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Original Article

A Model Predicting Healthcare Capacity Gaps For Alzheimer's Disease-Modifying Treatment in Canada

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ABSTRACT: ***Background:*** Alzheimer's disease (AD) is experienced by > 600,000 Canadians. Disease-modifying therapies (DMTs) for earlier stages of disease are in development. Existing health system capacity constraints and the need for biomarker-driven diagnostics to confirm DMT eligibility are concerning. This study aimed to characterize the capacity gap related to early AD (eAD) treatment with DMTs in Canada. ***Methods:*** A capacity model was developed to simulate the flow of a patient from screening to treatment for eAD to quantify the gap between available and required healthcare resources and qualify the bottlenecks restricting the patient journey at a provincial and national level. The model inputs (epidemiological, human resource, and clinical) were evidence-based, healthcare professional-, and patient advocate-informed. ***Results:*** The model estimated that nationally < 2% of patients would have access to the required healthcare resources for treatment with a DMT. Eligibility assessment represented the step with the largest capacity gap across all provinces, with a wait list of about 382,000 Canadians one year following DMT introduction. The top three resource gaps included AD specialist time and positron emission tomography and magnetic resonance imaging exam slots. Sensitivity analysis showed that full reliance on cerebrospinal fluid for eligibility testing increased capacity for assessment by about 47,000 patients. ***Conclusion:*** This model highlights that the Canadian health system is critically under-resourced to diagnose, assess, and treat patients with eAD with DMT. It underscores an urgent need for national policy and provincial resource allocation to close the gap.

RÉSUMÉ : Un modèle prédisant les lacunes du système de santé en ce qui concerne le traitement modificateur de la maladie d'Alzheimer au Canada ***Contexte :*** Plus de 600 000 Canadiens sont atteints de la maladie d'Alzheimer (MA). Des traitements modificateurs de la maladie (TMM) sont en cours de développement pour les stades précoces de la maladie. Cela dit, les contraintes existantes du système de santé en matière de capacité et le besoin de diagnostics basés sur des biomarqueurs pour confirmer si l'on peut débuter un TMM sont préoccupants. Cette étude vise ainsi à caractériser les lacunes du système de santé canadien en lien avec le traitement précoce de la MA par les TMM. ***Méthodes :*** Un modèle de capacité de ce système de santé a été développé pour simuler le parcours d'un patient entre le dépistage et le traitement de la MA précoce, et ce, afin de quantifier l'écart entre les ressources disponibles et les ressources requises et de caractériser les goulets d'étranglement (*bottlenecks*) qui limitent le parcours des patients au niveau provincial et pancanadien. Les données d'entrée du modèle (épidémiologiques, ressources humaines et cliniques) ont été fondées sur des données probantes, sur l'avis de professionnels de la santé et sur celui des défenseurs des patients. ***Résultats :*** À l'échelle nationale, le modèle a estimé que moins de 2 % des patients auraient accès aux ressources nécessaires du système de santé en vue d'un TMM. L'évaluation de l'admissibilité à un tel traitement est l'étape qui présente le plus grand déficit de capacité dans toutes les provinces, la liste d'attente totalisant environ 382 000 Canadiens un an après l'introduction des TMM. Les trois principales lacunes en matière de ressources étaient la disponibilité des spécialistes de la MA, les créneaux horaires disponibles pour des examens de tomographie par émission de positons (TEP) et les créneaux horaires disponibles pour des examens d'IRM. Une analyse de sensibilité a par ailleurs montré que le recours intégral au liquide cérébrospinal (LCS) pour des tests d'admissibilité aux TMM augmentait la capacité d'évaluation d'environ 47 000 patients. ***Conclusion :*** En somme, ce modèle montre que le système de santé canadien manque cruellement de ressources pour diagnostiquer, évaluer et traiter par TMM les patients atteints de la MA à un stade précoce. Il souligne également l'urgence d'une politique pancanadienne et d'une allocation des ressources provinciales pour combler ce déficit.

Keywords: Alzheimers; epidemiology; cognitive impairment; dementia; health services research; biomarkers; magnetic resonance imaging; neurodegenerative diseases; neurological practice; therapeutics

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Introduction

Alzheimer's disease (AD) is a devastating, incurable, neurodegenerative condition experienced by more than 600,000 Canadians.[1] The disease is prevalent in 10%–30% of people over 65 years of age.[2,3] More than 95% of cases are sporadic and occur late in life, with pathophysiological hallmarks of accumulated amyloid-β (Aβ) peptide and neurofibrillary tangles of tau protein in the brain.[2] Preclinical disease may be present for decades before the onset of clinical signs and symptoms which, once overt, typically progress over 8–10 years, ultimately leading to death from complications.[2]

The burden of neurological conditions is high, with affected Canadians utilizing more healthcare personnel support than Canadians with other chronic health condition(s).[4] The patient, caregiver, and health system burden of dementia is heavy. Patients with dementia experience worsening deficits in cognitive, emotional, and physical function, and loss of independence.[5] Caregivers, many of whom are elderly and also at risk, contribute substantial hours to the care of people with AD and experience negative quality of life impacts as the disease progresses.[5,6] A 2016 study estimated combined Canadian healthcare system costs and out-of-pocket caregiver costs to be $10.4 billion; an amount expected to grow to $16.6 billion by 2031.[6] Growth in burden is primarily attributed to a growing prevalence of disease, with case numbers expected to double over a 20 year period.[7] A 2019 global burden of disease study estimated that in Canada, dementia-related spending accounted for 2.3% of total healthcare spending and would increase by 5.5% annually.[8]

While clinical criteria have been the primary basis for the diagnosis of AD dementia,[9] biological definitions of AD, based on biomarkers of Aβ deposition, pathologic tau, and neurodegeneration, have been used in research settings.[10] In Canada, national guidelines for the diagnosis of AD suggest that most screening and clinical workup be completed by a primary care physician (PCP), and that more advanced diagnostics require referral to specialty clinics.[10] Sadly, studies suggest that less than half of those living with dementia receive a diagnosis, so many progress while awaiting a diagnosis.[11–13] Furthermore, current Canadian guidelines discourage screening for mild cognitive impairment (MCI), a common precursor to AD dementia.[14]

AD management mainly involves the treatment of comorbid illnesses and extensive social support.[2] Until recently, although there had been continued progress in understanding AD pathophysiology, a disease-modifying therapy (DMT) remained elusive.[15,16] However, a number of drugs aimed at modifying the disease in its earlier stages (i.e. MCI due to AD and mild AD dementia) are currently under investigation or have recently reported promising results.[16–18] Many of these treatments target Aβ peptide, two of which have received US Food and Drug Administration approval for AD treatment: aducanumab and lecanemab.[19,20] Aβ-targeted therapies require detection of Aβ aggregation using cerebrospinal fluid (CSF) or positron emission tomography (PET) to determine treatment eligibility.[2,21–25] Unfortunately, low numbers of dementia specialists and access to imaging already lengthen wait times for such services in Canada.[26]

The promise of DMTs for AD is bittersweet, considering the challenges anticipated from a health system perspective. Experts across the globe have raised concerns that current infrastructure is not sufficient for the anticipated demand for early AD (eAD) diagnostics.[25–27] Furthermore, in Canada, healthcare resources in neurology and dementia care are already strained or scarce, as has been highlighted in numerous reports.[28–33]

In alignment with implementation science and practice improvement,[34] we sought to quantify and characterize the expected capacity constraints related to DMT availability for patients with eAD in Canada. By understanding where bottlenecks exist, health systems and policy makers can make more informed decisions related to future models of care and care investment.

Methods

Study Design and Objectives

A comprehensive capacity model, similar to system dynamics modeling,[35] was developed in Microsoft Excel to model the healthcare capacity in Canada for treatment of eAD with Aβ-targeted DMT. The primary objective of the study was to characterize the healthcare capacity to diagnose, assess eligibility, and treat prodromal and mild AD patients with an Aβ-targeted DMT in Canada. Secondary objectives included estimating the number of patients who would not receive a DMT due to resource constraints, identifying the resource bottlenecks constraining the flow of patients along the AD treatment journey, and quantifying the healthcare resources (personnel and infrastructure) needed to overcome any identified bottlenecks.

The research question, study design, and data inputs were validated by a steering committee, which included three AD experts from major regions in Canada (Western Canada - HN, Ontario - SB, Quebec - LV) and one representative from the patient support community (LTW). The study was designed between May and October 2022 with data outputs finalized in December 2022. The protocol for this modeling project was reviewed by Advara, an institutional review board (IRB), and was deemed exempt from IRB oversight.

Study Setting

The model was based on health system configurations and delivery of care common in Canada, where health care is largely public-funded and provincially delivered.[36] Canada, the second largest country in the world, is a geographically vast and regionally diverse country. This study included all Canadian provinces; however, due to lack of available data, it excluded the territories in the less populated northern areas of the country.

Overall, model assumptions were based on steering committee input, clinical trial design of Aβ-targeted DMTs under investigation for eAD,[37] and current Canadian guidelines.[10] Healthcare innovations not yet available for clinical use (e.g., diagnostic blood-based biomarkers, BBBMs) were not included.[10,38] Similarly, the clinical trial population was used as reference for patients eligible for treatment. For the model, patients were considered eligible for Aβ-targeted DMT if they had MCI or mild AD, and tested Aβ positive (i.e., by increased amyloid PET or decreased CSF-$A\beta_{42}$).

Generally, each input variable required data supported by, in order of priority, published scientific literature, clinical trial protocol, public data sources, or steering committee consensus. Every effort was made to identify the most relevant and recent data specific to Canada, first provincially, and then nationally. Average consensus of the steering committee was used for parameters where no data were currently available (e.g., time to treat an AD patient with Aβ-targeted DMT).

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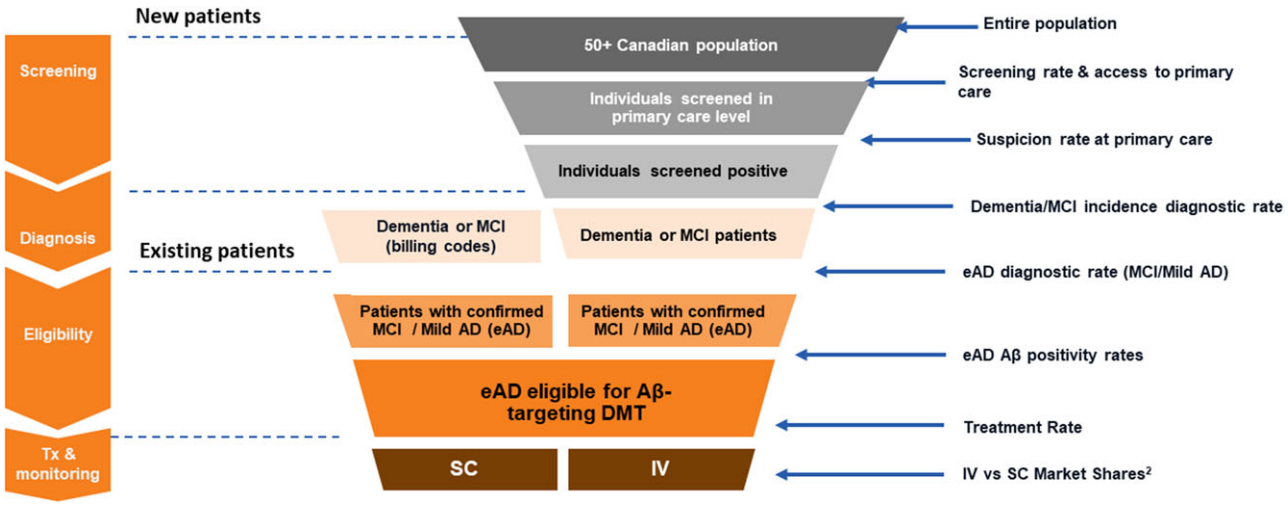

Figure 1: An illustration of the patient journey, from screening and diagnosis of early AD (eAD) to assessment of eligibility and treatment with an Aß-targeted DMT, estimating the expected demand at each step of the funnel.

Model configuration and assumptions

The model calculated the capacity gap as the difference between the total required resources and the currently available resources, for each step of the patient journey (diagnosis, eligibility, and treatment/monitoring). The model used a 3-year time horizon, assuming introduction of Aβ-targeted DMTs in year 1.

There were three essential elements of the model:

[Number of patients (Capacity demand) x Resource required per patient] – Available healthcare capacity = Capacity Gap

1. Healthcare capacity demand (i.e., prevalence, diagnostic rate, Aβ positivity rate, treatment rate, market shares; see Fig. 1),
2. Healthcare resources required (i.e., assignment of resource allocations or patient slots to various personnel or infrastructure)
3. Available healthcare capacity (i.e. number of health system personnel and infrastructure resources available, estimate of time available).

Healthcare capacity demand. The demand on the health system was determined based on the number of individuals expected to require access to healthcare personnel or resources. A patient journey funnel (Fig. 1) was designed to quantify the number of individuals flowing through the healthcare system toward treatment with an Aβ-targeted DMT. The model had a total of four stages (screening, diagnosis, eligibility, and treatment/monitoring) and two streams of patients. The two streams of patients were either new prevalent patients (i.e., an undiagnosed, prevalent pool of patients not currently managed by the healthcare system) or existing prevalent patients (i.e., diagnosed). Incident new patients were not captured in the model. Within the new patient stream, demand and associated rates (e.g., screening, suspicion, diagnosis) were assumed to be stable over the 3-year horizon of the model.

Assumptions related to healthcare capacity demand are detailed in Supplementary Table S1. Potential patients were assigned provincially, based on population distributions[39] after which applicable rates related to screening, diagnosis, eligibility, and treatment were applied nationally.

Healthcare resources required. At each stage of the demand funnel, individuals were assumed to require access to various healthcare resources, captured in units of time (personnel) or slots (infrastructure) required per patient. Personnel included AD specialists (neurologists, geriatricians, or psychiatrists with a focus in dementia care), AD nurses, pharmacists, imaging specialists (nuclear medicine specialists and radiologists), and technologists. For simplicity, some supportive resources (e.g., administrative, lab, and social services, intravenous infusion) were assumed to be unconstrained and were not included in the model. Infrastructure requirements included magnetic resonance imaging (MRI) and PET exam slots.

Assumptions related to healthcare resources required are detailed in Supplementary Table S2.

Available healthcare capacity. For each resource, an estimation of available time or exams/tests, based on the current health system, was incorporated in the model. Available resources were distributed to each step of the patient journey by type (i.e., AD specialist, nurse, PET, etc.), in a ratio proxying the required resources for each step. With the exception of PCPs, all resources were allocated provincially.

Inputs related to available healthcare capacity are detailed in Supplementary Table S3. After quantification of each available resource, an assumption regarding the proportion of time dedicated to AD was required. The steering committee agreed on an allocation for AD specialists: 10% of all neurologists and geriatricians and 2.3% of psychiatrists.[8] For all other healthcare resources (personnel and infrastructure), allocation of resources to dementia care was estimated using Canadian AD expenditure as a fraction of entire healthcare expenditure (2.3%), as a proxy estimate.[8]

Model simulation / Data analysis reporting

Microsoft Excel was used for modeling, data analysis, and visualization.

Flow through the system was supported or constrained by the resources required and available within each step. The model used the total potential patient demand, regardless of prior bottleneck (i.e., satisfied + unsatisfied) as the denominator to begin each step of the patient journey. The capacity gap within each step was computed as the number of patients for whom demand was satisfied versus unsatisfied in that step, with proportions reported as a function of the potential patients that could have entered that step. The unsatisfied demand of patients forming in a single treatment journey step (i.e., waitlist) was added to the following year's demand for that step.

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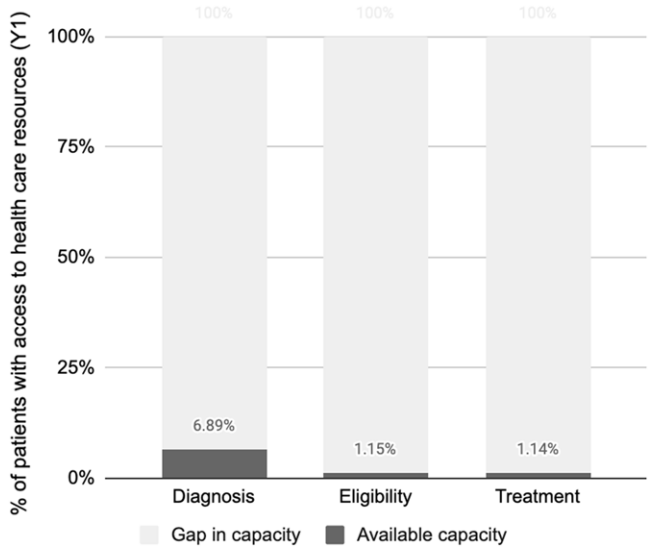

Figure 2: Percentage of patients with access to diagnosis, eligibility assessment, and treatment/monitoring with an Aß-targeted DMT for early AD, in Canada (year 1 following the introduction of a DMT). Nationally, <2% of patients will have access to the required healthcare resources for treatment with an Aß-targeted DMT in year 1.

Modeling assumed that a DMT treatment was only prescribed to a patient if there was available capacity for monitoring that patient. Mortality and treatment discontinuation were not included in the model, as they were assumed to be negligible over the short 3-year model horizon. Neither endogenous increases in available resources over time nor resources required for non-DMT eligible patients were included in the model.

For national analyses, data from all provinces were combined to provide Canadian capacity estimates. Results are reported using descriptive statistics. Human resource requirements are reported in units of full-time equivalent (FTE) with one FTE equal to 37.5 hours/week and 48 weeks/year. Reported patient numbers are rounded to the nearest 1,000 with the intention to illustrate directional estimates rather than specific numbers generated from modeling using extensive input assumptions with inherent variance.

Sensitivity Analysis

Based on the design of the model, there was an opportunity to perform sensitivity analyses where assumptions were uncertain or where changes in the care configuration were expected to result in capacity improvements. Two such scenarios were tested, independently. In one analysis, allocation of healthcare resource time (FTE) and infrastructure (slots) was increased from the base assumption of 2.3% to the upper limit of the reported range for percentage of total healthcare expenditure (i.e., 4.6%).[8] In the second scenario, Aβ testing was shifted from 50% PET and 50% CSF to 100% CSF. Increased potential capacity was reported for each of these scenarios as described above.

Results

Capacity Gaps Related to the Provision of Aβ-targeted DMTs in eAD

In modeling resources available, anticipated patient demand, and required resources for the treatment journey, the model estimated that only 6.89%, 1.15%, and 1.14% of potential patients nationally would have access to diagnosis, DMT eligibility assessment, and DMT treatment/monitoring, respectively, in year 1 (Fig. 2).

Ontario, Manitoba, and Saskatchewan were the provinces with the highest proportion of patients (8.6%, 8.6%, and 8.3%, respectively) with access to resources for diagnosis. In contrast, these provinces were among those with the lowest proportion of patients (< 1.0%) having access to eligibility assessment (see Supplementary Table S2). This drop in capacity was a result of increased patient demand, owing to the entry of prevalent patients with existing MCI or mild AD diagnoses into the model. Eligibility assessment, which could include either PET or CSF testing (including imaging specialist and technologist time), AD specialist assessment, and AD nurse support, represented the step with the largest capacity gap across all provinces (see Supplementary Table S4).

The number of Canadians anticipated to be waiting for eligibility assessment after year 1 was approximately 382,000. This number grows annually for each step of the patient journey (data not shown). All provinces are expected to have waitlists for eligibility in year 1, with the highest being in Ontario (approximately 148,000 patients) (Fig. 3).

Bottlenecks Constraining Capacity and Top Resources Required for Aβ-targeted DMT Provision in eAD

Nationally, and considering the entire patient journey, AD specialist time represents the largest capacity gap, equating to a 14-times increase in FTE, amounting to over 3,500 more AD specialists, required to satisfy demand in year 1. However, MRI and PET slot availability is the largest limiting resource constraining diagnosis and eligibility along the patient journey. This finding was largely similar when detailed by province (data not shown).

The difference between required and available resources (i.e., incremental resource required) for MRI and PET slots equates to nearly 26- and 86-fold increases in slots, respectively, in year 1 (data not shown).

Sensitivity Analysis Findings

Shifting from 50% PET / 50% CSF to 100% CSF for detection of Aβ resulted in an increased capacity to assess patients for DMT eligibility across all provinces (Fig. 4), opening access for nearly 47,000 patients nationally in year 1.

Increasing the time that ancillary resources are dedicated to AD care also increased capacity to assess patients for DMT eligibility across all provinces (Fig. 5), opening access for nearly 6,000 patients nationally in year 1.

Interpretation

Summary of Key Findings

Results of this model simulation show the Canadian healthcare system has an extremely low capacity to diagnose, assess eligibility, and treat (<7% of potential patients) eAD with an Aβ-targeted DMT. Importantly, our findings magnify the issues highlighted by a previous Canadian model[32] and corroborate findings from other countries, including the USA[15] and Brazil.[26] Indeed, our data underscore the need for AD specialist resources called for by Liu *et al.*[32] in their modeling, especially considering only a fraction of Canadian neurologists, geriatricians, and psychologists specialize in AD care. Combined, these modeling data demonstrate that the capacity of the Canadian healthcare system is grossly inadequate

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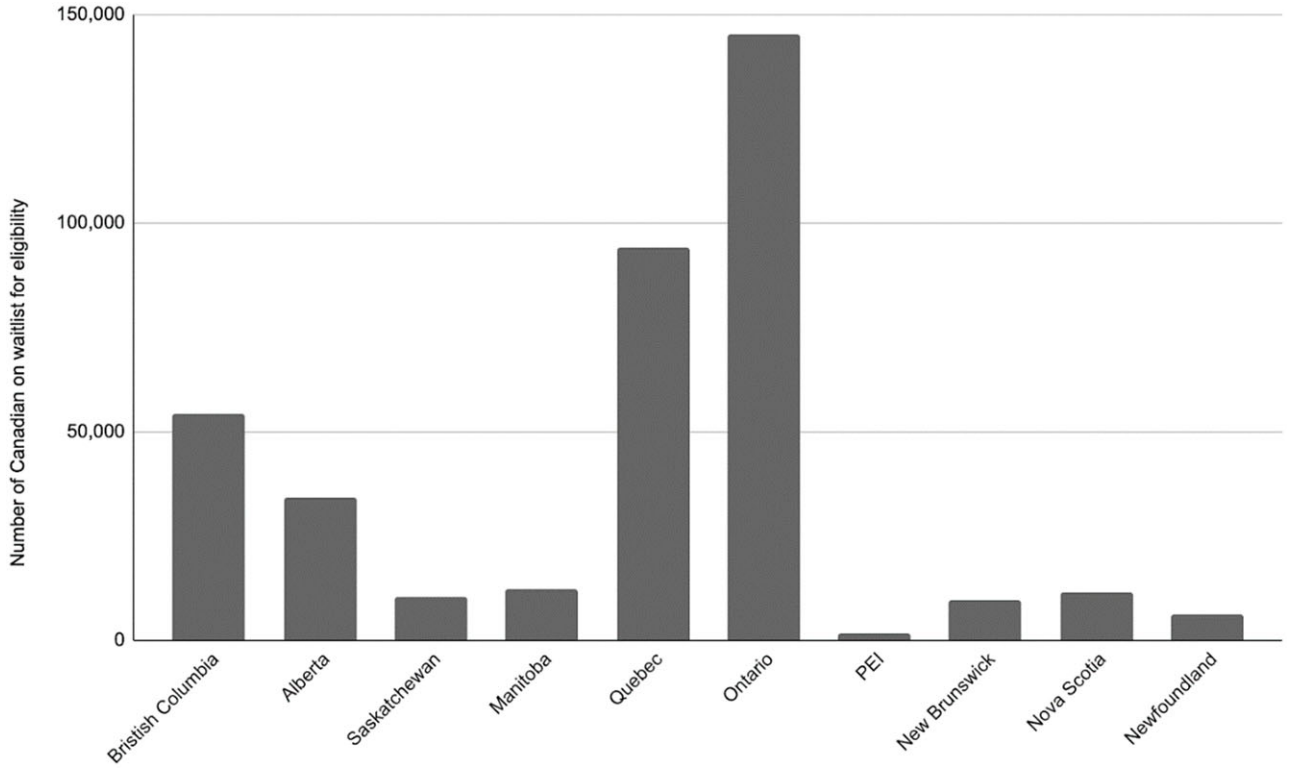

Figure 3: Anticipated provincial waitlist for eligibility assessment in year 1, following Aß-targeted DMT introduction. Approximately 382,000 Canadians could be awaiting eligibility assessment following introduction of a DMT.

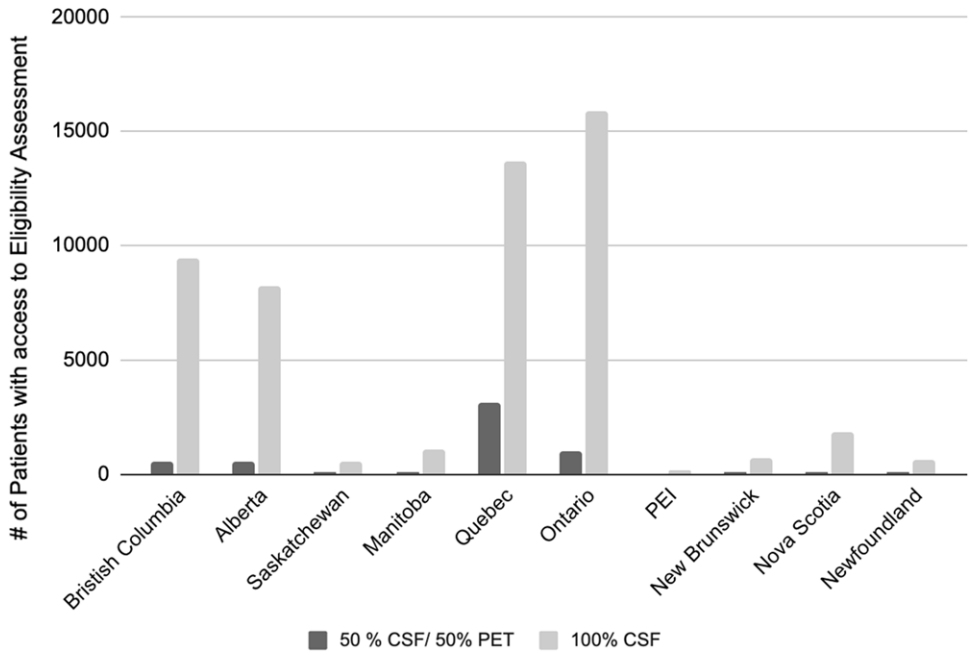

Figure 4: Impact of shifting from 50% CSF / 50% PET for Aβ determination compared to 100% CSF.

across all stages of the eAD patient journey and that national policy and investment supporting AD care will be required to realize the benefit of DMTs in this space.

Further, considering the large bolus of prevalent patients expected to present for Aβ testing initially, eligibility assessment represents the most constrained step along the patient journey to treatment with an Aβ-targeted DMT. In this step, imaging specialist FTE and PET imaging slots impart the greatest limitations to the flow of patients. In fact, capacity limitations for eligibility assessment predict a wait list of nearly 382,000 patients just 1 year after the introduction of an Aβ-targeted DMT. These findings differ in scale compared to the findings from the disease state and system dynamics model reported by Liu *et al.*[32] In their study, the year 1 waitlist was less than 100,000 patients

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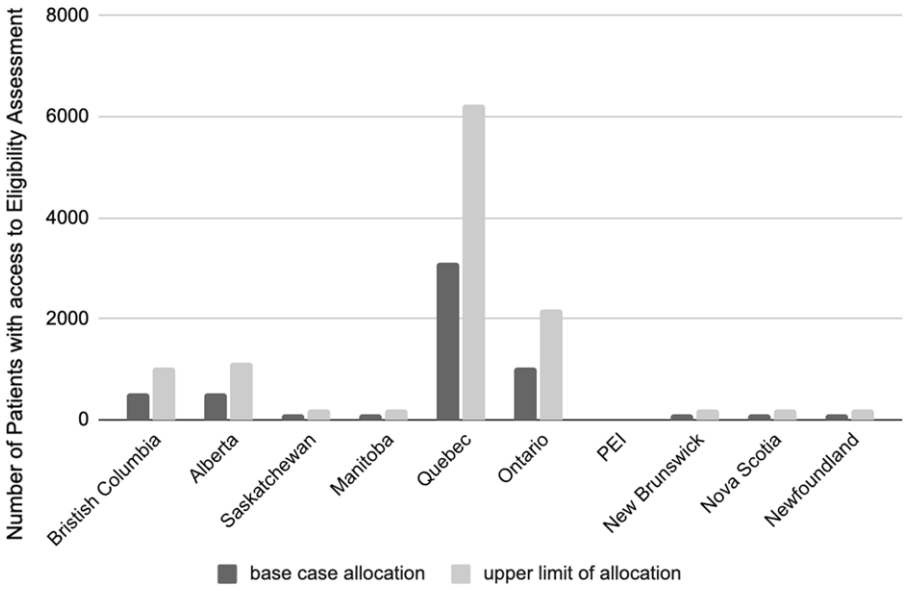

Figure 5: Impact of increased ancillary resources on capacity to assess eligibility for an Aß-targeted DMT (year 1).

for biomarker (eligibility) assessment. This gap widens when accounting for imaging specialist time and AD sub-specialization; additional considerations that reflect important constraints with respect to available and required resources within our model.

Our analysis also provides a unique view of the provincial nuances related to capacity constraints. Given the diversity of provincial challenges and health system models, solutions for increasing capacity will need to be customized and implemented at a provincial level but should focus on AD specialist resourcing and improving access to imaging.[40] Of particular concern and need for consideration will be the equitable provision of care, including access to imaging for diagnosis or eligibility assessment, in remote or rural populations.[34]

One solution to this bottleneck is to decrease reliance on PET (and thereby imaging specialist time) and increase the use of CSF for Aβ assessment, as explored in the sensitivity analysis. Such a shift allowed the assessment of nearly 47,000 additional patients nationally in year 1. Alternately, increasing the proportion of time ancillary resources allocate to dementia care (proxied by an increase in the proportion of healthcare expenditure for dementia care) allowed for close to 6,000 additional patients to be assessed for Aβ-targeted DMT eligibility. While these analyses highlighted potential priority areas for action, it should be recognized that major gaps in capacity remained, and the solutions required to adequately support disease-modifying treatment in eAD will be varied and systemic.

Limitations of the Study

Modeling complex systems has inherent limitations as flows are simplified and best assumptions are made. In this model, key limitations included the focus on a single, presumably prominent model of care. This meant potential capacity gains or losses true for other models of care (e.g., family health teams, centralized image interpretation, etc.) were not accounted for. In addition, the assumptions made for each variable provincially/nationally may not be accurate representations of the provincial/national reality. For example, a national assumption of 50% PET / 50% CSF does not accurately reflect the clinical reality of care in a province where PET is not funded. As was seen with the shift to 100% CSF testing in the sensitivity analysis, alternate resourcing configurations can appreciably impact patient access. Importantly, as data become available at more accurate and detailed levels, the model can be adjusted and re-run.

Another limitation is of course the scope of the model and resources not considered. As an example, dementia care in the Yukon (and other northern regions not included in the model) is unique (e.g., prominent role of nurse practitioner) and remote/rural access challenges are expected to be compounded in these areas. Likewise, resources not accounted for in the model, such as social worker support, should be considered as capacity solutions are contemplated. Additional questions require further study, including the capacity and need for social support, the resources required to manage diagnosed but non-DMT eligible patients, the impact of the pandemic on various assumptions, and the potential influence of blood-based biomarker use for clinical AD diagnosis.

Next Steps

This study can serve as a framework for modeling capacity needs related to future DMTs and changes to clinical care (e.g., BBBMs for the identification of Aβ) for AD, other neurological conditions, and beyond. Presumably, the future clinical use of validated and robust blood-based biomarkers in AD has the potential to not only simplify the diagnosis and evaluation of DMT eligibility but also enable a timelier assessment at the primary care level and a triaging of demand for amyloid PET and specialty consult. With the diagnostic accuracy of assays for phosphorylated-tau improving (particularly p-tau217),[41] the reality of BBBMs impacting the AD patient pathway to treatment is near. In theory, this would lessen the strain on key bottlenecks identified in our model (i.e., imaging resources and AD specialist time) but would require thorough consideration of other resource capacities (i.e., primary care). For now, stakeholders involved in AD care must heed the red flags raised by this and other research and consider the multitude of health system changes required to provide eligible patients with DMT early in their disease trajectory.

We also encourage complementary research such as investigating alternative models of care to help identify impactful interventions for capacity building.[42,43] Further, while some

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models have predicted overall economic benefit associated with DMT-driven delays in disease progression[44–46] it will be important to evaluate the economic implications of modified models of care or resource allocation in the context of the clinical benefit realized by a DMT.[47] Furthermore, the true impact of new interventions for eAD will only become clear once people living with AD enter into and pressure the existing health system. With an abundance of health, social, and economic considerations at play, the reshaping of AD care infrastructure and appropriate DMT provision will require a variety of solutions, including informed resource allocation, in order to deliver value.

Conclusion

In Canada, the modeled system of AD care and currently allocated resources are insufficient to support the provision of Aβ-targeted DMTs for patients with or seeking an eAD diagnosis. These capacity constraints are driven by the increased demand for services and treatment, coupled with limited resources. Resources particularly lacking include AD specialists and imaging availability. This model highlights the urgent need for increased national policy and provincial resource allocation to support AD diagnosis, eligibility assessment, and treatment/monitoring.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/cjn.2023.270.

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Statement of authorship. NB, SV, and MW contributed substantially to study conception and data acquisition. SEB, NB, HBN, LV, SV, LTW, and MW contributed to the study design and confirmation of acquired data. NB and MW conducted the primary data analysis. SEB, NB, HBN, LV, SV, LTW, and MW were responsible for data interpretation and the critical review of the draft and final manuscript, and all approved the final version for submission.

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Nathalie Budd, Shikha Virdi, and Melanie Wilson are employed by Hoffmann-La Roche Ltd (Mississauga, ON, Canada).

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