NEWS RELEASE

Study in Frontiers in Neurology Affirms Amyloid Blood Test Can Help Identify Patients Who May Forgo Imaging Evaluation for Alzheimer's Disease

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Findings suggest the test can reduce the need for PET imaging in some patients with mild cognitive decline to enable therapeutic focus on non-Alzheimer's disease causes, broadening access to quality evaluation and lowering healthcare costs

SECAUCUS, N.J., March 26, 2024 /PRNewswire/ -- A blood test that analyzes levels of amyloid proteins by highly sensitive mass spectrometry could help physicians establish that Alzheimer's disease (AD) is likely not the cause of patients' mild cognitive impairment, finds a new study published in **Frontiers in Neurology** by researchers from Quest Diagnostics (NYSE: DGX), the University of Florida and Mount Sinai Medical Center in Miami Beach.

According to the analysis, up to 99% of patients with a negative result for amyloid proteins in the brain using an imaging procedure called positron emission tomography (PET) would likely be negative using a blood test that evaluates a ratio of amyloid beta 42 and 40 proteins (Aβ42/40), which are found in the brain and also circulate in the blood stream. With this level of prediction, the investigators determined the test could help reduce PET brain scan evaluations by about 40%, with potentially substantial savings in healthcare costs for these patients.

While amyloid PET imaging is an established method for aiding diagnosis of AD, it is significantly more expensive, invasive and specialist-dependent than blood tests.

"The findings of this analysis in a large cohort have significant implications for AD care management, because they potentially mean many patients could benefit from this type of blood-based assay that has advantages relative to current approaches," said co-author David E. Vaillancourt, PhD, Orchid Professor and Chair Applied Physiology and Kinesiology, College of Health and Human Performance, Fixel Institute of Neurological Disorders and Director,

1Florida ADRC Biomarker Core.

The study, Clinical utility of plasma Aβ42/40 ratio by LC-MS/MS in Alzheimer's disease assessment, is believed to be one of the largest published studies to evaluate amyloid blood testing for AD assessment. The investigators analyzed 6,192 deidentified laboratory test results from patients whose physicians submitted specimens for testing by Quest's Aβ42/40 ratio test (brand name Quest AD-Detect® Beta-amyloid ratio testAB42/40). Clinical performance of the Quest test was established using 250 specimens from participants with amyloid PET imaging and demographic data from the 1Florida Alzheimer's Disease Research Center. Quest introduced the AD-Detect™ test to physicians in early 2022.

The investigators also evaluated the performance of the blood test by different interpretative ranges based on different cutoffs, or amyloid levels in the blood. Proposed guidelines from the National Institutes of Aging recommend blood biomarker testing account for different ranges by cutoff levels, including an intermediate range, to support clinical decision making.

Key findings:

High NPV across populations: The test's negative predictive value (NPV) was 99% (at the highest cutoff of 0.170) in a population with moderate prevalence of AD (40%) as determined by PET-positivity. NPV represents the likelihood a disease is not present in a given population. The investigators then applied the NPV of 99% to the population of 6,192 deidentified specimens tested by Quest for Aβ42/40. They determined that 40% of that population could reliably forgo additional evaluation by PET, which costs about $5,000 per scan.

High sensitivity for AD PET-positivity at lower cut off: The test was 91% sensitive for detecting AD, as determined by PET scan at a cutoff of 0.160 in a population with moderate prevalence of PET-positivity of 40%.

In the same population and cutoff, the specificity was 76%. The same investigative team recently published results of a **study** in Alzheimer's & Dementia that showed the "novel and important" finding that abnormal Aβ42/40 blood testing "associates with quantifiable changes in the tissue and extracellular microstructural environments" of the brain, even in PET-negative patients.

"These findings show Aβ42/40 testing is very helpful in identifying amyloid pathology in populations with a high prevalence of AD, particularly older individuals," said study co-author Michael Racke, MD, Medical Director of Neurology at Quest Diagnostics. "We believe the comparatively low specificity reflects the limits of PET scans to identify the earliest stages of AD pathology and that many of these patients will progress to be PET-positive as the disease worsens."

APOE4 did not influence accuracy, possibly due to population diversity: APOE4 alleles did not substantially improve accuracy of the Aβ42/40 test, in contrast to other research. Investigators theorize this was due to a higher than typical percentage of patients of Hispanic heritage in the study population. APOE4 is a genetic trait that raises risk of AD and is more likely to correlate with PET-positive results in patients who are White than Hispanic.

"Our findings are a cautionary note that algorithms incorporating Aβ42/40 and APOE4 allele status may not be generally applicable for all races and ethnicities," wrote the authors.

Nearly **7 million Americans** have Alzheimer's, the most prevalent dementia, a number projected to reach 14 million by 2060. New blood tests offer the potential for primary care physicians as well as specialists to identify people at risk for Alzheimer's disease even before symptoms manifest.

To access the complete study, including methodology, strengths and limitations: **Frontiers | Clinical utility of plasma Aβ42/40 ratio by LC-MS/MS in Alzheimer's disease assessment (frontiersin.org**)

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