Canadian healthcare capacity gaps for disease-modifying treatment in Huntington’s disease: a survey of current practice and modelling of future needs

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ABSTRACT

Objectives Disease-modifying therapies in development for Huntington’s disease (HD) may require specialised administration and additional resource capacity. We sought to understand current and future capacity for HD management in Canada considering the possible introduction of an intrathecal (IT) disease-modifying treatment (DMT).

Design, setting and participants Using a case study, mixed methods framework, online surveys followed by semistructured interviews were conducted in late 2020 and early 2021. Neurologists from Canadian HD (n=16) and community (n=11) centres and social workers (n=16) were invited to complete online surveys assessing current HD management and potential capacity to support administration of an IT DMT.

Outcome measures Survey responses, anticipated demand and assumed resource requirements were modelled to reveal capacity to treat (ie, % of eligible patients) by centre. Resource bottlenecks and incremental support required (full-time equivalent, FTE) were also determined.

Results Neurologists from 15/16 HD centres and 5/11 community centres, plus 16/16 social workers participated. HD centres manage 94% of patients with HD currently seeking care in Canada, however, only 20% of IT DMT-eligible patients are currently seen by neurologists. One-third of centres have no access to nursing support. The average national incremental nursing, room, neurologist and social worker support required (full-time equivalent, FTE) were also determined.

Conclusions In Canada, there is little to no capacity to support the administration of an IT DMT for HD. Current inequitable and inadequate resourcing will require solutions that consider regional gaps and patient needs.

INTRODUCTION

Huntington’s disease (HD) is a rare, inheritable, autosomal-dominant, neurodegenerative disorder that affects an estimated 4700 people living in Canada1,2 and its prevalence is increasing.3 HD is caused by an expansion of the CAG (cytosine, adenine, guanine) trinucleotide repeat in the huntingtin (HTT) gene, which translates into an aberrant HTT protein. Mutant huntingtin (mHTT) leads to neuronal dysfunction and death, with progressive motor, cognitive and psychiatric impairments.4,5 The disease typically presents during the prime of adulthood, with a median survival of 18 years from motor symptom onset or ‘manifest’ disease.1,4 Despite over 100 years of research, HD remains incurable and multidisciplinary symptom management is the mainstay of treatment.1,4,5

Knowing the genetic cause of HD, however, has been advantageous to the development of targeted therapeutics, with recent research focused on HTT/mHTT-lowering strategies.4,6-9 One class of agents, antisense oligonucleotides (ASOs), showed promise as a disease-modifying treatment (DMT) in early studies.7,10 Although some ASOs have since failed in later stage trials, new treatments...
continue to be studied.\textsuperscript{11} Many emerging therapies will also require specialised modes of administration.\textsuperscript{9,11,12} Health Canada has acknowledged the need for a national drug strategy that enables fair, consistent and evidence-based access to specialised drugs for rare diseases such as HD.\textsuperscript{13}

Considering the late stage exploration of intrathecal (IT) agents for movement disorders\textsuperscript{14,15} and anticipated healthcare capacity limitations,\textsuperscript{16–18} challenges were expected in the geographically vast, regionally diverse healthcare system.\textsuperscript{19} In alignment with implementation science and practice improvement,\textsuperscript{20} we sought to understand current and future capacity for HD management in Canada and to qualify potential gaps arising from the theoretical introduction of an IT DMT.

**METHODS**

**Study design**

Using a case study, mixed methods framework,\textsuperscript{21} cross-sectional online surveys and follow-up phone interviews were modelled on a global study,\textsuperscript{16} modified by the Canadian study team, and validated by both Canadian neurologists with experience administering an IT DMT\textsuperscript{15,16} and a Canadian HD patient organisation representative. Clinical trial experience indicated that an HD IT DMT could be administered by a trained neurologist in a hospital or community setting, given adequate supports and capacity. The study recruited neurologists from Canadian movement disorder clinics\textsuperscript{25} or social workers meeting the following criteria (see online supplemental appendix table S1 for full criteria):

1. A movement disorder neurologist managing >20 patients with HD and a dedicated HD neurologist (‘HD centres’),
2. A movement disorder neurologist managing <20 HD patients (‘Community centres’),
3. Social workers (also referred to in Canada as ‘Resource Center Directors’) focused on HD client support (‘Resource centres’).

HD centres were identified by the steering committee or referral by survey participants. Identification of Community centres was based on environmental scans conducted on the Canadian Movement Disorder Group website, with the guidance of the steering committee, and by referral within the survey. Resource centre directors were identified directly by the Huntington Society of Canada and Société Huntington du Quebec. Surveys were emailed to each centre (see online supplemental appendix table S2 for invited centres and online supplemental appendix file 2-4 for copies of the survey) in November 2020 requesting that one be completed by the person most familiar with HD healthcare capacity for that centre. Survey questions varied by centre type and were designed to collect dependent variables required for capacity modelling and qualitative data reporting. Guided phone interviews were conducted by a single interviewer to support common question interpretation among participants and validate survey data (see online supplemental appendix file 5 for a copy of the interview guide).

The primary participants in this study were physicians and other healthcare professionals (HCP) (eg, social workers). Informed consent was requested prior to study participation. No patient identifiers, like name, age, gender, address, phone number or health insurance information were collected. Thereby, according to the Tri-Council Policy, site-specific ethics approval and patient consent are not required for use of deidentified secondary data (the Tri-Council Policy Statement, 2019).

**Study objectives and data analysis**

The first objective of the study was to characterise HD patient care across Canada, with a focus on capacity for IT DMT provision. This included understanding the proportion, age and stage of patients with HD currently linked to care as well as the healthcare capacity dedicated to their management.

The second objective was to model the needed capacity of HD centres to deliver an IT DMT in Canada and to highlight key bottlenecks to achieving full provision. Linear quantitative capacity modelling was used to estimate the current and needed capacity (ie, resources and infrastructure). To achieve this, two sets of assumptions, based on a phase III IT DMT trial\textsuperscript{15} and expert Canadian steering committee feedback, were necessary. First, the steps and resources (ie, time and infrastructure) required to administer an IT DMT were assumed (see online supplemental appendix table S3). Second, the anticipated IT DMT demand was calculated as the number of Canadians (national population 38 005 23828) with a diagnosis of manifest HD (prevalence of 13.7 per 100 000\textsuperscript{5}) meeting IT DMT criteria (67.2% with stage 1 or 2 HD and 25–65 years of age\textsuperscript{24}) and expected to seek treatment (70%). Eligible patients were assigned provincially based on population distributions\textsuperscript{23} and then by centre based on the relative proportion of patients with HD currently seen in each centre (per survey response). Percentage of patients linked to care (ie, neurologist-seen) was calculated as the number of eligible patients currently in care (per survey response) divided by the anticipated IT DMT demand (per calculation above) multiplied by 100. Required social worker full-time equivalent (FTE) was based on an assumption of one social worker per HD centre.

The capacity gap was then determined, by centre, as the difference between current capacity (dependent variables) and required future capacity (independent variables). Capacity was modelled for two demand scenarios: (1) capacity to treat patients ‘linked to care’; the percentage of patients with HD currently linked to care and theoretically eligible for an IT DMT that could be treated considering the resources available and (2) capacity to treat ‘all eligible’ patients, that is, the percentage of patients with HD theoretically eligible for an IT DMT that could be treated considering the resources available. The model
used the scarcest resource as the upper limit of a centre’s capacity.

Data reporting
Survey methods are reported according to the CHERIES methodology (see online supplemental appendix table S4). Results are reported using descriptive statistics by centre (anonymous), region (Western Canada, Ontario, Quebec and Atlantic Canada; online supplemental appendix table S2) or nationally. In cases where national extrapolations were made, data points for non-responding centres were assumed to be equal to the national average of the responding centres (ie, archetyped). For continuous variables, measures of central tendency (medians and means) and dispersion (SD, range) are reported. Any binary or categorical variables are described with frequencies and percentages. Time is reported in units of FTE with one FTE=40 hours/week and 48 weeks/year. Microsoft Excel was used for data analysis and visualisation.

Post hoc analysis
To test the impact of an extended dosing interval (ie, every 16 weeks vs every 8 weeks) on capacity for treatment, changes to the model’s assumptions were applied (ie, half of the required resource time). The same methods outlined above were then used to assess the key outcomes of interest; number of centres with capacity, % of IT DMT-eligible patients treated, and incremental FTE required to treat all eligible patients.

Patient and public involvement
Importantly, the design, analysis and reporting of this study involved a representative (author and registered social worker, Angèle Bénard) from Huntington Society of Canada, a non-profit organisation that supports Canadians impacted by HD.

RESULTS
HD centres and HD patient distribution
A total of 16 HD centre neurologists, 11 community neurologists and 16 social workers met eligibility for inclusion in the surveys. Responses were received by a total of 15/16 (93.8%) HD centre neurologists, 5/11 (45.5%) community neurologists and 16/16 (100%) social workers responded to the survey. Follow-up with non-responding community centres indicated that low survey participation was due to a lack of HD case load in those clinics and, thus, a perceived lack of value in participating in the study.

Most HD centres (69.2%, n=9/13) have more than a quarter of patients living >2 hours’ drive away, with Western and Atlantic Canada reporting the highest remote patient populations (three centres had up to 75% of patients living >2 hours’ drive away). Ten centres (66.7%) support remote patients by telephone, telemedicine and/or satellite clinics (see online supplemental appendix table S5). Average wait time for a first visit at an HD centre is 7.1 (SD: 7.7) months.

Patients with HD represent a fraction of the entire movement disorder patient population (mean 17.2%; n=2193/12740) currently seeking care within HD centres. However, survey responses and extrapolation suggest that HD centres (n=15 responding +n=1 archetyped) manage 94% of patients with HD currently seeking care in Canada, with community centres (n=5 responding +n=6 archetyped) supporting 6%. The average number of patients with HD per HD centre varies by region (figure 1), with the national average being 146 (SD: 121), of which 38 (SD: 32) are in stage 1/2. HD centre neurologists spent 2.5 (SD 2.0) hours/week and 36 (SD: 12) min/visit on care of patients with HD.

Access to multidisciplinary care
The challenge of administering IT therapy rests not just on the procedure itself, but also providing patients in this vulnerable population a support network through a multidisciplinary team (MDT). Of the 10 HCP-types asked about in the survey, HD centres had variable onsite access to each (range: 3–11 HCP types) (figure 2). Notably, 66.7% of centres (10/15) reported having onsite nursing staff, each of whom dedicate an average of 0.6 (SD 0.8) hours/week to HD patient care. Five centres had no access to nursing support. Social workers, additional neurologists, psychiatrists and nurses were the most likely members to be working onsite as part of an MDT (figure 2), with nurses typically being seen at the same visit as the neurologist, but other HCPs requiring separate visits (online supplemental appendix figure S1). Social workers support an average of 263 clients each (160 patients, 64 caregivers and 39 others) from the HD community and spend approximately 28.0 (SD: 11.6) hours/week supporting HD clients (see online supplemental appendix figure S2 for proportion of time per task).

Anticipated demand for an IT DMT in manifest HD
An estimated 18.4% of IT DMT eligible patients are currently linked to care within HD centres (n=15 + n=1

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Figure 1 Regional distribution of Huntington’s disease (HD) patients (stage 1 or 2 vs other) currently seen within Canadian HD centres (n=15). HD, Huntington’s disease.
archetyped), and 1.0% (n=5 + n=6 archetyped) are linked to care in community centres; 80.6% are likely not currently under the care of a neurologist. Regionally, Quebec had the highest proportion of eligible patients not linked to care (87.3%), and the Atlantic had the highest proportion linked to HD or community centres (24.8% and 2.9%, respectively) (figure 3).

**Modelled capacity for an IT DMT, HD centres only**

When only considering patients linked to care in HD centres, five centres (33.3%) are estimated to have capacity to treat nearly all their IT DMT-eligible patients with HD. Another two centres (13.3%) would be able to provide support to the majority (>50%), but eight centres (53.3%) would have no capacity to support IT DMT administration (figure 4A). The number of centres with available capacity decreases once all IT DMT-eligible patients are accounted for. Just one HD centre (6.7%) is expected to be able to treat all eligible patients at peak demand, six (40.0%) would have some capacity and eight (53.3%) would have none (figure 4B). Considering HD centre capacity alone, there is an 85.9% gap in the capacity to treat all IT DMT-eligible patients with HD.

The average national incremental nursing, room and neurologist/proceduralist time required to support all IT DMT-eligible patients is 0.73, 0.36 and 0.30 FTE per HD centre, respectively (see online supplemental appendix table S6). The most common bottleneck for HD centres was nursing staff (n=9/15), while neurologist time and room/bed availability were limiting for a few (n=4/15 and 2/15, respectively). Interestingly, while 11 HD centre neurologists (73.3%) agreed or completely agreed to be willing to perform IT DMT, four completely disagreed. In interviews, barriers to willingness to administer an IT DMT included lack of time and lack of funding.

**Modelled capacity for an IT DMT, including community centres and resource centres**

Expanding the modelling to include the resources available in community centres and the support required from social workers results in a 93.7% gap in the capacity to treat (nationally) following the introduction of an IT DMT (figure 5). This is driven by limited social worker time. An incremental 0.21 FTE of social worker support per centre would be required to provide IT DMT to all eligible patients with HD (see online supplemental appendix table S6).
fibrosis and Parkinson’s disease. It can be expected that separate visits with social workers and other HCPs place added burden on patients and their families, particularly those living a distance from care.

In a survey of US Huntington Study Group sites, it was estimated that 70% of patients with HD evade care. Our data similarly show that less than 20% of IT DMT-eligible patients with HD are currently managed in Canadian community or HD centres. As such, introduction of and demand for a DMT would strain the system. We confirmed that Canadian HD centres have limited current capacity to administer IT DMTs due to nursing, neurologist or room time. Overall, the incremental FTEs required in Canadian centres appear similar to those predicted internationally. Neurologist capacity and willingness to administer IT DMTs are also serious areas of concern, with shortages and waning interest in the specialty already a threat to the system. Furthermore, when limitations in social worker capacity were accounted for, national capacity to treat decreased to only 6% of IT DMT-eligible patients with HD. Not surprising, given the full absence of resources in some centres, extension of IT DMT dosing to every 16 weeks rather than every 8 weeks had no impact on the number of HD clinics in Canada that have capacity to treat at peak demand (see online supplemental appendix figures S3 and S4): eight centres have zero capacity to treat in either scenario (patients currently linked to care or all eligible). Total gap in the capacity to treat, including support from community centres and social workers, would be 88.9% (a 4.8% absolute improvement) with a halving of administration. Using the every 16-week dosing interval, an additional 0.34 nurse, 0.16 room, 0.13 neurologist and 0.09 social worker FTE would be needed.

**Post hoc analysis**

Applying an IT DMT dosing of every 16 weeks rather than every 8-weeks had no impact on the number of HD clinics in Canada that have capacity to treat at peak demand (see online supplemental appendix figures S3 and S4); eight centres have zero capacity to treat in either scenario (patients currently linked to care or all eligible). Total gap in the capacity to treat, including support from community centres and social workers, would be 88.9% (a 4.8% absolute improvement) with a halving of administration. Using the every 16-week dosing interval, an additional 0.34 nurse, 0.16 room, 0.13 neurologist and 0.09 social worker FTE would be needed.

**DISCUSSION**

In Canada, HD patient care is concentrated in HD centres, where neurologists manage an average of 146 patients with HD per centre; about 10 times the number seen in community centres. This is in line with centres in the USA, where 135 patients with HD/site are seen. In approximately two-thirds of Canadian centres, more than a quarter of patients live over a 2 hours’ drive away, which creates unique issues for follow-up and management of patients receiving therapies between visits. Sixty per cent of HD centres in our survey offered telemedicine services. This is higher than an international survey of HD centres in our survey offered telemedicine services. This is higher than an international survey of HD centres, in which less than a quarter did and suggests that access to HD treatments requiring specialist administration will pose a unique challenge for remote Canadian patients.

Unfortunately, access to multidisciplinary care is inconsistent across the country, with nursing support inaccessible to 5/15 responding centres. Onsite nursing support, nursing time and social worker capacity are prominent areas of need if IT medications are introduced in Canada for HD. The current literature strongly promotes a multidisciplinary approach to HD patient care and research has shown the benefit of MDTs for similar chronic and degenerative conditions, such as cystic fibrosis and Parkinson’s disease. It can be expected that separate visits with social workers and other HCPs place added burden on patients and their families, particularly those living a distance from care.

In a survey of US Huntington Study Group sites, it was estimated that 70% of patients with HD evade care. Our data similarly show that less than 20% of IT DMT-eligible patients with HD are currently managed in Canadian community or HD centres. As such, introduction of and demand for a DMT would strain the system. We confirmed that Canadian HD centres have limited current capacity to administer IT DMTs due to nursing, neurologist or room time. Overall, the incremental FTEs required in Canadian centres appear similar to those predicted internationally. Neurologist capacity and willingness to administer IT DMTs are also serious areas of concern, with shortages and waning interest in the specialty already a threat to the system. Furthermore, when limitations in social worker capacity were accounted for, national capacity to treat decreased to only 6% of IT DMT-eligible patients with HD. Not surprising, given the full absence of resources in some centres, extension of IT DMT dosing to every 16 weeks rather than every 8 weeks had minimal impact on the available capacity to treat all IT DMT-eligible patients.

While our study is unique in its characterisation of existing systems of care for Canadian patients with HD, challenges related to the servicing of remote communities, centralised specialist care, long wait times and inequitable access to MDTs align with known systemic complexities plaguing the Canadian healthcare system as a whole. These challenges, together with the burden of illness, put tremendous strain on patients with HD and their caregivers. Furthermore, constrained capacity to treat patients with HD with novel DMTs is a barrier to achieving the benefits that those therapies may offer.

**Future directions**

Our study explores the practical facets of IT-DMT implementation on healthcare capacity; however, the introduction of a DMT would raise several potential additional avenues of research. First, prevalence estimates could be impacted by a DMT that could prolong disease duration. Second, overall healthcare utilisation throughout the course of the disease, including both early and late phases, would likely be impacted by the introduction of a DMT. Third, economical burden associated with changes in healthcare utilisation should also be considered. Combined, following the release of data on the clinical benefit of the DMT in question, future studies should integrate measures of disease burden, estimates of health resource utilisation and assessment of overall economic value.

Our study highlights the current variability of care delivery across Canada for HD. Given the diversity of challenges among the provincial health systems, solutions for increasing capacity, should a DMT become available, need to be customised by region. Further research...
should be conducted to correlate care delivery characteristics with quality of care and patient outcomes to help identify the most impactful interventions for capacity building.\textsuperscript{40,41} Our study can serve as a model for assessing capacity needs for future DMTs or alternative administration schedules. Importantly, policymakers, administrators and healthcare providers need to consider the time required to implement change and the benefits of doing so; improving the existing system and building a foundation to support future treatments.

Limitations of the study
To mitigate the risk of implicit bias in questionnaire design, diverse steering committee input was incorporated, and a third party was used to administer questionnaires and interviews. Some model assumptions were based on the best available data or steering committee opinion; although these may differ in actuality, they can be adjusted and the model rerun accordingly. Finally, survey responses were subjective and the perspective of one respondent at each centre; however, respondents were those most involved in HD patient care. One of the limitations of our study was the low response rate from community centres. Although, there was a high response rate from HD centres, which service the majority of patients. Indeed, some non-responding centres indicated lack of patients with HD as the reason for not participating. Therefore, responding community centres may not be accurate representations of all community centres and the proportion of patients seen in the community may be lower than our numbers suggest.

It should also be noted that the model used considers only the resources required for IT DMT administration and not ancillary tasks that may be associated with the influx of new patients or increased complexity of existing cases (e.g., administrative impact of patients new to clinic or other social worker tasks that may expand).

CONCLUSION
Current systems of HD care in Canada have little to no capacity to support a new IT DMT. Capacity constraints are driven by the high proportion of patients with HD not currently seeking care and are compounded by limitations in neurologist, nurse and social worker time or access. Considerable planning and collaboration would be required to ensure unburdened access for eligible patients.

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Competing interests AB reports employment by Huntington Society of Canada, which has received unrestricted grants from F. Hoffmann-La Roche, uniQure, Prilenia, PTC Therapeutics, Novartis, Triplet Therapeutics, and Wave Life Sciences; and has participated in research projects with F. Hoffmann-La Roche. SC reports receiving honoraria from F. Hoffmann-La Roche. BRL reports receiving personal compensation in the 3 past years as a paid scientific advisor or consultant to Novartis, Roche Canada, Remix Therapeutics, Sintetica, PTC Therapeutics, sRNAlytics, Teva, Triplet Therapeutics, F. Hoffmann-La Roche, Pfizer, Takeda, Design Tx, and uniQure regarding the development of new therapies for Huntington disease and similar disorders; receiving contract research funding from F. Hoffmann-La Roche, Teva, and uniQure to perform basic research projects in mouse models of Huntington disease; and receiving compensation for administrative expenses as the Co-Editor-in-Chief of the Journal of Huntington’s Disease. SC reports receiving honoraria from F. Hoffmann-La Roche. BRL has patients related to and is a co-founder and CEO of Incisive Genetics Inc. NB and JWW are employed by the study sponsor, F. Hoffmann-La Roche Ltd. KS reports receiving research funding from F. Hoffmann-La Roche and Prilenia Therapeutics.

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Patient consent for publication Not applicable.

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