

Alzheimer's Tests: Pros and Cons of the 6 Main Tests for Alzheimer's

By Paula Spencer Scott, Caring.com senior editor



First, the bad news: No single test can tell with certainty if someone has Alzheimer's disease. If that surprises you, you're not alone. Almost half of adults surveyed in five countries believed a reliable Alzheimer's test exists, according to a 2011 survey by the Harvard School of Public Health and Alzheimer's Europe.



Now the good news: Exciting research developments mean an Alzheimer's diagnostic test *is* nearer than ever. That's because probable signs of the disease now can be found in the brain and bloodstream up to ten years before symptoms become apparent (during what's called the "preclinical" stage of Alzheimer's disease). These new "biomarker" tests will be most helpful for identifying likely early cases and for helping to develop preventions and treatments.

For those concerned about current symptoms of dementia, however, doctors must rely on a clinical assessment. A clinical assessment to diagnose Alzheimer's dementia usually involves several kinds of testing. That's because, for now, diagnosing Alzheimer's is still largely a process of elimination.

Tests can check for causes of dementia that aren't Alzheimer's, help identify other problems that can affect the brain, and monitor cognitive changes over time.

"It's not always high tech, but it is in fact how we make the diagnosis," says neuroscientist and physician Paul Aisen, director of the Alzheimer's Disease Cooperative Study, a consortium of 80 academic institutions conducting Alzheimer's clinical trials.

Here are the six main options:

1. Brief cognitive screening tests

Also called: Mental status testing, office-based cognitive assessment

What they do: Brief cognitive tests check for the presence of problematic thinking skills that might indicate mild cognitive impairment or a dementia such as Alzheimer's.

The Mini-Mental Status Exam (MMSE) is the best-known cognitive functional status exam. An alphabet soup of similar tests also often used includes the Modified Mini-Mental State Exam (MMMSE), the Mini-Cog exam, the Montreal Cognitive Assessment (MoCA), the St. Louis Mental Status Exam (SLUMS), Addenbrooke's Cognitive Examination-Revised (ACE-R), the Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI), the Blessed Orientation-Concentration-Memory Test (BCOM), the Cognitive Function Test, the 7-Minute Screen, and others.

Pros: Brief cognitive tests can be completed in 5 to 15 minutes (depending on the test) in almost any setting. They can help flag possible Alzheimer's cases that may warrant further examination. They're also used to track changes in cognitive function over time in people with dementia.

Cons: These are preliminary tests; brief cognitive screenings can't diagnose Alzheimer's disease. An abnormal result can have many explanations other than Alzheimer's. They can also miss cognitive impairment in those who are highly educated or very intelligent. Nor can cognitive screens paint a detailed view of which functions (language, reasoning, etc.) are most affected.

Where to get tested: Most primary care physicians, geriatric social workers, and memory clinics can administer the test. Some cognitive screens can be administered by a layperson at home.

Cost: These are nominal or free, other than the cost of a memory workup or medical checkup.

2. Neuropsychological tests

What they do: Neuropsychological testing, a combination of interviews plus written and oral exams, provides a detailed picture of cognitive strengths and weaknesses. Thinking skills that are explored include memory, language, visual-spatial perception, attention, motor function, and executive function.

Clinicians may use multiple tests and interpret their collective data. Neuropsychological tests used for Alzheimer's include the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), the Cambridge Neuropsychological Test Automated Battery (CANTAB), the Neuropsychiatric Inventory (NPI), and many others.

Pros: Neuropsychological testing is especially useful for identifying very early or subtle cognitive changes. It also identifies in detail what areas of mental functioning are affected, which can help distinguish Alzheimer's disease from other forms of dementia. This information can help tailor individualized therapies.

Cons: Testing can take two to eight hours and is usually done separately from a standard neurological or medical exam. It can be tiring and stressful for the person being tested.

Where to get tested: Testing requires a referral to a specialist (clinical psychologist or psychiatrist) who's trained to interpret results. Memory clinics often have neuropsychologists on site.

Cost: The costs vary; they can run from \$500 to \$5,000 (usually the cost of the test plus an hourly clinician fee); some testing is usually covered by Medicare and may be covered by other insurance.

3. Brain imaging tests - What they do: CT scans and MRI (magnetic resonance imaging) look inside the brain at structural changes. PET (positron emission tomography) scans can show metabolic changes. (A new type of PET scan for Alzheimer's exists but isn't widely available; see below.)

Pros: The main purpose of imaging tests is to find other causes of memory problems and other dementia symptoms (such as brain trauma, tumor, or stroke). PET scans can help distinguish Alzheimer's from frontotemporal dementia.

Cons: Brain imaging may require the use of intravenous "tracing" agents, which can cause side effects in some patients. MRI scanners can feel claustrophobic and may not be compatible with pacemakers or other devices.

Where to get tested: CT and MRI scans can be done at a major hospital or brain imaging center, by referral. PET scans are less widely available. (Search online or ask your doctor).

Cost: It costs about \$1,500 to \$3,000 for MRI; \$3,000 to \$6,000 or more for PET scans. These may be covered by Medicare or private insurance. Tests are free to research subjects.

Occasionally done tests for Alzheimer's

4. Genetic tests

What they do: Genetic tests for Alzheimer's disease analyze an individual's DNA for several gene variants known to be associated with an elevated risk of developing the disease. Genetic tests aren't usually part of the basic workup when someone reports memory-related symptoms.

Single-gene mutations on three particular chromosomes can identify those at risk of an inherited form of early onset Alzheimer's (the kind that develops before age 60). Genetic tests also look for which of three variations of the apolipoprotein E gene (APOE) the subject has. Just over a quarter of the population has the APOE-4 variant, which is linked to a slightly higher rate of developing late-onset Alzheimer's.

Pros: The main beneficiaries of genetic testing are those who have a family history of early onset Alzheimer's (only about 1 percent of all cases). Having one of the three known mutations is considered highly predictive of developing Alzheimer's.

Testing of the APOE gene is generally considered beneficial only for sorting research subjects.

Cons: The tests have limited individual value for the near-99 percent of Alzheimer's cases that are late-onset (the kind that develop after age 60). Having the APOE-4 gene variation indicates a somewhat increased risk of developing Alzheimer's but doesn't mean that you'll definitely get the disease. The APOE-4 gene variation accounts for only about a third of the factors that seem to influence who gets Alzheimer's. Also, many people who don't have the APOE-4 variation still develop Alzheimer's.

Where to get tested: Doctors can refer you to a geneticist (specialist in genetics and genetic counseling). Or you may try to enroll in a genetic research study through the National Cell Repository for Alzheimer's Disease. Direct-to-consumer genetic testing companies found online, such as 23andme and Navigenics, analyze DNA for the APOE-4 gene.

Cost: These cost about \$150, plus genetic counseling fees; they're free to research subjects. Personal DNA analysis online can cost \$200 to \$400 or more.

Newer Alzheimer's tests not yet widely available

5. Spinal fluid tests

What they do: Cerebrospinal fluid is extracted via spinal tap and analyzed for "signature" amounts of biomarkers known to be present in the brains of people with Alzheimer's, including two proteins: amyloid beta, which forms plaques in the brain, and tau, which accumulates in dying brain cells to form so-called tangles.

Pros: Spinal tests can identify which subjects *don't* have Alzheimer's or preclinical signs of it, when biomarkers aren't seen. The presence of a biomarker called amyloid precursor protein (APPB) in people with mild cognitive impairment seems to predict with 80 to 90 percent accuracy who will go on to develop Alzheimer's, although research is ongoing.

Cons: A lumbar puncture is an invasive test that must be done by an experienced specialist, and the procedure can be uncomfortable. There's a small risk of complications such as infection, bleeding, and pain. Many laboratories may not be equipped to run this new and specialized test. Patients haven't been followed long enough to fully understand what the presence of biomarkers means.

Where to get tested: A specialty memory center run by neurologists is best, since neurologists routinely perform lumbar punctures -- and those working at a memory clinic will know how to interpret results. You may need to be a participant in a clinical trial to get tested.

Cost: Expect to pay \$200 to \$800 for the procedure, plus the cost of related prep tests and a professional fee. These tests are free to research subjects.

6. PET scans for amyloid

What they do: A new type of PET scan is now being used by researchers to try to detect a substance called amyloid, which appears in all Alzheimer's patients' brains.

Pros: PET scans can now help rule out Alzheimer's disease (when no amyloid deposits are seen). Eventually PET scans may be able to accurately identify Alzheimer's at an early stage of disease -- years before any memory problems become apparent. Testing may also be useful in determining which patients with mild cognitive impairment are likely to progress to Alzheimer's disease.

Cons: Brain imaging studies to detect amyloid are currently only being used for research purposes; they aren't yet approved to diagnose and treat patients. Brain imaging is also expensive and unlikely to be used as a widely available test unless treatment becomes available to delay the onset of the disease in people with preclinical Alzheimer's.

Where to get tested: For now, you have to be part of a clinical trial using PET scans to study amyloid.

Cost: This test is free to research subjects.

Future tests for Alzheimer's

Future tests for Alzheimer's aim to identify the disease before symptoms develop (although their value is limited until researchers also identify how to stop or reverse the course of the disease, which can't yet be done). Blood tests, for example, may be able to find biomarkers such as amyloid even in people with no signs of memory loss or other problems. Another kind of blood test in development looks for antibodies used to fight

Alzheimer's. Yet another noninvasive test involves photographing blood vessels in the retina of the eye to look for telltale damage.

For now, a definitive diagnosis of Alzheimer's can only be made by examining brain tissue after death. Doctors use the currently available tests to rule out other explanations, after which they can assign a "probable Alzheimer's" diagnosis.

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