THE ARISING

The Future of Memory

DEMENTIA & BRAIN HEALTH



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The question beneath the diagnosis

The first signs can be hard to name. A person who managed every household bill now needs to check the numbers three times. A familiar drive becomes disorienting. Someone who has always found the right word begins to substitute descriptions, gestures, and silence. Or the first change is not memory at all: a loss of judgment, a shift in personality, a new difficulty interpreting what the eyes can see.

The question that follows is rarely confined to medicine. What is happening? How much can we change? And how do we preserve the life being lived while we seek answers?

For decades, public discussion of dementia has often oscillated between two unsatisfying extremes. One depicts an inevitable descent, leaving families little agency. The other treats every promising molecule, brain scan, supplement, or laboratory discovery as though a cure were almost here. The science has become much more interesting than either story. We now have genuine, if limited, treatments that slow the disease for selected patients with early Alzheimer's disease; more accessible diagnostic tools; controlled evidence that some structured health interventions can improve cognitive-test performance; and an expanding understanding of the people and systems that make living with dementia better or worse.

Those advances need to be understood together. A brain exists inside a body, a household, a neighborhood, a medical system, and a lifetime. Dementia research becomes most useful when it examines how those levels meet.

First, there is no single thing called dementia

Dementia means a decline in memory, thinking, or other mental abilities severe enough to interfere with managing everyday life independently. Alzheimer's disease is the most familiar cause, but the syndrome may arise from damage to brain blood vessels, Lewy body disease, frontotemporal degeneration, a mixture of these conditions, or other illnesses. The course can differ strikingly. A person with Alzheimer-related brain changes may first struggle to form new memories; someone with frontotemporal degeneration, which affects areas near the front and sides of the brain, may show early behavioral or language changes; Lewy body disease may bring changes in alertness, seeing things that are not there, stiffness or slowed movement, or acting out dreams during sleep; vascular disease may alter walking, attention, planning, or speed of thinking. Having more than one disease process is common in older people. [DETeCD guideline; NICE NG97]

A sudden change deserves a different kind of attention. Delirium (sudden confusion), infection, medication effects, disturbances in body chemistry, sleep deprivation, pain, severe depression, reduced hearing or vision, and other urgent medical problems can mimic or compound chronic impairment. Dementia and delirium can coexist. A blood test for a sign of disease does not excuse a clinician from examining what changed, when it changed, what the person can still do, and which reversible contributors might be present.

This is where the clinical encounter matters most. A good assessment begins with a story: the timeline, the everyday consequences, a medication review, a neurological and functional examination, and information from someone who knows the patient-obtained with consent and respect for the patient's own voice. Brain scans and selected laboratory tests help answer the questions raised by that assessment. Specialists may add detailed tests of thinking and memory, scans that detect particular disease-related substances, or tests of spinal fluid or blood when these can make the diagnosis clearer or guide treatment. DOI:10.1002/alz.14333 / NICE:NG97

The result should be more than a label. It should explain the likely syndrome and causes, what uncertainties remain, what care is available now, and which choices deserve discussion.

The long interval before the first forgotten appointment

Alzheimer-related changes can develop years before obvious impairment. Amyloid and tau, proteins that can build up abnormally in the brain, are central to its biology, but the aging brain is also shaped by blood vessels, inflammation, metabolism, sleep, hearing, vision, exposure, education, social circumstances, and the capacity to recover from illness. The modern prevention story therefore begins well before anyone seeks a memory-clinic appointment.

The 2024 *Lancet* Commission identified fourteen potentially modifiable risk factors across the lifespan. The two added to its prior list were high LDL (often called “bad”) cholesterol in midlife and untreated vision loss in later life. The Commission estimated that addressing the included factors might prevent or delay approximately 45% of dementia cases at a population level. That number is an estimate calculated from population data and assumptions about how the risks interact, not an experimental finding that a particular individual can cut personal risk by 45%, nor a guarantee that removing all risks is feasible. PMID:39096926

The practical implications are still substantial. Blood pressure control, treatment of vascular disease, smoking avoidance, physical activity, treatment of diabetes and unhealthy blood-fat levels when medically appropriate, avoidance of excessive alcohol, attention to hearing and vision, and opportunities for learning and connection have benefits that do not depend on an unproven dementia-prevention promise. Some may also modify the conditions in which cognitive decline emerges. The degree to which each separately prevents dementia remains an ongoing scientific question.

The distinction between a persuasive biological argument and a measured human outcome appears clearly in three major randomized trials, in which chance determines which program or treatment each participant receives.

The Finnish FINGER trial enrolled 1,260 at-risk adults aged 60-77. A two-year program combined diet, exercise, thinking and memory exercises, and checks on risks to heart and blood-vessel health. It produced a modest advantage on a comprehensive cognitive-test score compared with general health advice. It did not establish fewer cases of dementia during the trial. PMID:25771249

The U.S. POINTER trial, published in 2025, enrolled 2,111 older adults with risk factors for decline. Both assigned programs encouraged physical and cognitive activity, a healthy diet, social engagement, and cardiovascular monitoring. One was more structured and intensive, with regular support and accountability. Over two years, the combined thinking-and-memory test score improved in both groups, and the more structured program improved more: 0.243 versus 0.213 standard deviations per year, a between-group difference of 0.029 standard deviations per year (95% CI, 0.008-0.050; P = .008). These numbers describe a small difference on a test scale, not a percentage reduction in dementia. A standard deviation is a way to express score differences relative to how widely people's scores vary. The 95% confidence interval (CI), 0.008-0.050, shows the range of differences reasonably compatible with these data under the analysis's assumptions. The P value of .008 indicates evidence against no average difference; it does not tell us how much daily life improved. Both groups received a program, and the trial did not establish fewer new cases of dementia. PMID:40720610

The most interesting question is not whether the result proves prevention. It is what organized support makes possible. Advice alone often asks people to become their own coaches, schedulers, transportation coordinators, nutritionists, and accountability partners. A structured program offers a different way to turn sound goals into repeated actions. We do not yet know which component accounts for the measured advantage; that is precisely why the design of care deserves to be studied alongside the components of lifestyle.

SPRINT MIND adds a complementary lesson. Adults with high blood pressure but without diabetes or prior stroke were randomized to targets for systolic blood pressure, the top number in a reading, below 120 or below 140 mm Hg. Over follow-up, probable dementia occurred at 7.2 versus 8.6 cases per 1,000 person-years (HR 0.83, 95% CI 0.67-1.04): roughly 7 versus 9 diagnoses if 1,000 people were each followed for a year. The hazard ratio (HR) compares how quickly diagnoses occurred in the two groups: 1 means no difference. Here the uncertainty range, 0.67-1.04, includes 1, so the trial did not establish a dementia benefit. Mild cognitive impairment, a decline less severe than dementia, did decrease (HR 0.81, 95% CI 0.69-0.95). That estimate suggests about a 19% lower rate over time, with an uncertainty range consistent with about 5% to 31% lower. The trial's treatment phase ended early and dementia events were fewer than expected. This is a meaningful argument for caring about vascular health, not permission to prescribe an intensive pressure target to everyone regardless of falls, adequate blood supply to organs, kidney function, dizziness on standing, or other individual risks. PMID:30688979

Hearing a conversation is part of brain health today

The ACHIEVE trial randomized 977 older adults with untreated hearing loss to hearing care or health education and followed changes in overall thinking and memory for three years. Across all participants, the main result showed no clear difference: a between-group difference of 0.002 standard deviations (95% CI -0.077 to 0.081; P = .96). The difference was almost zero, and its uncertainty range included both a small benefit and a small disadvantage. An analysis planned before the results were known suggested slower decline in one subgroup: older participants drawn from a study of people with greater heart-and-blood-vessel risk. That subgroup is worth studying, but the trial did not establish universal dementia prevention through hearing aids. PMID:37478886

Hearing care matters even without that claim. The person who no longer follows conversation may withdraw from company not because they have lost interest, but because participation has become exhausting. Helping someone hear can restore access to a shared life. We should measure that benefit directly, and study any longer cognitive consequences honestly.

Vision deserves the same respect. The latest Commission highlighted untreated vision impairment as a potential population-level risk factor. Clinical work can respond to the much simpler, immediate problem: preserving safe navigation, reading, social participation, and the ability to see the people one loves.

A diagnosis is changing: blood tests can help, but the patient comes first

On May 16, 2025, the FDA cleared the Lumipulse G plasma pTau217/Aβ1-42 ratio, a blood test comparing two Alzheimer-related protein measurements, for use as an aid in assessing abnormal amyloid buildup in symptomatic adults age 55 or older. On August 24, 2026, Roche announced FDA clearance of its Elecsys plasma pTau217 assay, which measures one protein marker in blood, for symptomatic adults 55 or older with signs, symptoms, or complaints of cognitive decline, with tested decision thresholds intended for primary and specialty settings. These are material improvements in the accessibility of the diagnostic pathway. They are not universal screening tests for people with no cognitive concern, and an amyloid-related result is not itself a complete diagnosis of the cause of a person's symptoms. FDA:LUMIPULSE:2025 / ROCHE:ELECSYS:2026-08

A 2025 Alzheimer's Association guideline for specialist care is particularly helpful because it is performance-based rather than brand-based. In a cognitively impaired population undergoing evaluation, a blood test reaching at least 90% sensitivity (detecting at least 90 out of 100 people with the target brain changes) and 75% specificity (correctly ruling them out in at least 75 out of 100 people without them) may help decide who needs further testing. A sufficiently validated test reaching 90% sensitivity and 90% specificity may substitute for an amyloid PET scan, which looks for the protein in the brain, or a test of cerebrospinal fluid (CSF), the fluid around the brain and spinal cord, in defined specialist diagnostic

settings. These are thresholds for tests used in context, not guarantees about every assay in every clinic. DOI:10.1002/alz.70535

New digital tools are entering the same conversation. An October/November 2026 *EClinicalMedicine* study assessing participants at one point in time evaluated a tablet-based motor, speech, and augmented-reality platform in 638 adults, with an additional 75-person independent cohort. Its ability to distinguish clinically classified mild cognitive impairment from unimpaired cognition had an area-under-the-curve score (AUC) of 0.90 in the main dataset and 0.87 (95% CI 0.80-0.93) in the independent cohort. AUC measures how well a test separates two groups: 0.5 is chance-level separation and 1.0 is perfect separation. Scores of 0.90 and 0.87 are encouraging, but do not mean that 90% or 87% of everyone screened will receive a correct diagnosis. The independent group's uncertainty range was 0.80-0.93. It does not establish that population screening improves health, predicts future dementia reliably, or helps clinicians make better decisions in ordinary practice. Developer funding also deserves attention. PMID:42964515

For someone considering a memory-testing app, that distinction matters. The most useful cognitive technology will not merely assign people to red, yellow, and green boxes. It will identify a specific question worth evaluating, explain uncertainty, respect accessibility and literacy differences, protect sensitive data, and support an appropriate clinical conversation without converting every imperfect test into a frightening forecast.

The amyloid era: an achievement measured in months and real tradeoffs

The central therapeutic advance is no longer hypothetical. Lecanemab and donanemab have demonstrated modest slowing of clinical decline in randomized trials of carefully selected patients with early symptomatic Alzheimer's disease and evidence of abnormal amyloid buildup. Their approval marks an important change: there are treatments targeting disease pathology rather than only symptoms, even though they do not restore lost function or cure dementia.

In the 1,795-participant CLARITY AD trial, average worsening on the Clinical Dementia Rating-Sum of Boxes, which assesses thinking and everyday function, over 18 months was 1.21 points with lecanemab and 1.66 with placebo. The adjusted difference was -0.45 points on an 18-point scale. At the group level the treatment slowed measured decline. It does not mean that each treated person experiences a perceptible 0.45-point advantage, and individual response varies. PMID:36449413

In TRAILBLAZER-ALZ 2, 1,736 participants were randomized to donanemab or placebo. In participants selected for analysis in advance because they had low or medium levels of tau buildup, the 76-week decline on the integrated Alzheimer's Disease Rating Scale was -6.02 versus -9.27 points, a 3.25-point difference (95% CI 1.88-4.62). Both groups worsened on average, but the treated group worsened less. The uncertainty range for that advantage was 1.88-4.62 points. A different scale, patient selection, study

duration, and tau subgroup mean these numbers cannot serve as a head-to-head comparison with lecanemab. PMID:37459141

The benefits must be considered beside amyloid-related imaging abnormalities (ARIA): brain swelling or bleeding that can appear on scans; rare severe events and deaths have occurred. Having two copies of the APOE ε4 gene variant increases that risk. Current U.S. prescribing information includes counseling and requirements for repeated MRI brain scans, and lecanemab now has options given into a vein or under the skin described in its July 2026 label. The practical treatment question is therefore not only “does it slow decline?” but “for whom, at what risk, with what monitoring capacity, and with which goals?” DM:LEQEMBI:v24 / DM:KISUNLA:v8

These medicines also reveal why earlier diagnosis has value only when it connects to good care. A clinic must recognize appropriate candidates, distinguish mixed or alternative syndromes, review medications and cerebrovascular risks, discuss genetic testing with consent, organize timely imaging and infusion or injection visits, and respond rapidly to unexpected neurological symptoms. Diagnosing amyloid in a person whose clinical picture or treatment preferences do not support that pathway can create uncertainty rather than value.

Care is a treatment domain, too

A person with dementia does not spend most days inside a randomized drug trial. They live at home, navigate routines, manage symptoms, speak with family, attend appointments, eat, move, and sleep. Care is the work of making those days more possible.

In the D-CARE randomized trial designed to test care in everyday settings, 2,176 person-with-dementia/caregiver pairs were assigned to health-system-based care management, community-based care management, or usual care. At 18 months, the two intervention strategies did not outperform usual care on the trial's main measures of behavioral and emotional symptoms and caregiver strain. A prespecified analysis of the same cohort found better caregiver satisfaction with the organized care approaches, without demonstrated improvements in patient cognition, function, quality of life, or overall caregiver burden. Those reports describe one trial population, not independent replications. PMID:39878968 / PMID:40892399

The result is worth taking seriously. People may appreciate help coordinating care even when a standardized score does not move. That is a real kind of value, but a different one from reducing symptoms, disability, or crises. Designing a better system requires us to measure all of them rather than assuming that satisfaction proves effectiveness-or that a score showing no clear improvement makes navigation worthless.

Behavioral distress deserves similar precision. Agitation can arise from pain, fear, overstimulation, fatigue, disrupted routines, infection, medication effects, and unmet needs. Environmental adjustments and careful assessment remain first steps. For selected adults with agitation specifically associated with

Alzheimer's dementia, there are now two U.S. FDA-approved medicine options with distinct profiles: brexpiprazole (approved 2023) and dextromethorphan-bupropion (Auvelity; expanded approval April 30, 2026). Auvelity was supported by a short-term randomized symptom trial and a study testing whether continuing treatment prevented symptoms returning after initial improvement; it is not a drug to use only “as needed” for agitation. It carries important seizure, blood pressure, interaction, and psychiatric warnings. Brexpiprazole is an antipsychotic carrying the class warning about increased mortality in older patients with dementia-related psychosis. Neither treats the underlying loss of brain cells and function. FDA:REXULTI:2023-05 / FDA:AUVELITY:2026-04 / DM:AUVELITY:v18

Care partners require more individualized attention than a single “burden” score. A 2026 review of accounts of caregiving describes relationship strain, emotional exhaustion, and technology that does not fit people’s needs, all problems existing services often overlook. A review mapping twelve studies of technology for people with dementia and their care partners from six middle-income countries found research concentrated on feasibility and acceptability rather than durable measured health outcomes for both members of the pair. These studies are useful design evidence, not a license to declare chatbots, robots, or sensors clinically effective. PMID:42964287 / PMID:42956288

A separate U.S. survey of adults at elevated cardiovascular risk found that informal caregivers were more likely than non-caregivers to skip meals or report housing instability. Its 7,215-person sample was not restricted to dementia caregiving, so it should not be quoted as a dementia-specific estimate. The connection still warrants investigation: giving care can change the caregiver's own health, financial security, and time for prevention. A good dementia service should attend to both people. PMID:42956859

New clues from blood vessels and the brain’s immune cells

The biomedical frontier continues to widen beyond amyloid. Two 2026 papers illustrate both the excitement and the discipline required.

In a *Science Advances* study, investigators identified oxidized guanosine triphosphate, or 8-oxoGTP, a chemically damaged form of a molecule cells use, as a trigger for inflammation in the brain’s resident immune cells, called microglia, in mice. Changing this molecule and a group of signaling enzymes called Src family kinases altered connections between nerve cells, tau-related changes, and thinking-and-memory measures in experimental systems. This is a fresh mechanistic hypothesis about how chemical damage can become inflammatory signaling. It is not evidence that taking antioxidants, Src inhibitors, or a particular supplement will treat human dementia. PMID:42950057

A *Cell* paper examined perivascular macrophages, the immune cells positioned beside cerebral blood vessels. In experimental models, changing cMAF, a protein that helps switch genes on and off, altered communication with the cells lining blood vessels. This included changes involving IGF1, a growth-related signal. Human tissue showed a related program and an APOE4-associated difference in Alzheimer samples. The experimental intervention supports a causal mechanism in the studied model; the

human observation remains an association. It does not create a new APOE-based prescribing or screening recommendation. PMID:42600613

A recent review of the glymphatic system, proposed routes through which fluid helps clear waste from the brain, brought sleep, blood-vessel function, metabolism, and waste removal into one picture. It is an important map of proposed biological interactions, not proof that manipulating a sleep schedule or clearance marker prevents Alzheimer's disease. The idea is scientifically attractive. Its value will depend on human experiments that tie a specific intervention to meaningful outcomes over time. PMID:42957838

For researchers, the connecting question is whether several apparently different aging pathways converge on blood-vessel function, immune activation, the ability of nerve-cell connections to withstand damage, and the ability to maintain ordinary life. For readers, it offers a more accurate view of discovery: biology is becoming richer, but treatments must earn their claims one comparison at a time.

Menopause, genes, and the risks of premature certainty

A new 2026 *Neuron* review describes menopause as a change involving hormone signals, the brain’s use of energy, connections between nerve cells, blood vessels, and inflammation. It proposes reasons that timing and prior hormonal history may matter to later-life cognition. It does not show that menopausal hormone therapy prevents dementia. The practical decisions around symptoms, bones, cardiovascular risk, and individual treatment eligibility remain separate questions requiring their own evidence. PMID:42962664

Genetics also needs careful framing. Rare disease-causing changes in genes such as APP and PSEN1/PSEN2 can cause inherited early-onset Alzheimer’s disease, with one altered copy enough to cause disease in affected families. APOE ε4 is different: it raises risk but does not mean someone will develop Alzheimer’s; its clinical role is particularly consequential when considering the risk of ARIA with anti-amyloid treatment. The meaningful service is not unrestricted genomic prediction. It is genetic counseling, informed consent, interpretation matched to family history and clinical context, and appropriate protection of the person's data.

What medicine, technology, and public investment should do next

Economic estimates can be impressive without telling us precisely how to improve a life. A June 2026 computer model of individual lives across the U.S. population estimated 5.7 million people age 51 and older living with dementia and comprehensive annual costs of $818 billion in 2025 dollars. The estimate includes $237 billion in valued unpaid care and $320 billion in quality-of-life losses among people with dementia. It is a modeled total spanning medical spending, informal care, earnings, and intangible burden-not a single healthcare bill or an amount any one organization pays. Its population and methods differ from other widely reported Alzheimer's prevalence estimates, which should not be combined mechanically. PMID:42340126

The U.S. Centers for Medicare & Medicaid Services (CMS) GUIDE model, operating since July 2024, is testing comprehensive dementia support and care navigation. Such systems could have real value if they reduce crises, improve caregiver experience, preserve time at home, and coordinate difficult transitions. An operating model or enrollment announcement is not by itself proof that it achieves those outcomes. CMS:GUIDE

For AI and robotics, the next useful generation of products will likely be less cinematic than a robot doctor. It may make appointments understandable, organize medication lists, help families document changes, flag conflicting notes for a clinician, make transport easier, and reduce duplicated work. The clinical study design matters: did the system prevent an avoidable emergency visit, reduce missed appointments without increasing burden, preserve autonomy, or simply produce a polished demonstration? Did it work for people with visual, hearing, language, motor, or cognitive impairments? Was the person able to decline constant monitoring?

The most valuable technology will not be the system that speaks most confidently about a future illness. It will be the one that makes a difficult present more manageable while respecting the people living through it.

A research enterprise that can correct itself

An October 2026 retraction is a reminder that published findings can later be withdrawn. A notice indexed under PMID 42959433 retracts a paper on chronic and nonchronic pain associations with dementia, DOI 10.3389/fnins.2026.1772559. That does not establish the opposite of the original claim. It means readers should no longer rely on that paper as support for the claim. PMID:42959433

A recent 60-participant study of virtual-reality reminiscence, using past experiences to prompt memories, raises a different problem: the brief published summary does not clearly identify which comparison group some results belong to, the order of reported outcomes, or how many people those results describe. Without that detail, the summary cannot support a confident treatment claim. PMID:42957174

For families, a useful question is whether an exciting claim rests on a study that others can check, understand, and repeat. Changing a conclusion when evidence changes is part of reliable science.

The future of memory

A loved person is not defined by the answers they give on a cognitive test. Nor is meaningful progress confined to the number of years before a diagnosis. We should care about safe mornings, conversations, moments of recognition, walks taken with a friend, familiar music, relief from distress, and the ability to make one's own choices for as long as possible.

There is reason for cautious hope. Medicine can now do more to investigate particular biological causes of dementia, measure some disease processes, and modestly alter the course of early Alzheimer's in selected patients. Preventive health programs can improve measured cognitive performance in at-risk people, though the long-term consequences still need study. Better support for care partners is both a scientific and a moral priority.

Our horizon is larger than any one of those advances. The aim is not merely to add treatments to a disorder. It is to make more of life possible-through the years of health before illness, the years of uncertainty, and the days when care itself becomes an expression of what matters most.

Sources and further reading

• **PMID:39096926** - 2024 Lancet dementia prevention, intervention and care Commission

• **PMID:25771249** - FINGER two-year multidomain randomized trial

• **PMID:40720610** - US POINTER randomized multidomain lifestyle

• **PMID:30688979** - SPRINT MIND cognitive outcomes randomized BP trial

• **PMID:37478886** - ACHIEVE hearing intervention vs health education

• **PMID:36449413** - CLARITY AD lecanemab phase 3

• **PMID:37459141** - TRAILBLAZER-ALZ 2 donanemab phase 3

• **DM:LEQEMBI:v24** - LEQEMBI current US label

• **DM:KISUNLA:v8** - KISUNLA current US label

• **FDA:LUMIPULSE:2025** - FDA clearance of first Alzheimer blood test

• **ROCHE:ELECSYS:2026-08** - FDA decision: Elecsys pTau217 Plasma, K261686, August 19, 2026

• **DOI:10.1002/alz.70535** - Alzheimer Association blood biomarker clinical practice guideline

• **DOI:10.1002/alz.14333** - DETeCD-ADRD guideline for primary care

• **PMID:39878968** - D-CARE pragmatic randomized clinical trial

• **PMID:40892399** - D-CARE prespecified secondary outcomes

• **PMID:42964515** - Multimodal NeuroMarker digital MCI discrimination

- **PMID:42950057** - 8-oxoGTP neuroinflammation in aging mouse brain
- **PMID:42600613** - Perivascular macrophage cMAF program in mouse and human
- **PMID:42957838** - Glymphatic dysfunction multisystem Alzheimer review
- **PMID:42962664** - Neurobiology of menopause and brain aging
- **PMID:42964287** - Taxonomy of dementia caregiver mental health and tech needs
- **PMID:42956288** - Dyadic dementia technology interventions in middle-income countries
- **PMID:42956859** - Caregiving unmet social needs and cardiovascular risk
- **PMID:42959433** - Retraction notice: chronic/nonchronic pain and dementia
- **PMID:42340126** - Cost of dementia in the US in 2026
- **CMS:GUIDE** - CMS GUIDE dementia experience model
- **NICE:NG97** - NICE dementia assessment management guideline
- **FDA:AUVELITY:2026-04** - FDA Auvelity approval for AD agitation
- **DM:AUVELITY:v18** - Auvelity US label current
- **FDA:REXULTI:2023-05** - FDA brexpiprazole agitation AD approval
- **PMID:42957174** - VR group reminiscence therapy in Alzheimer’s disease

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