**GSA**
**GERONTOLOGICAL
SOCIETY OF AMERICA®**

**OXFORD**

# Proceedings of the Alzheimer's Diagnosis in Older Adults With Chronic Conditions Network Inaugural Annual Conference

**Michelle M. Mielke, PhD,**[1,*] **Nicole R. Fowler, PhD, MHSA,**[2,3] **Heather E. Whitson, MD, MHS,**[4,5] **Heidi D. Klepin, MD, MS,**[6] **Antoine R. Trammell, MD, MPH,**[7] **Ambar Kulshreshtha, MD, PhD,**[8] **Kyra S. O'Brien, MD, MSHP,**[9] **Margaret Manchester, MPH,**[10] **Marcel E. Salive, MD, MPH,**[11] **and Jeff Williamson, MD, MHS**[12,13]

[1]Department of Epidemiology and Prevention, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA.
[2]Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana, USA.
[3]Indiana University Center for Aging Research and Regenstrief Institute, Inc., Indianapolis, Indiana, USA.
[4]Departments of Opthalmology, Medicine, and Neurology, Duke School of Medicine, Durham, North Carolina, USA.
[5]Durham VA Geriatrics Research and Education and Clinical Center, Durham, North Carolina, USA.
[6]Section on Hematology and Oncology, Wake Forest University School of Medicine, Winston Salem, North Carolina, USA.
[7]Department of Medicine and Neurology, Emory University School of Medicine, Atlanta, Georgia, USA.
[8]Department of Family and Preventive Medicine, School of Medicine, Emory University, Atlanta, Georgia, USA.
[9]Department of Neurology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA.
[10]School of Public Health, Georgia State University, Atlanta, Georgia, USA.
[11]National Institute on Aging, Bethesda, Maryland, USA.
[12]Section on Gerontology and Geriatric Medicine, Wake Forest University School of Medicine, Winston Salem, North Carolina, USA.
[13]Center for Healthcare Innovation, Wake Forest University School of Medicine, Winston Salem, North Carolina, USA.
*Address correspondence to: Michelle M. Mielke, PhD. E-mail: mmielke@wakehealth.edu

Decision Editor: Lewis A. Lipsitz, MD, FGSA (Medical Sciences Section)

## Abstract

The Alzheimer's Disease in Older Adults with Chronic Conditions (ADACC) Network is funded by the National Institute on Aging as a U24 cooperative agreement. ADACC is an inclusive, multidisciplinary group across multiple institutions that is charged with the task of developing evidence-based strategies for the use and implementation of Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD) biomarkers among older adults with cognitive impairment and multiple chronic conditions (MCCs). This report summarizes highlights of the First Annual Symposium of ADACC, which was held in Winston-Salem, North Carolina, in April 2024. An overview of the ADACC Network and goals were initially described, followed by a state of the science integrating biomarkers, AD/ADRD, and MCCs. Multiple presentations on a variety of topics were featured, including the significance of MCCs in AD/ADRD, the effects of MCCs on Alzheimer's blood-based biomarkers, the incorporation of AD/ADRD biomarkers into cancer care, the need to address racial and biomarker disparities, clinician and patient perspectives on plasma AD/ADRD biomarker testing, and ethical considerations. ADACC emphasized the importance of supporting emerging researchers and fostering a collaborative environment.

**Keywords:** Biomarkers, Comorbidity, Dementia, Diagnosis

The patient journey for older adults with multiple chronic conditions (MCCs) and cognitive impairment is complex. The diagnosis, prognosis, and management of cognitive impairment and each of the MCCs requires careful consideration of patient preferences, goals of care, and the evolving prognosis for each specific condition. The rapidly emerging development and access to Alzheimer's disease and Alzheimer's disease-related dementia (AD/ADRD) biomarkers, especially blood-based biomarkers (BBMs), have the potential to enhance or increase the burden of care for patients with MCCs. For this reason, numerous questions exist regarding the utility and implementation of the biomarkers in primary and specialty care settings.

To begin addressing this gap in the evidence, the National Institute on Aging (NIA) dedicated specific research funding to create the Alzheimer's Disease in Older Adults with Chronic Conditions (ADACC) Network (U24 AG082930). The ADACC Network is an inclusive, multidisciplinary group charged with the task of building a national infrastructure to develop evidence-based strategies for the use and implementation of AD/ADRD biomarkers among older adults with cognitive impairment and MCCs. As a national

collaborative funded by a U24 cooperative agreement, the ADACC Network: (i) assembles and analyzes existing data to assess the performance and accuracy of biomarkers (fluid and neuroimaging) in older patients living with MCCs; (ii) provides funds for pilot studies; and (iii) holds an annual conference to enhance scientific dialog on this topic and to disseminate the progress and findings from the ADACC. The ADACC Network held its inaugural conference in Winston-Salem, North Carolina, on April 29 and 30, 2024, with a focus on overviews of the state of the science, the initially funded pilot projects, the data coordinating center, and working groups. Attendees participated in breakout sessions for guided discussions on the practical and ethical implications of incorporating biomarkers into the medical care of aging adults with MCCs in both primary and specialty care settings. This report provides a brief overview of the presentations.

## The Significance of MCCs in AD/ADRD

The prevalence of MCCs among people with AD/ADRD is high. Dr. Heather E. Whitson, Professor of Neuroscience, Medicine, Neurology, Ophthalmology and Head & Neck Surgery and Communication Sciences at Duke University discussed the importance of considering MCCs when caring for aging older adults. Not only do MCCs significantly increase healthcare costs, with about 96% of Medicare spending used for two-thirds of beneficiaries with MCCs [1], but an individual's risk of complications, disability, dementia, and death also increases with number of comorbidities. Thus, MCCs pose a threat to an individual's independence. With increasing life expectancy, many previously deadly conditions are now chronic conditions, and rates of obesity and metabolic syndrome have increased [1,2]. Because of the interconnectedness of biological systems, injury or disease in any organ or subsystem can diminish biological resilience, making a person vulnerable to AD/ADRD.

About 95% of people with AD/ADRD have at least one other chronic condition, and someone with dementia is more than 3.8 times more likely to have 6+ chronic conditions than someone without. MCCs affect both the development and the detection of Alzheimer's disease (AD)-related pathology and dementia [3]. For example, frailty is related to both odds of AD/ADRD dementia and clinical expression, which has implications for clinical management because individuals with even a low level of AD pathology might be at risk for dementia if they are frail [3].

The diagnosis of AD/ADRD or its precursor, mild cognitive impairment (MCI), is challenging and can be somewhat lengthy, particularly among older adults with MCCs. As primary care providers (PCPs) predominantly provide care to older adults [4], and there is a limited capacity of AD/ADRD specialists, there is an urgent need for training and involvement of PCPs in the detection, diagnostic evaluation, care management, and coordination of persons with cognitive impairment in the context of other MCCs [5]. MCCs and cognitive impairment cannot be treated in isolation, but must be treated and managed in gestalt.

## Use of Biomarkers in Medical Care

Dr. Marcel E. Salive, Health Scientist Administrator for the Division of Geriatrics and Clinical Gerontology at the National Institute on Aging, provided examples and considerations when incorporating biomarkers in clinical care. Biomarkers are useful because they can help detect or confirm the presence of a disease, pathology, or biological presence of interest, as well as a disease subtype [6]. For example, blood glucose or hemoglobin A1c results are used to identify patients with type 2 diabetes mellitus; ejection fraction is used to identify heart failure severity and subtypes. However, biomarker cut points can differ by patient characteristics, which makes interpretation difficult. For example, cardiac troponin concentrations reflect ongoing cardiomyocyte injury and are used to diagnose myocardial infarction. However, cardiac troponin concentrations change with age and vary by sex; ranges of normal values for older adults may overlap with abnormal values for younger adults. This overlap confounds the interpretation of troponin results, potentially leading to false-positive diagnoses in older adults and men, and false-negative diagnoses in younger women [7]. As such, biomarkers should not be used in isolation, but in addition to the clinical characterization of the disease, other chronic conditions, and the sociodemographics of the patient population.

### Biomarkers Associated With AD

Biomarkers currently used to diagnose AD include those related to amyloid-beta (Aβ) plaques, neurofibrillary tau tangles, and neurodegeneration. Historically, amyloid positron emission tomography (PET), and a low cerebrospinal fluid (CSF) Aβ42/40 ratio or an elevated CSF phosphorylated tau (P-tau)/Aβ42 ratio have been the gold standard in vivo biomarkers to aid in the diagnosis of AD. Although these biomarkers have excellent diagnostic clinical accuracy, there are many limitations to their use at the population level including limited to no availability in many geographical areas, invasiveness, contraindications (eg, spinal stenosis increases with age), and cost (ie, not reimbursed and/or high out-of-pocket copays), and need for specialist interpretation [8].

Given the limitations of CSF and PET, BBMs are increasingly being utilized to aid in the diagnosis of AD; plasma measures of the Aβ42/40 ratio, P-tau181, and P-tau217 are clinically available as in vitro diagnostics to help determine the etiology of cognitive symptoms. However, despite the potential of BBMs for a more accurate and earlier diagnosis of AD, it remains unknown how to best utilize and implement AD BBMs at the population level. There is also a need to understand the real-world performance and clinical utility of these biomarkers in primary care settings in the context of MCCs.

## Considerations for Implementation of AD/ADRD BBMs

There are numerous factors that need to be considered when implementing and interpreting BBMs in primary care for the diagnosis of AD. Dr. Michelle M. Mielke, Professor of Epidemiology and Prevention and of Gerontology and Geriatric Medicine at Wake Forest University School of Medicine, discussed the impact of comorbidities and copathologies on BBM interpretation. For example, chronic kidney disease (CKD) increases concentrations of some AD/ADRD BBMs [9,10]. Without knowledge of this BBM level increase, a patient with CKD could be falsely diagnosed with AD. Additionally, higher body mass index (BMI) values are associated with decreased concentrations of the BBMs because increasing BMI leads to increasing blood volume [9–11]. Cardiac

conditions and medications can also affect biomarker concentrations (12,13). Therefore, a patient's recent weight gain or loss, MCCs, and prescription medications should be considered when interpreting AD/ADRD BBM results. Developing an algorithm to account for such factors when interpreting BBM levels might be beneficial in aiding physicians in more accurately interpreting the BBMs and diagnosing AD; this is 1 goal of ADACC.

Implementing the BBMs in primary care may also be challenging. AD pathology begins decades before symptoms appear and increases with age; 40% of cognitively unimpaired individuals will have amyloid pathology by age 80, but not all will develop cognitive symptoms (14). The AD/ADRD BBMs cannot currently predict which individuals will develop symptoms or when. Because of the risk of false-positive and false-negative results, a blood test should not be ordered without a clinical assessment that includes objective evidence of cognitive decline.

## Assessing Cognitive Impairment and Determining Etiology Among Patients With Cancer

Determining the cause of cognitive impairment among individuals with MCCs, such as cancer or cardiovascular disease, is difficult. There are currently no guidelines as to when and if AD/ADRD biomarkers should be used. Dr. Heidi D. Klepin, Professor of Hematology and Oncology, and Dr. Jeff Williamson, Professor of Gerontology and Geriatric Medicine, both at Wake Forest University School of Medicine, discussed diagnosing cognitive impairment and determining etiology among cancer patients.

Treating an older patient with cancer differs in important ways from treating a younger patient because the older patient is more likely to be frail, have MCCs requiring several additional medications, or have cognitive impairment. In 2018, the American Society of Clinical Oncology recommended that all adults aged 65 years and older with cancer undergo a geriatric assessment, assessing both physical and cognitive function, to inform cancer management (15). Results of a clinical trial comparing outcomes in older patients who did and did not undergo a geriatric assessment before beginning cancer treatment showed that patients who had geriatric assessments experienced significantly fewer serious toxic effects from cancer treatment (16). Thus, the overall picture of the patient's physical and cognitive function obtained from the geriatric assessment could be viewed as a biomarker that helps the oncologist predict how a patient may react to cancer treatment so that the treatment plan can be adjusted accordingly. However, it is important to ensure that cancer patients understand the purpose of an assessment focused on physical and cognitive function. Cognitive screening during an oncology intake may result in fear of disqualification from cancer treatment due to the results of the screening. Explaining to patients that the results can inform the specific type and intensity of chemotherapy and/or adjuvant treatment often helps address an older adult and their family's concerns.

Another feared complication of ongoing cancer therapy is "chemobrain," the onset of thinking and memory problems that some patients experience after cancer treatment. This self-reported symptom is not well correlated with objective tests and imaging results, and the underlying mechanism is unclear. The use of AD/ADRD BBMs for patients with

a cancer diagnosis can assist in personalizing cancer care. However, the BBM results need to be considered in the context of the entire patient presentation and symptoms because many factors can contribute to cognitive impairment over a patient's cancer journey.

## Addressing Health Disparities in AD/ADRD Biomarkers

There are multiple racial, ethnic, and geographic differences related to AD/ADRD risk, BBM expression, and access to healthcare. Dr. Antoine R. Trammell, Assistant Professor of Medicine and Neurology, and Dr. Ambar Kulshreshtha, Associate Professor of Family and Preventive Medicine and of Epidemiology, at Emory University, described health disparities in the use and interpretation of biomarkers for diagnosing AD/ADRD. Rates of dementia are highest among African American, American Indian/Alaska Native, and Latino populations, with the lowest rates for non-Hispanic White and Asian American groups (17). Compared with their White counterparts, African Americans and Latino Americans are 2 and 1.5 times more likely, respectively, to develop AD/ADRD, which may be related to more prevalent risk factors like obesity, diabetes, heart disease, and stroke. Additionally, African American decedents are more likely than their White counterparts to have another pathology in addition to AD (18).

In addition to racial/ethnic differences in the prevalence of AD/ADRD, there are racial/ethnic differences in access to healthcare. Murchison et al. (19) showed that African American patients were more likely than White patients to seek care for cognitive impairment in primary care, rather than specialty care, clinics. Because specialty clinics order PET neuroimaging and prescribe dementia-related medications at a higher rate than primary care clinics, African Americans had less access to PET neuroimaging or dementia-related medications.

Biomarkers for AD/ADRD may differ by race/ethnicity. Some studies have shown racial/ethnic differences in plasma AD/ADRD BBMs, while others have not. Studies have shown that African Americans have a greater contribution of microvascular dysfunction to cognitive impairment than White participants. Other factors can affect disease biomarkers, which can also vary by race. For example, higher perceived stress scores were associated with greater tau-related AD biomarkers among African Americans with cognitive impairment compared to their White counterparts, suggesting a potential biological connection for stress with AD and its racial disparity (20). Preventing disease with more education, modifying risk factors, timely screening, and implementing culturally appropriate interventions earlier in life will be key to reducing racial and ethnic disparities in AD/ADRD.

## Clinician and Patient Perspectives on Plasma AD/ADRD Biomarker Testing

Although AD/ADRD BBMs are now clinically available, there is little knowledge of clinician and patient perspectives on the use of the biomarkers. Dr. Kyra S. O'Brien, Assistant Professor of Neurology at the University of Pennsylvania, discussed clinicians varying perspectives on using AD/ADRD BBMs in practice. A study of semistructured interviews with 30 physicians, 15 with significant clinical dementia expertise, showed that clinicians' perspectives on biomarkers revolved around

4 main categories: impact on the patient's medical and psychosocial care, impact on the patient and family, patient characteristics, and test attributes. Some physicians felt that biomarker results would be useful for care planning and obtaining needed care support. In contrast, others believed biomarker results were not meaningful unless they could inform pharmacologic treatment options. Dementia experts generally felt biomarkers would be more clinically useful (21). Clinicians without dementia expertise identified several supports needed before they would adopt BBMs, including access to specialists and clear guidelines for appropriate use and interpretation.

Dr. Nicole R. Fowler, Associate Professor of Medicine at Indiana University School of Medicine, discussed AD/ADRD BBM use from the patient's perspective. Although BBMs are less invasive, burdensome, and costly than CSF or PET testing, there is a lack of consistent coverage across insurance programs and limited accessibility to laboratories that can process the samples. Although medical test results can provide reassurance to some patients, they can also induce anxiety and influence patient behavior.

A pilot study tested the feasibility and acceptability of using BBMs in primary care among patients who screened positive on a digital cognitive assessment. It also evaluated patients' perceptions of a decision guide to help patients decide whether to participate in biomarker testing. Of 1 722 patients aged 65 or older who completed the digital cognitive assessment, 236 (13.7%) screened positive for cognitive impairment. Of those approached for a blood test, 60% refused BBM testing. Of those who consented to BBM testing, 8% did not follow up on the disclosure discussion. Based on pre- and post-disclosure measures of anxiety and depression, it was determined that disclosure of BBM results did not increase depression, anxiety, distress, or concerns. However, given the high percentage of patients who refused BBM testing, focus groups are needed to understand why so many patients initially refused testing.

## Ethical Implications of AD/ADRD Biomarkers Testing

Ethical challenges will arise with the adoption of AD/ADRD BBM testing in clinical practice. Ms. Margaret Manchester, at the Georgia State University School of Public Health, highlighted 3 challenges including barriers to access, decision to pursue, and potential legal and social consequences of AD/ADRD biomarker testing.

Access to AD/ADRD biomarker testing can either mitigate or engrain existing health disparities. One potential barrier is payer coverage. In 2013, Centers for Medicare & Medicaid Services (CMS) announced conditional coverage of amyloid PET if individuals agreed to participate in clinical trials, marking early barriers to biomarker testing access. More recently, with the Food and Drug Administration approval of lecanemab and donanemab, therapies that require biomarker confirmation of AD pathology, this policy has been modified. Yet, disparities exist, and access is limited. Physicians and patients must consider cost when deciding whether to pursue AD/ADRD biomarker testing, especially when MCCs might affect AD biomarker test results.

Legal and social consequences of biomarker testing may exist. A major ethical concern around biomarker testing is possible discrimination against an asymptomatic patient with a positive AD/ADRD biomarker test result. Including this result in a patient's medical record might affect the patient's insurability or put the patient's employment at risk. Federal laws (eg, Genetic Information Nondiscrimination Act) are designed to protect against employment and insurance discrimination, but do not apply to biomarker results (22). How results are documented in the patient's medical record could influence how clinicians in other settings (eg, emergency department) judge the patient's decision capacity, perhaps incorrectly.

## Discussion

The evolving science around promising AD/ADRD biomarkers has great potential to democratize screening and risk reduction for AD/ADRD, but also brings additional challenges. Biomarkers have been useful in reducing the fear associated with diseases such as cancer and HIV when they become a doorway to effective treatments. This same scenario of reducing the fear of cognitive impairment is also possible if AD/ADRD biomarkers can be linked to the initiation of effective therapies. However, before these gains can be realized, substantial work is needed to establish the evidence base for when biomarkers are useful and reliable, particularly in the context of MCCs across diverse clinical settings. The ADACC is charged with (i) developing a systematic approach to examining and assimilating reliable evidence on the proper application of ADRD biomarkers in the setting of MCC in diverse populations; (ii) providing seed funding for promising research in this area; and (iii) fostering the growth of a network of both producers (researchers) and consumers (patients and providers) of the evidence base for appropriate AD/ADRD biomarkers use. Success in these areas is critical to establishing the trust necessary to leverage the rapid growth of cognitive health.

## Funding

## Conflict of Interest

M.M.M. has served on scientific advisory boards and/or has consulted for Althira, Biogen, Cognito Therapeutics, Eisai, Lilly, Merck, Novo Nordisk, and Roche. K.S.O. has served on an advisory board for Lilly. The other authors declare no conflict.

## Author Contributions

All authors made significant conceptual contributions to the manuscript, provided editing, and approved the final manuscript.

## References

1. Anderson C. *Chronic Conditions: Making the Case for Ongoing Care*. In: Anderson C, ed. Robert Wood Johnson Foundation. Princeton; 2010 update.

2. Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *JAMA.* 2005;294(6):716–724. https://doi.org/10.1001/jama.294.6.716

3. Wallace LMK, Theou O, Godin J, Andrew MK, Bennett DA, Rockwood K. Investigation of frailty as a moderator of the relationship between neuropathology and dementia in Alzheimer's disease: a cross-sectional analysis of data from the Rush Memory and Aging Project. *Lancet Neurol.* 2019;18(2):177–184. https://doi.org/10.1016/S1474-4422(18)30371-5

4. Yang M, Chang C-H, Carmichael D, Oh ES, Bynum JPW. Who is providing the predominant care for older adults with dementia? *J Am Med Dir Assoc.* 2016;17(9):802–806. https://doi.org/10.1016/j.jamda.2016.04.026

5. Lam J, Hlávka J, Mattke S. The potential emergence of disease-modifying treatments for Alzheimer's disease: the role of primary care in managing the patient journey. *J Am Board Fam Med.* 2019;32(6):931–940. https://doi.org/10.3122/jabfm.2019.06.180328

6. Group F.-N.B.W. *BEST (Biomarkers, EndpointS, and Other Tools) Resource*. Bethesda, MD: Co-published by National Institutes of Health (US); 2016.

7. Forman DE, de Lemos JA, Shaw LJ, et al.; Geriatric Cardiology Section Leadership Council. Cardiovascular biomarkers and imaging in older adults: JACC council perspectives. *J Am Coll Cardiol.* 2020;76(13):1577–1594. https://doi.org/10.1016/j.jacc.2020.07.055

8. Mattke S, Hanson M. Expected wait times for access to a disease-modifying Alzheimer's treatment in the United States. *Alzheimers Dement* 2022;18(5):1071–1074. https://doi.org/10.1002/alz.12470

9. Mielke MM, Dage JL, Frank RD, et al. Performance of plasma phosphorylated tau 181 and 217 in the community. *Nat Med.* 2022;28(7):1398–1405. https://doi.org/10.1038/s41591-022-01822-2

10. Syrjanen JA, Campbell MR, Algeciras-Schimnich A, et al. Associations of amyloid and neurodegeneration plasma biomarkers with comorbidities. *Alzheimers Dement* 2022;18(6):1128–1140. https://doi.org/10.1002/alz.12466

11. Rebelos E, Rissanen E, Bucci M, et al. Circulating neurofilament is linked with morbid obesity, renal function, and brain density. *Sci Rep.* 2022;12(1):7841. https://doi.org/10.1038/s41598-022-11557-2

12. Zhu F, Wolters FJ, Yaqub A, et al. Plasma amyloid-β in relation to cardiac function and risk of heart failure in general population. *JACC Heart Fail* 2023;11(1):93–102. https://doi.org/10.1016/j.jchf.2022.09.006

13. Brum WS, Docherty KF, Ashton NJ, et al. Effect of Neprilysin inhibition on Alzheimer's disease plasma biomarkers: a secondary analysis of a randomized clinical trial. *JAMA Neurology* 2024;81(2):197–200. https://doi.org/10.1001/jamaneurol.2023.4719

14. Roberts RO, Aakre JA, Kremers WK, et al. Prevalence and outcomes of amyloid positivity among persons without dementia in a longitudinal, population-based setting. *JAMA Neurol* 2018;75(8):970–979. https://doi.org/10.1001/jamaneurol.2018.0629

15. Mohile SG, Dale W, Somerfield MR, et al. Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric oncology. *J Clin Oncol.* 2018;36(22):2326–2347. https://doi.org/10.1200/JCO.2018.78.8687

16. Mohile SG, Mohamed MR, Xu H, et al. Evaluation of geriatric assessment and management on the toxic effects of cancer treatment (GAP70+): a cluster-randomised study. *Lancet.* 2021;398(10314):1894–1904. https://doi.org/10.1016/S0140-6736(21)01789-X

17. Mayeda ER, Glymour MM, Quesenberry CP, Whitmer RA. Inequalities in dementia incidence between six racial and ethnic groups over 14 years. *Alzheimers Dement* 2016;12(3):216–224. https://doi.org/10.1016/j.jalz.2015.12.007

18. Barnes LL, Leurgans S, Aggarwal NT, et al. Mixed pathology is more likely in black than white decedents with Alzheimer's dementia. *Neurology.* 2015;85(6):528–534. https://doi.org/10.1212/WNL.0000000000001834

19. Murchison CF, Kennedy RE, McConathy JE, Roberson ED. Racial differences in Alzheimer's disease specialist encounters are associated with usage of molecular imaging and dementia medications: an enterprise-wide analysis using i2b2. *J Alzheimers Dis.* 2021;79(2):543–557. https://doi.org/10.3233/JAD-200796

20. Trammell AR, McDaniel DJ, Obideen M, et al. Perceived stress is associated with Alzheimer's disease cerebrospinal fluid biomarkers in African Americans with mild cognitive impairment. *J Alzheimers Dis.* 2020;77(2):843–853. https://doi.org/10.3233/JAD-200089

21. O'Brien K, Coykendall C, Kleid M, et al. Determinants of plasma Alzheimer's disease biomarker use by primary care providers and dementia specialists. *J Gen Intern Med.* 2024;39(9):1713–1720. https://doi.org/10.1007/s11606-023-08583-9

22. Arias JJ, Karlawish J. Confidentiality in preclinical Alzheimer disease studies: when research and medical records meet. *Neurology.* 2014;82(8):725–729. https://doi.org/10.1212/WNL.0000000000000153