

Preserving America's Cognitive Strength

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Introduction

By our nature, we take for granted our ability to think. But cognitive strength—the blend of our mental, physical, and spiritual fitness—is our most valuable asset. It empowers us to think critically and independently so we can shape the world we want to live in. It prevents us from becoming slaves to small thinking and institutional dictates that serve a select few at the expense of the many. And it enables us to provide support for our family, friends, and fellow Americans. By maintaining our mental, physical, and spiritual well-being, we hold the potential to be loving parents to our children, caregivers for our family and friends, and active members of communities that form a thriving society.

Nothing drains America's cognitive strength like Alzheimer's disease, the most common form of dementia that affects more than seven million people over 65.¹ It's a chronic, fatal disease that starves the brain of vital energy, prevents the formation of new memories, and traps a person in the “eternal now” as the mind, body, and spirit fade away. Much of the research on Alzheimer's in recent decades has focused on the role of amyloid protein plaques, which seem to be the first discernible biological change in the linear progression and inflammation cascade. But we are learning that the disease is far more complex, and there is still so much we don't understand.

As a practicing neurologist and clinician, I'm following research developments to give my patients the best care possible while guiding them to prevent Alzheimer's disease, and I've never been more optimistic. In this paper, I will discuss the importance of lifestyle changes in preserving cognitive abilities and preventing dementia, new insights into its genetic, environmental, and behavioral causes of Alzheimer's disease; the role of repurposed generic treatments and other therapies; and actionable recommendations for building a better system of care for patients and families. These developments can advance President Trump and Secretary Kennedy's work to understand the root causes of disease, improve prevention, and create a better system of care that preserves America's cognitive strength for generations to come.

Understanding Alzheimer's Disease: Mechanisms, Causes, and Lifestyle Changes That May Help Prevent It

Alzheimer's poses an existential threat as we age, stealing decades of productive, enjoyable life. We are seeing the signs and symptoms much earlier in life—patients in their fifties and even forties are no longer uncommon. These are people in the prime of their productive years, who may have young children in the home. By some estimates, the number of people living with Alzheimer's will nearly double to 13 million by 2050.²

Discovered in 1906, Alzheimer's disease has traditionally been characterized by the accumulation of two types of proteins in the brain—beta amyloid and tau—which kill neurons, shrink the brain, and ultimately result in death.

Recent discoveries have significantly increased our understanding of the complex causes and mechanisms behind this disease. There is strong evidence supporting genetic, environmental and behavioral factors, many of which can be addressed with clinicians through recommendations for lifestyle changes based on individual needs and risk profiles. The 2024 Lancet Commission on Dementia Prevention, Intervention and Care reported that fully addressing 12 lifestyle risk factors can prevent or delay up to 40% of dementia cases.³ An

ongoing international study continues to reinforce what practicing neurologists have long known: a low-inflammation diet, regular exercise, quality sleep, fundamental brain exercises, and validated nutritional supplements can preserve cognitive abilities⁴ and may help prevent the development of disease.

As with all chronic conditions, the challenge is delivering this essential information to patients and the American people in a persuasive and actionable way—cutting through the clutter of modern life to make people feel educated and empowered, rather than confused, ashamed, or intimidated. Below is a summary of the current state of research into the causes and potential opportunities to prevent Alzheimer's disease.

Genetic/Prenatal

- APOE4. A large body of evidence confirms that genes, and one allele in particular – apolipoprotein 4, or APOE4 – predispose individual carriers to the accumulation of amyloid protein plaques in the brain, significantly increasing risk. One quarter of the population carries APOE4, and 2-3% are believed to carry two copies of the gene,

putting them at very high risk of developing dementia. Crucially, APOE4 interacts with multiple other genetic, environmental, and behavioral risk factors to further increase risk.⁵

- Prenatal nutrition is a significant risk factor for adult cognitive dysfunction. Good nutrition in utero creates stores of key neural building blocks such as folate, iodine, choline, and omega-3 found in leafy green vegetables, legumes, seafood, and eggs—all of which can help prevent amyloid deposition.^{6–8} These compounds are also widely available as nutritional supplements, as well as part of “fortified” foods.

Behavioral

- Education. Completing secondary education is a key variable determining the likelihood of developing Alzheimer’s, with economic opportunity, adolescent socialization, school- based nutrition programs, and athletic participation all potential contributing factors.^{9–13}
- Head injuries. Concussions and other serious brain trauma experienced in childhood and young adulthood are known risk factors.¹⁴ Research has implicated aggravating injury in combination with genetic predisposition, especially the APOE4 allele.^{15,16}
- Sleep. Poor sleep patterns in middle age (50s-60s), including prolonged irregular or insufficient sleep, are strongly correlated with increased risk of disease in subsequent decades.¹⁷
- Diet. Many of the foods popular in the western diet have been identified as Alzheimer’s risk factors, responsible for metabolic changes, obesity, and gut biota dysbiosis, contributing to impairment of the blood-brain barrier and neuroinflammation.^{18,19}
- Alcohol consumption. Heavy drinking in midlife is associated with multiple Alzheimer’s risk factors, including chronic thiamine deficiency and amyloid plaque deposition. Again, research points to a combination of behavior with genetic factors, especially the presence of the APOE4 allele, as strong predictors of negative outcomes.²⁰
- Smoking. Individuals who smoke two or more packs a day have more than double the incidence of Alzheimer’s.²¹ Studies have suggested multiple potential mechanisms, but there appears to be a strong role for vascular effects in combination with the APOE4 allele, leading to increased amyloid deposition.²²
- Social activity. Social isolation and subjective feelings of loneliness in later life are firmly established risk factors for Alzheimer’s.^{23,24} In one recent study, senior citizens who maintained an active social network delayed the onset of dementia by an

average of about five years (from 87.7 to 92.2).²⁵ Studies of long-term care facilities that employ intensive socialization activities have shown significant decreases in dementia incidence.²⁶

- Brain training: The Lifestyle Intervention to Reduce Risk (U.S. Pointer) study²⁷ reinforces what integrated neurology practitioners have long understood: relatively simple lifestyle changes can help preserve cognitive function over years. Significant improvements were evident in a group that combined 30 minutes of exercise four times a week with 30 minutes of computer-based brain training each week and a Mediterranean diet, compared with a control group. The study is ongoing.

Environmental

- Sunlight. Studies suggest regular exposure to safe amounts of direct sunlight is linked to decreased Alzheimer's risk, with a central role indicated for vitamin D, a complex physiological regulator.²⁸⁻³²
- Air pollution. Long-term exposure to air pollution from automobile traffic is causally related to Alzheimer's, with fine particulate matter found to contribute to the formation of amyloid plaques in the brain.³³

Medical

- Untreated hearing loss. Millions of Americans experience incremental hearing loss due to natural aging processes during midlife (ages 30-60). Age-related hearing loss is correlated with an increased risk.³⁴
- COVID. New research shows that the SARS-CoV2 virus can cause accumulation of beta proteins that lead to amyloid deposition, potentially increasing the risk of Alzheimer's disease.³⁵⁻³⁷
- Obesity. A growing body of evidence connects obesity in midlife (age 35-65) to an increased risk of Alzheimer's later in life. Findings show neuroinflammation correlated with obesity leads to activation of microglia and amyloid deposition in the brain.³⁸⁻⁴⁰
- Diabetes. Diabetes in later life is a major risk factor for dementia, with a 73% higher risk of developing Alzheimer's, concentrated in individuals with the APOE4 allele.^{41,42} Lifestyle interventions to control diabetes have also been shown to be effective in slowing the progress of Alzheimer's, including diet, exercise, and weight loss.^{43,44} For example, a Mediterranean diet is associated with fewer signs of Alzheimer's in older individuals.^{45,46}

The Landscape for Treatment

New therapeutic options are being explored to treat Alzheimer's, with numerous generic drugs being studied for potential repurposing. Typically, these studies must evaluate key issues for any proposed repurposing of an existing drug, including drug interactions and dosing, as well as questions specific to Alzheimer's treatments, such as the compound's ability to cross the blood-brain barrier.^{47,48} The following is a partial list of drugs that are currently under investigation.

Fasudil	A Rho-associated protein kinase (ROCK) inhibitor, Fasudil was shown in mice to protect against amyloid beta (A β) pathology, increase oxidative substances, and decrease lipid peroxides in the brain. ⁴⁹
Fluticasone	An inhaled anti-inflammatory corticosteroid, fluticasone use was shown to be correlated with lower incidence of Alzheimer's disease in a large retrospective study. ⁵⁰
Ibudilast	A phosphodiesterase inhibitor and toll-like receptor 4 (TLR4) antagonist, ibudilast has been shown in rats to alleviate cognitive deficits associated with Alzheimer's dementia, via TLR signaling and the ubiquitin/proteasome pathway. ⁵¹
Lithium	A well-known mood stabilizer, research with mice suggests lithium may reduce amyloid deposition and formation of abnormal clumps of tau proteins, slowing progression of Alzheimer's. ⁵²
Semaglutide	Widely used for treatment of diabetes, semaglutide has recently been shown to be associated with a lower incidence of first-time Alzheimer's diagnosis, likely due to overlapping disease mechanisms of Alzheimer's and diabetes. ⁵³
Sildenafil	Better known by trade name Viagra, computational modeling research in 2024 shows sildenafil is associated with a 30%-54% reduced prevalence of Alzheimer's disease, perhaps by lowering levels of neurotoxic tau proteins in the brain. ⁵⁴

The Role of Anti-Amyloid Therapies

There are currently two FDA-approved drugs for treatment in early Alzheimer's disease. These therapies have come under criticism from Secretary Kennedy and other members of the Trump administration. Many of my colleagues and I in the medical MAHA movement understand these concerns. On balance, there is a place for them in the current system of care for patients who understand the risks and wish to use them. Here is what we know:

- The FDA approved two monoclonal antibodies, lecanemab and donanemab, based on trials showing they slowed progression of Alzheimer's in early stage patients by clearing amyloid plaques from the brain. In addition there is anecdotal evidence of patient benefit.^{55,56}
- The drugs have known risks and side effects, such as brain swelling or bleeding, so patients are closely monitored and treatment is stopped at the first sign of concern.
- The drugmakers claim the therapies show a delay in Alzheimer's disease progression over 36 months.^{57,58}
- Trials are underway to understand potential to prevent symptoms by treating people with amyloid therapies when younger and still cognitively normal.⁵⁹

Building a Better System of Care

The most important thing we can do to preserve America's cognitive strength is prioritize the prevention and care of Alzheimer's disease. I believe we have reached a watershed moment in recognizing the factors that lead to the decline of brain health. We have the potential to do today for the brain what we did 70 years ago for the heart.

In the early 20th century, heart disease was not a major public health problem in America. But by the 1940s, its prevalence shot up and accounted for about half of all deaths.⁶⁰ A concerted public effort was made to understand and address the causes of this epidemic. Guidelines for prevention were created and updated over the years as we came to understand the many factors that contributed to disease—smoking, cholesterol, high blood pressure, obesity, among others. Today these are all common knowledge. As a result, our ability to prevent heart disease has massively improved. Between 1970 and 2022, deaths from heart disease fell by two-thirds.⁶¹

We can do the same for Alzheimer's disease right now. Lifestyle changes have been found in study after study to improve brain health and lower the risk of cognitive decline. Educating Americans about simple steps they can take to improve brain health and potentially prevent disease must be an urgent national priority. Primary care providers must be empowered to help patients make these changes, improve diagnosis, treat when appropriate, and ensure patients and families receive compassionate care at every stage of the disease. Here are the steps our leaders in government can take to accelerate this process:

- The U.S. Department of Health and Human Services. Our federal government should launch a nationwide educational campaign to encourage and educate Americans about the role of lifestyle changes in preserving cognitive strength and staving off brain disease. It is never too early to be focused on brain health. Knowing the signs and symptoms of brain disease early in life empowers people to seek care for themselves or their loved ones. The agency has already taken some positive steps to improve prevention through changes to the physician fee schedule and by including a prevention RFI to incentivize earlier diagnosis.⁶² It should prioritize actions to encourage specialists and primary care physicians to further focus on upstream prevention and diagnosis.
- Medical schools. Just as medical schools do not require in-depth learning about nutrition and root causes of chronic disease,⁶³ they similarly have given short shrift to educating students on brain health. The importance of a good diet, regular exercise, adequate sleep, exposure to sunlight, and nutritional supplements in preventing brain disease should be a fundamental part of an American medical education. Physicians of all disciplines should guide patients in their care not only towards treating disease, but also towards making essential lifestyle choices that can protect their brains and preserve cognitive strength over the course of a lifetime.
- Fortifying primary care: Given the scale and urgency of Alzheimer's disease, the most important system shift we can make is training more primary care physicians to increase their brain health IQ and become stewards of cognitive strength. Early intervention can delay the progression of Alzheimer's disease and preserve cognitive strength through naturopathic and therapeutic interventions. Primary care physicians should be empowered to recognize and act on the signs of cognitive impairment, armed with the knowledge about preventing disease and preserving cognitive function. Dr. Barak Gaster's Cognition in Primary Care program is one of several promising models for scaling national capacity.⁶⁴ This is the most important place within the health care system where we can have the greatest impact for patients

and families right now, while priming the system to act quickly on new insights, discoveries, and therapeutic interventions as they arise.

- **Therapeutics:** We need an all-of-the-above approach to treatment guided by wherever gold-standard science takes us. That includes a systematic study of naturopathic and generic repurposed drugs in partnership with the federal government. It also includes new medicines backed by solid evidence. It could also include use of validated Alzheimer's biomarkers to investigate preventive interventions through lifestyle modifications and therapeutics. The federal government should play a central role in this effort by funding and systematizing the collection and reporting of observational data nationwide. It can incentivize pharmaceutical industry discoveries by providing patent protections for new uses of old drugs and understanding the role generic repurposed treatments can play in adjunctive therapies for Alzheimer's and ultimately preventing brain disease.

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