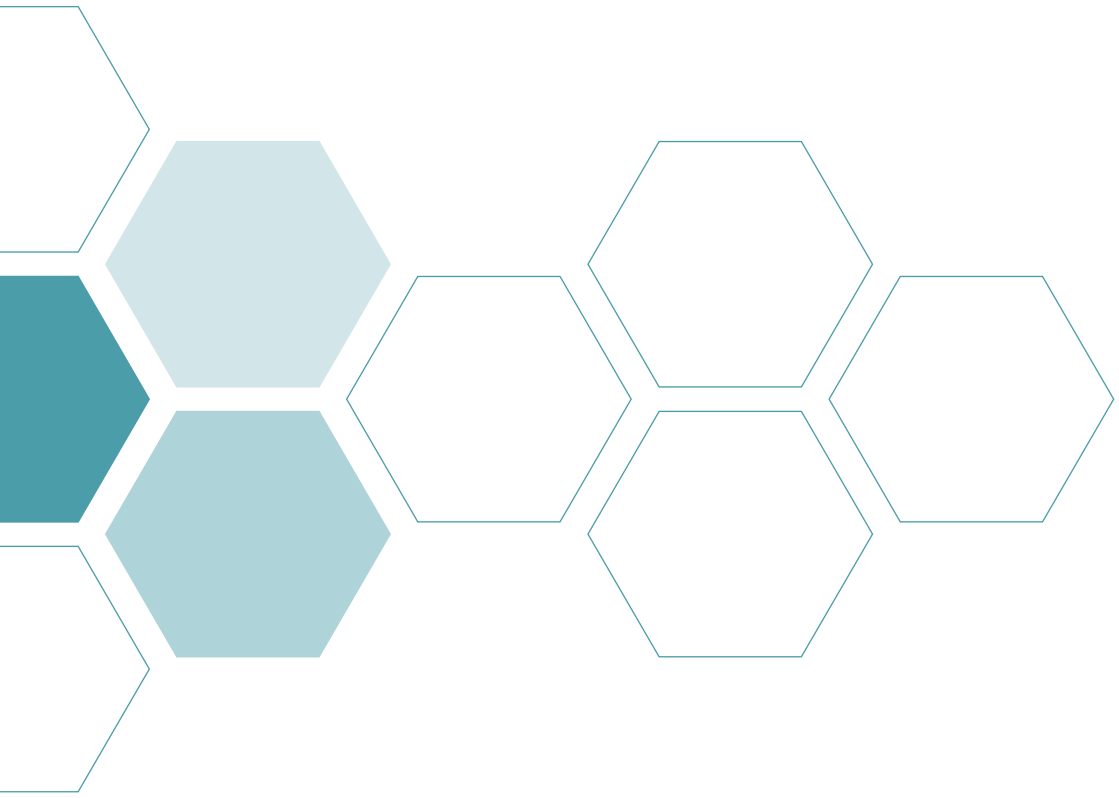
Diagnostic Challenges and Opportunities in Alzheimer's Disease Management



JOURNAL of MANAGED CARE MEDICINE

NAMCP
MEDICAL DIRECTORS INSTITUTE

JMCM

JOURNAL
OF MANAGED CARE
MEDICINE

4435 Waterfront Drive, Suite 101
Glen Allen, VA 23060
(804) 527-1905
fax (804) 747-5316

EDITOR-IN-CHIEF
Thomas Morrow, MD

PUBLISHER
Jeremy Williams

JOURNAL MANAGEMENT
Douglas Murphy Communications
Richmond, Virginia
(804) 387-7580
grant.murphy@douglasmurphy.com

GRAPHIC DESIGN
Douglas Murphy Communications

ISSN: 1094-1525. The *Journal of Managed Care Medicine* is published by NAMCP Medical Directors Institute. Corporate and Circulation offices: 4435 Waterfront Drive, Suite 101, Glen Allen, VA 23060; Tel (804) 527-1905; Fax (804) 747-5316. Editorial and Production offices: P.O. Box 71895, Richmond, VA 23255-1895; Tel (804) 387-7580; Fax (703) 997-5842. Advertising offices: Sloane Reed, 4435 Waterfront Drive Ste 101, Glen Allen, VA 23060 Tel (804) 527-1905, Fax (804) 747-5316.

POSTMASTER: Send address changes to The Journal of Managed Care Medicine, 4435 Waterfront Drive, Suite 101, Glen Allen, VA 23060.

JOURNAL of MANAGED CARE MEDICINE

The Official Journal of the NAMCP MEDICAL DIRECTORS INSTITUTE

A Peer-Reviewed Publication

TABLE OF CONTENTS

Diagnostic Challenges and Opportunities in Alzheimer's Disease Management

Ian N. Kremer, JD; Suzanne E. Schindler, MD, PhD; Joel B. Braunstein, MD, MBA
Gary M. Owens, MD (Moderator)

Key Message:

Early diagnosis of Alzheimer's disease (AD) is important because the early stages of the disease represent the time when the most benefit can be seen from the anti-amyloid disease modifying therapies (DMTs). Early diagnosis, also importantly, allows patients and families more time to engage in shared decision-making for both clinical and non-clinical care options. Biomarker testing is required to demonstrate brain amyloid presence before initiation of the new DMT treatments, enhance clinical management of co-occurring health conditions, and provide payers greater confidence that limited resources are being utilized appropriately.

Blood biomarker (BBM) testing for AD can remove diagnostic testing barriers with a simple blood draw, especially if incorporated into primary care practice. Blood tests may be the only modality that will enable adequate access to testing. Blood tests are less invasive, more accessible—including to populations in medically underserved communities—and potentially less expensive than cerebrospinal fluid (CSF) biomarker tests or positron emission tomography (PET) scans. The PrecivityAD2 test has high concordance with amyloid PET status and has demonstrated comparable performance to CSF analysis. This test provides results with positive or negative results that reflect a high or low likelihood for the presence of brain amyloid pathology. Compared to amyloid PET and CSF biomarker analysis, it is expected to provide a more acceptable, accessible, equitable, and scalable option for timely and accurate diagnosis.

Once these BBMs are reimbursed uniformly with reasonable copays, they are expected to become the preferred biomarker for AD pathology assessment and likely will enhance the standard of care in the assessment of cognitive impairment. Clinical implementation of BBM tests is likely to increase diagnostic certainty and impact clinical management in patients with mild cognitive impairment (MCI) or dementia by helping clinicians to rule in AD and identifying patients who may benefit from DMTs as well as to rule out AD in patients to allow for other diagnostic consideration for their cognitive symptoms.

The Value of Early Diagnosis of Alzheimer's Disease

Ian N. Kremer, JD

Alzheimer's disease (AD) is of interest to public and private payers due to the aging of the United States (U.S.) population with subsequent increases in those diagnosed with mild cognitive impairment (MCI) or mild dementia due to AD and substantial expansion in the therapeutic options, especially with the introduction of the anti-amyloid disease modifying therapy (DMT).

Dementia is an umbrella term that refers to cognitive impairment typified by a decline in memory and thinking that impairs function in everyday activities, and there are many causes of such cognitive impairment. AD is a specific brain disease that is a leading cause of cognitive impairment and is biologically defined by the presence of amyloid plaques and tau tangles in the brain. Amyloid plaques begin accumulating in the brain at least 10 to 20 years before the onset of AD clinical symptoms. Once amyloid plaques and tau tangles reach higher levels, individuals are likely to develop cognitive impairment and may progress to dementia. AD is the most common cause of MCI and dementia, although many patients with AD MCI or AD dementia have co-pathologies contributing to their cognitive impairment.

Until a dozen years ago, the diagnosis of AD pathology could not be made until the post-mortem brain examination. Now, there are several rigorously validated imaging and fluid biomarker tests that can determine whether AD specific brain pathology is present and may be causing or contributing to cognitive impairment. Clinically available AD biomarker tests include amyloid PET scans, CSF tests for amyloid and tau proteins, and blood-based amyloid and tau protein tests.

Diagnosing the cause or causes of cognitive impairment has significant value to patients, their families, clinicians, and payers (Exhibit 1). Numerous disorders that are treatable can cause cognitive impairment, such as strokes, medication side effects, sleep disorders, and depression. Even when AD is the primary cause of cognitive impairment, patients often benefit from the diagnosis and management of additional co-occurring conditions that are exacerbating cognitive impairment. Now that anti-amyloid DMTs are available, AD biomarker testing is essential to determining whether patients are candidates for these treatments, which are indicated only when biomarkers demonstrate evidence of amyloid pathology. Notably, anti-amyloid treatments are most effective very early in the disease course (MCI or mild dementia), making the early diagnosis of AD more urgent.

An accurate diagnosis also can be helpful to the management of other medical conditions. Most people with AD have multiple serious health conditions such as hypertension, diabetes, or cardiovascular disease, which require treatment. Identifying and diagnosing cognitive disorders helps physicians and patients prioritize treatment of co-occurring conditions and more vigilantly monitor and support treatment adherence. With or without an AD diagnosis, clinicians are managing people with AD. Denying the clinician the opportunity to access information about whether a patient has a cognitive disorder is neither a clinically appropriate strategy, nor is it ethical in terms of caring for the whole person. Knowing the diagnosis allows clinicians to provide the most thorough, wholistic, and person-centered patient care. Clinicians, patients, families, and payers benefit from confirming what diseases the patient faces and avoiding potential misdiagnoses with consequent mistreatment. Informed patients and families can make better choices about clinical and non-clinical options. With knowledge of timely and accurate AD diagnosis, patients and families can maximize the time they have to engage in shared decision-making, pursue their preferred clinical treatment pathways, optimize overall health, plan for legal, financial, emotional supportive care, and spiritual needs. Clinical trial participation and personal goals also

Exhibit 1: The Value of Early Diagnosis of Alzheimer's Disease

Treat Reversible Causes of Symptoms	• Some disorders mimic Alzheimer's disease (AD) but are not AD. • If identified early, dementia-like symptoms may be treatable and reversible.
Improve Clinical and Non-Clinical AD Support	• Disease modifying and symptomatic treatment are therapeutic options. • Referrals to appropriate community-based services are enhanced.
Improve Clinical Management of Other Conditions	• Most people with AD have multiple serious health conditions. • Identifying and diagnosing cognitive disorders helps physicians and patients prioritize treatment of co-occurring conditions. • With or without a diagnosis, clinicians are managing people with AD.
Empower Patients and Families	• Clinicians/patients/families benefit from knowing what diseases they face or not. • Informed patients and families can make better choices about clinical and non-clinical options.
Raise Efficiency with Blood-Based Biomarkers (BBMs)	• Specialist shortages and PET/CSF testing capacity undermine timely AD diagnosis. • Generally, BBMs are practical for PCPs, faster and more scalable, and less expensive. • Some BBMs are most appropriately used by PCPs only to triage patients before referral. • The best BBMs can be used by PCPs to make a diagnosis.

can be considered with as much time as possible to maximize quality of life.

From a clinical and payer perspective, coverage, and affordability for early diagnosis matter. Public and private payers should lean into equitable coverage by proactively educating clinicians and patients that coverage is available, streamline the process and eliminate any rate-limiting bureaucracy, and make copays affordable for all beneficiaries. No one should be excluded or left behind because of their financial situation or their ability to navigate complex coverage rules. This will help address healthcare disparities. AD disproportionately affects medically underserved populations and often has more ramifications given these populations' overall health situation. Delayed diagnosis exacerbates both AD specific and overall health disparities. At a minimum, it delays access to DMTs and symptomatic treatments, non-clinical support, and quality of life decision-making. At worst, delayed diagnosis causes people to lose the opportunity to consider DMTs, lose the opportunity to make decisions about their own quality of life, and potentially shortens their lives by not having other health conditions properly managed due to unrecognized cognitive deficits and consequent poor adherence to treatment regimens for such co-occurring conditions. An optimal diagnostic process must be equitable, timely, accurate, compassionate, and actionable (ETACA). ETACA diagnosis is an opportunity to build trust with, and improve health outcomes for, all patients and particularly for often marginalized populations.

Overall, earlier diagnosis means more time, and more time matters to patients. It gives patients more time in earlier stages of AD when that time is most precious and contributes most to quality of life, more time when improved DMTs may become available.

Specialist shortages, testing capacity, and overall cost for PET scans and CSF testing present substantial challenges to ETACA AD diagnosis. In many places in the U.S., a timely diagnosis is functionally impossible due to limited PET and CSF health system capacity. More scalable diagnostic tools are necessary. The use of BBMs can improve the efficacy, democratization, and equitability of AD diagnosis. Generally, BBMs are practical for primary care providers (PCPs), faster and more scalable, and less expensive than other testing. Some BBMs are most appropriately used by PCPs only to triage patients before referral to specialists. The best BBMs can be used by PCPs to make a diagnosis faster and less expensively with accuracy roughly equivalent to amyloid PET and CSF testing.

Use of Blood Biomarkers in the Diagnosis of Dementia due to Alzheimer's Disease

Suzanne E. Schindler, MD, PhD

The Memory Diagnostic Center (MDC), the dementia specialty practice associated with Barnes-Jewish Hospital/Washington University School of Medicine, saw 3,492 unique patients with memory complaints over the past year. The center has a recent average of 44 AD biomarker tests per month, with approximately 15% of patients undergoing CSF, PET, or blood tests. All three major biomarker modalities are now being used but the current selection of biomarker modality depends on practical factors including reimbursement. A few years ago, only CSF tests were used because that is what was available and paid for by insurance (Exhibit 2). Then blood tests were used in some patients who did not want to undergo a spinal tap or had a contraindication to a spinal tap. In 2023, amyloid PET scans became available and any patient who was being considered for DMTs had to have one of these tests. Recently, Medicare has started paying for the amyloid PET scans so their use has dramatically increased.

There are significant drawbacks to CSF tests and amyloid PET that limit their use and lead to disparities in diagnosis and care of those with memory difficulties. For the CSF tests, capacity and access are limited because most clinicians do not perform lumbar punctures (LPs), and it is time-consuming and expensive to train staff, set up LP clinics, and perform LPs. Most patients have never undergone an LP and some refuse due to perceived risks. Individuals identifying with minoritized groups are more likely to refuse an LP. Amyloid PET requires expensive and specialized equipment and personnel. Similar to LP, capacity and access are limited for amyloid PET. Amyloid PET cost is typically greater than $6,000 per scan which may be associated with a significant patient co-pay. Additionally, some patients are concerned about radioactivity and decline testing (Exhibit 3).

There are major advantages to blood tests. Blood collection is well accepted by patients and already performed as part of typical dementia evaluation. Providers are very accustomed to performing blood tests and blood tests are associated with minimal costs and burden. There is also high capacity to perform blood tests. Blood collection is well accepted by patients and already performed as part of typical dementia evaluation.

A barrier to BBM testing in AD diagnosis has been variability in the accuracy of these tests, but performance standards were recently published

Exhibit 2: Use of Biomarker Tests at Washington University

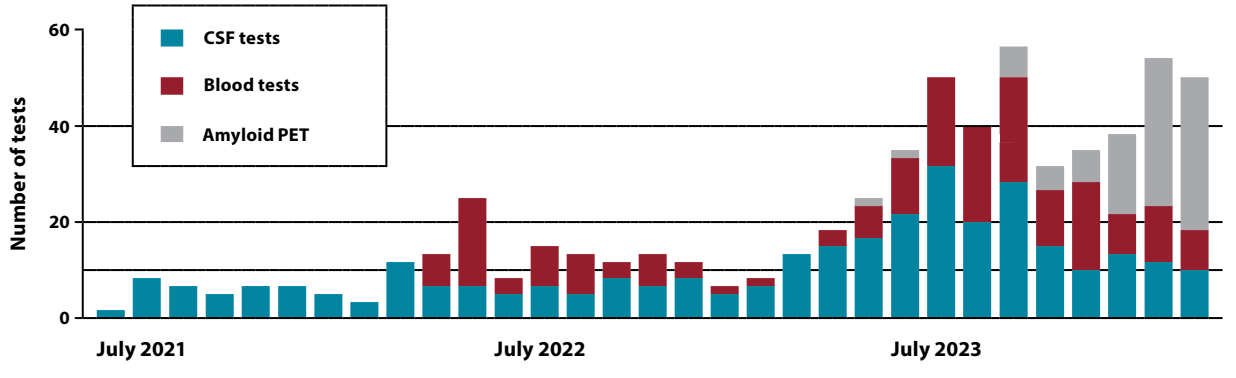


Exhibit 3: Why Do We Need Blood Tests for AD?

- There are **significant drawbacks** to CSF tests and amyloid PET that limit their use and lead to disparities in diagnosis and care.

- **CSF Tests**
  - **Provider**: most clinicians do not perform LP and it is time-consuming and expensive to train staff, set up clinics, and perform LPs; capacity/access is limited.
  - **Patient:** most patients have never undergone lumbar puncture (LP) and some refuse due to perceived risks; individuals identifying with minoritized groups are more likely to refuse LP.

- **Amyloid PET**
  - **Provider**: testing requires expensive and specialized equipment and personnel; capacity/access is limited.
  - **Patient**: cost is typically > $6,000/scan which may be associated with a significant co-pay; some patients are concerned about radioactivity.

- There are **major advantage**s of blood tests
  - **Provider**: minimal costs and burden for providers as well as very high capacity and access are possible.
  - **Patient**: blood collection is well accepted and already performed as part of typical dementia evaluation.

and there is increased regulation of diagnostic tests by FDA. The Global CEO Initiative on Alzheimer's Disease recommended that confirmatory BBM tests have similar accuracy to CSF tests, which have approximately 90 percent sensitivity and 90 percent specificity for amyloid PET status.[1]

Results from a study examining how well individual tests and combination of tests correlate with amyloid PET, early tau PET, cortical thickness, and cognitive impairment demonstrated that tests that use plasma p-tau217 have high agreement with amyloid PET.[2] Combining plasma p-tau217 with the amyloid-β 42 and amyloid-β 40 (Aβ42/Aβ40) plasma ratio also improves performance. In another study, the ratio of plasma phosphorylated tau 217 (p-tau217) to non-phosphorylated tau 217 (np-tau217) (expressed as a percentage, %p-tau217) was compared to matched CSF samples analyzed with clinically used and FDA-approved automated blood-based immunoassays for Aβ42/40 and p-tau181/Aβ42.[3] Plasma %p-tau217 was equivalent to FDA-approved CSF tests in classifying amyloid PET status, with an area under the curve (AUC) for both between 0.95 and 0.97. Plasma %p-tau217 was superior to CSF tests in classification of tau PET with AUCs of 0.95 – 0.98. Overall, plasma %p-tau217 demonstrated performance that was equivalent or superior to clinically used FDA-approved CSF tests in the detection of AD pathology.

Of note, 63 percent of Washington University Memory Diagnostic Center patients tested with the PrecivityAD2 test since its introduction to clinical care during late 2023 have an APS2 score on the PrecivityAD2 test between 80 and 100 (positive predictive value [PPV] for this range of score of having positive amyloid PET scan is 96% from the Meyer study[8]), and 18 percent have an APS2 score of 0 to 20 (negative predictive value [NPV] 95%).[8] For the 81 percent of values that are clear positive or negative (≥ 80 or ≤ 20) healthcare providers using the test believed that there was no further need for a follow-up test. Comparing the PrecivityAD2 test result to CSF p-tau181/Aβ42, the PrecivityAD2 test result provides increased separation of positive and negative results; more CSF cases require a follow-up amyloid PET. The 0 to 100 scale for APS2 appears easier to interpret than CSF test results. These data suggest that a positive or negative result on the blood test equates to a positive or negative result on the amyloid PET and reduces the need for performing an amyloid PET scan.

Another barrier to BBM use is a lack of reimbursement or inconsistent reimbursement. Clinicians are not going to order a test their patient cannot afford. Paradoxically, for many patients it is currently more affordable to get a $6,000 or more, amyloid PET scan than a substantially less expensive but just as accurate blood test.

A High-Performance Alzheimer's Disease Test: The PrecivityAD2 Blood Test

Joel B. Braunstein, MD, MBA

Major barriers to access have led to growing support for the use of blood biomarkers in clinical diagnosis.[1,4-7] The European Union-North American Clinical Trials in Alzheimer's Disease (EU/US-CTAD) Task Force noted that BBMs have the potential to be accurate, cost effective, and easily accessible for widespread clinical use, and could facilitate timely diagnosis.[4] The 2024 Alzheimer's Association (AA) Workgroup introduced a new approach to AD diagnosis, which noted that an abnormal Core 1 biomarker result is sufficient to establish a diagnosis of AD and to inform clinical decision-making throughout the disease continuum.[7] Core 1 BBMs that suffice as standalone diagnostic tests for AD are those with a minimum accuracy of 90 percent to detect abnormal amyloid PET in the intended-use population, or, more simply, plasma tests whose diagnostic performance is equivalent to that of approved CSF assays.[7] A BBM that achieves this diagnostic performance benchmark should be considered on equal footing with established PET and CSF biomarkers for diagnosis of AD.[7]

C2N Diagnostics is one of the companies that has developed a BBM for use as an aid to AD diagnosis (Exhibit 4). The PrecivityAD2 test is a multi-analyte, proteomic blood test with an algorithm that detects and quantifies specific peptides associated with AD pathology and evaluates presence of brain amyloid plaques (likelihood of positive amyloid PET, Exhibit 5). The algorithm that generates the test result is a logistic regression model that provides a probability score ranging between 0 and 100. The closer a patient's result is to 0, the greater the confidence in the negative test result; and the closer a patient's result is to 100, the greater the confidence in the positive test result. The test

Exhibit 4: C2N Diagnostics Clinical Care Test Components

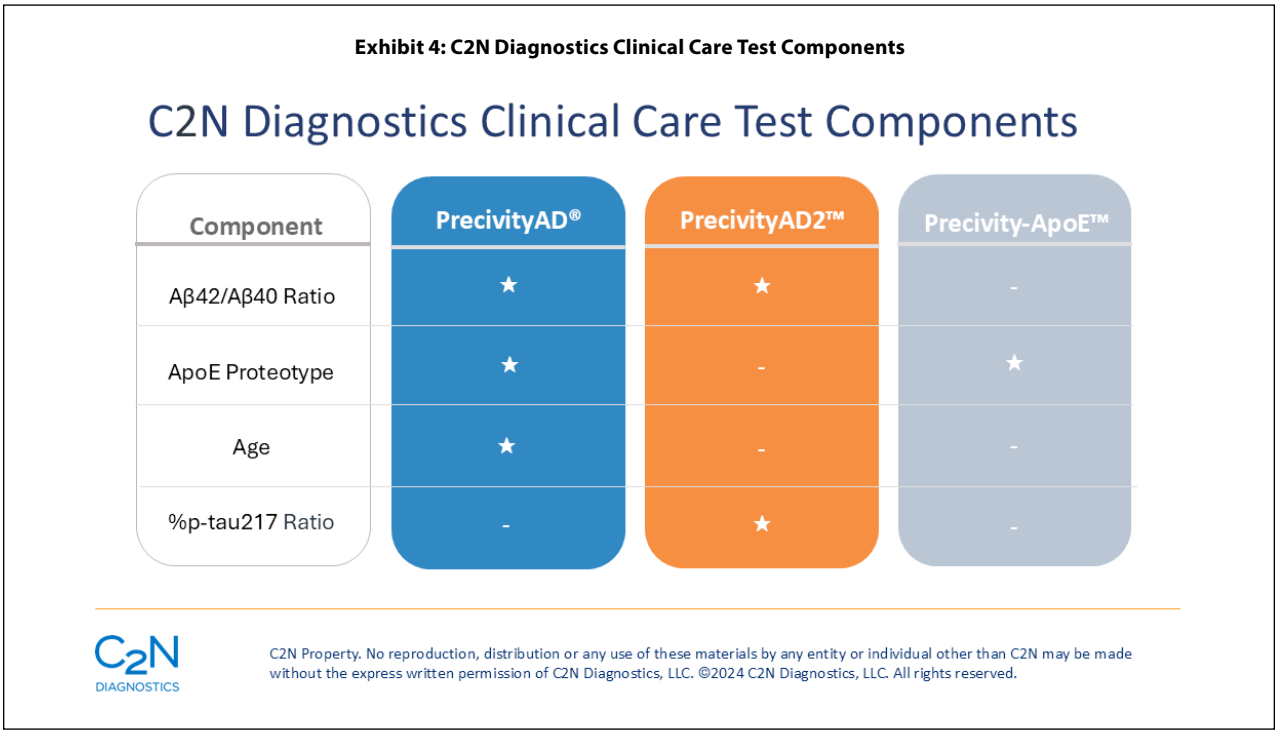


Image courtesy of C2N Diagnostics, LLC. Used with Permission.

Exhibit 5: PrecivityAD2™ Blood Test in Clinical Care

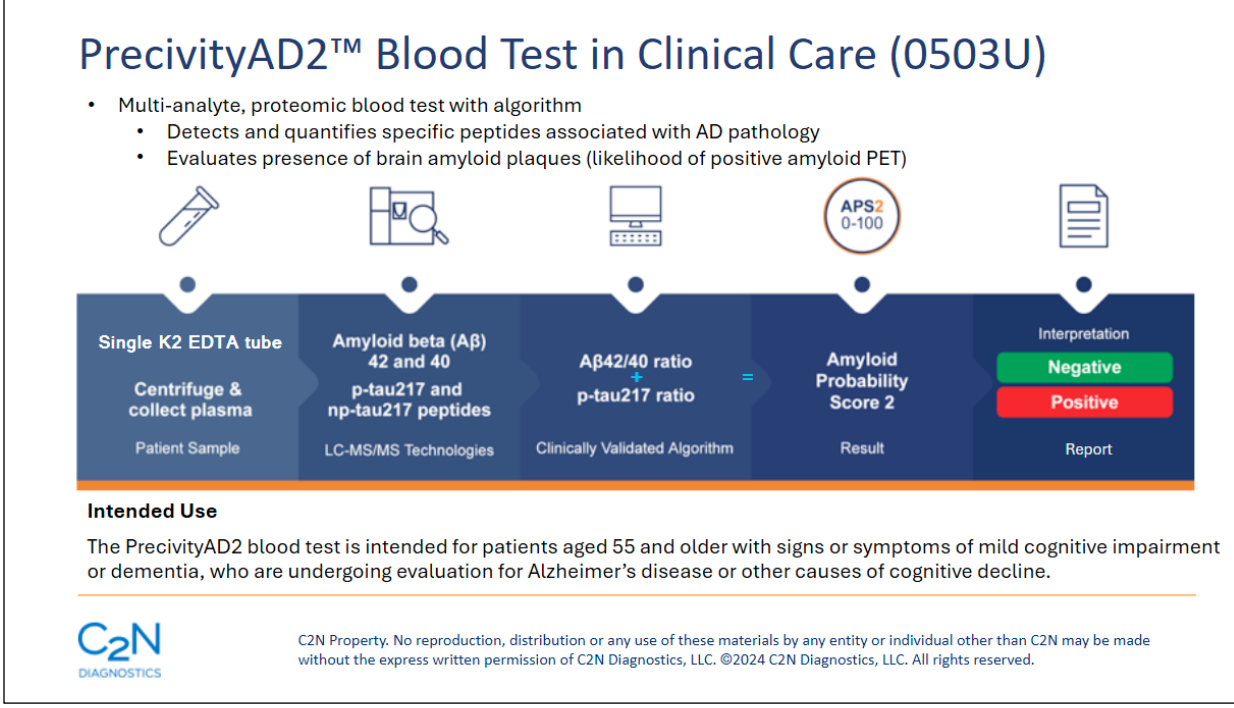


Image courtesy of C2N Diagnostics, LLC. Used with Permission.

Exhibit 6: Blood Biomarker Diagnostic Performance in Discriminating Clinical Alzheimer's Disease was Higher than that of PCPs and Memory Specialists[10]

Measurement	Performance of Clinical Judgment in Primary Care (95% Confidence Interval)	Performance of APS2 Algorithm in Primary Care (95% Confidence Interval)	Performance of Clinical Judgment in Secondary Care (95% Confidence Interval)	Performance of APS2 Algorithm in Secondary Care (95% Confidence Interval)
Accuracy	61% (53-69%)	91% (86-96%)	73% (68-79%)	91% (88-95%)
PPV	64% (53-76%)	88% (81-96%)	75% (68-81%)	93% (90-97%)
NPV	59% (47-70%)	95% (89-100%)	71% (62-80%)	89% (83-94%)

Performance of PrecivityAD2 blood test APS2 algorithm was evaluated in a population of 1213 patients using predefined cutoffs using CSF analysis and amyloid PET imaging as reference standards.[10]

returns either a Negative (APS score 0 – 47) or Positive (APS score 48 – 100) test result. The PrecivityAD2 blood test is intended for patients aged 55 years and older with signs or symptoms of MCI or dementia, who are undergoing evaluation for AD or other causes of cognitive decline. The Washington University Memory Diagnostic Center, among many other clinical sites throughout the U.S., is using the PrecivityAD2 test.

In an analysis, the PrecivityAD2 blood test showed strong clinical validity, with excellent agreement with brain amyloidosis by PET.[8] Amyloid Probability Score 2 (APS2) output from this test was similar by ethnicity, sex, age, and apoE4 status. APS2 is the combination of plasma %p-tau217 and Aβ42/Aβ40 ratio. The overall percent agreement with PET was 88 percent (53% prevalence amyloid positivity). The PPV

Exhibit 7: Using PrecivityAD2 as a Confirmatory Test

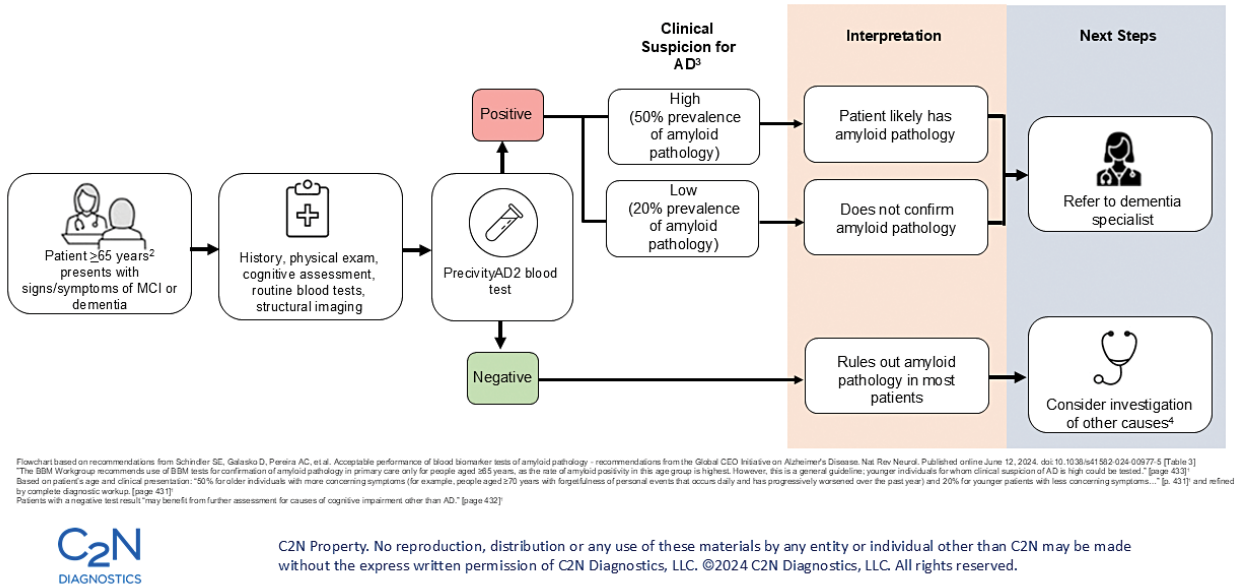


Image courtesy of C2N Diagnostics, LLC. Used with Permission.

was 90 percent (95% CI: 86% – 93%) and NPV was 87 percent (95% CI: 82% – 90%). The PrecivityAD2 test performance is believed to meet the Global CEO Initiative on Alzheimer's Disease standard of comparability to CSF diagnostic test performance and qualifies as a high performance BBM. It is also believed to meet the criteria for a Core 1 biomarker in the Alzheimer's Association revised diagnostic criteria.[1,7]

A Markov simulation showed that without BBM testing for early AD diagnosis the projected wait times for a diagnosis start at approximately 12 months in 2024 and increase to over 100 months by 2033.[9] Utilizing a BBM test (with performance similar to the PrecivityAD2 Test), the projected wait times drops to three months in 2024 and increases to slightly more than 12 months in 2033. More efficient use of specialist appointments and reduced need for amyloid PET and CSF tests decrease the anticipated waiting times. Reducing diagnosis wait times may lead to better outcomes.

One way to improve the early diagnosis of AD is to allow testing at the primary care level with BBMs. One clinical care study involving 1,213 individuals with signs or symptoms of cognitive impairment compared use of %p-tau217 alone and when combined with Aβ42/Aβ40 ratio (APS2) for AD diagnosis by both primary care and dementia specialists.[10] Primary care physicians had a diagnostic accuracy of 61 percent (95% CI, 53% – 69%) for identifying clinical AD after clinical examination, cognitive testing, and a computed tomographic scan versus 91 percent (95% CI, 86% – 96%) using the APS2 (Exhibit 6).[10] Dementia specialists had a diagnostic accuracy of 73 percent (95% CI, 68% – 79%) versus 91 percent (95% CI, 88% – 95%) using the APS2. It is important to note that the population in the primary care group was older (median 77.3 versus 74.1 years) with more chronic comorbidities (cardiovascular disease, hyperlipidemia, chronic kidney disease, and diabetes) compared to the secondary care group. A BBM needs to be robust when confounding factors such as comorbidities are present, and the APS2 was shown to be robust here. In the overall population, the diagnostic accuracy using the APS2 (90% [95% CI, 88% – 92%]) test result did not differ from the diagnostic accuracy using the %p-tau217 alone (90% [95% CI, 88% – 91%]). This study does demonstrate a significant rate of misdiagnosis by both primary care and specialists when biomarker testing is not used as part of the clinical care evaluation process. A potential workflow for incorporating BBMs into primary care practice has been developed (Exhibit 7).[11]

Author Bios

Ian N. Kremer, JD is the Executive Director of the LEAD (Leaders Engaged on Alzheimer's Disease) Coalition. Ian Kremer became the LEAD Coalition's Executive Director in 2012 and has worked on dementia policy for almost three decades. Throughout his career, Kremer has served as a board or advisory committee member for a variety of public service organizations, non-profits, and government appointed panels in the fields of aging, technology, and health. Kremer holds degrees from Washington University and the University of Michigan School of Law. He is a member of the Virginia State Bar and the American Bar Association.

Suzanne E. Schindler, MD, PhD is a clinical neurologist and neuroscientist focused on improving the diagnosis and treatment of Alzheimer's disease. She completed the MD/PhD program, a Neurology residency, and a fellowship in dementia at Washington University. Dr. Schindler sees patients with memory concerns and coordinates biomarker testing for the Washington University Memory Diagnostic Center. She leads the Fluid Biomarker Core for the Knight Alzheimer's Disease Research Center. Her research is focused on the clinical validation of blood tests for Alzheimer's disease. She is an Associate Professor of Neurology at Washington University School of Medicine, in St. Louis, MO.

Joel B. Braunstein, MD, MBA is the CEO and Co-Founder of C2N Diagnostics, LLC and has led the company's commercial growth since its inception. Dr. Braunstein has played a senior executive role in numerous emerging life sciences companies since 2004. He received his M.D. with Highest Distinction from Northwestern University Medical School in 1996. Subsequently, he trained in internal medicine at Brigham and Women's Hospital, Harvard Medical School, and was a Fellow in Cardiovascular Medicine and Robert Wood Johnson National Clinical Scholar at the Johns Hopkins Medical Institutions. Additionally, he completed an MBA with management and health policy focus and maintained an Assistant Professorship in Cardiology at Johns Hopkins University. In 2010, he was named a Distinguished Alumnus of Johns Hopkins University. Dr. Braunstein also serves on the Executive Advisory Board for the Chemistry of Life Processes (CLP) Institute at Northwestern University.

Gary M. Owens, MD is President of Gary Owens Associates in Ocean View, DE.

References

1. Schindler SE, Galasko D, Pereira AC, et al. Acceptable performance of blood biomarker tests of amyloid pathology — recommendations from the Global CEO Initiative on Alzheimer's Disease. *Nat Rev Neurol*. 2024;20(7):426-39.
2. Warmenhoven N, Salvadó G, Janelidze S, et al. A comprehensive head-to-head comparison of key plasma phosphorylated tau 217 biomarker tests. *Brain*. 2024:awae346.
3. Barthélemy NR, Salvadó G, Schindler SE, et al. Highly accurate blood test for Alzheimer's disease is similar or superior to clinical cerebrospinal fluid tests. *Nat Med*. 2024;30(4):1085-95.
4. Angioni D, Delrieu J, Hansson O, et al. Blood Biomarkers from Research Use to Clinical Practice: What Must Be Done? A Report from the EU/US CTAD Task Force. *J Prev Alzheimer's Dis*. 2022;9(4):569-79.
5. Hansson O, Edelmayer RM, Boxer AL, et al. The Alzheimer's Association appropriate use recommendations for blood biomarkers in Alzheimer's disease. *Alzheimer's Dement*. 2022;18(12):2669-86.
6. Mielke MM, Anderson M, Ashford JW, et al. Recommendations for clinical implementation of blood-based biomarkers for Alzheimer's disease. *Alzheimer's Dement*. 2024;20(11):8216-8224. doi:10.1002/alz.14184
7. Jack CR Jr, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. *Alzheimer's Dement*. 2024;20(8):5143-69.
8. Meyer MR, Kirmess KM, Eastwood S, et al. Clinical validation of the PrecivityAD2 blood test: A mass spectrometry-based test with algorithm combining %p-tau217 and Aβ42/40 ratio to identify presence of brain amyloid. *Alzheimer's Dement*. 2024;20(5):3179-92.
9. Mattke S, Chen J, Hanson M. A Markov decision process model evaluating the diagnostic journey until biomarker confirmed diagnosis of early-stage AD was conducted. Poster presentation. AAIC 2024, Philadelphia.
10. Palmqvist S, Tideman P, Mattsson-Carlgren N, et al. Blood biomarkers to detect Alzheimer's disease in primary care and secondary care. *JAMA*. 2024;332(15):1245-57.
11. Monane M, Maraganore DM, Carlile RM, et al. Clinical Utility of an Alzheimer's Disease Blood Test Among Cognitively Impaired Patients: Results from the Quality Improvement PrecivityAD2 (QUIP II) Clinician Survey Study. Diagnostics (Basel). 2025;15(2):167. Published 2025 Jan 13. doi:10.3390/diagnostics15020167