The Need for a Fast-track Pathway to Streamline Disease-modifying Treatments in Early Alzheimer's Disease

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To the Editor,

I read with great interest the commentary by Montero-Odasso, Lee, and Hogan regarding the resource challenges facing Canadian brain health care in the present times.[1] The authors rightly argue that it should be more than solely deciding on who can receive amyloid targeting treatments. While the need for a holistic approach towards improving brain health is deeply appreciated, at least part of the argument seems to have a problematic premise that these therapies are a niche intervention relevant to too small a fraction of patients. By citing restrictive "real-world eligibility" figures of 6–8%, the authors inadvertently rely on a denominator illusion that mischaracterizes clinical utility.

The 6–8% figure represents all unselected patients entering a general memory clinic, including those with advanced dementia or even non-Alzheimer's pathologies. When the analytical lens is adjusted to the true target population of early Alzheimer's disease (AD)—as seen from both European tertiary clinics[2] and population-based cohorts like the Mayo Clinic Study of Aging[3]—eligibility climbs to 15–21% of patients strictly in the early stages of AD (mild cognitive impairment or mild dementia) who lack major safety contraindications. A therapy that could alter the disease trajectory for nearly one in five early-stage patients represents a substantial clinical cohort, particularly with analyses showing clinically meaningful effects on cognition and function.[4] These figures should also account for delays in specialist assessment, which allow a proportion of patients to already progress beyond eligibility criteria even before evaluation, leading to an underestimation of the actual eligibility numbers.

In this context, one can draw a curious analogy with the revolutionization of ischemic stroke therapy by the advent of intravenous (IV) thrombolysis, more than two decades ago. It may be more than a mere coincidence that contemporary registry analyses suggest eligibility is approximately 5–10% of all ischemic stroke presentations.[5] Modern workflow improvements, including the implementation of stroke codes, have increased the treated proportion in some stroke systems to >10%, but that does not mean the overall eligible proportion of all ischemic stroke patients has become much higher than earlier even after a long experience with this modern treatment. Yet, in the modern day, it is next to impossible to imagine a higher neurology centre without access to IV thrombolysis.

In this reader's opinion, one way to timely capture early AD patients is through a streamlined, fast-track pathway embedded within our existing system. By arming primary care providers with rapid screening tools, including plasma p-tau 217 in the right clinical context,[6] patients demonstrating early cognitive impairment can bypass traditional, lengthy waitlists and flow directly into a streamlined diagnostic triage protocol to confirm amyloid status. This targeted workflow rapidly filters out ineligible individuals at the frontline, ensuring that only select candidates reach tertiary specialists for final infusion clearance, while the others continue to receive the traditional and preventative care that the authors have quite expertly outlined. Such a pathway, once established, can function for other future disease-modifying treatments in AD that may well be approved in the coming years.

We can better optimize brain health delivery by integrating therapeutic modernization within the existing framework of care. To keep our eye on the main prize, Canada must build a system capable of both multi-domain lifestyle prevention and cutting-edge molecular care in AD as we enter the "golden age of Alzheimer's research"[7].

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