



# Curing Alzheimer's by Investing in Aging Research

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## Summary

Congress allocates billions of dollars annually to Alzheimer's research in hopes of finding an effective prophylactic, treatment, or cure. But these massive investments have little likelihood of paying off absent a game-changing improvement in our present knowledge of biology. Funds currently earmarked for Alzheimer's research would be more productive if they were instead invested into deepening understanding of aging biology at the cell, tissue, and organ levels. Fundamental research advances in aging biology would directly support better outcomes for patients with Alzheimer's as well as a plethora of other chronic diseases associated with aging — diseases that are the [leading cause](#) of mortality and disability, responsible for 71% of annual deaths worldwide and 79% of years lived with disability. Congress should allow the National Institute on Aging to spend funds currently restricted for research into Alzheimer's specifically on research into aging biology more broadly. The result would be a society better prepared for the imminent health challenges of an aging population.

## Challenge and Opportunity

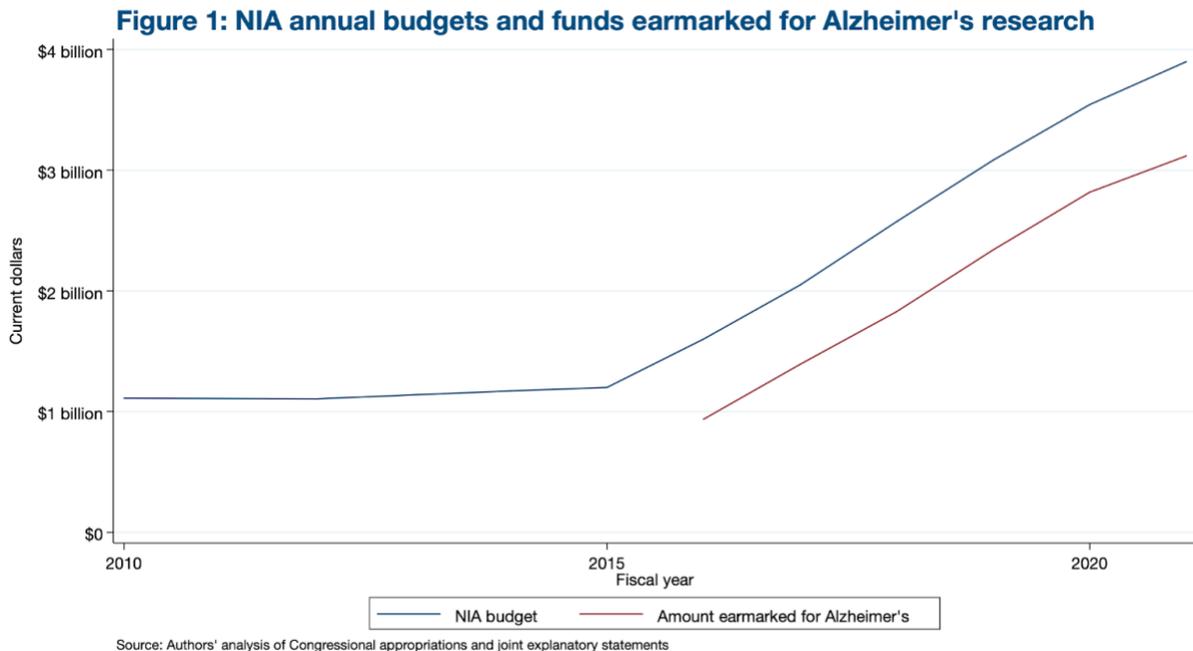
The NIH [estimates](#) that 6.25 million Americans now have Alzheimer's disease, and that due to an aging population, that number will more than double to 13.85 million by the year 2060. *The Economist* similarly [estimates](#) that an estimated 50 million people worldwide suffer dementia, and that that number will increase to 150 million by the year 2050. These dire statistics, along with astute political maneuvering by Alzheimer's advocates, have led Congress to earmark billions of dollars of federal health-research funds for Alzheimer's disease.

President Obama's [FY2014](#) and [FY2015](#) budget requests explicitly cited the need for additional Alzheimer's research at the National Institutes of Health (NIH). In FY2014, Congress responded by giving the NIH's National Institute on Aging (NIA) a small but disproportionate increase in funding relative to other national institutes, "[in recognition](#) of the Alzheimer's disease research initiative throughout NIH." Congress's [explanatory statement](#) for its FY2015 appropriations laid out good reasons not to earmark a specific portion of NIH funds for Alzheimer's research, stating:

*"In keeping with longstanding practice, the agreement does not recommend a specific amount of NIH funding for this purpose or for any other individual disease. Doing so would establish a dangerous precedent that could politicize the NIH peer review system. Nevertheless, in recognition that Alzheimer's disease poses a serious threat to the Nation's long-term health and economic stability, the agreement expects that a significant portion of the recommended increase for NIA should be directed to research on Alzheimer's. The exact amount should be determined by scientific opportunity of additional research on this disease and the quality of grant*

applications that are submitted for Alzheimer's relative to those submitted for other diseases.”

But this position changed suddenly in FY2016, when Congress [earmarked](#) \$936 million for Alzheimer's research. The amount earmarked by Congress for Alzheimer's research has risen almost linearly every year since then, reaching [\\$3.1 billion](#) in FY2021 (Figure 1).



This tsunami of funding has been unprecedented for the NIA. The seemingly limitless availability of money for Alzheimer's research has created a perverse incentive for the NIH and NIA to solicit additional Alzheimer's funding, even as agencies struggle to deploy existing funding efficiently. The NIH Director's [latest report](#) to Congress on Alzheimer's funding suggests that with an additional \$226 million per year in funding, the NIH and NIA could effectively treat or prevent Alzheimer's disease and related dementias by 2025.

This is a laughable untruth. No cure for Alzheimer's is in the offing. Progress on Alzheimer's research is stalling and commercial interest is declining. Of the [413 Alzheimer's clinical trials](#) performed in the United States between 2002 and 2012, 99.6% failed. Recent federal investments seemed to be paying off when in 2021 the Food and Drug Administration (FDA) [approved Aduhelm](#), the first new treatment for Alzheimer's since 2003. But the approval was based on the surrogate endpoint of amyloid plaques in the brain as observed by PET scans, not on patient outcomes. In its first months on the market, Aduhelm visibly flopped. Scientists subsequently [called on](#) the FDA to withdraw marketing approval for the drug. If an effective treatment

were likely by 2025, Big Pharma would be doubling down. But Pfizer announced it was [abandoning](#) Alzheimer's research in 2018.

The upshot is clear: lavish funding on treatments and cures for a disease can only do so much absent knowledge of that disease's underlying biological mechanisms. We as a society must resist the temptation to waste money on expensive shots in the dark, and instead invest strategically into understanding the basic biochemical and genetic mechanisms underlying aging processes at the cell, tissue, and organ levels.

## Plan of Action

Aging is the number-one risk factor for Alzheimer's disease, as it is for many other diseases. All projections of an increasing burden of Alzheimer's are based on the fact that our society is getting older. And indeed, even if a miraculous cure for Alzheimer's were to emerge, we would still have to contend with an impending onslaught of other impending medical and social costs.

Economists and scientists have [estimated](#) extending average life expectancy in the United States by one year is worth \$38 trillion. But funding for basic research on aging remains tight. Outside of the NIA, several foundations in the United States are actively [funding](#) aging research: the American Federation for Aging Research (AFAR), The Glenn Foundation for Medical Research, and the SENS Foundation each contribute a few million per year for aging research. Privately funded [fast grants](#) have backed bold aging projects with an additional \$26 million.

This relatively small investment in basic research has generated billions in private funding to commercialize findings. Startups raised [\\$850 million](#) in 2018 to target aging and age-related diseases. Google's private research arm Calico is armed with billions and a pharmaceutical partner in Abbvie, and the Buck Institute's Unity Biotechnology launched an initial public offering (IPO) in 2018. In 2021, Altos Labs raised hundreds of millions to commercialize cellular reprogramming technology. Such dynamism and progress in aging research contrasts markedly with the stagnation in Alzheimer's research and indicates that the former is a more promising target for federal research dollars.

Now is the time for the NIA to drive science-first funding for the field of aging. Congress should maintain existing high funding levels at NIA, but this funding should no longer be earmarked solely for Alzheimer's research. In every annual appropriation since FY2016, the House and Senate appropriations committees have issued a joint explanatory statement that has force of law and includes the Alzheimer's earmark. These committees should revert to their FY2015 position against politically directing NIH funds towards particular ends. The past six years have shown such political direction to be a failed experiment.

Removing the Alzheimer's earmark would allow the NIA to use its professional judgment to fund the most promising research into aging based on scientific opportunity and the quality of the grant applications it receives. We expect that this in turn would cause agency-funded research to flourish and stimulate further research and commercialization from industry, as privately funded aging research already has. Promising areas that the NIA could invest in include building tools for understanding molecular mechanisms of aging, establishing and validating aging biomarkers, and funding more early-stage clinical trials for promising drugs. By building a better understanding of aging biology, the NIA could do much to render even Alzheimer's disease treatable.

## Frequently Asked Questions

### 1. How did Congress get so interested in Alzheimer's disease? What recent actions has Congress taken on funding for Alzheimer's research?

In 2009, a private task force calling itself the Alzheimer's Study Group released a [report](#) entitled "A National Alzheimer's Strategic Plan." The group, co-chaired by former Speaker of the House Newt Gingrich and former Nebraska Senator Bob Kerrey, called on Congress to immediately increase funding for Alzheimer's and dementia research at the NIH by \$1 billion per year.

In response to the report, Senators Susan Collins and Evan Bayh introduced the [National Alzheimer's Project Act \(NAPA\)](#), which was signed into law in 2011 by Barack Obama. NAPA requires the Department of Health and Human Services to produce an [annual assessment](#) of the nation's progress in preparing for an escalating burden of Alzheimer's disease. This annual assessment is called the National Plan to Address Alzheimer's Disease. The first National Plan, released in 2012, established a goal of effectively preventing or treating Alzheimer's disease by 2025. In addition, the Alzheimer's Accountability Act, which passed in the [2015 omnibus](#), gives the NIH director the right and the obligation to report directly to Congress on the amount of additional funds needed to meet the goals of the national plan, including the self-imposed 2025 goal.

### 2. Why is treating Alzheimer's so hard?

Understanding diseases that progress over a long period of time such as Alzheimer's requires complex clinical studies. Lessons learned from [past research](#) indicate that animal models don't necessarily translate into humans when it comes to such diseases. Heterogeneity in disease presentation, imprecise clinical measures, relevance of target biomarkers, and difficulty in understanding underlying causes exacerbate the problem for Alzheimer's specifically.

Alzheimer's is also a whole-system, multifactorial disease. Dementia is [associated](#) with a decreased variety of gut microbiota. Getting cataract surgery seemingly [reduces](#) Alzheimer's risk. Inflammatory responses from the immune system can [aggravate](#) neurodegenerative diseases. The blood-brain barrier [uptakes](#) less plasma protein with age. The list goes on. Understanding Alzheimer's hence requires understanding of many other biological systems.

### 3. What is the amyloid hypothesis?

Alzheimer's is named after Alois Alzheimer, a German scientist credited with [publishing](#) the first case of the disease in 1906. In the post-mortem brain sample of his patient, he identified extracellular deposits, now known as amyloid plaques, clumps of amyloid-beta (A $\beta$ ) protein. In 1991, David Allsop and John Hardy [proposed](#) the

amyloid hypothesis after discovering a pathogenic mutation in the APP (A $\beta$  precursor protein) gene on chromosome 21. Such a mutation led to increased A $\beta$  deposits which present as early-onset Alzheimer's disease in families.

The hypothesis [suggested](#) that Alzheimer's follows the pathological cascade of A $\beta$  aggregation  $\rightarrow$  tau phosphorylation  $\rightarrow$  neurofibrillary tangles  $\rightarrow$  neuronal death. These results indicated that A $\beta$  could be a drug target for Alzheimer's disease.

In the 1990s, Elan Pharmaceuticals proposed a vaccine against Alzheimer's by stopping or slowing the formation of A $\beta$  aggregates. It was a compelling idea. In the following decades, drug development centered around this hypothesis, leading to the [current approaches](#) to Alzheimer's treatment: A $\beta$  inhibition ( $\beta$ - and  $\gamma$ -secretase inhibitors), anti-aggregation (metal chelators), A $\beta$  clearing (protease-activity regulating drugs), and immunotherapy.

In the last decade, the growing arsenal of A $\beta$  therapies fueled the excitement that we were close to an Alzheimer's treatment. The [2009 report](#), the [2012 national plan](#), and [Obama's funding requests](#) seemed to confirm that this was the case.

However, the strength of the amyloid hypothesis has declined since then. Since the shutdown of the first Alzheimer's vaccine in 2002, numerous other pharmaceutical companies have [tried and failed](#) at creating their own vaccine, despite many promising assets shown to clear A $\beta$  plaques in animal models. Monoclonal antibody treatments (of which *aducanumab* is an example) have [reduced](#) free plasma concentrations of A $\beta$  by 90%, [binding to](#) all sorts of A $\beta$  from monomeric and soluble A $\beta$  to fibrillar and oligomeric A $\beta$ . These treatments have suffered high-profile late-stage clinical trial failures in the last five years. Similar failures surround other approaches to Alzheimer's drug development.

There is no doubt these therapies are successful at reducing A $\beta$  concentration in pre-clinical trials. But combined with the continuous failure of these drugs in late-stage clinical trials, perhaps A $\beta$  [does not play](#) as major a role in the mechanistic process as hypothesized.

## About the Authors



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## About the Day One Project



The Federation of American Scientists' Day One Project is dedicated to democratizing the policymaking process by working with new and expert voices across the science and technology community, helping to develop actionable policies that can improve the lives of all Americans. For more about the Day One Project, visit [dayoneproject.org](http://dayoneproject.org).

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