Statement Testimony Prepared For:
Hearing titled "Alzheimer's and Other Diseases: An Arizona Perspective"
United States Senate Special Committee on Aging

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November 1, 2019

Chairman Collins, Ranking Member Casey, Senator McSally and members of the Special Committee on Aging, thank you for providing me this opportunity to present a brief perspective on our understandings, challenges and opportunities related to Alzheimer's disease (AD) and Related Dementias (ADRD); their current and projected impact on our health care systems and economics; and the exciting prospects for better diagnosis, treatments and prevention, and progress towards a "cure" in the coming decade.

I am a cognitive neurologist and neuroscientist, and director of the Banner Sun Health Research Institute, Sun City, AZ. I take care of patients, families, and caregivers impacted by cognitive disorders and AD/ADRD; and conduct and lead international research on early detection, treatments, socioeconomic impacts, and best clinical practices in AD/ADRD. I am also a former caregiver, both for my aunt and for my father, whom we took care of at home for over 10 years and who died of dementia.

Alzheimer's disease (AD) is the most common cause of cognitive impairment/dementia above age 65, With rising longevity, a worldwide pandemic of dementia due to AD/ADRD is anticipated[1-5]. AD is the sixth leading cause of death in the United States, and is the only top-10 cause still significantly increasing[1]. The increasing prevalence and costs of AD/ADRD pose a potent threat to our health and social care systems, and our economy.

AD/ADRD are brain diseases. They are not a normal part of aging. These diseases insidiously cause brain damage; damage that over decades leads to, at first subtle, impairments in cognition and behavior, and later to dementia, a gradual decline and ultimate loss of independence. These diseases slowly ravage the brain by depositing toxic clumps of proteins, which first pollute and then light a spreading fire in the brain, causing damage to the brain's infrastructure through inflammation; vascular damage; and disruption of cell energy mechanisms, connections, structures and networks – and which ultimately lead to neurodegeneration (cell death). The "signature" of AD pathological changes is now measurable during life using "biomarkers" – we can measure the toxic proteins related to AD in cerebrospinal fluid collected through spinal taps and see them on novel, though expensive, brain scans. Soon we will be able to measure these and signs of cellular damage and degeneration with 85-90% accuracy using blood tests – these tests will revolutionize early detection efforts and greatly accelerate the pace of research to develop successful personalized diagnosis and therapies; therapies to prevent, retard, or even potentially reverse damage, disease progression, and clinical symptoms. These will allow us to intervene earlier, before widespread and irreversible loss of brain cells and connections have occurred, thus allowing a better

chance of stopping or slowing disease progression. It is estimated that an intervention that can start to delay dementia stages of AD/ADRD by 5 years beginning in 2025 would reduce projected Medicare costs by nearly 50%, and would spare 2.5-4 million Americans from dementia between 2030-2035[6].

We continue to face challenges in the clinical setting regarding providing timely detection, accurate diagnosis, and appropriate disclosure, management, and care. All too often, cognitive and behavioral symptoms due to AD/ADRD go undiagnosed or are misattributed [1,3,7-12]. This is despite more than two decades of advances in definitions, criteria, and imaging and biomarker technologies [13-18] and known meaningful benefits of timely diagnosis for the patient and caregiver [1,2,19-23]. Most persons with AD/ADRD are not diagnosed until the moderate stages of dementia, and 40-50% of persons with dementia never receive a specific diagnosis. Most individuals and their caregivers desire to know the diagnosis, and the value of diagnostic disclosure is supported by evidence and consensus [21,24,25]. Regrettably, as a result of delayed or lack of diagnosis and proper disclosure, patients and their families experience distressing, costly, and potentially harmful delays in receiving appropriate care [1,20]. Barriers to timely diagnosis and appropriate disclosure of cognitive impairment or dementia due to AD/ADRD are multifactorial but can be mitigated. A major opportunity to mitigate this gap is through dissemination and implementation of national best practice guidelines for evaluation, diagnosis and disclosure of AD/ADRD – I co-chair the Alzheimer's Association Workgroup that has, for the first time, developed such a guideline; the report is being finalized and will be available to the medical field and public in early 2020.

The projected burden and costs of AD/ADRD are staggering. About 5.8 million Americans have AD dementia but this number is estimated to increase to 8.4 million by 2030 and to 13.8 million by 2050[26]. Between 2019 and 2025 every state is expected to experience an increase of at least 12 percent in the number of people with AD, and greater increases are expected in Western and Southeastern states[26]. These increases will have a marked impact on states' health care systems, as well as the Medicaid program, which covers the costs of long-term care and support for some older residents with dementia. In Arizona in 2019 there are 140,000 people with AD dementia, this is projected to increase by 43% to 200,000 people with AD dementia in 2025[26]. Almost two-thirds of Americans with AD are women, and the socioeconomic costs and burdens are disproportionally borne by women and minorities[27]. In 2018, over 16 million caregivers provided over 18.5 billion hours of informal (unpaid) care at a low estimate cost of $234 billion[26].

The socioeconomic costs of AD/ADRD typically begin in the years before a diagnosis is made[27]. There are staggering inconsistencies between how costs of AD/ADRD are calculated across studies and our research strongly supports that current estimates fail to recognize the true societal costs[27]. For example, out of pocket expenses for people with dementia are up to one third of their household wealth in the final five years of their life, and caregivers have healthcare costs that are twice as high as non-caregivers. We also found evidence that costs begin rising up to 10 years prior to diagnosis. The opportunities to surmount these challenges will come from better timely diagnosis and care; improving measurement of costs through technologies, real-time data, and big data integration (e.g., of health records and insurance databases); gathering real-world evidence via establishing longitudinal patient registries; adoption of biomarkers; better capturing which stakeholder pays for what and when; development of resource utilization and cost models to support rational resource allocation and investment decisions; and better value recognition illness frameworks that consider direct, indirect (e.g. by caregivers via informal/unpaid care), and intangible costs (e.g. quality of life, effects on economy)[27].

Our community, greatly appreciates the strong bipartisan support that has led to large increases in U.S. federal funding in the last five years for AD/ADRD-related research and that is already bearing fruit. Continued commitment and resolve are needed for discovery and implementation of solutions to avert the impending national health crisis from AD/ADRD that will strain our health and social care systems, workforce, and the economy in the next 1-2 decades. This existential threat to our healthcare systems,

particularly Medicare and Medicaid as we know them, also presents an opportunity for growth and return on investment: to do good and do well; and for our nation to lead the world in diagnostics, treatments, prevention, knowledge- and technology-based solutions and development of dementia-ready and dementia-friendly work force and communities. In this respect, the state of Arizona has been particularly forward thinking. In the last 20 years state funding provided through the Arizona Alzheimer's Consortium (AAC)(http://azalz.org/) has been used as seed money to obtain matched-funding for Arizona-based organizations, including institutes at Banner Health and other AAC partner institutions, to build successful and world-leading programs in research, care, education and training that have produced impactful results, pushed the field forward through global prevention trials and biomarker development and validation, attracted world-class scientists and clinicians, and established innovative and comprehensive care programs that are foundational to defeat AD/ADRD.

It is a very exciting time in our field. We now appreciate that AD/ADRD-related brain changes, and thus "the disease(s)", begin 15-20 or more years before individuals show clear symptoms and that many older individuals, 80 years or older, harbor multiple types of pathological changes, often due to AD along with vascular-ischemic brain injury (or another ADRD) causing a mixed dementia[2,28-32]. Thus, age-related increases in dementia risk can be attributed to accumulation of multiple pathological changes, each of which contributes to dementia risk, and multipronged approaches are likely to be necessary if we are to develop more efficient diagnostics and effective therapies. This makes the picture more complex and accounts, at least partially for the last 2 years having been "the best of times" and "the worst of times" in our community. We have had many disappointments related to experimental drug failures, but also have learned a tremendous amount from these setbacks. We have made great progress regarding tests to detect the hallmarks of the AD using "biomarkers"; using these tests we can show that we finally have drugs in our arsenal that can "remove" amyloid protein plaques, one of the hallmarks of AD, from the brain – and are continuing to test whether these drugs can, at least modestly, both modify disease and slow clinical decline. Importantly, we have learned to diversify our portfolio of drugs beyond amyloid, and to include multiple other mechanisms, targets and interventions; including studying brain healthy lifestyles (such as exercise, proper nutrition, mitigation of cerebrovascular risk factors, and engaging in cognitive and social engaging activities) that, if implemented early enough, may prevent up to 30-35% of cases of dementia worldwide[2].

We are in a critical period that requires strategic planning, investment and collaborative action, because the impact of AD/ADRD is not a "them problem", it is an "us problem". It is too big for one sector to solve by itself; it requires collaborative solutions across multiple stakeholders and for public-private partnerships. I am confident that with continued bipartisan support and leadership, we will rise to the challenge and do what we must: provide better care now, and prevent and cure AD/ADRD for the sake of the future generations.

Thank you, and I am happy to answer any questions you may have.

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