Are Blood-Based Biomarkers Ready to Screen for Alzheimer's? An Evidence Brief

This policymaker brief assesses whether plasma phosphorylated-tau 217 (p-tau217) blood tests are ready to be evaluated as screening tools for Alzheimer's disease in cognitively unimpaired adults, and what that readiness means for the policy question the ASAP Act addresses. This brief holds throughout the distinction between *diagnostic* use — for which the FDA has cleared two tests in symptomatic patients — and *screening* use in the cognitively unimpaired population a Medicare screening coverage program would serve. The screening case rests on a separate, peer-reviewed evidence base, not on the FDA diagnostic clearances.

Key findings

- **On positive predictive value — a key measure of how a screen performs in practice — the Alzheimer's blood test is the strongest in the illustrative comparison made below.** Its PPV for amyloid pathology in cognitively unimpaired adults (45–79%, depending on population and threshold) exceeds mammography (4.4%), low-dose CT (~3.6%), FIT (~5%), an ATHENA cytology-triage figure (~14%), biopsy yield after abnormal PSA screening (~25–30%), and the multi-cancer early-detection test PATHFINDER evaluated (38%), for which Congress created a Medicare pathway in February 2026. These figures are measured at different pathway points, so Section 4 labels each comparator explicitly.
- **The evidence base in cognitively unimpaired adults is now substantial and replicated.** For example, a meta-analysis of 7,834 such individuals found pooled discrimination (AUC) of 0.87, and the result holds across independent populations, multiple manufacturers, and several continents.
- **The ASAP Act creates coverage authority, not a coverage mandate.** It adds FDA-cleared or FDA-approved Alzheimer's and related-dementia early-detection screening tests as a Medicare Part B benefit (for tests furnished on or after January 1, 2028), removing the statutory bar that today blocks Medicare from covering screening for beneficiaries without symptoms. FDA still gates clearance; CMS still applies its ordinary reasonable-and-necessary standard to determine if coverage should be extended and, if so, sets the operational terms.
- **Routine screening involves more than test accuracy.** Real questions remain (Section 6). These are reasons to stage clinical deployment deliberately, not reasons to keep the statutory door closed. They are exactly what the FDA and CMS weigh in their evaluations and preparation for coverage.

1. The right standard: a comparative one

Every screening test Medicare covers was adopted not because it was perfect, but because it reliably identified the people who needed further evaluation. An appropriate way to evaluate the suitability of Alzheimer's blood tests for screening is by comparing their performance to mammography and to lung, colorectal, cervical, prostate, and multi-cancer screening tests. Sections 2 through 4 provide this evaluation; Section 5 describes the confirmatory pathway a positive result triggers.

2. Screening is not diagnosis

Screening tests are not intended to provide a diagnosis, and that is not the appropriate accuracy standard to apply to them. A screen identifies the people who warrant further evaluation; diagnostic evaluation follows for those with a positive screening test result. A lead measure of a screen's performance is **positive predictive value (PPV)** — of those who test positive, the share who actually have the disease. Mammography, one of the most consequential screening programs of the last half-century, operates at a PPV of about 4.4%: roughly 95% of positive screens are not cancer. Screening is judged not by whether every positive result is accurate, but by whether the test improves population health by reliably routing the indicated people to the next step of a more thorough evaluation.

The FDA has cleared two blood tests that identify biomarkers of Amyloid pathology:

- **Fujirebio Lumipulse pTau217/β-amyloid 1-42 plasma ratio** (510(k) K242706, cleared May 16, 2025) — for adults 50+ in a *specialized care setting* with signs and symptoms of cognitive decline; and
- **Roche Elecsys Phospho-Tau (181P) plasma test** (510(k) K252163, cleared October 8, 2025) — for adults 55+ as an aid in the *initial assessment* of cognitive decline (a primary-care, pre-specialist indication).

Both are **diagnostic aids for patients who already have cognitive symptoms** — and the Lumipulse summary states explicitly that the test "is not intended as a screening or stand-alone diagnostic test." Neither clearance covers screening.

Accordingly, the case for *screening* does not rest on these FDA clearances, though these clearances do indicate the verified performance and reliability of these tests in adjacent contexts. Instead, it rests on the body of peer-reviewed evidence in cognitively unimpaired adults summarized in Section 3.

3. The evidence in cognitively unimpaired adults

The central scientific question is whether a blood test can reliably distinguish a cognitively unimpaired person who has Alzheimer's pathology from one who does not. Recent evidence answers this question consistently.

Meta-analyses.

- The largest meta-analysis specific to cognitively unimpaired adults pooled **7,834 individuals across 18 studies** and found that plasma p-tau217 discriminated Alzheimer's pathology with an area under the curve (AUC) of **0.87 (95% CI, 0.85–0.90)**, concluding that "plasma p-tau217 can reliably detect AD pathology in the preclinical stage" (Malek-Ahmadi et al., *JAMA Neurology*, 2026). AUC ranges from 0.5 (pure chance) to 1.0 (perfect discrimination); 0.87 represents strong discrimination.
- An independent meta-analysis of **2,566 cognitively unimpaired Asian adults** found an AUC of **0.88** for p-tau217, rising above 0.92 in combination with Aβ42/40 (Terao & Kodama, *Ageing Research Reviews*, 2026), extending the evidence base to cognitively unimpaired Asian cohorts.

The largest primary study. A 12-cohort diagnostic-accuracy study of **2,916 cognitively unimpaired adults** across the United States, Europe, Australia, and Canada found that plasma p-tau217 identified preclinical Alzheimer's with a PPV as high as **79%**, varying with the threshold chosen and the age of the population (Salvadó et al., *JAMA Neurology*, 2025). The authors described plasma p-tau217, used alone or in a 2-step approach with PET or CSF, as a "cost-effective, scalable, and minimally burdensome strategy for identifying preclinical AD."

Robustness across tests and populations. The finding is not an artifact of a single assay, vendor, or research-grade cohort. A head-to-head comparison of five leading p-tau217 tests found all five detected amyloid pathology with AUCs of **0.91–0.96** in a mixed BioFINDER-2 cohort spanning cognitively unimpaired and impaired participants, with consistent high-performance results reported in the cognitively unimpaired subgroup (Warmenhoven et al., *Brain*, 2025). In cognitively unimpaired adults specifically, a separate immunoassay reached an AUC of **0.91** (Hibar et al., *Alzheimer's & Dementia*, 2026); and in community-dwelling populations, the closest analog to a screening setting, four different assays again showed similar high performance, with AUCs of **0.84–0.90** (Deek et al., *Alzheimer's Research & Therapy*, 2026). Performance holds across the commercial landscape and across the populations closest to a screening setting.

Taken together these results spanning many thousands of cognitively unimpaired adults, plus tens of thousands more across mixed cognitive status, multiple manufacturers, and several continents, find plasma p-tau217 discriminates Alzheimer's pathology with accuracy (AUC) in

the high-0.8s to low-0.9s. This is a substantial and rapidly maturing evidence base rather than simply a preliminary signal.

4. Positive predictive value, compared with other screening programs

The most direct comparison is on the measure that most directly governs a screen's performance — positive predictive value — set against the screens Medicare covers or has newly authorized.

Screening test or comparator metric	**Endpoint**	**PPV / yield**	**What a Positive Triggers**
Mammography screening exam	Breast cancer	4.4% PPV1	Diagnostic mammogram, ultrasound, biopsy
Low-dose CT (LDCT) screen	Lung cancer	~3.6%, derived from NLST false-positive share	Follow-up CT, PET scan, biopsy
FIT (stool test)	Colorectal cancer	~5%	Colonoscopy
ATHENA ASC-US+ cytology triage among HPV-positive women	High-grade cervical precancer (CIN3+)	~14%†	Colposcopy, biopsy
Biopsy after abnormal PSA screening	Prostate cancer	~25–30% biopsy yield	MRI, biopsy
MCED (Galleri, PATHFINDER)	Multiple cancers	38%	Targeted diagnostic workup

Screening test or comparator metric	Endpoint	PPV / yield	What a Positive Triggers
p-tau217 blood test	**Amyloid pathology associated with Alzheimer's disease**	**45–79%**	**Cognitive evaluation, confirmatory testing**

† The cytology figure is not a general Pap-screen PPV; it is the PPV of ASC-US-or-worse cytology used as triage among HPV-positive women in ATHENA. The PSA figure is biopsy yield after abnormal PSA screening, not the PPV of a positive PSA blood test itself. PPV is prevalence-dependent and reflects the population screened, endpoint, threshold, and pathway point in each study; the primary source and exact derivation for each figure are listed in Sources.

On PPV, the Alzheimer's blood test has the **highest value in this comparison** — though the comparison is illustrative: these tests target different endpoints (cancer, precancer, downstream biopsy-confirmed cancer, or, for p-tau217, the biological pathology of Alzheimer's) at different points in the workup. When a mammogram is positive, it is wrong about cancer roughly 95% of the time, yet Medicare rightly covers it because of its overall benefit. When the Alzheimer's blood test is positive, the probability of true amyloid pathology runs from about **50% in lower-prevalence community cohorts to 79% in older, higher-prevalence groups screened at a stringent threshold** (Balogun et al.; Salvadó et al.), and a confirmatory second step lifts it to 91–99% (Section 5).

Medicare has, in effect, already resolved the underlying question many times over, by covering screening tests with a *fraction* of the predictive value robustly confirmed for p-tau217 blood tests. The conclusion this supports is, on the evidence, clear: a test of this strength **warrants the same evidence-based coverage determination every other screen received** rather than being foreclosed by a statutory gap that blocks the question of suitability from being examined.

5. The clinical pathway after a positive screen

A common and reasonable concern about any screen is the false positive. The clinical pathway following a **positive** Alzheimer's blood test would follow the same "screen, confirm, act" logic used throughout medicine. A positive screen triggers a closer look: in the 12-cohort cognitively unimpaired study, a positive blood test followed by a confirmatory CSF test reached a **91%** predictive value, and followed by amyloid PET reached **99%** (Salvadó et al., 2025). Confirmatory testing could include a complementary blood test, CSF or amyloid PET depending on clinical context, access, and coverage terms.

A **negative** screen — the majority of results — reassures with age-dependent confidence: in Salvadó's cohorts, negative predictive value was about **91%** under age 60 and declined with age, reaching about **66%** in participants 80 and older.

> **A note on a commonly misinterpreted figure.** In that same 12-cohort study (Salvadó et al.), the researchers deliberately set the test to a stringent cutoff so it would only rarely flag a person who did not have Alzheimer's pathology. At that setting, the test caught about **46%** of the people who actually did have preclinical disease — it missed the other 54%. This is the result of a deliberate choice, not a limit of the test. For any screening test, the threshold can be set toward either of two priorities: making each positive result more likely to be real (fewer false positives), or catching a larger share of the people who truly have the disease (at the cost of more false positives). The researchers here chose the first, because their goal was to select participants for a clinical trial where a false positive is relatively costly. A population screening program would likely choose the second and accept more false positives in order to miss fewer people who have Alzheimer's pathology. That is the standard screening approach, exemplified by cancer screens such as mammography: a sensitive screen paired with a confirmatory follow-up that clears the extra false positives a more sensitive setting produces. This tradeoff is inherent in how screening tests work; it does not, by itself, mean a test is weak.

6. Other objections to screening

Accuracy is necessary but not sufficient to justify a screening program, and several of the studies cited above say so in the context of the p-tau217 blood test. These studies validate the test's performance while declining to endorse routine screening and instead call for standardized thresholds, external validation, and prospective evaluation first (e.g., Gebril et al., 2026; Terao & Kodama, 2026). The concerns raised are valid, but none justifies withholding the coverage authority the ASAP Act would create.

Concern: There is no approved treatment for preclinical Alzheimer's, and no trial has yet shown that screening itself improves outcomes. Both are true today — and neither is the obstacle it appears. Today's approved anti-amyloid therapies are directed to the earliest *symptomatic* stage: FDA labeling for Leqembi and Kisunla states that treatment should be initiated in patients with mild cognitive impairment or mild dementia stage of disease. Yet fewer than 1 in 10 expected mild cognitive impairment cases are diagnosed in primary care (Liu et al., 2024); a positive screen is what prompts the proactive cognitive monitoring that identifies impairment while treatment may still be relevant. And when a blood biomarker does reach the clinic it sharply improves detection — in primary care, physician accuracy for Alzheimer's rose from 61% to 91% with a biomarker in hand (Palmqvist et al., 2024); that study was in *symptomatic* patients, but it shows the tool's real-world value once deployed. Detection can also

enable action that needs no drug. For instance, a structured lifestyle program improved cognition in cognitively unimpaired older adults at elevated risk (US POINTER; Baker et al., 2025), providing evidence that risk reduction is actionable in this population, though that trial selected participants by lifestyle and cardiometabolic risk rather than biomarker status. Early knowledge can support financial, legal, medical, and care planning while people still have capacity (Alzheimer's Association, *Early Detection and Diagnosis*).

Concern: Disclosing preclinical status could harm patients. Regarding psychological harms, much evidence points the other way. Across the REVEAL trials (genetic risk) and the A4 study (amyloid status), telling cognitively unimpaired adults they carry elevated risk produced only mild, transient distress — with no increase in clinical depression, severe anxiety, or suicidality — when paired with appropriate counseling (Green et al., 2009; Grill et al., 2020); the strongest predictor of distress is pre-existing anxiety, not the result. The discrimination exposure is real and should be addressed in parallel. GINA protects against genetic-information discrimination in health coverage and employment, but it does not reach life, disability, or long-term-care insurance, and Title II applies only to employers with at least 15 employees (NHGRI; EEOC, 2010). The ADA defines disability broadly, and *Bragdon v. Abbott* recognized asymptomatic HIV infection as an ADA disability, but whether those principles would protect an asymptomatic person with only neurodegenerative biomarker evidence remains unsettled (42 U.S.C. § 12102; *Bragdon v. Abbott*; Arias et al., *Neurology*, in press, 2026, manuscript on file). Published Alzheimer's biomarker-disclosure scholarship likewise documents employment, insurance, documentation, and long-term-care discrimination risks and calls for legal and policy safeguards (Arias et al., 2018; Largent et al., 2021; Vaishnav et al., 2024). The right course is to advance those protections alongside coverage, not to withhold people's knowledge of their own health while the law catches up.

Concern: Screening would overdiagnose — labeling people who may never become symptomatic. This is true of nearly every screen Medicare covers: we identify high cholesterol, hypertension, prediabetes, and early prostate cancer in millions who may never suffer the feared event, because the information guides prevention, treatment and care decisions, and planning. Alzheimer's should not be held to a different standard. The result is also graded, not binary. Higher p-tau217 levels carry a higher and earlier risk of progression (Ossenkoppele et al., 2025), so even false positive screen results may well convey actionable information. And, most importantly, Americans overwhelmingly want access to this test: 90% support Medicare covering it, and 91% want their own insurer to (AIM National Voters Survey, 2026). Withholding it on the premise that patients cannot handle knowing their own risk is a paternalism to a level that would be rare elsewhere in medicine.

Concern: Real-world performance and thresholds are not yet standardized. This is important but routine laboratory medicine. Thresholds may need biologically informed adjustment for kidney function, body mass, and anemia (Yun et al., 2026), and assays

harmonize over time, as they did for cholesterol, HbA1c, and PSA. Postmarket oversight matters too. Certain Lumipulse calibrator lots were subject to a 2026 Class II recall for falsely elevated positive or indeterminate results. This is exactly the lot- and assay-level quality control that FDA recall oversight and CLIA/laboratory quality systems are built to identify; CMS coverage terms can also require appropriate follow-up if coverage is extended. These are implementation tasks, not barriers in principle, and a coverage pathway can help create the incentive to finish the standardization work.

Concern: Validation in diverse populations is incomplete. This is a genuine and important gap (Cousins et al., 2025), but deferring coverage leaves the populations that bear the greatest Alzheimer's burden with the least access, widening the disparity the objection means to guard against. The right course is to deploy only under coverage terms that require stratified validation and monitoring, which a coverage pathway can help drive.

Concern: The screening protocol — whom to screen, at what age, how often — is undefined. That is precisely what CMS coverage determinations and clinical guidelines specify once the authority exists, and is the ordinary sequence for every covered screen, not a reason to foreclose the question.

A common thread to several objections: Each concern is important, and several are the ordinary work of deploying any screen. In particular, note the logic of many of these concerns arguably pushes for ASAP as a remedy rather than against it. A coverage pathway can accelerate standardization, population validation, insurance protection, and screening protocols by giving FDA, CMS, researchers, and insurers a concrete pathway to evaluate. Waiting for every question to be answered before acting risks ensuring that none will be because the incentive to address them will never materialize.

Most fundamentally across these objections, not only does the ASAP Act not mandate coverage, it also does not mandate that anyone be screened. What it does is create the authority that lets the FDA, CMS, researchers, and insurers do the work these questions require which is the subject of Section 7.

7. ASAP provides authority, not a mandate

Clinical adoption of blood-based tests in diagnosis is early, and in screening it is earlier still. But this is a typical development cycle that has characterized other screening tests Medicare covers: the science arrives first, clinical practice follows, and guidelines track the accumulating evidence. Caution at this stage reflects sound medicine; it is not an argument against the ASAP Act.

Coverage *authority* and clinical *rollout* operate on different timelines, and that distinction is central to the bill. The ASAP Act does not direct Medicare to cover these tests. Under current

law, Medicare cannot cover a screening test for beneficiaries without symptoms unless the U.S. Preventive Services Task Force recommends it with an A or B grade — a process that typically takes many years — or Congress specifically authorizes coverage. The ASAP Act is that authorization: it adds FDA-cleared or FDA-approved Alzheimer's and related-dementia early-detection screening tests as a Medicare Part B benefit, for tests furnished on or after January 1, 2028, paid under the laboratory fee schedule.

What it does not do is dictate the result. The FDA still determines whether a given test is cleared or approved for a screening use, and CMS still applies its ordinary "reasonable and necessary" standard — the baseline for all discretionary Medicare coverage — and sets the operational terms: which beneficiaries are eligible, how often, and what confirmatory pathway follows a positive result. Congress opens the door; the agencies decide who walks through it, when, and on what terms.

Conclusion

By the standards medicine uses to judge a screening test — whether it identifies the right people, routes them to an appropriate next step, and improves on current practice — the evidence for the Alzheimer's blood test is strong, and it keeps strengthening as reinforcing evidence rapidly accumulates. On positive predictive value it is the strongest screen in the illustrative comparison in Section 4, ahead of the screens Medicare covers today. The evidence is strong enough to justify creating Medicare authority, while FDA and CMS must still evaluate qualifying tests under defined terms, including benefits, harms, thresholds, and implementation.

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