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EDITION 3 · SEPTEMBER 2026



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Dr Sukh Rashpal Sandhu | Subscribe free on LinkedIn

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INTRODUCTION

The HealthTech Herald: September 2026

By Dr Sukh Rashpal Sandhu

Edition 3 of The HealthTech Herald: 5 pieces for September 2026.

Your trusted source for the latest breakthroughs at the intersection of health and technology.

This edition brings together 5 new features written for this edition. New features are marked "Written for this edition".

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Thank you to every reader who subscribes, shares and responds.

Warm regards,
Dr Sukh Rashpal Sandhu
Author, The HealthTech Herald

THE HEALTHTECH HERALD

A Blood Test That Looks a Decade Ahead: Alzheimer's Diagnosis Moves Out of the Memory Clinic

By Dr Sukh Rashpal Sandhu | Written for this edition

Two studies presented in London in July 2026 suggest that a simple blood draw can help family doctors diagnose Alzheimer's disease almost as accurately as specialists, and can estimate the risk of future decline in people who have no symptoms at all. Here is what the research found, what it does not yet prove, and why the questions it raises are as important as the answers.

Why this matters

For most of the past century, a definite diagnosis of Alzheimer's disease could only be made after death, when a pathologist examined brain tissue under a microscope and found the two hallmark proteins of the disease: clumps of amyloid beta between nerve cells, and twisted tangles of a protein called tau inside them. During life, doctors relied on memory tests, interviews with family members and the process of ruling out other causes.

That changed over the past two decades with two powerful tools. Amyloid PET scans can show amyloid deposits in the living brain, and a lumbar puncture (a spinal tap) can measure amyloid and tau in the cerebrospinal fluid that bathes the brain and spinal cord. Both are accurate. Both are also expensive, invasive or hard to access, and largely confined to specialist memory clinics in major cities.

That bottleneck matters more now than it did ten years ago. A new generation of antibody medicines that remove amyloid from the brain has been approved in several countries for people in the early stages of Alzheimer's disease. These treatments are only suitable for people with confirmed amyloid pathology, which means accurate, early, accessible diagnosis has become the gateway to treatment rather than a matter of academic interest.

Blood tests promise to widen that gateway. And at the Alzheimer's Association International Conference (AAIC) 2026, held in London and online in mid July, two studies offered some of the strongest evidence yet about how these tests perform in the real world, and about what they might tell us long before symptoms appear.

Study one: family doctors with a blood test perform like specialists

What the researchers did

The first study, led by neurologist Associate Professor Sebastian Palmqvist of Lund University in Sweden, was presented on 14 July 2026. It asked a deceptively simple question: when doctors in everyday practice receive the result of an Alzheimer's blood test, does it actually change, and improve, what they do?

The interim results included 1,310 patients in Sweden who had either mild cognitive impairment (MCI, a stage of noticeable memory or thinking problems that do not yet interfere seriously with daily life) or dementia. Of these, 927 were assessed by specialists in secondary care and 383 were seen in primary care by general practitioners. In all, 165 physicians took part.

Each patient's blood was analysed using a commercial test called PrecivityAD2, which combines two measurements: the proportion of tau protein that is phosphorylated at a particular site (called p-tau217), and the ratio of two forms of amyloid beta (Aβ42 and Aβ40). The results were sorted into negative, intermediate or positive.

Crucially, doctors recorded their working diagnosis and their care plan before seeing the blood test result, and then again after. The "true" diagnosis was established separately by a consensus of experts using clinical assessment plus either spinal fluid testing or amyloid PET, with the adjudicators blinded to the blood test result.

The patients seen in primary care were also independently assessed by dementia specialists, which allowed a direct, head-to-head comparison of family doctors and specialists looking at the same people.

What they found

The headline numbers are striking:

Group	Accuracy before blood test result	Accuracy after blood test result
Specialists (secondary care, 927 patients)	74%	89%
General practitioners (primary care, 383 patients)	65%	93%

In the head-to-head comparison among primary care patients, specialists were more accurate than general practitioners before the blood test (76% versus 65%). After the result was disclosed, the difference disappeared: 94% for specialists and 93% for general practitioners, a gap that was not statistically meaningful.

The test also changed what doctors did. General practitioners changed their diagnosis for 30% of patients, and clinical management (referrals, further investigations and treatment decisions) changed in 55.9% of primary care cases. Specialists changed their diagnosis in 21.6% of cases and revised management in 49.2%.

Perhaps the most revealing finding was how the two groups used the test differently. General practitioners became much more willing to rule Alzheimer's out after a negative

result: their readiness to make an immediate decision in those cases rose from 12.9% to 25%. But after a positive result, they did not become more willing to make an immediate Alzheimer's diagnosis; they still preferred to refer the patient on. Specialists, by contrast, became far more willing to diagnose Alzheimer's straight away when the result was positive, with the share rising from 1.9% to 55.4%.

Dr Palmqvist described the aim of the work in plain terms. "We wanted to find out whether a simple blood test for Alzheimer's changes how doctors actually diagnose and manage their patients in everyday clinical care," he said.

He also stressed a point that is easy to miss. A negative result rules out Alzheimer's as the likely cause, not every cause. People whose test is negative may still have another neurological condition and may still need specialist assessment.

Why the primary care result is the big one

In most health systems, including Australia's, the general practitioner is the first and often the only doctor a person with early memory concerns will see. If that first consultation can produce an accurate answer about whether Alzheimer's pathology is likely to be present, several things become possible: people who do not have Alzheimer's can be spared long waits and anxious months; people who do have it can be referred quickly; and scarce specialist appointments, PET scans and lumbar punctures can be reserved for the patients who really need them.

The caution shown by the general practitioners in the study, using a positive result as a reason to refer rather than as a final verdict, is arguably exactly the right behaviour at this stage. The Alzheimer's Association said it is preparing a concise decision tool to help primary care clinicians use these tests appropriately, and it has already published clinical practice guidelines for their use in specialist care.

Study two: a blood test that estimates risk years before symptoms

What the researchers did

The second study, presented on 15 July 2026 and published in *JAMA* the day before, took the question in a different direction. Rather than asking whether a blood test can help diagnose people who already have symptoms, it asked whether p-tau217 levels in people with no symptoms can predict who will go on to develop cognitive impairment, and over what time frame.

The lead author was Associate Professor Rachel Buckley of the Mass General Brigham Neuroscience Institute and Harvard Medical School, with neurologist Professor Reisa Sperling as senior author.

The team pooled and harmonised data from six observational cohorts and clinical trial groups in North America, Japan and Australia. According to the published paper, the analysis included 2,684 cognitively unimpaired older adults with a median age of about 70; 63% were women. Enrolment in the contributing cohorts began as early as 2004, and follow-up ran to 2025, with a median of 5.4 years and a maximum of 13.5 years.

The researchers measured p-tau217 in each participant's first available blood sample and then tracked who progressed to mild cognitive impairment, dementia, or two consecutive abnormal scores on the Clinical Dementia Rating scale, a standard measure of everyday functioning.

What they found

There were 478 progression events in the published analysis. Each one standard deviation increase in baseline p-tau217 was associated with a 38% higher hazard of progressing to cognitive impairment (hazard ratio 1.38). That association held even after the researchers accounted for how much amyloid each person had on a PET scan, with the hazard ratio only modestly reduced to 1.32. In other words, the blood test carried information beyond what the brain scan alone provided.

When the researchers translated those statistics into estimated absolute risks, the picture became more concrete:

- In the published paper, the estimated five year risk of progression was 24% for people in the "high" p-tau217 group and 38% for those in the "very high" group.
- In the Alzheimer's Association's conference release, people with very high levels (more than twice the study average) had an estimated 78% likelihood of developing cognitive impairment within ten years, while those with moderately elevated levels had an estimated 15% risk over five years and 45% over ten.

Readers should notice that the conference abstract, the press release and the journal article report slightly different figures and category labels. That is common: conference abstracts are often written months before final analysis, and the press release itself warns that its data may not match the abstract. The published *JAMA* paper is the version of record, and it notes that ten year estimates are constrained by limited long-term data.

Professor Buckley summed up the significance of the work. Her team's findings, she said, "provide some of the clearest evidence yet that elevated p-tau217 levels may help detect dementia risk years earlier."

The cholesterol analogy, and its limits

The Alzheimer's Association drew an analogy that is helpful for general readers. A cholesterol or blood pressure reading is used not only to diagnose disease but to estimate future risk and guide what to do about it. A p-tau217 result in a symptom-free person could, in principle, play a similar role for Alzheimer's.

But the analogy has an important limit. For high cholesterol, we have decades of evidence that lowering it in people without symptoms prevents heart attacks and strokes. For Alzheimer's, we do not yet have proof that treating people before symptoms appear prevents or delays dementia. Prevention trials are under way, and Professor Sperling noted that the information from blood testing "may become more relevant" if those trials show that early treatment works.

Until then, a high p-tau217 result in a healthy person is a probability, not a destiny, and one that cannot yet be acted on with a proven medicine.

What exactly is p-tau217?

Tau is a protein that normally helps stabilise the internal scaffolding of nerve cells. In Alzheimer's disease, tau becomes abnormally modified with chemical tags called phosphate groups. One particular modification, at position 217 on the protein chain, appears to be especially closely linked to the disease process. The resulting molecule is called phosphorylated tau 217, or p-tau217.

Small amounts of p-tau217 leak from the brain into the bloodstream, where modern laboratory techniques can detect them at extremely low concentrations. Interestingly, while p-tau217 is a form of tau, its blood levels track very closely with the amount of amyloid in the brain, which is why it has become such a useful window on both hallmarks of the disease.

The test does not measure memory, and it does not measure dementia. It measures biology. That distinction sits at the centre of a lively scientific and ethical debate about whether Alzheimer's disease should be defined by its biology (the presence of amyloid and tau) or by its symptoms (memory and thinking problems that affect daily life).

How these tests have reached the clinic

The London studies did not appear in a vacuum. In May 2025, the United States Food and Drug Administration (FDA) cleared the first blood test to aid in diagnosing Alzheimer's disease, the Lumipulse G pTau217/β-Amyloid 1-42 Plasma Ratio made by Fujirebio Diagnostics. The FDA's clearance covered adults aged 55 and older with signs and symptoms of cognitive decline, tested in specialised care settings.

In the clinical study supporting that clearance, which used 499 plasma samples, 91.7% of people with positive results had amyloid confirmed by PET or spinal fluid testing, and 97.3% of people with negative results had negative PET or spinal fluid results. Fewer than 20% of patients received an indeterminate result.

The FDA was explicit about the limits. The test is not a screening test and not a stand-alone diagnosis. Results must be interpreted alongside other clinical information. The main risks are false positives, which could lead to an inappropriate diagnosis and unnecessary treatment, and false negatives, which could delay effective care.

The Swedish study adds something the FDA clearance did not: evidence from real consultations, with real doctors, showing how the information changes decisions in practice, including in primary care.

The questions that still need answering

Not all blood tests are equal

There are now many Alzheimer's blood tests on the market or in development, measuring different combinations of proteins with different laboratory methods. They do not all perform to the same standard. As Dr Sheena Aurora of the Alzheimer's Association put it in the conference release, "not all blood-based biomarker tests meet the same standards for accuracy, clear evidence-based guidance is essential."

The Swedish study tested one specific commercial product. Its results cannot automatically be assumed to apply to other tests.

Who was studied, and who was not

Both studies drew on carefully selected groups. The Swedish patients were people already presenting to doctors with cognitive symptoms in a well-resourced European health system. The prognostic study pooled research cohorts and trial participants, people who volunteered for long-term brain research, and its authors note that further validation in unselected populations is needed.

The researchers also cautioned that factors including age, genetics, kidney function, obesity and racial and ethnic background can influence biomarker levels and dementia risk. Kidney function is a particularly practical concern, because many older people have some reduction in kidney function, which can affect the concentration of proteins in the blood.

Intermediate results

Many blood tests produce three categories of result: clearly negative, clearly positive, and an uncertain zone in between. People in that middle zone still need confirmatory testing. How large that group is, and how quickly they can be referred, will shape how much these tests actually reduce pressure on specialist services.

Testing people without symptoms

The prognostic study is about people with no symptoms. At present, the major guidelines and regulatory clearances are for people who already have cognitive concerns. Testing healthy people raises different questions:

- What would a person do with the knowledge that they have a 1 in 3 chance of cognitive impairment within five years, when no preventive treatment has been proven?
- How should such results be communicated, and by whom, with what counselling?
- What are the implications for insurance, employment and family members?

The researchers themselves framed the near-term use mainly in research: identifying at-risk people who could join prevention trials. That is a sensible, cautious position.

What it means for Australians

Australia's dementia burden is large and growing, and many Australians live far from specialist memory clinics or face long waits to see a geriatrician or neurologist. For these reasons, the prospect of an accurate test that a general practitioner can order from a regional surgery is genuinely significant.

The *JAMA* prognostic analysis drew on cohorts that included participants in Australia, a reminder that Australian research groups have been central to the long-term study of Alzheimer's biology.

At the same time, readers should not assume that what is available or recommended in Sweden or the United States is automatically available here, or covered by Medicare.

Access to tests, their approval status, cost and guidance on use differ between countries and can change. Anyone with concerns about memory or thinking, their own or a family member's, should start with their general practitioner, who can assess the many treatable causes of memory problems (such as thyroid disease, vitamin deficiencies, depression, sleep problems and medication side effects) before any question of Alzheimer's testing arises.

Reading the numbers wisely

Health stories about Alzheimer's blood tests often reduce to a single headline figure: "93% accurate" or "78% risk". A few principles help put such numbers in context.

1. **Accuracy depends on who is tested.** A test that is 90% accurate in people with memory symptoms, where Alzheimer's is common, can perform very differently in the general population, where it is much rarer. In low-prevalence settings, even a good test generates a higher proportion of false positives.
2. **Relative and absolute risk are different.** A 38% increase in hazard per standard deviation sounds dramatic, but what matters to an individual is their absolute risk over a defined period, which depends heavily on their starting point.
3. **Estimates have uncertainty.** Ten year risk estimates in the prognostic study were based on fewer people followed for that long, so they are less certain than five year estimates.
4. **A biomarker is not a diagnosis of dementia.** Many people with amyloid in their brains never develop dementia in their lifetimes, often because they die of something else first.

The bigger picture

These two studies point to a future in which the diagnosis of Alzheimer's disease is faster, cheaper, less invasive and more widely available. That future is arriving in stages: first in specialist clinics, then increasingly in primary care, and eventually, perhaps, as a risk assessment for people without symptoms.

Each stage brings genuine benefits and new responsibilities. Faster diagnosis means earlier access to support, planning and, for eligible patients, treatment. But a test is only as useful as the care pathway behind it. If general practitioners can identify likely Alzheimer's in their surgeries, health systems need enough specialists, infusion capacity, MRI scanners for safety monitoring and support services to respond.

In this writer's view, the most encouraging aspect of the Swedish data is not the headline accuracy figure but the way doctors used it. The general practitioners treated a negative result as reassurance and a positive result as a reason for referral, not as a final word. That is what responsible adoption of a powerful new test looks like.

The blood test will not replace the clinician. What it can do, if used well, is give the clinician a far clearer view, far sooner, of what is happening inside the brain.

This article explains research findings for general readers and is not medical advice. Anyone with concerns about memory or thinking should speak to their general practitioner.

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THE HEALTHTECH HERALD

Statins After Seventy: An Australian Trial Finally Answers a Question Millions Have Asked

By Dr Sukh Rashpal Sandhu | Written for this edition

For years, doctors and older patients have faced the same uncertainty: should a healthy person over 70, with no history of heart disease, take a cholesterol-lowering statin? In late August 2026, a decade-long Australian trial of almost 10,000 people gave the clearest answer yet. The answer is a qualified yes for the heart, and a more complicated story for longer, healthier lives.

The question nobody had properly tested

Statins are among the most studied medicines in history. They lower low-density lipoprotein (LDL) cholesterol, the so-called "bad" cholesterol, and in people who have already had a heart attack or stroke, or who are at high risk, they reduce the chance of further events. Tens of millions of people take them worldwide.

Yet one group has been conspicuously underrepresented in the big statin trials: older people without known cardiovascular disease. Most landmark trials either excluded people over a certain age or enrolled too few of them to draw reliable conclusions for that group specifically. As the European Society of Cardiology (ESC) noted when the new results were released, the balance of benefits and risks for older people without cardiovascular disease, diabetes or dementia had remained uncertain.

That uncertainty matters enormously. Older adults are the age group most likely to have heart attacks and strokes. They are also the group most likely to be taking multiple medicines, most vulnerable to side effects, and most concerned with something beyond simply living longer: staying independent, mentally sharp and physically capable.

In practice, this meant that a 75 year old with no heart problems who asked their doctor "Should I be on a statin?" was often met with a judgement call, informed by evidence from younger people and by extrapolation, rather than by direct trial evidence.

STAREE was designed to fill that gap.

How statins work, in brief

Cholesterol is not simply a villain. The body needs it to build cell membranes and make hormones. Most of the cholesterol in the blood is made by the liver rather than eaten in food. Problems arise when too much LDL cholesterol circulates for too long, because LDL particles can lodge in the walls of arteries, where they contribute to fatty, inflamed

deposits called plaques. Over decades, plaques narrow arteries, and if one ruptures, a blood clot can form on top of it and block blood flow, causing a heart attack or an ischaemic stroke.

Statins work by blocking an enzyme in the liver, called HMG-CoA reductase, that is a key step in making cholesterol. When the liver makes less cholesterol, it responds by pulling more LDL out of the bloodstream. The result is lower LDL levels in the blood and, over time, a lower risk of plaque-related events.

Atorvastatin, the statin tested in STAREE, has been widely prescribed for decades and is now available as an inexpensive generic medicine in Australia and many other countries. The 40 mg dose used in the trial is commonly prescribed in everyday practice.

A key question for older people has always been whether that well-established mechanism translates into the same benefit later in life, when arteries have already been shaped by seven decades of living, and when other health problems compete for attention.

What STAREE is

STAREE stands for STAtins for Reducing Events in the Elderly. It was led by Professor Sophia Zoungas of the School of Public Health and Preventive Medicine at Monash University in Melbourne. According to its registration on ClinicalTrials.gov, the trial began in July 2015, with Monash University as lead sponsor and the National Health and Medical Research Council (NHMRC) and the National Heart Foundation of Australia as collaborators.

The results were presented in a Hot Line session at ESC Congress 2026 in Munich on 29 August 2026 and published simultaneously in the *New England Journal of Medicine* (NEJM), one of the world's most influential medical journals.

The design

STAREE was a double-blind, randomised, placebo-controlled trial, the gold standard for testing whether a treatment works.

- **Who took part:** 9,971 people aged 70 and over, recruited through Australian general practice. None had a history of clinical cardiovascular disease, diabetes or dementia.
- **Age and sex:** The average age was 74.7 years, and 52% were women.
- **Treatment:** Participants were randomly assigned, in equal numbers, to take either atorvastatin 40 mg daily (a dose classed as high intensity in major guidelines) or an identical-looking placebo.
- **Blinding:** Neither the participants nor the researchers assessing them knew who was taking which.
- **Follow-up:** The median follow-up was 5.9 years.

Recruiting through general practice was a deliberate and important choice. It means the participants looked more like the older Australians who actually sit in GP waiting rooms than the highly selected volunteers recruited through hospital clinics in many trials.

Two questions, not one

STAREE had two co-primary endpoints, and understanding both is the key to understanding the result.

1. **Major cardiovascular events:** a combination of death from cardiovascular causes, nonfatal heart attack, stroke, or coronary revascularisation (procedures such as stents or bypass surgery to restore blood flow to the heart).
2. **Disability-free survival:** remaining alive and free of both dementia and persistent physical disability.

The first question asks whether a statin protects the heart and brain circulation. The second asks a broader question that matters deeply to older people: does it help them live longer, independently and with their minds intact?

What the trial found

The heart: a clear benefit

Over the follow-up period, major cardiovascular events occurred in 6.0% of people taking atorvastatin and 8.3% of people taking placebo. That corresponds to a hazard ratio of 0.70, meaning a 30% relative reduction in risk. The 95% confidence interval ran from 0.61 to 0.82, and the result was highly statistically significant.

In plain language: among healthy older Australians, a daily statin reduced the chance of a heart attack, stroke, cardiovascular death or need for a heart procedure by roughly 30%.

It is worth translating that into absolute numbers, because a relative reduction of 30% can sound larger or smaller than it really is depending on the starting risk. The difference between 8.3% and 6.0% is 2.3 percentage points over roughly six years. As a rough illustration (this is a simple calculation from the published percentages, not a figure reported by the investigators), that means about one major cardiovascular event avoided for every 43 or 44 people treated for that period.

For a preventive medicine taken by people without symptoms, that is a meaningful benefit.

Disability-free survival: no significant difference

The second co-primary outcome told a different story. Death, dementia or persistent physical disability occurred in 12.8% of the atorvastatin group and 13.6% of the placebo group. The hazard ratio was 0.94, with a 95% confidence interval from 0.84 to 1.05, and a p-value of 0.25. That is not statistically significant.

In other words, the trial could not show that statins helped older people live longer free of dementia and disability.

According to the American College of Cardiology's summary of the presentation, around 80% of deaths in the trial were from non-cardiovascular causes. That offers one plausible explanation: in this age group, cancer, infections, falls, frailty and other conditions account for much of what determines whether someone remains alive and independent. A

medicine that reduces cardiovascular events will only move the dial on disability-free survival if cardiovascular events are a large share of what threatens it.

Safety

Statins have a long and sometimes contentious reputation when it comes to side effects, so the safety data were watched closely.

- Muscle-related, liver-related and diabetes-related adverse events were more frequent in the atorvastatin group.
- Serious adverse events, however, were uncommon and occurred in exactly the same proportion in both groups: 2.7%.

The published conference summaries did not give separate percentages for each type of non-serious side effect, so readers should look to the full NEJM paper for precise figures. The headline message is that side effects were more common with the statin, but serious harms were not.

What the lead researcher said

Professor Zoungas placed the result in an Australian context. "An estimated 21,000 older Australians suffer from major cardiovascular events, like heart attack and stroke, each year," she said in the ESC's release.

She described STAREE as the first large randomised trial to address this question in this population, and she was direct about what she hopes will happen next. "We hope to see updated guidelines to help clinicians make use of these new findings," she said.

How to read this result fairly

STAREE can be described in two very different ways, both technically accurate:

- "Statins cut heart attacks and strokes by 30% in healthy older people."
- "Statins fail to help older people live longer without disability or dementia."

Neither headline tells the whole story. The fair reading is this: STAREE provides strong evidence that atorvastatin prevents cardiovascular events in healthy people over 70, at the cost of more frequent but mostly non-serious side effects. It does not show that this translates into longer life free of dementia and disability over about six years.

Why the two results do not contradict each other

It might seem puzzling that a medicine can prevent heart attacks and strokes without improving disability-free survival. After all, strokes are a major cause of disability and dementia.

Several factors could explain it:

1. **Competing risks.** In people in their 70s and 80s, many different conditions compete to cause death or disability. Preventing one cause does not prevent the others.
2. **Time.** The median follow-up was just under six years. Some benefits of preventing cardiovascular events, such as reduced vascular contributions to dementia, may take longer to appear.

3. **Statistical power.** The disability-free survival result trended in the direction of benefit (12.8% versus 13.6%), but the difference was small and the confidence interval included no effect. The trial may not have been large or long enough to detect a modest difference in this broader outcome.
4. **Side effects.** If muscle-related side effects affected some participants' activity levels, that might offset benefits in physical function, although the trial's overall serious adverse event rate was identical between groups.

Each of these is a hypothesis, not a finding. The full publication and future analyses will help clarify which, if any, apply.

Muscle aches: what blinded trials tell us

Muscle symptoms are the most commonly reported reason people give for stopping statins. STAREE found that muscle-related adverse events were more frequent with atorvastatin, which is consistent with earlier evidence.

The broader research picture is helpful here. In 2022, the Cholesterol Treatment Trialists' Collaboration published in *The Lancet* an analysis of individual participant data from large, randomised, double-blind trials of statins, involving more than 120,000 people in its main comparison of statin against placebo. It found that statins caused a small excess of muscle symptoms, mostly in the first year of treatment, but that more than 90% of the muscle symptoms reported by people taking statins were not actually caused by the statin. Many of the same aches occurred at similar rates in people taking a placebo.

This matters for older people in particular, because muscle aches and stiffness are common with age, whatever the cause. A person who develops aches after starting a statin may reasonably wonder whether the medicine is responsible. Sometimes it is. Often, the evidence suggests, it is not. A doctor can help work out which, sometimes by pausing and restarting the medicine, or trying a different dose or statin.

None of this dismisses genuine side effects. Rare but serious muscle problems do occur, and STAREE confirms a higher rate of muscle, liver and diabetes-related events with atorvastatin. But it does suggest that fear of side effects, on its own, should not be the deciding factor without a proper conversation.

A sibling study with a very different answer

STAREE has a famous Australian sibling. Between 2010 and 2017, the ASPREE trial, also led from Monash University and also conducted largely through general practice, tested whether daily low-dose aspirin helped healthy older people. Its results, published in the NEJM in 2018, showed that aspirin did not prolong disability-free survival and increased the risk of major bleeding. That finding changed practice worldwide and led many older people to stop taking aspirin for primary prevention.

The contrast with STAREE is instructive. Aspirin offered no meaningful net benefit and caused harm. Atorvastatin, by contrast, delivered a clear cardiovascular benefit with no increase in serious adverse events. Neither improved disability-free survival, which may say as much about how hard it is to move that outcome with any single medicine as it does about the medicines themselves.

Together, these trials show the value of testing preventive medicines directly in the population that will use them, rather than assuming that what works in a 55 year old will work, or work the same way, in a 75 year old.

What it means for older Australians

Guidelines are likely to be reviewed

STAREE's results will almost certainly feed into future revisions of cardiovascular prevention guidelines, both in Australia and internationally. Professor Zoungas explicitly called for that. Guideline committees will need to weigh the clear cardiovascular benefit against the side effect profile and the absence of a disability-free survival benefit, and decide how strongly to recommend statins for healthy people over 70.

The conversation with your GP may change

Until now, a doctor discussing statins with a healthy 75 year old had to rely largely on extrapolated evidence. STAREE gives that conversation a firmer foundation. A reasonable discussion might cover:

- the person's own cardiovascular risk, based on blood pressure, cholesterol, smoking, kidney function, family history and other factors;
- how much they value reducing their risk of heart attack and stroke specifically;
- their tolerance for possible side effects, such as muscle aches;
- how many other medicines they already take; and
- their own priorities and preferences.

STAREE tested one medicine, atorvastatin, at one dose, 40 mg daily. The results cannot automatically be assumed to apply equally to other statins or doses, although statins share a common mechanism.

Questions worth asking

For healthy older readers wondering what STAREE means for them, a few questions may help structure a conversation with a general practitioner:

1. What is my estimated risk of a heart attack or stroke over the next five years?
2. How much would a statin be likely to reduce that risk, in absolute terms?
3. What side effects should I look out for, and what should I do if I notice them?
4. How would a statin fit with the other medicines I already take?
5. If I start, how will we know whether it suits me, and when would we review it?

Who the results do not cover

STAREE excluded people with existing cardiovascular disease, diabetes or dementia. People who have already had a heart attack or stroke are in a different situation altogether, where the evidence for statins is long established. People with diabetes were also excluded, and different guidance applies to them. Anyone currently taking a statin should not stop or change it based on news reports; any change should be discussed with their doctor.

The bigger lesson: what we choose to measure

STAREE's design reflects a welcome shift in how prevention research in older people is framed. For a long time, cardiovascular trials measured cardiovascular outcomes and little else. But for a person in their late 70s, avoiding a heart attack is only part of the goal. What most people want is to remain themselves: independent, mobile and mentally sharp for as long as possible.

By making disability-free survival a co-primary endpoint, alongside cardiovascular events, the STAREE investigators asked the question that older people themselves care about most. That the answer was not a simple yes is not a failure of the trial. It is precisely the kind of honest, useful evidence that lets patients and doctors make better decisions.

In this writer's view, STAREE is a model of what publicly funded medical research can do. It was led from an Australian university, supported by the NHMRC and the Heart Foundation, run through ordinary general practices, and designed to answer a practical question that pharmaceutical companies had little commercial incentive to address, because atorvastatin has long been available as an inexpensive generic medicine.

The result gives older Australians and their doctors something they have lacked for decades: direct evidence, from people like them, about what a statin can and cannot do.

Key facts at a glance

Feature	Detail
Trial	STAREE (STAtins for Reducing Events in the Elderly)
Lead	Professor Sophia Zoungas, Monash University
Participants	9,971 adults aged 70 and over, no cardiovascular disease, diabetes or dementia
Treatment	Atorvastatin 40 mg daily versus placebo
Median follow-up	5.9 years
Major cardiovascular events	6.0% versus 8.3% (hazard ratio 0.70)
Disability-free survival outcome	12.8% versus 13.6% (hazard ratio 0.94, not significant)
Serious adverse events	2.7% in both groups
Published	*New England Journal of Medicine*, 29 August 2026

This article explains research findings for general readers and is not medical advice. Do not start, stop or change any medicine without speaking to your doctor.

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THE HEALTHTECH HERALD

The Mammogram That Reads the Heart: AI Finds Signs of Cardiovascular Disease in Breast Screening Images

By Dr Sukh Rashpal Sandhu | Written for this edition

Millions of women have a mammogram every year or two to check for breast cancer. Research presented at the European Society of Cardiology Congress in August 2026 suggests that artificial intelligence could also read those same images for signs of heart disease, high blood pressure and stroke. The idea is compelling. The evidence is early. Here is what was found, and what still needs to happen.

A screening opportunity hiding in plain sight

Cardiovascular disease is the leading cause of death in women worldwide. Yet, as the lead researcher noted in the European Society of Cardiology (ESC) announcement of the new research, it is often underdiagnosed and undertreated in women, and women who do seek care often present with more advanced disease.

There are many reasons for this. Heart attack symptoms in women can be less "classic" than the crushing chest pain often associated with men. Women have historically been underrepresented in cardiovascular trials. And many women simply do not have regular contact with cardiovascular health services until a problem arises.

Breast screening is different. In many countries, organised programs invite women in midlife and beyond for regular mammograms, whether or not they have any symptoms. In Australia, BreastScreen Australia actively invites women aged 50 to 74 for a free screening mammogram every two years. In the United States, the American College of Cardiology has noted that about 40 million mammograms are performed each year.

That creates an intriguing possibility. If a routine mammogram already captures images of breast tissue and the blood vessels running through it, could those images carry information about cardiovascular health that we are currently ignoring?

The study presented in Munich

Who did it

The research was led by Dr Viana Copeland of Chaim Sheba Medical Center and Tel Aviv University in Israel. It was presented at ESC Congress 2026 in Munich, in a session on 30

August 2026, under the title "Detecting cardiovascular diseases from mammography using deep learning". The ESC issued a press release about it on 27 August 2026.

The study was funded by the AI Research Center at Sheba Tel Hashomer, ARC (the Center for Digital Innovation in Israel), and a Meirim Prize grant for medical innovation. The ESC release notes that Dr Copeland is an inventor on pending patent applications related to cardiovascular artificial intelligence, a disclosure readers should keep in mind.

What they did

This was a retrospective cohort study, meaning the researchers looked back at existing records rather than recruiting women and following them forward.

- **Data:** 29,921 women who had undergone 97,364 mammography examinations at a single tertiary referral centre between 2011 and 2025.
- **Age:** The median age was 54.
- **Diagnoses:** Cardiovascular diagnoses were drawn from electronic medical records, medication prescriptions, and procedure and imaging findings.
- **Prevalence:** In this population, 16% of women had hypertension (high blood pressure), 2.5% had ischaemic heart disease (narrowing of the heart's arteries, the cause of most heart attacks) and 2.5% had had a stroke.

The team trained a deep learning model, a type of artificial intelligence that learns to recognise patterns in images by being shown many labelled examples, to identify features in mammograms associated with each of these three conditions.

What they found

The researchers measured performance using a statistic called the area under the receiver operating characteristic curve, or AUROC. An AUROC of 0.5 means the model is no better than a coin toss; an AUROC of 1.0 means it separates people with and without the condition perfectly.

Condition	AUROC
Hypertension	0.79
Ischaemic heart disease	0.78
Stroke	0.86

According to the ESC, the results were consistent when the researchers accounted for whether a woman had breast cancer and for her age. The release did not give separate figures for those subgroups.

Reporting in *The ASCO Post* added further detail from the presentation. About 18% of the women in the dataset had breast cancer, the median follow-up was 7.3 years, and the model was a convolutional neural network, a type of deep learning architecture widely used for image analysis. Performance improved slightly when the model used mediolateral oblique views (the angled side views taken in a standard mammogram), with the AUROC rising to 0.80 for hypertension and ischaemic heart disease and 0.88 for stroke.

How a deep learning model learns from images

Deep learning is a branch of artificial intelligence loosely inspired by the way networks of neurons process information. A convolutional neural network, the type described in this study, is built from many layers of mathematical filters. The early layers learn to pick out simple features such as edges, lines and textures. Deeper layers combine those simple features into more complex patterns.

To train such a model, researchers show it a very large number of images, each labelled with the correct answer: in this case, whether the woman in the image had a recorded diagnosis of hypertension, ischaemic heart disease or stroke. The model makes a prediction for each image, compares it with the correct label, and adjusts its internal settings slightly to reduce its error. Repeated many thousands of times, this process gradually tunes the model to recognise whatever patterns best distinguish the groups.

Two features of this process are important for understanding the results.

First, the model learns from correlations in the data, not from medical knowledge. If something in the images happens to be associated with a diagnosis, the model may learn to use it, whether or not it reflects the underlying biology. That is why testing on completely independent data, from different hospitals and machines, is essential.

Second, the model's reasoning is not directly visible. Researchers can use various techniques to highlight which regions of an image most influenced a prediction, but deep learning models do not explain themselves in the way a radiologist can. For a screening tool, that lack of transparency is one of the issues regulators and clinicians weigh.

What an AUROC of 0.8 really means

For a general reader, an AUROC around 0.8 can be hard to interpret. A useful way to think about it is this: if you picked one woman with the condition and one woman without it at random, a model with an AUROC of 0.8 would correctly rank the woman with the condition as higher risk about 80% of the time.

That is genuinely informative. It shows the images contain real signal about cardiovascular health, and that the model has learned to detect it. But it is not, by itself, good enough for a screening test. Two reasons explain why.

The problem of low prevalence

Ischaemic heart disease and stroke each affected only 2.5% of women in this dataset. When a condition is uncommon, even a fairly accurate test will produce many more false alarms than true detections, simply because there are so many more people without the condition to be wrongly flagged. Researchers describe this as low positive predictive value, and it is a well-known challenge for any population screening tool.

The researchers themselves acknowledged this. They said they plan to improve the model's accuracy and to reduce both false positives and false negatives.

Detecting what is already known

The study identified women who already had a recorded diagnosis of these conditions. That is a sensible first step to prove the concept. But the real clinical value of a screening tool lies in finding disease, or high risk, that has not yet been recognised, and in predicting future events. Whether the model can do that has not yet been tested.

What might the AI be seeing?

The ESC release did not specify which image features the model relies on, and deep learning models are often difficult to interpret. But there is a well-established body of research on one visible clue.

Mammograms sometimes show calcium deposits in the walls of the small arteries in the breast, called breast arterial calcification. These are distinct from the tiny calcifications radiologists look for as possible signs of cancer. Radiologists typically do not quantify or report breast arterial calcification, because it is not relevant to cancer detection.

Previous research has linked these calcifications to cardiovascular risk. In March 2025, at the American College of Cardiology's annual scientific session, researchers from Emory University and Mayo Clinic presented an AI model that measured breast arterial calcification in mammograms from more than 56,000 patients. Women with the most severe calcification had a five year event-free survival of 86.4%, compared with 95.3% for those with little or none. The ACC noted that earlier studies had found women with arterial calcium buildup had a 51% higher risk of heart disease and stroke. That tool was not available for clinical use and required external validation.

The Sheba study goes a step further, at least in ambition. Rather than measuring a single predefined feature, it asked a deep learning model to find whatever patterns in the image best predicted each condition. That approach can capture subtler signals but makes it harder to explain what the model is detecting, a known trade-off in medical AI.

Why women's heart health needs new tools

The interest in finding cardiovascular disease through breast screening reflects a long-standing gap. For much of the twentieth century, heart disease was widely regarded as a men's problem, and the research base reflected that assumption. Many of the risk scores and diagnostic pathways still used today were developed largely in men.

Women's cardiovascular risk also changes across life in ways that standard checks may miss. Pregnancy complications such as pre-eclampsia and gestational diabetes, and the hormonal changes of menopause, are increasingly recognised as signals of later cardiovascular risk. Women may also be more likely than men to have forms of heart disease that affect the smallest blood vessels of the heart, which do not always show up on tests designed to find blockages in the large arteries.

Against that background, any reliable way to flag women who might benefit from a closer look at their cardiovascular health deserves serious investigation. The Sheba study is one such attempt. Its value will depend on whether it can be shown to identify women whose risk would otherwise have been overlooked.

The case for "opportunistic screening"

The idea behind this research has a name: opportunistic screening. It means using medical images, tests or encounters that have already happened for one purpose to look for other conditions as well, at little or no extra cost or inconvenience to the patient.

Opportunistic screening is attractive for several reasons:

1. **No extra test.** The woman has already had the mammogram. No additional radiation, appointment or procedure is required.
2. **Scale.** Breast screening programs reach very large numbers of women, including many who rarely see a doctor otherwise.
3. **Equity.** It could reach women who are less likely to have their cardiovascular risk assessed through other routes.
4. **Timing.** Many women begin breast screening at an age when cardiovascular risk is starting to rise, and when preventive action can make a meaningful difference.

The ESC release made exactly this argument: analysing the same images for cardiovascular information could offer a scalable approach without requiring an additional imaging examination.

The case for caution

Associate Professor Elena Arbelo, speaking for the ESC Communication Committee, welcomed the concept but was clear about the work ahead. "The challenge now is to establish accuracy and reliability," she said, adding that the goal was to move from experimentation to clinical implementation.

Several hurdles stand between a promising conference presentation and a tool that could be used in breast screening services.

Validation beyond a single centre

All the data came from one hospital in Israel. AI models trained in one setting frequently perform less well in another, because of differences in scanners, imaging protocols, patient populations and how diagnoses are recorded. Before any clinical use, the model would need to be tested on independent data from other hospitals and countries, ideally prospectively.

Peer review

The ESC release describes a congress presentation. It does not mention publication in a peer-reviewed journal. Conference presentations are an important part of science, but they have not been through the full scrutiny of journal peer review.

What happens after a positive result?

Any screening program must answer a practical question: what happens to a woman who is flagged? She would need to be referred for a cardiovascular assessment, probably through her general practitioner, involving blood pressure checks, blood tests and possibly further investigations. That pathway must exist, be funded and be acceptable to women. A screening flag with no clear next step can create anxiety without benefit.

Consent and expectations

Women attend breast screening to check for breast cancer. If their images were also analysed for cardiovascular risk, they would need to be told, and arguably given a choice. Screening programs would also need to make sure that cardiovascular analysis does not distract from, or delay, the primary purpose of cancer detection.

Regulation

In Australia, software that is intended to diagnose or screen for disease is generally regulated as a medical device by the Therapeutic Goods Administration (TGA). Any such tool would need to meet regulatory requirements for safety and performance before it could be supplied for clinical use here. Similar requirements apply in the United States, Europe and elsewhere.

Five questions to ask about any medical AI headline

Stories about artificial intelligence detecting disease appear almost weekly. A few simple questions can help readers judge how close a given finding is to making a difference in real care.

1. **Was the model tested on data it had never seen, from somewhere else?** Results from a single hospital are a starting point, not an endpoint.
2. **Did it find disease that was already known, or predict disease that was not?** Recognising recorded diagnoses is easier than predicting future events.
3. **How common is the condition in the people who would be tested?** The rarer the condition, the more false alarms even a good test produces.
4. **Has it been peer reviewed, and has it been tested prospectively?** Conference findings and retrospective analyses are early evidence.
5. **What happens to a person who is flagged?** A useful tool needs a clear, available next step.

Applied to this study, the answers are clear: it is promising early-stage research, presented as an initial model, that has not yet passed the tests needed for clinical use.

Where this fits in the wider AI story

This study is part of a broader trend in which AI is being used to extract hidden information from routine medical tests. Researchers have explored AI analysis of eye photographs, electrocardiograms and chest X-rays to estimate cardiovascular risk, age-related changes and other conditions that the tests were not originally designed to detect.

The common thread is the realisation that medical images contain far more information than the human eye routinely extracts. A radiologist reading a mammogram is, rightly, focused on breast cancer. An AI model can be trained to look for many things at once.

That opportunity comes with a responsibility. The more a single image is asked to reveal, the more important it becomes to know how accurate each of those predictions is, how they were validated, and how the results will be used.

What the researchers plan next

According to the ESC release, the Sheba team describes the current model as an initial one. Their stated next steps are to improve its accuracy, to reduce both false positives and false negatives, and to test whether mammograms can reveal other cardiovascular conditions beyond the three examined so far.

Those are sensible priorities. A logical sequence from here would include external validation on images from other hospitals and countries, testing whether the model can predict future cardiovascular events rather than recognise existing diagnoses, and, eventually, prospective studies in which women attending screening are followed to see whether flagging their risk leads to better care and outcomes. Each of those steps takes time, and each could change the picture.

What it means for women now

For now, this research does not change anything about how women should approach breast screening or heart health. The AI model is not available for clinical use, and no screening program currently uses mammograms to assess cardiovascular risk.

What the study does do is underline two messages that hold true regardless:

- **Breast screening matters.** Women in eligible age groups should continue to take up invitations to breast screening.
- **Heart health in women matters.** Cardiovascular disease remains the leading cause of death in women. Regular checks of blood pressure, cholesterol and blood sugar, along with attention to smoking, physical activity, diet and weight, remain the foundations of prevention. In Australia, eligible adults can discuss a heart health check with their general practitioner.

The bigger picture

In this writer's view, the most valuable thing about the Sheba study is not the specific accuracy numbers, which come from what the ESC release describes as an initial model. It is the question it puts on the table: are we using the medical tests we already do as wisely as we could?

Every year, health systems perform enormous numbers of scans, blood tests and recordings. Each is ordered for a specific reason and read for that reason. AI raises the possibility that the same data could support broader preventive care, particularly for groups, such as women and cardiovascular disease, where existing care has gaps.

Turning that possibility into practice will take rigorous validation, careful design of care pathways, honest communication with patients, and regulatory oversight. If those pieces come together, a mammogram might one day help protect not only a woman's breasts, but her heart.

This article explains research findings for general readers and is not medical advice. Speak to your doctor about breast screening and heart health checks.

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THE HEALTHTECH HERALD

Silencing a Toxic Protein: The First Approved Treatment for Alexander Disease

By Dr Sukh Rashpal Sandhu | Written for this edition

On 3 September 2026, the United States Food and Drug Administration approved the first medicine for Alexander disease, an ultra-rare and relentlessly progressive brain disorder. The drug, zilganersen, does not replace a missing gene or add a missing enzyme. Instead, it tells the body to make less of a harmful protein. Its approval is a landmark for a small community of families, and a signal of how far a once-experimental class of genetic medicines has come.

A disease most people have never heard of

Alexander disease is so rare that most doctors will never see a case. The FDA describes it as affecting fewer than 1 in a million people. Other estimates, cited in coverage of the approval, put it at roughly 1 in 1 to 3 million people worldwide.

The condition is named after the New Zealand pathologist W. Stewart Alexander, who described the first case in 1949. For decades it was recognised mainly by what pathologists saw in brain tissue after death: unusual clumps of protein, called Rosenthal fibres, in a particular type of brain cell.

What goes wrong

The brain is made of more than nerve cells. A large share of its cells are support cells called glia. Among the most important are astrocytes, star-shaped cells that help maintain the chemical environment around nerve cells, support the blood-brain barrier, and help keep the brain's insulating white matter healthy.

Astrocytes contain a structural protein called glial fibrillary acidic protein, or GFAP. In Alexander disease, a mutation in the GFAP gene causes the protein to be abnormal. The faulty protein builds up inside astrocytes, forming the toxic aggregates that damage the nervous system over time.

Unlike many genetic diseases, Alexander disease is usually not caused by inheriting two faulty copies of a gene. In most cases, a single altered copy is enough, and many cases arise from a new mutation that neither parent carries. Scientists describe this as a "gain of function" problem: the trouble is not that something is missing, but that something harmful is being made.

How it affects people

Alexander disease can begin in infancy, childhood, adolescence or adulthood, and its features vary with age of onset. According to the FDA and coverage of the approval, complications can include:

- seizures;
- loss of developmental milestones in children;
- difficulty walking and problems with balance;
- muscle weakness; and
- increased pressure inside the brain.

In older children and adults, problems with swallowing, speech and coordination are common. The disease is progressive, meaning it worsens over time. Until September 2026, there was no approved treatment that targeted its cause. Care focused on managing symptoms: medicines for seizures, nutrition support, physiotherapy and other supportive measures.

How the disease is diagnosed

Because Alexander disease is so rare, and because its early features overlap with many other neurological conditions, diagnosis has historically been slow. Today, two tools are central.

The first is magnetic resonance imaging (MRI) of the brain. In many forms of Alexander disease, MRI shows characteristic patterns of change in the brain's white matter and other regions, which can prompt specialists to suspect the diagnosis.

The second is genetic testing. Because nearly all cases are linked to changes in the GFAP gene, finding a disease-causing variant in that gene confirms the diagnosis. The growing use of broad genetic testing in children with unexplained neurological problems has made it more likely that Alexander disease will be recognised, and recognised earlier.

Earlier diagnosis has taken on new importance now that a treatment exists. In a progressive disease, damage that has already occurred may not be reversible. A medicine that slows the build-up of toxic protein is likely to be most useful when started before extensive damage has accumulated, although the trial evidence does not yet tell us exactly how much timing matters.

How zilganersen works

Zilganersen, which will be sold under the brand name Zanvastro, was developed by Ionis Pharmaceuticals, a company based in California that has spent more than three decades developing a technology called antisense.

A short lesson in antisense

Every protein in the body is made from instructions in DNA. But DNA does not build proteins directly. First, the relevant gene is copied into a temporary message called messenger RNA (mRNA). The cell's protein-making machinery then reads that message and assembles the protein.

An antisense oligonucleotide, or ASO, is a short, synthetic strand of genetic material designed to match a specific mRNA message, like a key cut for one lock. When it binds to its target message, it can prevent that message from being used, or mark it for destruction, so that less of the corresponding protein is made.

In the case of zilganersen, the target is the message for GFAP. By reducing the production of GFAP, including the abnormal form, the drug aims to stop the toxic build-up before it accumulates and causes further damage. The FDA described it as the first therapy to directly target the protein build-up that drives the disease.

Getting the drug to the brain

ASOs are relatively large molecules that do not readily cross from the bloodstream into the brain. So zilganersen is given by intrathecal injection: a needle is passed into the fluid-filled space around the spinal cord in the lower back, in a procedure similar to a lumbar puncture. From there, the drug can spread through the cerebrospinal fluid to reach brain tissue.

According to the prescribing details reported with the approval, the dose is 50 mg, given by a trained healthcare professional once every 12 weeks, or four times a year.

The evidence behind the approval

The trial

The approval was based on a multicentre, randomised, controlled study registered on ClinicalTrials.gov as NCT04849741. Ionis describes it as a global, multicentre, randomised, double-blind, controlled phase 1 to 3 study of intrathecally administered zilganersen (originally known as ION373) in patients with Alexander disease. The registry shows it began in June 2021 and lists 54 participants as enrolled.

According to the FDA, the randomised study included 49 paediatric and adult patients aged 2 and older, and a separate open-label substudy included 4 patients younger than 2. Reporting by *The American Journal of Managed Care* (AJMC), citing the trial data, described participants ranging in age from 2 to 53, with a median age of 11, and 65.3% female. In the double-blind period, participants were randomised in a 2 to 1 ratio to zilganersen or control.

For a disease this rare, recruiting a randomised, controlled trial of this size, across multiple countries, was itself a considerable achievement.

Walking speed: the main measure

Choosing how to measure benefit in a rare, variable disease is difficult. The researchers chose walking speed as the primary outcome for participants aged 5 and older, measured with the 10-Metre Walk Test, a simple, well-validated test of how quickly a person can walk a set distance.

At week 61, participants aged 5 and older who received zilganersen had significantly better walking speed than those in the control group. AJMC reported that the least squares mean difference was 33.3%, with a p-value of 0.041. The FDA described the

treated patients as having "significantly better walking speed" than untreated patients among those who had measurable walking difficulties at the start.

It is important to understand what "better" means here. In a progressive disease, the natural course is decline. The benefit described in coverage of the trial was a stabilisation of gait speed compared with control, in other words, slowing or halting the expected worsening rather than restoring lost function.

Younger children

Walking speed is not a reliable measure in children aged 2 to 4, who are still developing their motor skills. For this group, the researchers used a broader assessment of motor skills, the Gross Motor Function Measure. According to the FDA, treated children improved, while children in the control group declined.

For children younger than 2, direct trial evidence was limited, both because of the rarity of the disease and because there was no concurrent control group. The FDA said it relied on pharmacokinetic modelling (how the drug moves through and is handled by the body) and safety data from the four young patients in the substudy to support use in this age group.

Other measures

AJMC reported that key secondary measures, including patients' most bothersome symptoms and global impressions of change from patients and clinicians, trended in favour of zilganersen, with the patient global impression of change reaching statistical significance.

An exploratory analysis found that levels of GFAP in the blood fell by 33.6% compared with control. Exploratory findings are not proof of benefit on their own, but this one fits the way the drug is supposed to work: less GFAP is being made.

Safety

The most common adverse reactions were:

- vomiting;
- back pain;
- cough;
- headache; and
- post-lumbar puncture syndrome (a headache and related symptoms that can follow a spinal injection).

AJMC reported that most treatment-emergent adverse events were mild or moderate, and that serious adverse events were less frequent with zilganersen than with control (37.5% versus 47.1%). The high rate in both groups is a reminder of how serious Alexander disease itself is.

The FDA highlighted one specific warning: aseptic meningitis, an inflammation of the membranes around the brain and spinal cord that is not caused by infection, has been reported. Patients and caregivers are advised to tell their healthcare provider if meningitis-like symptoms, such as fever, headache, neck stiffness or sensitivity to light, develop.

What the regulators and the company said

Dr Emily Freilich, director of the FDA's Division of Neurology I in the Center for Drug Evaluation and Research, acknowledged the long wait for families. "For patients with Alexander disease and their families, there have been no approved treatment options," she said, describing the approval as a landmark moment for the community.

Ionis chief executive Dr Brett Monia said the approval "begins a new chapter for people living with Alexander disease."

The drug received several FDA designations intended to encourage and accelerate development for serious and rare conditions: Orphan Drug, Fast Track, Breakthrough Therapy, and Rare Pediatric Disease, along with Priority Review. Ionis also received a Rare Pediatric Disease Priority Review Voucher, a transferable certificate that entitles the holder to a faster FDA review of a future product.

Zanvastro will be Ionis' first independently launched neurology medicine. At the time of the announcement, the company said the drug would be available in the United States in the coming weeks. The following day, Reuters reported that Ionis had set a list price of US$285,000 per dose.

How regulators weigh evidence in ultra-rare disease

The zilganersen approval offers a useful window into how regulators approach diseases with very few patients.

In common conditions, regulators can expect large trials with thousands of participants and long follow-up. In a disease affecting fewer than one in a million people, that is impossible. Regulators instead look for the strongest evidence that can reasonably be obtained, which in this case was a randomised, controlled trial of about 50 patients, supplemented by supporting data.

Several features strengthened the case:

1. **Randomisation and a control group.** Unlike many rare-disease programs, the main study compared treated patients with a concurrent control group, which reduces the risk that differences reflect chance or bias.
2. **A plausible mechanism, confirmed by a biomarker.** The drug is designed to reduce GFAP production, and blood GFAP levels fell, which supports the idea that it is doing what it was designed to do.
3. **Consistency across measures.** The main walking outcome, the motor assessment in younger children and some secondary measures all pointed in the same direction.
4. **A serious unmet need.** With no other treatments, regulators may accept somewhat more uncertainty about the size and durability of benefit than they would for a condition with existing options.

At the same time, the FDA was transparent about where evidence was thin, particularly for children under 2, where it relied on modelling and limited safety data. That transparency is important: it allows doctors and families to understand how strong the evidence is for their particular situation.

Antisense medicines come of age

Zilganersen is part of a lineage of antisense medicines for neurological disease that has transformed expectations over the past decade.

The best known is nusinersen (Spinraza), developed by Ionis with Biogen and approved by the FDA in December 2016 for spinal muscular atrophy, a genetic disease that was once a leading genetic cause of death in infancy. Like zilganersen, it is given by intrathecal injection. In 2023, the FDA granted accelerated approval to tofersen (Qalsody), another Ionis-discovered, Biogen-developed antisense medicine, for a form of amyotrophic lateral sclerosis (ALS, or motor neurone disease) caused by mutations in the SOD1 gene.

There is an important difference between those medicines and zilganersen. Nusinersen works by modifying how a gene's message is processed so that more of a needed protein is made. Tofersen and zilganersen, by contrast, reduce the production of a harmful protein. This "knock-down" strategy is especially well suited to gain-of-function diseases, where the problem is a toxic protein rather than a missing one.

The approval of zilganersen strengthens the case that, for at least some genetic brain disorders, if scientists can identify the harmful protein and its gene, they can design a medicine to turn it down.

What families should understand

For families affected by Alexander disease, a few practical points follow from the evidence and the approval:

- The medicine is designed to slow or stabilise the disease by reducing production of the harmful protein. It is not expected to reverse damage that has already occurred.
- The strongest trial evidence relates to walking speed in people aged 5 and older; evidence in infants is more limited.
- Treatment involves regular spinal injections, four times a year, for as long as treatment continues.
- Possible side effects, including the warning about aseptic meningitis, should be discussed in advance with the treating team.

Questions that remain

How durable is the benefit?

The main measure of benefit was assessed at week 61, just over a year. Alexander disease unfolds over many years. Longer follow-up will be needed to understand whether stabilisation of walking speed is maintained, and whether the drug alters other aspects of the disease, such as swallowing, seizures, cognition or survival.

Which patients benefit most?

Because Alexander disease varies so much with age of onset, it is possible that benefit differs between infants, children and adults. The evidence base is strongest for people aged 5 and older with measurable walking difficulty, and more limited for very young children.

The burden of treatment

Lifelong intrathecal injections every three months are a significant commitment, particularly for young children, who may need sedation for the procedure, and for people whose spinal anatomy makes injections difficult.

Access and cost

Medicines for ultra-rare diseases are typically very expensive, reflecting high development costs spread over very small patient populations. Reuters reported a US list price of US$285,000 per dose, with four doses a year at the approved schedule. How the medicine will be funded, and whether and when it will be available outside the United States, are open questions. In Australia, any such medicine would need to be evaluated by the Therapeutic Goods Administration (TGA) before it could be registered, and funding through the Pharmaceutical Benefits Scheme or other programs would require separate assessment.

Life beyond the trial

Approval is not the end of the evidence-gathering process. Medicines approved for rare diseases are typically followed through ongoing open-label extension studies, in which trial participants continue treatment and are monitored over longer periods, and through post-marketing safety surveillance once the medicine is used more widely. For a disease as variable as Alexander disease, that real-world experience, gathered from patients of different ages and stages, will be essential to understanding who benefits most, and by how much.

The bigger picture

For most of the history of medicine, ultra-rare genetic diseases have been treated as tragic but untouchable. There were too few patients to attract investment, too little understanding of mechanism to design a drug, and too few people to run a trial.

The approval of zilganersen challenges each of those assumptions. The disease mechanism was understood well enough to pick a target. A platform technology, antisense, made it possible to design a drug against that target without starting from scratch. Regulatory incentives for rare paediatric diseases helped justify the investment. And patients and families across multiple countries made a randomised trial possible.

In this writer's view, the significance of this approval extends well beyond Alexander disease. Each time a rare-disease medicine is approved on the basis of a well-conducted trial, it builds the scientific, regulatory and commercial pathway for the next one.

For the small number of families living with Alexander disease, the change is more immediate. For the first time, there is a medicine that targets the cause of their condition, not just its symptoms. It is not a cure, and its long-term effects remain to be seen. But after more than seven decades since the disease was first described, it is a beginning.

This article explains a regulatory decision and research findings for general readers and is not medical advice. People affected by Alexander disease should discuss treatment options with their specialist.

Key terms

Term	Meaning
Astrocyte	A star-shaped support cell in the brain and spinal cord
GFAP	Glial fibrillary acidic protein, a structural protein in astrocytes; the abnormal form builds up in Alexander disease
Antisense oligonucleotide (ASO)	A short synthetic strand of genetic material designed to bind a specific RNA message and reduce production of a protein
Intrathecal injection	An injection into the fluid around the spinal cord
10-Metre Walk Test	A timed test of how quickly a person can walk a set distance
Aseptic meningitis	Inflammation of the membranes around the brain and spinal cord that is not caused by infection

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THE HEALTHTECH HERALD

One Infusion, a Lifetime of Hope: The First Gene Therapy for Sanfilippo Syndrome Type A

By Dr Sukh Rashpal Sandhu | Written for this edition

On 17 September 2026, the United States Food and Drug Administration approved Fayuvi, the first approved treatment for children with Sanfilippo syndrome type A, a fatal inherited disease sometimes described as childhood dementia. Given once, through a drip, it delivers a working copy of a missing gene to cells throughout the body, including the brain. It is a scientific milestone, a hard-won victory for families, and a test of how health systems will pay for medicines priced in the millions.

A disease that takes away what children have learned

Sanfilippo syndrome is named after the American paediatrician Sylvester Sanfilippo, who described it in 1963. Its medical name is mucopolysaccharidosis type III, or MPS III, and it exists in several subtypes, labelled A to D, each caused by a fault in a different gene. Type A, known as MPS IIIA, is the subject of this approval.

What goes wrong inside cells

Every cell contains small compartments called lysosomes, which act as recycling centres. They contain enzymes that break down large, complex molecules so their building blocks can be reused.

One of those molecules is heparan sulfate, a long sugar chain found on cell surfaces and in the tissue around cells. Breaking it down requires a sequence of enzymes working in order, like workers on a disassembly line. In MPS IIIA, a fault in a gene called SGSH means the body cannot make enough of one of those enzymes, called sulfamidase.

Without it, partly broken-down heparan sulfate accumulates inside cells throughout the body. The brain is especially vulnerable. Over time, the build-up damages nerve cells and leads to progressive neurological decline.

What families experience

The FDA describes MPS IIIA as a rare, inherited condition that progressively damages the brain and nervous system. Children often seem to develop typically in the first years of life. Then development plateaus, and children begin to lose skills they had already acquired, including language and other cognitive and developmental abilities.

According to coverage of the approval, the average lifespan of children with the condition is about 15 years. Until September 2026, treatment was limited to managing symptoms and providing comfort care. There was no medicine that addressed the cause.

MPS IIIA is inherited in an autosomal recessive pattern, meaning a child must inherit a faulty copy of the SGSH gene from each parent. Parents who carry one faulty copy are usually healthy and often have no idea they are carriers until a child is diagnosed. Ultragenyx, the company behind Fayuvi, estimates there are 3,000 to 5,000 affected patients in the developed world.

Why the brain has been so hard to reach

To understand why Fayuvi matters, it helps to know why diseases like MPS IIIA have resisted treatment for so long.

For several other lysosomal storage diseases, doctors have used enzyme replacement therapy: regular infusions of a manufactured version of the missing enzyme. In conditions that mainly affect the body's organs, such as the liver, spleen, bones or heart, this approach can help considerably. But the brain sits behind the blood-brain barrier, a tightly sealed layer of cells lining the brain's blood vessels. It protects the brain from toxins and infections, but it also blocks most large molecules, including enzymes, from entering.

MPS IIIA is primarily a disease of the brain. An enzyme infused into the bloodstream may reduce heparan sulfate in the body but is unlikely to reach the nerve cells where the most important damage occurs. Researchers have explored workarounds, including injecting enzymes directly into the fluid around the brain and engineering enzymes that can "ride" transport systems across the barrier. Bone marrow transplantation, used in some related conditions, has not proved effective in Sanfilippo syndrome.

Gene therapy offers a different route. Rather than repeatedly delivering the enzyme, it aims to equip the body's own cells, including cells in the brain, to make the enzyme themselves.

How Fayuvi works

Fayuvi's scientific name is rebisufligene etisparvovec, and it was known during development as UX111. It is a gene therapy, meaning it treats disease by delivering genetic material into a patient's cells.

The delivery vehicle

Getting a gene into cells requires a vehicle, called a vector. Fayuvi uses a modified, non-infectious adeno-associated virus serotype 9, or AAV9. Adeno-associated viruses are small viruses that are not known to cause disease in people. Scientists remove the virus's own genes and replace them with the therapeutic gene, in this case a working copy of SGSH.

AAV9 is a particularly useful vector for brain diseases because, when given in sufficient doses into the bloodstream, it can cross the blood-brain barrier, the protective layer that normally keeps most substances in the blood away from brain tissue.

Once inside cells, the delivered gene provides instructions for making sulfamidase. With the enzyme restored, cells can once again break down heparan sulfate, reducing its build-up in the body and brain.

A one-time treatment

Fayuvi is given once, as an intravenous infusion. According to the FDA, it must be given in a healthcare setting equipped to manage infusion reactions. Patients receive corticosteroids, medicines that dampen the immune system, starting the day before the infusion and continuing for at least eight weeks afterward. This is because the immune system can react to the viral vector, and suppressing that response helps protect the patient and the treatment.

Ultragenyx said the therapy will be available through a network of qualified treatment centres, specialist sites trained to administer gene therapy, and that it expected centres to begin offering it within 30 to 60 days of approval.

The evidence behind the approval

The study

According to the FDA, its assessment of effectiveness was based on an open-label, single-arm, multicentre study in paediatric patients with MPS IIIA. The trial is registered on ClinicalTrials.gov as NCT02716246, a phase 1 to 3 gene transfer trial that began in April 2016. The registry lists an estimated enrolment of 36 participants, and the entry still carries an original study code from Abeona Therapeutics, the company that developed the therapy before Ultragenyx took it forward.

"Open-label" means everyone involved knew who received the treatment. "Single-arm" means there was no randomised comparison group within the trial. Instead, the researchers compared the treated children with an untreated historical control cohort: children with MPS IIIA whose disease course had been documented in natural history studies.

What it showed

The study measured changes in cognitive scores in children aged 2 to 5. According to the FDA, treated children maintained or improved cognitive function compared with the historical control cohort. The agency described this as a divergence from the expected course of the disease, in which development typically plateaus and then declines.

In a progressive disease that normally erodes a child's abilities, holding cognitive function steady, or improving it, is a profound result. It does not mean the disease has been cured. It means the downward trajectory that defines MPS IIIA appears to have been altered in the children studied.

The FDA's Dr Megha Kaushal, acting deputy director of the Office of Therapeutic Products, highlighted the broader scientific significance, saying the approval showed that "systemic AAV9-mediated gene delivery can reach the central nervous system at therapeutically relevant levels."

Why a single-arm study?

For readers used to hearing that randomised controlled trials are the gold standard, the basis for this approval may raise questions. In ultra-rare, rapidly progressive childhood diseases, randomising children to receive no treatment, while their condition worsens, raises serious ethical problems. There are also simply too few patients to run large trials.

Regulators therefore sometimes accept single-arm studies compared against carefully documented natural history, especially when the expected course of the disease is well established and the treatment effect is clear. This approach has real limitations, including the risk that the treated and historical groups differ in ways that affect outcomes, but it is a recognised pathway for rare diseases.

Safety

The FDA listed the most common adverse reactions, occurring in more than 5% of patients, as:

- increased levels of the liver enzyme AST;
- nausea and vomiting;
- fever;
- decreased appetite;
- decreased white blood cell and platelet counts; and
- increased amylase (an enzyme associated with the pancreas).

The FDA also highlighted two warnings:

1. **Thrombotic microangiopathy (TMA).** This is a potentially serious condition involving damage to small blood vessels, low platelet counts and possible organ injury. It is a recognised risk with high-dose AAV gene therapies.
2. **Potential long-term risk of tumour development.** As with other AAV-based gene therapies, there is a theoretical risk that the delivered genetic material could integrate into a patient's own DNA and contribute to tumour development. This requires long-term monitoring.

A difficult road to approval

Fayuvi's approval did not come easily. Ultragenyx first filed its application with the FDA in early 2025. In July 2025, the FDA issued a complete response letter, a formal decision not to approve the application at that time, citing manufacturing issues and asking for more data.

Ultragenyx addressed the manufacturing observations, prepared updated long-term clinical data and resubmitted the application on 30 January 2026. The FDA accepted it with a target action date of 19 September 2026. The approval came two days early, on 17 September. Although Ultragenyx had sought accelerated approval, MedCity News reported that the FDA granted full approval, and that the label covers children with preserved neurodevelopmental function.

The Cure Sanfilippo Foundation, a patient advocacy organisation, has noted that the therapy had been in clinical trials for nearly ten years and that the foundation contributed funding that helped advance it into clinical testing. That long, collaborative journey,

involving academic researchers, small biotechnology companies, a larger company and patient foundations, is typical of rare-disease medicine.

Glenn O'Neill of the Cure Sanfilippo Foundation and Terri Klein of the National MPS Society, in a joint statement, called the approval "a remarkable scientific achievement."

The value of natural history research

The approval of Fayuvi rests heavily on comparison with an untreated historical control cohort. That comparison is only possible because, over many years, researchers and families documented in detail how MPS IIIA unfolds in children who receive no disease-modifying treatment.

This kind of natural history research is unglamorous. It involves repeated assessments of children whose condition is worsening, careful recording of developmental scores over time, and the cooperation of families at an extraordinarily difficult point in their lives. It rarely makes headlines. Yet without it, the effect of a treatment in a single-arm trial would be almost impossible to interpret.

In that sense, families whose children were never treated have contributed directly to the approval of a treatment that may help children diagnosed in the future. It is one of the quieter but most important truths of rare-disease medicine.

The price question

Ultragenyx set the US list price of Fayuvi at US$3.95 million before rebates or discounts, according to MedCity News and Pharmaceutical Technology, placing it among the most expensive medicines in the world. The company argues that the lifetime cost of caring for a child with MPS IIIA can exceed US$8 million.

That argument, that a one-time treatment can be cheaper over a lifetime than ongoing care, is now a familiar feature of gene therapy pricing. It has some logic. But it also raises hard questions:

- **Who pays upfront?** Health systems and insurers must find millions of dollars at once, even if savings accrue over decades.
- **What if the benefit fades?** Long-term durability of gene therapy effects is still being established for many conditions.
- **How are budgets balanced?** Money spent on very expensive treatments for very rare conditions is not available for other care, a tension that health technology assessment bodies in every country must manage.

The FDA also awarded Ultragenyx a Rare Pediatric Disease Priority Review Voucher, a certificate that can be used to speed up review of a future product or sold to another company. Reports cited by *Pharmaceutical Technology* put the value of such vouchers at US$150 million to US$200 million.

Fayuvi is Ultragenyx's second approved gene therapy, after Genglycos, a gene therapy for glycogen storage disease type Ia that the FDA approved in August 2026.

Where Fayuvi fits in the gene therapy story

Fayuvi joins a small but growing group of gene therapies that use AAV vectors to treat neurological disease. The best known is onasemnogene abeparvovec (Zolgensma), also an AAV9-based therapy, approved by the FDA in 2019 for spinal muscular atrophy in young children.

What makes Fayuvi notable is the target. Lysosomal storage diseases that affect the brain have been especially difficult to treat. Enzyme replacement therapy, in which a manufactured enzyme is given by regular infusion, has helped people with some lysosomal storage diseases, but enzymes given into the bloodstream generally cannot cross into the brain. Delivering a gene that lets cells make their own enzyme, including cells behind the blood-brain barrier, is a different and potentially more powerful strategy.

The FDA's description of Fayuvi as a demonstration that systemic AAV9 delivery can reach the central nervous system at therapeutically relevant levels is significant for this reason. If the approach works for MPS IIIA, researchers will be keen to apply it to related conditions, including other subtypes of Sanfilippo syndrome.

What remains uncertain

Long-term durability

The children treated in early trials are being followed over many years. Whether the benefit is maintained into adolescence and adulthood, and whether treated children can live substantially longer, are questions only time can answer.

Timing and severity

In progressive neurological diseases, damage that has already occurred may not be reversible. The evidence presented to the FDA focused on children aged 2 to 5. The approved label is limited to children whose neurodevelopmental function is preserved. It is likely that the earlier a child is treated, the better the outcome, which places a premium on early diagnosis.

Early diagnosis

That raises a broader challenge. Because children with MPS IIIA often appear to develop typically at first, diagnosis is frequently delayed, sometimes until significant damage has occurred. Some families endure years of uncertainty, with symptoms initially attributed to developmental or behavioural conditions. A treatment that works best early creates a strong case for faster diagnosis, through greater clinician awareness and, potentially in future, newborn screening.

Access beyond the United States

The FDA approval applies in the United States. Availability in other countries, including Australia, depends on separate regulatory decisions, such as by the Therapeutic Goods Administration, and on funding arrangements, which for medicines of this cost typically involve lengthy assessment and negotiation.

What families should understand

For families affected by MPS IIIA, several practical points follow from the approval and the evidence:

- The evidence presented to the FDA concerned children aged 2 to 5, and early treatment is likely to matter.
- The therapy is given once, but it involves a course of corticosteroids and close monitoring, including for thrombotic microangiopathy and liver effects.
- Long-term monitoring is recommended because of the theoretical risks associated with AAV gene therapy.
- The therapy is delivered through specialist treatment centres, and eligibility, timing and access should be discussed with a metabolic or genetic specialist team.

What it means

For families of children with MPS IIIA, the approval changes the landscape. For the first time, there is a treatment designed to alter the course of the disease rather than simply ease its symptoms.

For the wider field, Fayuvi offers evidence that a single intravenous infusion of an AAV9 gene therapy can deliver meaningful benefit for a brain disease. That evidence will shape research into many other childhood neurological conditions.

For health systems, it is another reminder that the arrival of one-time, multi-million dollar treatments demands new ways of assessing value, paying for care and making sure that access is fair.

In this writer's view, the most striking element of this story is the timeline. The trial began in 2016. The first application was rejected in 2025 over manufacturing questions. Approval came in 2026. Throughout, families of children with a rapidly progressive disease waited, and in many cases their children could not. That is a sobering reminder of why getting manufacturing, regulation and access right matters so much, and why speed, where it can be achieved safely, is not merely a convenience in rare disease. It is the difference between treatment and too late.

This article explains a regulatory decision and research findings for general readers and is not medical advice. Families affected by Sanfilippo syndrome should discuss treatment options with their specialist team.

Key terms

Term	Meaning
MPS IIIA	Mucopolysaccharidosis type IIIA, also called Sanfilippo syndrome type A
Lysosome	A compartment inside cells that breaks down and recycles large molecules
Heparan sulfate	A complex sugar molecule that builds up in MPS IIIA
Sulfamidase	The enzyme missing in MPS IIIA, made from instructions in the SGSH gene
AAV9	Adeno-associated virus serotype 9, a modified,

Term	Meaning
	non-infectious virus used to deliver genes
Single-arm study	A trial in which all participants receive the treatment, with no randomised comparison group
Historical control	A comparison group drawn from previously documented, untreated patients
Thrombotic microangiopathy	Damage to small blood vessels with low platelets and possible organ injury

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Masthead

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