Testimony of Maria Carrillo, Ph.D., Chief Science Officer, Alzheimer's Association
Senate Committee on Finance Health Subcommittee hearing on "The Alzheimer's Crisis: Examining Testing and Treatment Pipelines and Fiscal Implications"
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Chairman Toomey, Ranking Member Stabenow, and members of the Committee, my name is Maria Carrillo and I serve as the Chief Science Officer of the Alzheimer's Association. Thank you for holding this important hearing today and for the opportunity to testify on the Alzheimer's and other dementia therapeutic and diagnostic pipelines, and on the federal policies that will help address barriers to foster much-needed breakthroughs in diagnosis and treatment.

Founded in 1980, the Alzheimer's Association is the world's leading voluntary health organization in Alzheimer's care, support, and research. The Alzheimer's Association is the nonprofit with the highest impact in Alzheimer's research worldwide and is committed to accelerating research toward methods of treatment, prevention, and, ultimately, a cure. The Alzheimer's Impact Movement (AIM) is the advocacy arm of the Alzheimer's Association, working in strategic partnership to make Alzheimer's a national priority. Together, the Alzheimer's Association and AIM advocate for policies to fight Alzheimer's, including increased investment in research, improved care and support, and development of approaches to reduce the risk of all dementia.

Alzheimer's is a progressive brain disorder that damages and eventually destroys brain cells, leading to a loss of memory, thinking, and other brain functions. Ultimately, Alzheimer's is fatal. We have yet to celebrate the first survivor of this devastating disease.

In addition to the suffering caused by the disease, Alzheimer's is also an enormous strain on the healthcare system, on families including my own, and federal and state budgets. Alzheimer's was projected to be the most expensive disease in America in 2020, with costs set to skyrocket at unprecedented rates. While there are over 5 million Americans currently living with the disease, without significant action, nearly 14 million Americans will have Alzheimer's by 2050. In 2020, Alzheimer's and other dementia will cost the nation $305 billion, including $206 billion in Medicare and Medicaid payments. Unless a treatment to slow, stop, or prevent the disease is developed, in 2050, Alzheimer's is projected to cost more than $1.1 trillion (in 2020 dollars).

BARRIERS TO PIPELINES

Medical Research

We have seen great scientific progress with the historic funding increases Congress has made in Alzheimer's and related dementia research at the National Institutes of Health (NIH). In fact, since Congress passed the National Alzheimer's Project Act (NAPA) 10 years ago, Alzheimer's NIH research funding has increased more than six-fold. This investment has been critical to progress toward the primary research goal to effectively treat and prevent Alzheimer's by 2025, including advances into new biomarkers to detect the disease.

Biomarkers offer the most promising paths because they can detect the earliest brain changes. The Food and Drug Administration (FDA) has approved positron emission tomography (PET)

scans to identify the hallmark amyloid plaques and tau tangles in the brain and is currently reviewing an application for cerebrospinal fluid (CSF). We are also closer to a blood test for Alzheimer's than ever before: breakthrough research presented at the Alzheimer's Association International Conference (AAIC) 2020 - the largest convening of dementia scientists in the world - this past July found that specific markers in the blood may be able to detect changes in the brain 20 years before Alzheimer's symptoms occur. These biomarkers will be new diagnostic tools in the toolbox for primary care doctors and specialists to assist in the early and more accurate diagnosis of Alzheimer's. In addition to these great advances, there is a drug under review at FDA, for the first time, that may treat the underlying biology of the disease.

However, even with these great strides, there is still much left to be done. Investment in Alzheimer's research is still only a fraction of what's been applied over time to address other major diseases. Between 2000 and 2017, the number of people dying from Alzheimer's increased by 145 percent while deaths from other major diseases have decreased significantly or remained approximately the same.

Alzheimer's is one of the most complex challenges science and medicine has ever faced. The reality is that we don't yet know as much as we would like to about the underlying causes of Alzheimer's, compared to some other major diseases. It is a heterogeneous disease, marked by the accumulation of beta-amyloid plaques and tau tangles in the brain, and neurodegeneration. We are still learning about other brain changes such as inflammation, changes in the way our brain cells process energy and nutrients, the role of the immune system and how our brain cells communicate. This heterogeneity underscores the need for diversification of research targets. Funding diverse avenues of investigation and understanding the causes of the disease will ultimately enable us to discover effective Alzheimer's diagnostics and treatments.

It is critical to note that while the field of Alzheimer's biomedical research has made great gains over the years in understanding the brain changes associated with the disease and how the disease progresses, much of the research to date has not included sufficient numbers of Blacks/African Americans, Hispanics/Latinos, Asian Americans/Pacific Islanders, and Native Americans to be representative of the U.S. population. Studies indicate that older Blacks/African Americans are about twice as likely to have Alzheimer's or other dementia as older whites. Some studies indicate older Hispanics/Latinos are about one and one-half times as likely to have Alzheimer's or other dementia as older whites. However, Hispanics/Latinos comprise a very diverse group in terms of cultural history, genetic ancestry and health profiles, and there is evidence that prevalence may differ from one specific Hispanic/Latino ethnic group to another, for example Mexican Americans like myself, compared with Caribbean Americans. Moreover, because Blacks/African Americans and Hispanics/Latinos are at increased risk for Alzheimer's, the underrepresentation of these populations not only hinders the ability of researchers to understand these health disparities, it also restricts their knowledge of how an approved therapy or diagnostic may affect the population most likely to need the drug.

Current and future Alzheimer's research must include greater numbers of underrepresented populations in clinical trials, observational studies, and other investigations to ensure everyone benefits from advances in Alzheimer's science. In order to increase the recruitment and retention of these populations, researchers must understand how to foster and maintain partnerships with

trusted community-based organizations, ensure that members of their research team reflect underrepresented groups, and budget adequately for recruitment and retention efforts. These strategies are outlined in the National Institute on Aging's *Alzheimer's Disease and Related Dementias Clinical Studies Recruitment Planning Guide* and *National Strategy for Recruitment and Participation in Alzheimer's and Related Dementias Clinical Research***.** Congress should prioritize policies that will help apply these strategies, and others, to increase the participation of underrepresented populations in Alzheimer's clinical trials. The Alzheimer's Association and AIM look forward to working with the Committee and other Congressional members to accomplish this.

It is crucial that we continue to increase investment in research in order to maximize every opportunity for success. This will enable us to learn all of the ways Alzheimer's affects the brain, develop better diagnostics, and discover effective treatments for the disease. The Alzheimer's Association and AIM urge Congress to finalize an additional $354 million for NIH Alzheimer's funding in fiscal year (FY) 2021, which was included in the recent Senate draft. We cannot afford to leave any stone unturned. With every study, we are illuminating the biology of Alzheimer's and finding another piece of the Alzheimer's research puzzle.

Coverage of Diagnostics

With all of the scientific progress researchers are making in the field of Alzheimer's biomarkers, we need to ensure there is access to these diagnostic tests. Coverage for diagnostics would help spur private sector engagement on both diagnostics and therapeutics.

Diagnostic testing with a validated biomarker for Alzheimer's is critical. Even in the absence of a treatment, early and accurate diagnoses allow individuals to plan, participate in clinical trials, and express preferences to friends and family. The Alzheimer's Association has worked with the Centers for Medicare & Medicaid Services (CMS) since 2013 to explore coverage of amyloid PET scans, resulting in the IDEAS Study, of which I am a co-chair. The IDEAS Study seeks to gather evidence to support reimbursement by Medicare and third party payers to determine if amyloid PET scans can help clinicians accurately diagnose the cause of cognitive impairment, provide the most appropriate treatments and recommendations, and improve health outcomes. Building on what we have learned from IDEAS, we are now partnering with CMS to launch New IDEAS, which will study the impact of amyloid PET scans on more diverse and historically underrepresented populations.

The IDEAS Study demonstrated amyloid PET scans changed medical management in nearly two-thirds of cases, demonstrating that PET imaging can be a powerful tool to improve the accuracy of the causes of cognitive impairment, including Alzheimer's diagnosis, and lead to better medical management, especially in difficult-to-diagnose cases. If a treatment that addresses the underlying biology of the disease were to become available, accurate diagnostic testing would be a crucial first step in determining appropriate access to the drug. Additionally, the increasing availability of therapeutics in the coming years will also raise the awareness of Alzheimer's and other dementia and drive the public's desire for assessment. Our health care system, including the FDA and CMS, must be prepared to evaluate and provide coverage of these assessment and diagnostic services.

Clinical Practice Guidelines
Despite more than two decades of advances in diagnostic criteria and technology, symptoms of Alzheimer's disease and other dementia too often go unrecognized or are misattributed. This causes delays in accurate diagnoses and appropriate care that are harmful and costly. There currently are no consensus Alzheimer's diagnostic recommendations for primary care physicians. Guidelines were created some years ago but were only developed for neurologists.

As reported at AAIC 2018, a workgroup convened by the Alzheimer's Association under leadership by Dr. Bradford Dickerson, Dr. Alizzera Atri and I, developed 20 recommendations for physicians and nurse practitioners to provide practical and specific U.S. guidelines that are relevant to both primary and specialty settings. The recommendations range from enhancing efforts to recognize symptoms to compassionately communicating to individuals and their caregivers. They can then guide U.S. health care practitioners in the evaluation of individuals for memory, thinking, communication and personality changes, and symptoms of cognitive impairment, Alzheimer's or another dementia. There are several benefits of early and accurate diagnosis including participation in clinical trials which allows individuals to enroll in clinical trials that advance research and may provide medical benefits.

The Alzheimer's Association looks forward to working with physician groups and medical societies to encourage primary care doctors, dementia experts, and nurse practitioners to adopt the new guidelines.

Risk Reduction
As the scientific field continues to search for a way to cure, treat, or slow the progression of Alzheimer's, it is crucial that we also focus on reducing the risk of developing the disease in the first place. Researchers are increasingly studying the impact that lifestyle behaviors may have on the risk of developing Alzheimer's and other dementia. The future of reducing Alzheimer's could be in treating the whole person with a combination of drugs and modifiable risk factor interventions, as we do now with heart disease.

The Alzheimer's Association is leading a two-year clinical trial to evaluate whether lifestyle interventions that simultaneously target multiple risk factors can protect cognitive function in older adults at increased risk for cognitive decline. The U.S. Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk (U.S. POINTER) is the first such study to be conducted in a large group of Americans and will enroll approximately 2,000 older adults, with a particular focus on enrolling underrepresented populations. The study will evaluate the effects of lifestyle interventions, like physical exercise, a healthier diet, cognitive and social stimulation, and self-management of heart and vascular health, on changes in cognitive function. Vascular and metabolic health, physical function, mood, and quality of life will also be assessed, and we look forward to sharing the study results in 2023. Leveraging the Alzheimer's Association investment in U.S. POINTER, NIH funding has enabled several important ancillary studies to look deeper into the science of the main study. There is a neuroimaging ancillary study, which is the first large-scale investigation of how lifestyle interventions affect biological changes in the brain associated with Alzheimer's and dementia. There is a sleep ancillary study to examine whether changes in sleep predict changes in overall cognitive function or in specific areas, such as memory. And researchers from the Alzheimer's Gut Microbiome Project will examine the

effects of dietary interventions on microbiome composition and function in samples collected from three clinical trials, including U.S. POINTER, to understand how variations in the gut microbiome relate to cognitive decline and other Alzheimer's-relevant outcomes.

We are already seeing promising advances in risk reduction research. Last year, the *Journal of the American Medical Association* (*JAMA)* published the groundbreaking results of the SPRINT MIND study, the first randomized clinical trial to demonstrate that intensive medical treatment to reduce blood pressure can significantly reduce risk of mild cognitive impairment (MCI). The study found a statistically significant 19 percent reduction in risk of MCI, which is important because everyone that develops dementia passes through MCI. Preventing new cases of MCI therefore prevents new cases of dementia. NIH just announced additional funding to build upon this initial finding and further explore the effects of lowering systolic blood pressure.

It is crucial that significant research findings like SPRINT MIND are translated into effective public health interventions across the country. In 2018, Congress passed the BOLD Infrastructure for Alzheimer's Act (P.L. 115-406), which would do just that, by investing in a robust Alzheimer's public health infrastructure across the country. This infrastructure includes Alzheimer's and Related Dementias Public Health Centers of Excellence and funding to state, local, and tribal public health departments. Congress appropriated $10 million for the first year of BOLD's implementation in FY 2020, which allowed the Centers for Disease Control and Prevention (CDC) to award funding to three Public Health Centers of Excellence and 16 public health departments across the country this fall. Importantly, one of those Centers of Excellence is focused entirely on risk reduction, and the Alzheimer's Association is grateful for the opportunity to lead this center. While this is a meaningful step forward, CDC must receive the full $20 million authorized for BOLD's second year of implementation in FY 2021 to ensure the full and necessary impact that Congress intended. \

FEDERAL POLICIES FOR BREAKTHROUGHS

Care Planning

One barrier to the increasing availability of therapeutics in the future is the underdiagnosing of Alzheimer's and other dementia. When diagnoses are made, they are too often undisclosed by clinicians. Without detection and diagnosis, people living with dementia cannot get the help they need and may not be able to access therapeutics in a timely manner when available. Education of clinicians and individuals features prominently in the *National Plan to Address Alzheimer's Disease.*

Since January 1, 2017, Medicare has reimbursed physicians and other health care professionals for providing comprehensive care planning to individuals with cognitive impairment – a critical step in improving the quality of care and quality of life for those with Alzheimer's and their caregivers. A care planning visit includes an evaluation of cognition and function, measuring neuropsychiatric symptoms, a safety evaluation, identifying and assessing a primary caregiver, development of advance care directives, and referrals to community services.

The bottom line is that care planning helps ensure those with Alzheimer's get on the right care path. Analyses show dementia-specific care planning can lead to fewer hospitalizations, fewer

emergency room visits, and better medication management. It allows diagnosed individuals and their caregivers to access medical and non-medical treatments, clinical trials, and support services available in the community. Alzheimer's and related dementia also complicate the management of other chronic conditions, so care planning is key to better care coordination and management of comorbid conditions. The availability of the care planning code, CPT® code 99483, is an important step in that direction.

The Alzheimer's Association and AIM contracted with the Health Care Cost Institute to analyze the use of the care planning benefit among Medicare fee-for-service (FFS) beneficiaries and among those in some Medicare Advantage (MA) plans. Unfortunately, the results illustrate that very few Medicare beneficiaries received care planning in 2017, the first year it was available. Specifically:

- 18,669 FFS Medicare beneficiaries received care planning, a rate of 55.6 per 100,000 beneficiaries.
- 2,857 individuals in the Medicare Advantage plans that were analyzed received the services, a rate of 39.4 per 100,000 beneficiaries.
- In seven states and Washington, D.C., not a single FFS Medicare beneficiary received care planning services.

In short, fewer than one percent of those living with Alzheimer's and other dementia received care planning in 2017.

For the benefits of care planning to reach more Americans affected by Alzheimer's, more clinicians must use the care planning benefit. Introduced by Senator Stabenow, the bipartisan *Improving HOPE for Alzheimer's Act* (S. 880/H.R. 1873), would help achieve that goal by requiring the Department of Health and Human Services to (1) educate clinicians on the existence and importance of Medicare's care planning benefit; and (2) report to Congress on the barriers to individuals receiving care planning services and how to increase their use. This bill has already garnered significant bipartisan support in both chambers.

Robust care planning is the first step to learning about long-term care options and selecting the preferred, most appropriate services for persons with dementia, families, and caregivers. Because persons living with Alzheimer's and other dementia often use a variety of supports over the course of the disease and because many--if not most--people need help coordinating those services, a care plan can help these individuals sort through options and choose the long-term services and supports that can contribute the most to the quality of their life. The Alzheimer's Association and AIM urge Congress to pass this critical, bipartisan legislation which garnered support from over half of Congress in its 20 months since introduction, to support individuals living with Alzheimer's and other dementia, and their families, while they await treatment options.

IMPROVEMENTS TO HEALTH CARE PROGRAMS FOR CARE COORDINATION, DIAGNOSIS, AND TREATMENT

Alternative Payment Model

In a recent letter from Chairman Toomey and Ranking Member Stabenow to Department of Health and Human Services Secretary Alex Azar, recommendations were offered on how to strengthen care and services for persons living with dementia as well as foster innovation in Alzheimer's and dementia research. We support the recommendation to the Center for Medicare and Medicaid Innovation (CMMI) to create and test alternative payment and coordinated care models targeted toward Medicare and/or Medicaid beneficiaries with Alzheimer's and other dementia.

A person with dementia is 4.4 times more likely to have six or more other chronic conditions as someone without dementia. Managing these chronic conditions is impeded by an individual's cognitive impairment. As a consequence, health care utilization is significantly higher among seniors with dementia than among seniors without dementia. The annual hospitalization rate is twice as high; the use of skilled nursing facilities is nearly four times higher; and hospital/skilled nursing facility stays are nearly four times longer. In addition, on average, a senior with dementia will visit the emergency room more than once each year.

Many of these costs are simply unnecessary and could be avoided if care was properly managed including better coordination of care, seamless navigation across the multitude of providers, and timely access to care and interventions. There are proven ways to improve the quality of care and quality of life – and reduce Medicare spending – if the payment barriers standing in the way are broken down. Much of the discussion surrounding Alzheimer's disease has focused, importantly, on the need for biomedical research to find means to prevent it and treatments. It is important to not forget that millions of people living with Alzheimer's and other dementia need better care.

CONCLUSION

It is imperative that Congress and the private sector continue to invest in research as we work - together - toward the primary research goal to effectively treat and prevent Alzheimer's by 2025. In the absence of a treatment that would change the underlying course of the disease, we must do all we can to ensure the best quality of care and quality of life for those living with Alzheimer's and the people who care for them. We look forward to working with the Committee to advance bipartisan solutions that will have a meaningful impact on people living with Alzheimer's and other dementia, including passage of the *Improving HOPE for Alzheimer's Act*. Thank you for your continued leadership on investment in NIH funding for Alzheimer's disease and other dementia, and improving care, supports, and services for those living with Alzheimer's and their caregivers, and we appreciate the opportunity to be a resource to the Committee.