Recent Updates in Alzheimer's Disease

Hydro Pensioners Association of Ontario

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Objectives

To provide updates since we last met in 2024:

- Recently approved new treatments for AD
- System changes prompted by new treatments
- What does the future hold (current drugs in development)
- A call to action for those wishing to be involved

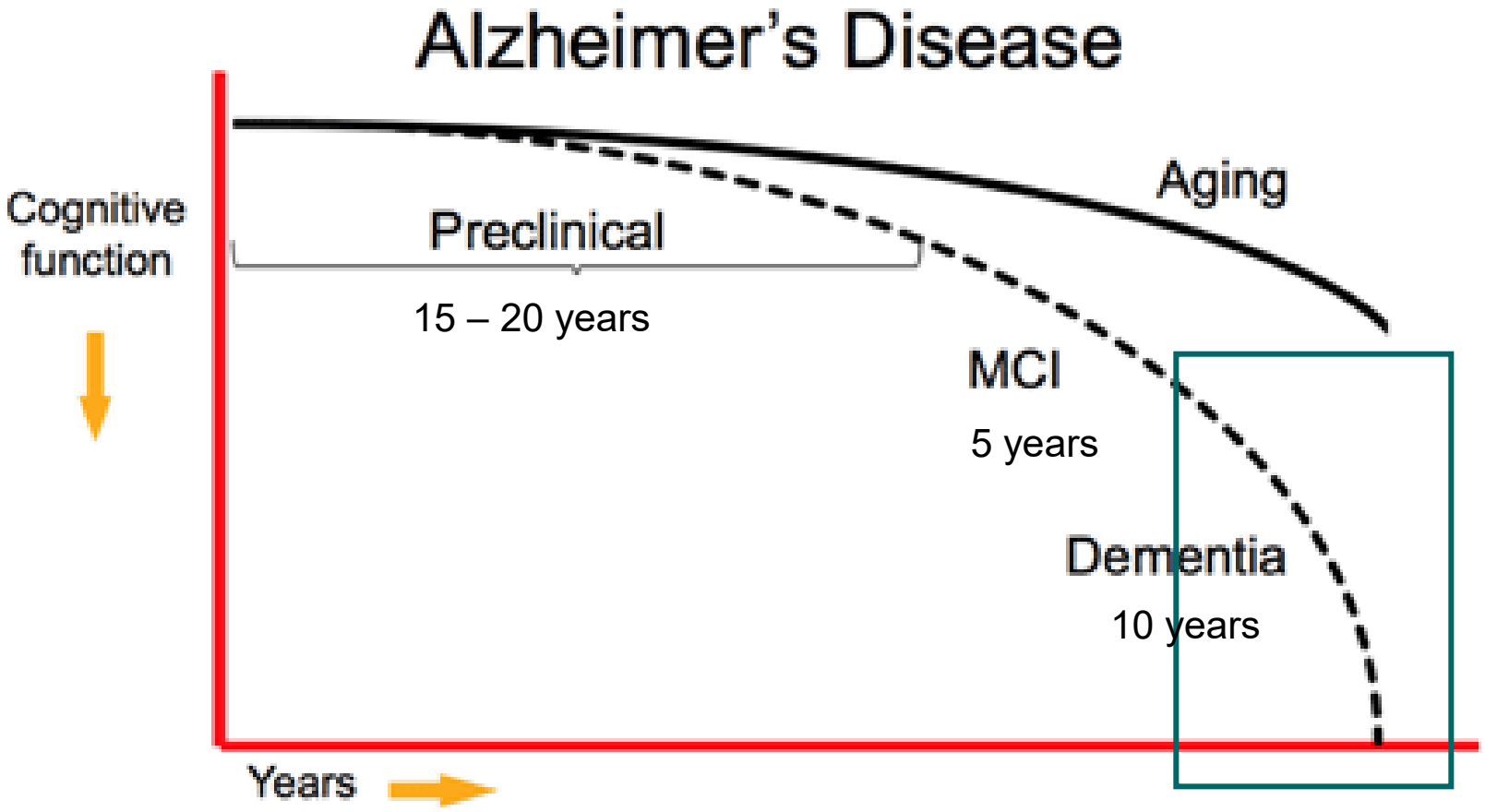
What Hasn't Changed

Alzheimer's disease remains:

- a serious, progressive disease causing:
  - impairment in memory and thinking
  - loss of independence
  - altered mood and behaviour
- A highly feared disease with no cure
- An expensive disease for patients and society
- The commonest cause of dementia
- Frequently underdiagnosed and misdiagnosed

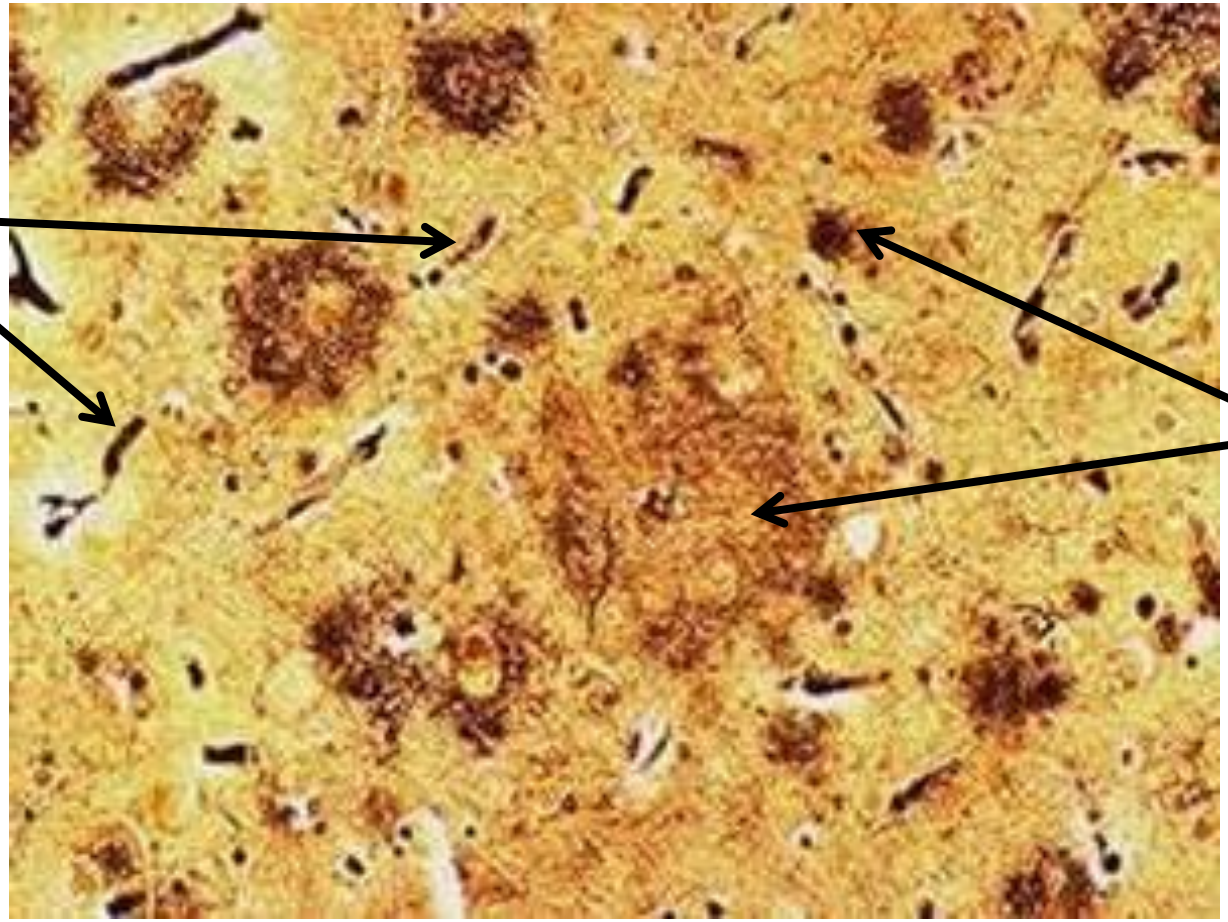
AD Remains an Urgent Healthcare Priority

- Staggering numbers; severe morbidity; enormous costs of care
- Fraught with under-diagnosis and late diagnosis:
  - Diagnosed in only 50% of patients
  - Diagnosis after several years of symptoms
- Prior approved medicines address symptoms only, are insufficient (too little; too late), and none approved for the MCI stage of AD



A 30 yr disease: 15 + 5 + 10

Abnormal Proteins: Amyloid & Tau



Increasing Recognition of the Importance of Early Diagnosis But There are Challenges

- Patients may not recognize and report symptoms
- Fear of stigma and loss of independence
- Historically, physicians lack of skill and interest
- Early symptoms often conflated with normal aging
- Cognitive tests may be insensitive for early disease
- Clinical diagnosis without biomarker confirmation is often inaccurate

What's New In AD Treatment?

The Dawn of a New Era in AD Treatment

- July 2023: FDA full approval of lecanemab (Leqembi)
- July 2024: FDA full approval of donanemab (Kisunla)
- Each of these medicines are:
  - antibodies targeting amyloid
  - given by intravenous infusion
  - indicated for early stages of AD
  - Purpose is to slow disease
- Currently approved in more than 53 countries

Robust Clearance of Amyloid with Antibody Treatment

Canada Finally Comes Onboard!

- Oct. 2025: Health Canada approves lecanemab
  - Marks the first disease slowing treatment for AD
  - First time there is any treatment for MCI stage
  - >200 patients now on treatment since drug arrived in Canada and many more lined up to start

- April 2026: Health Canada approves donanemab
  - First patients will be treated in late July 2026

Eligibility for Lecanemab or Donanemab

Health Canada indication is for individuals with:

- Mild cognitive impairment or mild dementia
- Biomarker confirmation of amyloid
- Cannot have 2 copies of ApoE4/E4
- Must not be on anticoagulants
- Must be able to undergo MRI scans
- A pretreatment MRI must be free of specific risk factors for side effects

One Class; Two Different Treatments

- Lecanemab and donanemab robustly clear plaque but lecanemab also clears other more toxic forms of amyloid
- Lecanemab is a continuous treatment while donanemab has a hard stop at 18 mos.
- Lecanemab has longer term data (4 yrs vs 3 yrs of benefit)
- Those who start lecanemab with very low amyloid or tau have stable to *improved* cognition & function out to 4 years
- Quality of life data is unique to lecanemab
- Other differences as well

What's New In System Readiness and Treatment Access

New Treatments Trigger Change

- Medical educational initiatives re: early detection
- Restructuring of specialist clinics to fast-track referrals
- Increasing access to AD biomarkers (cost-coverage for some tests; local lab access for blood biomarkers and ApoE)
- Network of infusion centres established country-wide
- Increasing number of MRI centres trained to provide the baseline and post-initiation scans and reports needed
- **July 16/26, Canada Drug Agency announced a positive recommendation for cost coverage of lecanemab**

PET and CSF: The Original Gold Standard Tests to Confirm Amyoid

Amyloid PET Scan

Spinal Tap for CSF

Blood Tests Now Available to Confirm Presence of Brain Amyloid

- pTau217 blood test has the same accuracy as spinal fluid analysis and PET scans, i.e., >90% accuracy
- Blood tests are less expensive, less invasive, more accessible, and more acceptable to patients and health care providers than other biomarker modalities

New Infusion Centres Inaugurated

Lecanemab Autoinjector: Approved by FDA and Under Review by Health Canada

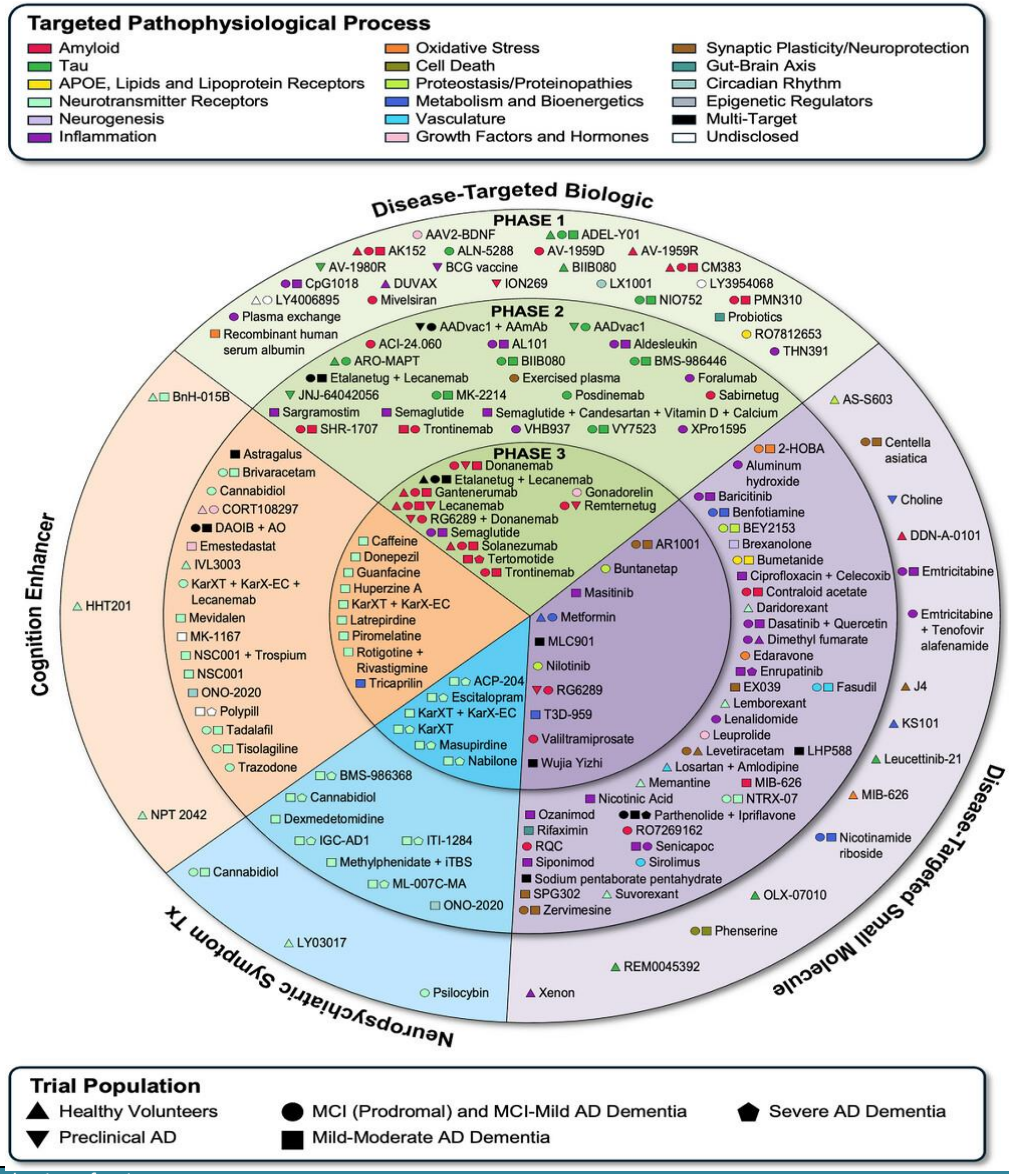
Once approved in Canada, patients will no longer be tied to infusion centres and can self-administer treatment at home.

What's Next for Lecanemab and Donanemab

- Additional Phase 3 studies for preclinical AD are fully enrolled and results are highly anticipated
  - Lecanemab: AHEAD study read out in 2028
  - Donanemab: Trailblazer-ALZ 3 read out in 2027
- If positive, this will be the catalyst for major change, including the likelihood of population screening with a blood test for those over age 55

What Other Treatments May be Coming in the Future

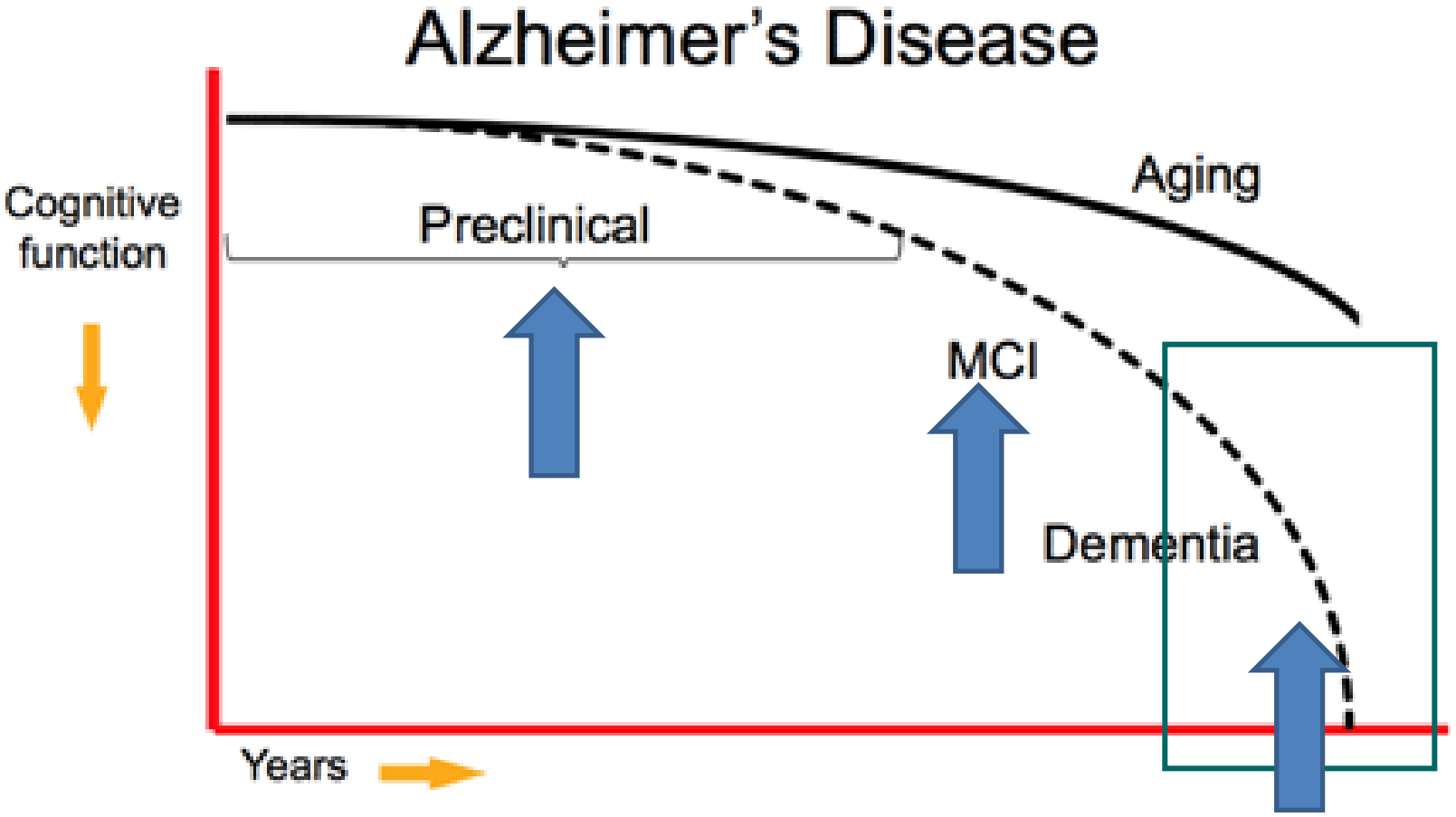
2026 Alzheimer's Drug Development Pipeline



AD, Alzheimer's disease; MOA, mechanism of action.
Cummings J et al. Alz&Dem:TRCI. 2024

2026 AD Drug Development Pipeline

- 158 unique drugs under development
- Across different stages of AD and different mechanisms
- 73% are disease modifying treatments
  - 39% small molecules; 34% biologics
- 27% symptomatic treatments
  - 18% cognitive enhancers; 10% behaviour symptoms
- 35% (46 drugs) repurposed agents



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A Few Programs of High Interest

- A next generation anti-amyloid antibody: trontinemab
  - Uses a brain shuttle technology to get drug into brain
  - rapid amyloid clearance with almost no ARIA
  - Study in Early AD fully enrolled; study in preclinical AD will start this summer

- Genetic approaches to **shut off** production of proteins:
  - Mivelsiran achieves dramatic reduction of amyloid without side effects in phases 1, 2; under study for AD, CAA, Down's
  - Diranersen becomes 1st drug to lower tau production and show clinical benefit (July 2026). Will move into Phase 3.

A Few Programs of High Interest

- Valiltramiprosate: an oral drug which blocks formation of the most toxic form of amyloid, namely oligomers
  - With recent phase 2 success of valiltramiprosate in those with MCI and ApoE4/E4, a Phase 3 trial will begin in Q4 providing options for those with 2 copies of ApoE4 as well as those with high burden of microbleeds (i.e., those excluded from the currently approved treatments)

Reasons to Join a Clinical Trial

- Access to specialized diagnostic tests not otherwise readily available
- Access to cutting edge treatments under development and not yet available by prescription
- Access to an expert team of specialists
- Close monitoring of one's condition
- Satisfaction of doing everything one can for oneself, one's family, and for future generation

Key Take Aways

- AD is a long, complex disease with many opportunities to intervene
- Diagnosing and treating early are key to best outcomes
- Accurate diagnosis is possible with PET scans, spinal fluid analysis, and now, blood tests
- 2 disease slowing treatments, lecanemab & donanemab, have now been approved in Canada
- Additional treatments, including those to prevent AD are under active study
- Research participation provides the hope for the future

Don’t Doubt Progress; Help Accelerate It!

- People who know this disease want to be involved and have many options:
  - Have a baseline memory test
  - Join our prevention and treatment registry
  - Undergo a cheek swab to check for AD risk
  - Find out if a clinical trial is right for you

Without Medical Heroes
The Pharmacy Would Be Bare

We all have a role to play to end AD

Protect Next Generations

Help Make a Difference!

Connect with us at: 416-386-9606
or: Research@memorydisorders.ca

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