

Advancements Build Momentum: 10 Years of Alzheimer's Disease and Related Dementias Research



National Institutes of Health



Table of Contents

Introduction.....	3	Advanced Clinical Research on Lifestyle Interventions	16
Advanced Understanding of the Risk Factors, Genetics, and Mechanisms of Disease in Dementia.....	5	Increased Understanding of How Social and Physical Environmental Factors Affect Dementia Risk and Disparities	18
Diversified and De-Risked the Therapeutic Pipeline for Disease-Modifying Drugs	8	Expanded Research on Dementia Care and Care Partner Supports.....	20
Advanced Drug Repurposing and Combination Therapy Development	11	Looking Forward.....	22
Discovered Tools to Detect, Diagnose, and Monitor Dementia	13	Appendix: References and Citations	23

SPOTLIGHTS

Translating Discoveries to the Clinic	4	Population Studies Reveal Dementia Prevalence and Disparities	19
Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) Study	10	Population Studies Uncover Dementia Risk and Protective Factors	19
Digital Health Technologies Come of Age	15		



Over the past **10 years**, the NIH, led by NIA and NINDS, significantly **expanded its investments** in Alzheimer's and related dementias research.

Introduction

An estimated 6.7 million Americans are currently living with [Alzheimer's disease](#). Worldwide, more than 50 million people have dementia, a diagnosis that may include Alzheimer's or a related disorder such as [frontotemporal disorders](#), [Lewy body dementia](#), or [vascular dementias](#).

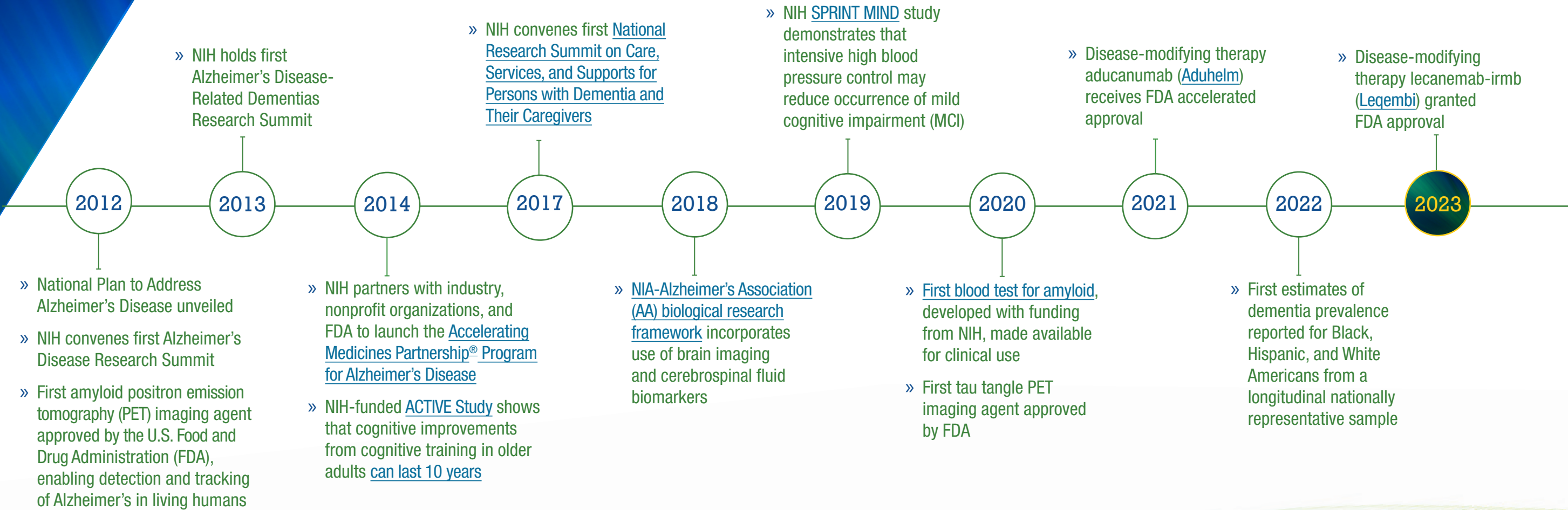
This public health challenge takes a tremendous emotional, physical, and financial toll on those living with these diseases and their caregivers.

The [National Plan to Address Alzheimer's Disease](#), which arose from the [National Alzheimer's Project Act](#), spurred a substantial increase in federal funding for dementia research. As a result, over the past 10 years, the [National Institutes of Health](#) (NIH), led by its [National Institute on Aging](#) (NIA) and [National Institute of Neurological Disorders and Stroke](#) (NINDS), significantly expanded its investments in Alzheimer's and related dementias research across the United States and beyond. Through enhanced collaboration and innovative partnerships with industry, other agencies, and people living with dementia and their families, NIH has:

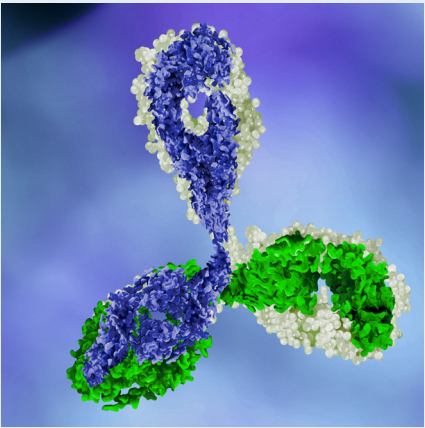
- » Advanced understanding of the risk factors, genetics, and mechanisms of disease in dementia
- » Diversified and de-risked the therapeutic pipeline for disease-modifying drugs
- » Advanced drug repurposing and combination therapy development
- » Discovered tools to detect, diagnose, and monitor dementia
- » Advanced clinical research on lifestyle interventions
- » Increased understanding of how social and physical environmental factors affect dementia risk and disparities
- » Expanded research on dementia care and care partner supports

*Worldwide, more than **50 million people** have dementia, a diagnosis that may include **Alzheimer's** or a related disorder such as frontotemporal disorders, Lewy body dementia, or vascular dementias.*

A Decade of Progress



SPOTLIGHT



Translating Discoveries to the Clinic

The increased federal investment in Alzheimer's and related dementias research in recent years yielded discoveries that advanced diagnostics, treatments, and potential preventions.

For example, the anti-amyloid antibody lecanemab-irmb ([Leqembi](#)) received FDA

approval in 2023 based on a demonstrated effect in slowing cognitive decline. It is the first traditional (full) approval of a treatment that affects the underlying disease process of Alzheimer's instead of only treating the symptoms of the disease. NIH support laid essential groundwork for the pharmaceutical company trials that led to this decision. Not only was the agency's funding integral in

understanding the role of amyloid, the protein targeted by lecanemab, the industry trials hinged on the use of amyloid PET imaging, a technology developed with NIH-funded research. Researchers also recently found that [donanemab](#), another anti-amyloid drug, was effective in slowing the rates of cognitive and functional decline in participants who have early symptoms of Alzheimer's.

Advanced Understanding of the Risk Factors, Genetics, and Mechanisms of Disease in Dementia

Ten years ago, scientists knew of only 10 genes linked to Alzheimer's disease; today, we know of more than 70 relevant genetic regions, findings made in large part thanks to NIH funding. And although we knew years ago that the *APOE* ϵ 4 variant of the *APOE* gene is a significant genetic risk factor for Alzheimer's, we did not know why. Today, scientists know much more about the function of APOE protein — for example, it seems to influence all forms of dementia.



NIH-funded research suggests that the *APOE* ϵ 4 gene can cause brain cells to build up abnormal amounts of [lipids](#) instead of using them to insulate nerve fibers. Another study found that high levels of *APOE*4 protein in neurons trigger an [immune pathway](#) that leads to tau tangles and cell death. These findings are leading to new approaches in developing potential dementia therapeutics.

Still, the genetics of Alzheimer's is complex. NIH-funded researchers found that *APOE* ϵ 4 is not as strong a predictor of risk in certain ethnic and racial groups, including those of African and [American Indian](#) ancestry, as it is in people of European ancestry. These findings underscore the importance of conducting more diverse population studies to determine specific genetic risk factors across racial and ethnic groups.

Beyond risk genes, scientists are also uncovering rare gene variants that may help protect against Alzheimer's disease. These include an *APOE* variant called [APOE3ch](#) and a variant of the *RELN* gene called *RELN-COLBOS*. Understanding how these rare variants promote dementia resilience opens up new avenues for developing treatments.

Decoding the genetics of Alzheimer's-related dementias

Scientists have also advanced our understanding of the genetic underpinnings of related dementias. For example, we now know that genetic cases of frontotemporal dementia are mostly caused by mutations in one of three genes: *C9ORF72*, *MAPT*, or *GRN*. A recent NIH-funded study revealed how specific mutations in these genes [affect the age of onset and duration](#) of frontotemporal dementias, which vary considerably. Understanding the causes of variation in age of onset could provide important clues about what causes frontotemporal dementias.

NIH scientists have also found [two new genes involved in Lewy body dementia](#), demonstrating how risk genes often overlap across neurodegenerative diseases: One of these genes, *BIN1*, is also linked to Alzheimer's disease, while the other, *TMEM175*, is involved in Parkinson's disease.

Identifying shared mechanisms of Alzheimer's disease and mixed dementias

As research continues, scientists are finding more commonalities across different forms of dementia. Once considered completely separate, brain changes found in Alzheimer's, Lewy body dementias, frontotemporal dementias, and vascular dementias often overlap. This includes sharing risk factors, such as *APOE* ϵ 4 and other genes, and associated disease processes, such as buildup and spread of misfolded proteins in the brain and loss of synaptic connections between neurons.

It is now understood that the pathologies thought to define distinct forms of dementia commonly co-occur: This is called mixed dementia. For example, Alzheimer's pathology (beta-amyloid plaques and tau tangles) most commonly co-occurs with cerebrovascular disease (problems with blood vessels and blood flow in the brain) or Lewy bodies (alpha-synuclein clumps).

Moreover, abnormal forms of a protein called TDP-43 are not limited to frontotemporal dementia but are commonly found with Alzheimer's pathology and hippocampal sclerosis. Recently, another misfolded

protein, TMEM106B, was also linked to diagnoses of Alzheimer's, Lewy body dementia, and frontotemporal dementias.

Scientists continue to learn how having multiple dementias may shape the course of disease, paving the way for personalized treatment approaches.

Discovering a common and under-recognized form of dementia

Our appreciation of the complexities and forms of dementia continues to evolve. Research from the [NIA Alzheimer's Disease Research Centers](#) recently led to the [discovery and classification of a new form of dementia](#) called limbic-predominant age-related TDP-43 encephalopathy (LATE). [LATE is relatively common](#), and clinical symptoms associated with it mimic the clinical features of Alzheimer's, meaning that some people clinically diagnosed with Alzheimer's may have more LATE pathology than typical Alzheimer's pathology.

Though it is not yet possible to identify LATE during life, researchers are investigating ways to diagnose it in living people. This would help in determining the most effective treatments, including personalized therapies, and in the selection of appropriate participants for dementia studies.

Investigating the higher risk of Alzheimer's in women and other groups

Women have a higher risk than men of developing Alzheimer's over their lifetimes. NIH-funded researchers are working to discover why. Recently, studies pointed to having an [additional copy of certain genes](#), [hormonal changes](#) during menopause, and differences in [how the brain makes energy as potential causes](#) of the differences.

Additionally, people with [Down syndrome](#) are at high risk of developing Alzheimer's because they carry an extra copy of the amyloid precursor protein gene. NIH-funded researchers found that Alzheimer's progression in Down syndrome is [similar to other genetic, early onset forms of the disease](#). This suggests that those living with Down syndrome may benefit from participating in studies — some of which are already in progress — on Alzheimer's therapies aimed at slowing formation of amyloid plaques.

Some individuals have a higher risk than others of developing Alzheimer's over their lifetimes. NIH-funded researchers are working to discover why.

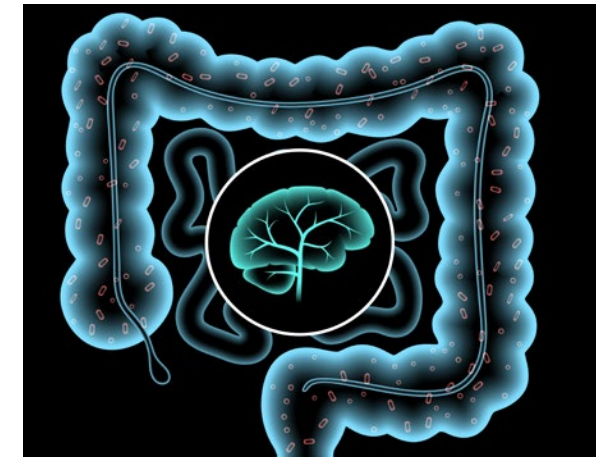
Looking beyond the brain to the gut and liver

Ten years ago, dementia research focused almost solely on the brain. Today, NIH-funded researchers are exploring other organ associations, including links between the digestive and vascular systems. For example, the gut [microbiome's](#) role in inflammation and other disease processes has been associated with dementia in several studies. Ongoing NIH-funded microbiome research may also help explain why subgroups of people with Alzheimer's respond differently to dietary and other interventions.

Research also points to a gut-liver-brain connection in dementia through the production of bile acids as well as key lipids that are needed by the brain.

Uncovering vascular contributions to cognitive impairment and dementia

[Vascular dementias](#) are no longer considered a separate form of dementia. More than 50% of



dementia cases also show damage to the brain's vascular system, which is made up of blood vessels that supply oxygen and other nutrients to the brain. Commonly identified through MRI scans, this damage is termed “diffuse white matter disease.” NIH-funded scientists are exploring this connection — known as vascular contributions to cognitive impairment and dementia — to better understand how and when vascular damage occurs. For example, their research has shown that key dementia proteins such as beta-amyloid can build up in the brain's blood vessels or alter blood vessel formation and function. Injury to these affected blood vessels is a fairly common complication of the anti-amyloid therapies and can lead to brain swelling and bleeding in the brain.



Understanding neuropsychiatric symptoms in dementia

Neuropsychiatric symptoms such as psychosis, agitation, depression, sleep disturbance, and apathy are quite common in dementia. They can be among the most terrifying symptoms to patients, distressing to their care partners and families, and greatly affect quality of life. Among other initiatives to further study these symptoms, NIA collaborated with the NIH National Institute of Mental Health to launch the [Psych-AD program](#), which is designed to better understand the molecular underpinnings of neuropsychiatric symptoms in dementia. The aim is to discover better biomarkers and targets for treatment of these symptoms.

Diversified and De-Risked the Therapeutic Pipeline for Disease-Modifying Drugs

Over the past decade, NIH funding has enabled the development and testing of 18 new dementia drug candidates in clinical trials, with two more ready to enter trials.

NIA-Supported Drug Candidates That Have Advanced To Clinical Development



Drug Candidate/
Therapy Type



Targeted Biology
(CADRO Theme)

PHASE I

AV-1959D (DNA vaccine)	Amyloid beta
AAV2-BDNF (Gene Therapy)	Growth Factors and Hormones
ACU193 (Immunotherapy - Monoclonal Antibody)	Amyloid beta
BMS-984923	Neurotransmitter Receptors
MW150	Inflammation
MW151	Inflammation
Posiphen	Proteostasis/Proteinopathies
OLX-07010	Tau
CS6253	ApoE, Lipids and Lipoprotein Receptors
NNI-362	Neurogenesis
J147	Metabolism and Bioenergetics
CMS121	Multi-target

PHASE II

Allopregnanolone	Multi-target
PU-AD/PU-HZ151/lcapamespib	Proteostasis/Proteinopathies
MW189	Inflammation
LM11A-31	Amyloid beta
CT1812	Amyloid beta
BPN14770/Zatolmilast	Neuroprotection/Resilience

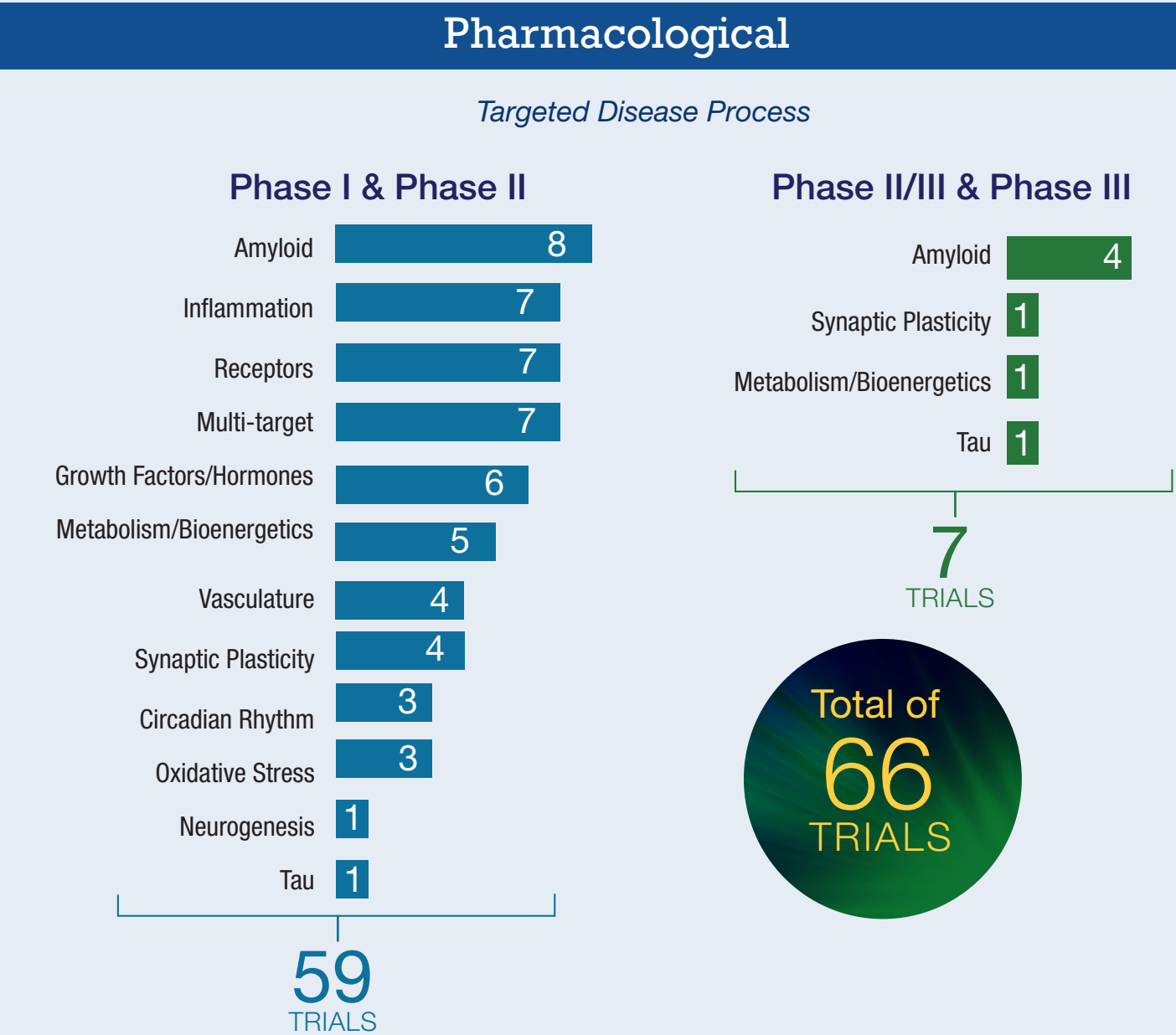
Because of the substantial progress in understanding how dementia unfolds and NIH’s robust investment in drug development programs, the portfolio of drug candidates continues to expand and help de-risk further investment by the private sector. These drug candidates are intended to stop or slow the disease process rather than only treat symptoms, and some target amyloid plaques and tau tangles in new ways. Building upon our understanding of [mechanisms of disease in dementia](#), most new drug candidates target other aspects of the disease, including problems with the immune system, proper protein assembly and removal, lipid balance, or metabolism.



SPOTLIGHT

Diversity of drug targets in active clinical trials

The breadth of mechanisms under study is increasing.



SPOTLIGHT

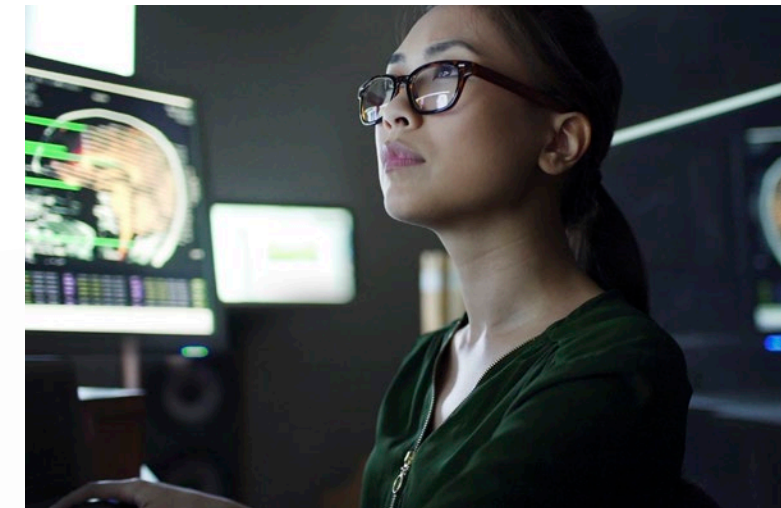
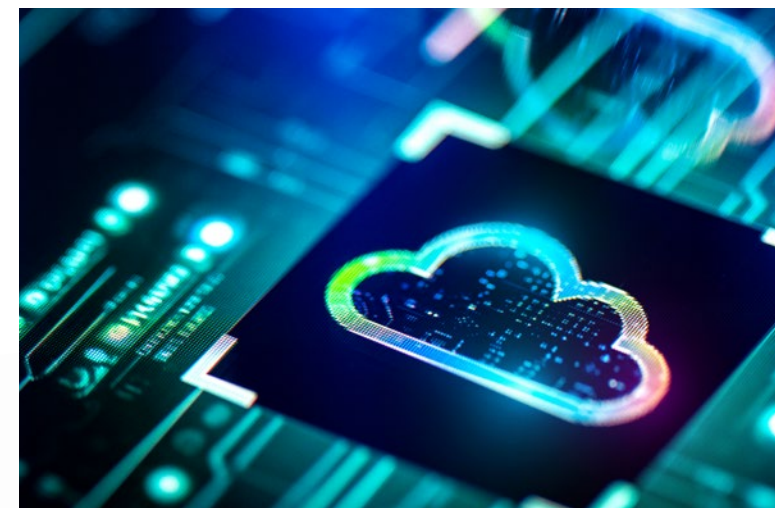
Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) Study



The [Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease \(A4\) study](#), launched in 2014, is an ongoing prevention trial to test whether the drug solanezumab could slow cognitive decline associated with high brain amyloid if started before clinical symptoms of Alzheimer's appeared. The findings were not positive, but they were definitive. Preliminary results showed [solanezumab did not slow cognitive decline](#) before clinical symptoms developed. However, information from the study has [advanced our understanding of Alzheimer's disease](#), and biosamples and detailed, patient-level data from the approximately 1,300 participants in the A4 trial will be available to the research community soon, enabling further discoveries about the disease and differences in the responsiveness to treatment.

Investing in Innovation for Tomorrow's Breakthroughs

Through its open science approaches, NIH has accelerated the pace and efficiency of dementia research progress. Specifically, the agency's investments in [centralized data-sharing platforms and other technologies](#) make it possible for scientists to more freely share data, tissue samples, and other crucial research resources more broadly and effectively.



Advanced Drug Repurposing and Combination Therapy Development

Drugs that are already FDA-approved to treat diseases other than dementia may hold a key to effectively treating Alzheimer's and related disorders.



Researchers are exploring multiple ways to repurpose drugs either alone or in combination with another therapeutic through initiatives such as the [NIA Advancing Combination Therapy and Drug Repurposing for Alzheimer's Disease \(ACTDRx AD\)](#) program. The [Metformin in Alzheimer's Dementia Prevention \(MAP\) study](#), another late-stage trial in Phases 2b and 3, tests metformin, an FDA-approved medication for diabetes that has been repurposed to treat MCI and early-onset Alzheimer's. MAP is testing the safety and effectiveness of metformin and is currently recruiting participants. This trial is projected to be completed in 2026.

An antiepileptic drug to treat Alzheimer's

Thirty years of NIH-funded basic and translational research led to the discovery of a new mechanism for memory loss and the development of AGB101 as a possible new treatment for Alzheimer's. AGB101 is a long-lasting version of the FDA-approved

antiepileptic drug levetiracetam. Results from a recently completed [Phase 3 clinical trial](#) on the effectiveness of AGB101 for MCI caused by Alzheimer's disease are forthcoming.

A water pill for people at high genetic risk of Alzheimer's

By combining precision medicine and big data methods, an NIH-funded study identified [bumetanide as a candidate](#) for lowering the risk of Alzheimer's disease in people who carry the *APOE* $\epsilon 4$ variant. Bumetanide is a common FDA-approved diuretic; further tests and clinical trials for its use in reducing Alzheimer's risk are needed.

*An NIH-funded study found a water pill may be a candidate for lowering the risk of Alzheimer's disease in people who carry the *APOE* $\epsilon 4$ variant*



Discovered Tools to Detect, Diagnose, and Monitor Dementia

A timely and accurate dementia diagnosis is crucial for determining treatment options and selecting participants for the most relevant clinical trials. Before the early 2000s, autopsy was the only sure way to diagnose Alzheimer's. Currently, **biomarkers** are helping researchers diagnose dementia, monitor its progression, and gauge response to treatments. Often found in body fluids or with imaging, biomarkers are signs of what is happening in the body. Importantly, newer biomarkers can be collected non-invasively, which will make both clinical research and personalizing treatments for individual patients considerably easier.



Toward a biological definition of Alzheimer's disease

NIH-funded research enabled the development of PET scans that detect abnormal beta-amyloid plaques in the brain, which can rule out other causes of cognitive impairment and support an Alzheimer's diagnosis. More recently, [PET scans have been developed to detect tau tangles](#), another hallmark of Alzheimer's.

We can also measure proteins in an individual's cerebrospinal fluid, sampled through a lumbar puncture, as a biomarker for abnormal beta-amyloid or tau in the brain.

These imaging and spinal fluid biomarkers formed the basis of the [2018 NIA-AA Biological Research Framework](#), which has helped substantially in developing a biologically based definition of Alzheimer's.

Blood-based biomarkers as a less expensive and less invasive option

An ideal biomarker test is minimally invasive and can be used in virtually any doctor's office. Thanks in large part to NIH funding, the [first blood-based biomarker test for Alzheimer's](#) is now available to many doctors, dependent on state-specific availability reflecting FDA guidelines, to help support diagnosis. Developed by C₂N Diagnostics, the [PrecivityAD™ blood test](#) can accurately predict the [presence of beta-amyloid plaques in the brain](#) based on blood beta-amyloid levels, age, and APOE status.

The blood test is also being used in many clinical trials, such as to help select participants for the NIH-funded [AHEAD Study](#). This trial

is testing whether the newly FDA-approved drug lecanemab can prevent Alzheimer's disease in at-risk people without symptoms.

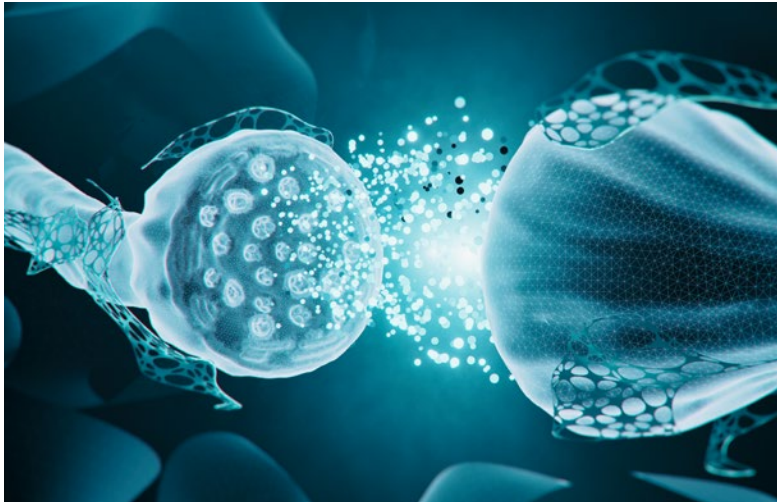
Scientists also continue to study different forms of the tau protein as a biomarker, including how well they work to predict dementia risk in different racial and ethnic groups. For example, in a multi-ethnic community-based sample, one form of tau was recently found to be a [more accurate Alzheimer's marker](#) than beta-amyloid in diverse populations.

Emerging biomarkers

Discoveries in recent years point to new potential biomarkers, such as measuring brain inflammation or detecting [abnormal TDP-43](#), which is found in frontotemporal dementias. Because of NIH funding, other biomarkers in development for detecting or monitoring dementia include the following:

» **Alpha-synuclein:** Clumped forms of alpha-synuclein are found in the brains of people with Parkinson's disease and Lewy body dementias. A [cerebrospinal fluid test](#) for abnormal alpha-synuclein received FDA breakthrough device designation in 2019. Researchers are also developing a skin test for this biomarker that would be less invasive than a lumbar puncture.

- » **Brain damage:** Researchers found that a protein called neurofilament light chain (NfL), which is released when nerve cells are damaged, may be a [useful biomarker for familial Alzheimer's](#) and frontotemporal dementia.
- » **Problems at the synapse:** Synapses are the spaces where neurons communicate with each other, but in Alzheimer's and some other dementias, the synapses can stop working. In 2021, [Alzheimer's Disease Neuroimaging Initiative \(ADNI\)](#) researchers identified a promising biomarker, NPTX2, for synaptic dysfunction and Alzheimer's progression.
- » **Vascular changes:** White matter lesions, which can be seen as bright white areas on brain images, have been linked with dementia. They have many causes, some of which are related to vascular changes, or changes in blood flow. [A large, diverse cohort study](#) is examining the role of white matter lesions in cognitive impairment and dementia.



Discovering early indicators of dementia

In addition to these biomarkers, NIH-funded research has revealed other indicators that could help identify people in the earliest stages of dementia:

- » **Money management:** People with dementia were more likely to [miss credit card payments](#) as early as six years before their diagnosis.
- » **Driving behavior:** Several recent studies show how tracking driving behavior with GPS can help identify people with preclinical Alzheimer’s (who have biomarkers for the disease but do not have symptoms). These behaviors, such as hard braking, increased over time, corresponding with an increase in the biomarkers.
- » **Early chronic pain:** People with dementia may experience [increased levels of pain](#) as early as 16 years before their dementia diagnosis. Though it is unlikely that pain causes or increases the risk for dementia, chronic pain may be an early indicator before other signs appear.

As early as six years before their diagnosis, people with dementia were more likely to miss credit card payments.

SPOTLIGHT



Digital Health Technologies Come of Age

NIH-funded researchers are advancing up-and-coming digital biomarkers for dementia, such as the use of digital devices to evaluate memory or learning through computer tasks. Recently, a tool that uses electronic health record data to [detect unrecognized dementia](#) was developed and validated.

For people diagnosed with dementia, wearable devices could enable doctors to monitor daily function and possible disease progression by tracking sleep patterns, gait, and mobility.



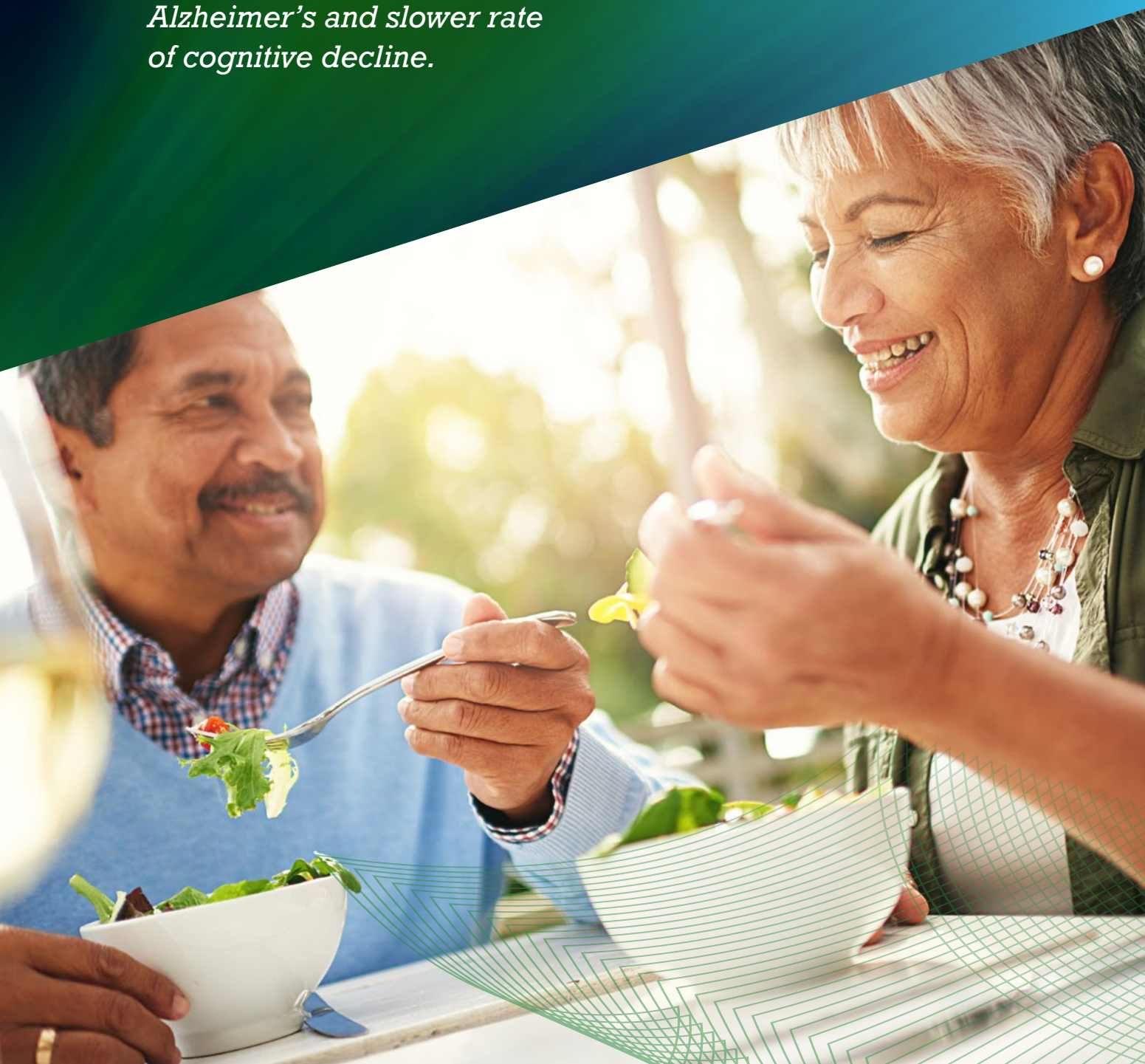
Advanced Clinical Research on Lifestyle Interventions

More scientific evidence is still needed, but strategies are emerging to potentially reduce dementia risk or delay its onset and progression. A **2017 evidence-based, NIA-commissioned report** concluded that evidence on lifestyle factors to prevent Alzheimer's, such as physical activity, blood pressure management, and cognitive training, is "encouraging although inconclusive."

Since then, scientists have strengthened this knowledge base. For example, the NIH-funded **SPRINT MIND trial** indicates intensive blood pressure control may **slow age-related brain damage** and **reduce the risk of MCI**.

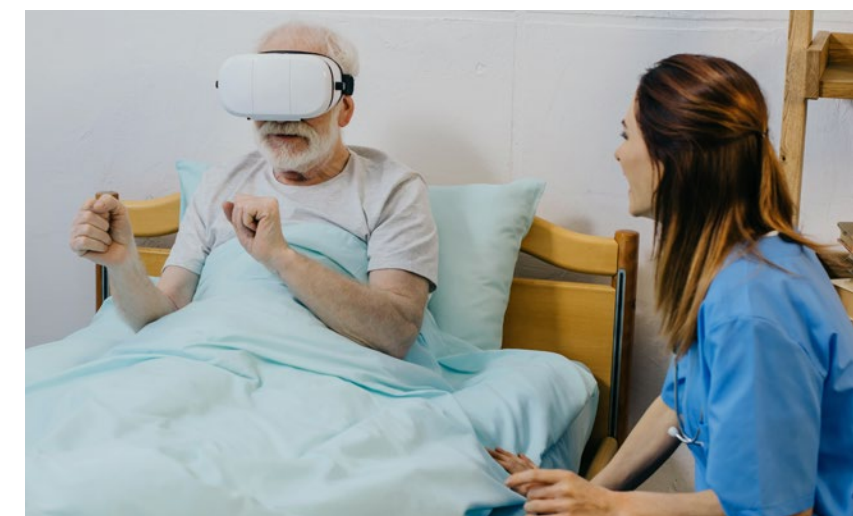


NIA-funded research found that a hybrid Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diet, called the MIND diet, was associated with a lower incidence of Alzheimer's and slower rate of cognitive decline.



Brain training may improve some cognitive function

Past NIH-funded research has suggested that [cognitive training improves certain aspects of cognitive function](#) in older adults. A large, multisite [clinical trial](#) is currently assessing the efficacy of a similar cognitive training program to prevent or delay dementia onset. According to another NIH-funded study, engaging with new 3D virtual environments, such as 3D video games, may improve recognition memory.



Clinical trials are now in progress to test the effect of physical activity on cognitive function and dementia risk.

Dietary and physical activity interventions

Dietary interventions continue to be a key focus of NIH research on dementia risk reduction. NIA-funded research found that in observational studies, the MIND diet, a hybrid Mediterranean-Dietary Approaches to Stop Hypertension (DASH) diet, was associated with a lower incidence of Alzheimer's and a slower rate of cognitive decline. Other areas being investigated include [multivitamins](#) and a modified [ketogenic diet](#).

Emerging areas of focus

An emerging area of investigation is on interventions to enhance cognitive reserve, the mind's ability to cope with the effects of aging. Other evolving focuses include interventions to potentially compensate for premature cognitive decline and dementia linked to adverse exposures in early life, such as neglect, abuse, and malnutrition.

Increased Understanding of How Social and Physical Environmental Factors Affect Dementia Risk and Disparities

Alzheimer's and related dementias do not affect all populations equally. Compared with White Americans, Hispanic Americans are 1.5 times as likely to develop dementia, and Black Americans are twice as likely. Despite this, NIH-funded research shows that dementia is under-diagnosed in these populations, pointing to the need for approaches to improve diagnoses in underserved communities.



Diving deeper into health disparities

Scientists are now uncovering biological mechanisms that underpin health disparities. Social stress, including discrimination, has been shown to contribute to [accelerated aging of the immune system](#), which can play a key role in Alzheimer's disease.

In addition, [high blood pressure is a risk factor for dementia](#) and is more prevalent in Black Americans than in other racial and ethnic groups in the United States.

Through ongoing [clinical studies](#), researchers are testing culturally sensitive interventions aimed at reducing dementia disparities by addressing risk factors and improving the well-being of people with dementia. Other scientists are examining how to tackle larger-scale issues, including [health care access](#) and [delivery](#).



Environment influences brain health

Many aspects of a person's life can affect their risk of developing dementia. These factors include everything from education and social status to where someone lives to their physical activity level. NIH-funded researchers are discovering how all these factors, collectively called the "[exposome](#)," affect dementia.

For example, [higher education levels](#) may help preserve cognitive function and reduce the risk for dementia. Living near green spaces, such as parks and gardens, is also linked with [higher cognitive function](#). In contrast, long-term exposure to air pollution raises the risk of dementia. Ongoing research is exploring how other aspects of the exposome, such as [workplace exposures](#) and [heavy metals](#), may contribute to dementia risk and disparities.

SPOTLIGHTS

Population Studies Reveal Dementia Prevalence and Disparities

A recent NIH-funded study estimates that 10% of Americans age 65 and older have dementia and that 22% have MCI. Consistent with other studies, the researchers found higher prevalence for both Black and Hispanic Americans, as well as for people with lower levels of education.



Population Studies Uncover Dementia Risk and Protective Factors

NIH-funded research has uncovered new environmental, sociocultural, and behavioral factors throughout life that are associated with dementia. Understanding whether and how these factors affect dementia risk can point to potential prevention strategies to help lower that risk.

- » **Social engagement:** [Regularly seeing friends and family in midlife](#) is linked to a lower risk of a dementia diagnosis later in life. In another study, [women who were employed](#) during early adulthood and midlife had slower rates of memory decline than those who did not work.
- » **Sleep:** [Insufficient sleep in middle age](#) is associated with a higher risk of dementia later in life.
- » **Personality traits:** Certain [personality traits in adolescence](#) are linked with lower dementia risk 50 years later. In another study, [neuroticism](#) (a tendency to feel self-doubt, anxiety, and other negative feelings) was linked with more amyloid and tau buildup in the brain, while conscientiousness was linked with less buildup.

Expanded Research on Dementia Care and Care Partner Supports

Informed by its National Research Summit on Care, Services, and Supports for Persons Living with Dementia and Their Care Partners/Caregivers, NIH has significantly expanded research on how to improve dementia care and support for care partners over the past decade.



Identifying costs and challenges in dementia care

A [2021 NIH-funded study](#) found that people with dementia who have an adult child available for caregiving are less likely to require paid care and transition into a nursing home. A growing movement to care for people with dementia outside of a nursing home setting means more hands-on care delivered in the community. Other studies are illuminating the costs of care, challenges, and need to support family care partners and have found the following:

- » People with dementia and their families [shoulder more of the costs of care](#) when these individuals live in the community, such as at home or with family members, than when they live in a nursing home or other residential facility. These costs do not factor in lost wages from caregiving.
- » Paid care partners, such as home health aides, can help family caregivers to enable people with dementia to live safely at home and in the community. However, according to a [2020 study](#), only one in four community-dwelling individuals with dementia received paid care. People in the middle-income range were less likely than those with higher incomes or on Medicaid to receive paid care, underscoring the need to make paid care more accessible.



Improving quality of life for people with dementia and their care partners

Supporting care partners means assisting with the day-to-day challenges of caring for a loved one with dementia. In a [2021 evidence-based, NIH-commissioned report](#), the National Academies of Sciences, Engineering, and Medicine found two promising intervention types. These were collaborative care models that coordinate a dementia care team of experts to support care partners and REACH (Resources for Enhancing Alzheimer's Caregiver Health) interventions that provide care partners with knowledge and resources.

Further dementia care intervention research will continue to expand the evidence base. In addition, [telehealth programs](#) developed and tested by NIH-funded researchers show promise in boosting dementia care and care partner support. Through these programs, people with dementia and their caregivers are provided with at-home access to care expertise and online care partner education.

Making an IMPACT

Launched in 2019, researchers in the [IMbedded Pragmatic Alzheimer's disease and related dementias Clinical Trials \(IMPACT\) Collaboratory](#) test interventions to improve care of people with dementia in real-world settings. [Projects currently underway](#) include empowering emergency department nurses to improve detection of dementia in patients and strategies to improve dementia training and care management across interdisciplinary teams.

A 2021 IMPACT Collaboratory study found that [COVID-19 was more severe](#) in nursing home residents who were more cognitively impaired.

Looking Forward

Through sustained NIH investment, scientists have made significant strides in understanding Alzheimer's and related dementias, and progress toward how to effectively diagnose, treat, and prevent them. Milestone therapeutic advancements mark the beginning of a new era of promise for the field and have reinforced the importance of pursuing amyloid as a strategic therapeutic target. These discoveries would not have been possible without the hard work and dedication of researchers, study participants, caregivers, and other stakeholders.

To ensure that dementia discoveries are broadly applicable, a top priority is for [clinical trials and observational studies to better represent the diversity](#) of the United States. Equally important is [supporting a diverse dementia research workforce](#) through [Scientific Workforce Diversity Programs](#).

NIH is also expanding its dementia research portfolio into emerging scientific areas including precision environmental health. Researchers in this field study how factors in the environment, such as pollution, chemicals, and metals, interact with an individual's genetics to affect the risk of dementia.

With continued commitment to scientific collaboration, data sharing, and innovative research, NIH is well positioned to fuel tomorrow's breakthroughs.



Learn about future efforts in *[A New Era: Driving Momentum in Alzheimer's and Related Dementias Research](#)*

Appendix: References and Citations

Introduction

Rajan KB, et al. [Population estimate of people with clinical Alzheimer’s disease and mild cognitive impairment in the United States \(2020 - 2060\)](#). *Alzheimer’s & Dementia*. 2021;17(12):1966-1975. doi: 10.1002/alz.12362.

Alzheimer’s Disease International. [Numbers of people with dementia worldwide: an update to the estimates in the World Alzheimer Report 2015](#). 2017.

Section 1. Advanced Understanding of the Risk Factors, Genetics, and Mechanisms of Disease in Dementia

Blanchard JW, et al. [APOE4 impairs myelination via cholesterol dysregulation in oligodendrocytes](#). *Nature*. 2022;611(7937):769-779. doi: 10.1038/s41586-022-05439-w.

Zalocusky KA, et al. [Neuronal ApoE upregulates MHC-I expression to drive selective neurodegeneration in Alzheimer’s disease](#). *Nature Neuroscience*. 2021;24(6):786-798. doi: 10.1038/s41593-021-00851-3.

Bakulski KM, et al. [Cumulative genetic risk and APOE ε4 are independently associated with dementia status in a multiethnic, population-based cohort](#). *Neurology Genetics*. 2021;7(2):e576. doi: 10.1212/NXG.0000000000000576.

Suchy-Dicey A, et al. [APOE genotype, hippocampus, and cognitive markers of Alzheimer’s disease in American Indians: data from the Strong Heart Study](#). *Alzheimer’s & Dementia*. 2022;18(12):2518-2526. doi: 10.1002/alz.12573.

Aguillon D, et al. [APOE3 Christchurch mutation carriers from the Colombian kindred with autosomal dominant Alzheimer’s disease due to PSEN1 E280A](#). *Alzheimer’s & Dementia*. 2022;18(S3):e068060. doi: 10.1002/alz.068060.

Lopera F, et al. [Resilience to autosomal dominant Alzheimer’s disease in a Reelin-COLBOS heterozygous man](#) [published online ahead of print, 2023 May 15]. *Nature Medicine*. 2023;10.1038/s41591-023-02318-3. doi: 10.1038/s41591-023-02318-3.

Moore KM, et al. [Age at symptom onset and death and disease duration in genetic frontotemporal dementia: An international retrospective cohort study](#). *Lancet Neurology*. 2020;19(2):145-156. doi: 10.1016/S1474-4422(19)30394-1.

Robinson JL, et al. [Neurodegenerative disease concomitant proteinopathies are prevalent, age-related and APOE4-associated](#). *Brain*. 2018;141(7):2181-2193. doi: 10.1093/brain/awy146.

Jin Y, et al. [APOE ε4 exacerbates α-synuclein seeding activity and contributes to neurotoxicity in Alzheimer’s disease with Lewy body pathology](#). *Acta Neuropathologica*. 2022;143(6):641-662. doi: 10.1007/s00401-022-02421-8.

Dickson DW, et al. [APOE ε4 is associated with severity of Lewy body pathology independent of Alzheimer pathology](#). *Neurology*. 2018;91:e1182-e1195. doi: 10.1212/WNL.00000000000006212.

Jiang YX, et al. [Amyloid fibrils in FTL-D-TDP are composed of TMEM106B and not TDP-43](#). *Nature*. 2022;605:304-309. doi: 10.1038/s41586-022-04670-9.

Chang A, et al. [Homotypic fibrillization of TMEM106B across diverse neurodegenerative diseases](#). *Cell*. 2022;185(8):1346-1355.e15. doi: 10.1016/j.cell.2022.02.026.

Schweighauser M, et al. [Age-dependent formation of TMEM106B amyloid filaments in human brains](#). *Nature*. 2022;605(7909):310-314. doi: 10.1038/s41586-022-04650-z.

Cornblath EJ, et al. [Defining and predicting transdiagnostic categories of neurodegenerative disease](#). *Nature Biomedical Engineering*. 2020;4(8):787-800. doi: 10.1038/s41551-020-0593-y.

Demarest TG, et al. [Biological sex and DNA repair deficiency drive Alzheimer’s disease via systemic metabolic remodeling and brain mitochondrial dysfunction](#). *Acta Neuropathologica*. 2020;140(1):25-47. doi: 10.1007/s00401-020-02152-8.

Yan Y, et al. [X-linked ubiquitin-specific peptidase 11 increases tauopathy vulnerability in women](#). *Cell*. 2022;185(21):3913-3930.e19. doi: 10.1016/j.cell.2022.09.002.

Xiong J, et al. [FSH blockade improves cognition in mice with Alzheimer’s disease](#). *Nature*. 2022;603(7901):470-476. doi: 10.1038/s41586-022-04463-0.

Seo D-O, et al. [ApoE isoform- and microbiota-dependent progression of neurodegeneration in a mouse model of tauopathy](#). *Science*. 2023;379(6628):eadd1236. doi: 10.1126/science.add1236.

Sampson TR, et al. [A gut bacterial amyloid promotes α-synuclein aggregation and motor impairment in mice](#). *eLife*. 2020;9:e53111. doi: 10.7554/eLife.53111.

Vogt NM, et al. [Gut microbiome alterations in Alzheimer’s disease](#). *Scientific Reports*. 2017;7(1):13537. doi: 10.1038/s41598-017-13601-y.

Hemraj B. et al. [Sex-specific effects of microbiome perturbations on cerebral Aβ amyloidosis and microglia phenotypes](#). *Journal of Experimental Medicine*. 2019;216(7):1542–1560. doi: 10.1084/jem.20182386.

Kling MA, et al. [Circulating ethanolamine plasmalogen indices in Alzheimer’s disease: relation to diagnosis, cognition, and CSF tau](#). *Alzheimer’s & Dementia*. 2020;16(9):1234-1247. doi: 10.1002/alz.12110.

Nho K, et al. [Altered bile acid profile in mild cognitive impairment and Alzheimer’s disease: relationship to neuroimaging and CSF biomarkers](#). *Alzheimer’s & Dementia*. 2019;15(2):232-244. doi: 10.1016/j.jalz.2018.08.012.

Bourassa P, et al. [Beta-amyloid pathology in human brain microvessel extracts from the parietal cortex: relation with cerebral amyloid angiopathy and Alzheimer’s disease](#). *Acta Neuropathologica*. 2019;137(5):801-823. doi: 10.1007/s00401-019-01967-4.

Bennett RE, et al. [Tau induces blood vessel abnormalities and angiogenesis-related gene expression in P301L transgenic mice and human Alzheimer’s disease](#). *Proceedings of the National Academy of Sciences*. 2018;115(6):E1289-E1298. doi: 10.1073/pnas.1710329115.

Section 3. Advanced Drug Repurposing and Combination Therapy Development

Taubes A, et al. [Experimental and real-world evidence supporting the computational repurposing of bumetanide for APOE4-related Alzheimer's disease](#). *Nature Aging*. 2021;1(10):932-947. doi: 10.1038/s43587-021-00122-7.

Section 4. Discovered Tools to Detect, Diagnose, and Monitor Dementia

Klunk WE, et al. [Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B](#). *Annals of Neurology*. 2004;55(3):306-319. doi: 10.1002/ana.20009.

Verhoeff NP, et al. [In-vivo imaging of Alzheimer disease beta-amyloid with \[11C\]SB-13 PET](#). *American Journal of Geriatric Psychiatry*. 2004;12(6):584-595. doi: 10.1176/appi.ajgp.12.6.584.

Li Y, et al. [Validation of plasma amyloid-β 42/40 for detecting Alzheimer disease amyloid plaques](#). *Neurology*. 2022;98(7):e688-e699. doi: 10.1212/WNL.00000000000013211.

Brickman AM, et al. [Plasma p-tau181, p-tau217, and other blood-based Alzheimer's disease biomarkers in a multi-ethnic, community study](#). *Alzheimer's & Dementia*. 2021;17(8):1-12. doi: 10.1002/alz.12301.

Janelidze S, et al. [Plasma P-tau181 in Alzheimer's disease: relationship to other biomarkers, differential diagnosis, neuropathology and longitudinal progression to Alzheimer's dementia](#). *Nature Medicine*. 2020;26:379-386. doi: 10.1038/s41591-020-0755-1.

Thijssen EH, et al. [Diagnostic value of plasma phosphorylated tau181 in Alzheimer's disease and frontotemporal lobar degeneration](#). *Nature Medicine*. 2020;26:387-397. doi: 10.1038/s41591-020-0762-2.

Janelidze S, et al. [Plasma P-tau181 in Alzheimer's disease: relationship to other biomarkers, differential diagnosis, neuropathology and longitudinal progression to Alzheimer's dementia](#). *Nature Medicine*. 2020;26:379-386. doi: 10.1038/s41591-020-0755-1.

Thijssen EH, et al. [Plasma phosphorylated tau 217 and phosphorylated tau 181 as biomarkers in Alzheimer's disease and frontotemporal lobar degeneration: a retrospective diagnostic performance study](#). *Lancet Neurology*. 2021;20(9):739-752. doi: 10.1016/S1474-4422(21)00214-3.

Wang Z, et al. [Skin α-synuclein aggregation seeding activity as a novel biomarker for Parkinson disease](#) [published correction appears in *JAMA Neurol*. 2021;78(1):120]. *JAMA Neurology*. 2020;78(1):1-11. doi: 10.1001/jamaneurol.2020.3311.

Quiroz YT, et al. [Plasma neurofilament light chain in the presenilin 1 E280A autosomal dominant Alzheimer's disease kindred: a cross-sectional and longitudinal cohort study](#). *Lancet Neurology*. 2020;19(6):513-521. doi: 10.1016/s1474-4422(20)30137-x.

Gendron TF, et al. [Comprehensive cross-sectional and longitudinal analyses of plasma neurofilament light across FTD spectrum disorders](#). *Cell Reports Medicine*. 2022;3(4):100607. doi: 10.1016/j.xcrm.2022.100607.

Libiger O, et al. [Longitudinal CSF proteomics identifies NPTX2 as a prognostic biomarker of Alzheimer's disease](#). *Alzheimer's & Dementia*. 2021;17(12):1976-1987. doi: 10.1002/alz.12353.

Nicholas LH, et al. [Financial presentation of Alzheimer's disease and related dementias](#). *JAMA Internal Medicine*. 2021;81(2):220-227. doi: 10.1001/jamainternmed.2020.6432.

Bayat S, et al. [GPS driving: a digital biomarker for preclinical Alzheimer disease](#). *Alzheimer's Research & Therapy*. 2021;13:115.

Doherty JM, et al. [Adverse driving behaviors increase over time as a function of preclinical Alzheimer's disease biomarkers](#). *Alzheimer's & Dementia*. 2023;19(5):2014-2023. doi: 10.1002/alz.12852.

Kumaradev S, et al. [Timeline of pain before dementia diagnosis: a 27-year follow-up study](#). *Pain*. 2021;162(5):1578-1585. Doi: 10.1097/j.pain.0000000000002080.

Bock JR, et al. [Application of digital cognitive biomarkers for Alzheimer's disease: identifying cognitive process changes and impending cognitive decline](#). *Journal of Prevention of Alzheimer's Disease*. 2021;8(2):123-126. doi: 10.14283/jpad.2020.63.

Hajjar I, et al. [Development of digital voice biomarkers and associations with cognition, cerebrospinal biomarkers, and neural representation in early Alzheimer's disease](#). *Alzheimer's & Dementia (Amsterdam, Netherlands)*. 2023;15(1):e12393. doi: 10.1002/dad2.12393.

Bock JR, et al. [Application of digital cognitive biomarkers for Alzheimer's disease: identifying cognitive process changes and impending cognitive decline](#). *Journal of Prevention of Alzheimer's Disease*. 2021;8(2):123-126. doi: 10.14283/jpad.2020.63.

Barnes DE, et al. [Development and validation of eRADAR: a tool using EHR data to detect unrecognized dementia](#). *Journal of the American Geriatrics Society*. 2020;68(1):103-111. doi: 10.1111/jgs.16182.

Section 5. Advanced Clinical Research on Lifestyle Interventions

The SPRINT MIND Investigators for the SPRINT Research Group. [Effect of intensive vs. standard blood pressure control on probable dementia: a randomized clinical trial](#). *JAMA*. 2019;321(6):553-561. doi: 10.1001/jama.2018.21442.

The SPRINT MIND Investigators for the SPRINT Research Group. [Association of intensive vs standard blood pressure control with cerebral white matter lesions](#). *JAMA*. 2019;322(6):524-534. doi: 10.1001/jama.2019.10551.

Rebok GW, et al. [Ten-year effects of the ACTIVE cognitive training trial on cognition and everyday functioning in older adults](#). *Journal of the American Geriatrics Society*. 2014;62(1):16-24. doi: 10.1111/jgs.12607.

Clemenson GD, et al. [Enriching hippocampal memory function in older adults through video games](#). *Behavioural Brain Research*. 2020;390:112667. doi: 10.1016/j.bbr.2020.112667.

Morris MC, et al. [MIND diet associated with reduced incidence of Alzheimer's disease](#). *Alzheimer's & Dementia*. 2015;11(9):1007-1014. doi: 10.1016/j.jalz.2014.11.009.

Morris MC, et al. [MIND diet slows cognitive decline with aging](#). *Alzheimer's & Dementia*. 2015;11(9):1015-1022. doi:10.1016/j.jalz.2015.04.011

Section 6. Increased Understanding of How Social and Physical Environmental Factors Affect Dementia Risk and Disparities

Power MC, et al. [Trends in relative incidence and prevalence of dementia across non-Hispanic Black and White individuals in the United States, 2000-2016](#). *JAMA Neurology*. 2021;78(3):275-284. doi: 10.1001/jamaneurol.2020.4471.

Lennon JC, et al. [Black and White individuals differ in dementia prevalence, risk factors, and symptomatic presentation](#). *Alzheimer's & Dementia*. 2022;18(8):1461-1471. doi: 10.1002/alz.12509.

Zhu Y, et al. [Sex, race, and age differences in prevalence of dementia in Medicare claims and survey data](#). *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*. 2021;76(3):596-606. doi: 10.1093/geronb/gbaa083.

Bettcher BM, et al. [Peripheral and central immune system crosstalk in Alzheimer disease — a research prospectus](#). *Nature Reviews Neurology*. 2021;17(11):689-701. doi: 10.1038/s41582-021-00549-x.

Klopack ET, et al. [Social stressors associated with age-related T lymphocyte percentages in older U.S. adults: evidence from the U.S. Health and Retirement Study](#). *Proceedings of the National Academy of Sciences*. 2022;119(25):e2202780119. doi: 10.1073/pnas.2202780119.

Levine DA, et al. [Association between blood pressure and later-life cognition among Black and White individuals](#). *JAMA Neurology*. 2020;77(7):810-819. doi: 10.1001/jamaneurol.2020.0568.

Manly JJ, et al. [Estimating the prevalence of dementia and mild cognitive impairment in the U.S.: the 2016 Health and Retirement Study Harmonized Cognitive Assessment Protocol Project](#). *JAMA Neurology*. 2022;79(12):1242-1249. doi: 10.1001/jamaneurol.2022.3543.

Zahodne LB, et al. [The role of education in a vascular pathway to episodic memory: brain maintenance or cognitive reserve?](#) *Neurobiology of Aging*. 2019;84:109-118. doi: 10.1016/j.neurobiolaging.2019.08.009.

Jimenez MP, et al. [Residential green space and cognitive function in a large cohort of middle-aged women](#). *JAMA Network Open*. 2022;5(4):e229306. doi: 10.1001/jamanetworkopen.2022.9306.

Semmens EO, et al. [Air pollution and dementia in older adults in the Ginkgo Evaluation of Memory Study](#). *Alzheimer's & Dementia*. 2023;19(2):549-559. doi: 10.1002/alz.12654.

Sommerlad A, et al. [Association of social contact with dementia and cognition: 28-year follow-up of the Whitehall II cohort study](#). *PLOS Medicine*. 2019;16(8):e1002862. doi: 10.1371/journal.pmed.1002862.

Mayeda ER, et al. [Association of work-family experience with mid- and late-life memory decline in US women](#). *Neurology*. 2020;95(23):e3072-e3080. doi: 10.1212/WNL.00000000000010989.

Sabia S, et al. [Association of sleep duration in middle and old age with incidence of dementia](#). *Nature Communications*. 2021;12(1):2289. doi: 10.1038/s41467-021-22354-2.

Chapman BP, et al. [Association between high school personality phenotype and dementia 54 years later in results from a national US sample](#). *JAMA Psychiatry*. 2020;77(2):148-154. doi: 10.1001/jamapsychiatry.2019.3120.

Terracciano A, et al. [Personality associations with amyloid and tau: results from the Baltimore Longitudinal Study of Aging and meta-analysis](#). *Biological Psychiatry*. 2022;91(4):359-369. doi: 10.1016/j.biopsych.2021.08.021.

Section 7. Expanded Research on Dementia Care and Care Partner Supports

Choi H, et al. [Family care availability and implications for informal and formal care used by adults with dementia in the US](#). *Health Affairs (Millwood)*. 2021;40(9):1359-1367. doi: 10.1377/hlthaff.2021.00280.

Kelley AS, et al. [Residential setting and the cumulative financial burden of dementia in the 7 years before death](#). *Journal of the American Geriatrics Society*. 2020;68(6):1319-1324. doi: 10.1111/jgs.16414.

Reckrey JM, et al. [Living in the community with dementia: who receives paid care?](#) *Journal of the American Geriatrics Society*. 2020;68(1):186-191. doi: 10.1111/jgs.16215.

National Academies of Sciences, Engineering, and Medicine. [Meeting the Challenge of Caring for Persons Living with Dementia and Their Care Partners and Caregivers: A Way Forward](#). *National Academies Press*; 2021. doi: 10.17226/26026.

Possin KL, et al. [Effect of collaborative dementia care via telephone and internet on quality of life, caregiver well-being, and health care use: the Care Ecosystem randomized clinical trial](#). *JAMA Internal Medicine*. 2019;179(12):1658-1667. doi: 10.1001/jamainternmed.2019.4101.

Lykens K, et al. [Impact of a community-based implementation of REACH II program for caregivers of Alzheimer's patients](#). *PLOS ONE*. 2014;9(2):e89290. doi: 10.1371/journal.pone.0089290.

Possin KL, et al. [Effect of collaborative dementia care via telephone and internet on quality of life, caregiver well-being, and health care use: the Care Ecosystem randomized clinical trial](#). *JAMA Internal Medicine*. 2019;179(12):1658-1667. doi: 10.1001/jamainternmed.2019.4101.

Griffiths PC, et al. [Tele-Savvy: an online program for dementia caregivers](#). *American Journal of Alzheimer's Disease & Other Dementias*. 2018;33(5):269-276. doi: 10.1177/1533317518755331.

Casey JJ, et al. [An integrative group movement program for people with dementia and care partners together \(Paired PLIÉ\): initial process evaluation](#). *Aging & Mental Health*. 2020;24(6):971-977. doi: 10.1080/13607863.2018.1553142.

Panagiotou OA, et al. [Risk factors associated with all-cause 30-day mortality in nursing home residents with COVID-19](#). *JAMA Internal Medicine*. 2021;181(4):439-448. doi: 10.1001/jamainternmed.2020.7968.