



LEAD

Leaders Engaged on Alzheimer's Disease

The Path Ahead

A Framework for a Transformative National Plan
to Defeat Alzheimer's Disease

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Alzheimer's Foundation of America	Johnson & Johnson
Alzheimer's Research and Prevention Foundation	Mayo Clinic
American Association for Geriatric Psychiatry	National Association of State Units on Aging
American Geriatrics Society	National Alliance for Caregiving
AHAF Alzheimer's Disease Research	National Association of States United for Aging and Disabilities
American Life Science Pharmaceuticals, Inc.	National Association of Area Agencies on Aging
Banner Alzheimer's Institute	National Council on Aging
Baylor College of Medicine	National Family Caregivers Association
Critical Path Institute	Parkinson's Action Network
Cure Alzheimer's Fund	Pfizer Inc.
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In developing these recommendations LEAD established four workgroups -- one each in the areas of research, clinical care, long-term care support and services, and drug discovery and development -- to carefully select priority recommendations representative of the sentiment and unique needs of the Alzheimer's community. Participation in LEAD or in the development of this report does not constitute an endorsement of each of the recommendations within this document by any particular organization or workgroup contributor.

Recommendations to the Advisory Council on Research, Care and Services

Leaders Engaged on Alzheimer's Disease (LEAD) was created in February 2008 as an open network of Alzheimer's-serving organizations to link key stakeholders from the government, business, and civic sectors to increase attention to and awareness of Alzheimer's disease, its care, treatment, prevention, research, and eventual cure. Recent LEAD efforts have included advocating for increased funding for Alzheimer's disease research at the National Institutes of Health (NIH) and National Institute on Aging (NIA), supporting the inclusion of a cognitive assessment as part of Medicare's Annual Wellness Visit, and ensuring that the needs of Alzheimer's-affected individuals and families are addressed within the new Accountable Care Organization regulations.

More than 40 of the nation's leading Alzheimer's-serving organizations have collaborated within LEAD to develop a series of recommendations which, if adopted, will bring laser-like focus to the issue of Alzheimer's disease. The strength of LEAD is its capacity for a vibrant exchange of information and promotion of outcome oriented strategies utilizing our collaborative strengths. Our goal, simply stated, is to stop Alzheimer's disease by aggressively supporting policies and strategies known to be both effective and innovative.

The subsequent recommendations, if adopted as policy and effectively executed, would bring transformative change in the trajectory of Alzheimer's, saving millions of lives and trillions of dollars, and dramatically accelerate the velocity of progress in Alzheimer's disease research, care, and prevention.

Alzheimer's is the only disease in the top ten leading causes of death that cannot be prevented, cured, or modified.¹ It currently affects more than five million Americans, a number that is expected to grow exponentially by 2050.² The National Alzheimer's Project Act (NAPA) presents a unique opportunity -- indeed a moral imperative -- to put in place a bold yet achievable strategy to prevent Alzheimer's disease from becoming America's biggest public health, fiscal and economic threat to date.

The time is now for America to rally the nation behind the challenging but achievable goal of preventing or controlling the disabling symptoms of this disease by 2020 by accelerating development of preventative treatments, focusing federal investments on innovative, outcomes-oriented research, and facilitating high quality, more affordable care for Alzheimer's-impacted families. Committing our efforts towards the advancement and achievement of this objective and these strategies is indeed bold, but only by aiming high will the best and brightest in our nation be inspired -- and the resources of many

¹Centers for Disease Control and Prevention, *Healthy Aging: Alzheimer's Disease*, <http://www.cdc.gov/aging/aginginfo/alzheimers.htm> (October 2011)

²National Institutes of Health, *Alzheimer's Disease Fact Sheet*, <http://www.nia.nih.gov/NR/rdonlyres/7DCA00DB-1362-4755-9E87-96DF669EAE20/18196/ADFACTSHEET.pdf>, NIH Publication No. 11-6423 (July 2011)

sectors and stakeholders be mobilized -- to address the grave and growing challenge of Alzheimer's disease to our nation, our growing fiscal imbalances and our families. Incremental steps and half measures are not enough to confront the growing Alzheimer's disease crisis.

LEAD members and participants, including nationally renowned experts representing the voices of the Alzheimer's serving community, actively supported the passage of NAPA and are now willing to be a resource to the Advisory Council as it moves forward with the development and implementation of a strategic plan. We respectfully submit to you our recommendations for consideration. In developing these recommendations LEAD established four workgroups -- one each in the areas of research, clinical care, long-term care support and services, and drug discovery and development -- to carefully select priority recommendations representative of the sentiment and unique needs of the Alzheimer's community. Additional recommendations were solicited from LEAD member organizations and subject matter experts through an online survey, phone calls, and interviews.

Below, LEAD has identified five strategies we believe are essential to achieving the goal of stopping Alzheimer's disease in this decade. We urge the Advisory Council to include each in the draft of the strategic plan.

- **Triple the amount of funding for Alzheimer's disease research through NIH, reduce duplication and spur outcomes-oriented innovation.** We must ensure that the main driver of basic and translational research in the United States is fully supported and our research and researcher infrastructure continues to build. Even as additional resources are provided, it must be a priority to develop and make funding decisions based on an outcome-measured process to ensure effective utilization of limited and targeted taxpayer dollars. In order to reduce the potential for waste and duplication of efforts, we must identify and coordinate activity across public and private research-funding agencies, here and around the world, to maximize the potential for public-private innovation in scientific advances.
- **Support the implementation of proven models of care for people with Alzheimer's disease that adequately reimburse healthcare professionals for improved quality of care.** There are several successfully proven care programs supported by the Centers for Medicare and Medicaid Services (CMS) for people with Alzheimer's disease that reduce healthcare clinical care costs and, at the same time, improve quality of care. Those programs should be taken to scale and held accountable for achieving the higher quality/lower cost performance demonstrated in pilot or research programs. In tandem, systems of reimbursement designed for acute as opposed to chronic conditions and based on procedures as opposed to outcomes must be re-formed, and healthcare professionals adequately reimbursed, to incent the improved and unique dementia-oriented care and services required by people with Alzheimer's disease.
- **Support dementia-centric training requirements for healthcare professionals that manage or care for people with Alzheimer's disease and ensure services and support care are accessible to all people with Alzheimer's in need.** As the American population ages and the number of people with Alzheimer's disease increases it is imperative that a dementia-trained workforce is in place to

execute proven, high quality, successful long-term care programs and support services to meet the unique needs of this population. There are currently a number of federal and state programs that require adequate resources to meet the demand of people with Alzheimer's in the coming years and to improve the quality of care for individuals with Alzheimer's disease and reduce the long term health care costs associated with that care. Those federal and state programs should be linked and executed jointly to assure effective execution with an appropriately-trained workforce.

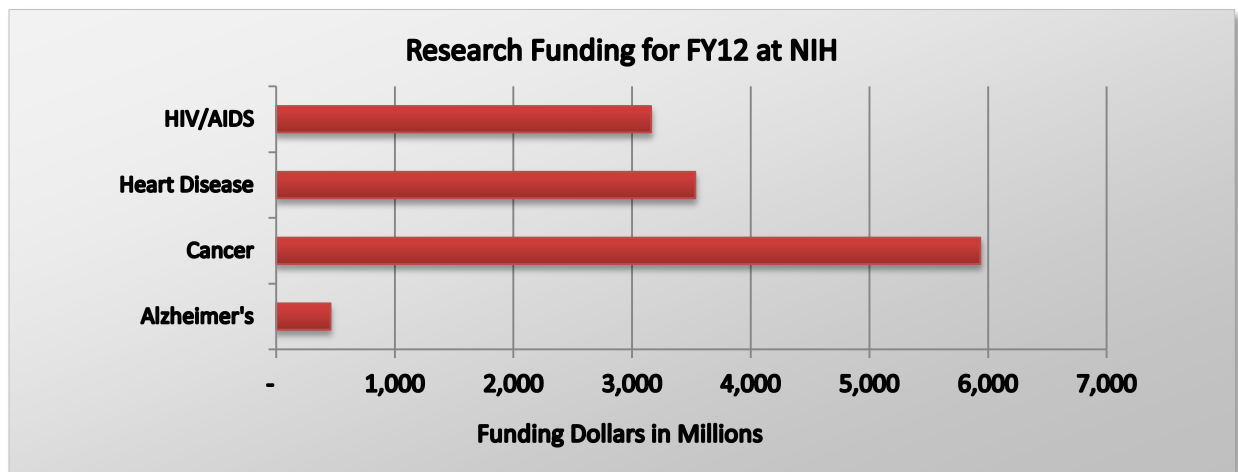
- **Create incentives to drive development of new Alzheimer's disease therapies through enhanced market exclusivity, development of large scale patient registries, and expedited development of qualified biomarkers.** In order to maintain and increase robust investment for Alzheimer's disease and care support from the private sector, new incentives and policy interventions are needed to reduce the time-to-market for potential therapies in the pipeline and to create an positive environment for private sector investment in the care-at-home sector.
- **Establish a dedicated fund at the U.S. Department of Health and Human Services (HHS) to focus on aggressively investing in small businesses that are developing treatments and therapies that present the best likelihood for reducing Medicare and Medicaid spending on Alzheimer's disease.** If we fail to address the 'valley of death' in early drug discovery, the therapeutic pipeline will remain under-populated, under-invested and sluggish. Public investment in the early drug discovery segment of the market will leverage significantly greater private investment and advance earlier stage drug development, thus adding to the odds of getting innovative therapies to market within the decade. Accelerating the drug discoveries, development and approval of therapies intended to significantly modify, stop, or reverse Alzheimer's disease and related dementias, is essential if we are to prevent Alzheimer's disease from becoming our nation's biggest public health, fiscal and security threat.

LEAD stands ready to support the Advisory Council's efforts to contribute to a national strategic plan for Alzheimer's disease. Within the following pages of this report, LEAD participants have outlined additional and more detailed recommendations in the areas of research, clinical care, long-term care and support services, and drug discovery and development. LEAD sincerely hopes that these recommendations will be considered for inclusion in the draft strategic plan.

Increase Support for Research

Basic research is the platform from which effective qualified therapeutic targets to slow, end, and/or prevent diseases are developed. No matter what the approval and distribution processes for drugs and other therapies might be, it is basic research, the “discovery” and description of the fundamental mechanisms of disease pathogenesis that drive the development of effective therapies. Currently, that basic research platform for Alzheimer’s disease within the federal government, academia and industry in the area of Alzheimer’s disease is **underfunded, uncoordinated, and un-focused**. A true, integrated national plan to end Alzheimer’s disease must address these issues head on.

Alzheimer’s disease now threatens to overwhelm the healthcare system. If current trends are not arrested, the U.S. will have spent over \$2 trillion by 2020 to care for Americans with this disease.³ These frightening numbers do not include the 12.5 billion hours of care delivered by 15 million caregivers valued at over \$144 billion for the more than 5 million estimated people with Alzheimer’s disease.^{4 5}



Source: U.S Department of Health & Human Services, *Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)*, <http://report.nih.gov/rcdc/categories> (February 2011)

(Note: Heart Disease includes funding for Heart Disease and Cardiovascular Disease)

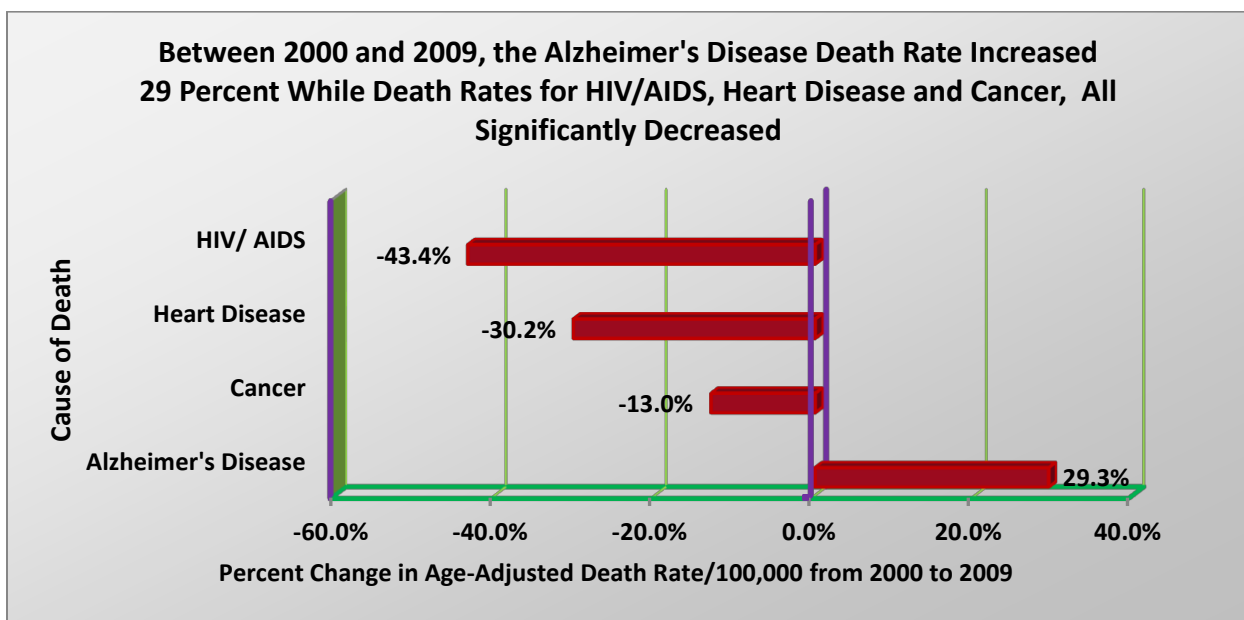
³ USAgainstAlzheimer’s, *The Facts: The Cost to Our Children*, <http://usagainstalzhimers.org/facts/the-cost-to-our-children/>

⁴ Alzheimer’s Association, 2011 Alzheimer’s Disease Facts and Figures, *Alzheimer’s & Dementia*, Volume 7, Issue 2

⁵ National Institutes of Health, *Alzheimer’s Disease Fact Sheet*, <http://www.nia.nih.gov/NR/rdonlyres/7DCA00DB-1362-4755-9E87-96DF669EAE20/18196/ADFACTSHEET.pdf>, NIH Publication No. 11-6423 (July 2011)

In the year 2010, the U.S. spent close to \$172 **billion** for Alzheimer’s care (70% through taxpayer-funded Medicare and Medicaid support), but only \$469 **million** for basic and translational research grants through NIH that drive the search for the effective therapies that would reduce the costs of care.⁶ The 2012 proposed budget for Alzheimer’s disease at the NIH is \$458 million and includes funding for basic research, clinical research, training and support.⁷ The ratio of “cure” to “care” is about 1 to 400. These ‘care’ costs will continue to escalate as a result of the aging demographics with more than 10,000 people turning 65 every day for the next 19 years, creating a larger at risk population.⁸

There have been great scientific advances that give us confidence that increased research efforts will lead to an effective treatment; however, there simply is not enough money being invested in basic and translational research through the NIH to “bend the cost and suffering curve” of Alzheimer’s disease. According to the NIH Almanac, only 3.6 cents of every NIH dollar goes toward supporting the work of the National Institute on Aging—compared to 16.5 cents to the National Cancer Institute, 14.6 cents to the National Institute of Allergy and Infectious Diseases, 10 cents to the National Heart, Lung and Blood Institute, and 6.3 cents to the National Institute of Diabetes and Digestive and Kidney Diseases.⁹



Source: National Vital Statistics Reports, Vol. 49, No. 4, March 16, 2011.
National Vital Statistics Reports, Vol. 50, No. 15, September 16, 2002.

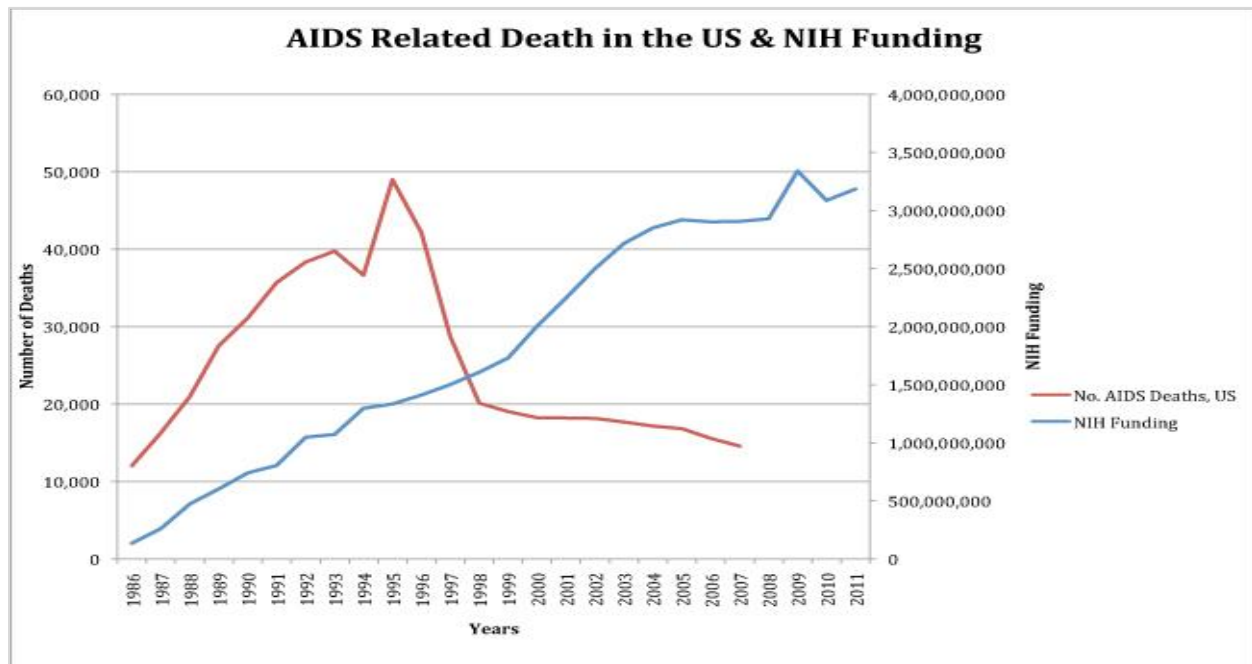
⁶ Lewin Group for the Alzheimer's Association, Changing the Trajectory of Alzheimer's Disease: A National Imperative, May 2010; National Institutes of Health Office of the Budget <http://report.nih.gov/rcdc/categories/>.

⁷ U.S Department of Health & Human Services, *Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)*, <http://report.nih.gov/rcdc/categories/> (February 2011)

⁸ AARP, *Approaching 65: A Survey of Baby Boomers Turning 65 Years Old*, <http://assets.aarp.org/rgcenter/general/approaching-65.pdf> (December 2010)

⁹ National Institutes of Health, *Appropriations*, <http://www.nih.gov/about/almanac/appropriations/index.htm> (October 2011)

As we have learned from the experience with polio and HIV/AIDS medical research, breakthroughs can have a profound impact on not only reducing mortality and morbidity, but on reducing healthcare costs. For example, the cost-effectiveness of the polio vaccine since 1955 in the United States is estimated at \$180 billion.¹⁰ According to former NIH Director Elias Zerhouni, M.D., the \$10 billion invested in basic research in HIV/AIDS between 1985 and 1995 saved \$1.4 trillion in healthcare costs.¹¹



Source: Stanley B. Prusiner, M.D., based on data from National Vital Statistics Reports and NIH Office of the Budget.

Under these circumstances and faced with certain disaster without substantial changes in funding and approach, we recommend these specific recommendations for incorporation into the Advisory Council’s strategic plan.

RECOMMENDATIONS

Increase Funding for Alzheimer’s Disease Research as a Priority Among Public and Private Entities.

There are no effective therapies for Alzheimer’s disease. On the other hand, there have been tremendous scientific advances in this area over the last 25 years that lead the field to believe that truly effective therapies are in sight. Despite this, early and even mid-career researchers are leaving the

¹⁰ Thompson KM, Duintjer Tebbens RJ. Retrospective cost-effectiveness analyses for polio vaccination in the United States. *Risk Analysis*. 2006;26:1423–1440.

¹¹ BJ Culliton, "Interview: Extracting Knowledge from Science: A Conversation with Elias Zerhouni," *Health Affairs*, 25 (2006): w94-w103.

research field because their work in Alzheimer's disease research cannot be funded. Tripling the amount of funding for Alzheimer's disease research through NIH will assure that the basic research infrastructure that is aimed at stopping this disease and 'bending the cost curve' remains in place. This increase should *not* come at the expense of the Alzheimer's Disease Centers program, the Alzheimer's Disease Genetics Consortium, the National Cell Repository for Alzheimer's Disease, and the National Alzheimer's Coordinating Center — all of which provide a huge and unprecedented collaborative infrastructure that facilitates basic, clinical and translational research, enabling many R01s to be proposed and completed. Significant federal investments to speed basic research will lead to the identification of novel drug targets, and follow-on translational studies will examine the efficacy of targets in preclinical studies and clinical trials. Clinical research should also be increased to determine best methods for all aspects of patient care. Additional funding recommendations include:

- Incentives to triple the amount of funding for research via foundation, private support, and industry to facilitate breakthroughs in multiple areas necessary to make advances.
- Provide appropriate incentives for private industry to invest in the accelerated development of the most promising Alzheimer's therapies.
- Fund the Cures Acceleration Network (CAN), within the office of the Director of the NIH, to aid in speeding the translation of basic scientific discoveries into treatments for Alzheimer's and other diseases.
- Provide adequate support for and direction to the FDA to ensure new approaches to accelerate therapeutic development through incentives for innovation.

Enhance Coordination of National and Global Efforts in Alzheimer's Disease Research.

Federal agency coordination will help to rationalize and focus funding efforts. There should be a central Alzheimer's disease coordinating entity established within the Office of the HHS Secretary with the authority and ability to convene inter-agency and non-government constituencies, here and around the world, to gather and distribute data, and make recommendations to the Secretary for federal policy regarding funding strategies for stopping Alzheimer's disease. An international Alzheimer's disease action plan developed by nations with national Alzheimer's disease plans in place or in progress is an important first step in global coordination against this global challenge.

Focus Research Resources on the Most Promising Areas.

With limited resources, private and public funders of Alzheimer's research must develop methods to coordinate research funding to assure that resources are spent strategically on the most promising areas and that investments are outcomes-oriented and accountable for results. Specifically, we recommend:

- Better ways to determine diagnosis, prognosis, and response to therapies quickly using appropriate biomarkers and genetic markers.
- Development of methods to measure the outcomes of interventional approaches that are more sensitive—but relevant—indicators of therapeutic effectiveness. While such research should

include biomarkers and genetic markers, the primary focus should be related to the identification of more relevant clinical endpoints that may ultimately be used to demonstrate the effectiveness of novel therapeutic approaches. It is essential that such research be closely aligned with the FDA so that any progress in the field can be rapidly adopted by regulators, thereby expediting regulatory review and ultimately patient access to successful therapeutics.

- Development of better methods to study non-symptomatic or mildly cognitive impaired individuals to effect better prediction of risk factors, primary and secondary prevention, and effective delay in progression. These methods should include:
 - Development of a large-scale national registry to allow scientists quick and inexpensive access to well-defined populations for multiple research and treatment trials, and
 - Adoption of standardized protocols, procedures and processes for the conduct of clinical trials and the standardization of data capture and exchange of clinical trial results.

Improve Clinical Care Quality and Reduce its Cost

It is now known that the neuropathological and neurodegenerative changes precede Alzheimer's symptoms by decades. As a result, the earliest clinical manifestations are often missed by individuals and healthcare providers. Detecting, diagnosing and managing the care of people with Alzheimer's disease will require ingenuity and integration across the traditional silos of public and private health agencies like the Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services, National Institutes of Health, and Food and Drug Administration as well as healthcare providers and payers. As a nation, we should focus on developing and continuously improving the care of our citizens in home or community settings by offering the best risk management, prevention strategies, early detection, precise diagnosis and long-term management available at any given time, recognizing that, in doing so, we can reduce utilization of traditional providers, hospitals and institutional services and the attendant costs to Medicare and Medicaid.

RECOMMENDATIONS

Recruit, Develop and Continuously Train a Workforce of Able and Dedicated Healthcare Professionals for People with Alzheimer's Disease.

There are not enough family or geriatric physicians trained in caring for individuals with dementia and a paucity of training in Alzheimer's disease for existing healthcare professionals generally. All providers who take care of people with Alzheimer's disease should have geriatric medical training so that they are able to provide quality care. Specific recommendations include:

- Develop affordable companion services, study-partner, and medication management services in the public and private sector
- Develop trained dementia aides to help individuals with dementia with their emotional and physical needs when memory failure prevents independent function
- Enhance and make affordable long-term care options for those who choose residential care due to memory disorders and dementia. These settings can be networked with Memory Disorders Centers to ensure that the goals of maintaining cognition and function as well as manageable behavior are retained for residents in long-term care, with no reduction in their quality of life due to the change of living arrangement.

Primary Care Doctors, Geriatricians, Geriatric Psychiatrists and Neurologists Should be Adequately Reimbursed for Patient Care and the Evaluation of Cognitive Function Including Psychometrics and Caregiver Education and Counseling.

Unless doctors are appropriately reimbursed, they will not take the necessary time to address the complex needs of individuals with Alzheimer's disease. Anticipatory management in a setting where

transitions and treatable concomitants of Alzheimer's disease are understood will result in better care at all stages. Such practices may delay the onset and progression of disabling clinical symptoms, and allow meaningful function, reduce healthcare costs and improve the quality of life for individuals with the disease and their family caregivers.

CMS Should Implement Proven Pilot and Demonstrations Programs System-Wide.

Several studies demonstrate that programs such as REACH (Resources for Enhancing Alzheimer's Caregiver Health) and Independence at Home (IAH) for high-cost Medicare beneficiaries with two or more chronic conditions—including Alzheimer's disease—reduce healthcare expenditures, improve quality of care and enhance health outcomes.¹² Successful programs like IAH should be implemented across the country so that all people with Alzheimer's disease have access to high quality care.

Develop Models of Care and Training Materials to Assist Primary Care Providers Manage Co-Existing Medical Conditions in People with Alzheimer's Disease.

It is estimated that two thirds of people with Alzheimer's disease also have at least one other co-existing chronic condition—such as diabetes, heart disease, or high blood pressure-- complicating care management.¹³ Providing training resources on care management for healthcare professionals will help individuals with dementia ensure the highest possible level of functioning and avoid excess disability.

Create a Network of Accessible Memory Disorder Centers.

The Centers should be engaged in both clinical care and research, and focused on developing, improving and disseminating best practices in clinical care for people with Alzheimer's disease and their family caregivers. The Centers are necessary to ensure the translation of clinical research into practice, especially advances related to identification of persons with genetic mutations and persons with genetic, biological and environmental risk factors and to the implementation of biomarker based risk assessments. Such Centers will also serve to mobilize assessed populations for clinical trials of new prevention and disease modifying treatments. An example of such a network of centers can be seen in France, where efforts are successfully underway to integrate research, treatment and support through multi-disciplinary centers.

The Centers should be for-profit, at-risk comprehensive management facilities dedicated to optimizing the overall health care of all people with Alzheimer's disease. Funding would be dually-sourced through Medicare and pharmaceutical company support. Pharmaceutical clinical research will be an essential component of these Centers, generating income and advancing the field of clinical care research and

¹² Veteran's Affairs Home Based Primary Care," J. Beales, T. Edes, Clinics in Geriatric Medicine, vol. 25, no. 1 (Feb. 2009); "Geriatric Care Management for Low Income Seniors, A Randomized Control Trial," S. Counsell, et al. JAMA (Dec. 12, 2007); "Consider Medical Care At Home," R. Meyer, Geriatrics (June 2009); "Home Delivery: Bringing Primary Care to the Housebound Elderly," S. Okie, New England Journal of Medicine (Dec. 4, 2008); "Programs Bring Care To Homebound Seniors," M. Friedrich, JAMA (June 11, 2008); "Elderpact: A Housecall Program Teamed With An Area Agency on Aging to Provide Coordinated Chronic Care," B. Kinosian, et al., Journal of the American Geriatric Society (2004).

¹³ Cummings JL, Doraiswamy PM, Leoon J, Martin D, Neumann PJ. Prevalence and impact of medical comorbidity in Alzheimer's disease, J Gerontol A Biol Sci Med Sci. 2002 Mar

offering people with Alzheimer's innovative new therapies through clinical trials. These settings should also be eligible for research dollars from the NIH and other agencies and for enhanced reimbursement from CMS for the integrated assessments and services provided to patients.

Improve Emergency Department and Inpatient Hospital Care for People with Alzheimer's Disease.

Improved emergency department and inpatient hospital care can be achieved by increasing recognition of Alzheimer's disease in acute care settings and providing information and training for physicians, nurses, nursing aides and other staff to help them manage the care of these patients more appropriately. This should include psychiatric care for patients with escalating levels of depression, agitation or psychosis, hospital care for acute agitation or psychosis in both public and private hospital settings. In addition, psychosocial support services must be available to families that will allow for the continued care of loved ones with Alzheimer's disease at home when an illness or other emergency strikes the primary caregiver.

Improve Long Term Care & Support Services

As our nation's population ages there is a greater need for long term care and support services for people with Alzheimer's disease and their families. Alzheimer's disease is often viewed as a "family disease" because of the tremendous responsibilities on family members who care for the person with Alzheimer's disease. Currently 80% of care for people with Alzheimer's disease provided at home is delivered by family caregivers.¹⁴ The annual estimated cost to care for a person with Alzheimer's disease is more than \$42,000 per year, more than three times the average cost incurred by individuals over 65 without Alzheimer's disease.¹⁵ In order to meet the unique care requirements of this population we need to support proven federal, state and local programs that support both the diagnosed individual and family. In addition, we must ensure that the healthcare workforce is capable of providing quality care, and that new initiatives are established that address the unmet needs of this population.

RECOMMENDATIONS

Support Federal Programs that Strengthen Care and Resources for People with Alzheimer's Disease and Their Families.

Successful programs are in place at the federal, state and local levels that provide adequate care and support for people with Alzheimer's disease and their families. Through increased funding and resources these programs will be able to reach populations that are in need of such services. Below is a list of successful federal programs that should continue to receive support to ensure that people with Alzheimer's disease and their families receive quality care:

- Older Americans Act - Reauthorization of this legislation would ensure grants to states for community planning and social services, research and development projects, and personnel training in the field of aging.
- Lifespan Respite Care Act – Reauthorization of this legislation would authorize grants to statewide respite-care service providers. Grants can be used for various purposes, including training and recruiting workers and volunteers, training family caregivers and providing information about available services.
- National Family Caregivers Support Program - At a minimum HHS should ensure that funding levels meet the recommended levels of the President's FY12 budget (\$192 million). This program provides grants to states and territories to pay for a range of programs that assist family and informal caregivers to care for their loved ones at home and for as long as possible. In addition, this program

¹⁴ The Family Caregiver, *New Survey Discusses Impact of Alzheimer's Disease on Family Caregivers*, http://www.thefamilycaregiver.org/press_room/detail.cfm?num=165

¹⁵ Alzheimer's Association, 2011 Alzheimer's Disease Facts and Figures, *Alzheimer's & Dementia*, Volume 7, Issue 2

should add the family caregiver assessment to the list of services for which states can use program funds.

Enhance Training Requirements for Healthcare Professionals Working with People with Alzheimer's Disease and Their Families.

It is important that any healthcare professional managing or providing care for people with Alzheimer's disease or at-risk populations is adequately trained. As our nation's population ages and cases of Alzheimer's disease increase there is a need to ensure that physicians, caregivers, social workers and all other healthcare professionals are well trained to provide quality care and support services. Therefore, we encourage both government and private agencies that regulate, accredit, license and certify residential care and community care providers and settings to require training for anyone caring for people with Alzheimer's disease and other dementias. Such providers should include directors of nursing, nurse supervisors, nursing assistants and respite caregivers. The settings requiring certification should include assisted living, adult day care, nursing home and home care. The training should be based on evidence-based guidelines that have been developed through consensus processes that included providers, family caregivers, other advocates and people with dementia.

Develop New Programs and Initiatives to Address the Unmet Need of Alzheimer's Care and Support.

While there are many community programs and resources to assist with care for people with Alzheimer's disease and their families, more can be done to ensure safe and affordable delivery of care.

- Ensure enforcement of existing CMS regulations about the use of antipsychotic drugs for nursing home residents with Alzheimer's disease or related dementias. Although these drugs may be necessary in some cases, they are presently used excessively, and often without the required documentation and monitoring.
- Fund research to identify programs and interventions that can reduce preventable emergency department visits and hospitalizations and prevent or delay nursing home placement for people with Alzheimer's disease and other dementias.
- Identify effective programs and services for people with early stage dementia, including people with young onset dementia (individuals under age 65), and support wider availability of these programs and services nationwide.

Improve the Drug Development Process

Significant challenges exist to develop and deliver Alzheimer's disease treatments and therapies to the marketplace. There are currently only five licensed drugs for the treatment of Alzheimer's disease. Four of the approved drugs help slow the progression of the disease at its earliest stages, while only one drug has been approved to treat people with moderate to severe Alzheimer's disease. Lack of tools, such as biomarkers, and an understanding of the biological agents that cause Alzheimer's disease impede our ability to address the impending need of people with Alzheimer's disease and their families. Targeted funding for research and incentives to accelerate the therapeutic pipeline and more rapidly translate basic science into new therapies will help to enhance our ability to reduce the costs and risks associated with Alzheimer's disease drug development. In addition, increasing clinical trial enrollment through patient registries, and outreach and education to the public and private sectors will be critical to ensuring continued investment in new Alzheimer's disease therapies. In sum, reducing the time and cost to move a therapy from research to FDA approval -- now 11 to 13 years and <\$1 billion -- is critical to the economic competitiveness of the country as well as to the health and well-being of families without a therapy to address their loved one's Alzheimer's disease.

RECOMMENDATIONS

Expedite Efforts to Qualify Biomarkers for Alzheimer's Disease.

It is essential that drug discovery and development for Alzheimer's disease keep pace with new discoveries in order to improve the chance of success of novel therapies. To ensure this, the following recommendations should be considered:

- Early Mild Cognitive Impairment (MCI) should be included in the drug development paradigm. Many experts believe that some failed drugs may have shown efficacy had they been initiated earlier in the disease. The identification of individuals at prodromal stages will increase the chance of success of disease-modifying therapies.
- Combinatorial biomarkers for Alzheimer's disease should be explored. Recent evidence suggests that a combination of biomarkers can be applied to defining patient subtypes that will respond to particular treatments. The process to qualify one single biomarker for regulatory approval is long and tedious. It is essential that a path be defined for qualifying combinatorial biomarkers in order to keep pace with advances in the field.
- Accelerate methods and processes to standardize and harmonize biomarker assays. Phase II and Phase III clinical trials in Alzheimer's disease patients are very long and costly. Regulatory acceptance and approval of biomarkers is dependent on standardization and harmonization across diverse geographic boundaries. Many biomarkers suffer from technical challenges inherent to the assay or mediator being measured which makes harmonization very challenging. Effective

implementation of biomarkers requires coordination, standardization, and compliance at all stages of implementation.

- Public–private partnerships should be created to evaluate promising presymptomatic treatments and to develop consensus for surrogate markers in the most rapid and rigorous way. Any partnership should include academia, industry, federal and regulatory agencies, and other necessary stakeholders.
- Increase resources for FDA to qualify biomarkers. The process to achieve regulatory approval of biomarkers currently depends upon the FDA workload to meet Prescription Drug User Fee Act (PDUFA) deadlines. It is essential that accelerated paths for qualifying biomarkers be given sufficient resources in order to advance effective therapies to treat people with Alzheimer’s disease.

Incentivize Innovation for Industry and Government Researchers Through Market Exclusivity.

Such exclusivity has been granted to other areas of development where there have been complicating factors in bringing drugs to market and particular negative consequences, including Orphan drugs and those studied in pediatric populations. Market incentives for innovation can be achieved in several ways:

- Extended market exclusivity would provide pharmaceutical companies with a compelling financial incentive to continue their efforts to develop Alzheimer’s disease treatments. Offering extended marketing exclusivity for demonstrably effective presymptomatic Alzheimer’s disease treatments, perhaps starting the intellectual property time clock upon completion of the expensive, large and time-consuming pivotal prevention trials, would galvanize the evaluation of promising presymptomatic treatments and help avert an overwhelming financial crisis.
- Provide federal funding to develop presymptomatic Alzheimer’s disease treatments. Treatments without a sufficient marketing incentive at all, such as currently available medications with limited or no patent coverage, dietary supplements and health-promoting lifestyle interventions that have been suggested to reduce the risk of Alzheimer’s disease, could be funded with federal support or targeted market exclusivity.
- Provide federal funding or tax credits for the inclusion of multiple complementary brain imaging and other biomarker measurements in randomized control trials of promising Alzheimer’s disease-slowing treatments and require pharmaceutical companies to make the data publicly available after the trials are completed. This policy would accelerate the development of reasonably likely surrogate end points for the evaluation of promising Alzheimer’s disease slowing treatments, and it would provide a path for the accelerated regulatory agency approval of presymptomatic treatments.

Reduce the Time and Cost for Recruitment of Individuals for Large Scale Clinical Trials.

As manufacturers work to bring new therapies to market, there must be a renewed focus on the cost, time and delays in recruiting members for clinical trials. The use of large-scale patient registries, funded by philanthropic, industry and public funding, would facilitate faster and less expensive clinical trial recruitment. The public and private sectors should also work together to address the unique

circumstances of individuals with Alzheimer's disease and their ability to provide informed consent for clinical trial participation. Finally, data that is held by the FDA should be pooled or made available voluntarily by companies to improve the design of trials and to learn from past failures.

Direct the Administrator of CMS to Conduct and Submit to the Secretary of HHS and to Congress a Study on Alzheimer's Treatments and Therapies.

The report should address the following issues:

- Quantify current and future CMS spending – within both Medicare and Medicaid- on Alzheimer's disease and other high-cost diseases;
- Identify and prioritize targeted strategies and therapies that, if developed and implemented, could significantly reduce CMS spending on Alzheimer's and the other diseases included in the study;
- Identify particular therapy/care needs and specific technology and product as well as more general needs to be addressed;
- Request Congressional authorization to establish a fund to invest through a private venture vehicle in those early-stage private companies targeting treatments and therapies that present a reasonable likelihood of reducing Medicare and Medicaid spending on Alzheimer's and other high cost diseases; to provide funding to support the development of priority therapies identified in the report – including drugs, diagnostics, and devices; and to work with HHS agencies including the Biomedical Advanced Research and Development Authority (BARDA), In-Q-Tel, and other public-private partners to discharge this work.

Waive the Unmet Medical Need Requirement for New Alzheimer's Disease Treatments.

The unmet medical need requirement should be interpreted or waived so that all investigational submissions for products intended to improve Alzheimer's disease symptoms or alter the progression of the disease receive Fast Track status. In addition, to the enhanced communication provided to sponsors under the Fast Track process, this approach should enable any new Alzheimer's disease treatment to be considered for accelerated approval based on a surrogate endpoint that is reasonably likely to predict the expected health benefit.

Encourage the FDA to Enhance Risk-Benefit Decision Making.

The FDA should take into consideration patient impact factors that are particularly relevant to people with Alzheimer's disease, including disease burden on the affected individuals, family members and society, lack of any cure, and population size. The FDA should develop a process by which it can solicit input from diagnosed individuals and caregivers at earlier stages of the drug review process when risk-based decisions are being made. These might include pre- investigational new drug/device exemption discussions, decisions to disapprove, delay discontinue or restrict a clinical trial, submission of a marketing application, decision on status of review (accelerated, priority etc.), evaluation of the data, advisory committee discussions, approval or rejection decisions, writing of the labeling, discussion of risk mitigation elements (REMS), consideration of advertising and promotion materials review, and post-

marketing surveillance and studies, and labeling or status changes. Such a process would be beneficial to people living with other diseases in addition to Alzheimer's by allowing them to contribute to decisions that will affect their access to new treatments.

Establish a Definition for Preventing the Onset of Alzheimer's Disease.

Consider the term "presymptomatic Alzheimer's disease treatment" to refer to those interventions that are initiated before apparent cognitive decline and intended to reduce the chance of developing Alzheimer's disease-related symptoms. Establishing and accepting this definition would help address uncertainties surrounding the term "prevention" and be more acceptable to regulatory agencies.

Conclusion

As a nation we must take bold steps to tackle the increasing cost of care, rising prevalence, and dearth of treatments and therapies for Alzheimer's disease while at the same time identifying new methods of halting and preventing this disease. The strategies and recommendations presented in this document represent the collective thinking of our nation's leading researchers, clinicians, caregivers and patient advocates in the fight against Alzheimer's disease. The Advisory Council is strongly urged to consider these recommendations for inclusion in the draft of the strategic plan, and LEAD is prepared to support the Advisory Council as the way forward is determined.