






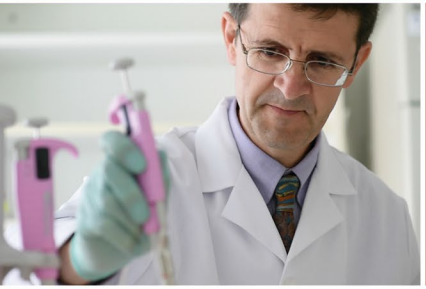


R13/U24 Conference: The Intersection of Multiple Chronic Conditions, Alzheimer's Disease and Related Dementias

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NIH National Institute on Aging DESIGNATED Alzheimer's Disease Research Center

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Disclosures

- I have received grants from NIA/NIH, Department of Veterans Affairs, State of Wisconsin, and UW-Madison to support my research program

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- UW-Madison has received grants from pharmaceutical companies for me to serve as a site PI to conduct treatment trials involving patients with MCI and dementia
- I have **no conflicts for this presentation**

Conference Theme and Goals

<u>Theme</u>: "The Intersection of Multiple Chronic Conditions and Alzheimer's Disease and Related Dementias (ADRD)

<u>Goals</u>:

- Characterize the nature of interaction between multiple chronic conditions (MCC) and ADRD mechanistically, clinically, and therapeutically
- Discuss how biological aging serves as a mechanistic link between brain and body
- Review breakthrough advances in AD biomarkers and co-occurring pathologies and their application in clinical settings
- Define how treatment and prevention of comorbidities would improve ADRD outcomes
- Outline responsible care for patients with MCC in the era of breakthrough advances in AD therapeutics

Prevalence and Socioeconomic Impact of Alzheimer's Disease

- In recent estimates, **6.9 million** Americans have Alzheimer's disease; by 2050, over 13 million Americans will have AD
- AD is the seventh leading cause of death in the United States and leads to **100,000 deaths each year**
- **Lifetime risk** of dementia after **age 55 is 42%.** Risk is higher in women, Black adults, and APOE4 carriers
- Total **cost** of care in the US currently **exceeds $600 billion**
- Over 11 million Americans provide unpaid care to people with AD. This involves $18.4 billion hours of **informal care** for an estimated value of **$346.6 billion**
- The **death rate** from AD has **increased by 140%** over the past 20 years

1) Fang et al. Nature Medicine; 13 January 2025:https://doi.org/10.1038/s41591-024-03340-9
2) Alzheimer's disease facts and figures, Alzheimer's Association, 2024

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Multiple Chronic Conditions and Dementia

- Over 95% of patients with AD have one or more other chronic conditions
- AD patients are nearly 4 times more likely to have six or more other chronic conditions
- Diagnosis of AD in the presence of MCC can be difficult, especially in primary care settings and delay the diagnosis
- People with AD and MCC have higher care costs, functional deficits, hospitalization, institutionalization, and mortality
- The impact of dementia on management of MCC and vice versa is currently unknown and needs more research

Percentage of People with Alzheimer's or Another Dementia Who Also Have . . .

Hypertension	56%
Heart Disease	46%
Chronic Kidney Disease	46%
Diabetes	37%
Congestive Heart Failure	34%
COPD	20%
Stroke	13%
Cancer	10%

1) Kulshreshtha et al. JAMA Network Open;2024;7(10),e2440411
2) Alzheimers Assoc Fact Sheet, March 2022

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Imaging and Fluid AD Biomarkers

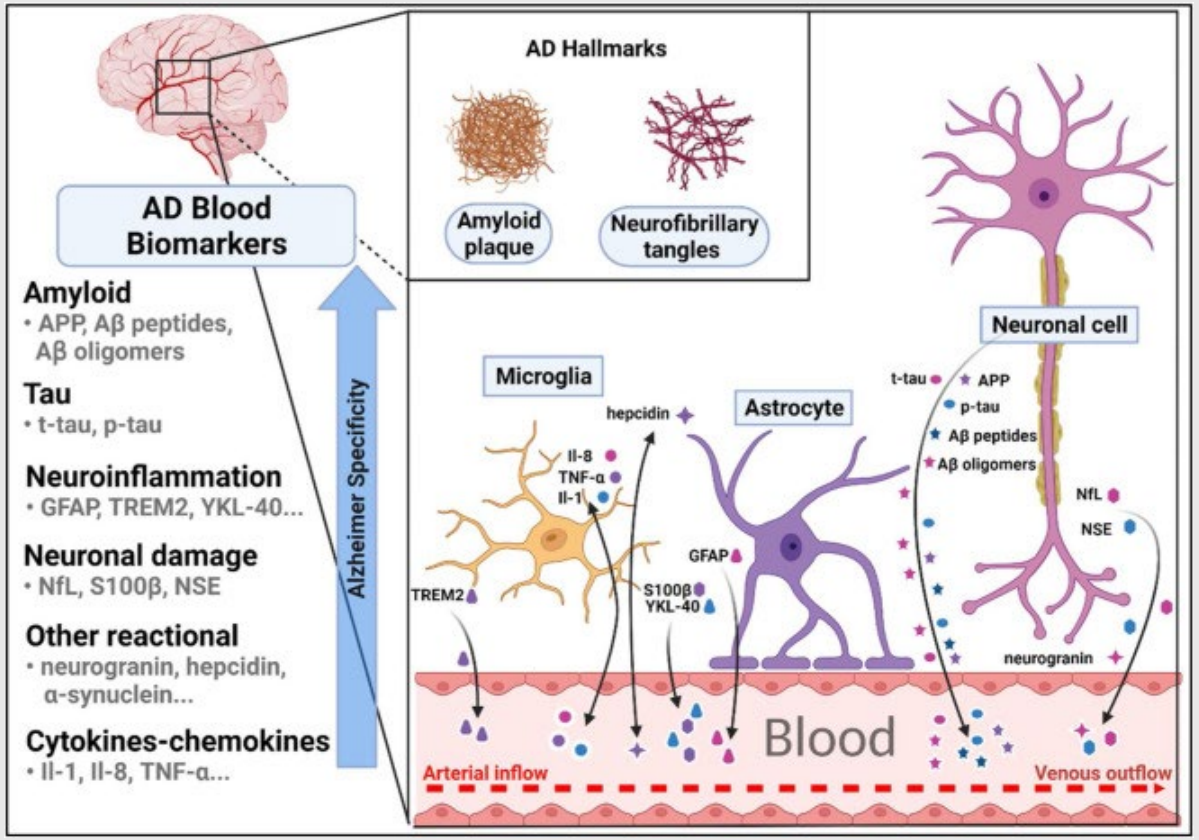
Discovery of neuroimaging and fluid AD biomarkers has transformed early diagnosis and treatment of AD dementia

For the first time, AD biomarkers will **provide a biological confirmation** of a clinical diagnosis and screen for people at risk for AD

Misdiagnosis of dementia in primary care settings can be **as high as 75%,** especially in **marginalized populations**

Use of AD biomarkers, especially fluid biomarkers, will significantly reduce the prevalence of under- and mis-diagnosis of AD

Blood-based AD biomarkers are less invasive, cost-effective, accessible, scalable, and diagnostic



1) Michelle Mielke et al., Alzheimer's Dement;2024:20;8216-8224
2) Delaby et al., Rev Neurologique; 2023:179, 161-173
3) Arslan et al. Clin Chem Lab Med; 2024, 62(6):1063-1069

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Justification to Study the Interactions Between MCC and Dementia

- Coexistence of MCC and dementia is highly prevalent in older adults
- Vascular diseases are commonly associated with dementia
- The complex interplay between MCC and dementia pathology is currently unknown and needs to be evaluated
- The diagnosis of dementia in the presence of MCCs can be difficult, especially in primary care settings with limited expertise
- Adverse consequences of poorly managed MCCs, especially vascular diseases, on dementia pathology, symptoms, progression, and mortality are essentially unknown
- Need to assess the impact of co-occurring MCC and dementia on caregiving and related burden

1) Matthews Klee et al. 2025; Alzheimer's & Dementia; 21 e14589
2) Pui Ying Yew et al. 2024; Alzheimer's & Dementia;20:4818-4827

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MCCs and Dementia: Moving Forward

Gaps:

- How do underlying biological mechanisms of MCCs interact with the pathophysiology of AD/ADRD at a cellular and molecular level
- Which MCC or a combination have the greatest impact on dementia
- Do the interactions between dementia and MCC vary across populations
- What are the most effective strategies for managing chronic conditions in people with dementia
- How do socioeconomic factors and access to healthcare influence the management of MCC in people with dementia across different populations

Opportunities:

- Better understanding of molecular mechanisms underlying the interaction between MCCs and dementia
- Develop blood biomarkers for AD and co-occurring pathologies for biological diagnosis of each disease
- Examine how the interaction and impact of MCC on dementia and vice versa differs across populations
- Develop patient-centered, holistic approaches to treating patients with MCC and dementia
- How does the presence of multiple chronic conditions impact the burden on caregivers of people with dementia

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Plenary Presentations

1) Comorbidity and ADRD
Speaker – Heather Whitson, MD
Duke University School of Medicine


Heather Whitson

2) Social determinants of health, equity and health disparities
Speaker - Monica Parker, MD
Emory University School of Medicine


Monica Parker

3) State of science on ADRD biomarkers
Speaker – Michelle Mielke, PhD
Wake Forest University School of Medicine


Michelle Mielke

Topic Presentations

1) Biological aging as a mechanistic link between brain and body
Moderator – George Kuchel, MD
University of Connecticut School of Medicine


George Kuchel

2) Improving ADRD outcomes by preventing and treating comorbidities
Moderator - Cynthia Carlsson, MD
University of Wisconsin School of Medicine & Public Health


Cynthia Carlsson

3) Responsible care in the era of MCC and therapeutic revolution in aging brain
Moderator – Nicole Fowler, PhD
Indiana University School of Medicine


Nicole Fowler

4) Small Group Breakout Sessions