The Canadian Journal of Neurological Sciences (2024), **51**, 723–731
doi:10.1017/cjn.2023.322

Canadian Journal of Neurological Sciences
Journal Canadien des Sciences Neurologiques

Review Article

Health System Change for Alzheimer's Disease-Modifying Therapies in Canada: Beginning the Discussion

Andrew Frank[1], Zahinoor Ismail[2], Melanie Wilson[3], Serge Gauthier[4], Louis Verret[5], Ging-Yuek Robin Hsiung[6] and Michael Borrie[7]

[1]Bruyere Research Institute, and University of Ottawa, Ottawa, ON, Canada, [2]Departments of Psychiatry, Clinical Neurosciences, and Community Health Sciences, Hotchkiss Brain Institute and O'Brien Institute for Public Health, University of Calgary, Calgary, AB, Canada, [3]Hoffmann-La Roche Ltd., Mississauga, ON, Canada, [4]McGill Center for Studies in Aging and Dementia Education Program, McGill University, Montreal, QC, Canada, [5]Service de Neurologie, Clinique Interdisciplinaire de Mémoire, CHU de Québec-Université Laval, Hôpital Enfant-Jésus, Québec, QC, Canada, [6]Division of Neurology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada and [7]Division of Geriatric Medicine, Lawson Health Research Institute, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada

ABSTRACT: Alzheimer's disease (AD) is a neurodegenerative disorder that accounts for 60%–70% of patients with dementia, and it is estimated that over one million Canadians will be living with dementia by 2030. Disease-modifying therapies (DMTs) targeting the underlying pathophysiology of AD are currently in development. Several models have demonstrated that the potential arrival of Alzheimer's DMTs will most likely overwhelm the already-constrained Canadian healthcare system. Canada does not have a strategy to address the extensive requirements of using DMTs, including providing an early diagnosis of AD, confirming DMT eligibility via amyloid biomarkers, and conducting ongoing treatment monitoring. Thus, a multidisciplinary group of experts involved in AD care in Canada gathered to review (1) the current barriers to diagnosis and management of AD; (2) how existing clinic models, including those used in multiple sclerosis (MS), could be applied to address key barriers in AD; and (3) how to design and implement optimal care pathways in the future. The actions outlined in this review will help clinicians and healthcare systems improve readiness to integrate the use of disease-modifying therapies in Alzheimer's disease, if such therapies are approved in Canada.

RÉSUMÉ : Entamer la discussion au sujet des changements qui attendent le système de santé canadien en lien avec les traitements modificateurs de la maladie d'Alzheimer. La maladie d'Alzheimer (MA) est une affection neurodégénérative qui touche 60 à 70 % des patients atteints de démence. On estime que plus d'un million de Canadiens seront atteints de démence d'ici à 2030. Des traitements modificateurs de la maladie (TMM) ciblant la physiopathologie sous-jacente de la MA sont en cours de développement à l'heure actuelle. À ce sujet, nombreux sont les modèles qui ont démontré que l'arrivée potentielle des TMM pour la MA va très probablement entraîner une demande excessive affectant le système de santé canadien alors que ce dernier est déjà soumis à des contraintes. C'est ainsi que le Canada n'a pas de stratégie pour répondre aux nombreuses exigences liées à l'utilisation des TMM, notamment l'établissement de diagnostics précoces pour la MA, la capacité de déterminer l'admissibilité des patients aux TMM grâce aux biomarqueurs amyloïdes et le fait d'assurer un suivi continu des traitements. Un groupe multidisciplinaire d'experts impliqués dans les soins de la MA au Canada s'est donc constitué pour examiner : 1) les obstacles actuels à l'établissement d'un diagnostic de MA au pays et à la prise en charge des patients ; 2) la façon dont les modèles cliniques existants, y compris ceux utilisés dans le cas de la sclérose en plaques (SP), pourraient être mis en pratique pour surmonter les principaux obstacles liés à la MA ; 3) la manière de concevoir et de mettre en œuvre pour l'avenir des parcours de soins optimaux. En bref, les actions décrites dans cette étude aideront les cliniciens et les systèmes de santé à mieux se préparer à intégrer les TMM si ces derniers sont approuvés au Canada en ce qui regarde la MA.

Keywords: Alzheimers; cognitive impairment; dementia, geriatric health services; health services research; biomarkers; magnetic resonance imaging; neurological practice; therapeutics

(Received 9 June 2023; final revisions submitted 20 November 2023; date of acceptance 30 November 2023; First Published online 6 December 2023)

Corresponding author: M. Wilson; Email: melanie.wilson.mw2@roche.com

Cite this article: Frank A, Ismail Z, Wilson M, Gauthier S, Verret L, Hsiung G-YR, and Borrie M. (2024) Health System Change for Alzheimer's Disease-Modifying Therapies in Canada: Beginning the Discussion. *The Canadian Journal of Neurological Sciences* **51**: 723–731, https://doi.org/10.1017/cjn.2023.322

Introduction

The Alzheimer Society of Canada reported an estimated 597,300 individuals living with dementia in Canada in 2020, and this number is estimated to reach one million individuals in 2030.[1] Unfortunately, many people living with dementia do not receive a timely diagnosis, and reports show high levels of undetected dementia globally.[2,3] Today, dementia costs the Canadian economy and healthcare system an estimated $10.4 billion annually, and these costs are expected to continue to grow with the aging population.[4]

Alzheimer's disease (AD) is a neurodegenerative disorder that accounts for 60-70% of patients with dementia and is characterized by a decline in memory and cognition.[5–7] In Canada, there are currently no approved therapeutics which stop or delay the progression of this debilitating disease. Recently, there has been progress in monoclonal antibodies (mAbs) that target amyloid-β (Aβ), which have shown promising results in the earlier stages of the disease.[8,9] However, the arrival of a disease-modifying therapy (DMT) for AD will most likely overwhelm the Canadian healthcare system, as the influx of patients seeking a diagnosis and potential treatment would put a strain on already-limited healthcare capacity. Recent analyses show that Canada would have the longest and most persistent wait times for a DMT for AD among the G7 countries.[10] There is a clear need to assess and address barriers in the Canadian healthcare system that are delaying early diagnosis and treatment of AD, prior to the potential arrival of DMTs.

A group of Canadian stakeholders with expertise in dementia and other neurological illness convened in the Fall of 2022 to discuss ways in which models of care for AD would need to evolve ahead of the introduction of DMTs. There were three regional forums which took place in Calgary, Toronto, and Quebec City, comprised of a multidisciplinary group referred to here as the "Canadian Dementia Expert Group." The objectives were to prioritize key barriers in the AD patient pathway, understand how other existing healthcare models could be applied to address such barriers, and design solutions to evolve the care pathway for new innovations, including potential DMTs and novel biomarkers.

An important aspect of introducing potential Alzheimer's DMTs is the healthcare system cost associated with these treatments. This was explored by the Institute for Clinical and Economic Review's California Technology Assessment Forum, utilizing drug pricing in the United States.[11] At this time, Canada-specific drug pricing information is not yet available. One analysis showed potential cost recovery to the Canadian healthcare system through the use of DMTs, via reduced long-term care usage.[12] Ultimately, a true pharmaco-economic analysis, relevant to Canada, will be essential. However, this was beyond the capability of our Canadian Dementia Expert Group.

Here, we aim to review the recommendations from the Canadian Dementia Expert Group, focusing on the rationale behind early detection and diagnosis of AD, the barriers in the Canadian healthcare system which prevent access to timely biomarker testing, and recommendations to facilitate safe and appropriate access to Alzheimer's DMTs, if they are approved for use by Health Canada.

The AD Continuum & Pathophysiology

AD is defined biologically as the presence of two major hallmarks: extracellular amyloid-β (Aβ) plaque deposition and intracellular neurofibrillary tangles (NFT).[13,14] Inflammation, oxidative stress, disruption of intracellular nutrient transport, synaptic loss, and neuronal degeneration accompany accumulation of Aβ and NFT. These neurobiological changes lead to the onset of clinical symptoms, which can include changes in short-term memory, language, general cognition, mood, and behavior.[14,15] While the precise sequence of events remains unknown, it is believed that extracellular Aβ plaque deposition occurs prior to intracellular NFT formation.[15] Importantly, data suggest that Aβ deposition alone is not sufficient to cause cognitive deterioration directly, though its abundance is directly correlated with the extent of cognitive decline.[13,16]

The onset of AD neuropathological changes precedes the emergence of clinical symptoms by an estimated average of 10–20 years.[17–22] Historically, the diagnosis of AD has focused on clinical symptoms. In the mild cognitive impairment (MCI) stage, individuals may experience memory loss and show abnormality on cognitive tests, while daily independence remains generally intact.[23,24] In the dementia stage, memory and other cognitive symptoms become more severe, with individuals requiring assistance performing daily activities.[23,24] The AD dementia stage can further be broken down into mild, moderate, and severe stages depending on the severity of interference with daily activities.[7,24]

With the emergence of biomarkers that characterize the pathophysiological changes in AD, the National Institute on Aging and the Alzheimer's Association (NIA-AA) research framework provides a biological definition of AD.[13] The framework includes three general groups of biomarkers: (1) biomarkers of Aβ plaques (labeled "A") such as cortical amyloid PET ligand binding or low CSF Aβ42; (2) biomarkers of fibrillar tau (labeled "T") such as cortical tau PET ligand binding or elevated CSF phosphorylated tau (p-tau); and (3) biomarkers of neurodegeneration or neuronal injury (labeled "(N)") such as CSF total tau (t-tau), CSF neurofilament light protein (NfL), FDG PET hypometabolism, and cortical atrophy on MRI.[13,25] Further, the NIA-AA Clinical Staging system accounts for the AT(N) designation across the clinical cognitive continuum, from normal cognition to subjective cognitive decline, to mild cognitive impairment and syndromic dementia, incorporating potential behavioral change in advance of cognitive decline.[13] Stage 1 describes individuals with biomarker evidence of Alzheimer's disease who are asymptomatic.[13] Stage 2 describes individuals who have normal performance on objective cognitive tests but have a subjective concern of cognitive decline or neurobehavioral changes.[13] Stage 3 describes individuals who have objective cognitive impairment on testing not severe enough to impact general everyday functioning.[13] Stages 4 through 6 describe progressive loss of function and are characterized as mild, moderate, and severe dementia.[13]

It has been proposed that interventions in upstream events (Aβ or tau aggregation) can mitigate downstream deleterious events (synaptic loss or neuronal death), thus slowing development of dementia.[26] While there are therapies available to treat the symptoms of AD, there are currently no Health Canada-approved medications to treat and target the underlying pathology of AD. Promising results have been reported recently using monoclonal antibodies (mAbs) which reduce Aβ levels in early AD (broadly defined as MCI or mild AD dementia, or NIA-AA Clinical Stages 3 or 4),[13] leading to United States Food and Drug Administration approvals of such medications.[27,28] However, the process of introducing these new therapies into Canadian provincial health-care systems is far from straightforward. As the COVID-19 pandemic has shown, even the most sophisticated healthcare systems can be overwhelmed by a rapid surge in demand for

https://doi.org/10.1017/cjn.2023.322 Published online by Cambridge University Press

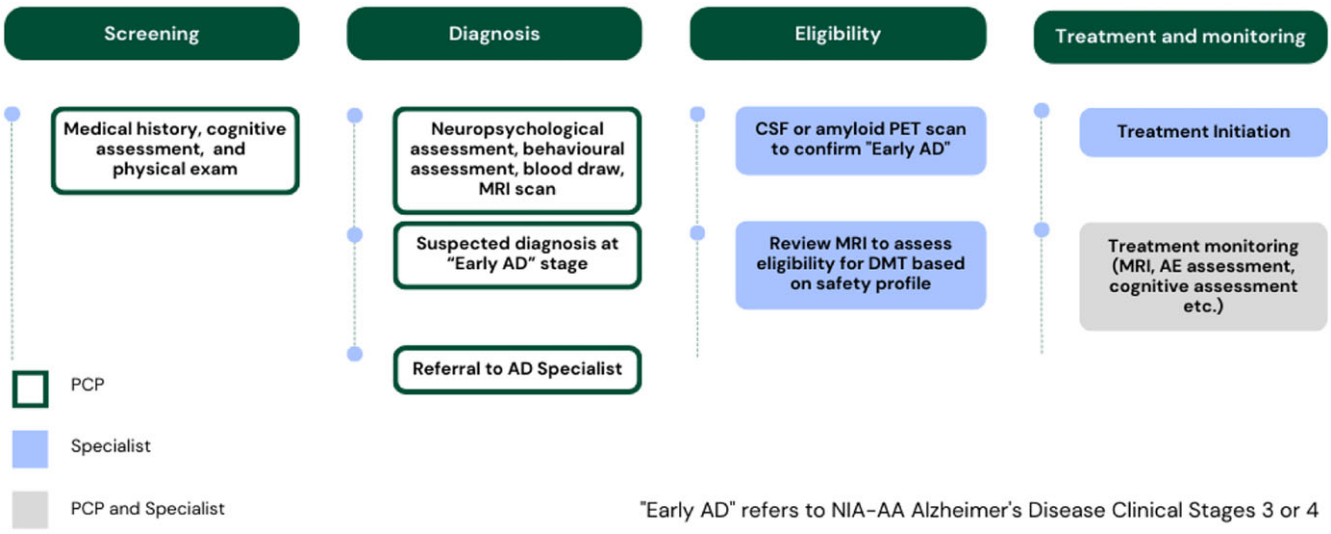

Figure 1: Early AD patient pathway to screen, diagnose, determine eligibility, and initiate DMTs, once available.

services. The introduction of a potential DMT for early AD may result in a similar development, in which the current healthcare system capacity is insufficient to cope with the expected volume of patients.[10] Shifts and adaptations of current models of care for AD patients will be required in order for such medications to be accessible to Canadians who are assessed as eligible to receive them.

Facilitating the Future Detection and Management of Early AD

The landscape of AD disease-modifying therapies is constantly evolving. If approved, such therapies will require fundamental changes in the way healthcare is delivered for people living with AD. While there are several compounds on the horizon, our focus is on the most advanced class of medication, monoclonal antibodies (mAbs) targeting Aβ-positive MCI and mild AD dementia. These passive immunotherapies activate microglia to engulf and remove fibrillar Aβ and/or block the aggregation of smaller Aβ species from forming plaques.[29] Recently, the anti-Aβ mAbs lecanemab and donanemab have demonstrated efficacy in slowing clinical decline in the MCI and mild dementia stages of biomarker-confirmed AD.[8,9] If approved, extensive medical infrastructure would be required to safely administer antibody therapy either by intravenous infusions or as subcutaneous injections.[30,31] Figure 1 conceptualizes a future pathway for early AD diagnosis, assessment for eligibility, and treatment with disease-modifying therapies, based on current clinical trial requirements.

In Canada, most care for dementia is currently provided by primary care physicians, but with the introduction of DMTs, there would be a need to shift to specialist-based dementia diagnosis with biomarkers.[31] Anti-Aβ mAbs require the evaluation of Aβ status prior to administration, either by amyloid PET scan or by lumbar puncture to analyze CSF for Aβ, total tau, and phospho-tau.[31–33] While there are many advancements underway developing blood/plasma Aβ and tau biomarkers, they are not ready for clinical use.[31,34]

A major potential side effect of treatment with anti-Aβ mAbs is amyloid-related imaging abnormalities (ARIA).[32,33,35] Since anti-Aβ mAbs target removal of Aβ from both the parenchyma and cerebral vasculature, vessels with preexisting Aβ vascular pathology might become transiently more susceptible to leakage of vascular contents.[35] This pathology results in ARIA-E (edema) if the leakage consists of proteinaceous fluid, and ARIA-H (hemorrhage) if the leakage consists of blood products.[35] Should patients decide to undergo treatment with an anti-Aβ mAb, a baseline pre-treatment MRI would be required to ensure there is no elevated risk of ARIA due to existing multiple microbleeds prior to treatment.[32,33] Once on treatment, monitoring with additional MRIs would be required, especially during the initial stages of treatment, as ARIA-E and ARIA-H typically occur early in the course of treatment.[36] Clinical trial protocols require up to four MRIs in the first year of treatment, a significant burden on healthcare resources.[32,33,37] Should a patient develop ARIA, mAbs therapy would be interrupted, and additional MRIs would be required.[32,33] In clinical trials, treatment often resumed once ARIA resolved.[32,33]

Overall, substantial healthcare resources and coordination between multiple stakeholders will be required to realize future care pathways with DMTs. Several models have shown that the Canadian healthcare system is not equipped to manage the influx of patients and the requirement for diagnosis, eligibility determination for DMTs, and safety monitoring.[10,38]

Canadian Dementia Expert Group Recommendations

Multiple groups of experts involved in dementia and other neurological care gathered in 2022 to discuss the future needs of the healthcare system and ways to create change ahead of potential DMT approvals. Forums took place in Western Canada (Calgary, AB), Ontario (Toronto, ON), and Quebec (Quebec City, QC) with a total of 6 meeting chairs and 30 participants. 18 Canadian cities were represented across the participants, with a balance of males and females, and healthcare professionals from academic and community practice settings. The objectives of the meetings were to (1) understand and prioritize key barriers in the current patient pathway that would affect the ability to treat patients with potential DMTs; (2) understand how other existing clinic models, including those used in multiple sclerosis (MS), could be applied to address key barriers in AD; and (3) assess how to best design optimal care pathways and implement these models in the future. The expert group was composed of AD specialists (neurologists, geriatricians,

https://doi.org/10.1017/cjn.2023.322 Published online by Cambridge University Press

Table 1: Summary of key barriers to integrating future AD DMTs into care pathways

Stage in AD Care Pathway	Barriers
Timely Identification of "Early AD"	• Many patients have limited access to primary care. These resource constraints are expected to worsen with more primary care physicians (PCPs) retiring and a surge of patients trying to access care if a DMT is available.
	• There is a lack of public awareness and education on AD, which limits knowledge in patients and families on the early signs and symptoms of AD.
	• There is stigma and discrimination toward AD in the community. This prevents people from speaking up when early signs are evident.
	• PCPs often lack education, time, and access to tools to support initial assessments and standardized testing. This leads to inconsistencies on how MCI and mild dementia are identified, evaluated, and managed.
Confirmatory Diagnosis/ Eligibility	• There is limited and delayed access to specialists for diagnosis confirmation and eligibility for DMTs. Many patients will progress to later stages while on wait lists.
	• PET or CSF testing is needed to confirm the presence of Aβ pathology. PET is costly and access is limited by location, while CSF testing reimbursement systems differ by province. Both PET and CSF are invasive and require significant clinician education for interpreting results. Greater capacity of personnel to administer and interpret these tests will also be required.
	• There is a lack of community knowledge of available resources to support post-diagnosis discussion with PCPs, patients, and families.
Treatment and Monitoring	• Current wait times for MRIs will be strained should DMTs become available. Greater expertise and capacity for MRI screening and monitoring specific to AD will be required, as well as increased coordination, resources, and trained personnel.
	• If patients are deemed appropriate for DMT use, there is also a need for added capacity in infusion clinics for treatment administration.
Overall Care Coordination	• There is a lack of specialized AD navigation pathways and interdisciplinary support teams. There is a need to better coordinate referrals, diagnosis, and treatment.

Table 2: Summary of recommended short-term recommendations to improve AD models of care in Canada

High-impact Recommendations to Address in the Foreseeable Future	Regional Forum that Made Recommendation
1. Develop an official "AD Treatment Community Network" to incorporate learnings from the prior introduction of DMTs in other therapeutic areas	All Regions (Western Canada, Ontario, and Quebec)
2. Collect evidence from the Multispecialty Interprofessional Team (MINT) model to support advocacy efforts and best practice sharing	Western Canada and Ontario Regions
3. Continue to expand the work of the Quebec Alzheimer Plan	Quebec Region
4. Educate healthcare providers (HCPs) and the general public on the early identification of AD and the role of biomarkers	All Regions (Western Canada, Ontario, and Quebec)
5. Expand amyloid PET and CSF biomarker access for Canadian patients, while building stronger evidence for future blood-based biomarkers	All Regions (Western Canada, Ontario, and Quebec)
6. Improve MRI monitoring capacity and DMT administration infrastructure	All Regions (Western Canada, Ontario, and Quebec)

psychiatrists), primary care providers (including general practitioners and nurse practitioners) with experience in AD care, AD biomarker experts, neuroradiologists, MS specialists, and dementia government policy experts.

Across the three regions in Canada, participants overwhelmingly identified similar barriers within the current AD care pathway, and there was alignment that addressing barriers within the diagnostic and treatment initiation stage of the pathway would be needed (Table 1). The groups prioritized the need to support the timely identification of early AD, which includes increasing capacity of primary care, and addressing general public stigma toward AD. All groups also felt that access to resources to confirm DMT eligibility (amyloid PET, CSF biomarkers, specialists) would only worsen if a DMT was approved. Currently, amyloid PET is limited to research settings and is very costly. CSF testing for amyloid status is available for clinical use and reimbursed by some provinces, but often through complicated mechanisms. For example, in the province of Quebec, CSF testing for Aβ is reimbursed using a process called "Authorization for Medical Biology Services Not Available in Quebec" which requires the signature of two physicians, including one that is a medical biochemist designated by the Health Ministry.[39] Historically, hospitals in Canada have sent CSF samples to laboratories outside of Canada, not only resulting in a delay in diagnosis but adversely impacting a critical window of opportunity for treatment, clinical trials, and other supportive services for patients and their families. In an effort to demonstrate the benefit of providing direct access to CSF biomarker testing to providers in Canada, St Paul's Hospital in Vancouver, Canada launched the National Alzheimer's Disease Biomarker Testing Program in 2021, through a special access designation.[40] While CSF testing is now available across Canada through this program, capacity investment levels and differing reimbursement pathways from province to province continue to create barriers to equitable access for all.

The challenges continue once patients are deemed eligible for treatment with DMTs. MRI monitoring and ongoing infusions or injections would put a strain on specialists, nurses, technologists, and radiologists. MRI wait times were seen as a barrier in all regions. As well, the infrastructure for administering intravenous or subcutaneous DMTs is non-existent within the current AD care pathway. Finally, across all of these barriers, a common challenge identified was the need to better coordinate care across multidisciplinary teams.

In order to overcome these challenges, the Canadian Dementia Expert Group prioritized six short-term recommendations (Table 2). The majority of the recommendations were consistent

https://doi.org/10.1017/cjn.2023.322 Published online by Cambridge University Press

and applicable in all three regions. Recommendations were prioritized as highly impactful if they could be implemented in the foreseeable future, and have a triple effect on patients, caregivers, and the healthcare system.

Recommendation to Develop an Official "AD Treatment Community Network" to Incorporate Learnings From the Prior Introduction of DMTs in Other Therapeutic Areas

The Canadian Dementia Expert Group included multiple sclerosis (MS) specialists and nurses who shared their experience introducing some of the first MS DMTs into their clinic models. The exchange between disease areas in these forums provided strong insights and parallels that could be leveraged to inform change in the healthcare system. Developing an "AD Treatment Community Network" would be helpful nationally to promote discussion about introducing AD DMTs if available, while incorporating learning from other fields. Conferences and other forums would be helpful in connecting clinicians and patient advocacy groups within these areas, to work together to create change in the model of care.

There are a number of insights gained by looking at the MS multidisciplinary clinic model. The first therapy proven to be effective in altering the natural history of relapsing-remitting MS was in 1993 (i.e. interferons).[41] Today, there are over 20 DMTs for patients with MS.[42] Parallels can be drawn between MS treatment in the early 1990s and AD treatment today. However, the scale of AD in the aging population is magnitudes greater than the population affected by MS, which is a limitation of our analysis.

MS stakeholders noted that it was critical that they quickly established and funded MS multidisciplinary clinics, which partnered with radiologists, specialized nurses (to support infusions and injections), social workers, occupational therapists, drug navigators, lab medicine specialists, and other ancillary resources. Radiology partnerships enabled clinics to secure ongoing access to MRI in MS. Specialized nurses developed extensive knowledge of MS pathology, diagnosis, symptom management, and treatment, contributing to therapeutic decisions, side effect management, and therapeutic response monitoring. Nurses also help manage patient expectations and play a key role in patient education. Specialized MS clinics were able to build evidence on improved health outcomes (e.g. slowed disease progression, improved quality of life) and cost savings of the clinic model. Government and other sources of funding were then approached based on this evidence. National programs were also developed to educate the public and PCPs on understanding the initial symptoms of MS, and why early MS diagnosis is important.

The MS community has built well-established consensus guidelines on the diagnostic criteria for MS, which are continuously updated as new evidence emerges. A similar approach should be taken in AD, especially on biomarker interpretation and MRI use for safety monitoring. Such guidelines should be disseminated nationally, as education of specialists will be important to reduce potential skepticism surrounding early AD diagnosis and treatment.

As noted, strategies employed in creating MS clinics across Canada may need to be scaled up significantly in AD, as the prevalence of AD is about six times that of MS.[1,43] It is also recommended that the AD community seek open dialogue with clinicians in other therapeutic areas that implement DMTs, such as cancer care, wherein patients often require regular MRI and PET scans to assess their initial eligibility for treatment and to monitor disease response. Developing systems of care for patients with early AD modeled to include the robust elements of integrated provincial cancer care systems would enhance provincial and thus national dementia care overall.

Recommendation to Collect Evidence from the MINT Model to Support Advocacy Efforts and Best Practice Sharing

Currently, referral numbers to AD specialists are high, as some PCPs may be unfamiliar with identification and assessment of cognitive symptoms, and initiation of standard-of-care symptomatic treatments.[44–46] In Canada, where there is a shortage of AD specialists, national guidelines emphasize that dementia care should be centered in primary care.[47–51] However, studies have shown this can be challenging, with many individuals with dementia going undiagnosed in the community.[3] Multispecialty Interprofessional Team (MINT) memory clinics across Canada offer multidisciplinary dementia care provided by primary care teams who have received standardized nationally accredited training. There are over 100 MINT sites in Canada, and the success of this model is based on collaboration between primary care, dementia specialist care, and community agencies.[52] This model, or one similar, could improve patient access to diagnostic tests, specialists, and follow-up resources.

The Canadian Dementia Expert Group noted that the economic benefit of the MINT model has been independently evaluated, with published data demonstrating MINT clinics to be less expensive, while improving quality of life as compared to usual care.[53] Several other studies have demonstrated high levels of patient and caregiver satisfaction within MINT clinics, improved care through partnerships between MINT clinics and the Alzheimer Society, high levels of healthcare provider satisfaction, and substantial capacity-building for dementia care within primary care.[54–58] Although this model can create local capacity, a major limitation is that sufficient funding may not be available to allow all regions to adopt this model. The reliance on multidisciplinary care may also be challenging to implement when there is already-limited access to primary care resources across Canada.[59]

In the short term, learnings and best practices from multidisciplinary models such as MINT memory clinics can be shared with primary, specialty, and community care in order to facilitate early diagnosis, which is central to appropriate DMT use.

Recommendation to Expand the Work of the Quebec Alzheimer Plan

Experts in the Quebec region recommended leveraging the already-established model of care known as the Quebec Alzheimer Plan, to continue to build capacity for AD diagnosis and treatment.[60] PCPs in Quebec work within multidisciplinary teams called Family Medicine Groups (FMGs), with access to nurses, social workers, and occasionally occupational therapists. The interdisciplinary model has been endorsed by the government of Quebec with two protocols available for AD: (1) diagnosis; and (2) post-diagnostic care.[61] Under the Plan, the province of Quebec has designated primary care as responsible for detecting MCI and early Alzheimer's disease, and within this model, nurses are empowered and trained to administer cognitive tests, reserving the more complex patients for tertiary care. This is very much in line with national dementia guidelines which emphasize that dementia care should be centered in primary care.[47–51] Not only has this structure been found to increase the quality of care provided to patients with

https://doi.org/10.1017/cjn.2023.322 Published online by Cambridge University Press

dementia, but physicians have also had increased confidence in their competence to diagnose and manage dementia.[62,63]

While there is a strong level of support for the Quebec Alzheimer Plan already, the Quebec Dementia Expert Group recommended continued investment in the Plan's Phase III implementation.[64,65] Appropriate levels of investment and resources should be made available to enhance support for timely diagnosis and care. A central recommendation was to continue to elevate the role of nurse practitioners in Quebec, as they can play a pivotal role in supporting earlier diagnosis. Additionally, the group recommended implementing a navigator model within FMGs (ensuring that patients and caregivers are supported throughout their journey, including moving between primary and specialty care), and assigning both an HCP and nurse champion to each team.

As part of Phase III of the Quebec Alzheimer Plan, strengthening of secondary and tertiary memory clinics will be essential, as these clinics will assist with interpretation of biomarker testing, confirmation of early AD diagnosis, and administration and monitoring of DMTs alongside PCPs and FMGs.[64,65] They will also be involved in training and education at all levels, including networking between medical specialties (imaging, laboratory, and clinical) around AD diagnosis and DMT use. The clinical and functional parameters of these memory clinics should be made official, and their status recognized.

There is a greater need for education of all stakeholders involved in the Quebec Alzheimer Plan. Education can be provided on disease awareness and diagnosis through FMGs, in partnership with academic and government bodies. There is also a need to evolve payment models, as the current system creates a disincentive to spending more time with patients during a cognitive assessment.

Recommendation to Educate HCPs and the General Public On the Early Identification of AD and Biomarkers

The Canadian Dementia Expert Group determined that a significant barrier is the lack of primary care education on using available tools to identify MCI and mild dementia.[62] Recommendations were made for primary care to use scales to measure cognition, behavior, and function, administered to both the patient and care partner.[66] Early detection fundamentally requires family member and friend participation, as ignoring them is a frequent cause of delayed diagnosis.[67] Addressing this barrier through education would increase primary care confidence in identifying which patients could potentially benefit from DMTs, and optimizing outcomes for those who are not eligible.

For specialized healthcare practitioners including neurologists, geriatricians, geriatric psychiatrists, and laboratory medicine specialists, education should focus on the utility and interpretation of PET and CSF biomarkers. This knowledge will be essential in managing the eligibility requirements for DMTs in a healthcare system with strained diagnostic resources. Education will need to be provided for radiologists on how to assess MRI scans for amyloid-related imaging abnormalities (ARIA). New educational initiatives could be accredited by the College of Family Physicians of Canada and the Royal College of Physicians and Surgeons of Canada, and disseminated in partnership with the Alzheimer Society of Canada and other local agencies, which can further advocate for government investment in healthcare practitioner education.

A recommendation was made to increase public education around the differences between healthy aging and mild cognitive impairment. Through partnership with patient groups such as the Alzheimer Society, social media campaigns were recommended as a potential means to educate the public and combat stigma. Testimonials from celebrities, patients with lived experience, and caregivers could be leveraged for such campaigns. Reducing public stigma tied to cognitive impairment should lead to earlier consultations with a healthcare provider.

Potential approval of DMTs for AD will lead to more people seeking opinions on whether they are eligible for treatment, or even if they are at risk for cognitive decline. Equipping primary care teams and other physicians with the knowledge to assess individuals at risk, how to communicate that risk, and how to provide prevention and/or cognitive enhancement strategies will be important in the future model of care. International roadmaps are already available on how to improve brain health services and implement models of dementia prevention.[68]

Recommendation to Expand Amyloid PET and CSF Biomarker Access for Canadian Patients, While Building Stronger Evidence for Future Blood-Based Biomarkers

Access to amyloid PET and CSF biomarker analyses was highlighted as a major barrier to overcome prior to the potential arrival of AD DMTs. There is a need to optimize access to existing resources, as well as secure funding for expansion. Contact should be made with nuclear medicine sites across the country, to gauge current PET capacity. Lumbar punctures for CSF analysis are scalable, less expensive, and more accessible than PET scans. Lumbar puncture has been demonstrated to be safe and effective in patients with AD, and given the demonstration of high diagnostic accuracy of measurement of Aβ and tau proteoforms in CSF, this technology should be used more widely in memory clinics.[69] Increasing ease of access to CSF testing for Aβ and tau through provincial reimbursement pathways, and increasing capacity to perform lumbar punctures, will help ensure patients who are eligible for DMTs can swiftly receive them.

Blood-based biomarkers may become an effective screening tool in primary care given the less-invasive specimen collection requirements. In the future, blood-based biomarkers may even replace PET and CSF for confirmatory diagnosis of Alzheimer's disease, which will aid in the determination of DMT eligibility. Currently, there are no Health Canada-approved blood-based biomarker products available, which in part reflects the need to collect more evidence to establish their validity in the diagnosis of AD. The Canadian Dementia Expert Group recommended a focused effort to build further evidence on blood-based biomarkers through research groups and industry partnerships in Canada. As new data become available, the NIA-AA Research Framework and Clinical Staging should be leveraged to review this information and assess how to best incorporate blood-based biomarkers into the future AD care pathway.[13]

A first pan-European workflow for biomarker use in "middle-old age" to diagnose AD at the MCI to mild dementia stage has been proposed.[70] Frailty and comorbidities, rather than age alone, may be more important future considerations when interpreting limited existing biomarker data in older individuals.

ApoE genetic testing has been proposed as an integral aspect of risk stratification for possible amyloid-related imaging abnormalities (ARIA) associated with DMT use.[33] ApoE genotyping capacity should be surveyed across the country, to assess current access. There is a need to create and distribute standardized ARIA risk

https://doi.org/10.1017/cjn.2023.322 Published online by Cambridge University Press

charts for each possible ApoE genotype, to assist AD specialists in interpreting results to patients, as there are insufficient dedicated genetic counselors to address this discussion in all cases.

Recommendation to Improve MRI Monitoring Capacity and DMT Administration Infrastructure

The availability of MRI will be a critical rate-limiting step for diagnosis, treatment eligibility, and safety monitoring of DMT use. The Canadian Dementia Expert Group recommended convening a forum in collaboration with neuroradiologists nationwide, to determine standardized sequencing protocols for MRI in dementia care, especially relating to monitoring and management of ARIA. Clinician education on the detection and management of ARIA will also be required, to enable technologists, neuroradiologists, and clinicians to align on key requirements across centers in Canada.

The neuroimaging forum suggested above could also explore how to optimize MRI access, beyond simply purchasing more scanners. Recommendations may include creating shorter MRI time slots, providing pre-filled MRI requisition forms, and creating automatic future booking systems, to help centers forecast workload. Fostering ongoing relationships with neuroradiologists across the country will be essential to accommodate the increased patient volume if DMTs become available.

If intravenous DMTs are approved in Canada, there will be a need to expand intravenous infusion clinic capacity to allow for more widespread administration of DMTs. Specialty care and memory clinics will need to evolve to coordinate care and enable more frequent visits for drug administration, monitoring, and counseling. Multiple Sclerosis (MS) clinic models can offer guidance on how this infrastructure can be created. Community-based intravenous administration clinic capacity may also be leveraged for AD care.

Conclusion

The Canadian healthcare system is not prepared for the potential arrival of Alzheimer's disease-modifying therapies (DMTs), as it currently cannot accommodate the need for early diagnosis, biomarker testing, and MRI monitoring that is essential for treatment with these agents. These challenges will only grow based on the increase in the number of people living with AD and existing barriers in the current care pathway. The Canadian Dementia Expert Group recommendations outlined in this review begin a discussion to support timely access to DMTs for eligible patients, if such agents are approved for use by Health Canada. These recommendations are aligned with priorities set out in both the Canadian National Dementia Strategy and the Quebec Alzheimer Plan and focus on awareness, education, and quality of care.[60,71] Ultimately, there is great need for provincial healthcare systems to prioritize dementia care and support infrastructure development. In the anticipated era of disease-modifying therapies, all stakeholders must be ready to work collaboratively with persons living with AD and their families, to enact change in the AD model of care.

Acknowledgments. The authors thank the participants of the Canadian Dementia Expert Group for their contributions to the recommendations provided in this review. Participants included:

Western Canada Forum: Dr Alexandre Henri-Bhargava, Dr Sheny Khera, Dr Michael Yeung, Fred Horne, Dr Mari L. DeMarco, George Andrews, Margaret Prociuk, Dr Oliver David, Karyn Fischer

Ontario Forum: Dr Mark Freedman, Dr Sandra Black, Dr Linda Lee, Dr Amer M. Burhan, Dr Deborah Norrie, Dr Sharon Cohen, Jennifer Whitlock, Kyle Fitzgerald, Dr Daniel Wong, Dr Donald Lee

Quebec Forum: Dr Pierre Duquette, Julie Brunet, Dr Claude Patry, Karoline-Mona Demers, Josée Poirier, Sylvie Grenier, Dr Pedro Rosa-Neto, Dr Guy Lacombe, Dr Christian Vinette, David Levine, Claire Webster

Funding. This manuscript and the Canadian Dementia Expert Group forums were funded by F. Hoffmann-La Roche Ltd (Mississauga, ON, Canada).

Competing interests. Dr Andrew Frank has received support for this manuscript and the Canadian Dementia Expert Group forums, as noted above.

Dr Michael Borrie has received funding/grants to his institution from MITNEC-C6, CIHR Institute on Aging for the Canadian Collaboration on Neurodegeneration in Aging, NIH Alzheimer Disease Neuroimaging Initiative, Biogen, Alector, Eisai, Abbvie, and Eli Lilly. He has received consultancy fees to his institution from Biogen and Hoffmann-La Roche Ltd He has received support for this manuscript and the Canadian Dementia Expert Group forums, as noted above.

Dr Serge Gauthier is a board member of the Sharon Francis Foundation. He has served on advisory boards/consultancies for ENIGMA US, AmyriAD, and TauRx. He has received honoraria from Lundbeck Korea, Eli Lilly Canada, and Eisai Canada. He has received support for this manuscript and the Canadian Dementia Expert Group forums, as noted above.

Dr Ging-Yuek Robin Hsiung is the current president of the Consortium of Canadian Centres for Clinical Cognitive Research (C5R). He has acted as Site Investigator in clinical trials in Alzheimer's Disease and was paid accordingly by Biogen, Cassava, and Eli Lilly. He has received consulting fees from Biogen, NovoNordisk, and Hoffmann-La Roche Ltd He has received support for this manuscript and the Canadian Dementia Expert Group forums, as noted above.

Dr Zahinoor Ismail is funded by the Alzheimer's Drug Development Foundation, Brain Canada, CCNA, CIHR, Gordie Howe CARES, NIA, and Weston Foundation. He has served on advisory boards/consultancies for Acadia, Biogen, Lundbeck, Otsuka, Hoffmann-La Roche Ltd., and the Canadian Agencies for Drugs and Technologies in Health, and is co-chair of the Government of Canada Ministerial Advisory Board for Dementia. He has received honoraria from Lundbeck/Otsuka and his institution has received fees from Acadia, Biogen, and Hoffmann-La Roche Ltd He has received support for this manuscript and the Canadian Dementia Expert Group forums, as noted above.

Dr Louis Verret has acted as Principal Investigator in clinical trials in Alzheimer's Disease and was accordingly paid by Hoffmann-La Roche Ltd., Biogen, IntelGenX, and NovoNordisk. He received personal fees for consulting work and advisory boards, speaker bureaus, and lectures from Hoffmann-La Roche Ltd and Biogen. He has received support for this manuscript and the Canadian Dementia Expert Group forums, as noted above.

Melanie Wilson is employed by Hoffmann-La Roche Ltd (Mississauga, ON, Canada).

Statement of authorship. AF, MB, SG, RH, ZI, LV, and MW contributed substantially to the review conception and strategy. AF, MB, SG, RH, ZI, LV, and MW were responsible for the critical review of the manuscript outline and draft reports, and all approved the final version for submission.

References

1. Alzheimer Society of Canada. Navigating the Path Forward for Dementia in Canada. The Landmark Study: Path [Internet]. 2022. Available from: http://alzheimer.ca/en/research/reports-dementia/landmark-study-report-1-path-forward. Accessed March 3, 2023.
2. Burke AD, Goldfarb D. Timely diagnosis of alzheimer disease. J Clin Psychiatry. 2022;83:LI21019DH1C. DOI: 10.4088/JCP.LI21019DH1C.
3. Lang L, Clifford A, Wei L, et al. Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. BMJ Open. 2017;7:e011146. DOI: 10.1136/bmjopen-2016-011146 Published 2017 Feb 3.
4. Manuel DG, Garner R, Finès P, et al. Alzheimer's and other dementias in Canada, 2011 to 2031: a microsimulation population health modeling (POHEM) study of projected prevalence, health burden, health services, and

https://doi.org/10.1017/cjn.2023.322 Published online by Cambridge University Press

caregiving use. Popul Health Metr. 2016;14:37. DOI: 10.1186/s12963-016-0107-z.
5. Garcia-Alloza M, Subramanian M, Thyssen D, et al. Existing plaques and neuritic abnormalities in APP: PS1 mice are not affected by administration of the gamma-secretase inhibitor LY-411575. Mol Neurodegener. 2009;4:19. DOI: 10.1186/1750-1326-4-19.
6. World Health Organization [Internet]. WHO; 2022. Dementia. Available from: https://www.who.int/news-room/fact-sheets/detail/dementia. Accessed March 1, 2023
7. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to alzheimer's disease: recommendations from the national institute on aging-alzheimer's association workgroups on diagnostic guidelines for alzheimer's disease. Alzheimers Dement. 2011;7:263–9. DOI: 10.1016/j.jalz.2011.03.005.
8. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. N Engl J Med. 2022;0:9–21. DOI: 10.1056/NEJMoa2212948.
9. Sims JR, Zimmer JA, Evans CD, et al. Donanemab in early symptomatic Alzheimer disease the TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA. 2023;330:512–527. DOI: 10.1001/jama.2023.13239.
10. Mattke S, Wang M. Why would Canada have the longest wait times for an Alzheimer's treatment among the G7 countries? A policy analysis. Alzheimers Dement. 2021;17:e057288.
11. Wright AC, Lin GA, Whittington MD, et al. The effectiveness and value of lecanemab for early Alzheimer disease: a summary from the institute for clinical and economic review's California technology assessment forum. J Manag Care Spec Pharm. 2023;29:1078–83.
12. Jun H, Shi Z, Mattke S. Projected savings to Canadian provincial budgets from reduced long-term care home utilization due to a disease-modifying Alzheimer's treatment. J Prev Alzheimers Dis. 2023. https://link.springer.com/article/10.14283/jpad.2023.95#citeas.
13. Jack CR, Bennett DA, Blennow K, et al. NIA-AA research framework: toward a biological definition of Alzheimer's disease. Alzheimers Dement. 2018;14:535–62. DOI: 10.1016/j.jalz.2018.02.018.
14. Pinheiro L, Faustino C. Therapeutic strategies targeting amyloid-β in Alzheimer's disease. Curr Alzheimer Res. 2019;16:418–52. DOI: 10.2174/1567205016666190321163438.
15. Ghahremani M, Wang M, Chen HY, et al. Plasma phosphorylated tau at Threonine 181 and neuropsychiatric symptoms in preclinical and prodromal alzheimer disease. Neurology. 2023;100:e683–e693. DOI: 10.1212/WNL.0000000000201517.
16. Resnick SM, Sojkova SM, Zhou Y, et al. Longitudinal cognitive decline is associated with fibrillar amyloid-beta measured by [^{11}C]PiB. Neurology. 2010;74:807–15. DOI: 10.1212/WNL.0b013e3181d3e3e9.
17. Villemagne VL, Burnham S, Bourgeat P, et al. Amyloid β deposition, neurodegeneration, and cognitive decline in sporadic Alzheimer's disease: a prospective cohort study. Lancet Neurol. 2013;12:357–67. DOI: 10.1016/S1474-4422(13)70044-9.
18. Reiman EM, Quiroz YT, Fleisher AS, et al. Brain imaging and fluid biomarker analysis in young adults at genetic risk for autosomal dominant Alzheimer's disease in the presenilin 1 E280A kindred: a case-control study. Lancet Neurol. 2012;11:1048–56. DOI: 10.1016/S1474-4422(12)70228-4.
19. Jack CR Jr, Lowe VJ, Weigand SD, et al. Serial PIB and MRI in normal, mild cognitive impairment and Alzheimer's disease: implications for sequence of pathological events in Alzheimer's disease. Brain. 2009;132:1355–65. DOI: 10.1093/brain/awp062.
20. Bateman RJ, Xiong C, Benzinger TL, et al., Med. NEngl J. Clinical and biomarker changes in dominantly inherited Alzheimer's disease [published correction appears in N. Engl J Med. 2012;367:795–804. DOI: 10.1056/NEJMoa1202753.
21. Gordon BA, Blazey TM, Su Y, et al. Spatial patterns of neuroimaging biomarker change in individuals from families with autosomal dominant Alzheimer's disease: a longitudinal study. Lancet Neurol. 2018;17:241–50. DOI: 10.1016/S1474-4422(18)30028-0.
22. Braak H, Thal DR, Ghebremedhin E, Del Tredici K. Stages of the pathologic process in Alzheimer disease: age categories from 1 to 100 years. J Neuropathol Exp Neurol. 2011;70:960–9. DOI: 10.1097/NEN.0b013e318232a379.
23. Aisen PS, Cummings J, Jack CR Jr, et al. On the path to 2025: understanding the Alzheimer's disease continuum. Alzheimers Res Ther. 2017;9:60. DOI: 10.1186/s13195-017-0283-5.
24. Jack CR Jr, Albert MS, Knopman DS, et al. Introduction to the recommendations from the national institute on aging-Alzheimer's association workgroups on diagnostic guidelines for alzheimer's disease. Alzheimers Dement. 2011;7:257–62. DOI: 10.1016/j.jalz.2011.03.004.
25. Zetterberg H, Bendlin BB. Biomarkers for Alzheimer's disease – preparing for a new era of disease-modifying therapies. Mol Psychiatry. 2021;26:296–308. DOI: 10.1038/s41380-020-0721-9.
26. Selkoe DJ, Hardy J. The amyloid hypothesis of Alzheimer's disease at 25 years. EMBO Mol Med. 2016;8:595–608. DOI: 10.15252/emmm.201606210.
27. U.S. Food & Drug Administration [Internet]. FDA News Release; c2021. FDA Grants Accelerated Approval for Alzheimer's Drug. Available from https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug. Accessed September 15, 2023.
28. U.S. Food & Drug Administration [Internet]. FDA News Release; c2023. FDA Converts Novel Alzheimer's Disease Treatment to Traditional Approval. Available from https://www.fda.gov/news-events/press-announcements/fda-converts-novel-alzheimers-disease-treatment-traditional-approval. Accessed September 15, 2023.
29. Avgerinos KI, Ferrucci L, Kapogiannis D. Effects of monoclonal antibodies against amyloid-beta on clinical and biomarker outcomes and adverse event risks: a systematic review and meta analysis of phase III RCTs in Alzheimer's disease. Ageing Res Rev. 2021;68:101339. DOI: 10.1016/j.arr.2021.101339.
30. Gauthier S, Rosa-Neto P. Chapter 18 disease-modifying drugs. World alzheimer's report. Alzheimer's Disease Int. 2022;2022:295–7.
31. Chertkow H, Rockwood K, Hogan DB, et al. Consensus statement regarding the application of biogen to health Canada for approval of aducanumab. Can Geriatr J. 2021;24:373–378. DOI: 10.5770/cgj.24.570.
32. Cummings J, Aisen P, Apostolova LG, Atri A, Salloway S, Weiner M. Appropriate use recommendations. J Prev Alzheimers Dis. 2021;8:398–410. DOI: 10.14283/jpad.2021.41.
33. Cummings J, Apostolova L, Rabinovici GD, et al. Lecanemab: appropriate use recommendations. J Prev Alzheimers Dis. 2023;10(3):362–377. DOI: 10.14283/jpad.2023.30.
34. Smirnov DS, Ashton NJ, Blennow K, et al. Plasma biomarkers for Alzheimer's disease in relation to neuropathology and cognitive change. Acta Neuropathol. 2022;143:487–503. DOI: 10.1007/s00401-022-02408-5.
35. Sperling RA, Jack JRJr, Black SE, et al. Amyloid-related imaging abnormalities in amyloid-modifying therapeutic trials: recommendations from the Alzheimer's association research roundtable workgroup. Alzheimers Dement. 2011;7:367–85. DOI: 10.1016/j.jalz.2011.03.003.
36. Barakos J, Purcell D, Suhy J, et al. Detection and management of amyloid-related imaging Abnormalities in patients with Alzheimer's disease treated with anti-amyloid beta therapy. J Prev Alzheimers Dis. 2022;9:211–20. DOI: 10.14283/jpad.2022.21.
37. Ostrowitzki S, Lasser RA, Dorflinger E, et al. A phase III randomized trial of gantenerumab in prodromal Alzheimer's disease. Alzheimers Res Ther. 2017;9:95. DOI: 10.1186/s13195-017-0318-y.
38. Liu JL, Hlavka JP, Coulter DT, et al. Assessing the preparedness of the Canadian health care system infrastructure for an Alzheimer's treatment. Rand Health Q. 2019;8:2.
39. Gouvernement du Québec [Internet]. Ministère de la Santé et des Services sociaux; c2022. Biologie médicale: Analyses. Available from: https://msss.gouv.qc.ca/professionnels/soins-et-services/biologie-medicale/analyses/. Accessed March 23, 2023.
40. Providence Health Care, St. Paul's Hospital [Internet]. Pathology and Laboratory Medicine; c2022. Test Catalog. Available from https://www.providencelaboratory.com/test_catalog.php?ID=628. Accessed March 3, 2023.
41. Murray TJ. The history of diagnosis and treatment of MS: a brief overview. Curr Neurol Neurosci Rep. 2022;22:545–9. DOI: 10.1007/s11910-022-01217-3.

https://doi.org/10.1017/cjn.2023.322 Published online by Cambridge University Press

42. MS Society of Canada [Internet]. MS Society of Canada; c2023. Disease-modifying Therapies. Available from: https://mssociety.ca/managing-ms/treatments/medications/disease-modifying-therapies-dmts. Accessed March 3, 2023.
43. Gilmour H, Ramage-Morin PL, Wong SL. Multiple sclerosis: prevalence and impact. Health Rep. 2018;29:3–8.
44. Chodosh J, Peitti DB, Elliott M, et al. Physician recognition of cognitive impairment: evaluating the need for improvement. J AM Geriatr Soc. 2004;52:1051–9. DOI: 10.1111/j.1532-5415.2004.52301.x.
45. Dubois B, Padovani A, Scheltens P, Rossi A, Dell'Agnello G. Timely diagnosis for Alzheimer's disease: a literature review on benefits and challenges. J Alzheimer Dis. 2016;49:617–31. DOI: 10.3233/JAD-150692.
46. Prins A, Hemke F, Pols J, Moll van Charante EP. Diagnosing dementia in Dutch general practice: a qualitative study of GPs' practices and views. Br J Gen Pract. 2016;66:e416–422. DOI: 10.3399/bjgp16X685237.
47. CMA. Assessing dementia: the Canadian consensus. Organizing committee, Canadian consensus conference on the assessment of dementia. Can Med Assoc J. 1991;144:851–53.
48. Patterson CJ, Gauthier S, Bergman H, et al. The recognition, assessment and management of dementing disorders: conclusions from the Canadian consensus conference on dementia. Can Med Assoc J. 1999;160:S1–S15.
49. Chertkow H. Diagnosis and treatment of dementia: introduction. Introducing a series based on the third Canadian consensus conference on the diagnosis and treatment of dementia. Can Med Assoc J. 2008; 178:316–21. DOI: 10.1503/cmaj.070795.
50. Gauthier S, Patterson C, Chertkow H, et al. Recommendations of the 4th Canadian consensus conference on the diagnosis and treatment of dementia (CCCDTD4) can. Geriatr J. 2012;15:120–26. DOI: 10.5770/cgj.15.49.
51. Ismail Z, Black SE, Camicioli R, et al. Recommendations of the 5th Canadian consensus conference on the diagnosis and treatment of dementia. Alzheimer's Dement. 2020;16:1182–95. DOI: 10.1002/alz.12105.
52. Lee L, Hillier LM. Best approaches to supporting the needs of people living with dementia and their carers. World alzheimer report 2022. Alzheimer's Disease Int. 2022;2022:142.
53. Wong WL, Lee L, Walker S, et al. Cost-utility analysis of a multispecialty interprofessional team dementia care model in Ontario, Canada. BMJ Open. 2023;13:e064882. DOI: 10.1136/bmjopen-2022-064882.
54. Lee L, Slonim K, Hillier LM, et al. Persons with dementia and care partners' perspectives on memory clinics in primary care. Neurodegen Dis Manag. 2018;8:385–97. DOI: 10.2217/nmt-2018-0024.
55. Lee L, Hillier LM, Harvey D. Integrating community services into primary care: improving the quality of dementia care. Neurodegener Dis Manag. 2014;4:11–21.
56. Lee L, Molnar F, Hillier LM, et al. Multi-specialty interprofessional team (MINT) memory clinics: enhancing collaborative practice and health care providers' experience of dementia care. Can J Aging. 2022;41:96–109. DOI: 10.1017/S0714980821000052.
57. Lee L, Hillier LM, Stolee P, et al. Enhancing dementia care: a primary care-based memory clinic. J Am Geriatr Soc. 2010;58:2197–204. DOI: 10.1111/j.1532-5415.2010.03130.x9.
58. Lee L, Hillier LM, Heckman G, et al. Primary care-based memory clinics: expanding capacity for dementia care. Can J Aging. 2014;33:307–19. DOI: 10.1017/s0714980814000233.
59. Ontario College of Family Physicians. [Internet]. Ontario College of Family Physicians; c2022. Life Without a Doctor. Available from: https://lifewithoutadoctor.ca/. Accessed September 15, 2023.
60. Arsenault-Lapierre G, Godard-Sebillotte C, Sourial N, et al. Le plan Alzheimer québécois, un plan basé sur les soins primaires. Sante Publique. 2020;32:375–80. DOI: 10.3917/spub.204.0375.
61. Gouvernement du Québec [Internet]. Ministère de la Santé et des Services sociaux; c2018. Processus clinique interdisciplinaire en première ligne. Available from: https://publications.msss.gouv.qc.ca/msss/document-001071/. Accessed March 3, 2023.
62. Vedel I, Sourial N, Arsenault-Lapierre G, Godard-Sebillotte C, Bergman H. Impact of the quebec alzheimer plan on the detection and management of alzheimer disease and other neurocognitive disorders in primary health care: a retrospective study. CMAJ Open. 2019;14:E391–E398. DOI: 10.9778/cmajo.20190053.
63. Vedel I, Couturier Y. Résultats de la Recherche Évaluative et Pistes D'Action. l'Initiative ministérielle sur la maladie d'Alzheimer et autres troubles neurocognitifs majeurs 2016. 39p.
64. Gouvernement du Québec [Internet]. Ministère de la Santé et des Services sociaux; c2022. Orientations ministérielles sur les troubles neurocognitifs majeurs - Phase 3. Available from: https://publications.msss.gouv.qc.ca/msss/document-003346/. Accessed March 3, 2023.
65. Gouvernement du Québec [Internet]. Ministère de la Santé et des Services sociaux; c2022. Trousse à l'intention des intervenants en troubles neurocognitifs majeurs. Available from: https://publications.msss.gouv.qc.ca/msss/document-003492/. Accessed March 3, 2023.
66. Tang-Wai DF, Smith EE, Bruneau M-A, et al. CCCDTD5 recommendations on early and timely assessment of neurocognitive disorders using cognitive, behavioral, and functional scales. Alzheimer's Dement (N Y). 2020;6: e12057. DOI: 10.1002/trc2.12057.
67. Briggs R, O'Neill D. The informant history: a neglected aspect of clinical education and practice. QJM. 2016;109:301–2. DOI: 10.1093/qjmed/hcv145.
68. Frisoni GB, Altomare D, Ribaldi F, et al. Dementia prevention in memory clinics: recommendations from the European task force for brain health services. Lancet Reg Health Eur. 2023;26:100576. DOI: 10.1016/j.lanepe.2022.100576.
69. Stiffel M, Bergeron D, Mourabit Amari K, et al. Use of Alzheimer's disease cerebrospinal fluid biomarkers in a tertiary care memory clinic. Can J Neurol Sci. 2022;49:203–9. DOI: 10.1017/cjn.2021.67.
70. Festari C, Massa F, Ramusino MC, et al. European consensus for the diagnosis of MCI and mild dementia: preparatory phase. Alzheimers Dement. 2023;19:1729–41. DOI: 10.1002/alz.12798.
71. Public Health Agency of Canada. [Internet]. PHAC; 2019. A Dementia Strategy for Canada. Available from: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/dementia-strategy.html. Accessed March 3, 2023.

https://doi.org/10.1017/cjn.2023.322 Published online by Cambridge University Press