and decreasing hospital stay to 4 days meets threshold at 1 and 5 years. Otherwise, model does not. WTP for QALY 20,000–30,000 GBP	Not cost effective at 1 year Extrapolation reveals increasing likelihood of cost effectiveness up to 5 years and reducing cost effectiveness between 5 and 10 years

Table 2 (continued)

Study	Country, healthcare system	Year Currency	Discount rate	Effectiveness data source	Cost data source	Horizon, cycles	Quality of life/severity assessment(s)	Patient population	ICER	Sensitivity analysis	Conclusion
Pietzsch et al. [34] Parkinson's disease	USA, multi-payer	2014 US$	3%	Based on Eggington et al. [39], and transition probabilities from Deuschl et al. [46]	Implantation costs: 2014 Medicare national average reimbursement amounts Drug costs (BMT): MarketScan data for medical supplement enrollees Drug costs (DBS): decreased based on study by Weaver et al. [52] assuming 40% decrease from baseline Medicare charges, costs related to falls from Bohl et al. [53]	10 years, 6-month cycles	H&Y	Not reported	US$23,404/QALY	Deterministic analyses, no effect	Cost effective across a wide range of assumptions, yielding substantial improvements in QoL at a favorable value profile

Table 2 (continued)

Study	Country, healthcare system	Year Currency	Discount rate	Effectiveness data source	Cost data source	Horizon, cycles	Quality of life/severity assessment(s)	Patient population	ICER	Sensitivity analysis	Conclusion
Fann et al. [38] Parkinson's disease	Taiwan, two-tier system	US$	3%	Literature review Zhao et al. [54]	Taiwan National Health Insurance	3 years, 3-month cycles	UPDRSIII, H&Y	All Parkinson's disease with STN stimulation	$147,065 per life-year gained and $123,436/QALY gained at 3 years $36,833 per LYG and $69,033/QALY gained at 10 years	Deterministic and probabilistic, no effect	Cost effective
Guo et al. [42] Parkinson's disease	China, single payer	2021 Chinese Yuan	Not reported	Retrospective cohort study, Palmer et al. [55]; Liou et al. [56]	China Healthcare Security	15 years, 6-month cycles	H&Y	Parkinson's disease	¥213,544/QALY (95% CI ¥208,177.35–218,910.10)	Unidirectional deterministic, no effect	Cost effective

Table 3: Patient Characteristics Among 14 Included Studies
All values are listed as mean (SD) unless otherwise specified
DBS=deep brain stimulation; BMT=best medical therapy; UPDRS=Unified Parkinson's Disease Rating Scale; H-Y=Hoehn and Yahr Scale

Table 3 Patient characteristics among 14 included studies

Study	Base-case age	Disease severity	Time to surgery
Tomaszewski et al. [3]	55	Not reported	Not reported
Yianni et al. [31]	Not reported	Not reported	Not reported
Valldeoriola et al. [33]	59.9 (6.8)	UPDRS 50 (3.2)	DBS group: 16.9 years (1.2) BMT group: 13.6 years (1.2)
Dams et al. [41]	60	H-Y off, % of population III 50% IV 30% V 20%	Not reported
Eggington et al. [39]	60.5 (7.4)	Mean baseline H&Y 3.4	DBS group: 13 years (5.8) BMT group: 13.8 years (5.6)
Zhu et al. [30]	55.5 (6.2); range 41–64	Mean UPDRSIII score 44 Mean H&Y stage 3.2 Mean Schwab ADL % 43%	8.6 years (2.4); range 6–13
Walter et al. [32]	Median 59.1 (range 52–67)	H&Y years 4.1 (4-5)	14.1 years (range 10–19.2)
Dams et al. [40]	52 (6.6)	Base case: H&Y I: 5 H&Y II: 65 H&Y III: 20 H&Y IV: 10 H&Y V: 0	DBS group: 7.3 years (3.1) BMT group: 7.7 years (2.7)
Fundament et al. [37]	52.22 (0.4)	All treatments UPDRS I = 1.06 (0.17) UPDRS II = 4.85 (0.57) UPDRS III = 12.29 (1.48) UPDRS IV = 5.54 (0.31)	Not reported
Kawamoto et al. [36]	Not reported	Not reported	Not reported
McIntosh et al. [35]	59 (range 37–79)	Not reported	DBS group: 11.5 years (range 2.0–32.2) BMT group: 11.2 years (1.0–30.0)
Pietzsch et al. [34]	60.5 (range 50–70)	Not reported	Not reported
Fann et al. [38]	Not reported	Not reported	Not reported
Guo et al. [42]	DBS: 64.33 (range 41–79) BMT: 64.91 (range 41–89)	H&Y stage before DBS = 3.92 (SEM 0.0769) BMT average H&Y = 3.62 (SEM 0.0653)	Not reported

Table 4: Incremental Net Benefit Estimation per Study
Values reported as estimate±standard deviation or estimate (95% confidence interval)
INB=Incremental net benefit; DBS=deep brain stimulation; BMT=best medical therapy; ΔC=change in cost; QALY=quality of life years; ΔE=change in efficacy; USD=United States Dollar
Method for INB Calculations Utilized:
1) $INB = K\Delta E - \Delta C$;
2) $INB = \Delta E(K - ICER)$,
where K is the willingness to pay threshold, and ΔC and ΔE are the incremental cost and incremental effectiveness, respectively.
Methods for INB Variance Calculations Utilized:
Scenario 1: The primary economic evaluation reports point estimates and variances (SE, SD) for every parameter required for calculation of INB and its variance. These outcomes were then calculated according to equations 1-4 (described in Appendix 2)
Scenario 4: The study does not report dispersion, but does provide CE plane graphs with a scatter plot of ΔC on the Y-axis and ΔE on the X-axis. Individual values of ΔC and ΔE were digitally extracted from the CE plane using Web-Plot-Digitizer software [58]. Means of ΔC and ΔE, and their variances and covariances were estimated. INB and its variance were estimated using equations 1 and 3 (described in Appendix 2)
Scenario 5: The study does not report any dispersion, nor a CE plane, but provides only point estimates of costs, outcomes, and ICER. Measures of dispersion were estimated from another study, as long as the study these measures were borrowed from fulfilled the following criteria:
-They were in the same income-level country.
-Their ICERs differ only by±50-75%.
-They are similar in intervention, comparator, time period, and country region.
-They have a similar model type and imputes (i.e. discounting and time horizon).
For full details of INB Calculations, please see Appendix 2.

Table 4 INB estimation per study

Study	Horizon	Country	Threshold (2022USD)	ΔC (2022 US$)	ΔC variance (2022 US$)	Method for variance	ΔE	ΔE variance	Method for variance	ICER (2022USD)	ICER variance (2022USD)	Method for variance	INB	Method for INB	INB variance	Method for INB variance
Tomaszewski et al. [3]	Lifetime	USA	85,016.73	59,511.71	Not available	Not applicable	0.72	0.01	SD (Monte Carlo simulation)	83,646.26	83,076.64–88,555.12	95% CI (median, sensitivity analyses)	986.74	2	72,280,948.32	1
Yianni et al. (dystonia) [31]	2 years	UK	696,419.82	76,382.01	Not available	Not applicable	0.47 (1 year) 0.94	0.078	SD (reported)	81,256.27	Not available	Not applicable	578,253.73	2	Not able to estimate	Not applicable
Valldeoriola et al. [33]	1 year	Spain	221,077.28	16,804.08	4554.19	SE (reported)	0.221	0.004	SE (reported)	76,026.26	97,446.44–137,417.21	95% CI (sensitivity analyses)	32,056.27	2	1,160,830.33	1
Dams et al. 2013 [41]	Lifetime	Germany	57,072	12,473.80	Not available	Not applicable	1.05	0.003	SD (Monte Carlo simulation)	11,908.43	8,025.75-18,007.04	95% CI (mean, sensitivity analyses)	47,421.75	2	9,774,751.09	1
		Finland	48,581.99	10,618.20			1.05	0.003	SD (Monte Carlo simulation)	10,136.94	6,831.84–15,328.32	95% CI (mean, sensitivity analyses)	40,367.31	2	7,083,277.92	1
		Spain	55,677.66	14,636.15			1.05	0.003	SD (Monte Carlo simulation)	13,972.78	9,417.03–21,128.59	95% CI (mean, sensitivity analyses)	55,642.40	2	9,303,656.39	1
Eggington et al. 2014 [39]	5 years	UK	57,998.58	40,071.22	Not available	Not applicable	1.002	0.091	(Estimate from Fundament [37])	39,976.49	34,799.15–44,272.25	95% CI (median, sensitivity analyses)	18,058.14	2	306,111,202.40	5
Zhu et al. [30]	1 year	Hong Kong	Not available	Not available	Not available	Not applicable	Not available	Not available	Not applicable	31,057.40	Not available	Not applicable	− 2069.67	2	Not able to estimate	Not applicable
	2 years	Hong Kong	25,227.36	5644.12	4831.14	SD (reported)	0.355	0.223	SD (reported)	6,273.54	8,086.36–61,414.73	Range (reported)	6728.61	2	141,949,724.70	1
Walter et al. [32]	Lifetime	UK	36,119.58	19,751.51	Not available	Not applicable	0.13	Not available	Not applicable	7,182.36	Not available	Not applicable	3761.84	2	Not able to estimate	Not applicable
		Germany	33,050.90	25,986.55			0.12			9,519.43			2823.78	2		
Dams et al. 2016 [40]	Lifetime	Germany	83,829.46	61,027.85	Not available	Not applicable	1.6	0.051	(Estimate from Dams 2013 [41])	38,058.58	32,442.00–45,603.23	95% CI (median, sensitivity analyses)	96,068.56	2	358,400,145.90	5
Fundament et al. [37]	15 years	UK	53,824.14	48,081.10	7525.18	Sensitivity analysis C-E plane	1.34	0.110	Sensitivity analysis C-E plane Covariance 135.34	35,680.02	34,187.30–35,703.34	95% CI (median, sensitivity analyses)	24,313.12	2	304,112,592.10	1

Table 4 (continued)

Study	Horizon	Country	Threshold (2022USD)	ΔC (2022 US$)	ΔC variance (2022 US$)	Method for variance	ΔE	ΔE variance	Method for variance	ICER (2022USD)	ICER variance (2022USD)	Method for variance	INB	Method for INB	INB variance	Method for INB variance
Kawamoto et al. [36]	10 years	Japan	529.43	975.20	22.10	C-E plane	3.2	0.510	C-E plane Covariance 0.196	293.36	Not available	Not available	755.41	2	142,765.59	4
McIntosh et al. [35]	1 year	UK	80,783.66	18,693.34	15,399.38–21,987.29	95% CI (reported)	0.0205	0.0003	95% CI (reported)	926,039.21	Not available	Not applicable	− 17,327.74	2		
	5 years		60,587.74	29,401.21	Not available	Not applicable	0.33	0.01	Not applicable	91,245.14	39,279.03–454,987.69	95% CI (reported)	− 10,116.94	2	36,894,325.21	1
	10 years		60,587.74	84,679.45			0.6	0.034		142,455.92	69,051.85–750,397.37	95% CI (reported)	− 49,120.90	2	125,119,898.30	1
Pietzsch et al. [34]	10 years	USA	Not available	Not available	Not available	Not applicable	1.69	Not available	Not applicable	28,947.54	Not available	Not applicable	Not able to estimate	Not applicable	Not able to estimate	Not applicable
Fann et al. [38]	3 years	Taiwan	6827.40	3405.81	14.21	C-E plane	0.519	0.00004	C-E plane Covariance − 0.048	9363.85	Not available	Not applicable	137.61	1	2534.18	4
	10 years		3110.26	4045.00	22.48	C-E plane	1.368	0.0003	C-E plane Covariance − 0.032	5236.84	Not available	Not applicable	209.83	1	3123.65	4
Guo et al. [42]	15 years	China	54,647.38	82,728	82,424.04–83,031.96	95% CI (reported)	1.5077	1.4711–1.5443	95% CI (reported)	54,870.35	53,491.45–56,249.24	95% CI (reported)	− 186.90	2	7,182,232,825,072.28	4

Table 5: Quality assessment among all included studies. Adapted from the CHEC checklist tool [16] Y=yes, N=no.

Table 5 Quality assessment among all included studies. Adapted from the Consensus on Health Economics Criteria Checklist (CHEC) tool [15]

	Tomaszewski et al. [3]	Yianni et al. [31]	Valldeoriola et al. [33]	Dams et al. (2013) [41]	Eggington et al. [39]	Zhu et al. [30]	Walter et al. [32]	Dams et al. (2016) [40]	Fundament et al. [37]	Kawamoto et al. [36]	McIntosh et al. [35]	Pietzsch et al. [34]	Fann et al. [38]	Guo et al. [42]
1. Is the study population clearly described?	N	Y	Y	Y	N	Y	N	Y	Y	N	Y	Y	N	Y
2. Are competing alternatives clearly described?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
3. Is a well-defined research question posed in answerable form?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
4. Is the economic study appropriate to the stated objective?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5. Are the structural assumptions and the validation methods of the model properly reported?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
6. Is the chosen time horizon appropriate in order to include relevant costs and consequences?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
7. Is the actual perspective chosen appropriate?	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
8. Are all important and relevant costs for each alternative identified?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Are all costs measured appropriately in physical units?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
10. Are costs valued appropriately?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
11. Are all important and relevant outcomes for each alternative identified?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
12. Are all outcomes measured appropriately?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
13. Are outcomes valued appropriately?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
14. Is an appropriate incremental analysis of costs and outcomes of alternatives performed?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
15. Are all future costs and outcomes discounted properly?	Y	N	N	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	N

Table 5 (continued)

	Tomaszewski et al. [3]	Yianni et al. [31]	Valldeoriola et al. [33]	Dams et al. (2013) [41]	Eggington et al. [39]	Zhu et al. [30]	Walter et al. [32]	Dams et al. (2016) [40]	Fundament et al. [37]	Kawamoto et al. [36]	McIntosh et al. [35]	Pietzsch et al. [34]	Fann et al. [38]	Guo et al. [42]
16. Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	Y	N	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y
17. Do the conclusions follow the data reported?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
18. Does the study discuss the generalizability of the results to other settings and patient/client groups?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
19. Does the article/report indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	N	N	N	Y	Y	N	Y	Y	Y	Y	Y	N	Y	Y
20. Are ethical and distributional issues discussed appropriately?	N	N	N	Y	Y	N	Y	Y	Y	Y	Y	N	Y	Y

Table 6: Methodological assessment of included studies with respect to heterogeneity of included studies

Table 6 Methodological assessment of included studies with respect to heterogeneity of included studies

Criteria	Considerations	Concerns
Model structure	All model-based included studies (10/14) utilized Markov or semi-Markov modeling structures	Consistent across model-based studies, one microsimulation model included
	4/14 included studies completed analyses of comparative original studies without modeling	
Model validity	Of the 10 model-based studies, 7/10 were based on H&Y stages 1–5 off states + death state	The majority of models utilized similar structures and inputs; however, the combination of Markov transition state models and microsimulations limit confidence in certainty in pooled estimates
	One study only considered H&Y stages 3–5 + death state	
	One study defined states as "outside nursing home, inside nursing home, dead", and another defined states as either "DBS continuation, DBS withdrawal or dead" for DBS patients, or survival/death for BMT	
Estimation of costs	Direct local hospital costs reported for 4/14 studies, national insurance costs reported for 6/14, questionnaire/expert opinion in 2/14, previous studies for 2/14	Inconsistent cost sources and itemized reporting decrease certainty in cost estimates for INB
	Reported costs include medication costs, implants, surgical cost, pre-operative work-up, complication costs, long-term care costs—all with inconsistent reporting between studies	
Estimation of health state utility	2/14 studies utilized literature reviews for estimation of utilities	Duplicate data likely included (e.g., EARLYSTIM trial data used in two included studies)
	4/14 studies utilized data from original comparative studies	Significant variance in change in efficacy between studies, even with similar time horizons
	2/14 studies utilized the EARLYSTIM dataset	These inconsistencies decrease certainty in health state utilities for INB
	6/14 studies utilized data from previously published studies	
	Mean ΔE (QALY) of all included studies for Parkinson's disease for longer duration time horizons (10 years to lifetime) is 1.12 (0.53)	
Variance reporting	Measure of variance in efficacy reported in 5/14 studies, estimated from reported C-E planes in 3/14, estimated using Monte Carlo simulation for 2/14, not estimable for 2/14 studies, estimated from similar studies in 2/14	Inconsistent reporting and estimation error decrease certainty in INB variance
Heterogeneity	Given above concerns, considerable heterogeneity exists based on the time horizon, GDP of included countries, perspectives, cost and effectiveness estimates, variance estimates, source of data, modeling structure and validity This limits the certainty of effect estimates for outcomes	

Table 7: Transferability assessment of included studies, adapted from Welte *et al* [18]
Low scores indicate high transferability
*Study by Yianni *et al* [32] was deemed to have poor transferability, given it is the only study assessing DBS for dystonia, and was therefore excluded from the transferability assessment
**Study country used is Germany, as Finland and Spain were also estimated in original study
1=Estimated relevance; 2=Estimated correspondence between study and decision country; 3=Estimation of Cost-Effectiveness Ratio (CER) of decision country based on CER of study country is (U=unbiased, TH=too high, TL=too low, THOL=too high or low)
VH=very high; H=high; L=low; VL=very low; NR=not relevant in the model; NA=not reported in the model

Table 7 Transferability assessment of included studies, adapted from Welte et al. [17]

Study/Country	Transferability factors (all studies compared to USA)																							
	Perspective			Discount rate			Medical cost approach			Productivity cost approach			Absolute and relative prices in healthcare			Practice variation			Technology availability			Disease incidence and prevalence		
	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
Tomaszewski et al.[3]/USA	VH	VH	U	VH	VH	U	H	H	U	NA		U	VH	VH	U	VH	VH	U	H	VH	U	H	VH	U
Yianni et al. [31][a]/UK (dystonia)																								
Valldeoriola et al. [33]/Spain	VH	VH	U	VH	NA	THOL	H	H	U	NA		U	VH	L	TH	VH	H	THOL	H	VH	U	H	L	THOL
Dams et al. [41][b]/Germany	VH	VH	U	VH	VH	U	H	H	U	NA		U	VH	L	TH	VH	VH	U	H	VH	U	H	H	THOL
Eggington et al. [39]/UK	VH	VH	U	VH	H	TL	H	H	U	NA		U	VH	L	TH	VH	H	TL	H	VH	U	H	H	THOL
Zhu et al. [30]/Hong Kong	VH	VH	U	VH	VH	U	H	H	U	NA		U	VH	L	TH	VH	VH	U	H	VH	U	H	H	THOL
Walter et al. [32]/UK and Germany	VH	VH	U	VH	VH	U	H	H	U	NA		U	VH	L	TH	VH	VH	U	H	VH	U	H	H	THOL
Dams et al. [40]/Germany	VH	VH	U	VH	VH	U	H	H	U	NA		U	VH	L	TH	VH	VH	U	H	VH	U	H	H	THOL
Fundament et al. [37]/UK	VH	VH	U	VH	H	TL	H	H	U	NA		U	VH	L	TH	VH	VH	U	H	VH	U	H	H	THOL
Kawamoto et al. [36]/Japan	VH	VH	U	VH	NA	THOL	H	H	U	NA		U	VH	L	TH	VH	H	THOL	H	VH	U	H	L	THOL
McIntosh et al. [35]/UK	VH	VH	U	VH	H	TL	H	H	U	NA		U	VH	L	TH	VH	H	THOL	H	VH	U	H	H	THOL
Pietzsch et al. [34]/USA	VH	VH	U	VH	VH	U	H	H	U	NA		U	VH	VH	U	VH	VH	U	H	VH	U	H	VH	U
Fann etal. [38]/Taiwan	VH	VH	U	VH	VH	U	H	H	U	NA		U	VH	L	TH	VH	H	THOL	H	VH	U	H	H	THOL
Guo et al. [42]/China	VH	H	THOL	VH	NA	THOL	H	H	U	NA		U	VH	L	TH	VH	H	THOL	H	VH	U	H	H	THOL

Study/Country	Transferability factors (all studies compared to USA)																		Overall assessment
	Case mix			Life expectancy			Health-status preferences			Acceptance, compliance, incentives to patients			Productivity and work-loss time			Disease spread			
	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	
Tomaszewski et al.[3]/USA	H	VH	U	H	VH	U	VH	VH	U	L	VH	U	NA		U	NR		U	U 0/14
Yianni et al. [31][a]/UK (dystonia)																			THOL N/A
Valldeoriola et al. [33]/Spain	H	VH	U	H	L	TL	VH	VH	U	L	H	U	NA		U	NR		U	THOL 5/14
Dams et al. [41][b]/Germany	H	VH	U	H	L	TL	VH	VH	U	L	H	U	NA		U	NR		U	THOL 3/14
Eggington et al. [39]/UK	H	VH	U	H	L	TL	VH	VH	U	L	H	U	NA		U	NR		U	TL 5/14
Zhu et al. [30]/Hong Kong	H	VH	U	H	L	TL	VH	H	THOL	L	H	U	NA		U	NR		U	THOL 4/14
Walter et al. [32]/UK and Germany	H	VH	U	H	L	TL	VH	VH	U	L	H	U	NA		U	NR		U	THOL 3/14

Table 7 (continued)

Study/Country	Transferability factors (all studies compared to USA)																	
	Case mix			Life expectancy			Health-status preferences			Acceptance, compliance, incentives to patients			Productivity and work-loss time			Disease spread			Overall assessment
	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	
Dams et al. [40]/Germany	H	VH	U	H	L	TL	VH	VH	U	L	H	U	NA		U	NR		U	THOL 3/14
Fundament et al. [37]/UK	H	VH	U	H	L	TL	VH	VH	U	L	H	U	NA		U	NR		U	TL 4/14
Kawamoto et al. [36]/Japan	H	VH	U	H	L	TL	VH	L	TH	L	H	U	NA		U	NR		U	TH 6/14
McIntosh et al. [35]/UK	H	VH	U	H	L	TL	VH	VH	U	L	H	U	NA		U	NR		U	THOL 5/14
Pietzsch et al. [34]/USA	H	VH	U	H	VH	U	VH	VH	U	L	VH	U	NA		U	NR		U	U 0/14
Fann etal. [38]/Taiwan	H	VH	U	H	L	TL	VH	H	THOL	L	H	U	NA		U	NR		U	THOL 5/14
Guo et al. [42]/China	H	VH	U	H	H	TL	VH	H	THOL	L	H	U	NA		U	NR		U	THOL 7/14

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CONTRIBUTORSHIP STATEMENT

Melissa Lannon contributed significantly to the study's concept and design, data collection and analysis, and interpretation of the results. She wrote the first draft of the manuscript, provided critical revisions, and gave final approval of the submitted manuscript.

Taylor Duda contributed to data collection and analysis. He provided critical revisions and gave final approval of the submitted manuscript.

Alexander Mastrolonardo contributed to data collection and analysis. He provided critical revisions and gave final approval of the submitted manuscript.

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Amanda Martyniuk contributed to data collection and analysis. She provided critical revisions and gave final approval of the submitted manuscript.

Forough Farrokhyar contributed to the study's concept and interpretation of the results. She provided critical revisions and gave final approval of the submitted manuscript.

Feng Xie contributed to data analyses and interpretation of the results. He provided critical revisions and gave final approval of the submitted manuscript.

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Suneil Kalia contributed to the study's concept and interpretation of the results. He provided critical revisions and gave final approval of the submitted manuscript.

Sunjay Sharma contributed to the study's concept and interpretation of the results. He provided critical revisions and gave final approval of the submitted manuscript.

APPENDIX 1 - Supplementary Table 1: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions (R) 1946 to May 24, 2022. Updated MEDLINE search on March 12, 2023 revealed 12 additional studies for screening.

Search strategy for MEDLINE (Ovid Platform ALL 1946 to May 24, 2022**)**		
#	**Searches**	**Results**
1	Electric stimulation therapy/ or deep brain stimulation/	31937
2	Device Removal/	14682
3	Electric stimulation/	115891
4	Neuromodulation.mp.	10596
5	Neurosurgical procedures/	35005
6	Neurostimulat*.mp.	4690
7	(electric stimulation therap* or deep brain stimulat* or Device Removal or Electric Stimulation).mp.	167718
8	Or/1-7	210955
9	"Anterior limb of internal capsule".mp.	91
10	Subthalamic nucleus/ or zona incerta/ or thalamus/ or thalamic nuclei/ or anterior thalamic nuclei/ or geniculate bodies/ or intralaminar thalamic nuclei/ or lateral thalamic nuclei/ or pulvinar/ or mediodorsal thalamic nucleus/ or midline thalamic nuclei/ or posterior thalamic nuclei/ or ventral thalamic nuclei/ or external capsule/ or internal capsule/	44201
11	Subthalamic nucle*.mp.	7599
12	Ventral Thalamic nuclei/	922
13	Globus Pallidus/	7065
14	(dbs or ventralis intermedius nuclei or globus pallidus* or subthalamic nucleus or zona incerta or thalamus or ventral thalamic or stn or vim or gpi).mp.	97283
15	Basal ganglia diseases/	5561
16	Parkinsonian disorders/ or Parkinson disease/	84308
17	Neurodegenerative diseases/	22818
18	(basal ganglia disease* or parkinsonian disorder* or Parkinson* disease).mp.	132698
19	Dystonic disorders/	3212
20	Essential tremor/	2542
21	(essential tremor or primary dystonia).mp.	5209
22	Or/9-21	251690
23	Exp "costs and cost analysis"/	258068
24	"health care economics and organizations"/ or economics/ or "compensation and redress"/ or "costs and cost analysis"/ or "cost allocation"/ or cost-benefit analysis/ or "cost control"/ or "cost savings"/ or health care costs/ or direct service costs/ or drug costs/ or employer health costs/ or hospital costs/ or health expenditures/ or capital expenditures/ or low-value care/ or economics, hospital/ or hospital charges/ or economics, medical/ or fees, medical/ or economics, pharmaceutical/ or "fees and charges"/ or capitation fee/ or fee-for-service	654963

	plans/ or fees, pharmaceutical/ or "rate setting and review"/ or financial support/ or health planning support/ or healthcare financing/ or financing, organized/ or financing, government/ or insurance, health, reimbursement/ or single-payer system/ or health care sector/ or health planning/ or "health care quality, access, and evaluation"/ or "exp delivery of health care"/ or "delivery of health care, integrated"/ or provider-sponsored organizations/ or health care reform/ or health priorities/ or health resources/ or health services accessibility/ or health care rationing/ or health equity/ or health facility closure/ or health facility environment/ or health facility size/ or "health services needs and demand"/ or healthcare disparities/ or learning health system/ or medical tourism/ or needs assessment/ or nurses improving care for health system elders/ or population health management/ or practice patterns, nurses'/ or practice patterns, physicians'/ or professional practice gaps/ or health services research/ or comparative effectiveness research/	
25	Decision support techniques/	22200
26	Decision trees/	11954
27	(decision model* or Markov or discrete event simulation or decision tree* or trial-based model).mp.	53167
28	(cost utility analys* or cost benefit analys* or economic* or health care economics or healthcare economics or cost analys* or cost effectiveness).mp.	810636
29	(cost adj1 (outcome* or benefit* or minim*)).mp.	101979
30	Monte carlo method/	31274
31	Monte carlo method.mp.	33532
32	Or/23031	1240752
33	8 and 22 and 32	300

APPENDIX 2 - Incremental Net Benefit Calculation Methodology:

Data harmonization was performed using COMER framework [7]. All currencies were first converted the 2022 value for the currency reported in each individual study using the historical CPI of the country of study [9]. Individual study currencies were then converted to 2022 US dollars (USD) by converting to purchasing power parity (PPP) using conversion rates from the International Monetary Fund [9]. This was completed for incremental costs, thresholds, and ICERs for each study. After currency conversions for cost and threshold (K), the INB was estimated.

After currency conversions for cost and threshold (K), the INB was estimated using one of the following two equations:

$$INB = K\Delta E - \Delta C \quad (1)$$

or

$$INB = \Delta E(K - ICER) \quad (2)$$

Where K is the willingness to pay threshold (as reported in each paper, or from study country), and ΔC and ΔE are the incremental cost and incremental effectiveness, respectively.

Variance of INB was estimated using one of the following two equations:

$$Var(INB) = K^2\sigma_{\Delta E}^2 + \sigma_{\Delta C}^2 - 2K\sigma_{\Delta E\Delta C} \quad (3)$$

or

$$Var(INB) = K^2\sigma_{\Delta E}^2 + \sigma_{ICER}^2 \quad (4)$$

Where $\sigma_{\Delta C}^2$, $\sigma_{\Delta E}^2$, and $\sigma_{\Delta E\Delta C}$ are the variances of ΔC and ΔE and their covariance, and σ_{ICER}^2 is the variance of ICER.

Economic evaluations have variable reporting for parameters, therefore the five scenarios , previously described by Bagepally *et al.*[56] were used, as needed.

Scenario 1: The primary economic evaluation reports point estimates and variances (SE, SD) for every parameter required for calculation of INB and its variance. These outcomes were then calculated according to equations 1-4.

Scenario 2: The study reports means and measures of dispersion (95% CIs) of incremental costs, outcomes, and ICER. Or the 95% CI is estimated from sensitivity analyses (mean or median of upper limits from sensitivity analyses, depending on normality of distribution of results) [57]. The variance of ICER was calculated using the following formulas:

$$SE = \frac{UL_{ICER} - \hat{\mu}_{ICER}}{Z_{a/2}} \quad (5)$$

then

$$\hat{\sigma}^2_{ICER} = SE^2 \quad (6)$$

Where UL_{ICER} represents the upper limit of ICER in the 95% confidence interval (or from the sensitivity analysis), $Z_{a/2}$ represents the standardized normal (1.96 if alpha=0.05), and $\hat{\mu}_{ICER}$ is the mean ICER. Once the variance of ICER has been calculated, the INB was estimated using equation 4.

Scenario 3: The study reports means and variances (95% CI, SD/SE) or costs and outcomes (ΔC and ΔE), but does not provide an ICER or its variance. Data for ΔC and ΔE were used to simulate ΔC and ΔE using Monte Carlo simulations with gamma and normal distributions for ΔC and ΔE, respectively, using 10000 separate replications. The ΔC and ΔE, and the covariance between them was then calculated. A sensitivity analysis was performed using different distributions to test the robustness of pooling results, and an estimate of the covariance ($\sigma_{\Delta E \Delta C}$) and $\sigma^2_{\Delta E}$ and $\sigma^2_{\Delta C}$

was calculated. In cases where the 95% CI was provided, this was converted to SD using equations 5 and 6.

Scenario 4: The study does not report dispersion, but does provide CE plane graphs with a scatter plot of ΔC on the Y-axis and ΔE on the X-axis. Individual values of ΔC and ΔE were digitally extracted from the CE plane using Web-Plot-Digitizer software [58]. Means of ΔC and ΔE, and their variances and covariances were estimated. INB and its variance were estimated using equations 1 and 3.

Scenario 5: The study does not report any dispersion, nor a CE plane, but provides only point estimates of costs, outcomes, and ICER. Measures of dispersion were estimated from another study, as long as the study these measures were borrowed from fulfilled the following criteria:

-They were in the same income-level country.

-Their ICERs differ only by ±50-75%.

-They are similar in intervention, comparator, time period, and country region.

-They have a similar model type and imputes (i.e. discounting and time horizon).

INB was then pooled across studies, using a random-effects model, DerSimonian-Liard in all cases [10].

$$INB_P = \frac{\sum_{i=1}^{S} w_i \, INB_i}{\sum_{i=1}^{S} w_i + \tau^2}$$

$$\tau^2 = \frac{Q - (S-1)}{\sum w_i - \frac{\sum w_i^2}{\sum w_i}}$$

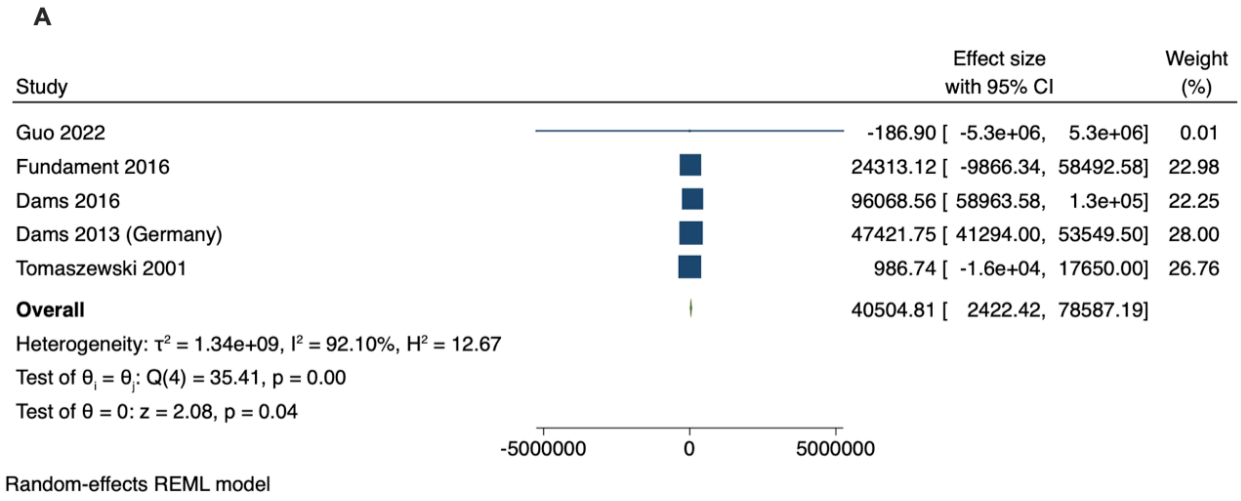
The heterogeneity of INB between studies was assessed using the Cochran Q test and the I^2 statistic, as follows:

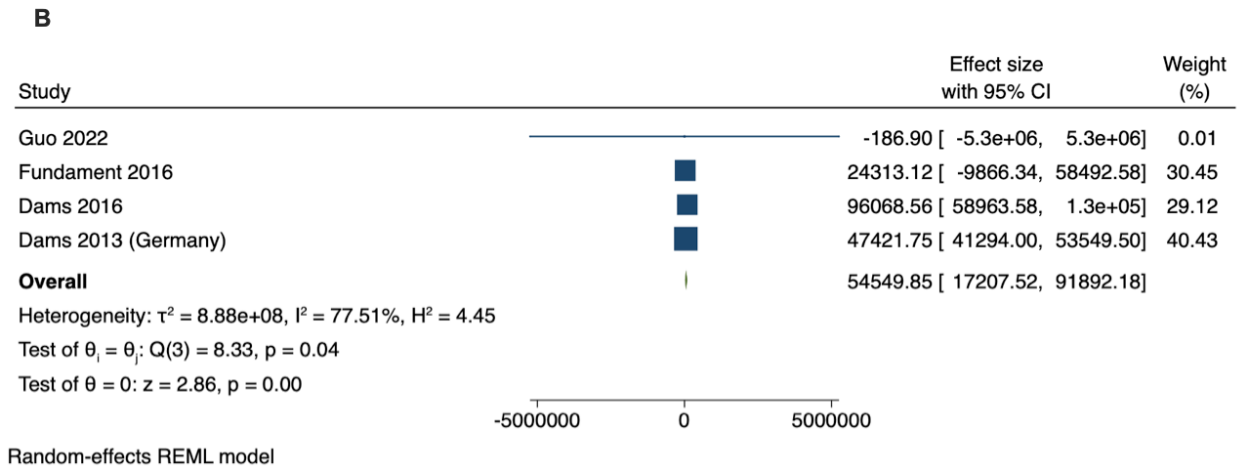
$$Q = \sum_{i=1}^{S} w_i(INB_i - INB_P)$$

$$w_i = \frac{1}{var(INB_i)}$$

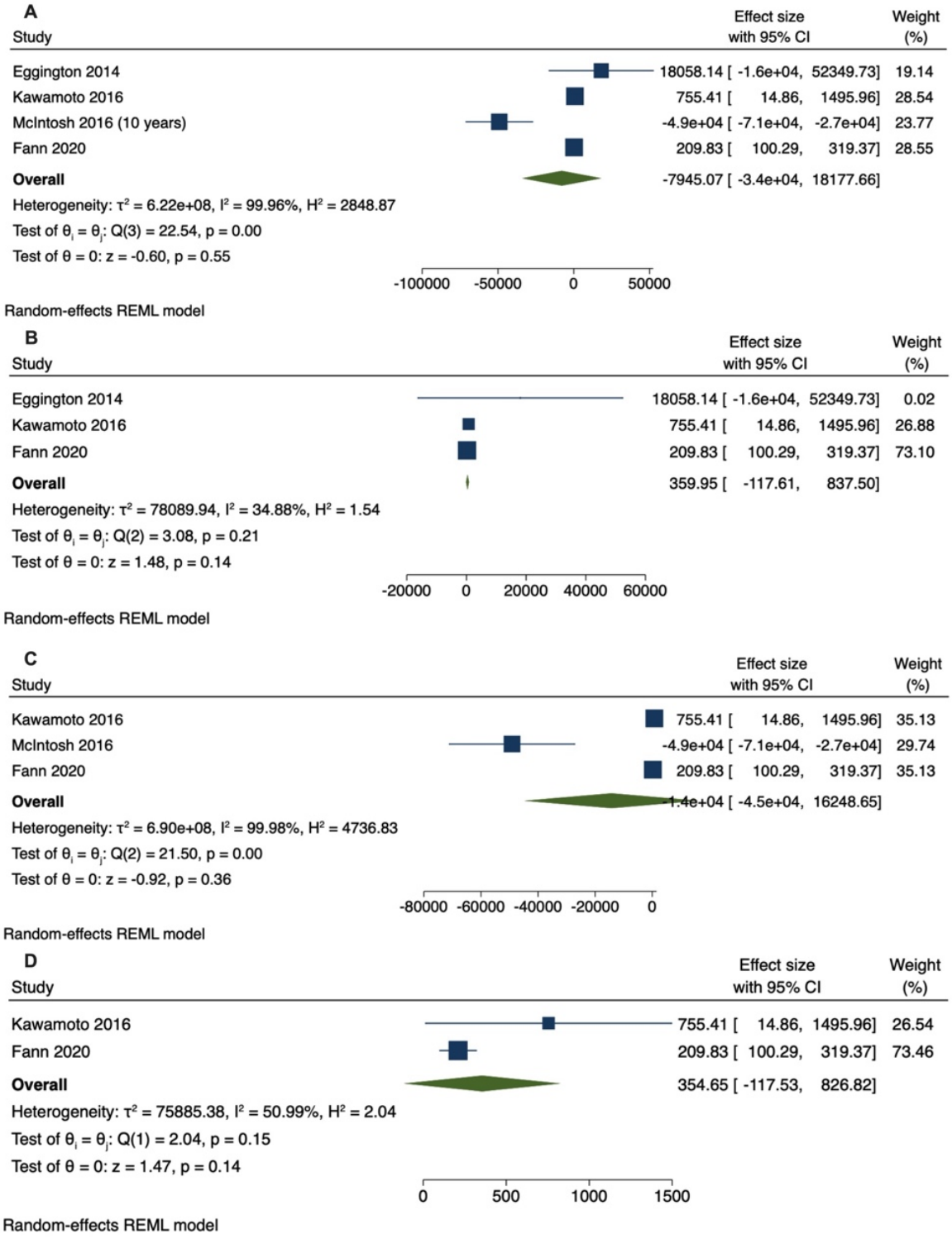
$$I^2 = \frac{(Q - S + 1) \times 100}{Q}$$

APPENDIX 3 – Supplementary Figure 1: Forest plots of 15 year-lifetime horizon meta-analyses with (A) and without (B) Tomaszewski [3], indicating no difference between analyses of studies from multi-payer and single payer countries, vs. single payer only.

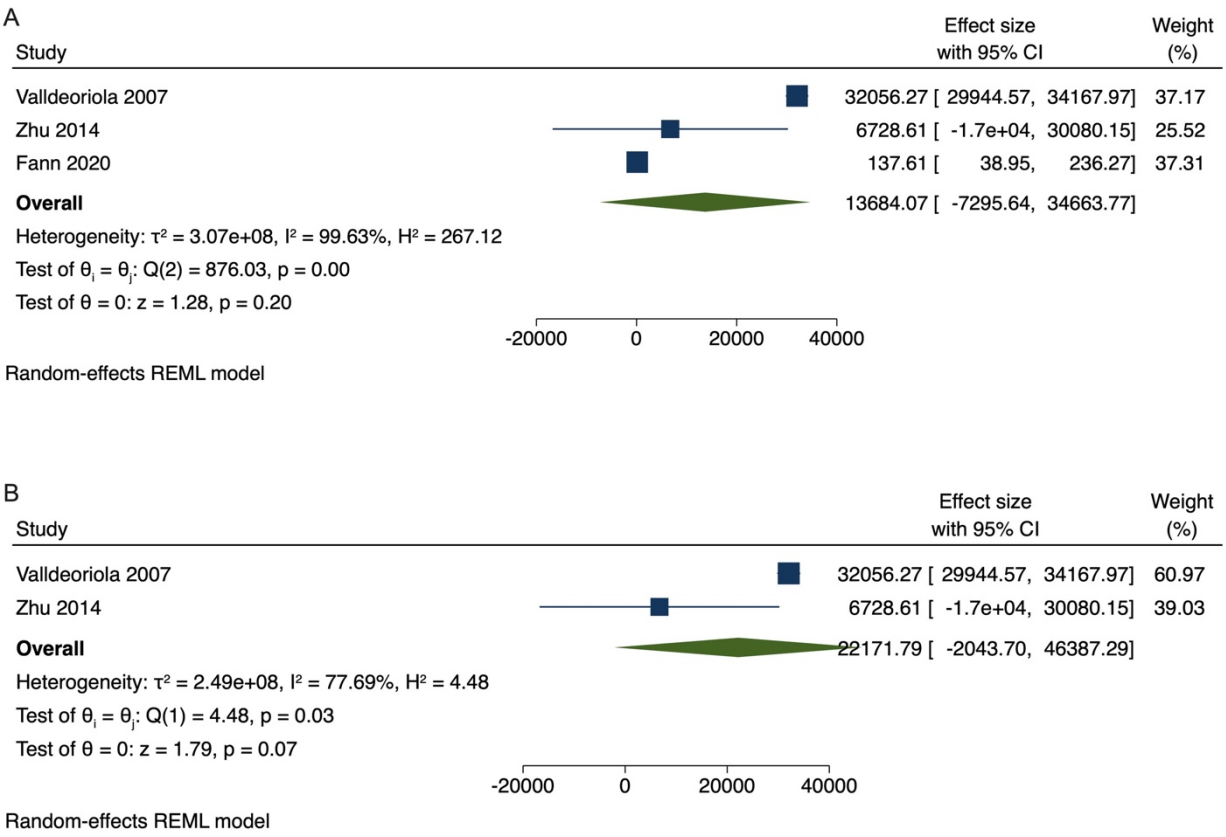




APPENDIX 4 – Supplementary Figure 2: Forest plots of 5-10 year horizon meta-analyses with (A) and without (B) McIntosh *et al* [36], and 10 year time horizon meta-analyses with (C) and without (D) McIntosh *et al* [36].



APPENDIX 5 – Supplementary Figure 3: Forest plots of 1-3 year horizon meta-analyses with (A) and without (B) Fann *et al* [39], indicating decreased heterogeneity and improved precision with a model-based evaluation eliminated.



CHAPTER 3: Mixed Methods Survey of Stakeholders to Identify Barriers to Accessing Deep Brain Stimulation for Movement Disorders in Canada

Mixed Methods Survey of Stakeholders to Identify Barriers to Accessing Deep Brain Stimulation for Movement Disorders in Canada

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ABSTRACT

Background

Movement disorders (Parkinson's disease, essential tremor, dystonia) are debilitating, progressive conditions that profoundly impact patients' quality of life. Surgical therapies, such as deep brain stimulation (DBS) can provide tremendous relief to patients, but remain costly, and therefore limited in availability. In order to determine if adequate access to this service is available, it is important to understand the prevalence of the disease and potential barriers to access.

Methods

This is a mixed methods survey of stakeholders (patients/family members, advocacy groups, family physicians, neurologists, neurosurgeons) assessing perceived barriers to DBS for movement disorders and attempt to estimate the prevalence of candidates for this therapy by region. Closed and open-ended questions were used. Descriptive statistics were used to highlight regions of Canada where perceived access is poor, and to identify barriers to access.

Results

A total of 220 responses were recorded (12 neurosurgeons, 22 neurologists, 30 family physicians, 153 patients and caregivers, and 3 advocacy group personnel). Themes included limited resources/centralization of resources, education, burdensome referral patterns, and personal patient factors. Barriers included costs associated with travel, waitlists, lack of specific resources, and poor understanding of movement disorders, DBS indications, and referral pathways.

Conclusions

A number of barriers to access to DBS have been identified, related to geography and centralization of services, referrals, and need for further education of indications, and safety. Use of virtual care, centralized referral pathways, and further research to determine the true prevalence of candidates for this therapy are required to improve access to DBS in Canada.

1 INTRODUCTION

From its inception in 1984, The Canada Health Act has maintained the tenants that provincial and territorial health insurance plans must adhere to. These principles are: 1) public administration, 2) accessibility, 3) comprehensiveness, 3) universality, and 4)portability (1). The unique geography and population distribution of Canada creates challenges when assessing the accessibility of health services. As the complexity of health care delivery has evolved, concerns have grown about accessibility to critical healthcare services, particularly those requiring significant technological investment (2).

One such area with advancing technology is functional neurosurgery. This subspecialty of neurosurgery involves the use of neurostimulators, implanted devices, and modulation of neurological circuits for the benefit of patients with neurological disease (for example, movement disorders including Parkinson's Disease, essential tremor, and primary dystonia). These treatments have a profound impact on the quality of life for these patients.

As the field of functional neurosurgery continues to evolve and the population of Canada ages, proper access to deep brain stimulation (DBS) is essential. Currently, gaps remain in our understanding of the prevalence of disease, burden of disability and access to care. Therefore, optimizing the opportunity to alleviate suffering and reduce health care costs associated with conditions amenable to functional neurosurgical intervention becomes challenging.

Previously identified barriers to DBS for movement disorder indications include race (3–11), gender (4,6,9–12), socioeconomic status/insurance status (3,4,6,9,10,13,14), lack of referrals to

tertiary centers/movement disorder clinics (15,16), and geographical distance from tertiary centers (17–20). The majority of studies have been conducted in the United States, however Honey *et al* provided a national snapshot of the geographic distribution of DBS services in Canada in 2018, revealing a clear disparity between provinces in terms of access (i.e. excellent access in Saskatchewan with extremely poor access in Newfoundland and Labrador)(21). What this study did not investigate was the patient need for these services to determine equitable access. Pooja *et al* investigated the demographics of patients treated with DBS in Edmonton, revealing that significant disparities in access exist based on gender and ethnicity (11). Crispo *et al* completed a retrospective cohort study utilizing ICES data in Ontario, revealing that of 46,237 individuals with Parkinson's Disease, only 1.2% went on to receive DBS. They also highlighted that Northern Ontario residents were more likely than their Southern counterparts to receive DBS (AOR 2.23, 95%CI 1.15-4.34), that neighbourhoods with the highest number of visible minorities were less likely to receive DBS, and that regular neurologist care and use of multiple Parkinson's medications were positively associated with patients receiving DBS (19). Again, these studies did not endeavour to investigate the need for this service, in terms of prevalence of candidates for DBS, thereby reporting the proportion of patients going on to receive DBS without defining what an expected number should be.

There have been no previous attempts to comprehensively analyze access to DBS in Canada, through investigation of need for these services, matched access, and investigation of barriers for patients and practitioners, as determining the prevalence of candidates for DBS is a challenging concept. The literature relies on retrospective data to determine a patient's ability to access functional neurosurgery, however this method is limited, in that patients have already overcome

existing barriers to receive surgical intervention in many of these studies. Population-level data from databases such as the Canadian Institute for Health Information does not provide the granularity to assess operative candidacy, which requires clinical acumen. As such, in the current study, expert opinion will be used for this estimation. A previous international study by Dewan *et al* used surveys of neurosurgeons to estimate the proportion of patients with a number of neurologic diseases that warrant neurosurgical consultation or operative management. Investigators reported high concordance rates between clinicians regarding estimates (22), providing evidence of utility for this methodology, recognizing inherent limitations to survey studies. Including clinicians from multiple specialties (family medicine, neurology, and neurosurgery) may limit the degree of bias for or against surgical consultation expected from certain respondent groups.

The current study utilizes a mixed methods survey approach to estimate prevalence of candidates for DBS across Canada with Parkinson's Disease, essential tremor, or primary dystonia through expert opinion, and determine barriers and facilitators to care from patient and health care provider perspectives.

The objectives of this study include identification of underserved populations where need far exceeds availability of treatment due to geographic location, cost associated with travel, or inadequate resources with long wait times; identification of barriers to efficient access to functional neurosurgery among patients with movement disorders; and identification of barriers to referral to functional neurosurgery for patients with movement disorders.

2 METHODS

This is a population-based mixed methods survey study. The study was approved by the local university ethics committee, the Hamilton Integrated Research Ethics Board (HiREB #15262).

2.1 Survey Development

Survey questionnaires were developed in English and French and adapted for each of the stakeholder groups of interest along the patient care pathway. Questions were based on previously identified barriers to accessing DBS (geography, access to subspecialty services, socioeconomic status, race, and gender). To estimate prevalence of candidates for DBS by region, participants were asked to estimate the number of candidates in their region, and then to define the region they were referring to.

2.2 Survey Validation

Surveys were piloted with two individuals from each target group (neurosurgeons, neurologists, family physicians, patients/caregivers, advocacy groups) for clarity and comprehensiveness. Neurosurgeons and neurologists reviewed all surveys for content validity, while individuals from each stakeholder group reviewed respective surveys for face validity.

2.3 Survey Administration

Surveys were distributed electronically using electronic link or QR code via email, newsletters, and websites to patients and caregivers through advocacy groups across Canada (Parkinson NL, Parkinson NS, Parkinson QC, Parkinson Canada, International Essential Tremor Foundation, and Dystonia Canada). Employees and volunteers of advocacy groups were asked, via email, to

complete a designated survey as well. Family physicians, neurologists, and neurosurgeons in Canada were provided a QR code to respective surveys through an electronic faxing service in Canada, utilizing publicly available physician contact information (Scott's Info). Additionally, the Canadian Neurological Sciences Federation listed surveys for neurologists and neurosurgeons on their website and newsletter. Finally, publicly available institutional email addresses were used to distribute surveys to neurologists and neurosurgeons in Canada. A total of two faxes and two emails were sent to maximize responses. See Supplementary Material for survey forms.

2.4 Statistical Analyses

Descriptive statistics were utilized to summarize patient demographics, region, physician years in practice, estimated number of movement disorder patients in practice, and estimated number of DBS candidates in region. We hypothesized that geographic location may predict perceived lack of access to care among all practitioners and patients, in addition to financial barriers with lack of available DBS implants among functional neurosurgeons. To test this hypothesis, a binary logistic regression analysis was planned to estimate lack of access to care, adjusting for geographic location, financial barriers, availability of DBS implants, and practitioners. In the event of low response rate, descriptive interpretation was used.

Rurality was assumed for non-responses, based on answers to other questions, and answers were amended if the described region fitted different criteria than described by the respondent. For example, if the population of the municipality reported by the respondent had a population in

keeping with an urban centre, but the respondent reported the region as rural, data was corrected as such.

To estimate prevalence in described populations, denominators were estimated based on populations reported by Statistics Canada for regions described by respondents, or catchment areas listed on health authority websites if described in that manner. For non-responders, prevalence was estimated based on other responses (i.e. “urban centre in New Brunswick” – the average population of the three urban areas in the province; Moncton, Saint John, Fredericton) was used. The numerators were mean responses from participants in each group or region. Intraclass correlation coefficients were calculated between groups (between all family physicians, between all neurologists, between all neurosurgeons, and between providers in each region) as measure of agreement between the stakeholders.

Access was converted to values on a Likhert scale (1=No problem with access; 2=reasonable access; 3=poor access; 4=very poor access) and averaged for each province. Heat maps were produced with open access software found at heatmapper.ca

Qualitative themes were extracted from open ended questions using open coding, utilizing in vivo coding, followed by axial coding, then selective coding to collate codes into potential themes. Themes were refined and named.

3 RESULTS

A total of 220 responses were obtained from all stakeholder groups surveyed. Details of response rates are available in Table 1.

3.1 Quantitative Responses

3.1.1 Neurosurgeons

A total of 12 responses (11 English, 1 French) were obtained from Canadian neurosurgeons, the majority practicing in Ontario (n=10), and less than 100km from a centre providing functional neurosurgery. Three neurosurgeons from Ontario and one from Quebec report performing DBS as part of their practice. All neurosurgeons practiced in urban areas.

The majority of surgeons reported less than five unique patients are implanted with DBS devices monthly at their centre, with one surgeon in Ontario reporting 5-10 patients, and one surgeon in British Columbia reporting 10-20 unique cases per month.

3.1.2 Neurologists

A total of 22 responses (21 English, 1 French) were obtained from Canadian neurologists. The majority of respondents practicing in Ontario (54.5%), followed by British Columbia (22.7%), Alberta (18.1%), and Quebec (4.5%). All but one neurologist report practicing in urban centres (population greater than 30,000 or less than 30 minutes away from a community with a population of more than 30,000). The majority report an estimated distance for their patients to travel to access functional neurosurgery of less than 100km (77.2%). The exceptions to this were five neurologists reporting an estimated distance of 100-500km (AB n=2; ON n=3). Nearly half

of respondents were located within the Greater Toronto Area, Southwestern Ontario, or Southeastern Ontario.

There were varied responses in terms of duration of practice, with many neurologists practicing for less than five years. Just over half of respondents report movement disorder sub-specialization. Of surveyed neurologists, 77.27% report referring patients for DBS as part of their practice.

3.1.3 Family Physicians

A total of 30 responses (28 English, 2 French) were obtained from Canadian family physicians. Nearly half of all respondents were practicing in Ontario (33.33%), followed by Newfoundland and Labrador (20.0%), British Columbia (16.67%), and low responses from all other provinces with no responses from Prince Edward Island or the territories. The majority of family physicians practiced in urban centres (60.0%), and the greatest number report practicing for more than 20 years (36.67%), followed by 30.0% practicing for less than five years.

In terms of distance required for patients to travel to see a functional neurosurgeon, a bimodal distribution was observed, with the majority of responses indicating either less than 100km or more than 1,000km. Nearly all family physicians reporting distances greater than 1,000km were from Newfoundland and Labrador (n=4), where all physicians reported patients would need to travel greater than 500km. The majority of responses indicating distances less than 100km were in Ontario (n=7) and British Columbia (n=4). All respondents in Ontario reported patients needing to travel less than 500km.

The majority (76.67%) of respondents reported having a poor understanding of indications for DBS. Of those reporting a good understanding of indications, when asked to describe the ideal candidate for DBS, no respondents were able to accurately describe a good candidate for the therapy, with examples of responses including “Parkinson’s disease” and “motor disorders”, without further descriptions. See Table 2 for details of demographics for all surveyed physicians.

3.1.4 Patients/Caregivers

A total of 153 responses were obtained by Canadians living with Parkinson’s disease, essential tremor, or primary dystonia and their loved ones. Of these respondents, 124 were patients, 13 respondents were family members of patients living with one of the aforementioned movement disorders, and reported completing the questionnaire on behalf of themselves, and a further 10 respondents were family members completing the questionnaire on behalf of a patient. Six respondents did not provide a description as to whether they were a patient or a family member.

The majority of respondents were located in urban regions (70.59%), and 42.48% of respondents were living in Ontario.

In terms of diagnoses, 41.18% of respondents were diagnosed with dystonia, 32.68% with essential tremor, and 25.49% with Parkinson’s disease. All respondents from Newfoundland and Labrador were living with Parkinson’s disease. Variable responses were obtained in terms of duration of disease, with 30.07% of respondents reporting diagnosis within the past five years.

The majority of patients report having been diagnosed by a neurologist (73.86%). Patients living in Alberta were most likely to be diagnosed by a family physician, with 41.18% of Albertan respondents reporting receiving their diagnosis from a family doctor as opposed to a neurologist. The majority of patients reported that no physician has ever discussed DBS with them (67.32%), and 5.88% of patients report never having heard of DBS at all. When questioned about interest in pursuing DBS if offered to them, nearly half of respondents (49.01%) stated that yes, they would be interested and 36.60% report that they are unsure if they would be interested in DBS as a therapy for their movement disorder.

Of the 153 patient/caregiver respondents, 19 (12.42%) had previously undergone DBS. Of those that had received the therapy, the majority (63.16%) had been diagnosed for over two years prior to receiving DBS, and nearly all of those who received DBS waited over six months for DBS once they had been referred. Patients who had undergone DBS were more likely to live in an urban region, and the majority of patients were from either Ontario or British Columbia. See Table 3 for demographics of included patients/caregivers, and for comparison of patients who have undergone DBS with those who have not. Additionally, see Figure 1for geographic distribution of patients who had previously undergone DBS in the study population.

3.1.5 Advocacy Groups

A total of three responses were obtained from Canadians working for advocacy groups in one of the three movement disorders of interest (Parkinson's disease, essential tremor, dystonia).

All responses were collected from individuals living in urban areas, with one each from Newfoundland and Labrador, Nova Scotia, and British Columbia. All respondents believed inadequate number of functional neurosurgeons and patient socioeconomic status were barriers to accessing DBS.

3.2 Estimated Prevalence of Candidates for DBS in Canada

Both family physicians and neurologists were surveyed to establish estimated prevalence of the movement disorders of interest in their region. Overall, family physicians estimated the median prevalence of patients with Parkinson's disease in their region to be 0.25 % (range 0.0002-28.6%), essential tremor 0.44% (range 0.0001-84.79%), and dystonia 0.17 % (range 0-35%). Neurologists reported a median estimated prevalence of Parkinson's disease at 0.53% (range 0.06-8.00%), essential tremor at 0.62% (range 0.03-16%), and dystonia at 0.03% (range 0.01-0.8%).

Additionally, physicians were surveyed regarding the estimated number of referrals for DBS at their respective centres, and to estimate how many of those referred patients go on to receive DBS.

Of patients referred for DBS at their centre, five surgeons reported estimating that less than 10% of patients go on to receive DBS. The surgeon in Quebec estimated 25-50% of referred patients receive DBS, and the remainder of respondents in Ontario report 10-25% (n=1), 50-75% (n=1), and 75-100% (n=2).

Of neurologists surveyed, 77.27% reported referring patients for DBS themselves, and the majority report less than 10 monthly DBS referrals in their region, with 45.45% reporting less than five monthly referrals. Of these referrals, nearly half (45.45%) of respondents report less than 10% go on to receive DBS.

The majority of family physicians reported estimating less than five patients are referred for DBS monthly in their region (80.0%), and 66.67% report that of referred patients, less than 10% go on to receive DBS. See Table 4 for comparison of estimated number of candidates and prevalence by medical specialty.

There was a high degree of heterogeneity of responses with respect to prevalence estimates. Among family physicians, mean estimated prevalence ranged from less than 0.1% (0.1) for Parkinson's disease in British Columbia and 4.32% in Ontario. This is compared with reported provincial prevalence for Parkinson's disease ranging from 0.03% in New Brunswick and 0.068% in Manitoba.

Poor concordance existed between family physicians in each province, with family physicians in Alberta having the highest intraclass correlation at 0.82 (-6.003, 0.995). However, no province had mean estimated prevalence near the previously reported national prevalence (23). Poor understanding of variations of prevalence of the other two conditions of interest exists between provinces and territories in Canada, however, the large discrepancy between estimates and previously reported prevalence of Parkinson's disease across Canada suggests the estimates for other conditions are likely inaccurate as well.

Neurosurgeons and neurologists were surveyed as to what the estimated number of candidates for movement disorders of interest would be for their respective regions. Neurologists estimated a mean prevalence of 0.03% (SD 0.06). There were variable responses between neurosurgeons, with 25% of neurosurgeons reporting estimating >500 DBS candidates with movement disorders in their region, and 17% reporting 10-25 candidates. It is notable that these were not reported as prevalence rates, but all neurosurgeons were practicing in urban locations. Similar distribution was observed among neurologists, where 27% reported estimating 10-25 candidates in their region and 23% estimating 100-200 candidates.

3.3 Perceived Access to DBS

Additionally, all respondents reported on their perception of access to DBS in their region. The majority of participants in each physician stakeholder group reported very poor or poor access to DBS in their region. For neurosurgeons, the poorest access was reported in Quebec and British Columbia (See Figure 1 for further details). Among family physicians, 16.7% reported adequate access to this service, all of whom practiced in urban settings in either Ontario (n=4) or Alberta (n=1).

Of included patients and caregivers, 35.29% reported very poor access to this service, and 32.02% reported reasonable access. Those who reported very poor access were primarily from Newfoundland and Labrador, where all patients reported either very poor or poor access to DBS. Those reporting adequate access to DBS were living in Ontario, with 36.92% of Ontarian

respondents reporting reasonable access. See Figure 2 for details of perceived access by stakeholders.

3.4 Barriers to Access

All participants were asked to select all factors they believe are barriers to delivery of DBS in their region from two lists of either systemic or cultural/socioeconomic patient factors. The systemic factors listed included geographic location, inadequate number of functional neurosurgeons, inadequate number of specialists to complete assessment prior to referral to neurosurgeon, poor understanding of indicators limiting referral, inadequate access to operative time for surgeons, inadequate device funding, and other. Cultural or socioeconomic patient factors included patient ethnicity, patient socioeconomic status, patient gender, and other.

The most commonly reported barrier across all physician groups was inadequate number of specialists to complete initial assessments (neurosurgery 75%; neurology 77.27%; family medicine 70%). It was also the second most commonly reported barrier among patients and caregivers (35.95%).

The second most commonly reported barrier for neurologists (59.09%) and family physicians (66.67%) was inadequate number of functional neurosurgeons. Additionally, this was the most commonly reported perceived barrier for patients and caregivers (40.52%). For neurosurgeons, however, this inadequacy was the third most frequently reported barrier, along with inadequate access to operative time for surgeons and poor understanding of indications limiting referral.

Access to subspecialist care (both functional neurosurgery and movement neurologists for initial assessments) were more frequently reported among patients and caregivers in Ontario and British Columbia, compared with Atlantic Canadians, who most commonly perceived geographic location as a barrier to access (73.33% of participants from Newfoundland and Labrador; 66.67% of participants from Nova Scotia; 60.0% of New Brunswick participants).

Geographical location was reported as a barrier by 43.33% of family physicians surveyed, however all family physicians in Newfoundland and Labrador reported geographical location and access to specialists as barriers. Geographical location was reported as a barrier by 45.45% of neurologists and only 16.67% of neurosurgeons. Again, all specialists surveyed reported practicing in urban areas.

Specialists did not commonly perceive poor understanding limiting referral as a barrier (40.90% of neurologists, with the same proportion reporting inadequate device funding as a barrier, and 41.67% of neurosurgeons). However, family physicians frequently reported a lack of understanding of indications for DBS, and 60% of family physicians surveyed did report lack of understanding as a barrier to patient access to DBS. Additionally, the majority of Ontario family physicians reported this factor as a barrier to access.

In terms of cultural and socioeconomic patient factors, socioeconomic status was the most commonly reported barrier among all groups surveyed (neurosurgery 50%; neurology 63.64%; family medicine 43.33%; patients/caregivers 22.22%; advocacy groups 100%).

Ethnicity and gender were far less commonly reported across all groups. Family physicians in from urban areas did commonly report ethnicity as a barrier. Gender was uncommonly reported across all groups, with no neurosurgeons reporting gender as a barrier to access. See Table 5 for summary of perceived barriers by stakeholder group.

3.5 Qualitative Themes

Four themes emerged from all stakeholders surveyed, including *Education*, *Limited Resources/Centralization of Resources*, *Patient Factors* and *Referral Process*. Ideas from four of five surveyed groups fit into these themes. See Table 6 for summary of themes and associated ideas for each group.

An insufficient number of advocacy group responses were available to generate qualitative themes; however, ideas were expressed regarding poor understanding of dystonia as a barrier to accessing treatment, and that limited resources and availability of DBS in some regions present physical and financial challenges to patients that require travel to access the service.

3.5.1 Education

All stakeholder groups for which qualitative analysis was possible reported ideas related to the concept of education. Ideas related to education from neurosurgeons include the concept that DBS is a good treatment that is underutilized due to lack of understanding of the treatment, stigma related to undergoing brain surgery, biases for pharmacological therapy, and delayed referrals due to poor understanding of the existence of this therapy.

Ideas from neurologists surveyed include physician understanding, with the notion that education around indications and follow-up for these patients would be beneficial for non-movement disorder neurologists, and that there exists an overestimation of surgical risk, with under appreciation of the value of DBS. This lack of education leads to a lack of timely referral of patients who may be good candidates for DBS.

Ideas surrounding education among family physicians primarily focused on physician understanding and misunderstandings about DBS. For example, many family physicians reported "know(ing) very little on this subject", being unsure of available centres and indications, and the invasiveness of DBS as a therapy. In terms of misunderstanding, family physicians echoed similar statements regarding uncertainty of availability of the service. For example, one physician reported that patients in their region (New Brunswick) would have to travel to Ontario for DBS, however the treatment is available in Nova Scotia, which is significantly closer.

For patient and caregiver participants, concepts related to education include patient understanding (for example, a number of patients reported uncertainty about what DBS is) misconceptions (such as the idea that DBS is not offered in Canada, or only in Ontario, and that it is only used as a "last resort"), physician understanding (including delayed diagnosis as a result of unfamiliarity on behalf of physicians), and that DBS is not discussed with patients as a potential therapy. Themes around education were most commonly reported by patients in Quebec, Ontario, and British Columbia, as well as in patients with essential tremor and dystonia.

3.5.2 Limited Resources and Centralization of Available Resources

All stakeholder groups for which qualitative analysis was possible reported ideas related to limited resources and centralization of available resources as a barrier to accessing DBS. Neurosurgeons identified ideas related to specific resources, specifically scarcity of movement disorder neurologists and device funding, centralization of access to larger cities, and presence of long wait times (reported as 2-3 years).

Ideas shared by neurologists related to this theme can be further broken down into limitations on number of patients/implants available for year provincially, limited access to alternative therapies such as high intensity focused ultrasound, limited access to specialists (neurologists, functional neurosurgeons), limited operating room availability, limited access to specialized nursing care and neuropsychology, and the consequences of centralization of services, including travel, limited funding directed to regions to regions outside of major centres, long wait lists resulting in medical complications while patients wait for surgical assessment, and that access to DBS may be improved by increasing utilization of virtual care.

Family physicians reported frustration with the limited number of patients that may receive DBS annually per province, that they have referred patients who are not deemed eligible after significant delay and inconvenience to the patients to undergo formal assessment, and reluctance to refer patients given significant burden of travel for initial assessment.

Ideas from patient/caregiver responses related to limited resources include long wait times, with patients reporting waiting for six months to four years for specialist appointments, a lack of availability in some regions (Newfoundland and Labrador, New Brunswick, Southwest Ontario,

Manitoba, and Mainland British Columbia), lack of specific resources in regions (including neurologists, movement disorder specialists, functional neurosurgeons, family physicians, interpreters, social support groups, treatment and counselling, device restrictions, operative time and hospital beds). Additionally, patients and caregivers identified ideas about the impact of COVID-19 on the delivery of functional neurosurgery. Ideas related to the theme of limited resources among patients and caregivers were most commonly reported in Atlantic provinces and in patients with Parkinson's disease.

In patients and caregivers, ideas relating to centralization of services include the perception of access in larger cities, whether access is truly available or not, the burden of travel and transportation on accessing functional neurosurgery, and the cost associated with travelling for appointments. Ideas relating to centralization were most commonly reported in Ontario, British Columbia, Alberta, and Atlantic provinces.

3.5.3 Patient Factors

Neurologists described a number of patient factors that limit access to DBS on an individual level. Primarily socioeconomic status in that patients may not be able to travel or obtain transportation for multiple appointments, even if they live close to a major centre. This burden is greater in populations who live further away from major centres where DBS is offered. Additionally, social support and language barriers were reported to affect access to DBS for patients.

Patients also cited personal factors as reasons they had not previously considered DBS, including mild symptoms or adequate medical management, advances age, or that they have learned to cope with their disease. Some patients reported no interest in pursuing DBS as they have a fear of undergoing surgery.

3.5.4 Referral Process

Family physicians described frustration with obtaining any specialty assessment for their patients, with onerous referral processes for patients living with movement disorders. This was not described for other stakeholder groups surveyed.

See Figure 3 for summary of barriers across referral pathway for DBS in patients with movement disorders.

4 DISCUSSION

Previous attempts have been made to describe access s to DBS, utilizing retrospective data from patients who have received DBS previously, and attempting to determine what facilitators exist in that population of patients that lead them to being successful in obtaining the service (3–6,10,11,20,24). This approach has considerable limitations, as these patients have already overcome barriers to receiving DBS. Additionally, this approach is unable to estimate the true prevalence of candidates for this service. Without understanding the number of individuals seeking therapy, an understanding of access cannot be achieved. Therefore, this study attempts to estimate the prevalence of candidates for DBS in the Canadian population, and understanding

barriers to accessing DBS from a population of primarily potential candidates for DBS and the healthcare providers treating these patients.

Although limited in number of responses, the representativeness of the Canadian population in patient responses is fair in terms of proportion of responses by province/territory. There is overrepresentation of patients/caregivers from Newfoundland and Labrador (9.8% of responses compared with 1.4% of Canadian population from NL(25)), and underrepresentation of respondents from Quebec (5.9% of responses vs. 22.2% of the Canadian population (25)), in spite of the survey being offered in both French and English. Unfortunately, there were no responses from Prince Edward Island, Yukon, Northwest Territories, or Nunavut. It is important to consider these patient perspectives, given the likely poor access to care in these regions (26,27), however low response rates may be expected, given the low populations in these areas (0.4% of the Canadian population for PEI, and 0.1% of the national population in each of the territories (25)). All other regions were represented within 2% of the national proportion of the population residing in the respective provinces.

In terms of physician groups, family physicians from Newfoundland and Labrador are again over-represented (20% of respondents compared with the 2.1% of Canadian family physicians practicing in NL), Quebec is again under-represented (3.3% of responses vs. 24.4% of Canadian family physicians (28)), and Alberta is under-represented (6.6% of respondents vs. 13.0% (28)). All other regions are within 4% of the proportion of Canadian family physicians for each province and territory. Again, no responses were obtained from family physicians practicing in Prince Edward Island (0.4% of Canadian family physicians (28)) or the territories, which

collectively represent 0.3% of family physicians in Canada (28) . The overrepresentation of physicians from Newfoundland and Labrador may have resulted from an active Parkinson's society in the province, with advocates eager to promote improved access in the region, as indicated by their contact with us in early stages of study design. Although we attempted to promote recruitment in Quebec through inclusion of French language studies, this may have not been clear to potential participants, as English language information about the study was presented prior to French study information in all correspondence.

Both neurology and neurosurgery were severely limited in responses, with only 22 neurologists responding from four provinces, and only 12 neurosurgeons responding from three provinces. This paucity of data from regions of Canada with probable limited access signifies an important missing voice in this narrative. While multiple attempts were made at recruiting participants from these groups, including two faxes and two separate emails, the low response rate may have been a result of recruitment strategies. Many physicians and surgeons receiving faxes would need to be provided the faxed information by administrative personnel in many office settings. Previous research suggests that physicians are more responsive to mail surveys, and that response rates to email are traditionally in the range of 25-30%, due to survey fatigue, competing demands, and privacy concerns (29). Additionally, nearly all responses from neurologists and neurosurgeons are from practitioners in urban settings. Barriers identified by these physicians and surgeons may be vastly different from those in rural settings elsewhere in the country. It is important to note, however, that of all groups surveyed, neurologists and neurosurgeons see patients who have already overcome many barriers to access specialist services, and the ability of these specialists to identify barriers to care may be skewed as a result. The ideas obtained from

family physicians and patients/caregivers are likely a more realistic picture of access to DBS in Canada.

4.1 Prevalence of DBS Candidates Nationally

Estimation of prevalence of DBS candidates was limited by response rate within respondent groups. A previous international study by Dewan *et al* (2018) utilized surveys of neurosurgeons to estimate the proportion of patients with a number of neurologic diseases that warrant neurosurgical consultation or operative management and found high concordance rates between clinicians regarding estimates (22). Estimates in the present study had low concordance, which may be a result of low response rate across all included specialties. Prevalence rate estimates were likely inaccurate as a result. Family physicians in particular, frequently reported "I don't know" as a response to the request for estimates. This was more common for dystonia and essential tremor than Parkinson's disease.

Additionally, prevalence rate was calculated by estimating the denominator of the prevalence based on descriptions of the region provided by respondents. As such, respondents may have had a smaller population in mind when describing the number of patients in their region, thus leading to a lower prevalence estimation used in the study. This approach was taken to limit the identifiability of respondents per ethics recommendations. In future studies, we would suggest asking respondents to provide a numerical value of the population they are thinking of when estimating prevalence.

Physicians were also queried to estimate the number of patients referred for DBS monthly in their region. The majority of respondents estimated less than five patients are referred for DBS in their region each year. It is likely that neurologists would have the greatest ability to estimate these numbers given their patient population, but it is interesting that neurologists from the most populous province in Canada (Ontario) estimated fewer referrals than other regions. Nearly all of the neurosurgeons surveyed were practicing in Ontario, with results consistent with those obtained from neurologists. It is therefore possible that there are a greater number of referrals in Western Canada for DBS, even though British Columbia has been reported to have a lower DBS rate compared with the national average (80%), and Alberta has a similar rate to Ontario when compared with the national average (120% vs. 126%, respectively). This would be a consideration for future work, as poor referral rate was mentioned across physician groups as a barrier to accessing DBS across Canada, and identification of regions with lower referral rates, and improving referral patterns would thereby improve access to DBS for patients.

Many respondents across all provider groups estimated that less than 10% of referred patients ultimately undergo DBS. However, the four neurosurgeons surveyed that reported performing DBS themselves reported much higher estimations. Neurologists and family physicians more frequently reported lower proportions of referred patients undergoing DBS, but neurologists specializing in movement disorders did more often estimate a higher proportion of patients referred would ultimately undergo surgery. Those more likely to formally assess potential candidates for DBS or ultimately perform surgery were therefore more likely to estimate that referred patients are implanted. One previous American study found that approximately half of

referred patients for DBS were found to be good candidates for surgery (30), consistent with our findings.

Estimates of number of candidates for DBS with movement disorders in each region were variable for both neurologists and neurosurgeons, with no discernable pattern. Again, perhaps having respondents quantify prevalence as a percentage of their population, or have them better define their population, may provide more accurate estimates.

4.2 Qualitative Themes

There was considerable overlap in ideas obtained from all groups. All groups identified themes around limited resources and centralization of resources. This was thought to be a common concern regarding travel as a barrier to access for patients, and the costs associated with travel. Additionally, respondents from every group expressed concerns about long wait times and the impact of a limited number of movement disorder specialists and functional neurosurgeons. All respondent groups also shared similar concerns about the need for education of patients and care providers regarding diagnosis and treatment of movement disorders, and the benefits and availability of DBS along with its indications.

In general, concerns regarding travel and lack of resources were more commonly expressed in respondents from Atlantic Canada and patients with Parkinson's disease, although the increased reporting of this concern in patients with Parkinson's may be due to the high number of Parkinson's disease patients/caregivers from Newfoundland and Labrador in our study

population. Therefore, it may be a reflection of a regional concern as opposed to disease-specific issues.

Ideas surrounding education were more common in Central Canada and British Columbia, as well as patients with essential tremor and dystonia. It is possible that these regions have better access to DBS (or at least the perception of better access), and therefore individuals are able to identify additional barriers beyond geographic and unavailability of services in their region. These themes may also be more common in essential tremor and dystonia as these diagnoses may be more poorly understood than Parkinson's disease. This is supported by family physician responses, where fewer respondents provided estimates for prevalence of these two conditions than Parkinson's disease, and commonly responded with comments like "I have no idea" when asked about these two diagnoses.

4.3 DBS Patients Surveyed

Included patients that have undergone DBS were not reflective of previously reported access to DBS. For example, 13% of patients receiving DBS in our study were residing in Newfoundland and Labrador, the province that has historically had the poorest access to this service, with one previous retrospective study of all DBS patients in Canada over a two year period reporting 0.006% of their cohort from Newfoundland and Labrador. This over-representation from NL may be a result of an enthusiastic Parkinson's disease advocacy group in the region that effectively recruited patients to the study.

Nearly all patients who had received DBS in this study received their formal diagnosis from a neurologist, as opposed to family physician. It is likely that neurologists have better understanding of indications and availability of DBS, and are therefore more likely to refer appropriate candidates. Literature supports the notion that movement disorder specialists are more likely to refer good candidates for DBS than other providers (30), so access to neurology and specifically movement disorder neurologists, is likely an important facilitator for accessing DBS.

In terms of timeline for diagnosis and treatment of these patients, nearly all patients reported being diagnosed greater than five years ago, with most being diagnosed greater than 20 years ago. Most patients report experiencing symptoms between 1-5 years prior to diagnosis. Once diagnosed, the majority of these patients were referred for surgery greater than two years after diagnosis, and underwent surgery more than six months after referral, with 40% of patients reporting a period greater than two years between patient referral and surgical implantation. Qualitative responses from all groups indicate waitlists of 2-5 years for DBS across Canada. It is unclear at what time patients who received DBS were implanted, so it is possible that delays associated with Covid-19, or any other number of factors, have increased wait list times since these patients underwent surgery. This is one area for future research to determine duration of waitlists and solutions to decrease surgical wait times for DBS patients.

4.4 Proposed Solutions

A number of policy changes are required to address access to DBS in Canada, with varying approaches between regions of the country. See Table 7 for facilitators and barriers to access identified in each of the five regions of Canada.

The first potential solution that comes to mind when considering increasing access to DBS is increasing available resources, including the number of movement disorder specialists and functional neurosurgeons in Canada. Of course, this would ameliorate some of the burden of waitlists and, to some extent, travel for individual patients, however beyond increasing the number of providers in population-dense regions with access to supporting resources required for a successful DBS program, this would not decrease the burden of travel and expenses for Canadians living in isolated regions of our country.

One frequently cited barrier, and one identified in previous literature (21), is provincial caps on the number of DBS implants available annually. All provinces except Saskatchewan and Nova Scotia have a limited amount of funding allocated to implants annually. By removing this restriction, Saskatchewan has been able to have the best access to DBS in Canada (21). Previous studies have shown that DBS is a cost-effective treatment strategy compared with best medical therapy alone, when considered over the lifetime of implanted patients. DBS has been shown to decrease medication costs, as well as hospitalizations and delay institutionalization of patients living with movement disorders, even accounting for costs of potential complications and hardware replacements (31). Therefore, providing increased access to operative time and implants at a provincial level may be a cost-effective approach that would, in turn, increase access to this beneficial therapy.

Increasing physical resources would not improve access to Canadians living outside of major cities, and in regions like Atlantic Canada, Manitoba, and Northern Canada, where patients must travel long distances for multiple appointments (assessments, surgical bookings, follow-up, reprogramming), and have limited to no access to emergency neurosurgical care should complications arise. In these cases, increased use of telemedicine may provide improved access to patients. The Covid-19 pandemic necessitated the use of telemedicine for many providers. Available literature suggests telemedicine provides an effective alternative to in-person care for patients living with movement disorders (16,17). Patients were able to access care for surgical assessments, follow-ups, and undergo re-programming, all without the inconvenience and costs incurred by travelling. Creation of telemedicine movement disorder clinics throughout the country may be an alternative to current healthcare allocation strategies, to ensure access to care is improved for all Canadians. Increasing funding to provide travel stipends to patients may alleviate some of the financial burden reported as a barrier to accessing this service as well.

It was very clear that improved education is required for patients and practitioners regarding diagnosis of movement disorders, indications for DBS, and how to access these services. Among family physicians, 76.7% reported not having a good understanding of indications for DBS, and among the seven family physicians reporting that they did have a good understanding, when asked to describe the ideal candidate for DBS, responses were vague (i.e. “someone with Parkinson’s”) or incorrect, with many family physicians believing the ideal candidate would be a patient with medically refractory symptoms, or that surgery is a “last resort”. These beliefs were reiterated by patient comments that they have been given similar information from physicians.

Providing education both to patients and care providers about indications for DBS would help ensure more potential candidates for this efficacious therapy are screened and potentially assessed for DBS.

Previous literature has described the ideal candidate for DBS in Parkinson's disease as having a disease duration of at least five years, allowing atypical forms of parkinsonism to manifest, that they should have a positive response to levodopa (defined as a greater than 30% improvement in Unified Parkinson's disease rating scale motor score), and should not have pre-existing dementia or severe depression. Additionally, patients should undergo magnetic resonance imaging to rule out secondary diagnosis or structural concerns, and should be medically optimized (32). Both patients and family physicians frequently cited age as an exclusion criteria for DBS, however while evidence suggests younger patients may have improved outcomes, there is no formal age cut off for the procedure (32). For essential tremor and primary dystonia, patients should have one of these diagnoses with symptoms that interfere with the patient's quality of life and functionality, intact cognition, and absence of severe psychiatric illness (30). For all diagnoses, patients should have realistic expectations about what symptoms can be improved by DBS, and should be willingness to participate in surgery.

With respect to willingness to participate in surgery, few patients reported fear of surgical intervention as a reason they would be unwilling to undergo DBS. The availability of "incisionless" lesioning procedures (for example, magnetic resonance imaging guided high intensity focused ultrasound) should also be explained, providing the understanding that these

procedures are also invasive with potential complications, and cause permanent brain lesions, compared with DBS, where stimulation can be switched off.

Combining the above approaches would require significant collaboration. Although the Canada Health Act stipulates that individual provincial/territorial governments are responsible for overseeing and carrying out the principles of the Act in their respective region, national collaboration may be warranted to improve access across Canada. Providing educational resources and clear referral pathways in each region with a regional triage system would ensure patients residing in provinces/territories without access to this service would have the ability to be referred to a centralized service for their region. For example, a patient living in Newfoundland and Labrador could, in collaboration with their family physician, receive referral to an expanded virtual movement disorder assessment clinic in Halifax, responsible for screening and triaging patients to determine if more comprehensive assessment is warranted. Literature suggests that patients referred for DBS by movement disorder specialist neurologists were more likely to be good candidates for DBS than patients referred from other providers (30). Therefore, ensuring patients are first assessed by movement disorder specialists, both for diagnosis, therapeutic optimization, and determination of candidacy, would ensure smooth referral pathway flow for patients.

Further investigation is required to better understand how the prevalence of DBS candidates varies across Canada. Currently, no national database exists to answer this question. It is possible that estimation using expert opinion could be utilized if higher response rates could be achieved. Additionally, requiring respondents to define the population they are considering when

estimating prevalence may be beneficial. Improved understanding of the distribution of prevalence of these conditions is critical. Particularly for essential tremor and dystonia, for which we do not have granular data for provincial/territorial prevalence. It is impossible to comprehensively assess access to a service without an in depth understanding of the candidates for that service, defining the need for it to determine if that need is being met.

4.5 Limitations

A number of limitations exist for the current study. Firstly, biases inherent to survey studies, including reporting bias and issues with response rate.

A primary aim of this study was to determine the prevalence of candidates for DBS across Canada. Unfortunately, due to the limited number of responses estimating prevalence of the three conditions of interest and estimating prevalence of candidates for DBS, low concordance rates exist between practitioners. As a result, confidence in these estimates is very low. Additionally, respondents did not clearly describe the population for which they were estimating prevalence. This introduces additional estimation error that could be avoided if strictly numerical responses were provided.

5 CONCLUSION

This study utilized mixed methods surveys of stakeholders for DBS in Canada to attempt to estimate prevalence of candidates for DBS among patients diagnosed with movement disorders across Canada in addition to identifying barriers to accessing DBS. This was in attempt to address limitations of previous studies investigating access to DBS in Canada, that were not able

to define the need for this service and match access to determine its adequacy. A number of themes were generated, describing the beliefs of stakeholders for DBS in Canada regarding barriers, including limited resources/centralization of resources, education, individual patient factors, and burdensome referral processed were determined to be common barriers to accessing DBS. We propose improving education, centralized referral pathways, and the use of virtual care to improve access to DBS across Canada, and further research to determine the true prevalence of candidates for this therapy to better understand variability in the need for this service across the country.

FIGURES

Figure 1: Geographical Distribution of Patients Previously Having Undergone Deep Brain Stimulation

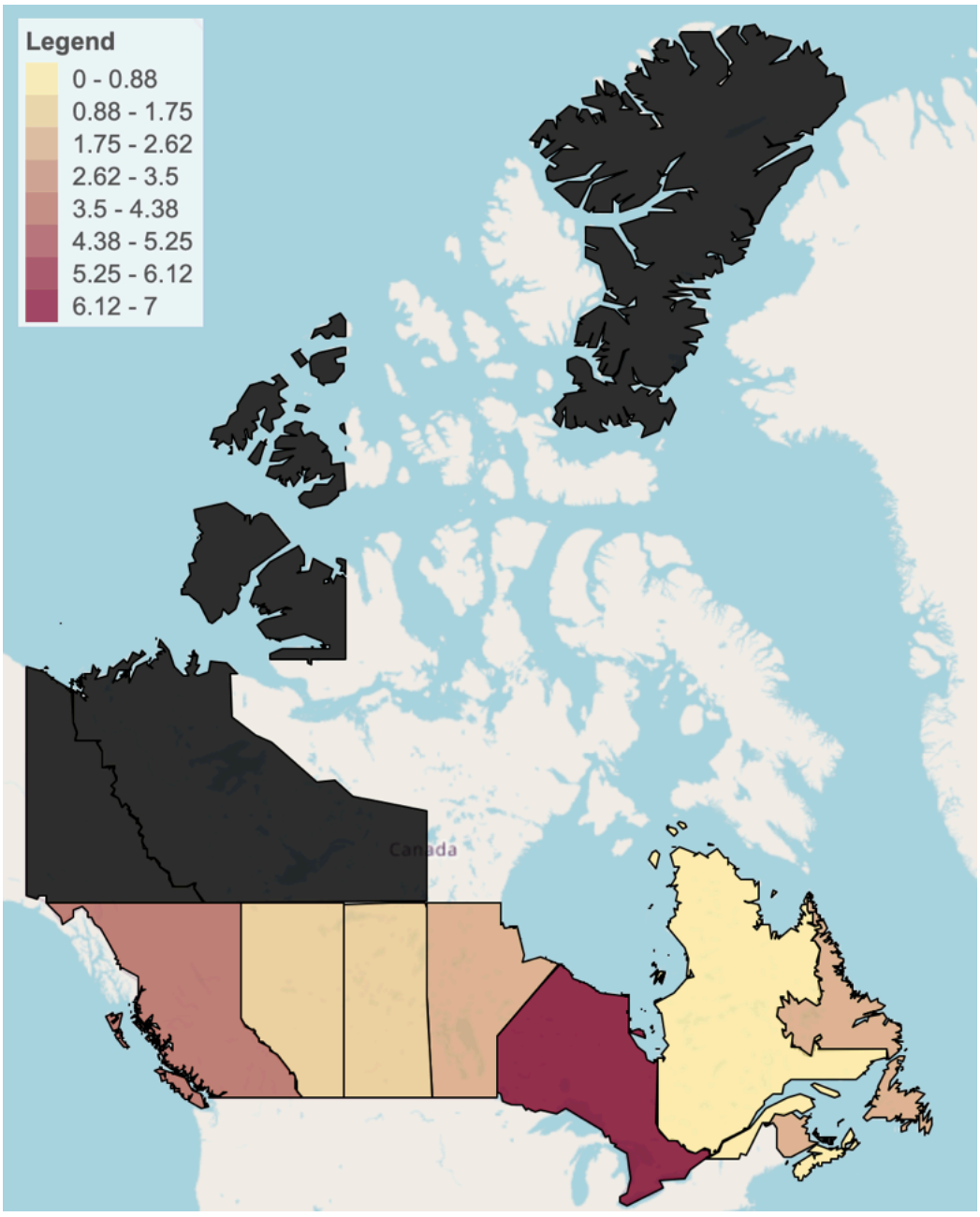


Figure 2: Perceived Access to Deep Brain Stimulation Across Canada by Respondent Group
A) Perceived Access by Neurosurgeon Respondents; B) Perceived Access by Neurologist Respondents; C) Perceived Access by Family Physician Respondents; D) Perceived Access by Patient and Caregiver Respondents

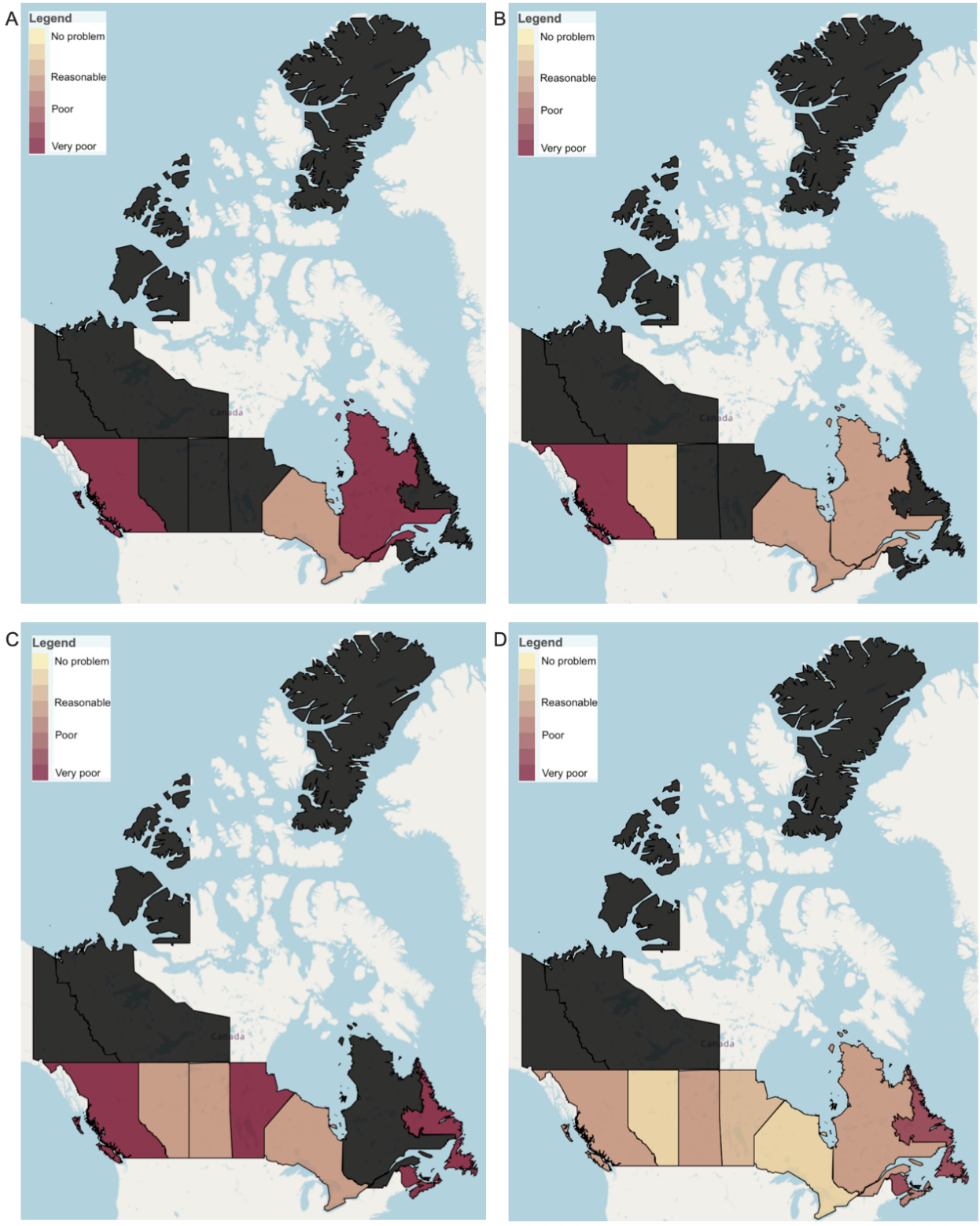
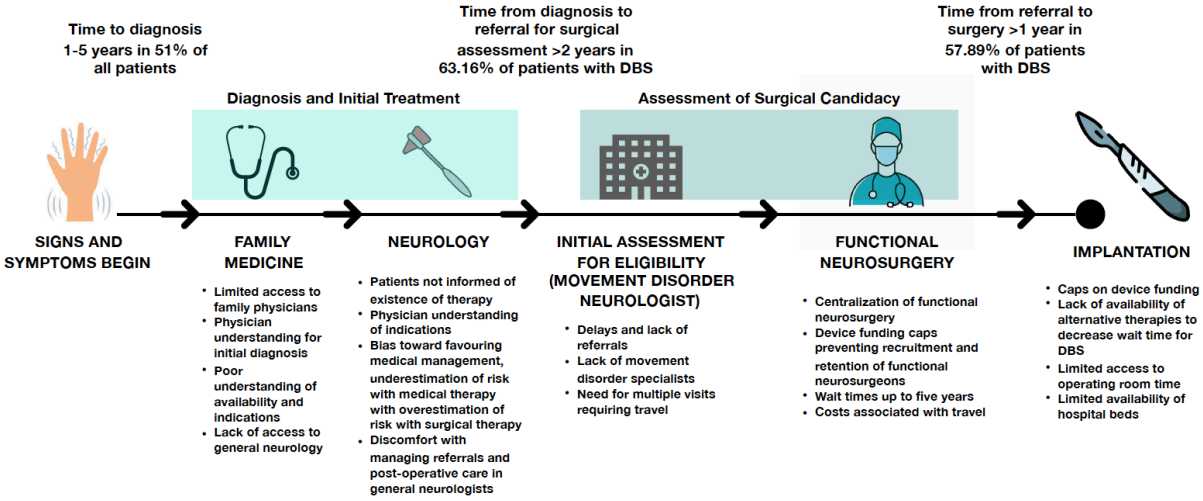


Figure 3: Summary of Referral Pathway for Patients and Associated Barriers



TABLES

Table 1: Response Rates Among Respondent Groups

Respondent Group	Means of Contact	Potential Respondents	Actual Respondents	Response Rate
Patients and caregivers	Parkinson QC	8,673 via newsletter	153 (146 English, 7 French)	0.6%
	Parkinson NL	200 via email		
	Parkinson NS	60 via Facebook		
	Parkinson Canada	13,000 via newsletters, email lists, website		
	International Essential Tremor Foundation	788 in Canada via email		
	Dystonia Canada	1,700 via email		
Advocacy groups	Parkinson QC	1	3 (3 English)	50%
	Parkinson NL	1		
	Parkinson NS	1		
	Parkinson Canada	1		
	International Essential Tremor Foundation	1		
	Dystonia Canada	1		
Family Physicians	Scott's Info database and electronic faxing service	17,442	30 (28 English, 2 French)	0.17%
Neurologists	Scott's Info database and electronic faxing service	855	22 (21 English, 1 French)	3.57%
	Canadian Neurological Sciences Federation	700 staff members between neurology and neurosurgery		
	Publicly available email	457		
Neurosurgeons	Scott's Info database and electronic faxing service	231	12 (11 English, 1 French)	5.04%
	Canadian Neurological	700 staff members between neurology and neurosurgery		

	Sciences Federation			
	Publicly available email	238		

Table 2: Demographics of Physician Respondent Groups

Survey Questions		Neurosurgery N=12	Neurology N=22	Family Medicine N=30
Province/Territory	Newfoundland and Labrador	0	0	6
	Nova Scotia	0	0	1
	Prince Edward Island	0	0	0
	New Brunswick	0	0	2
	Quebec	1	1	1
	Ontario	10	12	10
	Manitoba	0	0	1
	Saskatchewan	0	0	2
	Alberta	0	4	2
	British Columbia	1	5	5
	Territories	0	0	0
	No response	0	0	0
Urban vs. rural	Urban	12	16	18
	Rural	0	1	12
	No response	0	5	0
Duration of practice	<5 years	N/A	7	8
	5-10 years		3	6
	10-20 years		6	5
	>20 years		5	11
	No response		1	0
Movement disorder/functional neurosurgery subspecialisation	Yes	4	12	N/A
	No	8	10	
Distance required for patients to travel to see a functional neurosurgeon	<100km	7	17	14
	100-500km	4	5	7
	500-1000km	1	0	3
	<1000km	0	0	6

Table 3: Demographics of Patient and Caregiver Respondents

Survey Questions		Previously received DBS (N=19)	Have not received DBS (N=134)	Total (N=153)
Participant description	Patient	15	109	124
	Family member of patient participating on own behalf	1	12	13
	Family member of patient participating on behalf of patient	2	8	10
	No response	1	5	6
Region	Newfoundland and Labrador	2	13	15
	Nova Scotia	0	6	6
	Prince Edward Island	0	0	0
	New Brunswick	2	3	5
	Quebec	0	9	9
	Ontario	7	58	65
	Manitoba	2	3	5
	Saskatchewan	1	3	4
	Alberta	1	16	17
	British Columbia	4	19	23
	Territories	0	0	0
	No response	0	4	4
Urban vs. Rural	Urban	15	93	108
	Rural	4	35	39
	No response	0	6	6
Diagnosis	Parkinson's disease	6	33	39
	Essential tremor	3	47	50
	Dystonia	10	53	63
	No response	0	1	1
Time since diagnosis	<5 years	1	45	46
	5-10 years	5	36	41
	10-20 years	5	27	32
	>20 years	8	24	32
	No response	0	2	2
Duration of symptoms prior to diagnosis	<6 months	1	9	10
	6 months-1 year	4	17	21
	1-2 years	6	31	37
	2-5 years	5	37	42
	5-10 years	2	14	16
	>10 years	1	24	25
	No response	0	2	2
Diagnosing physician	Neurologist	17	96	113
	Family physician	2	35	37
	No response	0	3	3
Physician ever discussed DBS with patient/family	Yes	17	31	48
	No	1	102	103
	No response	1	1	2
Interested in pursuing DBS if offered	Yes	Not applicable	56	75
	No		13	13
	Unsure		56	56
	Have never heard of DBS		9	9
	No response/Not applicable		0	19
Of those who had received DBS, duration	<6 months	0	Not applicable	0
	6 months-1 year	1		1

between diagnosis and referral for surgery	1-2 years	5		5
	>2 years	12		12
	No response/Not applicable	0		135
Of those who have received DBS, duration between referral and implantation	<6 months	1	Not applicable	1
	6 months-1 year	7		7
	1-2 years	5		5
	>2 years	6		6
	No response/Not applicable	0		134

Table 4: Prevalence Estimates for Movement Disorders of Interest Among Physician Respondent Groups

Survey Questions		Neurosurgery (N=12)	Neurology (N=22)	Family Medicine (N=30)
Estimated prevalence of Parkinson's disease in region*			Median 0.53% Range 0.06-8.00% N=19	Median 0.25% Range 0.0002-28.26% N=22
Estimated prevalence of essential tremor in region*			Median 0.62% Range 0.03-16.00% N=19	Median 0.44% Range 0.0001-84.79% N=22
Estimated prevalence of dystonia in region*			Median 0.03% Range 0.01-0.80% N=18	Median 0.17% Range 0-35% N=17
Estimated number of new referrals for DBS in region	<5		10	24
	5-10		7	2
	10-20		4	1
	20-30		0	2
	No response		1	1
Of patients referred to centre, estimated percentage that go on to receive DBS	<10%	5	10	20
	10-25%	1	2	2
	25-50%	1	7	3
	50-75%	1	1	1
	75-100%	2	1	0
	No response	2	1	4
Estimated new DBS patients implanted at their centre per month	<5	9		
	5-10	1		
	10-20	1		
	No response	5		
Estimated number of DBS candidates with movement disorders in region	<10	1	0	
	10-25	2	6	
	25-50	0	2	
	50-75	1	2	
	75-100	0	0	
	100-200	1	5	
	200-500	1	2	
	>500	3	5	
	No response	3	0	

Table 5: Summary of Perceived Barriers Among Respondent Groups

Barriers	Neurosurgeons (n=12)	Neurologists (n=22)	Family Physicians (n=30)	Patients/Caregivers (n=153)	Advocacy Groups (n=3)
Inadequate number of specialists to complete initial assessment	75.00%	77.27%	70.00%	35.95%	66.67%
Inadequate number of functional neurosurgeons	41.67%	59.09%	66.67%	40.52%	100%
Inadequate device funding	58.33%	40.91%	30.00%	23.53%	0
Inadequate access to operative time for surgeons	41.67%	54.55%	26.67%	32.03%	66.67%
Geographical location	16.67%	45.45%	43.33%	32.68%	66.67%
Poor understanding of indications limiting referral	41.67%	40.91%	60.00%	30.07%	33.33%
Patient socioeconomic status	50.00%	63.64%	43.33%	22.22%	100%
Patient ethnicity	25.00%	31.82%	10.00%	4.58%	0
Patient gender	0	4.54%	3.33%	4.58%	33.33%

Table 6: Summary of Qualitative Themes Among Respondent Groups

	=Neurosurgery (N=12)	Neurology (N=22)	Family Medicine (N=30)	Patients/Caregivers (N=153)
Education	*Good treatment that is underutilized:* -"Under penetrated therapy with excellent evidence and under-utilized by a factor of 3-4." Education: -"Stigma related to brain surgery for treating a disorder remains." -"Patients are not informed of existence of therapy, referring physicians misinformed of existence of therapy, referring physicians misinformed of existence or criteria for DBS, evaluation of drug options before referral too long, long multidisciplinary assessments and greater neuropsychological fears for surgery compared to pharmacological treatments." -"Biases for pharmacological treatments exceed those for surgical treatments without necessarily there being an equivalent basis in the assessment of benefits and risks. Ex: medication-induced dyskinesia is often not perceived as a significant complication of pharmacological treatment but rather as the progression of the disease. This is then a risk which is not described as a complication. So we do not fear this risk of pharmacological treatment. DBS makes it possible to avoid increasing medication or even reducing medication and reduces the risk of this complication." *Delayed referrals:* -"No problem with access. Bottlenecks are related to referrals."	*Physician understanding:* -"Greater educational exposure to reasons for DBS are helpful for non-motor neurologists to be educated on." -"The challenge is determining eligibility and then follow up. I don't feel comfortable managing the referral process or after care adjustment of medications." *Overestimation of surgical risk:* -"Under appreciation of the value and over-estimation of adverse effects and complacency with non-surgical treatments by treating neurologists." *Lack of timely referral*	*Physician understanding:* -"Unsure of available centres and which patients qualify." -"Unfamiliar with this mode of treatment." -"I would like to know about indications and to know where to refer." -"I know very little on this subject." -"How invasive is this procedure?" *Misunderstanding:* -"Patients would need to travel to Ontario (from New Brunswick) for treatment."	*Patient understanding:* -"I'm not really sure what deep brain stimulation is exactly." *Physician understanding:* -"Initial diagnosis is an issue. Referral to movement disorders specialist can be problematic as most practitioners are not familiar with dystonia." *Misconceptions:* -"To my knowledge, DBS doesn't exist in Canada." -"Seems to be used more on Parkinson's patients and not much experience with dystonia." -"Only offered in Ontario." -"Doctors are advising against it unless absolutely the last resort." *Not discussed with patients:* -"I have never heard of any information concerning this therapy from anyone" Most commonly reported in Quebec, Ontario, and British Columbia, as well as in patients with essential tremor and dystonia.
Limited Resources and Centralization of Resources	*Limited specific resources:* -"Movement disorder neurologists." -Device funding: "the capacity to actually perform the procedure. Device funding is a major barrier that prevents the recruitment and/or retention of functional neurosurgeons at many tertiary centres." *Access in larger cities:* -"Currently patients need to be referred to London or Toronto for DBS. Hamilton has a large population that is underserved for DBS." -"Population base is large and mostly not serviced due to lack of availability at the academic neurosurgery regional centre."	*Provincial caps:* -"Currently in British Columbia… there is funding for 75 patients per year." *Alternative therapies to decrease strain on wait times:* -"There is also a lack of high intensity focused ultrasound in British Columbia which would be of benefit to patients with moderate to severe essential tremor that is medication-refractory. Many of these patients who are waiting for DBS would also benefit from HIFU, which would also help to reduce the wait list for DBS." *Neurologists (common in Quebec):*	*Device funding limits number of patients*: -"I was told that about 20 patients per year are funded for DBS in all of British Columbia, that would make my region eligible for only a handful whereas there must be several hundred good candidates out of the population of 5 million every year." *Specialists:* -"Only recently found out that (local functional neurosurgeon) is still performing this procedure, (they) have very limited surgical time." -"We don't even have a full-time neurologist in our region. Closest neurosurgeons are in St. John's (700km) and they do not perform this as far as I know." *Travel:*	*Long wait times:* -"I was scheduled for DBS. My movement disorder specialist recommended the duodopa pump in the meantime. The surgeon took me off the list." -"Travelled outside province as waitlist in British Columbia too long." Neurology: 6 months – 4 years Assessment: 6 months - 2 years Surgery: 7 months – 1 year *Lack of availability in many regions:* Newfoundland and Labrador, New Brunswick, Southwest Ontario, Manitoba, Mainland British Columbia *Lack of specific resources:*

	-"No access to DBS in large provincial region and all referrals need to go to the major referral centre in a different health authority." *Wait times:* -"Limited resource, patients will have to be referred to London or Toronto, where wait times can still be 2-3 years."	-"The main barrier is the lack of neurologists trained to manage these patients as well as access to the operating room." -"Wait times to see movement disorder specialists and specialists being mostly located centrally." *Functional neurosurgeons (common in British Columbia and Ontario):* -"Only one surgeon in all of British Columbia doing this procedure with a wait time of 3-5 years" -Nursing, neuropsychology *Travel:* -"No neurosurgery available in our region at all. Patients must travel at least 1.5 hours if not much more for neurosurgical assessment." *Centralization:* -"Government gives funding to Vancouver and not to other health regions that could create a service." *Patients develop medical complications waiting:* -"Four year waitlist to see the single surgeon and then 12-18 months from then to surgery. So referral isn't useful. Many patients lose time they would benefit from surgery. Some develop health complications or psychiatric issues before being able to benefit. We have to use duodopa for those who would be good DBS candidates. Very morally distressing not to have a standard of care treatment." -"It's waiting list times that are the biggest barrier in my region" *Role of virtual care:* -"I believe it is getting easier to refer as the current DBS expert is making inroads to optimizing selection with use of virtual care."	-"I have become reluctant to refer patients as it is a long drive to be evaluated and have not had one person get implanted." -"Travel distance, costs and lack of funded transport services for consults and procedures impacts patient care." -"To my understanding patients would have to leave the province which is not something they can afford,"	-Neurologists – underservice of general neurology as well as movement disorder specialists -Functional neurosurgeons – "one functional neurosurgeon for all of Atlantic Canada", "one functional neurosurgeon in British Columbia", "the one functional neurosurgeon in Manitoba left." -Family physicians -Interpreters and social support groups, treatment and counselling -Device restrictions -Operative time, hospital beds *Impact of COVID-19* *Perception of access in city:* -"would be provided in Calgary." -"Barriers to access… getting into a facility in Toronto or Hamilton." -"I live 2 hours drive from Toronto and Kingston. I feel that this option may be available if referred by my neurologist." *Travel/Transportation:* -Difficulty travelling with disability, unable to travel when caretaker for others -Many patients reported having to travel >2 hours to tertiary centre to access -Patients unable to drive themselves *Cost:* -Limited medical coverage for travel -Self-employed patients unable to travel for multiple appointments Limited resources most commonly reported in Atlantic provinces and patients with Parkinson's disease. Centralization most commonly reported in Ontario, British Columbia, Alberta, and Atlantic provinces.
Patient Factors		*Socioeconomic status:* -"Lower socioeconomic populations tend to live further away, have fewer means and support for repeated visits to surgery centre." -"Ability to drive or have access to a ride for that distance is an issue." -"Ability to attend appointments (e.g. self-employed, cannot afford gas or car to get to tertiary care centre)." *Support:* -"Social support (marital status) and education are contributing factors." *Language:*		*"Haven't considered DBS":* -Symptoms adequately managed with medical therapy -Symptoms mild -"Learned to deal with it" -Advanced age *Not interested* -Fear of undergoing surgery Reported across Canada

	-"No access to DBS in large provincial region and all referrals need to go to the major referral centre in a different health authority." *Wait times:* -"Limited resource, patients will have to be referred to London or Toronto, where wait times can still be 2-3 years."	-"The main barrier is the lack of neurologists trained to manage these patients as well as access to the operating room." -"Wait times to see movement disorder specialists and specialists being mostly located centrally." *Functional neurosurgeons (common in British Columbia and Ontario):* -"Only one surgeon in all of British Columbia doing this procedure with a wait time of 3-5 years" -Nursing, neuropsychology *Travel:* -"No neurosurgery available in our region at all. Patients must travel at least 1.5 hours if not much more for neurosurgical assessment." *Centralization:* -"Government gives funding to Vancouver and not to other health regions that could create a service." *Patients develop medical complications waiting:* -"Four year waitlist to see the single surgeon and then 12-18 months from then to surgery. So referral isn't useful. Many patients lose time they would benefit from surgery. Some develop health complications or psychiatric issues before being able to benefit. We have to use duodopa for those who would be good DBS candidates. Very morally distressing not to have a standard of care treatment." -"It's waiting list times that are the biggest barrier in my region" *Role of virtual care:* -"I believe it is getting easier to refer as the current DBS expert is making inroads to optimizing selection with use of virtual care."	-"I have become reluctant to refer patients as it is a long drive to be evaluated and have not had one person get implanted." -"Travel distance, costs and lack of funded transport services for consults and procedures impacts patient care." -"To my understanding patients would have to leave the province which is not something they can afford,"	-Neurologists – underservice of general neurology as well as movement disorder specialists -Functional neurosurgeons – "one functional neurosurgeon for all of Atlantic Canada", "one functional neurosurgeon in British Columbia", "the one functional neurosurgeon in Manitoba left." -Family physicians -Interpreters and social support groups, treatment and counselling -Device restrictions -Operative time, hospital beds *Impact of COVID-19* *Perception of access in city:* -"would be provided in Calgary." -"Barriers to access… getting into a facility in Toronto or Hamilton." -"I live 2 hours drive from Toronto and Kingston. I feel that this option may be available if referred by my neurologist." *Travel/Transportation:* -Difficulty travelling with disability, unable to travel when caretaker for others -Many patients reported having to travel >2 hours to tertiary centre to access -Patients unable to drive themselves *Cost:* -Limited medical coverage for travel -Self-employed patients unable to travel for multiple appointments Limited resources most commonly reported in Atlantic provinces and patients with Parkinson's disease. Centralization most commonly reported in Ontario, British Columbia, Alberta, and Atlantic provinces.
Patient Factors		*Socioeconomic status:* -"Lower socioeconomic populations tend to live further away, have fewer means and support for repeated visits to surgery centre." -"Ability to drive or have access to a ride for that distance is an issue." -"Ability to attend appointments (e.g. self-employed, cannot afford gas or car to get to tertiary care centre)." *Support:* -"Social support (marital status) and education are contributing factors." *Language:*		*"Haven't considered DBS":* -Symptoms adequately managed with medical therapy -Symptoms mild -"Learned to deal with it" -Advanced age *Not interested* -Fear of undergoing surgery Reported across Canada

Table 7: Regional Summary of Barriers and Facilitators to Accessing Deep Brain Stimulation

	Atlantic Canada	Central Canada	Prairie Provinces	Coastal Canada	Northern Canada
Description of Region	Easternmost region, including NL, NS, PEI, and NB.	Most populous region of the country, encompassing QC and ON.	Includes MB, SK, and AB.	BC only.	Canada's territories: YT, NT, NU.
Population	2,566,037 (24).	24,145,217 (24).	7,225,987 (24).	5,431,555 (24).	129,545 (24).
DBS Centre(s)	One functional neurosurgeon and multidisciplinary assessment team are located in Halifax, NS.	Multiple functional neurosurgeons at many sites, and multidisciplinary assessment teams, as appropriate. Referral sites in QC are ~~Université~~ de Montréal (one surgeon), McGill (one surgeon), Sherbrooke (one surgeon), and Laval (one surgeon). In ON, the largest referral sites are located in Toronto, with Toronto Western (three surgeons), and Sunnybrook (one surgeon). Additionally, there are centres in Ottawa (one surgeon), and London (one surgeon).	A total of four referral centres are located in this region. Two centres in SK, Regina and Saskatoon, with three practicing surgeons. AB has sites in Calgary (one surgeon) and Edmonton (one surgeon). MB previously had one functional neurosurgeon, who had retired several years ago. In recent years, a functional neurosurgeon has provided locum coverage to perform DBS cases for the region.	Vancouver. At the time of this survey's distribution, only one surgeon was practicing at the site. One additional surgeon has since been hired.	No available DBS centres in the region, and major referral sites would be in SK, AB, BC, and ON.
Identified Barriers and Facilitators	Atlantic Canada found to have the poorest perceived access among patients and family physicians, supported by previous literature finding NL in particular to have the poorest access to DBS in Canada (21). Most apparent theme is limited resources and centralization of resources, given all patients must be assessed in Halifax, NS. There are significant costs incurred for patients related to travel as a result. Many patients and providers have, therefore, reported cost as a barrier to access. There is no budgetary cap on the number of annual DBS cases in NS, therefore it has historically provided higher than national average rate of DBS in the province (108% of national average) (21). However, this does not appear to translate to improved access in the region as a whole.	Central Canada is the only region where a small number of participants from all cohorts reported adequate access to DBS. However, barriers to access remain, notably the need for education was evident in this region. A number of physicians reported having poor understanding of indications for DBS, as well as diagnosis of the conditions of interest. Patients reported similar perceptions, particularly for patients with essential tremor and primary dystonia. A number of patients reported significant delay in diagnosis for these conditions, calling for improved understanding on behalf of family physicians. Previous research has reported very poor access to DBS in QC (40% lower than national average) citing budgetary constraints as a cause for this (21,31). This idea was reiterated by neurologists respondents, with waitlists to see movement disorder specialists frequently cited as barriers. Nearly half of respondents who had previously undergone DBS in this study were located in ON, while no patients in QC had received DBS. One previous study considered disparities in DBS use for patients living with Parkinson's disease in ON, finding that individuals in northern ON were more likely to receive DBS. This surprising finding was not observed when medication use in older adults were accounted for (19). Unsurprisingly, regular neurologist care and multiple medications for Parkinson's disease were positively associated with DBS. This is reiterated in the current study, where nearly all patients who had received DBS were formally diagnosed by a neurologist. Readily available neurology services could therefore be considered a facilitator to accessing DBS. Additionally, greater than half of patients in ON reported that their care provider had discussed DBS as a therapy with them previously. This is higher than any other province.	In spite of locum coverage in MB, limited resources was commonly reported there, with a number of respondents citing the retirement of one functional neurosurgeon in the province as a significant barrier to access there. SK has been reported to have the best access to DBS in Canada, with a DBS rate 374% higher than the national average. This has been attributed to the absence of budgetary constraints in the province, and the presence of three functional neurosurgeons in the region. SK has been reported to have the highest ratio of practicing functional neurosurgeons to provincial population in Canada (1 per 0.37 million) (21). Interestingly, patients and providers in the province did not perceive adequate access there. Half of patient respondents in SK reported "very poor" access to DBS, while the remaining patients reported "adequate" access.	Like Central Canada, the predominant theme was the need for education, again regarding diagnosis, indications, and referral pathways regionally. The significant wait list of the single functional neurosurgeon in BC was frequently reported by both physicians and patients as a barrier to accessing the service in this region. A previous study found that DBS rates in the region were 80% of the national average. Given the recent hiring of an additional surgeon, one would expect that access to DBS in the province may improve as a result.	

Limitations	No responses from providers from NS or PEI, no neurologists or neurosurgeons from Atlantic Canada, limits ability to draw conclusions regarding access from expert opinion. All patients from NL diagnosed with Parkinson's disease (likely due to recruitment strategy with engaged advocacy group for Parkinson's disease distributing survey). No responses for PEI from any groups. Although province has small population and neurology is available, there is no provincial access to neurosurgery with referrals sent to NB and NS.	ON is the only province where patients and family physicians over-estimated access to DBS. Frequent responses included "would have to travel to Hamilton to see neurosurgery", or "would be available nearby in Kingston", although functional neurosurgery is not offered at either of the aforementioned sites. Improved understanding of referral patterns in the province may, in this case, lead to a decrease in perceived access.			No responses were obtained from Northern Canada. Limited evidence exists regarding the prevalence of movement disorders in this region, and given the sparse population, vast geographical sparse, and great distance patients would need to travel to access even basic healthcare in some areas, this is an important Canadian population to seek perspectives from.

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CONTRIBUTORSHIP STATEMENT

Melissa Lannon contributed significantly to the study's concept and design, data collection and analysis, and interpretation of the results. She wrote the first draft of the manuscript, provided critical revisions, and gave final approval of the submitted manuscript.

Amanda Martyniuk contributed to data collection and analysis. She provided critical revisions and gave final approval of the submitted manuscript.

Minoo Aminnejad contributed to data analysis. She gave final approval of the submitted manuscript.

Rami Hatoum contributed to the study's design and analysis. He gave final approval of the submitted manuscript.

David Paoloni contributed to the study's design. He gave final approval of the submitted manuscript.

Forough Farrokhyar contributed to the study's concept and interpretation of the results. She provided critical revisions and gave final approval of the submitted manuscript.

Mohit Bhandari contributed to the study's concept and interpretation of the results. He provided critical revisions and gave final approval of the submitted manuscript.

Suneil Kalia contributed to the study's concept and interpretation of the results. He provided critical revisions and gave final approval of the submitted manuscript.

Sunjay Sharma contributed to the study's concept and interpretation of the results. He provided critical revisions and gave final approval of the submitted manuscript.

APPENDIX 1 – Supplementary Figure 1: Survey forms for all stakeholder groups

Advocacy Groups

1	What region do you work in?	◯ Alberta ◯ British Columbia ◯ Manitoba ◯ New Brunswick ◯ Newfoundland and Labrador ◯ Nova Scotia ◯ Ontario ◯ Prince Edward Island ◯ Quebec ◯ Saskatchewan ◯ Northwest Territories ◯ Nunavut ◯ Yukon
2	How would the area you work in be classified?	◯ Urban (population greater than 30,000, or less than 30 minutes away from a community with a population of more than 30,000) ◯ Rural (population less than 30,000 that are greater than 30 minutes away from a community with a population of more than 30,000) ◯ Remote (without year-round road access, or which rely on a third party (e.g. train, airplane, ferry) for transportation to a larger centre)
3	The following questions will ask for estimates of patients "in your region", briefly describe the "region" you are referring to (i.e. health authority, town, encatchment area, province/territory)	_____
4	How many patients in your region do you estimate are referred for deep brain stimulation each month?	◯ < 5 ◯ 5-10 ◯ 10-20 ◯ 20-30 ◯ >30
5	How many of these referred patients do you estimate go on to receive deep brain stimulation implants?	◯ < 10% ◯ 10-25% ◯ 25-50% ◯ 50-75% ◯ 75-100%
6a	Do you believe there is a lack of access to deep brain stimulation in your region?	◯ Yes, access to deep brain stimulation is very poor in my region ◯ Yes, access to deep brain stimulation is poor in my region ◯ I believe patients who need deep brain stimulation have reasonable access to deep brain stimulation in my region ◯ No, there is no problem with accessing deep brain stimulation in my region
6b	Please elaborate on your beliefs regarding access to deep brain stimulation in your region.	_____

7	What system barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Geographical location ☐ Inadequate number of functional neurosurgeons to perform surgeries ☐ Inadequate number of specialists to complete assessment prior to referral to neurosurgeon ☐ Poor understanding of indications limiting referral ☐ Inadequate access to operative time for surgeons ☐ Inadequate device funding ☐ Other (please list below)
7	Please list other system barriers you perceive to accessing deep brain stimulation in your region	_____
8	What cultural or socioeconomic barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Patient ethnicity ☐ Patient socioeconomic status ☐ Patient gender ☐ Other (please list below)
8	Please list other cultural or socioeconomic barriers you perceive to accessing deep brain stimulation in your region	_____
9	Is there anything else you would like to tell us?	_____

Family Physicians

1	What region do you practice in?	◯ Alberta ◯ British Columbia ◯ Manitoba ◯ New Brunswick ◯ Newfoundland and Labrador ◯ Nova Scotia ◯ Ontario ◯ Prince Edward Island ◯ Quebec ◯ Saskatchewan ◯ Northwest Territories ◯ Nunavut ◯ Yukon
2	How would the area you practice in be classified?	◯ Urban (population greater than 30,000, or less than 30 minutes away from a community with a population of more than 30,000) ◯ Rural (population less than 30,000 that are greater than 30 minutes away from a community with a population of more than 30,000) ◯ Remote (without year-round road access, or which rely on a third party (e.g. train, airplane, ferry) for transportation to a larger centre)
3	How long have you been practicing independently?	◯ < 5 years ◯ 5-10 years ◯ 10-20 years ◯ >20 years
4	Estimate the distance patients in your clinic would need to travel to see a functional neurosurgeon for deep brain stimulation	◯ < 100km ◯ 100-500km ◯ 500-1000km ◯ >1,000km
5	The following questions will ask for estimates of patients "in your region", briefly describe the "region" you are referring to (i.e. health authority, town, encatchment area, province/territory)	_____
6a	How many patients do you estimate to have a diagnosis of Parkinson's Disease in your region? Note: As defined by the Movement Disorders Society, Parkinson's disease is defined as "a neurodegenerative disorder characterized primarily by loss of dopamine neurons in the substantia nigra. People may experience tremor, mainly at rest (described as pill rolling tremor in hands), bradykinesia, limb rigidity, gait and balance problems."	_____

6b How many patients do you estimate to have a diagnosis of essential tremor in your region?

Note: Essential tremor is defined by the Movement Disorder Society Task force as "an isolated tremor syndrome of bilateral upper limb action tremor with at least 3 years' duration. Tremor in other locations (e.g. head, voice, or lower limbs) may be present, but there are no other neurological signs such as dystonia, ataxia, or parkinsonism. Orthostatic tremor with a frequency >12Hx, task- and position-specific tremors and sudden onset and step-wise deterioration do not fall into the category of essential tremor."

_____

6c How many patients do you estimate to have a diagnosis of primary dystonia in your region?

Note: The Movement Disorders Society defines dystonia as "a movement disorder characterized by sustained intermittent muscle contractions causing abnormal, often repetitive movements, postures, or both. Dystonic movements are typically patterned, twisting, and may be tremulous. Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation." Primary dystonia is not due to any identifiable secondary cause.

_____

7 Do you believe you have a good understanding of indications for deep brain stimulation and what patients may benefit from this treatment?

- ◯ Yes
- ◯ No

8 Please describe the ideal motor disorder candidate for deep brain stimulation, as you understand.

_____

9 How many patients in your region do you estimate are referred for deep brain stimulation each month?

- ◯ < 5
- ◯ 5-10
- ◯ 10-20
- ◯ 20-30
- ◯ >30

10 How many of these referred patients do you estimate go on to receive deep brain stimulation implants?

- ◯ < 10%
- ◯ 10-25%
- ◯ 25-50%
- ◯ 50-75%
- ◯ 75-100%

11a Do you believe there is a lack of access to deep brain stimulation in your region?

- ◯ Yes, access to deep brain stimulation is very poor in my region
- ◯ Yes, access to deep brain stimulation is poor in my region
- ◯ I believe patients who need deep brain stimulation have reasonable access to deep brain stimulation in my region
- ◯ No, there is no problem with accessing deep brain stimulation in my region

11b Please elaborate on your beliefs regarding access to deep brain stimulation in your region.

_____

12	What system barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Geographical location ☐ Inadequate number of functional neurosurgeons to perform surgeries ☐ Inadequate number of specialists to complete assessment prior to referral to neurosurgeon ☐ Poor understanding of indications limiting referral ☐ Inadequate access to operative time for surgeons ☐ Inadequate device funding ☐ Other (please list below)
12	Please list other system barriers you perceive to accessing deep brain stimulation in your region	_____
13	What cultural or socioeconomic barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Patient ethnicity ☐ Patient socioeconomic status ☐ Patient gender ☐ Other (please list below)
13	Please list other cultural or socioeconomic barriers you perceive to accessing deep brain stimulation in your region	_____
14	Is there anything else you would like to tell us?	_____

Neurologists

1	What region do you practice in?	◯ Alberta ◯ British Columbia ◯ Manitoba ◯ New Brunswick ◯ Newfoundland and Labrador ◯ Nova Scotia ◯ Ontario ◯ Prince Edward Island ◯ Quebec ◯ Saskatchewan ◯ Northwest Territories ◯ Nunavut ◯ Yukon
2	How would the area you practice in be classified?	◯ Urban (population greater than 30,000, or less than 30 minutes away from a community with a population of more than 30,000) ◯ Rural (population less than 30,000 that are greater than 30 minutes away from a community with a population of more than 30,000) ◯ Remote (without year-round road access, or which rely on a third party (e.g. train, airplane, ferry) for transportation to a larger centre)
3	How long have you been practicing independently?	◯ < 5 years ◯ 5-10 years ◯ 10-20 years ◯ >20 years
4	Do you specialize in motor disorders?	◯ Yes ◯ No
5	Estimate the distance patients in your clinic would need to travel to see a functional neurosurgeon for deep brain stimulation	◯ < 100km ◯ 100-500km ◯ 500-1000km ◯ >1,000km
6	The following questions will ask for estimates of patients "in your region", briefly describe the "region" you are referring to (i.e. health authority, town, encatchment area, province/territory)	_____
7a	How many patients do you estimate to have a diagnosis of Parkinson's Disease in your region?	_____
7b	How many patients do you estimate to have a diagnosis of essential tremor in your region?	_____
7c	How many patients do you estimate to have a diagnosis of primary dystonia in your region?	_____
8	Do you refer patients for consideration of deep brain stimulation for these indications?	◯ Yes ◯ No

9	How many patients in your region do you estimate are referred for deep brain stimulation each month?	◯ < 5 ◯ 5-10 ◯ 10-20 ◯ 20-30 ◯ >30
10	How many of these referred patients do you estimate go on to receive deep brain stimulation implants?	◯ < 10% ◯ 10-25% ◯ 25-50% ◯ 50-75% ◯ 75-100%
11	How many patients do you estimate that would benefit from deep brain stimulation for motor disorder indications in your region?	◯ < 10 ◯ 10-25 ◯ 25-50 ◯ 50-75 ◯ 75-100 ◯ 100-200 ◯ 200-500 ◯ >500
12a	Do you believe there is a lack of access to deep brain stimulation in your region?	◯ Yes, access to deep brain stimulation is very poor in my region ◯ Yes, access to deep brain stimulation is poor in my region ◯ I believe patients who need deep brain stimulation have reasonable access to deep brain stimulation in my region ◯ No, there is no problem with accessing deep brain stimulation in my region
12b	Please elaborate on your beliefs regarding access to deep brain stimulation in your region.	_____
13	What system barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Geographical location ☐ Inadequate number of functional neurosurgeons to perform surgeries ☐ Inadequate number of specialists to complete assessment prior to referral to neurosurgeon ☐ Poor understanding of indications limiting referral ☐ Inadequate access to operative time for surgeons ☐ Inadequate device funding ☐ Other (please list below)
13	Please list other system barriers you perceive to accessing deep brain stimulation in your region	_____
14	What cultural or socioeconomic barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Patient ethnicity ☐ Patient socioeconomic status ☐ Patient gender ☐ Other (please list below)
14	Please list other cultural or socioeconomic barriers you perceive to accessing deep brain stimulation in your region	_____

15 Is there anything else you would like to tell us?

Neurosurgeons

1	What region do you practice in?	◯ Alberta ◯ British Columbia ◯ Manitoba ◯ New Brunswick ◯ Newfoundland and Labrador ◯ Nova Scotia ◯ Ontario ◯ Prince Edward Island ◯ Quebec ◯ Saskatchewan ◯ Northwest Territories ◯ Nunavut ◯ Yukon
2	Estimate the distance patients in your clinic would need to travel to see a functional neurosurgeon for deep brain stimulation	◯ < 100km ◯ 100-500km ◯ 500-1000km ◯ >1,000km
3	Do you perform deep brain stimulation surgeries?	◯ Yes ◯ No
4	How many unique patients implanted with deep brain stimulation electrodes would you estimate have their initial surgeries at your centre each month?	◯ < 5 ◯ 5-10 ◯ 10-20 ◯ 20-30 ◯ 30-40 ◯ >40
5	Of the patients referred for deep brain stimulation to your centre, what percentage would you estimate go on to receive deep brain stimulation implants?	◯ < 10% ◯ 10-25% ◯ 25-50% ◯ 50-75% ◯ 75-100%
6	How many patients do you estimate that would benefit from deep brain stimulation for motor disorder indications in your region?	◯ < 10 ◯ 10-25 ◯ 25-50 ◯ 50-75 ◯ 75-100 ◯ 100-200 ◯ 200-500 ◯ >500
7a	Do you believe there is a lack of access to deep brain stimulation in your region?	◯ Yes, access to deep brain stimulation is very poor in my region ◯ Yes, access to deep brain stimulation is poor in my region ◯ I believe patients who need deep brain stimulation have reasonable access to deep brain stimulation in my region ◯ No, there is no problem with accessing deep brain stimulation in my region

7b	Please elaborate on your beliefs regarding access to deep brain stimulation in your region.	_____
8	What system barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Geographical location ☐ Inadequate number of functional neurosurgeons to perform surgeries ☐ Inadequate number of specialists to complete assessment prior to referral to neurosurgeon ☐ Poor understanding of indications limiting referral ☐ Inadequate access to operative time for surgeons ☐ Inadequate device funding ☐ Other (please list below)
8	Please list other system barriers you perceive to accessing deep brain stimulation in your region	_____
9	What cultural or socioeconomic barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Patient ethnicity ☐ Patient socioeconomic status ☐ Patient gender ☐ Other (please list below)
9	Please list other cultural or socioeconomic barriers you perceive to accessing deep brain stimulation in your region	_____
10	Is there anything else you would like to tell us?	_____

Patients And Patient Families

1.	Please select which of the following describes you:	◯ Someone diagnosed with Parkinson's Disease, essential tremor, or primary dystonia, completing this questionnaire on behalf of myself ◯ A family member or caregiver of someone diagnosed with Parkinson's disease, essential tremor, or primary dystonia, completing this questionnaire on their behalf ◯ A family member of someone diagnosed with Parkinson's Disease, essential tremor, or primary dystonia, completing this questionnaire on behalf of myself
2.	Where do you or your family member live?	◯ Alberta ◯ British Columbia ◯ Manitoba ◯ New Brunswick ◯ Newfoundland and Labrador ◯ Nova Scotia ◯ Ontario ◯ Prince Edward Island ◯ Quebec ◯ Saskatchewan ◯ Northwest Territories ◯ Nunavut ◯ Yukon
3.	Which of the following would describe where you or your family member live?	◯ Urban (population greater than 30,000, or less than 30 minutes away from a community with a population of more than 30,000) ◯ Rural (population less than 30,000 that are greater than 30 minutes away from a community with a population of more than 30,000) ◯ Remote (without year-round road access, or which rely on a third party (e.g. train, airplane, ferry) for transportation to a larger centre)
4.	Which of the following has your doctor diagnosed you or your family member with?	◯ Parkinson's Disease ◯ Essential Tremor ◯ Primary Dystonia
5.	How long ago were you or your family member diagnosed with this condition?	◯ less than 5 years ◯ 5-10 years ◯ 10-20 years ◯ more than 20 years
6.	How long after experiencing symptoms were you or your family member first diagnosed?	◯ less than 6 months ◯ 6 months-1 year ◯ 1-2 years ◯ 2-5 years ◯ 5-10 years ◯ more than 10 years
7.	Which of the following care providers first diagnosed you or your family member with this condition?	◯ Family doctor ◯ Neurologist
8.	Has your doctor ever talked about deep brain stimulation surgery with you or your family member?	◯ Yes ◯ No

9.	Is this a treatment you or your family member would be willing to pursue if it was offered to you or your family member?	◯ Yes ◯ No ◯ Not sure ◯ I have never heard of deep brain stimulation
10.	If you or your family member have received deep brain stimulation, how long was it between diagnosis and referral for surgery?	◯ less than 6 months ◯ 6 months-1 year ◯ 1-2 years ◯ more than 2 years ◯ Not applicable
11.	If you or your family member have received deep brain stimulation, how long was it between referral for surgery and the operation?	◯ less than 6 months ◯ 6 months-1year ◯ 1-2 years ◯ more than 2 years ◯ Not applicable
12a.	Do you think there are barriers to you or your family member accessing this treatment?	◯ Yes, access to deep brain stimulation is very poor in my region ◯ Yes, access to deep brain stimulation is poor in my region ◯ I believe patients who need deep brain stimulation have reasonable access to deep brain stimulation in my region ◯ No, there is no problem with accessing deep brain stimulation in my region
12b.	Please tell us more about what you think of access to deep brain stimulation in your region.	_____
13.	What barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Distance from where I live to larger hospitals that provide deep brain stimulation ☐ Not enough functional neurosurgeons to perform surgeries ☐ Not enough specialists to assess patients prior to referral to neurosurgeon ☐ Poor understanding of who qualifies for deep brain stimulation ☐ Not enough hospital resources for surgeons to perform deep brain stimulation surgeries ☐ Not enough funding for deep brain stimulation implants ☐ Other (please list below)
13.	Please list other barriers you perceive to accessing deep brain stimulation in your region	_____
14.	What cultural or socioeconomic barriers do you perceive to accessing deep brain stimulation in your region? (Check all that apply)	☐ Patient ethnicity ☐ Patient socioeconomic status ☐ Patient gender ☐ Other (please list below)
14.	Please list other cultural or socioeconomic barriers you perceive to accessing deep brain stimulation in your region	_____

15. Is there anything else you would like to tell us?

Advocacy Groups

1	Dans quelle région pratiquez-vous?	◯ L'Alberta ◯ La Colombie-Britannique ◯ Le Manitoba ◯ Le Nouveau-Brunswick ◯ Terre-Neuve-et-Labrador ◯ La Nouvelle-Écosse ◯ L'Ontario ◯ L'Île-du-Prince-Édouard ◯ Le Québec ◯ La Saskatchewan ◯ Les Territoires du Nord-Ouest ◯ Le Nunavut ◯ Le Yukon
2	Lequel des énoncés suivants décrit votre milieu pratique?	◯ Urbain (population supérieure à 30000 habitants, ou à une distance de moins de 30 minutes d'une communauté comptant plus de 30000 habitants) ◯ Rural (population inférieure à 30000 habitants, et à distance de plus que 30 minutes d'une communauté comptant plus de 30000 habitants) ◯ Région éloignée (ne possédant pas un accès routier le long de l'année, ou dépendant d'une tierce partie (ie. Train, avion, croisière) pour les transports au centres larges)
3	Les questions suivantes portent sur des estimations concernant les patients "dans votre région". Veuillez décrire brièvement la "région" à laquelle vous faites référence (c.-à-d. autorité sanitaire, ville, zone de desserte, province/territoire)	_____
4	Dans votre région de pratique, combien de patients sont référés à la stimulation cérébrale profonde par mois?	◯ < 5 ◯ 5-10 ◯ 10-20 ◯ 20-30 ◯ >30
5	Selon vos estimations, quel pourcentage de ces patients référés recevront la stimulation cérébrale profonde?	◯ < 10% ◯ 10-25% ◯ 25-50% ◯ 50-75% ◯ 75-100%
6a	Croyez-vous qu'il existe un manque d'accès à la stimulation cérébrale profonde dans votre région?	◯ Oui, l'accès à la stimulation cérébrale profonde est très limité ◯ Oui, l'accès à la stimulation cérébrale profonde est limité ◯ Je crois que les personnes ayant besoin d□une stimulation cérébrale profonde auront un accès raisonnable à cette procédure ◯ Non, il n'y a pas de barrière à l'accès à la stimulation cérébrale profonde dans ma région
6b	Veuillez élaborer vos pensées quant au manque d'accès à la stimulation cérébrale profonde dans la région.	_____

7	Quel(s) obstacle(s) percevez-vous quant à l'accès à la stimulation cérébrale profonde dans votre région? (Veuillez sectionner tous les énoncés qui s'appliquent)	☐ L'emplacement géographique ☐ Nombre insuffisant de neurochirurgie(nes) fonctionnel(les), formé(es) pour performer cette procédure ☐ Nombre insuffisant de spécialiste ayant les compétences requises à l'évaluation du patient avant la référence en eurochirurgie ☐ Mécompréhension quant aux indications et à la sélection des candidats, limitant la référencés neurochirurgicale ☐ Manque de temps opératoire ☐ Financement inadéquat des appareils (nécessaire à la stimulation cérébrale profonde) ☐ Autres (veuillez décrire ci-dessous)
7	Veuillez décrire d'autres barrières, liée(s) au système de santé, causant un obstacle à l'accès à la stimulation cérébrale profonde dans votre région.	_____
8	Quelles barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région? (Veuillez sectionner tous les énoncés qui s'appliquent)	☐ L'appartenance ethnique ☐ Le statut socioéconomique ☐ L'identité du genre ☐ Autres (veuillez décrire ci-dessous)
8	Quelles autres barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région?	_____
9	Avez-vous d'autres informations ou pensées à nous partager?	_____

6b Combien de patients estimez-vous ont un diagnostic de tremblement essentiel dans votre région?

Remarque: Le tremblement essentiel est défini par le groupe de travail de la Société des Troubles de la Motricité (Movement Disorder Society) comme "un syndrome de tremblement isolé, originant des membres supérieurs bilatéralement, d'une durant au moins 3 ans. Des tremblements dans d'autres endroits (par exemple, la tête, la voix ou les membres inférieurs) peuvent être présents, en absence d'autres signes neurologiques tels que la dystonie, l'ataxie ou le parkinsonisme. Le tremblement orthostatique d'une fréquence > 12Hz, les tremblements spécifiques à une tâche et à une position ainsi que ceux associés à une apparition soudaine et une détérioration progressive ne sont pas considerés comme tremblements essentiels."

_____

6c Combien de patients estimez-vous ont un diagnostic de dystonie primaire dans votre région?

Remarque: La Société des Troubles de la Motricité (Movement Disorder Society) définit la dystonie comme "un trouble du mouvement caractérisé par des contractions musculaires intermittentes et soutenues provoquant des mouvements et/ou des postures anormaux et souvent répétitifs. Les mouvements dystoniques sont généralement structurés, de torsion et peuvent présenter un tremblement. La dystonie est souvent causée ou empirée par une action volontaire et associée à une activation musculaire excessive." La dystonie primaire n'est due à aucune cause secondaire identifiable.

_____

7 Croyez-vous avoir une bonne compréhension des indications de la stimulation cérébrale profonde et des patients pouvant bénéficier de ce traitement?

- ◯ Oui
- ◯ Non

8 Décrivez, selon votre compréhension, le candidat idéal pour la stimulation cérébrale profonde.

_____

9 Dans votre région de pratique, combien de patients sont référés à la stimulation cérébrale profonde par mois?

- ◯ < 5
- ◯ 5-10
- ◯ 10-20
- ◯ 20-30
- ◯ >30

10 Selon vos estimations, quel pourcentage de ces patients référés recevront la stimulation cérébrale profonde?

- ◯ < 10%
- ◯ 10-25%
- ◯ 25-50%
- ◯ 50-75%
- ◯ 75-100%

Family Physicians

1	Dans quelle région pratiquez-vous?	◯ L'Alberta ◯ La Colombie-Britannique ◯ Le Manitoba ◯ Le Nouveau-Brunswick ◯ Terre-Neuve-et-Labrador ◯ La Nouvelle-Écosse ◯ L'Ontario ◯ L'Île-du-Prince-Édouard ◯ Le Québec ◯ La Saskatchewan ◯ Les Territoires du Nord-Ouest ◯ Le Nunavut ◯ Le Yukon
2	Lequel des énoncés suivants décrit votre milieu pratique?	◯ Urbain (population supérieure à 30000 habitants, ou à une distance de moins de 30 minutes d'une communauté comptant plus de 30000 habitants) ◯ Rural (population inférieure à 30000 habitants, et à distance de plus que 30 minutes d'une communauté comptant plus de 30000 habitants) ◯ Région éloignée (ne possédant pas un accès routier le long de l'année, ou dépendant d'une tierce partie (ie. Train, avion, croisière) pour les transports au centres larges)
3	Depuis combien de temps pratiquez-vous de façon indépendante?	◯ < 5 ans ◯ 5-10 ans ◯ 10-20 ans ◯ >20 ans
4	Selon votre estimation, quelle serait la distance que les patients de votre clinique devraient parcourir pour voir un neurochirurgien(ne) fonctionnel (le) au sujet de la stimulation cérébrale profonde	◯ < 100km ◯ 100-500km ◯ 500-1000km ◯ >1000km
5	Les questions suivantes portent sur des estimations concernant les patients "dans votre région". Veuillez décrire brièvement la "région" à laquelle vous faites référence (c.-à-d. autorité sanitaire, ville, zone de desserte, province/territoire)	_____
6a	Combien de patients estimez-vous ont un diagnostic de la maladie de Parkinson dans votre région? Remarque: Selon la définition de la Société des Troubles de la Motricité (Movement Disorder Society), la maladie de Parkinson est "une maladie neurodégénérative caractérisée principalement par la perte de neurones dopaminergiques dans la substance noire. Les personnes atteintes peuvent présenter des tremblement (i.e. de la main au repos, rappellant le mouvement d'émiettement) , la bradykinésie, la rigidité des membres, et les troubles de démarche et de l'équilibre."	_____

11a	Croyez-vous qu'il existe un manque d'accès à la stimulation cérébrale profonde dans votre région?	○ Oui, l'accès à la stimulation cérébrale profonde est très limité ○ Oui, l'accès à la stimulation cérébrale profonde est limité ○ Je crois que les personnes ayant besoin d'une stimulation cérébrale profonde auront un accès raisonnable à cette procédure ○ Non, il n'y a pas de barrière à l'accès à la stimulation cérébrale
11b	Veuillez élaborer vos pensées quant au manque d'accès à la stimulation cérébrale profonde dans la région.	_____
12	Quels obstacles percevez-vous quant à l'accès à la stimulation cérébrale profonde dans votre région? (Veuillez sectionner tous les énoncés qui s'appliquent)	☐ L'emplacement géographique ☐ Nombre insuffisant de neurochirurgie(nes) fonctionnel(les), formé(es) pour performer cette procédure ☐ Nombre insuffisant de spécialiste ayant les compétences requises à l'évaluation du patient avant la référence en eurochirurgie ☐ Mécompréhension quant aux indications et à la sélection des candidats, limitant la référencés neurochirurgicale ☐ Manque de temps opératoire ☐ Financement inadéquat des appareils (nécessaire à la stimulation cérébrale profonde) ☐ Autres (veuillez décrire ci-dessous)
12	Veuillez décrire d'autres barrières, liée(s) au système de santé, causant un obstacle à l'accès à la stimulation cérébrale profonde dans votre région.	_____
13	Quels obstacles culturels ou socioéconomiques percevez-vous pour accéder à la stimulation cérébrale profonde dans votre région? (Veuillez sectionner tous les énoncés applicables)	☐ L'appartenance ethnique ☐ Le statut socioéconomique ☐ L'identité du genre ☐ Autres (veuillez décrire ci-dessous)
13	Quelles autres barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région?	_____
14	Avez-vous d'autres informations ou pensées à nous partager?	_____

Neurologists

1	Dans quelle région pratiquez-vous?	◯ L'Alberta ◯ La Colombie-Britannique ◯ Le Manitoba ◯ Le Nouveau-Brunswick ◯ Terre-Neuve-et-Labrador ◯ La Nouvelle-Écosse ◯ L'Ontario ◯ L'Île-du-Prince-Édouard ◯ Le Québec ◯ La Saskatchewan ◯ Les Territoires du Nord-Ouest ◯ Le Nunavut ◯ Le Yukon
2	Lequel des énoncés suivants décrit votre milieu pratique?	◯ Urbain (population supérieure à 30000 habitants, ou à une distance de moins de 30 minutes d'une communauté comptant plus de 30000 habitants) ◯ Rural (population inférieure à 30000 habitants, et à distance de plus que 30 minutes d'une communauté comptant plus de 30000 habitants) ◯ Région éloignée (ne possédant pas un accès routier le long de l'année, ou dépendant d'une tierce partie (ie. Train, avion, croisière) pour les transports au centres larges)
3	Depuis combien de temps pratiquez-vous de façon indépendante?	◯ < 5 ans ◯ 5-10 ans ◯ 10-20 ans ◯ >20 ans
4	Êtes-vous spécialiste en troubles moteurs?	◯ Oui ◯ Non
5	Selon votre estimation, quelle serait la distance que les patients de votre clinique devraient parcourir pour voir un neurochirurgien(ne) fonctionnel (le) au sujet de la stimulation cérébrale profonde.	◯ < 100km ◯ 100-500km ◯ 500-1000km ◯ >1000km
6	Les questions suivantes portent sur des estimations concernant les patients "dans votre région". Veuillez décrire brièvement la "région" à laquelle vous faites référence (c.-à-d. autorité sanitaire, ville, zone de desserte, province/territoire)	_____
7a	Combien de patients estimez-vous ont un diagnostic de la maladie de Parkinson dans votre région?	_____
7b	Combien de patients estimez-vous ont un diagnostic de tremblement essentiel dans votre région?	_____
7c	Combien de patients estimez-vous ont un diagnostic de dystonie primaire dans votre région?	_____

8	Référez-vous vos patients porteurs des maladies ci-dessus pour l'évaluation de la stimulation cérébrale profonde?	◯ Oui ◯ Non
9	Dans votre région de pratique, combien de patients sont référés à la stimulation cérébrale profonde par mois?	◯ < 5 ◯ 5-10 ◯ 10-20 ◯ 20-30 ◯ >30
10	Selon vos estimations, quel pourcentage de ces patients référés recevront la stimulation cérébrale profonde?	◯ < 10% ◯ 10-25% ◯ 25-50% ◯ 50-75% ◯ 75-100%
11	Selon vous, combien de patients bénéficieraient de la stimulation cérébrale profonde pour troubles moteurs dans votre région?	◯ < 10 ◯ 10-25 ◯ 25-50 ◯ 50-75 ◯ 75-100 ◯ 100-200 ◯ 200-500 ◯ >500
12a	Croyez-vous qu'il existe un manque d□accès à la stimulation cérébrale profonde dans votre région?	◯ Oui, l'accès à la stimulation cérébrale profonde est très limité ◯ Oui, l'accès à la stimulation cérébrale profonde est limité ◯ Je crois que les personnes ayant besoin d'une stimulation cérébrale profonde auront un accès raisonnable à cette procédure ◯ Non, il n'y a pas de barrière à l'accès à la stimulation cérébrale
12b	Veuillez élaborer vos pensées quant au manque d'accès à la stimulation cérébrale profonde dans la région.	_____
13	Quels obstacles percevez-vous à l'accès à la stimulation cérébrale profonde dans votre région? (Cochez toutes les réponses qui s'appliquent)	☐ L'emplacement géographique ☐ Nombre insuffisant de neurochirurgie(nes) fonctionnel(les), formé(es) pour performer cette procédure ☐ Nombre insuffisant de spécialiste ayant les compétences requises à l'évaluation du patient avant la référence en eurochirurgie ☐ Mécompréhension quant aux indications et à la sélection des candidats, limitant la référencés neurochirurgicale ☐ Manque de temps opératoire ☐ Financement inadéquat des appareils (nécessaire à la stimulation cérébrale profonde) ☐ Autres (veuillez décrire ci-dessous)
13	Veuillez décrire d'autres barrières, liée(s) au système de santé, causant un obstacle à l'accès à la stimulation cérébrale profonde dans votre région.	_____

14	Quelles barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région? (Veuillez sectionner tous les énoncés applicables)	☐ L'appartenance ethnique ☐ Le statut socioéconomique ☐ L'identité du genre ☐ Autres (veuillez décrire ci-dessous)
14	Quelles autres barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région?	_____
15	Avez-vous d'autres informations ou pensées à nous partager?	_____

Neurosurgeons

1	Dans quelle région pratiquez-vous?	◯ L'Alberta ◯ La Colombie-Britannique ◯ Le Manitoba ◯ Le Nouveau-Brunswick ◯ Terre-Neuve-et-Labrador ◯ La Nouvelle-Écosse ◯ L'Ontario ◯ L'Île-du-Prince-Édouard ◯ Le Québec ◯ La Saskatchewan ◯ Les Territoires du Nord-Ouest ◯ Le Nunavut ◯ Le Yukon
2	Selon votre estimation, quelle serait la distance que les patients de votre clinique devraient parcourir pour voir un neurochirurgien(ne) fonctionnel (le) au sujet de la stimulation cérébrale profonde	◯ < 100km ◯ 100-500km ◯ 500-1000km ◯ >1,000km
3	Pratiquez-vous la stimulation cérébrale profonde?	◯ Oui ◯ Non
4	Combien de patients porteurs d'électrodes de stimulation cérébrale profonde estimez-vous aient leur chirurgie initiale à votre centre par mois?	◯ < 5 ◯ 5-10 ◯ 10-20 ◯ 20-30 ◯ 30-40 ◯ >40
5	Parmi les patients référés à votre centre pour la stimulation cérébrale profonde, quel pourcentage estimez-vous avoir subi l'implantation de ces électrodes?	◯ < 10% ◯ 10-25% ◯ 25-50% ◯ 50-75% ◯ 75-100%
6	Selon vous, combien de patients bénéficieraient de la stimulation cérébrale profonde pour troubles moteurs dans votre région?	◯ < 10 ◯ 10-25 ◯ 25-50 ◯ 50-75 ◯ 75-100 ◯ 100-200 ◯ 200-500 ◯ >500
7a	Croyez-vous qu'il existe un manque d'accès à la stimulation cérébrale profonde dans votre région?	◯ Oui, l'accès à la stimulation cérébrale profonde est très limité ◯ Oui, l'accès à la stimulation cérébrale profonde est limité ◯ Je crois que les personnes ayant besoin d□une stimulation cérébrale profonde auront un accès raisonnable à cette procédure ◯ Non, il n'y a pas de barrière à l'accès à la stimulation cérébrale profonde dans ma région

7b	Veuillez élaborer vos pensées quant au manque d'accès à la stimulation cérébrale profonde dans la région.	_____
8	Quels obstacles percevez-vous à l'accès à la stimulation cérébrale profonde dans votre région? (Cochez toutes les réponses qui s'appliquent)	☐ L'emplacement géographique ☐ Nombre insuffisant de neurochirurgie(nes) fonctionnel(les), formé(es) pour performer cette procédure ☐ Nombre insuffisant de spécialiste ayant les compétences requises à l'évaluation du patient avant la référence en eurochirurgie ☐ Mécompréhension quant aux indications et à la sélection des candidats, limitant la référencés neurochirurgicale ☐ Manque de temps opératoire ☐ Financement inadéquat des appareils (nécessaire à la stimulation cérébrale profonde) ☐ Autres (veuillez décrire ci-dessous)
8	Veuillez décrire d'autres barrières, liée(s) au système de santé, causant un obstacle à l'accès à la stimulation cérébrale profonde dans votre région.	_____
9	Quelles barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région? (Cochez toutes les réponses qui s'appliquent)	☐ L'appartenance ethnique ☐ Le statut socioéconomique ☐ L'identité du genre ☐ Autres (veuillez décrire ci-dessous)
9	Quelles autres barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région?	_____
10	Avez-vous d'autres informations ou pensées à nous partager?	_____

Patients And Patient Families

1	Veuillez choisir l'énoncé qui vous décrit le mieux:	◯ Une personne ayant reçu un diagnostic de maladie de Parkinson, tremblement essentiel, ou dystonie primaire, complétant ce questionnaire en mon propre nom ◯ Un membre de la famille ou un proche-aidant à une personne ayant reçu un diagnostic de maladie de Parkinson, tremblement essentiel, ou dystonie primaire, complétant ce questionnaire au nom de la personne concernée par le diagnostic ◯ Un membre de la famille d'une personne ayant reçu un diagnostic de maladie de Parkinson, tremblement essentiel, ou dystonie primaire, complétant ce questionnaire en mon propre nom
2	Dans quelle province vous, ou le(s) membre(s) de votre famille résidez-vous?	◯ L'Alberta ◯ La Colombie-Britannique ◯ Le Manitoba ◯ Le Nouveau-Brunswick ◯ Terre-Neuve-et-Labrador ◯ La Nouvelle-Écosse ◯ L'Ontario ◯ L'Île-du-Prince-Édouard ◯ Le Québec ◯ La Saskatchewan ◯ Les Territoires du Nord-Ouest ◯ Le Nunavut ◯ Le Yukon
3	Lequel des énoncés suivants décrit le mieux votre milieu de vie, ou celui du membre de votre famille?	◯ Urbain (population supérieure à 30000 habitants, ou à une distance de moins de 30 minutes d'une communauté comptant plus de 30000 habitants) ◯ Rural (population inférieure à 30000 habitants, et à distance de plus que 30 minutes d'une communauté comptant plus de 30000 habitants) ◯ Région éloignée (ne possédant pas un accès routier le long de l'année, ou dépendant d'une tierce partie (ie. Train, avion, croisière) pour les transports au centres larges)
4	Lequel(s) des diagnostic(s) suivant(s), vous, ou un membre de votre famille avez-vous reçu?	◯ La maladie de Parkinson ◯ Le tremblement essentiel ◯ La dystonie primaire
5	Depuis combien de temps, vous, ou un membre de votre famille avez-vous reçu ce diagnostic?	◯ Moins que 5 ans ◯ 5-10 ans ◯ 10-20 ans ◯ Plus que 20 ans
6	Quel est l'intervalle de temps passé depuis les premiers symptômes jusqu'au diagnostic?	◯ Moins que 6 mois ◯ 6 mois-1 an ◯ 1-2 ans ◯ 2-5 ans ◯ 5-10 ans ◯ Plus que 10 ans
7	Lequel des professionnels de la santé suivants a-t-il posé le diagnostic en premier ?	◯ Médecin de famille ◯ Neurologue

8	Votre médecin vous a- t-il parlé de la stimulation cérébrale profonde?	◯ Oui ◯ Non
9	Considérez-vous ce traitement (stimulation cérébrale profonde) si on vous l'offre?	◯ Oui ◯ Non ◯ Pas certain ◯ Je n'ai pas entendu parler de la stimulation cérébrale profonde
10	Si vous, ou un membre de votre famille avez eu la stimulation cérébrale profonde, quel est l'intervalle de temps écoulé entre le diagnostic et la référence à un chirurgien?	◯ Moins que 6 mois ◯ 6 mois-1 an ◯ 1-2 ans ◯ Plus que 2 ans ◯ Non applicable
11	Dans le cas où vous ou un membre de votre famille avez eu une stimulation cérébrale profonde, quel était l'intervalle de temps entre la référence en chirurgie et la date de la chirurgie?	◯ Moins que 6 mois ◯ 6 mois-1 an ◯ 1-2 ans ◯ Plus que 2 ans ◯ Non applicable
12a.	Pensez -vous avoir un obstacle à l'accès à ce traitement?	◯ Oui, l'accès à la stimulation cérébrale profonde est très limité ◯ Oui, l'accès à la stimulation cérébrale profonde est limité ◯ Je crois que les personnes ayant besoin d'une stimulation cérébrale profonde auront un accès raisonnable à cette procédure ◯ Non, il n'y a pas de barrière à l'accès à la stimulation cérébrale profonde dans ma région
12b.	Veuillez nous partager vos pensées quant à l'accessibilité à la stimulation cérébrale profonde dans votre région.	_____
13	Quels obstacles percevez-vous quant à l'accès à la stimulation cérébrale profonde dans votre région? (Veuillez sectionner tous les énoncés qui s'appliquent)	☐ La distance entre votre milieu de résidence est l'hôpital offrant cette procédure ☐ Le manque de neurochirurgie(nes) fonctionnel(les), formé(es) pour performer cette procédure ☐ Le manque de spécialiste ayant les compétences requises à l'évaluation du patient avant la référence en neurochirurgie ☐ Mécompréhension quant à la sélection des candidats à la stimulation cérébrale profonde ☐ Manque de ressources hospitalières permettant au neurochirurgien de performer cette procédure ☐ Manque de fonds permettant l'achat des implants (nécessaire à la stimulation cérébrale profonde) ☐ Autres (veuillez décrire ci-dessous)
13	Quelles autres barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région?	_____

14	Quelles barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région? (Veuillez sectionner tous les énoncés qui s'appliquent)	☐ L'appartenance ethnique ☐ Le statut socioéconomique ☐ L'identité du genre ☐ Autres (veuillez décrire ci-dessous)
14	Quelles barrières culturelles ou socio-économiques, apercevez -vous, à l'accès à la stimulation cérébrale profonde dans votre région?	_____
15	Avez-vous d□autres informations ou pensées à nous partager?	_____

CHAPTER 4: Canadian Access to Deep Brain Stimulation for Movement Disorders: A Nationwide Retrospective Study

Canadian Access to Deep Brain Stimulation for Movement Disorders: A Nationwide Retrospective Study

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ABSTRACT

Background

The public healthcare system in Canada aims to provide accessible, medically necessary care to all Canadians. However, vast geography with sparsely populated Canadian presents unique challenges to this goal, that has become increasingly difficult with increasing complexity of healthcare as a result of improving technology and an aging population, as is the case with deep brain stimulation (DBS) for movement disorders.

The current study aims to define current access to DBS for movement disorders in Canada through the use of retrospective data from each of the 15 Canadian centres offering this service. Additionally, we aim to compare current access to that reported by Honey *et al* in 2018, to determine if improvements have been made in providing this therapy to patients who need it, and to determine the impact of the COVID-19 pandemic on delivery of DBS nationally, in terms of decrease in number of cases and recovery of delivery throughout the pandemic. Finally, similar to Honey et al, this study aims to determine if factors such as gender, socioeconomic status, indication, or geographic location impact patients' ability to access DBS.

Methods

A multi-centre, retrospective cohort study was conducted, utilizing retrospectively collected data from each of the 15 centres across Canada that offer DBS. Descriptive statistics were used to demonstrate the distribution of DBS cases across the country, and to compare socioeconomic status, age, gender, and proportion of minority populations in regions where patients reside.

Preliminary Results

A total of 162 patients have been included thus far from four sites (Queen Elizabeth II Health Sciences Centre, Halifax; Centre Hopital University de Sherbrooke, Sherbrooke; London Health Sciences, London; Centre Hospitalier de l'Universite de Montreal, Montreal). The majority of these patients were male, with a mean age of 62.41 years. The majority of cases were for Parkinson's disease (69.29%), and patients were found to reside in areas with higher than provincial median household income and the majority resided in areas with lower than provincial average minority population rate. Newfoundland and Labrador was found to have the poorest access to DBS per capita among included provinces. DBS cases decreased by approximately 50% in the first year of the COVID-19 pandemic, and had not recovered by 2022 to a point where the surgical backlog created can be adequately addressed.

Conclusions

Preliminary findings suggest that access to DBS has not improved since the publication of the study by Honey et al (2018), and that access was negatively affected by the COVID-19 pandemic, as is the case for nearly all surgical disciplines. Significant policy change at a governmental level is required to address the deficit in access to DBS, and further investigation is required to determine regions of the country where need for DBS (with assessment of true prevalence of DBS candidates) far exceeds current need.

1 INTRODUCTION

The public healthcare system in Canada, guided by the Canada Health Act, aims to provide accessible, comprehensive, universal, portable, and publicly administrated care (1). However, unique challenges resulting from vast geography with sparsely populated Canadian regions prevent truly accessible health services for all Canadians. This challenge has become increasingly difficult with increasing complexity of healthcare as a result of improving technology and an aging population (2).

Functional neurosurgery is one area of healthcare with rapidly advancing technology. This subspecialty of neurosurgery utilizes neurostimulators and implanted devices for neuromodulation of circuits for a variety of neurological diseases. Movement disorders have been a primary focus of neuromodulation within this specialty, including Parkinson's Disease, essential tremor, and dystonia.

Deep brain stimulation (DBS) is a mainstay of surgical treatment for movement disorders. However, access to this service is limited, resulting from centralization to academic centres in larger cities (3–6). Various socioeconomic and cultural differences have also been shown to impact access to DBS, including race (7–15), gender (8,10,13–16), socioeconomic status/insurance status (7,8,10,13,14,17,18), and lack of referrals to tertiary centers/movement disorder clinics (19,20).

In 2018, Honey *et al* utilized industry data to provide a snapshot of the geographic distribution of Canadian DBS, revealing a disparity in access between provinces, with excellent access to DBS in Saskatchewan and extremely poor access in Newfoundland and Labrador (21).

Since 2018, the Canadian healthcare system has continued to evolve. In 2020, the COVID-19 pandemic brought unforeseen strain to the system, resulting in significant delays in care for many patients. During the first 31 months after March 2020, approximately 937,000 (14%) fewer surgeries were performed than prior to the pandemic (2019) (22). For patients with movement disorders, overall care has been found to be significantly impacted by the COVID-19 pandemic, with one recent Canadian study reporting patients with Parkinson's disease experiencing amplification of pre-pandemic poor experiences with healthcare (23).

The current study aims to describe current access to DBS for movement disorders in Canada through the use of retrospective data from each of the 15 Canadian centres offering this service. Additionally, it aims to compare current access to that reported by Honey *et al* in 2018, to determine if improvements have been made in providing this therapy to patients who need it, and to determine the extent of the impact COVID-19 pandemic had on delivery of DBS nationally, in terms of decrease in number of cases and recovery of delivery throughout the pandemic. Finally, similar to Honey *et al*, this study aims to determine if factors such as gender, socioeconomic status, indication, or geographic location impact patients' ability to access DBS.

2 METHODS

Ethics approval was obtained through the Hamilton Integrated Research Ethics Board (HIREB#15846). Additionally, individual institutional research ethics board approval for each included site was obtained prior to site inclusion.

Included sites were Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia; Centre Hospitalier Universitaire de Quebec-Universite Laval, Quebec City, Quebec; Centre Hopital University de Sherbrooke, Sherbrooke, Quebec; Centre Hospitalier de l'Universite de Montreal, Montreal, Quebec; Montreal Neurological Institute, Montreal, Quebec; The Ottawa Hospital, Ottawa, Ontario; London Health Sciences, London, Ontario; Toronto Western Hospital, Toronto, Ontario; Sunnybrook Hospital, Toronto, Ontario; Health Sciences Centre, Winnipeg, Manitoba; Royal University Hospital, Saskatoon, Saskatchewan; Regina General Hospital, Regina, Saskatchewan; University of Alberta Hospital, Edmonton, Alberta; Foothills Medical Centre, Calgary, Alberta; Vancouver General Hospital, Vancouver, British Columbia.

Included patients were adults (18 years of age or older) with diagnosis of a movement disorder (Parkinson's disease, essential tremor, dystonia) treated with novel DBS implantation at a Canadian centre between January 1, 2019 and December 31, 2022.

Retrospective chart reviews were completed, capturing demographics (age at time of surgery, gender), as well as indication for DBS, and geographic location (recorded as forward sortation area codes - first three digits of postal code).

Individual forward sortation area codes were queried using publicly available Statistics Canada 2021 census data for median household income and 'total visible minority population' for regions. Statistics Canada utilizes The Employment Equity Act's definition of visible minority, "persons, other than Aboriginal peoples, who are non-Caucasian in race or non-white in colour."(24) This population primarily consists of South Asian, Chinese, Black, Filipino, Arab, Latin American, Southeast Asian, West Asian, Korean, and Japanese groups (25).

To determine distance of region to the centre in which patients received treatment, the open access service Cybo was utilized to capture regions associated with patients' forward sortation area codes. In instances where the first three digits corresponded to more than one municipality, the municipality with the largest population was utilized for analysis. Distance to centre was then estimated using Google Maps (26).

To determine rurality of included patients, the Canadian Alliance for Healthy Hearts and Minds map was used. Individual forward sortation areas were queried for the binary outcome "yes/no". This tool categorized communities rural based if less than 20% of postal codes fell within a metropolitan region known as a "census metropolitan area" or "census agglomeration" (27).

To visualize distribution of cases from each centre, a map was generated with individual data points representing forward sortation areas. A map was generated using Maptive (28). All other figures were generated using GraphPad Prism version 10.2.0 (29). Descriptive statistics were used for data analysis. Categorical variables are reported as counts and percentages and continuous variables are reported as mean with standard deviation (SD).

3 PRELIMINARY RESULTS

To date, 162 patients have been included from four sites (Queen Elizabeth II Health Sciences Centre, Halifax; Centre Hopital University de Sherbrooke, Sherbrooke; London Health Sciences, London; Centre Hospitalier de l'Universite de Montreal, Montreal). Data collection is ongoing at remaining sites.

The majority of patients were male (n=102, 63%), regardless of institution . This was also the case for Parkinson's disease (69.29%) and Essential tremor (54.17%), however nearly all patients receiving DBS for dystonia were female (9.09% male). Mean age of all patients was 62.41(SD 8.95). See Figure 1 for distribution of patient age. Ages of patients were similar across sites, however patients with dystonia were younger (50.27±13.28) than those with Parkinson's Disease (62.16±7.88) or essential tremor (69.33±4.86). See Table 1 for demographics of included patients.

A number of patients at the included sites traveled great distances for operative management (mean 173.93km ± 268.99). The sites with the greatest proportion of patients travelling from ≥100km away were Halifax (71.11%) and London (51.43%), followed by Sherbrooke (36.36%) and finally CHUM (16.12%), where the vast majority of patients resided nearby. The only included site where patients travelled from out of province was Halifax (NS 60.00%, PEI 17.78%, NB 17.78%, NL 44.44%). See Figure 2 for residence of patients receiving DBS at included sites.

In terms of rurality, the majority of patients lived in urban areas (85.19%). The site with the highest proportion of patients residing in rural areas was Halifax (33.33%), and the two provinces with the highest number of patients from rural areas were New Brunswick and Prince Edward Island (37.50%). See Table 2 for details on rurality of patient population.

The highest rate of DBS cases per capita in an included region thus far was Prince Edward Island (0.005%). When estimated prevalence of movement disorders for which patients were treated with DBS, patients in Prince Edward Island also had the highest rate per estimated patient prevalence in our population. Overall, patients with Parkinson's disease had the highest rates of DBS, however dystonia was better served in Newfoundland and Labrador and Prince Edward Island than other movement disorder indications. See Table 3 for further details of DBS cases per capita for included sites.

Included patients were found to live in areas with higher than provincial median household income, aside from Ontario. Additionally, patients were from areas with lower than provincial average visible minority rate, aside from patients from Newfoundland and Labrador and Prince Edward Island. See Table 4 for details regarding characteristics of patient residence compared with the general population of each province.

With respect to the impact of COVID-19, there were no DBS cases at any of the included centres during April or May of 2020, with the advent of the first wave of the pandemic in Canada. With the decrease in case numbers over the summer of 2020, DBS cases increased once again, decreasing following periods with higher numbers of COVID-19 cases throughout the pandemic.

January 2022 had the highest number of COVID-19 cases in Canada throughout the entire pandemic (1,054,300) (30), and no DBS cases were performed at included sites during that period. See Figure 3 for details regarding DBS cases performed per site vs. COVID-19 cases per month in Canada.

Overall, half as many cases per month were performed across all included sites in the first year of the pandemic. In the second year of the pandemic, 27% less cases were performed than in the period prior to the pandemic, however case numbers increased 12.5% higher than pre-pandemic cases in the third year of the pandemic, with two sites (London and Sherbrooke) increasing case numbers compared to pre-pandemic frequency. See Table 5 for details regarding average monthly cases performed by site.

4 DISCUSSION

The vast geographic landscape and sparse population density in Canada present unique challenges to the delivery of healthcare resources. Preliminary results of this study suggest that regions of Canada are better serviced in the delivery of DBS than others.

In terms of access per capita, Newfoundland and Labrador was underserviced compared to other provinces included in the preliminary analysis. This is notable given Quebec and Ontario have a number of additional sites that have not had data included thus far. Therefore, Newfoundland and Labrador is likely to be exceptionally underserved in terms of total population when compared with other provinces across Canada. This is in keeping with previous findings (21), providing evidence for Newfoundland and Labrador having the worst access to DBS across the country.

There is no functional neurosurgery site in the province, with patients needing to travel long distances to Halifax for assessment and surgery. This can be costly to patients and their families. Additionally, there is limited neurology services in the province, so many patients are diagnosed and managed by primary care physicians. It is interesting to note, however, that when patients are considered by indication, patients with dystonia appear to have better access to DBS in Newfoundland and Labrador than the other provinces included thus far. This may be due to early referral from rural physicians uncomfortable managing dystonia without subspecialisation, leading to improved access to DBS through movement disorder neurologists. Similarly to the study by Honey *et al* (21), it is worth considering that the small population in the province means that small fluctuations in numbers of implanted patients would considerably change the rate of DBS per capita.

The majority of patients in the study population were male. This is consistent with previous research into barriers to DBS access, which reveals that gender may be a barrier to access (8,10,14–16). The exception to this was dystonia patients, of which the majority were female. Given the male:female ratio of adult onset craniocervical dystonia is 1:1.5-2 (31), this may account for this difference. Parkinson's disease is twice as common in men than women (32), which may explain gender differences observed here and in previous studies. Essential tremor also has a similar prevalence between genders, however some studies have reported a slight male predominance (33). Therefore, gender differences noted here and in previously published studies may be a result of epidemiologic factors as opposed to referral or treatment bias on behalf of providers.

The mean age in this study was 62.41±8.95, similar to previous studies (21,34). Previous literature does suggest that patients with advanced age have comparatively less access to DBS than younger counterparts (34), consistent with current findings.

Similar to previous research, more patients were implanted with Parkinson's disease than other indications (34), in spite of higher prevalence of essential tremor than the other two indications of interest. Unsurprisingly, given the relatively high prevalence of essential tremor, it is therefore the most underserved of movement disorders. This may be due to adequate medical management for many patients, or due to need for education for both patients and care providers about the utilization of DBS therapy for this indication.

Many patients travelled a significant distance for DBS therapy (173.93±268.99), however there was a great deal of variation by site. Patients treated in Halifax travelled the greatest distance for treatment, and provincially, patients in Newfoundland and Labrador travelled the greatest distance for DBS (1,482.45km±6.15). This is an important consideration, given the relatively low DBS rate in the province. This far distance to travel and costs associated with travelling may be a significant barrier to access for DBS in Newfoundland and Labrador. Providing funding for travel or utilization of virtual care platforms to minimize visits for assessment, follow up, and reprogramming (20) may be an opportunity for future investigation to improve access in this region.

In terms of rurality, one third of all patients treated in Halifax were from rural communities, while the vast majority of patients treated in Quebec and Ontario were from urban centres. Given

the makeup of communities in the Atlantic provinces who travel to Halifax for DBS, this difference is understandable. Few cities exist in the Atlantic provinces, whereas a number of large cities in Southern Ontario are served by the site in London and the large population in Montreal would explain the proportion of urban patients at those sites.

Similar to findings by Honey *et al* (21), patients in the study population were found to have a higher median household income than the provincial median household income for their respective regions. The exception to this was Ontario where patients had a lower median household income than that of the province, although it will be interesting to see if this difference is minimized or results are in keeping with other provincial findings when patients from Toronto and Ottawa are included in the final analysis. This will likely be the case, given higher socioeconomic status patients residing in larger urban centres that would be referred to these sites.

In terms of average rate of minority populations living in regions where patients received DBS, the study population was found to reside in regions with lower than average rate of minority populations. This is in keeping with previous literature, which suggests patients living in regions with lower proportions of minority populations have better access to DBS (15,21). The exception to this was in Newfoundland and Labrador and Prince Edward Island. It is worth noting that these provinces have a relatively low rate of minority populations, and that the majority of patients in these provinces (all in Newfoundland and Labrador) were from urban centres, which typically have a higher proportion of minority populations than rural areas.

4.1 COVID-19 Impact on Delivery of DBS

Fluctuations in delivery of DBS occurred at three of the four included sites in this study. Similar to other surgical series (35-38), DBS cases decreased by 50% across all included sites in the first year of the pandemic, compared to the year prior. Overall, by year three, cases increased to a 12.5% compared to pre-pandemic numbers. This is largely due to a 51.9% increase in DBS cases in London compared to pre-pandemic numbers. Across all sites, assuming the number of DBS candidates remains constant over time, by the third year of the pandemic, a deficit across all sites of an average of 3.08 patients per month exists. As such, the increase in cases of 12.5% is not enough to address this deficit in delivery.

Literature from a number of surgical disciplines have highlighted the decrease in operative cases throughout the pandemic to the extent that a backlog has been created that is not being adequately addressed with resumption of pre-pandemic number of cases (35–38). A similar scenario is observed among this cohort, suggesting that policy changes are required to address the large number of patients waiting for DBS following the pandemic.

Given the impact of COVID-19 on delivery of DBS, it is difficult to ascertain whether delivery of DBS has improved since the 2018 paper by Honey *et al* (21), however comparing 2019 and 2022 to that earlier study period (2015-2016), the only province with a higher number of DBS cases is Prince Edward Island. This suggests further work is needed to improve access to this service in Canada.

It is important to consider provincial caps on device funding, utilize virtual care to minimize the impact of travel and socioeconomic status as barriers to access, and to increase access to movement disorder neurologists to expedite diagnosis and surgical referral.

4.2 Limitations

Limited conclusions can be drawn regarding access to DBS in Canada, given the preliminary nature of results with the absence of data for 11/15 Canadian sites for DBS at this point. Data collection is ongoing at remaining sites. This is particularly important to consider in evaluation of DBS delivery in Ontario and Quebec, given the absence of data from additional sites in these provinces (McGill, Ottawa and Toronto). Current data underrepresents access to DBS for individuals living in these provinces.

Evaluation of socioeconomic status in the current study is limited by estimations used for mean household income for individual patients. This data was not individually collected, but rather estimated based on forward sortation area codes, which may represent large populations (the average population per forward sortation area is 22,473.86, and the largest population in a single forward sortation area is 149,238) (39).

Forward sortation area was also used to estimate distance from patients' residence to surgical site, and average rate of minority populations. Additionally, average rate of minority populations is estimated by Statistics Canada using 25% of the population. Therefore, it may not be accurate for individual patients in our sample.

Ultimately, assessment of access to DBS requires an understanding of the need for this service across Canada. Previous studies have failed to identify the true prevalence of candidates for DBS nationally. This study attempts to define the need through estimated prevalence of indication diagnoses in each region, although certainly every patient with Parkinson's disease, for example, would not be an appropriate candidate for DBS. Quantification of need to match to access is important to identify regions where need far surpasses access to more appropriately direct funding. This is an area for future research.

5 CONCLUSIONS

While national access to DBS, the preliminary aim of this study, cannot yet be quantified, preliminary analyses from four included sites suggests that access to DBS has not improved following the study by Honey *et al* (21). Additionally, regional differences are apparent, including poor access in geographically isolated regions such as Newfoundland and Labrador, found to have the poorest access to DBS. As observed in other surgical disciplines, COVID-19 caused a decrease in the number of DBS cases performed over the course of 2020 and 2021, leaving a deficit of cases that is not being adequately addressed by all but one included site. Significant policy change is required at a provincial governmental level to DBS across Canada, and further investigation is required to determine regions of the country with the greatest need for improvement in services with respect to candidates for this life-changing procedure.

FIGURES

Figure 1: *Distribution of patient age at time of surgery. The number of DBS patients is shown for each 5-year age group.*

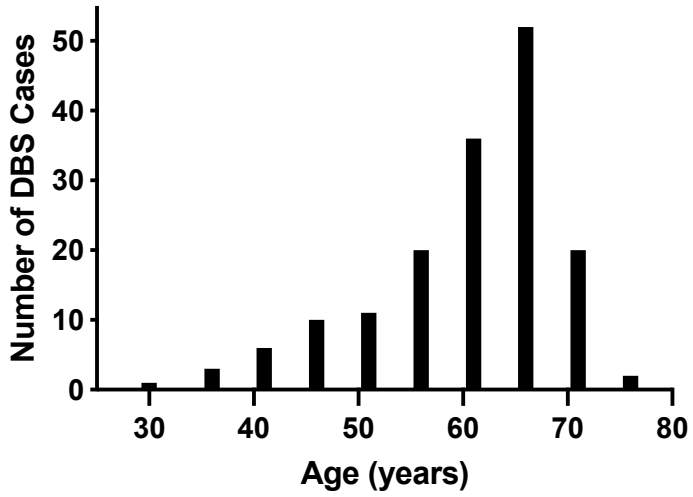


Figure 2: *Residence of patients receiving DBS at included sites*

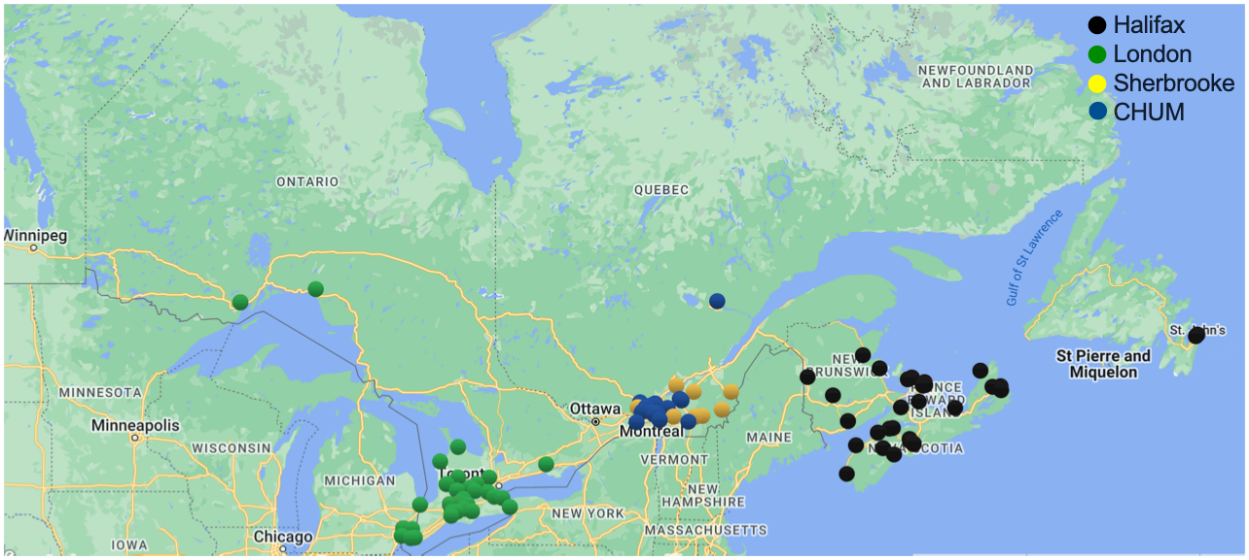
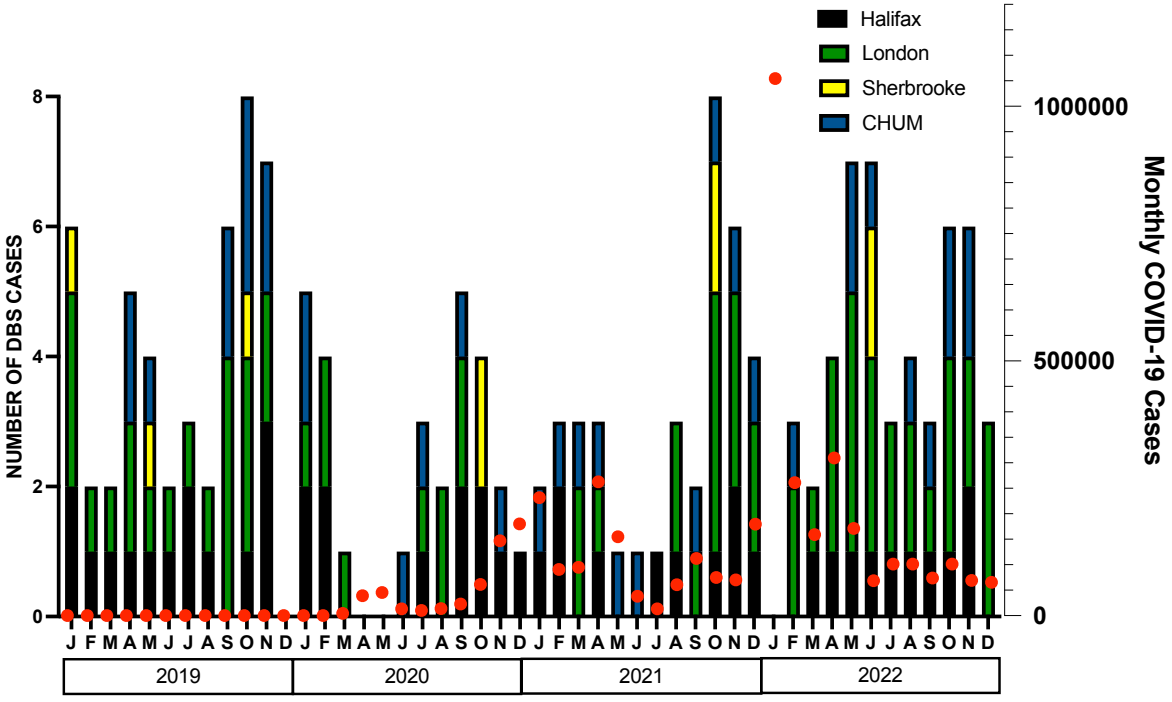


Figure 3: *Number of DBS cases per month of study period by site (columns) with number of COVID-19 cases per month in Canada (red points)(WHO COVID-19 dashboard (30)).*



TABLES

Table 1: *Patient demographics by centre*

		Halifax N=45	London N=70	Sherbrooke N=11	CHUM N=36	Total N=162
Indication n (%)	Parkinson's Disease	36 (80)	57 (81.4)	3 (27.2)	31(86)	127 (78.4)
	Essential Tremor	6 (13)	8 (11.4)	5 (45.5)	5 (14)	24 (14.8)
	Dystonia	3 (7)	5 (7.2)	3 (27.2)	0	11(6.8)
Sex (% Male)		62.22	65.71	63.64	58.33	62.96
Mean Age (SD)		60.96 (9.99)	63.40 (7.88)	61.45 (13.17)	62.61 (8.14)	62.41 (8.95)
Mean distance from patients' residence to centre (km)(SD)		280.87 (307.59)	173.16 (291.62)	93.83 (81.57)	66.23 (125.32)	173.93 (268.99)
Mean of estimated median household income (SD)		78,533.33 (16,726.70)	85,597.14 (16,880.38)	68,945.45 (12,588.04)	77,975.00 (21,503.64)	80,810.49 (18,214.70)
Average rate of visible minority population in patient region of residence (SD)*		8.56 (8.00)	15.37 (14.02)	4.26 (3.43)	16.39 (17.79)	12.95 (13.68)

*Estimated from 25% of population.

Table 2: *Rurality of included patients' residence*

Centre	Region of patient residence	Number of rural patients (%)	Total
Halifax (n=45)	NL (n=2)	0	15 (33.33%)
	NS (n=27)	9 (33.33%)	
	PEI (n=8)	3 (37.50%)	
	NB (n=8)	3 (37.50%)	
London (n=70)	ON (n=70)	4 (5.71%)	4 (5.71%)
Sherbrooke (n=11)	QC (n=11)	2 (18.18%)	5 (10.64%)
CHUM (n=36)	QC (n=36)	3 (8.33%)	
All included patients (n=162)			24 (14.81%)

Table 3: *DBS cases per capita*

Region	Population	Cases per capita	Estimated number of patients with movement disorders			DBS cases per estimated number of patients with movement disorders		
			PD[A]	ET[B]	D[C]	PD	ET	D
NL (n=2)	526,046	0.0004%	1,220	6,996	162	0.08%	0	0.62%
NS (n=27)	989,154	0.003%	2,440	13,156	305	0.90%	0.03%	0.33%
PEI (n=8)	159,179	0.005%	370	2,117	49	1.62%	0.05%	2.04%
NB (n=8)	783,814	0.001%	2,150	10,425	242	0.33%	0.01%	0
QC (n=47)	8,551,865	0.0006%	22,890	113,740	2,638	0.15%	0.009%	0.11%
ON (n=70)	14,757,582	0.0005%	45,500	196,276	4,553	0.13%	0.004%	0.003%
MB	1,381,809		3,985	18,378	426			
SK	1,165,963		2,655	15,507	360			
AB	4,412,013		9,725	58,720	1,361			
BC	5,173,896		15,280	68,813	1,596			
NT	44,395			590	14			
YT	42,109			560	13			
NU	39,581		20	526	12			
Canada (n=162)	38,027,406	0.0004%	106,225	505,764	11,731	0.12%	0.005%	0.09%

A - According to prevalence by province/territory for 2020-2021 (age standardized to ≥ 40 years) (40)
B – According to prevalence from global meta-analysis in 2021 (1.33% for all ages) (41)
C – According to prevalence from global meta-analysis in 2022 (0.03085% for all ages) (42)

Table 4: *Characteristics of study population compared with general population by region of patient residence*

Region	Median household income (2020)	Mean of median household incomes for patients in region (SD)	Difference	Visible minority rate*	Average visible minority rate for patient regions*	Difference	Average distance from site for patient regions
NL (n=2)	71,500	86,600.00 (38,749.45)	+15,100.00	3.4	6.15 (5.02)	+2.75	1,482.45 (6.15)
NS (n=27)	71,500	75,644.44 (16,907.24)	+4,144.44	9.8	9.13 (9.14)	-0.67	142.50 (147.63)
PEI (n=8)	73,500	81,562.50 (5,747.29)	+8,062.50	9.5	11.04 (7.69)	+1.54	310.60 (14.28)
NB (n=8)	70,000	83,237.50 (19,047.15)	+12,237.50	5.8	4.79 (1.72)	-1.01	417.71 (69.17)
QC (n=47)	72,500	75,861.70 (20,030.29)	+3,361.70	16.1	13.56 (16.44)	-2.54	72.69 (116.34)
ON (n=70)	91,000	85,597.14 (16,880.38)	-5,402.86	34.3	15.36 (14.02)	-18.94	173.16 (291.62)
MB	79,500			22.2			
SK	82,000			14.4			
AB	96,000			27.8			
BC	85,000			34.4			
NT	127,000			12.2			
YT	100,000			12.8			
NU	118,000			3.6			
Canada	84,000	80,810.49 (18,214.70)	-3,189.51	26.5	12.95 (13.68)	-13.55	173.93 (269.00)

Comparison of study population to Canadian population by province/territory. All data obtained from 2021 Canadian census (2020 data), Statistics Canada.
*Estimated from 25% of population.

Table 5: *Mean DBS cases per month throughout pandemic across all sites*

Date	Halifax	London	Sherbrooke	CHUM	Total
A)March 1, 2019-February 28, 2020	1.25	1.58	0.17	1	4
B)March 1, 2020-February 29, 2021	0.83 (33.6% fewer than A)	0.5 (68.35% fewer than A)	0.17	0.5 (50% less than A)	2 (50% less than A)
C)March 1, 2021-February 28, 2022	0.58 (53.60% fewer than A)	1.42 (10.13% fewer than A)	0.17	0.17 (83% less than A)	2.92 (27% less than A)
D)March 1, 2022-December 31, 2022	1 (20% fewer than A)	2.4 (51.9% more than A)	0.2 (17.65% more than A)	0.9 (10% less than A)	4.5 (12.5% more than A)

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CONTRIBUTORSHIP STATEMENT

Melissa Lannon contributed significantly to the study's concept and design, data analysis, and interpretation of the results. She wrote the first draft of the manuscript, provided critical revisions, and gave final approval of the submitted manuscript.

Amanda Martyniuk contributed to data collection and analysis. She provided critical revisions and gave final approval of the submitted manuscript.

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Forough Farrokhyar contributed to the study's concept and interpretation of the results. She provided critical revisions and gave final approval of the submitted manuscript.

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CHAPTER 5: Conclusions and Future Directions

5.1 Summary of findings

This doctoral thesis describes three main studies evaluating the landscape of deep brain stimulation (DBS) in Canada through the quadruple aim of health service research (cost, patient perspective, healthcare provider perspective, population level data) (1–4). The findings from these studies highlight the need for a multifaceted approach to improving equity in access to DBS. Chapter 2 addressed the aim 'reduce the per capita cost of healthcare' and described the cost-effectiveness of DBS compared with best medical therapy, highlighting the need to consider cost as it pertains to the duration of therapy for patients. Choosing DBS, a more cost-effective treatment strategy in Parkinson's disease, would allow reallocation of healthcare resources to provide solutions to barriers to access identified in Chapter 3. Drawing from healthcare provider and patient/caregiver perspectives to address the aims 'improve the patient and caregiver experience' and 'improve the work life of healthcare providers', the mixed methods survey of stakeholders for DBS for movement disorders in Canada (Chapter 3) identified barriers to accessing DBS along the entire trajectory of the patient referral pathway. Additionally, expert opinion from healthcare providers was used to attempt to estimate the prevalence of candidates for DBS with movement disorders across Canada to define the need for this service by region. Finally, Chapter 4 addresses the aim 'improve the health of populations' through identification of characteristics of patients who had previously undergone DBS therapy in Canada. This multicentre retrospective study assessed the estimated socioeconomic status and proportion of minority populations living in the regions where implanted patients resided, as well as geographical distance to a functional neurosurgical centre to identify potential facilitators to accessing DBS. Additionally, preliminary results assessed the impact of the COVID-19

pandemic on delivery of DBS in Canada as well as ability of the healthcare system to return to pre-COVID delivery of this service and address the backlog in cases created during the pandemic.

5.2 Strengths and limitations

This work presents a comprehensive assessment of access to DBS in Canada. The strength of this work is in the rigorous, comprehensive, and structured methods used.

A strength of the systematic review presented in Chapter 2 is the consideration of available evidence regarding the cost-effectiveness of DBS compared with best medical therapy to generate an overall effect estimate through meta-analysis. This provides a comprehensive assessment of cost of the intervention with regard to the Quadruple Aim of health service research. Decision makers can utilize these findings to allocate financial resources appropriately to increase access to DBS where it is most needed. Another strength is the comprehensive quality assessment performed, highlighting the need for rigorous economic evaluations based on primary datasets to inform decision-making. This study was limited by the quality of evidence available, with significant heterogeneity between evaluations, and insufficient evidence to allow for stratification by country income, study type, disease (only evidence available on Parkinson's disease), and disease severity as had been intended in the study protocol. Heterogeneity also exists between studies with regard to values and resources between countries. This was accounted for in the transferability assessment. Finally, the use of model-based evaluations in the absence of trials with long durations may introduce some degree of bias, as assumptions are

made with regard to stability of treatment effects and double-counting of study populations in evaluations where evidence was drawn from previous literature.

The novel approach used in Chapter 4 sought perspectives from healthcare providers and patients/caregivers to gain a comprehensive picture of barriers to accessing DBS across Canada and attempt to estimate candidates for DBS by region. The strength in this approach is the identification of solutions to improve access to DBS that vary by region. This study was limited by the response rate, and therefore estimates of prevalence were associated with low concordance rates and therefore confidence in these estimates is very low.

The strength of the work presented in Chapter 4 lies in the comprehensive nature, with inclusion of all sites across Canada. Preliminary analyses were able to determine the decrease in number of DBS cases at included sites during the COVID-19 pandemic, as well as the limited recovery in operative cases throughout the course of the pandemic and beyond. Additionally, comparison was drawn between a previous assessment of access to DBS and preliminary results suggest access has not improved and further action is required to provide equitable access to this service. Limitations include absence of data from 11/15 sites at this point, potential estimation error for socioeconomic status, distance to surgical site, and rate of minority populations by region as opposed to individual patient data.

Most notably in this doctoral thesis is the limitation that need for DBS in Canada remains poorly defined. Prevalence of candidates was poorly estimated in Chapter 3, and remains absent from the consideration of access in Chapter 4, as in previous literature. This remains a key determinant

of access, as it is impossible to determine if current access is adequate without an understanding of the need for the service.

5.3 Implications for practice

The findings from this doctoral thesis support decision makers in making changes to resource allocation to better serve populations across various regions. In terms of cost, Chapter 2 provides evidence that DBS can be considered a cost-effective solution, and therefore increasing funding for this therapy may provide a cost benefit. Financial resources can then be redirected to additional initiatives.

A number of potential solutions to increase access to DBS have been identified through the findings of this research. The first of these is increasing available human resources, including the number of available movement disorder specialists and functional neurosurgeons in Canada. This would ameliorate some of the burden of waitlists, however beyond increasing the number of providers in population-dense regions, this would not decrease the burden of travel and expenses for Canadians living in isolated, resource-poor regions of the country. Additional resources include operative time and removing provincial caps on the number of DBS implants available annually. Providing funding for unlimited DBS implants per year has been proven to be a successful strategy for improving access in Saskatchewan, boasting the best access to DBS in Canada as a result (5). Given the cost-effectiveness of DBS compared with standard therapy as demonstrated in Chapter 2, increasing funding for resources required to deliver this service is an appropriate strategy, but will not improve access in an equitable manner without additional measures.

As identified in the preliminary analyses presented in Chapter 4 and supported by previous literature, patients with lower socioeconomic status, racial minorities, and those residing great distances from sites offering DBS may be at risk of poorer access to DBS. In an effort to decrease the burdens socioeconomic status and geographic location place as barriers to access, the use of telemedicine may provide improved access through avoidance of travel for multiple appointments (assessments, surgical bookings, follow-up, reprogramming). Creation of regional telemedicine movement disorder clinics to complete assessments and streamline referral pathways may be an alternative mechanism of access for patients.

Even with improvements to referral pathways and improving access through use of telemedicine, education strategies are required to address misconceptions and poor understanding of movement disorders in general, as well as indications for DBS, risks and benefits of this therapy, and the process of referral for this treatment.

Applying these potential strategies would require significant collaboration between overseeing Provincial and Territorial ministries of health. The best utilization of resources would not see functional neurosurgery services in each province and territory. Therefore, collaboration will be required to ensure regions without this service do not suffer inadequate access as a result. Development of regional referral clinics utilizing telemedicine may standardize referral pathways to improve access across Canada.

5.4 Implications for future research

Further investigation is required with respect to economic evaluations in the Canadian context. Findings presented in Chapter 2 emphasize the need for economic evaluations conducted alongside primary studies.

Collaboration and methodology utilized in Chapter 4 provide a foundation for the development of a national database for DBS patients in Canada. This would allow further investigation of factors that potentially increase likelihood of accessing DBS for individual patients and regional populations.

Perhaps most importantly, further investigation is required to better understand how the prevalence of candidates for DBS varies by region in Canada. Development of a national database of movement disorder patients may be a means to answer this question, as the degree of granularity required to answer this question is not available in current health databases in Canada. Alternatively, utilizing methods outlined in Chapter 3 may be effective if higher response rates can be achieved. Understanding the distribution of prevalence of these conditions is crucial, as it is impossible to comprehensively assess access to a service without an in depth understanding of the candidates in need of the service, to determine if the need is being met.

5.5 Conclusion

This doctoral thesis comprises an assessment of access to DBS for movement disorders in Canada through the lens of the Quadruple Aim of health service research. Findings emphasize the importance of defining the need for this service through an understanding of the prevalence of candidates for this therapy, and lend potential solutions to increase access across Canada,

through increased human and technology resources, improved education, and further investigation.

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