Addressing Alzheimer's Disease: Target 2025

The Alzheimer's Association takes an in-depth look at the US National Plan to Address Alzheimer's Disease, which seeks to prevent and effectively treat Alzheimer's disease by 2025.

BY MARIA C. CARRILLO, PhD

An Alzheimer's disease epidemic is upon us. With Americans living longer than ever before, general practitioners and neurologists are seeing more and more people living with Alzheimer's. According to the Alzheimer's Association 2014 Alzheimer's Disease Facts and Figures report, there are currently more than five million Americans living with Alzheimer's, and those numbers will soar as more and more people reach the age of greatest risk unless something is done to change the course of the disease.

Unfortunately, we are not currently able to offer treatment to reverse, stop or even slow the progression of the disease. Instead, the US will spend $214 billion to care for people with Alzheimer's in 2014. Even with nearly one in five Medicare dollars spent on someone with Alzheimer's or another dementia, we must rely on the generosity of family and friends to provide care for people living with Alzheimer's for an average of four to eight years—but up to 20 years. According to Alzheimer's Disease Facts and Figures, 15.5 million Americans provided 17.7 billion hours of care for someone with Alzheimer's disease, valued—but uncompensated—at more than $220 billion in 2013. As many as 16 million Americans will be living with Alzheimer's by 2050 at a cost to the nation of $1.2 trillion. This cost, which does not include unpaid care, is simply unsustainable.

The Alzheimer's Association worked with Congress to ensure the unanimous passage of the National Alzheimer's Project Act (NAPA) in 2011. The Act mandated the creation of the first-ever National Plan to Address Alzheimer's Disease, which was released in May 2012 with the goal of preventing and effectively treating Alzheimer's disease by 2025.

As we know from the successes of other diseases, goals of this magnitude—goals aimed at changing the trajectory of a global health crisis—require significant investments to realize success. Currently, for every $26,500 that Medicare and Medicaid spend on caring for individuals with Alzheimer's, the National Institutes of Health (NIH) spends only $100 on Alzheimer's research. We must follow the proven model established by heart disease, cancer and HIV/AIDS and increase our federal investment in Alzheimer's disease research if we hope to reduce its crippling costs, staggering death toll and overwhelming burden on affected families.

PRACTICAL POINTER

In spite of the significant challenges associated with Alzheimer's disease research, the scientific community remains more optimistic than ever. Many prominent investigators believe the prospect of delaying the onset of disabling dementia symptoms within a decade is an attainable goal, provided we overcome scientific, administrative, and financial impediments. Inadequate funding remains the single most important barrier to achieving quicker and more significant advancements.

FEDERAL FUNDING & ACCOUNTABILITY

Since the creation of the National Alzheimer's Plan in 2012, two activities have assessed the scale and scope of the effort required to successfully reach the 2025 goal. The first was conducted by the Alzheimer's Association Expert Advisory Workgroup on NAPA, a task force of leading researchers in the field. In an effort to inform those implementing NAPA, this workgroup evaluated and proposed requirements in scientific and technological areas, infrastructure and research resources, and administrative and organizational domains. The workgroup estimated that a successful effort would require at least $2 billion per year over ten years. (Alzheimer's & Dementia 8 (2012), 357–371.)

Actions first by the administration and now, for the first time this year, by Congress, suggest a coalescing, bipartisan commitment to provide the resources needed to achieve significant progress. The administration demonstrated an early commitment by reallocating $50 million in fiscal year 2012 to provide an initial increase in Alzheimer's disease funding, enabling early progress, and $40 million from the NIH Office of the Director's budget in fiscal year 2013 to blunt the effects of sequestration. In addition, the Fiscal Year 2014 Consolidated Appropriations Act passed by Congress in January 2014 provided resources that will enable an allocation of an additional $100 million toward Alzheimer's research.

Earlier this spring, the Alzheimer's Accountability Act (H.R. 4351/S. 2192) was introduced to ensure that Congress is equipped with the best possible information to set funding priorities and reach the goal of the National Alzheimer's Plan. The Alzheimer's Accountability Act authorizes the NIH to submit a Professional Judgment Budget to Congress justifying funding for critical Alzheimer's research. This Professional Judgment Budget will be formulated by experts at the NIH to reflect the resources needed to accomplish the goals of the National Alzheimer's Plan in each fiscal year leading up to 2025. It will detail the state of Alzheimer's research and call out the most promising opportunities for investment.

IMPLEMENTATION & MILESTONES

The second effort was the Alzheimer's Disease Research Summit 2012: Path to Treatment and Prevention, held May 14-15, 2012 under the direction of the NIH and the National Institute on Aging (NIA). The summit convened more than 500 participants whose work culminated in an assessment of research requirements and a corresponding series of recommendations. While the Expert Advisory Workgroup on NAPA focused on the infrastructure required for this effort, recommendations from the summit identified specific research challenges that need to be resolved.

Based on the gap analysis, the NIA developed research milestones to reach the 2025 goal in the areas of drug development, development of non-pharmacological interventions, biomarkers of disease progression, epidemiology, research resources, infrastructure development, and study recruitment and participation. These milestones have subsequently been incorporated into the national plan and are now being used to prioritize and direct activities of the federal government and the broader field.

Administration officials have indicated that as they receive additional resources, these will be deployed against priority milestones. They have also cautioned that the timely completion of milestones depends, in turn, upon whether adequate resources are provided.

In February 2014, at the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies hearing on the economic impact of Alzheimer's disease in America, NIH Director Francis Collins, MD, PhD, stated, "We are not, at the moment, limited by ideas. We are not limited by scientific opportunities. We are not limited by talent. We are, unfortunately, limited by resources to be able to move this enterprise forward at the pace that it could take."

No complex plan ever unfolds exactly as anticipated. Continuous evaluation and adjustment will be required. Congress anticipated this when laying out its requirement that the national plan be updated annually. The next major evaluation of progress against the plan will occur when the NIH convenes a second international Alzheimer's Disease Research Summit in 2015.

ALZHEIMER'S TREATMENT AND PREVENTION RESEARCH

In spite of the significant challenges associated with Alzheimer's disease research, the scientific community remains more optimistic than ever. Many prominent investigators believe the prospect of delaying the onset of disabling dementia symptoms within a decade is an attainable goal, provided we can overcome scientific, administrative, and most importantly, financial impediments. Inadequate funding remains the single most important barrier to achieving quicker and more significant advancements in Alzheimer's research.

At the Alzheimer's Association, we are optimistic about the future, but our urgency continues to grow. We can and will solve the Alzheimer's disease epidemic. Other diseases have demonstrated that sustained investment in research can improve lives, reduce death rates and ultimately produce effective treatments and preventions. We

have the tools and the talent to achieve breakthroughs in Alzheimer's disease, but we need the resources to make this a reality.

The Association is especially hopeful about earlier diagnosis and treatment as methods to intervene in disease progression before irreversible cognitive decline occurs. Evidence suggests that the process of Alzheimer's disease begins more than a decade before clinical symptoms appear, suggesting we may need to intervene earlier to have a major impact on the course of the disease, particularly when using therapies designed to prevent the development of abnormal protein structures known as amyloid "plaques" and tau "tangles" that are abundant in the brains of people with Alzheimer's.

Among those helping to move the field toward methods of prevention are Reisa Sperling, MD, MMSc, professor of neurology at Harvard Medical School and director of the Center for Alzheimer Research and Treatment at Brigham and Women's Hospital and Massachusetts General Hospital, and Paul S. Aisen, MD, professor of neurosciences at the University of California San Diego and director of the Alzheimer's Disease Cooperative Study. They are the co-principal investigators of the Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) study, a pioneering trial that is one of five Alzheimer's prevention studies now in process or kicking off in the next year.

A4 is a clinical study for people aged 65 to 85 who have normal thinking and memory function but who may be at risk for developing Alzheimer's dementia sometime in the future. A4 is designed to evaluate the effectiveness, safety and tolerability of an investigational drug for Alzheimer's disease to determine whether decreasing amyloid with an investigational antibody treatment can help slow the memory loss associated with amyloid buildup in some people.

The Alzheimer's Association recently announced its largest-ever research grant—$8 million over four years—to support the Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN) study as a companion to A4. LEARN aims to help uncover which factors, in addition to amyloid plaques, should be pursued as potential causes of Alzheimer's. The grant will also fund a cutting-edge Tau Imaging sub-study to complement the A4 and LEARN research, allowing investigators to examine tau protein that forms tangles in the brain.

The Alzheimer's Association, thanks to a small group of donors, was also a catalyst in establishing the Dominantly Inherited Alzheimer's Network Trials Unit (DIAN TU), another secondary prevention trial that studies individuals with a rare genetic mutation that guarantees development of Alzheimer's. This international study will assess the safety, tolerability, and biomarker efficacy of the antibody drugs gantenerumab and solanezumab in individuals who have a genetic mutation for autosomal-dominant Alzheimer's disease.

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A third study, the Alzheimer's Prevention Initiative (API) Autosomal Dominant Alzheimer's Disease Treatment Trial, is also under way. It will be conducted in approximately 300 cognitively healthy individuals who have a rare genetic mutation that typically triggers Alzheimer's symptoms around age 45, and will investigate whether an antiβamyloid treatment can stave off the development of Alzheimer's disease. The API team will collaborate with researchers from DIAN to identify and recruit US participants.

API has initiated another new study, the APOE4 Treatment Trial. Banner Alzheimer's Institute, along with the NIH and Novartis, recently announced the five-year trial to determine whether two investigational anti-amyloid drugs—an active immunotherapy and an oral medication—can prevent or delay the emergence of symptoms of Alzheimer's in people at high genetic risk for developing the disease at older ages. Participants will carry two copies of the apolipoprotein E (APOE4) gene, which is strongly linked to late-onset Alzheimer's.

Takeda Pharmaceutical Company Limited and Zinfandel Pharmaceuticals, Inc. have initiated the TOMMORROW study, a global Phase III clinical trial investigating a genetic-based biomarker risk assignment algorithm to predict risk of mild cognitive impairment (MCI) due to Alzheimer's disease within a five-year period. TOMMORROW will evaluate the efficacy of low-dose pioglitazone in delaying the onset of MCI due to AD in cognitively normal individuals at high risk as determined by the group's risk assignment algorithm.

To connect the findings from different prevention studies, the Alzheimer's Association and Fidelity Biosciences

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Research Initiative convened the Collaboration for Alzheimer's Prevention (CAP). CAP facilitates the sharing of biomarker and imaging data among these prevention efforts in order to evaluate whether the drugs that are being tested demonstrate similar effectiveness in delaying, stopping or preventing the onset of cognitive decline or related disease processes.

The Alzheimer's Association is working with the principal investigators of these and a wide variety of other important studies to share their research data on the Global Alzheimer's Association Interactive Network (GAAIN™), a cloud-based collaborative initiative that provides scientists around the world with access to a vast repository of Alzheimer's research data and sophisticated analytical tools and computational power through a federated network infrastructure. The harmonization of data is necessary to advance and expedite the prevention effort; GAAIN is expected to have a transformational impact on these global projects.

While the focus of many ongoing Alzheimer's trials is disease modification, symptomatic approaches may provide substantial benefits to people with Alzheimer's, including the ability to maintain function, staying active and remain at home longer as the disease progresses. The Alzheimer's field has recognized the need to dramatically increase the efficiency of Phase II and III trials. Furthermore, the Alzheimer's research community requires additional drug targets for further investigation and significant increases in funding for the discovery and evaluation of existing and novel drug targets.

Funding is even more critical in the earliest phases of the drug development pipeline, where targets are most vulnerable to failure. Ensuring strong implementation of the National Alzheimer's Plan, including adequate funding of Alzheimer's research (the Alzheimer's Association is calling for an additional $200 million for this fiscal year), is necessary now to create a platform for progress.

We need to ensure that Alzheimer's is national priority. Contact your members of Congress to encourage funding of Alzheimer's research. In your own voice, share why additional funding is critical to your work and to the entire field investigating Alzheimer's disease and other dementias. Your participation is important, not only to your fellow researchers, but to the millions of individuals and families directly affected by dementia who are counting on you, and us to solve this problem. That is a story only you can tell. ■

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