Northern Light Health

Maine Initiative for Neurologic Aging and Health

MAINAH Webinar Fall 2023

10/5/2023 |

Agenda

6:00 ***Introduction:*** Cliff Singer MD

6:05 ***Loneliness, social isolation and healthy aging:***

Len Kaye PhD, Professor of Social Work and Director of Center on Aging, University of Maine

6:20 ***Mitochondrial function during aging and disease:***

Suzanne Angeli PhD, Assistant Professor of Molecular and Cellular Biology, University of Maine

6:35 ***Hearing Loss as a risk for cognitive impairment:***

Alice-Lee Vestner MD, Geriatric Psychiatrist, Maine Health and Clinical Associate Professor, Tufts University School of Medicine

6:50 ***A quick primer on precision medicine and the new treatments for Alzheimer's disease:*** Cliff Singer MD

7:00 ***Discussion and Q&A***

Precision Medicine and the New Treatments for Alzheimer's disease

Cliff Singer MD
Director, Center for Geriatric Cognitive and Mental Health
Northern Light Acadia Hospital
and Research Professor, University of Maine

What is Precision Medicine?

"Precision medicine" (aka PM and "personalized medicine") leverages technical and scientific advances to design treatments that are individualized to a person's specific genetic, lifestyle risk factors, medical, psychosocial and pathologic profiles.

Rather than rely on "average response" found in clinical trials, PM incorporates personal biomarkers to confirm diagnosis and personalize treatment.

PM identifies patients who meet criteria indicating they are likely to respond to treatments targeting specific pathology.

Precision Medicine in Oncology

Cancer specialists have led the way in precision medicine.

Maine Cancer Genomics Initiative (MCGI) is a state-wide consortium of oncologists meeting to determine the most appropriate treatments and targeted drug therapies for cancer patients.

Precision Medicine in Dementia Care

Scientific and technical advances over the last decade have made precision medicine in dementia diagnosis **possible**.

More recent breakthroughs in treatments specific to Alzheimer's disease have made precision medicine **necessary**.

Age-Associated Dementia

Although Alzheimer's disease is the most common of the age-associated dementias, it accounts for only about 2/3 of cases as primary cause. That's still over 35,000 people in Maine.

The other causes are also attributable to abnormal accumulation of specific proteins or vascular injuries to the brain.

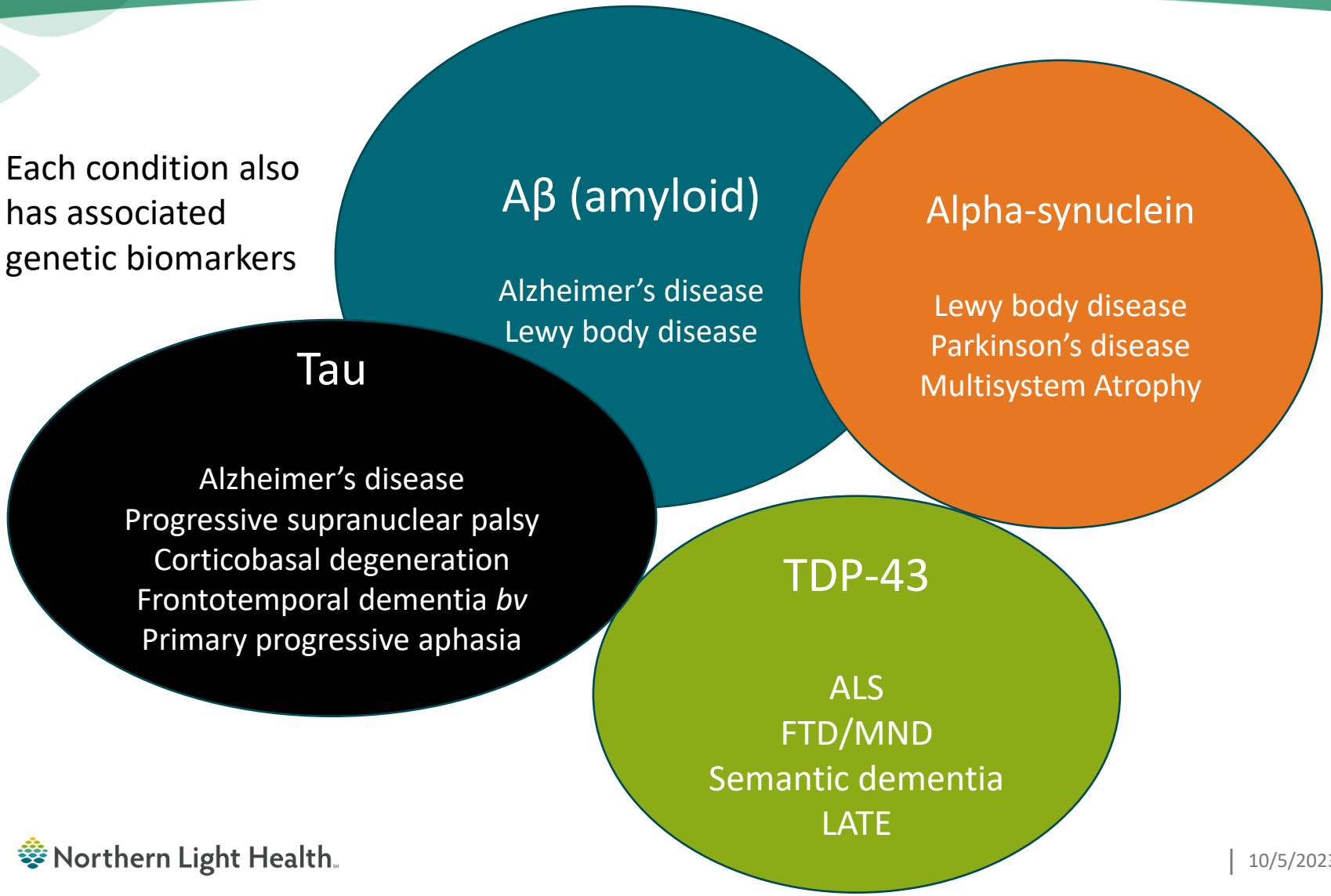
Some people develop these cognitive and behavioral disorders in mid-life and not old age.

All require a specialized approach to diagnosis.

Primary Protein Biomarkers of Common Dementias

Hampel H et al. Trends in Neurosciences 2023; 46:3:176-198

Each condition also has associated genetic biomarkers



Hypothetical Progression of AD Pathology

Jack CR et al. Lancet Neurology 2010

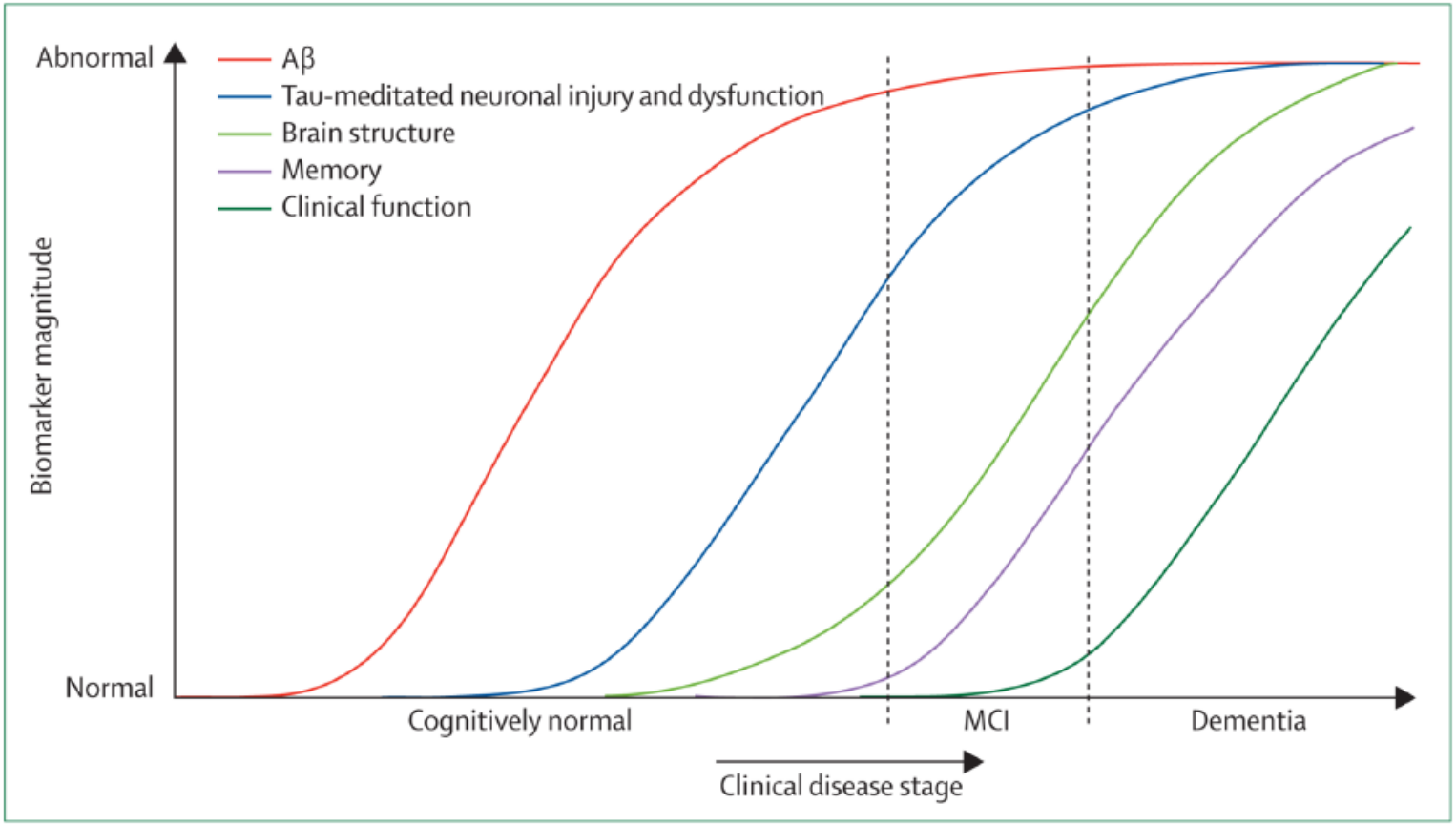
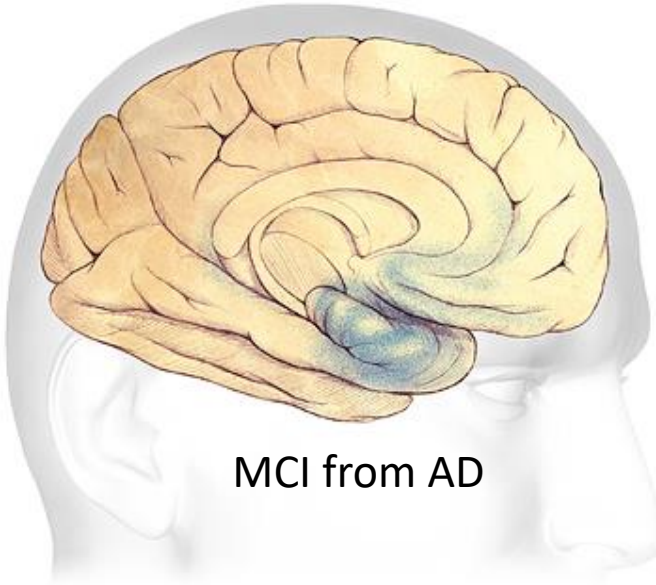
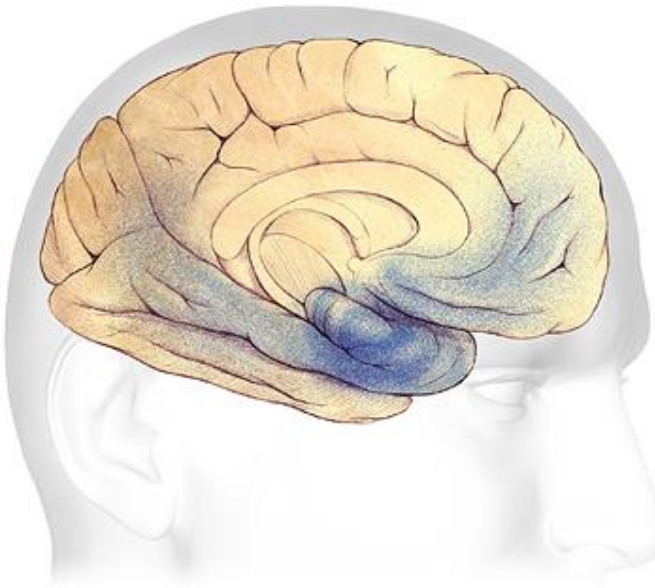


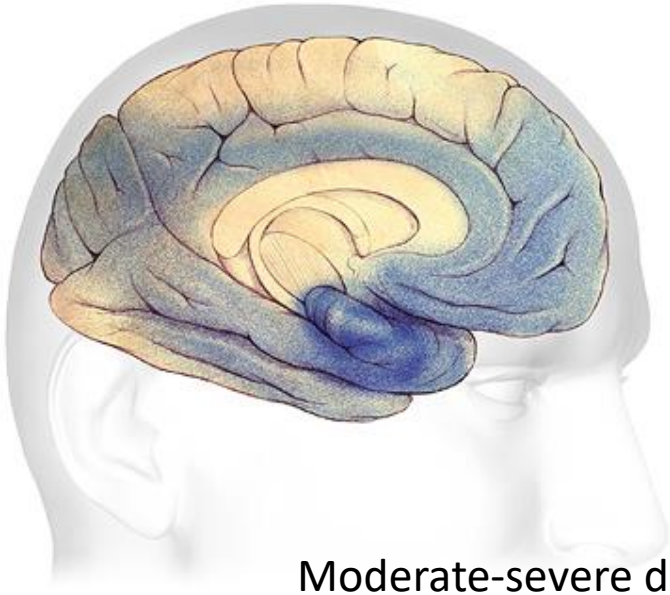
Figure 2. Dynamic biomarkers of the Alzheimer's pathological cascade
Aβ is identified by CSF $A\beta_{42}$ or PET amyloid imaging. Tau-mediated neuronal injury and dysfunction is identified by CSF tau or fluorodeoxyglucose-PET. Brain structure is measured by use of structural MRI. Aβ=β-amyloid. MCI=mild cognitive impairment.



MCI from AD



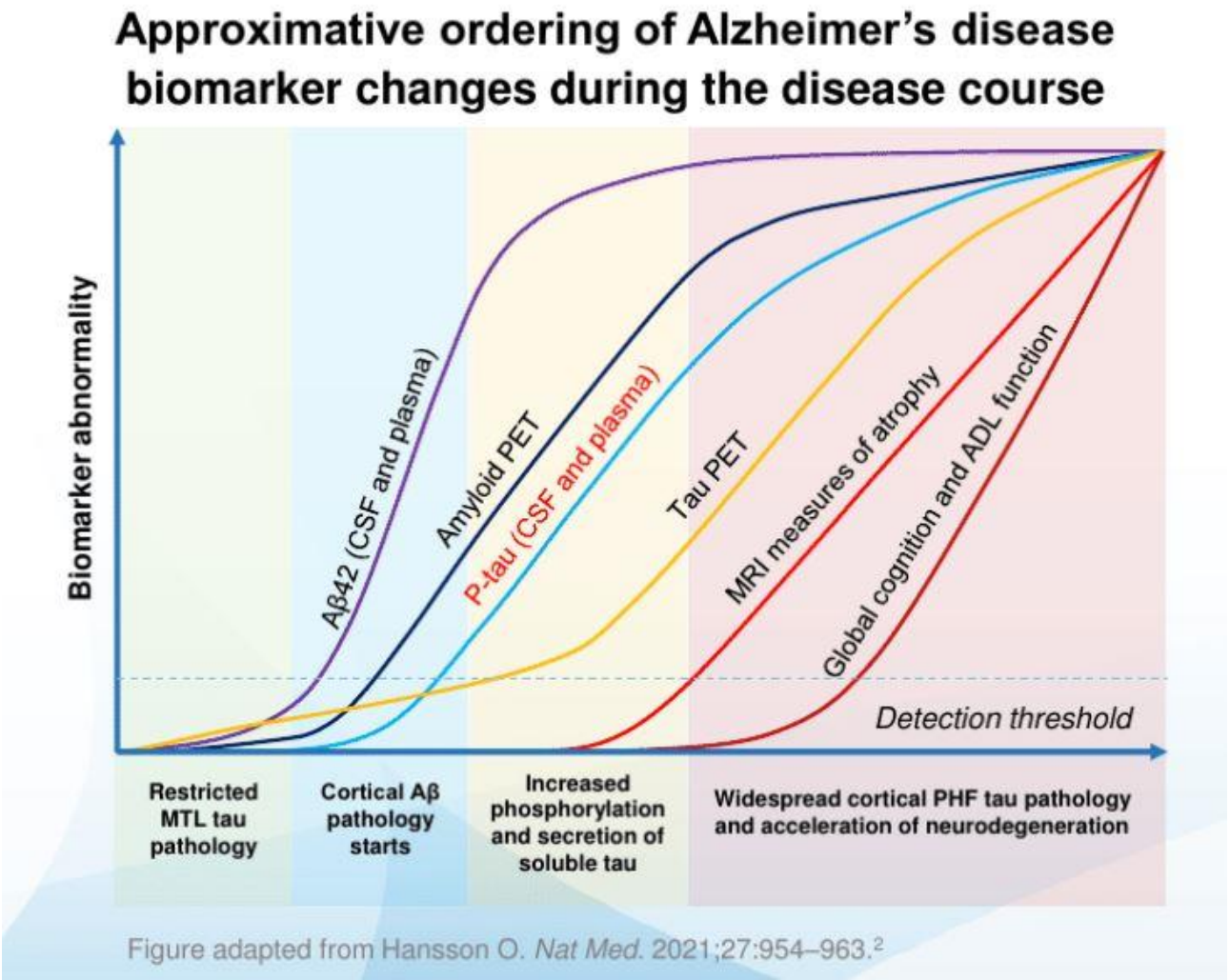
Mild Dementia



Moderate-severe dementia

Measured Biomarkers Sequence in AD

These are the biomarkers we use clinically and in research studies.



New Era in AD Therapy Has Arrived

The FDA has recently approved the first treatments specifically targeting the amyloid pathology of AD

The treatments are not cures, and are expensive and high risk, but slow disease progression and patients want access.

Using these, and future treatments on the near horizon, will require a new approach to diagnosis and treatment: a precision or personalized approach:

Confirm diagnosis with clinical evaluation, genomic, imaging and fluid biomarkers.

Expert review of diagnosis and risk factor analysis for new therapies.

Expert oversight of treatment with new modalities to monitor development of adverse events and therapeutic response.

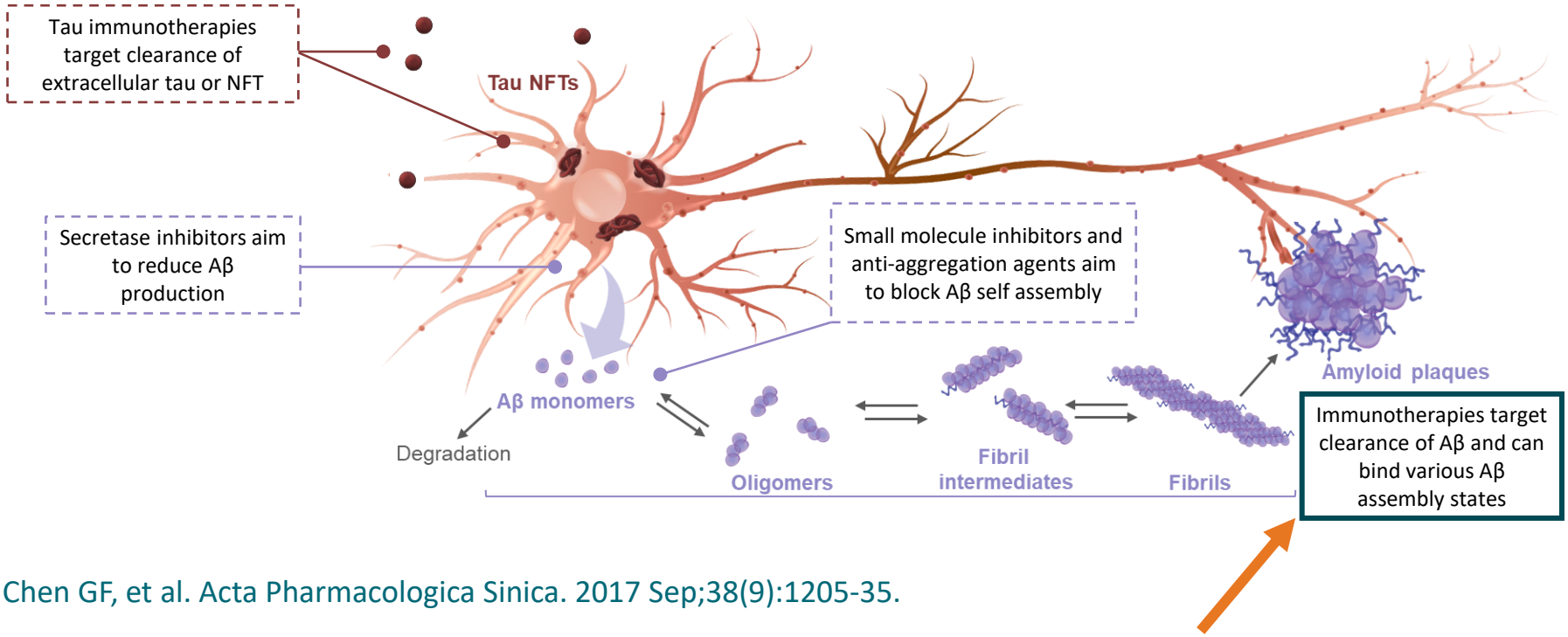
AMYLOID AND TAU PROVIDE OBVIOUS DISEASE-MODIFYING TARGETS

Anti-Tau therapeutic candidates

Target soluble extracellular tau or intracellular neurofibrillary tangles (NFTs)

Anti-Amyloid therapeutic candidates

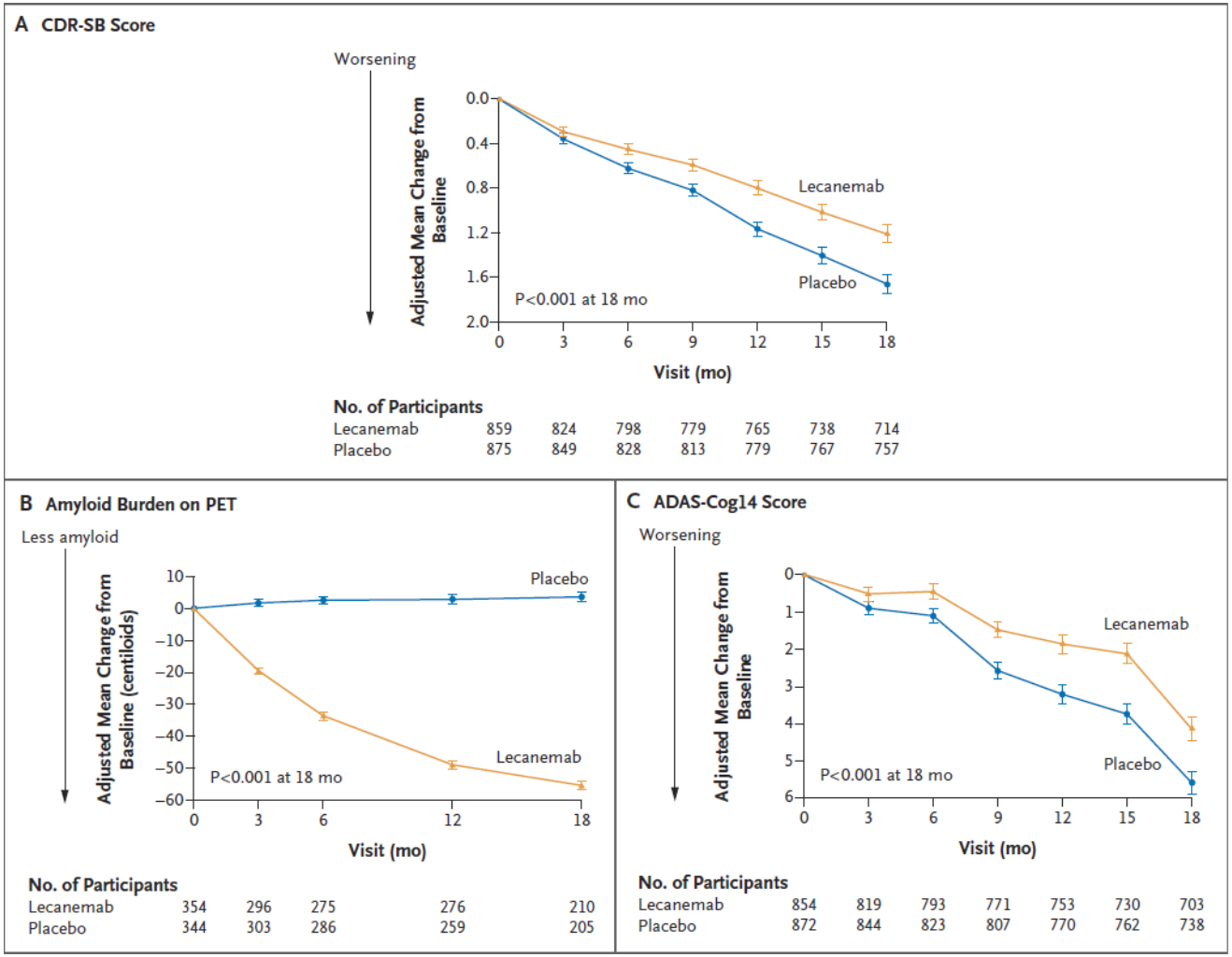
Target Aβ production, soluble Aβ monomers and oligomers (that can spread throughout the brain), and/or insoluble fibrils and amyloid plaques



Chen GF, et al. Acta Pharmacologica Sinica. 2017 Sep;38(9):1205-35.

Lecanemab in Early Alzheimer's Disease

van Dyck CH et al. NEJM January 5, 2023 388:1:9-21



Amyloid-Related Imaging Abnormalities (ARIAs) w lecanemab (van Dyck CH et al. 2023)

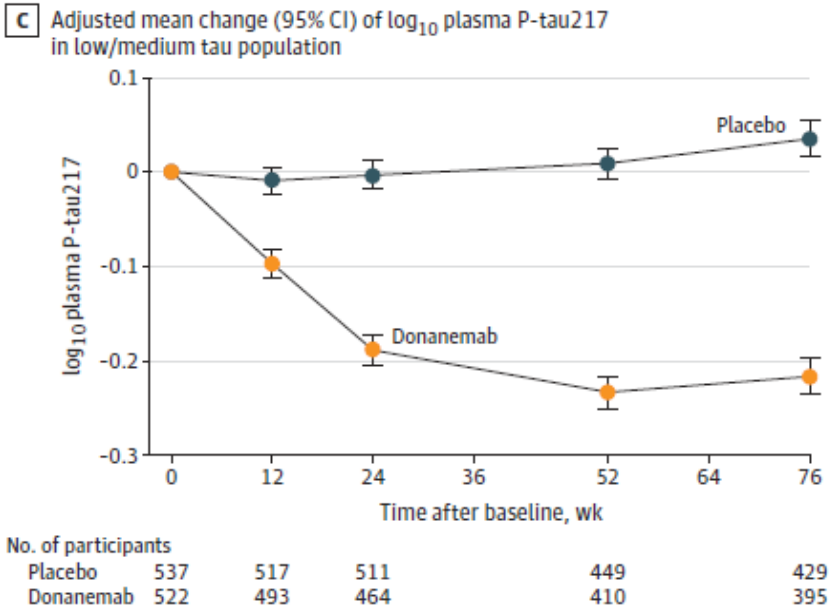
Table 3. (Continued.)

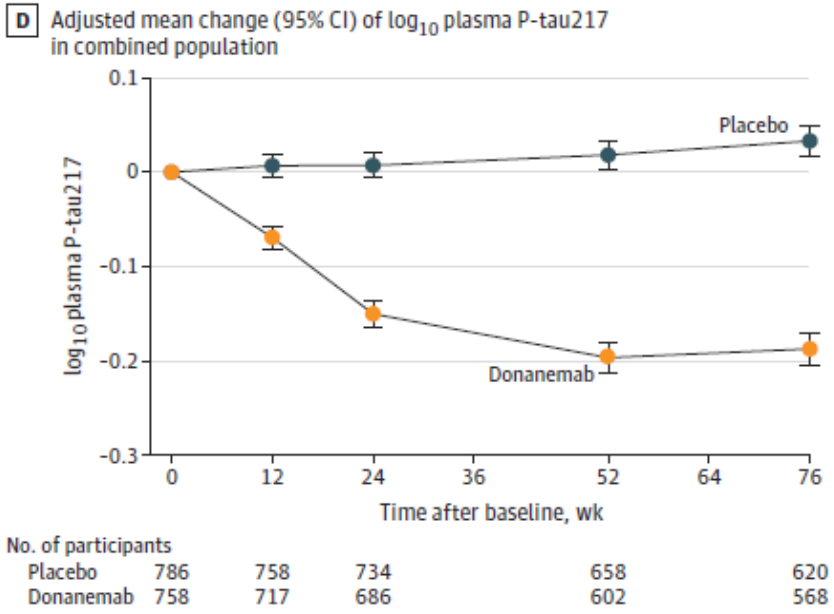
Event	Lecanemab (N = 898)	Placebo (N = 897)
ARIA-H according to ApoE ε4 genotype — no./total no. (%)		
ApoE ε4 noncarrier	33/278 (11.9)	12/286 (4.2)
ApoE ε4 carrier	122/620 (19.7)	69/611 (11.3)
ApoE ε4 heterozygote	67/479 (14.0)	41/478 (8.6)
ApoE ε4 homozygote	55/141 (39.0)	28/133 (21.1)
ARIA-E or ARIA-H — no. (%)	193 (21.5)	85 (9.5)
Concurrent ARIA-E and ARIA-H — no. (%)	74 (8.2)	9 (1.0)

* ARIA denotes amyloid-related imaging abnormalities, ARIA-E ARIA with edema or effusions, ARIA-H ARIA with hemosiderin deposits, and Covid-19 coronavirus disease 2019.
† The relatedness of adverse events to lecanemab or placebo was determined by the investigators.
‡ ARIA events were based on central review of MRI studies and include events that occurred after the double-blind intervention period.
§ Symptomatic ARIA-H concurrent with ARIA-E were included under ARIA-E.

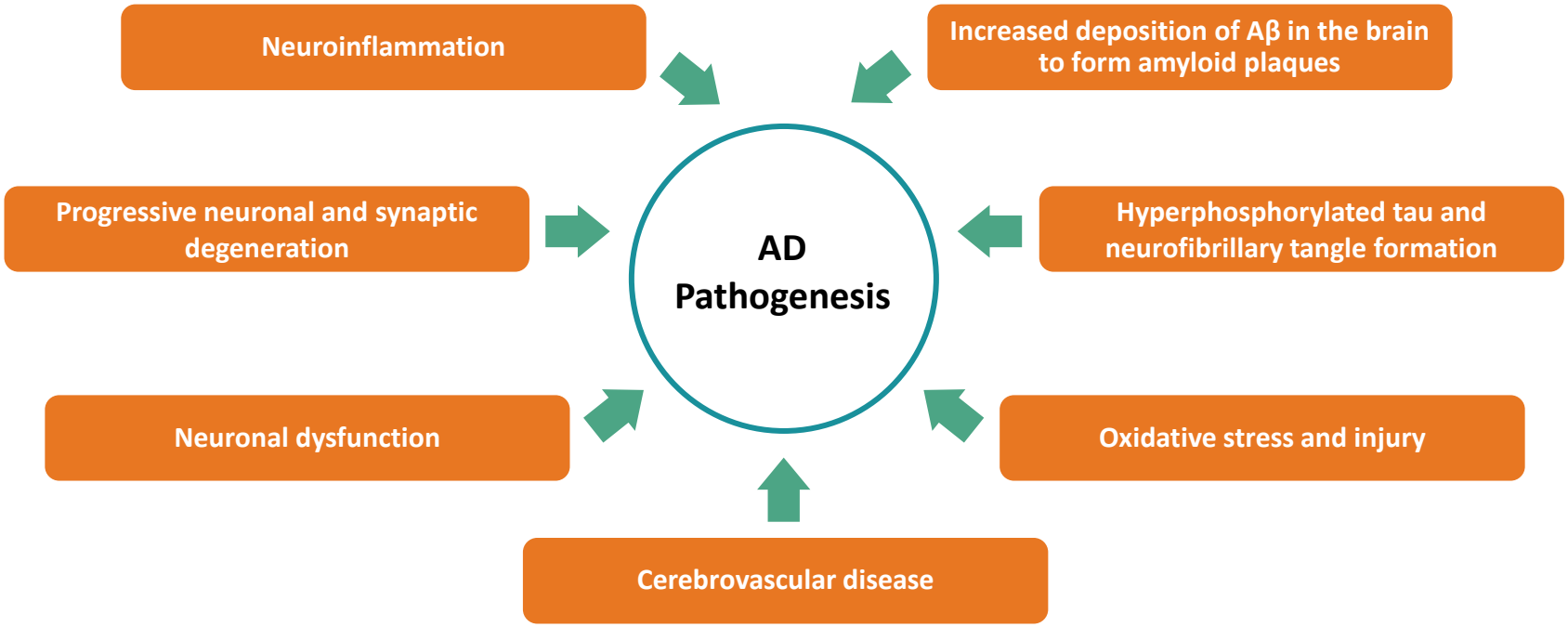
Donanemab in Early Symptomatic AD

Sims J et al. JAMA July 17, 2023 doi:10.1001/jama.2023.13239





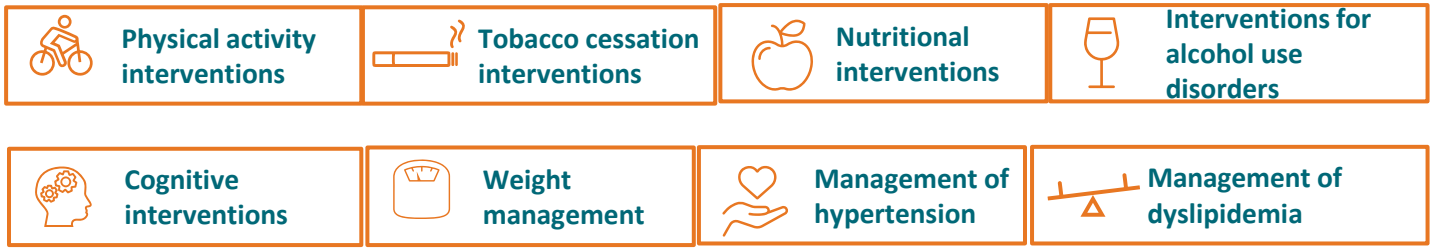
OTHER FACTORS IN AD PATHOGENESIS ARE ALSO POTENTIAL TARGETS for Precision/Personalized Approach



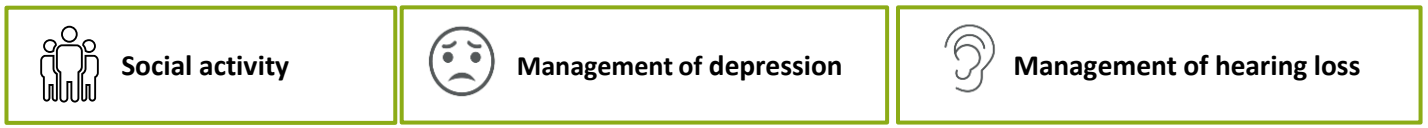
The

WHO 2019 GUIDELINES:
MODIFIABLE RISK FACTORS THAT CAN DELAY OR SLOW ONSET OF DEMENTIA

Areas for which WHO recommendations were strong/conditional for intervention



Areas for which WHO decided there was insufficient evidence to make firm recommendations for intervention



WHO 2019. https://www.who.int/publications/i/item/risk-reduction-of-cognitive-decline-and-dementia; Accessed July 24, 2021.


The End. Yay!!