Making Progress in Alzheimer's Research and Treatment

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Objectives

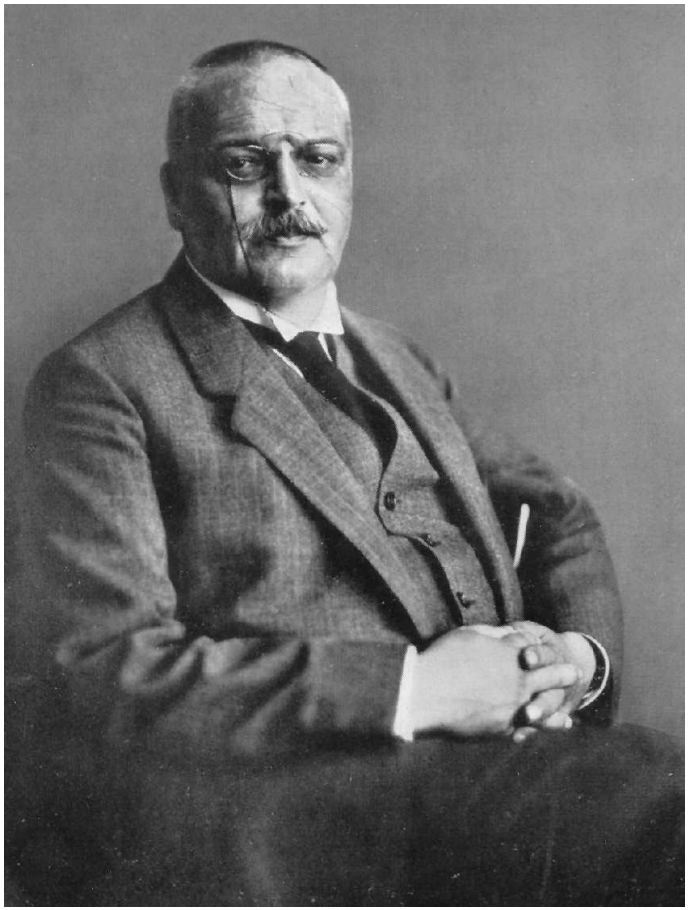
1. Enhance understanding of Alzheimer's disease
2. Provide updates on recent advances in
   - Diagnosis
   - Treatment
3. Provide a call to action to those interested

What is Alzheimer's Disease?

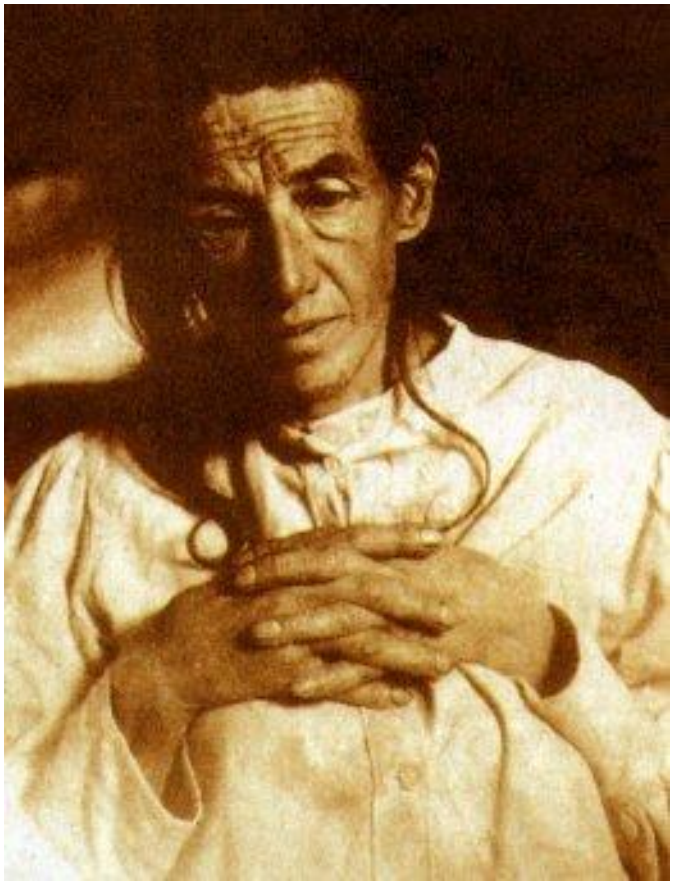
- A slowly progressive brain disease causing:
  - impairment in memory and thinking
  - loss of independence
  - altered behaviour
  - profound impact on care partners
- A highly feared disease
- An expensive disease
- The commonest cause of dementia

What's New in Diagnosis

AD 1906: “a rare disease”



Dr. Alois Alzheimer



Auguste Deter Age 51

Alzheimer's Disease 2025:
55 Million Worldwide; 75 M by 2030

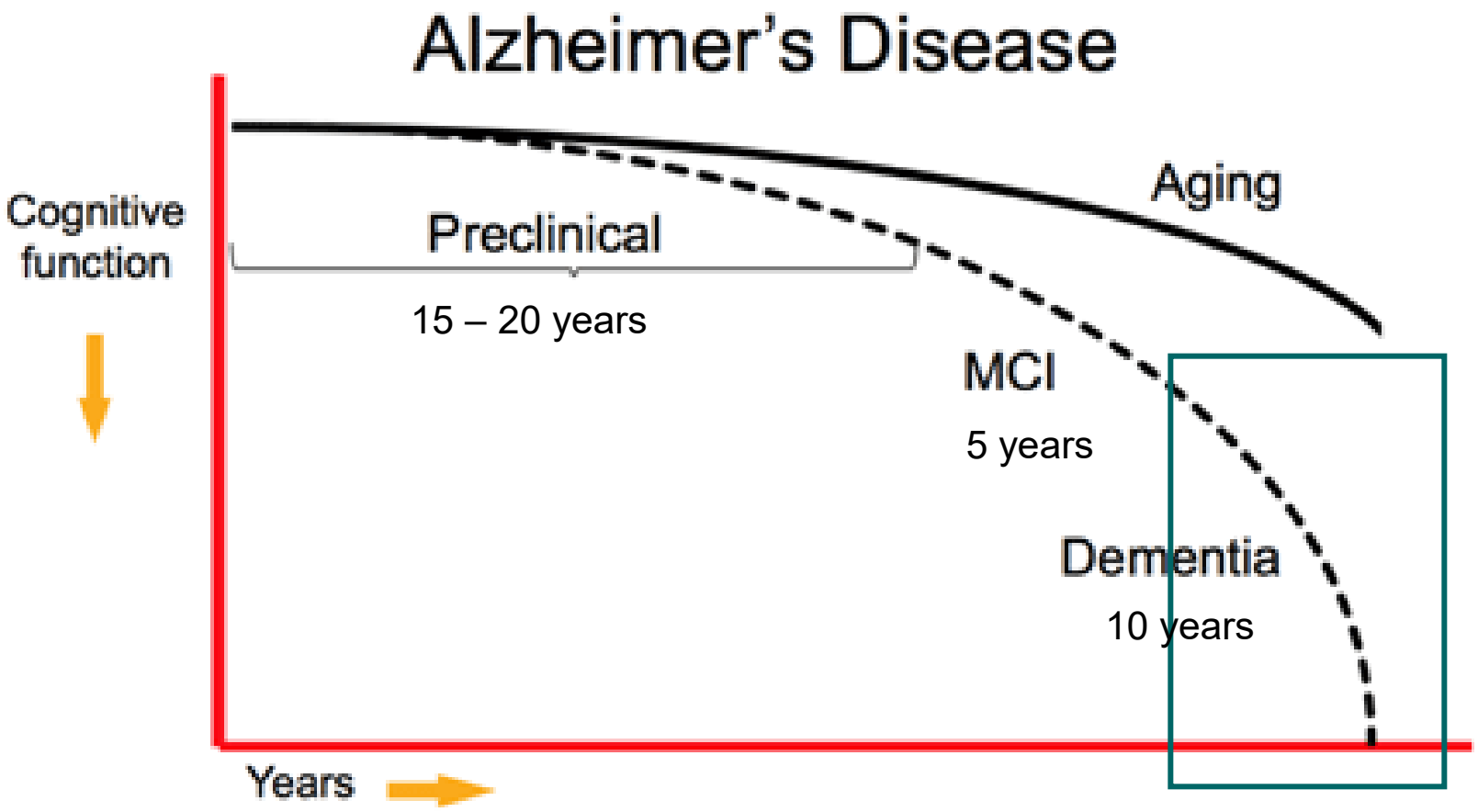
AD: An urgent health care priority

WHO 2012

- Staggering numbers; severe morbidity; enormous costs of care; enormous burden on families
- Fraught with under-diagnosis and late diagnosis:
  - Diagnosed in only 50% of patients
  - Diagnosis after several years of symptoms

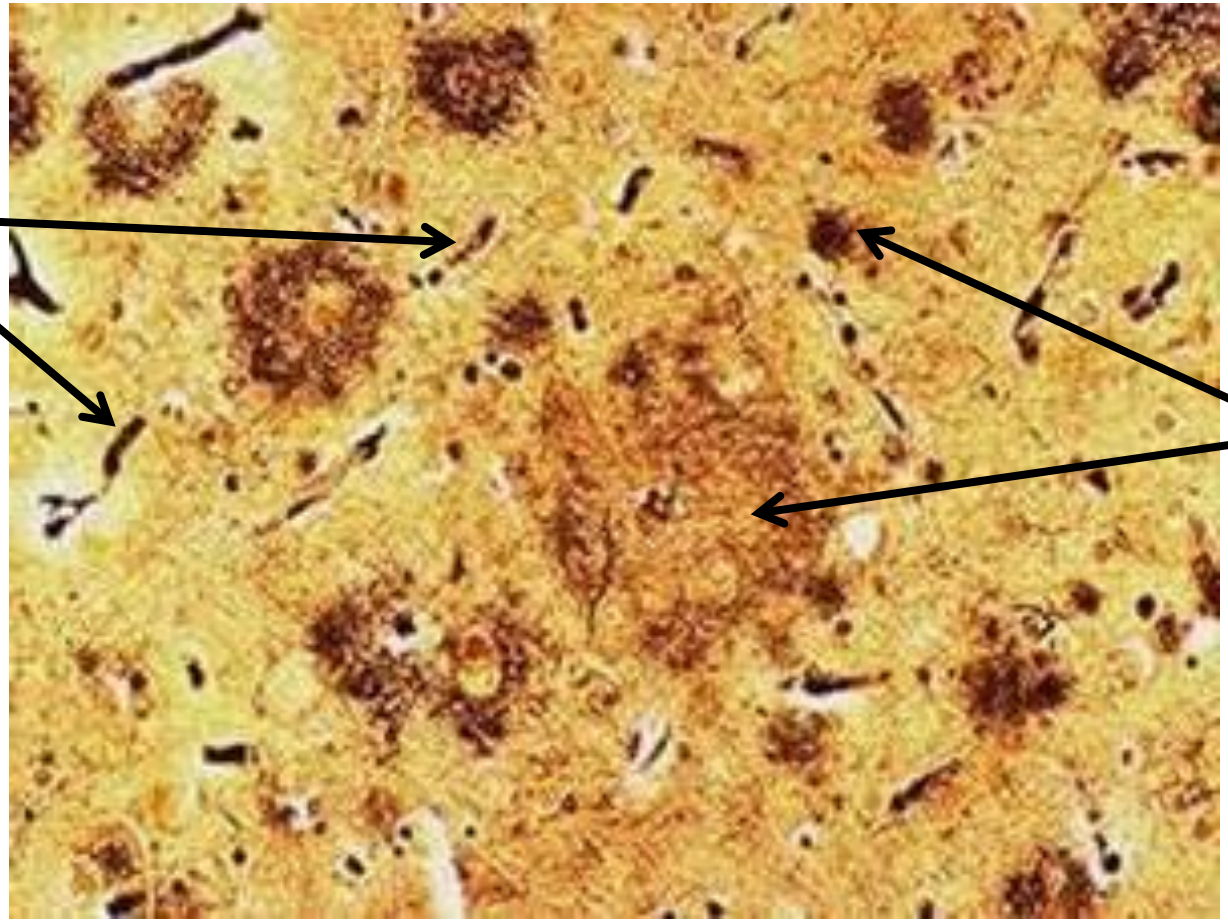
Diagnostic Challenges

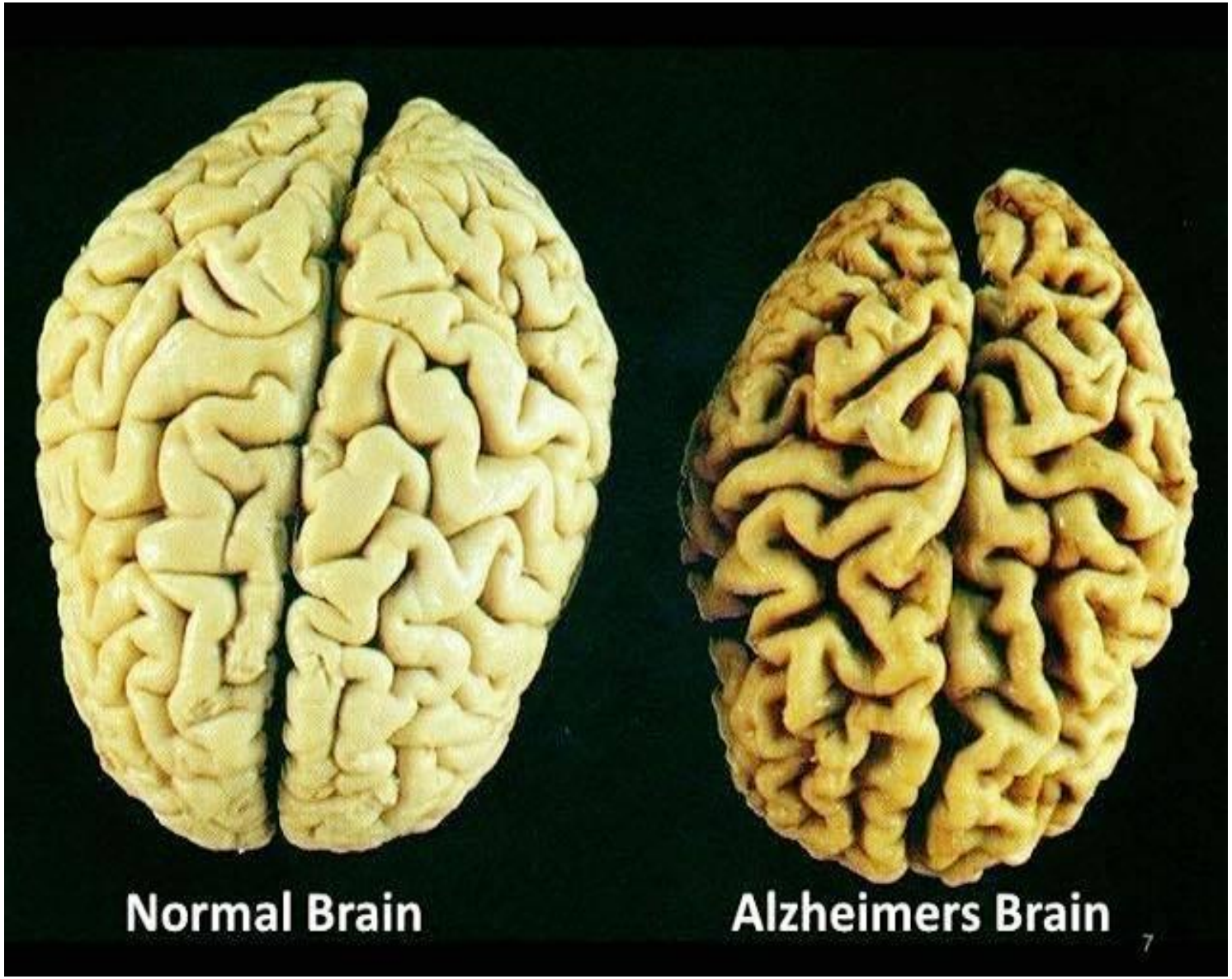
- Patients may not recognize and report symptoms
- Fear of stigma and of loss of independence
- Physicians lack skill and interest in diagnosing AD
- Symptoms are often confused with normal aging
- Cognitive tests may be insensitive for early disease



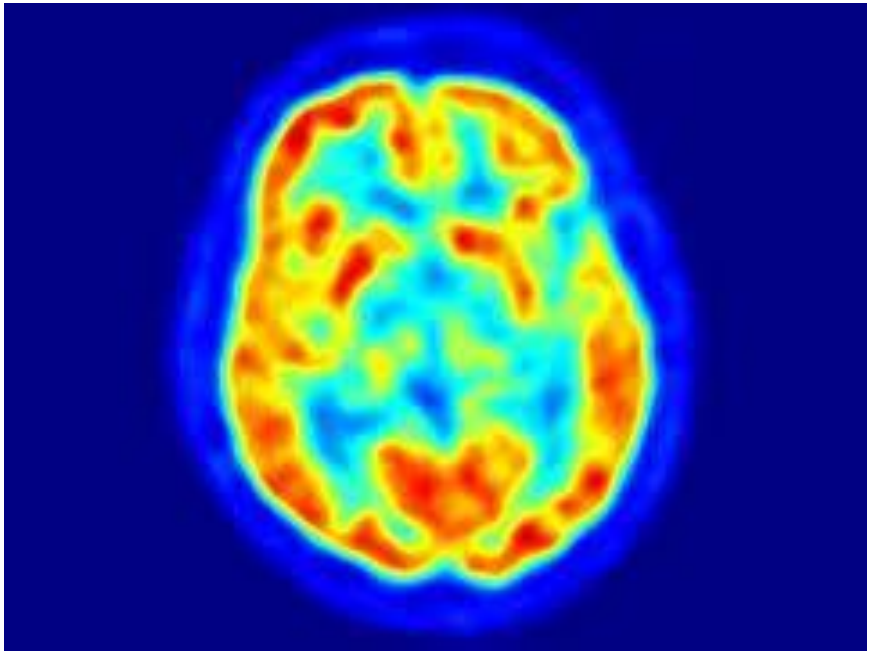
A 30-year disease: 15 + 5 + 10 years

Abnormal Proteins: Amyloid & Tau




Normal Brain
Alzheimers Brain
7

PET Amyloid Imaging



Amyloid can be detected at all stages of AD including prior to symptoms

Spinal Tap to Diagnosis Alzheimer's

Amyloid **and** Tau can be measured in spinal fluid

Blood Tests Can Now Detect Alzheimer's Brain changes

- Blood tests can diagnosis AD with over 90% accuracy
- Can measure levels of amyloid, tau, and other markers
- FDA approved first blood test for AD diagnosis in May 2025; others have been approved since then
- Many of these are now available in Canada

C2N DIAGNOSTICS:
Press Release Jan. 28, 2025

Toronto Memory Program is the First Canadian Clinic to Offer C2N's PrecivityAD2™ Blood Test to Help Healthcare Providers Diagnose Alzheimer's Disease, Joining Global Community in Embracing Breakthrough Technology

Retinal Scan for Detecting AD

RetiSpec Imaging

- Hyperspectral camera
- Detects amyloid in the back of the eye
- Non-invasive; no dye
- Validation study underway at TMP

Genetic Testing Can Help with Diagnosis

- Rare gene mutations which cause AD can be detected in a blood sample
- A major risk gene, ApoE4, can be detected in blood and from a cheek swab
- Individuals who have causative genes or risk genes have options for prevention and treatment through research studies

ApoE4 Risk Gene Can Be Assessed From a Cheek Swab in Just One Hour

1 copy of ApoE4: 3 X greater risk of AD
2 copies of ApoE4: 10X greater risk of AD

Cathy Barrick, CEO ASO

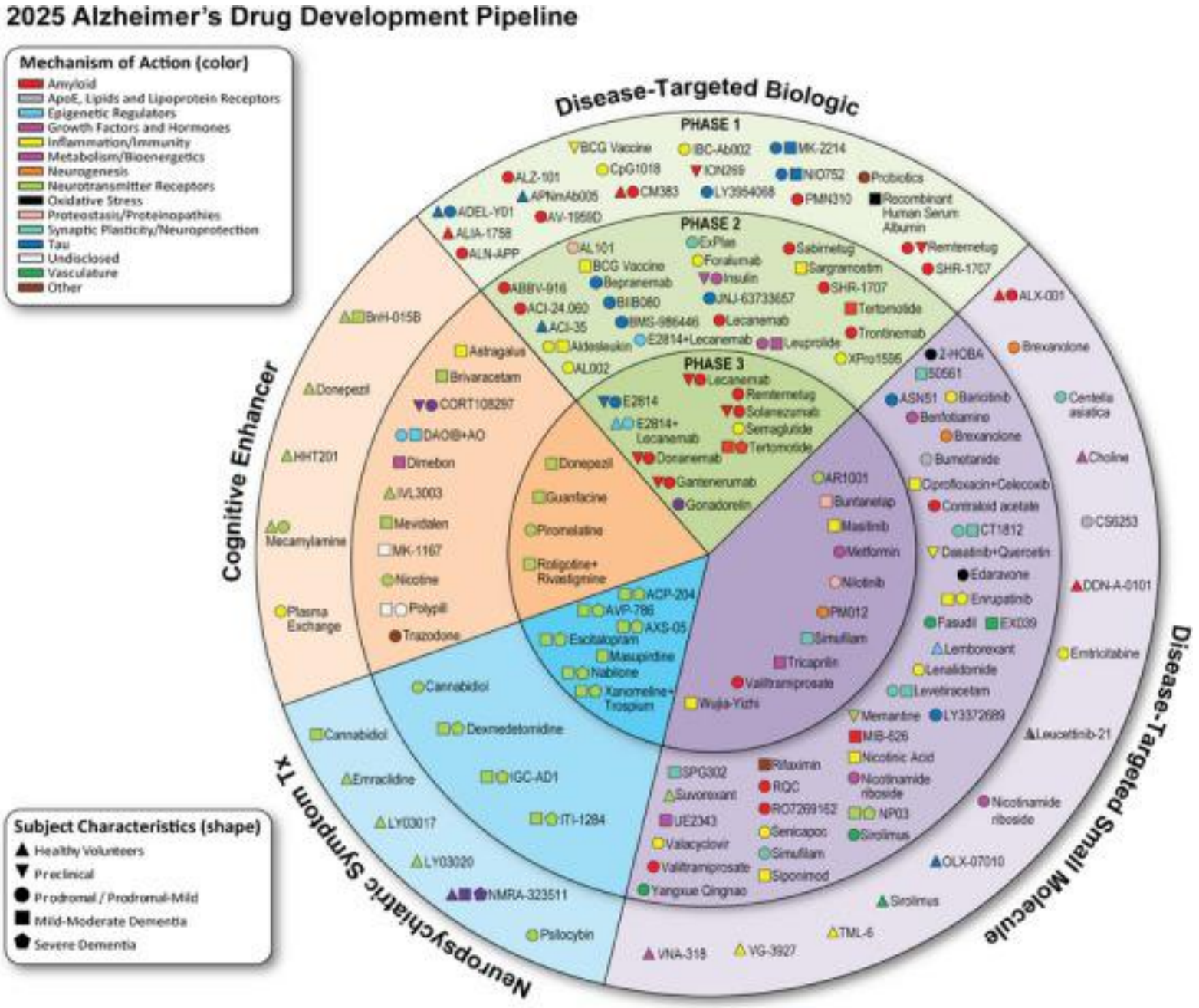
Genomadix Cube

What's New In AD Treatment

Existing Medications Are Not Enough

Previously approved medications:

- Treat symptoms and with modest effect
- Do not prevent or slow underlying disease
- Not approved for MCI stage of AD


2025 Alzheimer's Drug Development Pipeline
Mechanism of Action (color)
Amyloid
ApoE, Lipids and Lipoprotein Receptors
Epigenetic Regulators
Growth Factors and Hormones
Inflammation/Immunity
Metabolism/Bioenergetics
Neurogenesis
Neurotransmitter Receptors
Oxidative Stress
Proteostasis/Proteinopathies
Synaptic Plasticity/Neuroprotection
Tau
Undisclosed
Vasculature
Other
Disease-Targeted Biologic
Disease-Targeted Small Molecule
Neuropsychiatric Symptom Tx
Cognitive Enhancer
PHASE 1
PHASE 2
PHASE 3
BCG Vaccine
BC-Ab002
MK-2214
ALZ-101
CpG1018
ION269
NIO752
Probiotics
APNmAb005
CM383
LY3954068
PMN310
Recombinant Human Serum Albumin
ADEL-YD1
AV-1959D
ALIA-1758
ALN-APP
AL101
ExPlas
Sabirnetug
Remternetug
BCG Vaccine
Foralumab
Sargramostim
SHR-1707
ABBV-916
Bepranemab
Insulin
SHR-1707
ACI-24.060
BIIB080
JNJ-63733657
Tertomotide
ACI-35
BMS-986446
Lecanemab
Trontinemab
Aldesleukin
E2814+Lecanemab
Leuprolide
XPro1595
AL002
E2814
Lecanemab
Remternetug
E2814+ Lecanemab
Solanezumab
Semaglutide
Tertomotide
Donanemab
Gantenerumab
Gonadorelin
AR1001
Buntanetap
Masitinib
Metformin
Nilotinib
PM012
Simufilam
Tricaprilin
Valiltramiprosate
Wujia-Yizhi
ACP-204
AVP-786
AXS-05
Escitalopram
Masupirdine
Nabilone
Xanomeline+ Trospium
SPG302
Suvorexant
UE2343
Valacyclovir
Valiltramiprosate
Yangxue Qingnao
Rifaximin
RQC
RO7269152
Senicapoc
Simufilam
Sponimod
Memantine
LY3372689
MIB-626
Nicotinic Acid
Nicotinamide riboside
NP03
Sirolimus
OLX-07010
TML-6
VG-3927
VNA-318
BnH-015B
Donepezil
HHT201
Mecamylamine
Plasma Exchange
Astragalus
Brivaracetam
CORT108297
DAO/B+AO
Dimebon
IVL3003
Mevidalen
MK-1167
Nicotine
Polypill
Trazodone
Donepezil
Guanfacine
Piromelatine
Rotigotine+ Rivastigmine
Cannabidiol
Dexmedetomidine
Emraclidine
IGC-AD1
LY03017
ITI-1284
LY03020
NMRA-323511
Psilocybin
ALX-001
Brexanolone
Z-HOBA
50661
ASN51
Baricitinib
Centella asiatica
Benfotiamine
Brexanolone
Bumetanide
Choline
Ciprofloxacin+Celecoxib
Contrasoid acetate
CS6253
CT1812
Dasatinib+Quercetin
Edaravone
DDN-A-0101
Enrupatinib
Fasudil
EX039
Emtricitabine
Lemborexant
Lenalidomide
Levetiracetam
Leucettinib-21
Nicotinamide riboside
Sirolimus
Subject Characteristics (shape)
Healthy Volunteers
Preclinical
Prodromal / Prodromal-Mild
Mild-Moderate Dementia
Severe Dementia

2025 AD Drug Development Pipeline

- 182 trials assessing 138 unique drugs
  - phase 1: 48 trials assessing 45 drugs
  - phase 2: 86 trials assessing 75 drugs
  - phase 3: 48 trials assessing 31 drugs
- 74% DTTs
  - 59% small molecules; 41% biologics
- 25% symptomatic treatments
  - 14% cognitive enhancers; 11% behaviour symptoms
- 33% (46 drugs) repurposed agents
- 17% (24 drugs) target inflammation/immune processes

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Cummings J, et al. Alzheimers Dement. 2025.

15 of 18 CADRO Categories Represented in the 2025 Pipeline

- 25 (18%) drugs target Aβ pathophysiology
- 15 (11%) drugs target tau-related processes

- 30 (22%) target neurotransmitter receptors
- 24 (17%) target inflammation/immune processes
- 9 (6%) address synaptic plasticity/neuroprotection
- 8 (6%) target metabolism and bioenergetics
- 5 (4%) target growth factors and hormones

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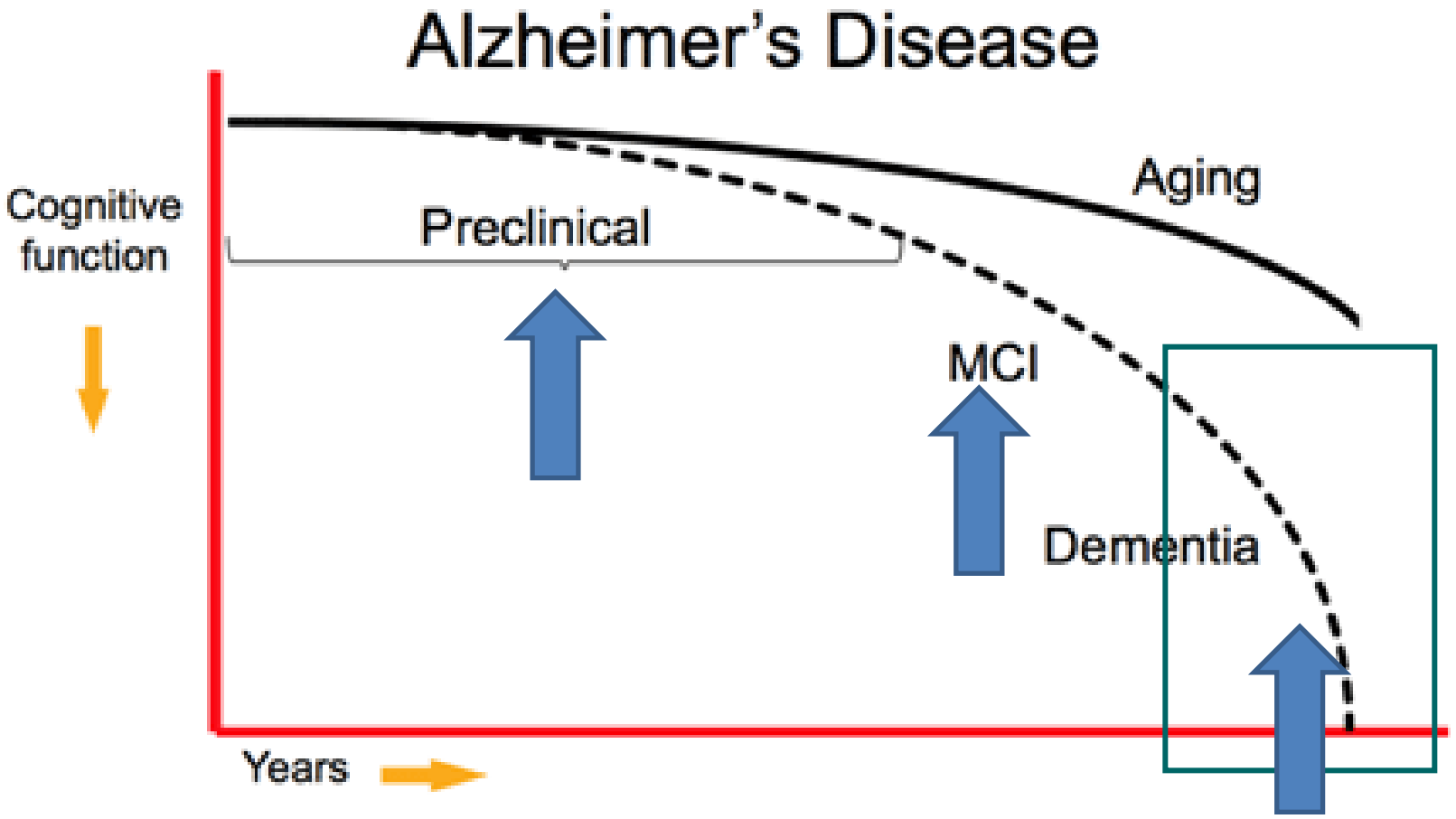
Cummings J, et al. Alzheimers Dement. 2025.



A 30-year disease: 15 + 5 + 10

A New Era in AD Treatment

- July 2023: FDA full approval of lecanemab
- July 2024: FDA full approval of donanemab
- Each of these are:
  - antibodies that clear amyloid
  - given by intravenous infusion
  - indicated for early stages of AD
  - intended to slow disease

Robust Clearance of Amyloid with Antibody Treatment

A New Era in AD Treatment

- By Sept. 2025: lecanemab and donanemab were approved in 50 countries
- Oct. 24, 2025: Health Canada finally approved lecanemab!
  - Marks the first disease slowing treatment for AD
  - Public cost coverage under review; recommendations expected in early 2026
  - Health Canada label excludes those with 2 copies of ApoE4

Lecanemab

- Robustly clears amyloid
- Slows decline in cognition
- Slows decline in daily function
- Reduces risk of transitioning to next stage of disease
- Preserves quality of life as assessed by patients
- Less care partner burden as reported by care partners
- Those treated early are stable or even *improve* up to 4 years after treatment initiation

What's Next for Amyloid Lowering Treatments

- Donanemab under Health Canada review for early AD
- Prevention trials of lecanemab and donanemab in preclinical stages of AD
- Subcutaneous formulation now FDA approved for maintenance dosing; under FDA review by FDA for initiation dosing
- Other anti-amyloid antibody programs ongoing, as well as other approaches to targeting amyloid
  - E.g., genetic approaches to **prevent** amyloid formation

Many Other Disease Modifying Treatments Are Under Active Study

- Anti-tau studies
  - Anti-tau antibodies to clear tau and reduce spread
  - Drugs to reduce tau formation
- Studies harnessing the immune system
  - To reduce inflammation in the brain
  - Activate immune cells to clear amyloid & other toxins
  - Boost protective functions of support cells in brain
- Combination therapies are starting to be tested

Lifestyle Strategies

Up to 45% of dementia may be preventable through lifestyle modification

- Mental Activity: pursue activities that are enjoyable, challenging, and entail problem-solving
- Physical Exercise: moderate intensity exercise 150 min/wk
- Dietary Pattern: ↑fruit, veggies, nuts; ↓animal fat, red meat
- Sleep: quantity and quality of sleep are important
- Stress Management: make time for things you find relaxing
- Control Vascular Risk Factors: e.g., smoking, cholesterol, hypertension, diabetes

Reasons to Join a Clinical Trial

- Access to specialized diagnostic tests not otherwise readily available (e.g., PET scan)
- 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

Without Medical Heroes
The Pharmacy Would Be Bare

Key Take Aways

- AD is a very long and complex disease with several stages providing multiple opportunities to intervene
- The later stages are particularly burdensome; diagnosing and treating early are key
- Accurate diagnosis is possible with a PET scans, spinal fluid analysis, and now, a blood test
- A new disease slowing treatment (lecanemab) has now been approved in Canada
- Additional treatments, including combination and preventative treatments are under active study

Don’t Doubt Progress; Help Accelerate It!

- People who know this disease want to be involved
- 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

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

Justine Reaume