The new definition of Alzheimer's disease

A Healthy Skepticism case study in three faults: probability reversal, arbitrary categories and the syndrome trap

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The claim

The news reports that a blood test can now detect Alzheimer's disease and that the disease can be diagnosed before any symptoms appear. In 2024 a workgroup convened by the Alzheimer's Association redefined Alzheimer's disease as a biological process, present whenever one biomarker is abnormal, whether or not the person has symptoms [10]. Since May 2025 the FDA has cleared four blood tests for that biomarker [6, 15]. Patients are asking their doctors for the test [8, 15], some with no symptoms at all.

A real claim rarely comes one fault at a time, and this one carries three: the test's accuracy is read in the wrong direction, a line through a continuous measurement turns a risk into a disease, and a single protein now names a condition that, at autopsy, usually has several causes. A healthy skeptic asks what a positive result means for someone like her, where the line sits and who drew it, and what two people with the same label actually share. This paper answers those three questions, then says what the new tests do well.

What the new criteria say

The 2024 criteria define Alzheimer's disease as a process that begins when amyloid plaques and tau tangles appear, while the person is still well. One abnormal "Core 1" biomarker is enough for the diagnosis: amyloid on a PET scan, a protein ratio in spinal fluid, or a blood test that agrees with those at least 90% of the time [10]. The clinical stages run from 1, "asymptomatic, biomarker evidence only," to 6, severe dementia. The authors add that the disease can be diagnosed in people without symptoms, but say this should not be done in the clinic yet [10, 11].

The four cleared blood tests measure forms of tau, amyloid, or both. All are cleared only for people who already have symptoms of cognitive decline, not for screening [6, 15]. The Association's 2025 guideline recommends them for patients with symptoms in specialty care, after a full clinical evaluation [14].

An international group of 46 specialists published a dissent in November 2024 that keeps the diagnosis for people with symptoms [5]. It calls a biomarker-positive person with normal cognition "asymptomatic at risk," not a patient, because most such people never become symptomatic [5].

Claim 1. A positive blood test means you have Alzheimer's disease

The fault: probability reversal.

For a healthy 70-year-old man with no symptoms, a positive blood test means a lifetime chance of Alzheimer's dementia of about 14%, with a range from about 7% to 23%. That number is the product of two conditional probabilities, because Alzheimer's dementia without amyloid is ruled out: P(dementia | positive) = P(amyloid | positive) × P(dementia | amyloid) = 14%.

The first factor. The test is sold on P(positive | amyloid), and a patient hears it as P(amyloid | positive), the chance that she has amyloid, but P(amyloid | positive) depends on how many in the group had amyloid to begin with. The first cleared test was checked against 499 people with cognitive impairment, about half of whom had amyloid, and in that group P(amyloid | positive) was 92% [6]. For a healthy 70-year-old, where about 20% have amyloid [12], a test at the guideline's accuracy standard gives about 69% [14].

The second factor. The criteria require amyloid for Alzheimer's dementia [10], so P(amyloid | dementia) is 100%, and that is heard as P(dementia | amyloid). The best estimate of that, from a model built on long-term studies [4], is about 20% over a lifetime for a 70-year-old man with amyloid and nothing else, with a range from about 10% to 34%. Multiply the two factors: 0.69 × 0.20 is about 14%, and the range on the second puts it between about 7% and 23%.

Claim 2. You either have Alzheimer's disease or you don't

The fault: arbitrary categories. **The question the course asks:** how concerned should you be if your systolic blood pressure goes from 119 to 120?

A person one tick above the cut point has Alzheimer's disease under the new definition, a person one tick below does not, and their chances of dementia differ by a little, because amyloid on a scan and tau in blood are amounts that rise with age along a smooth curve and the lifetime risk rises with them. The criteria draw a line through each amount and call one side disease.

The tests themselves admit the problem: the first cleared test uses two cut points and reports results between them as indeterminate, and in its clearance study up to 20% of results fell there [6]. The staging scheme adds more lines: biological stages A to D on the spread of tau, clinical stages 1 to 6, and a stage 2, "transitional decline," that can rest on the person's own report [10].

In December 2025, the maker of the first test recalled specific lots of its calibrators and reagents for falsely elevated ratios, "causing an incorrect classification of a patient as having amyloid pathology associated with Alzheimer's disease" [7]. Patients crossed the line into disease because a reagent lot was faulty, not because anything in their brains changed.

A viewpoint in Neurology called the biological definition a category error, the same one as defining diabetes by a single glucose reading [9]. The cut points are tuned to agree with PET scans, so they separate more amyloid from less, and the error is in reading them as separating the sick from the well.

Claim 3. Alzheimer's disease is amyloid in the brain

The fault: the syndrome trap. **The question the course asks:** if two people have the same diagnosis, what do they actually have in common?

Two people with the new diagnosis share one protein and nothing else. Under the 2024 criteria a 68-year-old with normal memory and a positive blood test has Alzheimer's disease, stage 1A, and an 84-year-old in a nursing home with severe dementia has Alzheimer's disease, stage 6D [10]. Everything a patient means by the word, the lost names and the lost independence, is absent from the first and defines the second.

Most dementia in old age comes from several brain pathologies at once [3]. In two long-running studies, 1,079 older people were tested every year and examined after death for nine kinds of brain pathology [3]. More than 230 different combinations turned up, each in fewer than 6% of people. Alzheimer's pathology accounted for about 50% of the cognitive loss on average, but in a given person anywhere from 22% to 100%.

The dissenting group put it in one line: a biomarker is a marker of a pathology, not a marker of a disease [2, 5]. The criteria's authors acknowledge that clinical and biological stages often do not align and propose a scheme to record the mismatch, but they retain the single-marker definition [10]. The definition is simple because it leaves the illness out, and that is the syndrome trap.

To summarize

For a healthy 70-year-old man, a positive blood test means a lifetime chance of Alzheimer's dementia, P(dementia | positive), of about 14% [4, 12, 14]. For people who already have symptoms, the tests are a major advance: in a Swedish study of 1,213 patients with cognitive complaints, primary care doctors identified Alzheimer's correctly 61% of the time after an exam, cognitive testing, and a CT scan, and the blood test alone was right 91% of the time [13]. The 2025 guideline recommends the tests for those patients after a full evaluation [14].

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