COMMENTARY

Improving the Delivery of Brain Health Care to All. Keeping our Eye on the Main Prize in an Era of Emerging Anti-Amyloid Therapies

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INTRODUCTION

The development of parenteral anti-amyloid therapies (AATs) for Alzheimer's disease (AD) marks a new era in cognitive therapeutics.(1) Currently or predicted soon-to-be available AATs (e.g., lecanemab, donanemab) appear modestly effective for patients with amyloid positive Mild Cognitive Impairment (MCI) or early-stage AD dementia. Though Health Canada granted conditional approval for lecanemab in October 2025, widespread access to these expensive agents will be delayed (annual drug acquisition costs for lecanemab when launched in the US were $26,500 USD(2)). It has been estimated that private insurance coverage in our country is a year away, and up to two years will be needed to decide if—and under what conditions—public funding may be provided. (Both Canada's Drug Agency and the Institut national d'excellence en santé et en services sociaux [INESSS] in Québec have recommended that lecanemab not be covered(3,4)). As well, their safe and appropriately targeted use will require a substantial upfront healthcare system investment and then on-going additional costs while maintaining necessary expenditures for other aspects of brain health care.(5,6)

Unfortunately, only a minority of patients considered for AAT meet eligibility criteria. For example, in a recently published study only 6–8% of 1,309 patients seen for cognitive concerns in a tertiary care memory clinic met clinical and amyloid status criteria and did not have a safety contraindication (i.e., >4 microbleeds or superficial siderosis on their MRI, *APOE4* homozygous status, anticoagulant therapy) for lecanemab.(7) Perhaps unsurprisingly relatively few persons (approximately 13,500) world-wide are estimated to have been treated with AATs outside of clinical trials.(2)

The gap between the hope and reality of AATs creates an urgent need to consider how we should deliver equitable and effective brain health care.(7) In our opinion, while the assessment of AAT eligibility should play an important role in overall brain health management, it cannot be the sole focus. These drugs are not a panacea. We have to consider both the wider needs of all patients and their families seen for cognitive concerns, and how best to specifically care for those who will be told they are ineligible or face potentially insurmountable barriers to accessing AATs.

DISCUSSION

It has long been recognized that comprehensive, multi-domain management of age-related cognitive impairment requires the creation, with the patient and caregiver (if present), of an individualized, periodically updated care plan incorporating anticipatory planning, caregiver support, neuropsychiatric symptom management, referrals when indicated, and both nonpharmacological and pharmacological (including deprescribing) interventions.(8) In Canada there has been general agreement that the majority of dementia care can be managed in primary care with only a minority needing to be referred on to specialty care.(9) We fear an excessive focus on AATs will distract from the need of maintaining this broad, primary-care based approach. While the appropriate use of AATs may require greater involvement of specialists focusing on decisions about their use, we must ensure the resulting system of care for optimizing brain health remains coordinated.

In older adults, mixed neuropathologies are common.(10) The benefits of lowering amyloid brain content with AATs will depend on how strongly an amyloid pathway underlies cognitive impairment in relation to coexisting pathophysiological processes. Detecting and understanding the extent of the multiple factors that might be driving cognitive decline is essential in clinical practice. A holistic approach that integrates

clinical evaluation, biomarkers, genotyping, and the detection of potential metabolic, vascular and lifestyle contributors coupled with multi-domain interventions, will represent a clinically sound, scalable, and ethical response to this new era in which we find ourselves. It should be more than solely deciding on who can receive AATs.

Growing evidence supports the use of nonpharmacological interventions that address lifestyle and vascular/metabolic risk factors for optimizing the brain health of older individuals at risk for cognitive impairment.[11] In the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) trial, a two-year multi-domain intervention of structured exercise, vascular/metabolic risk management, dietary guidance, and cognitive training was both feasible and helped to prevent cognitive decline in older participants.[12] These results have been replicated elsewhere (see—https://www.alz.org/wwfingers/overview.asp)[13] including the Canadian SYNERGIC Trial.[14] Progressive physical exercises, for example, seems to target mechanisms central to both Alzheimer's pathology (e.g., increases enzymatic clearance of Aβ, promotes glymphatic clearance during sleep that lead to better Aβ removal) and cerebrovascular dysfunction that are present in most persons with MCI or early AD seen in clinical practice.[15] These cognitive benefits are in addition to the improvements seen in general and cardiovascular health with the adoption of healthy lifestyles. Importantly, recent evidence shows that these interventions work even better in those *APOE4* homozygous,[16] which is a contraindication for AATs in some jurisdictions due to the higher incident of severe adverse events. While in no way minimizing the implementation challenges, we feel these interventions should be routinely offered and incorporated in the care plan of those seeking treatment for MCI or early dementia.

How best to do this in the Canadian context will present challenges. For one thing, there are deficiencies in required infrastructure and personnel. National shortages of family physicians[17] and the other specialists who are called upon (i.e., family physicians with care of the elderly training, geriatricians, geriatric psychiatrists, neurologists, psychiatrists[18-20]) for cognitive concerns are particularly salient. Approaches to address these shortages include creating a clinician resource plan with input from multiple stakeholders to address brain health needs; adding training spots in the noted specialties and facilitating entry into them; encouraging Canadian medical students and international medical graduates to consider these disciplines (e.g., through financial incentives); reducing the administrative burden on current physicians; increasing the use of telehealth (to reach those in rural and remote communities) and artificial intelligence for diagnostic assistance; and promoting innovative models of team-based care that include non-physician providers.

While an expanded network of specialty-based, stand-alone brain health (or memory) clinics have been proposed to meet the needs of those suspected of having impaired cognition, another consideration would be improving collaboration between secondary and tertiary care with primary care. An example of this could be through greater use of Multispecialty Interprofessional Team (MINT) Memory Clinics (previously known as Primary Care Collaborative Memory Clinics).[21] Roles and responsibilities would have to be clearly defined, but this may offer better integration with primary care and earlier access to the promotion of healthy lifestyles.

Independent of the care model chosen, a key element is offering something beneficial to all individuals with MCI or dementia, regardless of biomarker status, clinical stage, or AAT eligibility. The care offered should ideally include—as we have noted—intensive vascular/metabolic control (i.e., addressing hypertension[22], dyslipidemia, diabetes, and/or obesity), structured aerobic-resistance training, nutritional counseling (e.g., Mediterranean/MIND diet), cognitive training, sleep and stress management, and/or opportunities for social engagement. Monitoring and follow-up would include regular cognitive, vascular, functional, and adherence assessments.

The limited eligibility to receive ATTs for patients with MCI and early AD dementia can create potential ethical challenges concerning patients and families who will arrive with high expectations for ATT treatments but hear, "I'm sorry, you don't qualify." This can lead to profound emotional distress, pressure on practitioners to make exceptions, loss of trust, and disengagement from care. An unduly AAT-focused system risks serving only those who meet narrow eligibility criteria, while neglecting those who are older, at a later disease stage, and are more medically complex or have concurrent frailty. What could potentially emerge is a two-tier system for MCI and early-stage AD care: a small group receiving a costly and complex pharmacological intervention and a much larger group denied, admittedly often on justifiable grounds, this option. A comprehensive care model that holistically evaluates patients with a diverse range of cognitive presentations could offer meaningful personalized interventions to the majority, promoting fairness and equity in access to care for cognitive concerns.

CONCLUSION

The therapeutic promise of AATs for selected patients with AD pathology must not obscure the needs of the majority of patients who will never receive them. A comprehensive approach including clinical evaluation, biomarkers assessment, genotyping, and the detection of potential metabolic, vascular and lifestyle contributors coupled with multi-domain interventions, represents a clinically sound, scalable, and ethical response to this new era in which we find ourselves. It should be more than solely deciding on who can receive AATs. Delivering evidence-based interventions for all patients with MCI or dementia will help ensure that progress in therapeutics benefits the many, not just the few. The moment to act is now, before inequities in access and outcomes become entrenched.

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