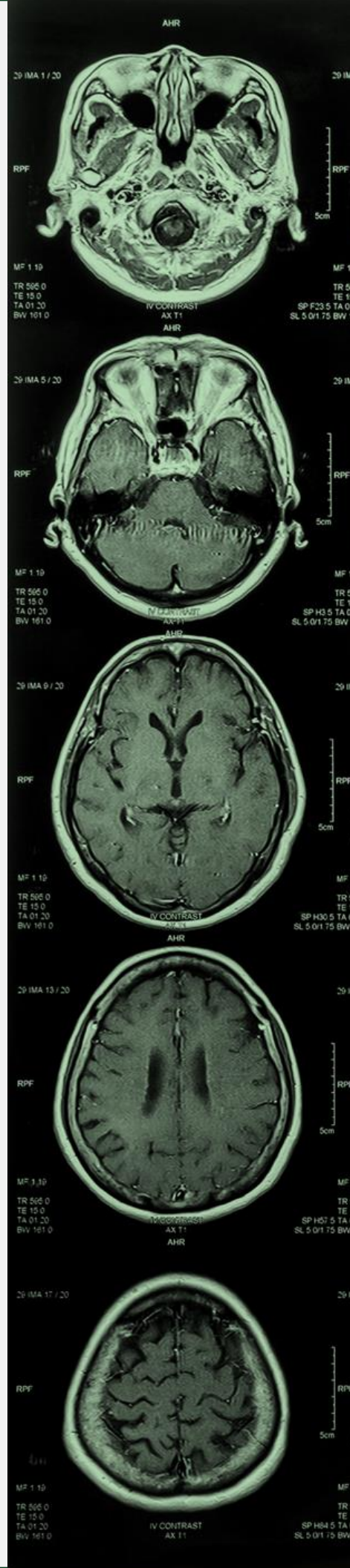




The Coming Alzheimer's Disease Healthcare Revolution

US Physician and Adult Perspectives on the Future of Diagnostics and Treatment

MAY 2022



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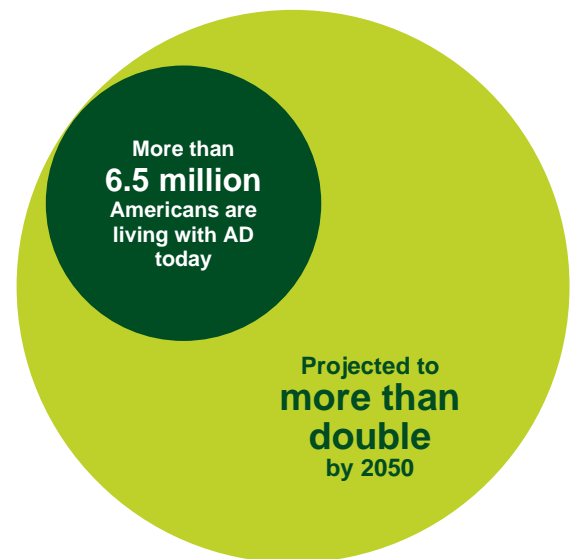
US Physician and Adult Perspectives on the Future of Diagnostics and Treatment



The field of Alzheimer's disease (AD) research and treatment seems better primed than ever to deliver new therapies with the potential to transform care.¹ The FDA's approval of aducanumab in June 2021, though contentious, marks the first authorization of a therapy that targets the fundamental pathophysiology of the disease.² More than 100 disease-modifying therapies are now in clinical trials—nearly 20 of which are in phase 3.³ The identification of biomarkers for AD has created new avenues for scientific exploration and increased hope that AD will one day be a treatable condition.

More than 6.5 million Americans are living with AD – a number projected to more than double by 2050 as the population ages.⁴ Without treatment, affected individuals face a progressive and ultimately lethal neurodegenerative disorder that destroys memory and thinking skills necessary to carry out simple daily tasks.⁵ As case numbers rise, healthcare and other societal costs associated with AD are predicted to reach \$1.1 trillion.⁶ But the greatest burden is experienced by the people living with AD, including their caregivers. Currently, more than 11 million Americans provide unpaid care for people with AD or other dementias.⁷ With no available cure and limited treatment options, patients and their loved ones inevitably experience a devastating and unstoppable disease progression.

New treatments for AD drive today's healthcare discourse in the space, but **diagnostics have been largely missing from the conversation.**



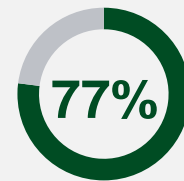
² *The Coming Alzheimer's Disease Healthcare Revolution: US Physician and Adult Perspectives on the Future of Diagnostics and Treatment*

The Coming Alzheimer's Disease Healthcare Revolution: US Physician and Adult Perspectives on the Future of Diagnostics and Treatment, a new report from Quest Diagnostics, reveals physician and US adult perspectives on the current and future landscape of dementia and AD evaluation, testing, treatment, and care. Findings highlight the important role diagnostics may play in the next era of AD healthcare.

Indeed, an individual being evaluated for AD will likely undergo a battery of tests. These may range from verbal cognitive assessments in a primary care physician's office to expensive or invasive procedures with neurologists and other specialists in outpatient facilities or hospitals, such as positron emission tomography (PET) scans, computerized tomography (CT) scans, and cerebrospinal fluid (CSF) taps. Weeks, months, or even years can elapse before a patient receives a diagnosis.⁸

Moreover, conventional diagnostic testing often takes place only after symptoms manifest—a time when irreversible damage may have already occurred, and meaningful intervention is limited. Limited diagnostics to accurately identify an affected individual, especially in early disease stages, has also contributed to the failure of therapies in clinical trials.⁹

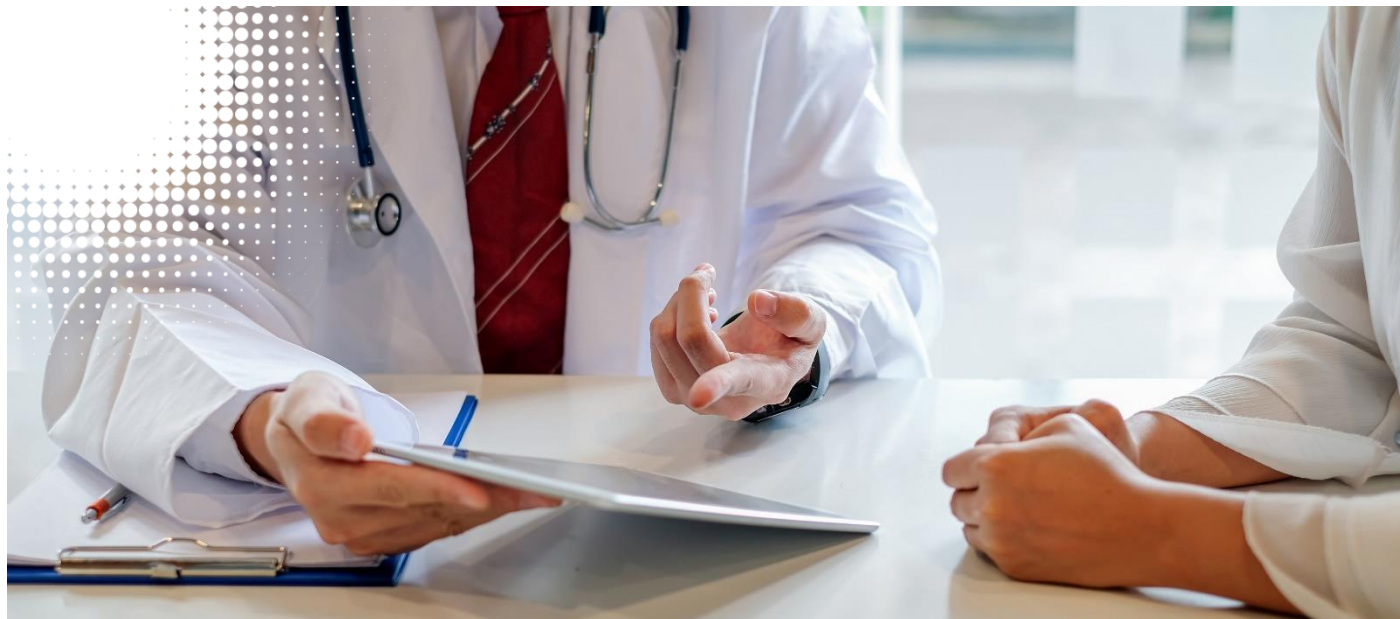
As new therapies come to the fore, and patients seek treatment in early disease stages—the need for scalable, less-invasive diagnostics, including in primary care settings, seems likely to grow. Preparing for this transformational shift now with increased education for both primary care providers and US adults is important in setting up the industry to succeed in this new AD environment.



of physicians say new therapies will transform Alzheimer's disease into a chronic, manageable disease.



Key findings



The Coming Alzheimer's Disease Healthcare Revolution: US Physician and Adult Perspectives on the Future of Diagnostics and Treatment is based on insights from online surveys of 501 primary care providers (PCPs) and 2,052 Americans aged 18 years and older. Quest Diagnostics commissioned the surveys, conducted in March 2022 by The Harris Poll, to glean insights into differing perspectives of PCPs, who are increasingly likely to be on the front lines of AD diagnosis, and ordinary US adults, whose expectations may ultimately shape the use of diagnostics and therapies in the future.

Key findings from the report include:

1

Physicians foresee a coming Alzheimer's disease treatment revolution

2

Physicians predict a blood test for the early detection of Alzheimer's disease risk will transform diagnosis and monitoring and lead to better care

3

Despite fear of a diagnosis, adult Americans want to be evaluated for dementia, including Alzheimer's disease, nearly 10 years earlier than current medical practice

4

Physicians are confident blood tests would enable quicker specialist referrals but fear the healthcare system is not equipped to handle a surge in diagnoses

5

Physicians and US adults both call for more education and guidance as the Alzheimer's disease diagnostic and treatment landscape shifts



Physicians foresee a coming Alzheimer's disease treatment revolution



A majority of physicians (66%) believe that we are on the precipice of groundbreaking new treatment options for AD, and **nearly all physicians (93%) say developments in testing and treatment for AD will help provide better care for their patients.**

Most physicians (84%) say testing will lead to earlier and improved disease management.

While many physicians (50%) believe a cure will remain out of reach, **most (77%) believe new therapies will transform AD into a chronic, manageable disease.**

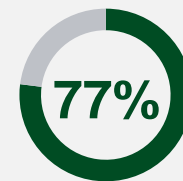
As pharmaceutical companies work to discover new treatment options, the diagnostics industry is also developing the next generation of tests to identify patients at risk for developing AD. Currently, an initial diagnosis of AD relies largely on documenting cognitive decline. In fact, many physicians screen and test for dementia only after their patient has overt signs of cognitive decline:

- PCPs most commonly evaluate and test for dementia, including AD:
 - If their evaluation of the patient's cognitive function causes them concern or worry (90%)
 - When the patient's caregiver expresses worry or concern about their cognitive function (88%)
 - If the patient asks for the testing to be done (78%) (eg, in the event they are experiencing symptoms)
- The primary signs of dementia that prompt physicians to refer patients to neurological specialists are memory loss (91%) and confusion (84%).

Given the invasive and sometimes complicated nature of current diagnostic procedures for AD and other forms of dementia, **it's not surprising that 91% of physicians say that less invasive diagnostic tools are needed to accurately and more easily detect AD risk and monitor disease progression.**



of physicians do not think there will ever be a cure for AD.



believe new therapies will transform AD into a chronic, manageable disease.

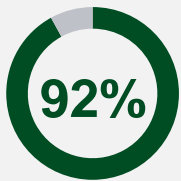
Two in 5 physicians (42%) worry their patients avoid or delay making an appointment to a referred neurological specialist for further evaluation or treatment for AD because of concerns about the cost of further evaluation or treatment for the disease.



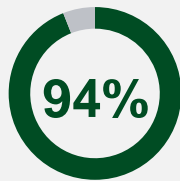
Physicians predict a blood test for the early detection of Alzheimer’s disease risk will transform diagnosis and monitoring—and lead to better care



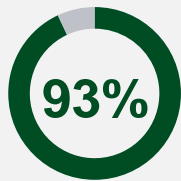
Nearly 9 in 10 physicians (87%) believe that blood tests for the early detection of AD risk will increasingly become the standard of care. Additionally, most physicians (91%) say such tests will revolutionize how physicians diagnose the disease, and 81% say they will revolutionize how AD is monitored over time.



of physicians say they are excited about the potential ability to use blood tests for the early detection of AD risk in their patient population.



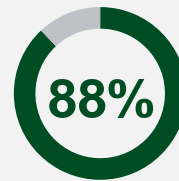
of physicians say blood tests would be more cost effective for the healthcare system compared to more invasive methods of detection (e.g., lumbar puncture).



of physicians say blood tests would help identify potential candidates for treatment.



of physicians see testing for early risk of AD as an overlooked part of the coming AD treatment revolution.



of physicians say blood tests for detection and monitoring of risk of AD paired with telehealth would lead to a new era of managing and monitoring AD.

Critically, early detection of risk:



Advances research and discovery of new treatments.

Identifying appropriate patients for clinical trials is essential for the research¹⁰ and discovery of treatments. Currently, a significant obstacle to AD research is the lack of ability to reliably identify individuals with AD or to identify them before cognitive function has been irreversibly impacted by the disease.

96%

of physicians say blood tests will help identify patients who may be appropriate for clinical trials for AD treatments. Additionally, 85% of physicians say blood tests will improve the quality and speed of clinical trials for AD treatments.



Helps provide an accurate diagnosis. There are several treatable conditions that can mimic dementia, from vitamin B12 deficiency, depression, and thyroid problems to medication side effects and drug withdrawal.

92%

of physicians say blood tests would help them rule out AD so they can better treat conditions that cause dementia-like symptoms.



Aids identification of individuals for pharmaceutical therapies.

In June 2021, the FDA granted accelerated approval for aducanumab, the first treatment designed to target AD pathophysiology. Although access remains limited, a range of drug therapies currently exist to help treat symptoms of AD, such as negative impacts to day-to-day function, agitation, and memory loss.

93%

of physicians say blood tests would help identify potential candidates for treatment.



Empowers preventive measures and participation in clinical trials. Early detection of risk of AD may inspire individuals to make lifestyle changes, such as quitting smoking or exercising more. While the research is unclear, studies show that behavioral changes could reduce risk and even potentially delay disease onset. It may also help spur individuals to investigate options for participating in clinical trials.



Provides added time for planning for the future. An earlier diagnosis of AD or assessment of risk allows patients and their families to plan for the future. Not only does this provide more time for the individual and their caregivers to cope with the diagnosis and symptoms, but it also allows for legal, financial, and end-of-life planning.



Supports equity in care.

Physicians also believe innovations in testing will improve health equity.

76%

of physicians agree that blood tests for the early detection of AD risk will support more equitable care and management of the disease



Reduces economic burden.

According to the Alzheimer's Association, early diagnosis could save costs of medical and long-term care for families and the US government. If all those who would get AD were diagnosed before dementia, it would save roughly \$7 trillion in health and long-term care costs¹¹.

Alzheimer's disease diagnostic innovation

A biomarker is a detectable or measurable indicator of the presence of, or a change in, disease or disease risk. In AD, research has found that the biomarkers beta-amyloid and tau may indicate the early stages of the disease. Currently, physicians assess these biomarkers through CSF and brain imaging, both of which can detect changes in beta-amyloid and tau levels. Blood tests and genetic risk profiles may also employ biomarker testing.



Genetic risk profiling: New research has identified three genes with rare mutations that cause AD as well as several genes that increase risk but don't guarantee a diagnosis. Genetic risk profiling may eventually serve as a valuable risk assessment tool and currently helps advance clinical trials by identifying participants at high risk for AD due to family history.



Blood tests: Blood tests tracking changes in levels of specific biomarkers have been identified as a viable, less invasive means for detecting risk of AD. Additional research suggests that blood tests could detect the early stages of Alzheimer's up to 20 years before the impact is felt by the patient or seen on a PET brain scan or in CSF collected via a lumbar puncture.¹² Blood tests not only support drug development and research but could also allow for a better understanding of disease progression over time.

Quest Diagnostics is at the forefront of innovation to improve the ability of healthcare providers to assess AD and other types of dementia, among other neurological and rare conditions. These services include genetic and immunological tests for dementia, including for AD, frontotemporal dementia, and autoimmune rapidly progressive dementia.

The QUEST AD-Detect™ Amyloid Beta 42/40 Ratio test, launched in early 2022, is a new analytically validated and less invasive blood test that aids in assessing the risk of AD.^{13,14} It evaluates the ratio of two peptides of amyloid beta, Aβ42 and Aβ40, in plasma sourced from a single blood test and is designed to monitor Aβ42/40 changes over time to assess the risk potential of AD progression. QUEST AD-Detect™ is a high-precision assay of a type shown in a study published in December 2021 to be as effective as traditional methods.¹⁵

With a physician's order, patients may supply a blood specimen at a Quest Diagnostics patient service center for testing with QUEST AD-Detect™. Quest Diagnostics operates a national network of 2,100 patient service centers, for convenient patient access. In addition to providing accessible insights into the risk of AD, QUEST AD-Detect™ blood-based biomarker testing may also help identify patients who are candidates for early antibody treatment.¹⁶



The QUEST AD-Detect™ test is the latest example of how Quest is innovating within the AD landscape. Its Athena Diagnostics division was the first company to launch a test to detect Alzheimer's biomarkers using CSF approximately 20 years ago. AD-Detect is based on a CSF test for aiding AD assessment developed by Quest Diagnostics in 2017. Other services include apoE genotype testing to help predict risk of early onset AD, and genetic and antibody tests for frontotemporal dementia and autoimmune rapidly progressive dementia. In addition, Quest has a long-standing history of advancing science in the field of dementia through academic research and other collaborations.

For more information about the QUEST AD-Detect™ blood test, visit: QuestfortheCure.com. For more information about Quest's Neurology portfolio, visit: QuestDiagnostics.com/Neurology.



Despite fear of a diagnosis, adult Americans want to be evaluated for dementia, including Alzheimer's disease, nearly 10 years earlier than current medical practice

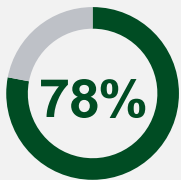


Nearly 9 in 10 adults (86%) have some fear about receiving an AD diagnosis and nearly half (47%) are scared to even be tested. Despite this fear, adults also expressed openness to being evaluated for dementia, including AD. Physicians say they begin evaluating patients for AD at about 66 years of age (mean). Yet, US adults want to be evaluated for dementia, including AD, around age 57 (mean)—a difference of nearly 10 years. Perhaps this willingness reflects optimism; 90% of adults say they are hopeful that new therapies will cure AD, and 89% are hopeful that new therapies will make the disease into a manageable chronic disease.

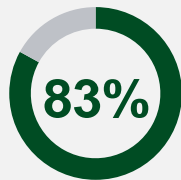
Top Three Fears Surrounding an Alzheimer's Disease Diagnosis:

1. Becoming a burden to loved ones **60%**
2. Loss of independence **58%**
3. No longer being able to enjoy life **51%**

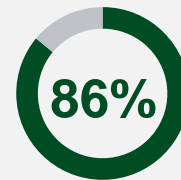
Adults also seem open to incorporating blood tests for AD into their annual wellness visits, not only to assess their own risk, but also to help contribute to ongoing research.



78% of adults would want to incorporate a blood test that detects early risk of AD into their preventative health visits so they can make plans for themselves and their families.



83% of adults say they would agree to take a blood test for the early detection of AD risk if their results might help researchers develop better treatments for the disease.



86% of adults believe blood tests for the early detection of AD risk will increasingly become a regular part of preventative care.



Physicians are confident blood tests would enable quicker specialist referrals but fear the healthcare system is not equipped to handle a surge in diagnoses



Most physicians (87%) agree that the ability to order one blood test that could detect risk for AD would enable them to refer their patients to a neurologist or other specialist more expeditiously.

While 84% of physicians say testing for early risk will lead to earlier and improved disease management, 92% say that blood tests for AD will lead to a surge in diagnoses.



More than half of physicians (60%) say that the current healthcare system/workforce would not be able to handle a surge in AD diagnoses.

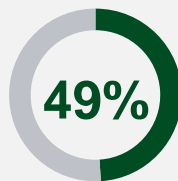
This is particularly troubling, as physicians are already expressing a lack of available resources for patients, spurring fears of missed diagnoses.



52% of physicians say they worry there are not enough neurological specialists for their patients to receive care in a timely manner.



70% of physicians who refer patients to neurological specialists for further treatment or evaluation for dementia including Alzheimer's have had patients face delays in getting an appointment in the past 12 months.

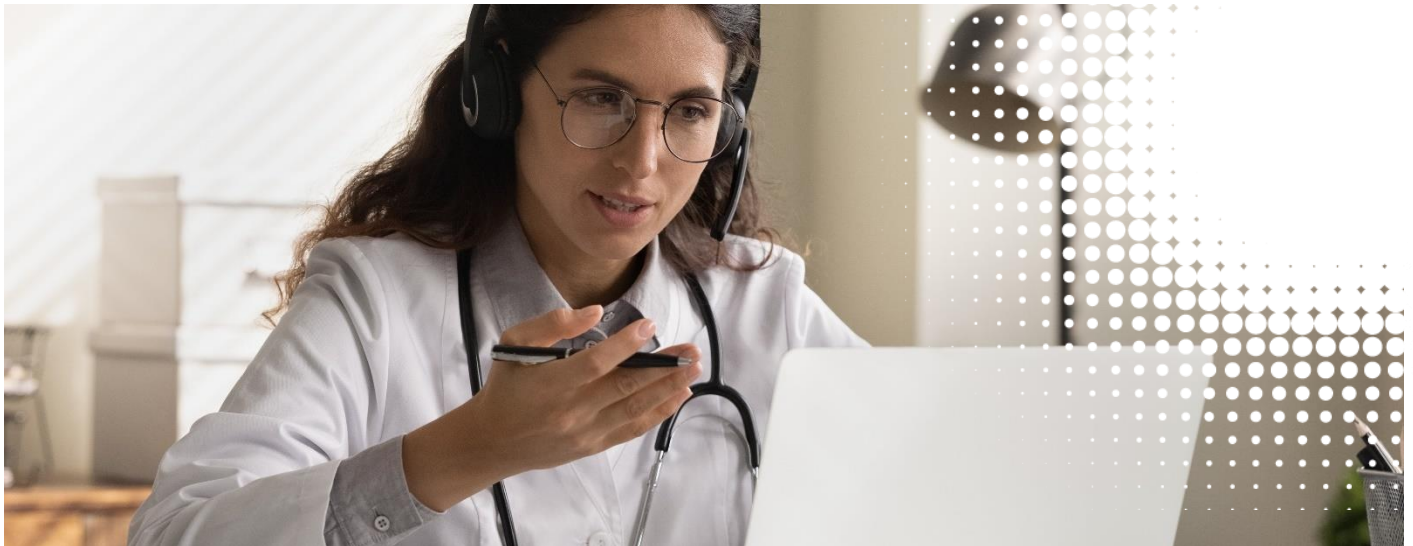


49% of physicians say that when patients face delays in getting an appointment with a neurological specialist, the patient's caregiver took on most of the care burden.

Physicians believe nearly 1 in 5 seniors (18%), on average, may be living with undiagnosed AD.



Physicians and US adults call for more education and guidance as the Alzheimer’s disease diagnostic and treatment landscape shifts



The vast majority of physicians (95%) agree that the value of a blood test for the early risk of Alzheimer’s disease depends on the quality of education around it.

Roughly two in three physicians (66%) say educational resources about the science behind blood tests would be very or extremely useful to their care for patients, in addition to:

Best practices on when and how to use such a blood test



How to use such a blood test in conjunction with other AD diagnostics



How to interpret results of such a blood test, including what it means if the test doesn’t show early risk of AD but there are still concerns about a patient’s cognitive function



How to counsel and support patients and patients’ caregivers around the results of such a blood test



How to counsel their patients or patients’ caregivers on the need for such a blood test



Additionally, with widespread interest among adults to incorporate the tests into their preventive health visits, physicians indicate they'd only be comfortable doing so when guidelines for how and when to use blood tests as well as reimbursement conditions were in place.



85% of physicians believe the value of a blood test for the detection of early risk of AD will depend on how widely reimbursed it is.



Nearly 1 in 4 physicians (24%) say they would not incorporate such a test into their preventive health visits for patients unless there were specific guidelines telling them when and under what circumstances to do so.



More than 8 in 10 US adults (83%) want more education about when they should be proactively evaluated for signs of AD and other forms of dementia.

Conclusion

Physicians and adult Americans are optimistic about advances in Alzheimer's disease treatment and diagnostics and open to employing blood tests to aid in the early detection of risk for the disease, including as part of preventive care.

But it's clear both groups need more education and resources. For physicians, top-of-mind resources include best practices for when and how to suggest and use AD diagnostics, how to interpret results, and how to counsel and support patients and their caregivers following such results.

For patients, more education about when they should be proactively evaluated for signs of AD and other forms of dementia is a priority. For those who receive a test showing an early risk factor for developing AD or indicating potential AD or another type of dementia, resources outlining how to join clinical trials may be useful.

The healthcare community may also need to prepare for how new therapies and diagnostics may alter care delivery, with primary care physicians playing a larger role in screening and caring for patients with dementia, including AD.

For more information on AD and other types of dementia, visit alz.org. For more information about clinical trials in Alzheimer's and dementia, visit www.alzheimers.gov/clinical-trials.



Methodology

On behalf of Quest Diagnostics, The Harris Poll conducted two online surveys in March 2022: one among 501 US duly licensed primary care providers (PCPs) with a patient load of two or more, and another among 2,052 Americans aged 18 and older. Data for the PCP survey were weighted where necessary by age, gender and specialty to bring them in line with their actual proportions in the population. Data for the general population survey were weighted where necessary by age, gender, race/ethnicity, region, education, marital status, household size, household income, and propensity to be online, to bring them in line with their actual proportions in the population. For more information, contact Kim Gorode, kimberly.B.Gorode@questdiagnostics.com or Ellen Murphy, Ellen.Murphy@syneoshealth.com.

About Quest Diagnostics

Quest Diagnostics empowers people to take action to improve health outcomes. Derived from the world's largest database of clinical lab results, our diagnostic insights reveal new avenues to identify and treat disease, inspire healthy behaviors, and improve health care management. Quest annually serves 1 in 3 three adult Americans and half the physicians and hospitals in the United States, and our nearly 50,000 employees understand that, in the right hands and with the right context, our diagnostic insights can inspire actions that transform lives. Learn more at www.QuestDiagnostics.com.

¹ The Promise the Alzheimer Disease Pipeline Holds Heading into 2020 | <https://www.neurologylive.com/view/promise-alzheimer-disease-pipeline-holds-2022>. Accessed April 11, 2022.

² FDA Grants Accelerated Approval for Alzheimer's Drug | <https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug>. Accessed June 2021.

³ 2021 Alzheimer's Clinical Trials Report | <https://www.alzdiscovery.org/uploads/media/ADDF-CTR-2021-06-singles.pdf>. Accessed April 10, 2022.

⁴ Alzheimer's Association. 2021 Alzheimer's disease facts and figures | <https://www.alz.org/media/Documents/alzheimersfacts-and-figures.pdf>. Accessed December 7, 2021.

⁵ What is Alzheimer's Disease? | <https://www.alzheimers.gov/alzheimers-dementias/alzheimers-disease>. Accessed April 11, 2022.

⁶ Alzheimer's Disease Facts and Figures | <https://www.alz.org/alzheimers-dementia/facts-figures#:~:text=years%20of%20diagnosis,-,Prevalence,living%20with%20Alzheimer's%20in%202022>. Accessed April 11, 2022.

⁷ Special Report: More Than Normal Aging: Understanding Mild Cognitive Impairment | <https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf>. Accessed April 11, 2022.

⁸ Medical Tests for Diagnosing Alzheimer's & Dementia | https://www.alz.org/alzheimers-dementia/diagnosis/medical_tests. Accessed April 11, 2022.

⁹ Due to Complex Barriers, the Overwhelming Majority of Alzheimer's Patients Do Not Participate in Clinical Trials | <https://healthpolicy.usc.edu/article/due-to-complex-barriers-the-overwhelming-majority-of-alzheimers-patients-do-not-participate-in-clinical-trials/>. Accessed April 9, 2022.

¹⁰ Alzheimer's Association Trial Match | https://www.alz.org/images/northcentraltexas/clinical_trials.pdf. Accessed April 13, 2022.

¹¹ Alzheimer's Association Why Get Checked | <https://www.alz.org/alzheimers-dementia/diagnosis/why-get-checked>. Accessed April 13, 2022.

¹² Blood Test Can Identify Alzheimer's 2 Decades before Symptoms | <https://www.medicalnewstoday.com/articles/326001>. Accessed April 11, 2022.

¹³ Data on file. Quest Diagnostics; 2022.

¹⁴ Burnham SC, Fandos N, Fowler C, et al. Longitudinal evaluation of the natural history of amyloid- β in plasma and brain. *Brain Commun.* 2020;2(1)fcaa041. doi:10.1093/braincomms/fcaa041

¹⁵ Li Y, Schindler SE, Bollinger, J, et al. Validation of plasma amyloid- β 42/40 for detecting alzheimer disease amyloid plaques. *Neurology*. Online ahead of print, December 14, 2021. doi:10.1212/WNL.00000000000013211

¹⁶ Cummings J, Lee G, Zhong K, et al. Alzheimer's disease drug development pipeline: 2021. *Alzheimers Dement (N Y)*. 2021;7(1): e12179. doi:10.1002/trc2.12179

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