

**ALZHEIMER'S AND OTHER COGNITIVE
DISEASES: AN ARIZONA PERSPECTIVE**

HEARING
BEFORE THE
SPECIAL COMMITTEE ON AGING
UNITED STATES SENATE
ONE HUNDRED SIXTEENTH CONGRESS

FIRST SESSION

SCOTTSDALE, ARIZONA

NOVEMBER 1, 2019

Serial No. 116-14

Printed for the use of the Special Committee on Aging



Available via the World Wide Web: <http://www.govinfo.gov>

U.S. GOVERNMENT PUBLISHING OFFICE

47-206 PDF

WASHINGTON : 2022

SPECIAL COMMITTEE ON AGING

SUSAN M. COLLINS, Maine, *Chairman*

TIM SCOTT, South Carolina
RICHARD BURR, North Carolina
MARTHA McSALLY, Arizona
MARCO RUBIO, Florida
JOSH HAWLEY, Missouri
MIKE BRAUN, Indiana
RICK SCOTT, Florida

ROBERT P. CASEY, JR., Pennsylvania
KIRSTEN E. GILLIBRAND, New York
RICHARD BLUMENTHAL, Connecticut
ELIZABETH WARREN, Massachusetts
DOUG JONES, Alabama
KYRSTEN SINEMA, Arizona
JACKY ROSEN, Nevada

SARAH KHASAWINAH, *Majority Acting Staff Director*
KATHRYN MEVIS, *Minority Staff Director*

C O N T E N T S

	Page
Opening Statement of Senator Susan M. Collins, Chairman	1
Opening Statement of Senator Martha McSally	3

PANEL OF WITNESSES

Alireza Atri, Ph.D, Director, Banner Sun Health Research Institute, Sun City, Arizona	4
Roberta Diaz Brinton, Ph.D, Director, Center for Innovation in Brain Science, University of Arizona, Tucson, Arizona	7
Lisa Capp, Previous Alzheimer's Disease Caregiver, Phoenix, Arizona	9

APPENDIX

PREPARED WITNESS STATEMENTS

Alireza Atri, Ph.D, Director, Banner Sun Health Research Institute, Sun City, Arizona	31
Roberta Diaz Brinton, Ph.D, Director, Center for Innovation in Brain Science, University of Arizona, Tucson, Arizona	37
Lisa Capp, Previous Alzheimer's Disease Caregiver, Phoenix, Arizona	40

ALZHEIMER'S AND OTHER COGNITIVE DISEASES: AN ARIZONA PERSPECTIVE

FRIDAY, NOVEMBER 1, 2019

U.S. SENATE,
SPECIAL COMMITTEE ON AGING,
Washington, DC.

The Committee met, pursuant to notice, at 10:15 a.m., (MST), at Granite Reef Senior Center, 1700 N. Granite Reef Road, Scottsdale, Arizona, Hon. Susan Collins, Chairman of the Committee, presiding.

Present: Senators Collins and McSally.

OPENING STATEMENT OF SENATOR SUSAN M. COLLINS, CHAIRMAN

The CHAIRMAN. The hearing will come to order.

Good morning. What a pleasure it is to be here in Arizona with my colleague, Senator Martha McSally, to convene this field hearing of the Senate Special Committee on Aging. Senator McSally has been a valued and active member of the Senate Aging Committee, which I chair. Her commitments and contributions to the Committee's work are many, and today's hearing reflects Senator McSally's work to advance research and care for families facing Alzheimer's disease.

As the founder and co-chair of the congressional Alzheimer's Task Force, this is an issue that is particularly important to me as well. Many families in our country, including mine, have been touched by Alzheimer's disease. Just last year, I lost my father to it, and like many of you who have gone through this experience, you know how painful it is when you reach the point where a loved one no longer knows your name.

Nearly 5.8 million Americans are living with this disease, including 140,000 here in Arizona. Your State has the fastest growth rate in the Country for Alzheimer's diagnoses, with the prevalence expected to grow by 43 percent in the next 6 years.

In addition to the human suffering it causes, Alzheimer's is our Nation's most expensive disease. It costs an astonishing \$290 billion a year, including \$195 billion in costs to the Medicare and Medicaid programs. If we continue along this trajectory, Alzheimer's is projected to claim the minds of nearly 14 million seniors and surpass \$1 trillion in annual costs by the year 2050.

It takes a tremendous toll on families too. Last year, family caregivers provided 18.5 billion hours of care for loved ones with dementia. It is often a 24/7 job that imposes a tremendous toll on the caregivers. I remembered my mother taking care of my father for

8 years at home prior to his going into the veterans home in our hometown of Caribou for the last 6 months of his life, and keep in mind, my mother is now 92. This was just last year when my father died. Even with help from my two younger brothers and their wives, she was the one who was there day in and day out, and I saw the toll that it took on her.

With the increased Federal investments and public-private partnerships, we are beginning to make progress. Last year, Senator McSally and I worked to secure the largest funding increase for Alzheimer's research in history, bringing us——

The CHAIRMAN. [continuing]. bringing us to \$2.34 billion, and we have worked together again this year to increase that number still more. That is going to make the difference.

Through advances in our understanding of the brain and imaging technologies, scientists, physicians, and pharmaceutical companies are able to conduct clinical trials that never would have been possible even just a few years ago. This investment will produce progress, and I am looking forward to learning about the new research being conducted in your State today.

Again, I am just delighted to be here with Senator McSally and all of you who care so much and share our passion for combating this devastating disease.

It now gives me great pleasure to officially turn over the gavel to my colleague, Senator McSally.

OPENING STATEMENT OF SENATOR MARTHA McSALLY

Senator MCSALLY. Thank you. Well, first, I really want to thank Senator Collins for holding this hearing today in sunny Arizona. We had some travel challenges last night. We arrived early this morning, East Coast Time, but it is really great that we were able to bring Washington, DC, to Arizona to talk about this really important issue, and your leadership on the Aging Committee, Susan, has just been extraordinary. It has just been amazing to be a part of this Committee and this effort and to partner with you on these important issues, and so welcome to the Grand Canyon State. We are glad to have you back.

I also want to say thanks to the Granite Reef Senior Center for hosting us today. This is a great venue, and thanks to everybody who has come out to listen to this important topic, and Mayor Lane from Scottsdale, thanks for also attending.

This just shows the example of how this community in Arizona and across really Arizona cares about these issues, is here to learn and identify the important things that we can do moving forward, and what is actually happening here in Arizona in this important space.

Today's hearing will provide an opportunity for us to hear testimony on Alzheimer's and other cognitive diseases which affect many aging Americans and their caregivers here in Arizona.

Today is also the first day of November. As many of our friends and partners in the Alzheimer's community know, the month of November is Alzheimer's Awareness Month. When President Ronald Reagan, who himself was diagnosed with Alzheimer's after leaving office, first made that designation in 1983, there were less

than 2 million people with the disease. Sadly, that number has grown threefold since that time.

In Alzheimer's, we have the fastest-growing rate of Alzheimer's disease in the U.S. Of the nearly 6 million estimated Americans aged 65 and older affected, 140,000 live here in our home State.

Furthermore, the death rate in Arizona is almost 20 percent higher than the U.S. average. We all know someone who has suffered from cognitive impairment, and the impact is immeasurable.

One of my uncles suffered for many years before passing from Alzheimer's Disease, and I have a dear friend named T.K. Warfield, who was also my veterinarian for all three dogs I have had as an adult, who is currently suffering from what his doctor now thinks is Lewy body dementia with Parkinson's-like symptoms. He had to stop caring for animals, which was his life passion, and has been through a challenging path to find a diagnosis and the best treatment. I have been heartbroken but inspired by how he and his wife, Donna, are enduring the fight against this awful disease.

I have been a strong advocate, as Senator Collins, for us really investing at the Federal level to address these issues and look for groundbreaking research. During my 5 years so far that I have been in Washington, DC, I have supported year-over-year increases in NIH funding, and we have seen an approximately 371 percent increase in those years. That is pretty amazing. That is overall NIH funding.

This year, we joined together, as Senator Collins mentioned, in requesting full and robust funding for the Fiscal Year 2020 Alzheimer's research through NIH. The funding has made an impact in our home State, as seen through University of Arizona's impressive research. I have and will continue to strongly support this much needed research.

It is fantastic to see Arizona leading the way in putting these dollars to use in Alzheimer's and other cognitive disease research. Between our public universities, community programs, local organizations, we are paving a path forward in fighting against these diseases.

Today we have three amazing witnesses in order to share their perspectives and their stories on this topic. We have got Dr. Roberta Brinton who is the director of the University of Arizona Center for Innovation in Brain Science, and Dr. Brinton will discuss the groundbreaking research they have been conducting as well as the impact of the Federal funding has had work.

We also welcome Dr. Alireza Atri—did I say that right? Okay.—who is the director of the Banner Sun Health Research Institute. This institute specializes in debilitating age-related diseases, and has had a significant impact on generating groundbreaking research.

Along with caring for his father for 10 years, his vital research in this field has led to potential, preventative treatments for Alzheimer's as well best practices and guidelines for aging adults. We welcome you and look forward to both your testimonies.

Despite many of these advances, however, we still have a long road to go. Today I hope not only to hear about the successes we have achieved but also the challenges that we still have to fight Alzheimer's and these cognitive diseases.

In 2017, in Arizona alone, there were over 300,000 caregivers—300,000 of our fellow Arizonans, who were caregivers providing more than 376 million hours of unpaid care to those affected by Alzheimer’s and other cognitive impairments, and it is usually a family member, like yours, like your mom. These unsung heroes sacrifice so much to care for their loved ones, and most of that time and effort goes unrewarded. They often quietly forgo their careers, and the consuming demands of caregiving can strain other relationships and roles such as spouse or parent in addition to their own physical and mental health.

Just last week, I met with a 26-year-old son who selflessly moved back home to care full-time for his mother, who has been suffering from Alzheimer’s now for 5 years. This young gentleman took what was a horrific diagnosis and actually created what is now a virtual reality company, which allows both cognitive and physical exercise for seniors. It is caregivers like him that allow those with these diseases to carry on as normally as possible.

I am pleased to welcome one of those caregivers today, Lisa Capp. Lisa cared for her mother for 18 years, sacrificing her time for her family. I have been moved by your story, Lisa, and I hope you can further shed light on the impact being a caregiver can have on an individual and a family.

Thank you all for being here, and again, thanks, Senator Collins, for joining us today and a big thanks to our witness panel who has given your time and your expertise to share your knowledge and with that, I will turn it over to Dr. Atri.

**STATEMENT OF ALIREZA ATRI, MD, Ph.D,
DIRECTOR, BANNER SUN HEALTH RESEARCH
INSTITUTE, SUN CITY, ARIZONA**

Dr. ATRI. Good morning, Chairman Collins, Senator McSally. Thank you very much for providing me this opportunity to present a brief perspective of our understandings, challenges, and projected impact of Alzheimer’s Disease and Related Dementias, ADRD.

I am a cognitive neurologist. I am a neuroscientist, and as you know, I also took care of my father at home for over 10 years. Before that, when I was 19, it was my aunt, who was like a mother to me, so this has a really personal perspective. I also take care of patients and families with early onset disease, so my patients in their 40’s and 50’s.

As you know, Alzheimer’s disease is the most common cause of cognitive impairment in individuals over 65, and we have a pandemic in the world because of longevity, and it is the sixth leading cause in the United States and is the only one in the top 10 that is really significantly increasing.

Alzheimer’s Disease and Related Dementias are brain diseases. They are not a normal part of aging, and that is really important because recently there was a survey with ADI that showed that still 60 percent of individuals around the world, including clinicians, still think of this as a normal part of aging, which it is not.

These diseases insidiously cause brain damage that over decades leads to, at first, subtle impairments in cognition and behavior and later to dementia, which is a gradual decline and ultimate loss of independence. They slowly ravage the brain by depositing toxic

clumps, we understand now, of proteins. First, these proteins pollute the brain, and then there is basically—they light a fire that spreads in the brain, and this causes damage to the brain’s infrastructure through inflammation, through vascular damage, and disruption of cell energy mechanisms, connections, structures, and networks, and ultimately leads to neurodegeneration, which is cell death.

The signature of Alzheimer’s disease changes is now measurable during life using things we call “biomarkers,” and so we can actually measure these toxic proteins in a spinal fluid through spinal taps, which is very common in Europe, but we do it less here, and also through novel brain scans that are expensive but possible to do.

Soon, what is really exciting, we will be to measure these through blood, and this is going to really revolutionize our understanding and also accelerate the basic research.

We think that, actually, probably with about 85 to 90 percent accuracy, these tests will be able to find these proteins and also give us suggestions about cellular damage, which is also important, and these are going to lead to personalized diagnoses and therapies, which we really, really need, because it is not just one disease actually. It is a number of things that come together that cause brain damage and therapies to prevent, retard, and even potentially reverse the damage and clinical symptoms and allow us to intervene earlier before there is widespread damage, which is really, really important.

As you know, if an intervention that could start delaying by 5 years Alzheimer’s disease and ADRD dementia phase, if we had the therapy by 2025, this would reduce about 50 percent of Medicare costs by 2030, and by 2030 to 2035, it will spare about 2.5 million to 4 million Americans with a dementia phase.

We also continue to face challenges in the clinical setting, unfortunately, because of timely diagnosis detection, accurate disclosure, management, and care. Too often, cognitive and behavioral symptoms go undiagnosed or are misattributed. This is despite decades of advances regarding criteria and imaging and knowing the meaningful benefits of timely diagnosis for the patients and caregivers.

Most individuals are not diagnosed until the moderate stages of dementia, and up to 40 to 50 percent of individuals with dementia never actually get a full accurate diagnosis or disclosure. This is regrettable, and the barriers to this are actually mitigatable, I think.

One of the barriers, I think, is of knowledge and guidelines. We do not actually have national best practice guidelines for evaluation, diagnosis, and disclosure of Alzheimer’s disease. I serve as co-chair of the U.S. Alzheimer’s Association Work Group for this, and so we will have this report being finalized and available to the public and the medical field in early 2020.

You went very eloquently over the staggering costs, both in terms of money and people. Every State is going to have an increase over the next decade, 12 percent at least in every State, and in Arizona, up to 43 percent, and that 18.5 billion hours of informal, unpaid caregiving, basically a low-estimate cost of that is \$234 billion that was spent but not counted in the economy.

It turns out the socioeconomic costs of ADRD really, typically began years before the diagnosis, and we have done some research that is international research to show that the cost, calculated across studies, really support that we are really failing to estimate the cost properly.

For example, out-of-pocket costs for people with dementia are up to a third of their household wealth in the final 5 years of their life, and caregivers have health care costs themselves that are twice as high as non-caregivers. We also found evidence that these costs are actually rising, up to 10 years before, lower savings, less employment, and all this is paid for by somebody. Employers are paying for it, and we are paying for it.

These are the costs, but this actually says that we have opportunities to mitigate this. The opportunities are going to come through technologies: possibly diagnosing and caring for people in a timely manner earlier; using real-time data and big data, for example, integrating health records with insurance data bases; gathering real evidence from longitudinal cohorts in the clinic, for example, and seeing how these costs are spread through the whole system; and capturing basically which stakeholder pays for what and when; developing resource utilization models that support the rational allocation and investment decisions; and to have better value recognition of illness frameworks that consider both the direct cost when money changes hands and also the indirect cost of this caregiving and then the hidden cost of quality of life and how it affects the economy. These need to be measured better.

This is a bipartisan effort, and we really appreciate the fact that the funding has gone up tremendously over the last 5 years, and this is actually paying dividends already in this sense.

The State of Arizona actually has been very forward-thinking in this way. The last 20 years, there is an Arizona Alzheimer's Consortium that has funded a lot of research, both at Banner and sister institutions, to actually have seed money that gets funded and matched with other things, and this has actually led to a number of big projects, including projects in Alzheimer's prevention that happen not just here but globally around the world, recruiting lovely people to the State. I have only been here for over a year, and you have been here for 3 years, so it is really helping with that and actually pushing care out in biomarkers. Biomarker development, we want the epicenters here.

It is a very interesting time in our field, and we now appreciate the damage that is starting silently, 15 to 20 years. Ultimately, we have that period that we can intervene.

We also appreciate that when people get in their 80's, they just do not have Alzheimer's changes. They have vascular changes. They have inflammatory changes. Maybe viruses and bacteria may be involved to trigger things, so those are all important. We still need multipronged approaches, not just one approach to do this.

In the last 2 years, it has been the best of times and the worst of times for us. We have had a lot of disappointments, but we have learned from those. From those setbacks, one of the major things we have learned is that we need biomarkers, better biomarkers to allow us to measure things and know where we are going.

Finally, we can actually have some therapies that are removing the amyloid protein from the brain, and we have shown this now, so the question is if you remove the amyloid, are we going to change clinical course? And there is some suggestion to that, and we need to go earlier.

We have also learned that we need to diversify our portfolio, that you will hear more about that, not to just look at amyloid, but also look at tau and inflammation and all kinds of other mechanisms and targets and interventions—and also always promoting basically lifestyles, such as exercise, proper nutrition, mitigating super-vascular risk factors, and engaging in cognitive and social activities. If we do this early enough, there is actually a fair bit of evidence that about 30 to 35 cases of dementia worldwide are actually preventable because people will not manifest the symptoms. Their brain will be much more protected.

We are in a really critical period that requires strategic planning and investment and collaboration. This is, as you know, not a “them” problem. It is an “us” problem. It is too big for one sector to solve by itself, and we need collaboration and continued support, and I am confident with continued bipartisan support and leadership that we will rise to the challenge because we have to do it. We have to provide better care now for families and patients who really depend on us and to prevent and cure Alzheimer’s disease and ADRD not just for our generation but also for the next generation.

Thank you very much.

Senator MCSALLY. Wonderful. Thank you, Dr. Atri.

Dr. Brinton?

**STATEMENT OF ROBERTA DIAZ BRINTON, Ph.D,
DIRECTOR, CENTER FOR INNOVATION IN BRAIN SCIENCE,
UNIVERSITY OF ARIZONA, TUCSON, ARIZONA**

Dr. BRINTON. Good morning, Senator Collins, Senator McSally. Thank you for the opportunity to address you on the Arizona Perspective on Aging: Alzheimer’s and Other Cognitive Diseases. I am Dr. Roberta Diaz Brinton, the director of the Center for Innovation in Brain Science at the University of Arizona. Our mission is to create innovations in brain science of the future for those who need a cure today.

We are an all-brains-on-deck translational ecosystem dedicated to addressing the urgent national health crisis of Alzheimer’s disease. I am honored to share with you the advances being made in Arizona to prevent and cure Alzheimer’s disease.

Curing Alzheimer’s disease is not rocket science. It is harder. That is the bad news, but I am here to deliver the good news.

Arizonans have a bold pioneering spirit, as Senator McSally knows, and an innovative culture that is exemplified through the Center for Innovation in Brain Science. Across the State, researchers and clinicians are working together to prevent, delay, and cure Alzheimer’s Disease through the Arizona Alzheimer’s Consortium, as Dr. Atri mentioned.

The University of Arizona’s Center for Innovation in Brain Science was created to address the challenge that in the 21st century there is not a single cure for a single neurodegenerative disease.

We operate as a university-biotech hybrid focused on age-associated neurodegenerative diseases, and it is unique in the Nation and likely the world. CIBS is a mission-driven all-brains-on-deck translational ecosystem that integrates the discovery prowess of academia with the best practices of biotech.

Our pipeline of innovative therapeutics for Alzheimer's disease include regenerative therapeutics that activate neural stem cells in the brain, promote energy production in the brain, reduce neuroinflammation, and prevent generation of Alzheimer's pathology.

A prime example of the success of our efforts and yours, after decades of painstaking research supported by National Institute on Aging, we are prime to conduct a Phase 2 clinical trial of allopregnanolone as the first regenerative therapeutic to regenerate the degenerated Alzheimer's brain. That is bold, and that is Arizona.

The National Alzheimer's Project Act is an ambitious plan, as you know, to prevent and effectively treat Alzheimer's disease in 5 years. Through the transformative and innovation leadership team at the National Institute on Aging, we are closer than ever to delivering on these goals. Federal investments have resulted in discovery of mechanisms and drivers of Alzheimer's and a broad portfolio of therapeutics currently in clinical trial. We now know one-size therapeutic will not fit all and will not fit all for all time. We will require a broad portfolio of therapeutic options that address both sex biology, Alzheimer's biology, and the progression of the disease.

To deliver prevention and treatment of Alzheimer's by 2025, two advances are critical. As Dr. Atri mentioned, we need big data analytics for precision prevention.

Electronic medical records held by the Federal Government hold the key to detecting and preventing Alzheimer's disease in at-risk populations. For example, using existing NIH-funded clinical trial data, we were able to identify women at increased risk of Alzheimer's disease while they were still healthy, and this provides the opportunity to intervene in this at-risk population when they are still healthy with FDA-approved therapeutics to reverse the trajectory of risk.

Using Medicare data, we demonstrated that specific statins reduced the risk of Alzheimer's disease in an ethnically diverse national population. Using insurance claims data, we were able to demonstrate that specific breast cancer therapies can reduce the risk of developing Alzheimer's disease in women later in life. We are currently conducting a comparable analysis of prostate cancer therapies and the risk of developing Alzheimer's in men.

We are now partnering with researchers at the Veterans Administration to determine which therapies for type 2 diabetes reduce or increase the risk of developing Alzheimer's. Through big data analytics, we can inform clinical care to prevent Alzheimer's disease in at-risk populations.

Our veterans face a unique constellation of risk-factors for Alzheimer's, including high stress, sleep deprivation, toxin exposure, and traumatic brain injury.

The challenges associated with accessing and analyzing veteran health records puts this group at risk when we could prevent Alzheimer's. Through their medical records, our heroic veterans on the battlefield can be heroes again in the fight against Alzheimer's.

I urge you to find a way to safely, securely, and efficiently expand access to electronic medical records held by the Federal Government and mandate the sharing of HIPAA-compliant patient-level data from federally funded clinical trials.

Precision medicine cures for Alzheimer's requires Arizona commercialization innovation. Big pharma and venture capital are abandoning Alzheimer's and other age-associated neurodegenerative diseases. However, their departure is Arizona's opportunity to become the new biotech hub for curing Alzheimer's.

A challenge to delivering our discoveries to patients is that commercialization of federally funded therapeutic development ultimately reaches a valley of death. Critical to delivering precision medicine cures for Alzheimer's is an accessible network of innovation experts to advance intellectual property opportunities, startup capital, business development, and the commitment to find a way to—yes, to achieve the goal for the American public.

The National Institutes of Health, SBIR, STTR, and Commercialization Accelerator Program are engines of commercialization that, with modest adjustments, could catapult therapeutic development across the valley of death.

The war against Alzheimer's Disease is being fought, as you said, already on many fronts, from the homes of patients and caregivers to the research laboratories of scientists and clinicians across this great Nation. Millions of Americans are counting on us to win this fight. We can, we will, we must win.

Arizona, with its bold pioneering spirit and entrepreneurial culture has a unique opportunity to lead the Nation and the world in the science of aging and innovative therapeutic development for Alzheimer's and age-associated neurodegenerative disease. Arizona can deliver precision medicine of the future for those who need a cure today.

Thank you for your commitment to our Nation and to Arizona, and for your efforts, we are closer to curing Alzheimer's. Thank you.

Senator McSALLY. Thank you, Dr. Brinton. I really appreciate it. Ms. Capp?

STATEMENT OF LISA CAPP, PREVIOUS ALZHEIMER'S DISEASE CAREGIVER, PHOENIX, ARIZONA

Ms. CAPP. Senator McSally, Senator Collins, and distinguished guests, thank you for the opportunity to testify about my experience as my mother's caregiver.

I am a blogger, an activist, and a dementia caregiving survivor after an 18-year journey through the disease with my mother, Vera Cappelletti. After her death in 2015, chairing the Board of the Vermont Alzheimer's Association and a recent move to Phoenix, I am now co-chairing the board of the Desert Southwest Alzheimer's Association Board. I write and speak regularly on the subject of dementia caregiving.

Why is that important? In 2014, comedian Seth Rogen addressed lawmakers in congressional testimony about the care of his wife's mother who was diagnosed with young-onset Alzheimer's. She was in her mid-50's. Back in 2014, Seth said, "I think until you see Alzheimer's firsthand, it is kind of hard to conceive how brutal it really is."

Today dementia caregiving remains equally brutal around a still-stigmatized disease driving family caregivers deeper into emotional, physical, and financial hardship.

Mom came to live with us after my dad passed away, and at the time, I was advancing my career in high tech. I was lucky. My husband, Tom, who is here with me today, shared fully in my role as caregiver, and without children due to my infertility, we did not count ourselves among those in the sandwich generation of care, as so many are.

My mother's dementia began with whimsical imaginings but turned to terrifying delusions and hallucinations. Tom and I continued care in our home until crisis, crisis that left us with no choice but to involuntarily commit my mom to a psychiatric ward in order to stabilize her condition.

My siblings, although living in other parts of the Country, participated in many ways, but most notably in our family's decision to move my mom not back to home from the hospital, but instead to live the remainder of her life in full-time memory care.

As my mom slid deeper into her dementia, the invisible battle became a struggle I had to watch progress while plaques and tangles took over her brain.

We were blessed by a relationship with a skilled geriatric psychiatrist who helped me to understand my mother's world just a little bit better.

Dr. Paul Newhouse asked, "Do you know what *deja vu* is, Lisa?" "Feeling you have been somewhere before, like it is familiar," I answered.

He said, "Yes. *Deja vu* means that the strange is familiar to you, but do you know what *jamais vu* is?" and I shook my head no. "*Jamais vu* is what our friends and family can experience in dementia. The familiar becomes strange. Imagine every moment of your life struggling with something you know and you have known your entire life, but now it is strange to you," the doctor shared with me.

My life was busy. I did not understand the nuances of my mom's brain disease. With the stress of having to leave work early to get mom to one of her many doctor appointments, she might pick up a comb and look at it as if she had never seen it before, confounded by its very function. I would grab the comb from her hand and smooth her hair as we rushed out the door late for our appointment, but waves of guilt kept building in me. The emotional web between someone you love living with dementia and you as the unexpected caregiver are made up of strands spun from loss, despair, sadness and intense feelings of inadequacy.

I think about the arc of my mother's life from wife, mother, and career; through the hallucinations and delusions; and on to the advanced stages of dementia. Bedridden with her ability to speak gone, I would lay my iPhone on her pillow and play Frank Sinatra

singing “Fly Me to the Moon.” Her beautiful green eyes would open, and light would dance in them but from a deep and far-away place.

Dementia is a set of perpetually evolving diseases requiring the act of caregiving to be both collaborative and yet co-dependent. As someone living with dementia progresses, so does the caregiver along the paths of physical, spiritual, and emotional coping. As one individual declines, the other must advance and the end of caregiving is not rewarded with a sense of freedom. It is marked instead by deep and intense grief at yet another loss to this despicable disease.

I am hopeful, more hopeful than I have ever been, that I will see the first survivor of this disease in my lifetime. The unprecedented funding you and your fellow legislators support is leading not only to critically important research discoveries like you have heard today, but to a renewed hope among caregivers for earlier detection, prevention, and an ultimate cure.

I thank you. I thank you, Senator Collins, for your leadership as Chair of the Senate Special Committee on Aging and for your support to programs, policies, and funding, critically important to the Alzheimer’s Association and those in our Nation requiring their services.

I thank you, Senator McSally, for your support to the younger onset bill, H.R. 1903, which passed the House this week. The bill will give access to critical resources for those living with dementia under the age of 60 as part of the Older Americans Act, services they do not have access to today, and I welcome the opportunity to work with you, Senator McSally, on initiatives that continue to benefit our great State and the Nation.

There are still so many opportunities yet to exploit. We need to educate and train primary care physicians, first responders, ER and hospital staff, caregivers and administrators in local care facilities, major employers and small business owners for whom caregivers currently work, barbers, lawyers and bankers, all who see the impact of this disease in their day-to-day lives and in their day-to-day work.

I applaud Mayor Mitchell and the city of Tempe for their work in becoming a dementia friendly city and to Mayor Gallego for considering similar steps in Phoenix. These actions enabled by your support to The Hope Act, H.R. 1873, go a long way in removing stigma around this disease and in making life a bit easier for caregivers.

I will end my comments by sharing although my legal name is Lisa Beilstein, I write and am active as Lisa B. Capp in my mom’s memory.

Thank you for giving me the opportunity to speak, for listening to my story, and for all you have done and will do in the fight we share together to ultimately live in a world without dementia and Alzheimer’s disease.

Senator MCSALLY. Wonderful. Thank you, Ms. Capp, for sharing your story in such a personal manner and your continued advocacy for caregivers and for victims of these diseases.

There is so much to talk here. I mean, we were taking copious notes.

I want to first start with—I opened up with this statistic that 20 percent more deaths are happening in Arizona than in other parts of the country from Alzheimer’s disease.

Dr. Atria or Dr. Brinton, do you have any sense of why that is such a higher significant percentage?

Dr. ATRI. I am not sure, but I think we probably have older individuals here with multifactorial disease, and so, in some ways, they may have some comorbidities that are made worse by dementia and that is one of the things that is interesting is that I think with Alzheimer’s disease, it is still underreported, even though it is a sixth leading cause. When somebody dies in the end stages, they may say it is their heart or their lungs or their infection, but really it is the Alzheimer’s disease that got them to that point where they could not swallow well and they got the pneumonia, et cetera.

Senator MCSALLY. Okay, great.

Dr. Brinton, do you have anything to add?

Dr. BRINTON. I do not have expertise in this area.

Senator MCSALLY. Okay.

Dr. BRINTON. One of the things that concerns me from my experience of conducting clinical trials is that women, who are disproportionately affected by Alzheimer’s disease oftentimes do not have the caregiving network that a man might have. If there is no daughter in the family or there is no daughter-in-law in the family, that actually poses a fairly large challenge for women with Alzheimer’s disease. They can experience dealing with the disease largely on their own, so that would be a concern that I would look into about why that might be.

Senator MCSALLY. Well, I want to followup on that, Dr. Brinton. We were talking in the back about how the gender split of how Alzheimer’s is so disproportionately impacting women than men, and you went through the other cognitive diseases and how that has got significant gender differences. Can you just share a little bit about the research and understanding related to specifically how these types of diseases are impacting men and women so differently?

Dr. BRINTON. Yes. To begin with, there has been an assumption in the Alzheimer’s field that there are more women living with Alzheimer’s than men because women live, on average, 4.5 years longer than men, but we all know that the disease is 10 to 20 years in the making. Average age of diagnosis of the disease is in their 70’s. Well, it does not take a rocket scientist to do that simple math of 70-ish minus 20-ish, and you run into 50-ish, which is the average age of menopause and that endocrine aging transition actually can unmask the risk of developing Alzheimer’s disease in women.

We are already able to detect beta-amyloid plaque in the brain of some women and particularly those women that carry the risk factor for Alzheimer’s disease, the APOE-e4 gene, and one of the exciting outcomes of an earlier study that we did was that those women who were at risk and still healthy but were developing significant cognitive decline were women who had dysfunction in their metabolic system. They were still within normal range, but they were on the wrong end of normal and it turns out they carried the APOE-e4 gene.

The APOE-e4 gene is not an absolute risk factor because what was really interesting is that in this entire study in 500 women, there was an equal distribution of the Alzheimer's risk factor APOE-e4. It only occurred that the cognitive decline only occurred in women who were postmenopausal. They were all postmenopausal, and they had metabolic dysregulation, and they were APOE-e4-positive, so you cannot change being chromosomally female. You cannot change your age, and you cannot change being menopausal but you can change your metabolic health because we had APOE-e4 women in the metabolic healthy group of women who showed who actually had fantastic cognitive function, so, again, early intervention.

At the time and I think part of what we really need to focus on is how can we deploy this scientific knowledge into the clinical space. I think we still have those hurdles to overcome that we can discover, and then how do we actually reach the clinician? How do we do that effectively?

I speak to many physician groups, but there has got to be this way that we communicate more effectively to the clinical world.

Senator MCSALLY. Just to followup, when you say metabolic function, can you put that in layman's terms?

Dr. BRINTON. Yes. It is really around glucose metabolism, and we know that type 2 diabetes is a risk for developing Alzheimer's disease and the reason for that is the brain consumes 20 percent of the glucose—20 percent of the glucose, 20 percent of the oxygen. It is 2 percent of the body weight and consumes—it punches above its weight, so from here down, we are a Prius. From here up, we are a Hummer, so the brain is—

Senator MCSALLY. I asked for layman's terms. Everybody can picture that.

Dr. BRINTON. Yes. The brain is an energy hog, and so when you look at type 2 diabetes, we typically think about type 2 diabetes as really from the neck down but the first organ affected is the one most dependent upon glucose.

Dr. ATRI. Let me add to that also because I think part of the metabolic syndrome, there is also the glucose metabolism. There is also obesity and also inflammation.

Dr. BRINTON. Yes.

Dr. ATRI. Micro inflammation.

Senator MCSALLY. Okay.

Dr. ATRI. That is huge. Things that are inflammatory to us are bad for the brain and bad for the vessels.

These interactions between glucose and insulin, they actually work in the Alzheimer's pathways—

Dr. BRINTON. Yes.

Dr. ATRI [continuing]. and they interact with APOE-e4.

Senator MCSALLY. Interesting.

Okay. One quick question for Ms. Capp, and then I will hand it over to Senator Collins.

You were with your mom when she was first diagnosed, right, through her whole journey? I mean not with her, but you have seen that whole journey that she has been through. Can you share some perspectives? The early prevention and the early indications that somebody may be prone to the disease are so critical, and in addi-

tion to some of the legislation that you mentioned, I am a proud cosponsor of another bill which is called the CHANGE Act, which requires testing for cognitive impairment or progression in both the Welcome to Medicare initial exam and the Medicare annual wellness visits.

I know a lot of the research is trying to catch it much earlier than that, but this seems like common sense, but can you just share just personally how it manifested and the journey of even trying to get a diagnosis and understand it all?

Ms. CAPP. Sure. I think the most difficult part of the early stages of dementia, whether it is younger onset or later onset, is the dynamics of denial.

When we are functioning at the levels, we are all functioning at, at the peak of our lives, at the peak of our careers, to recognize that something is wrong or for family members to admit that something just does not seem right is very difficult and that is why I focus on the stigma of the disease. It is critically important for us to remove stigma. It is a brain disease. It is no different than any other disease in terms of acceptance in our communities and support, and that is why dementia-friendly cities are so critically important.

Bankers often see it first before families. Family members often hear from neighbors that your mom or your dad are just not right. Things are not right. That part of overcoming denial and coming to acceptance allows people to finally get into a doctor's office to begin to try to get a diagnosis.

We did not have a diagnosis until very late because in the years that my mom was going through this, it was even more stigmatized.

It is critically important to be accepting, to understand, to learn the signs of Alzheimer's and dementia, so that everyone understands.

For those people who have not been touched by the disease—and we talk about how many families have, but for those who have not, the things that could be said can be very cruel. It is just about moving on.

It took a long time for us to understand what was going on. I am very interested in the research because my mom, although passing away in her late 80's, has a sister who is still alive at 101, so that Petri dish is pretty small and her sister traveled to Italy last year by herself. The dynamics are critically important for us to understand and for family members to know they can deal with this and get support.

Our geriatric psychiatrist was enormously successful. I will say there are far too few geriatric psychiatrists, and there are far too few primary care physicians who know how to detect and help family caregivers come to acceptance and out of denial.

Senator MCSALLY. Great. Thank you.

Senator Collins?

The CHAIRMAN. Dr. Atri, I am going to take up where Ms. Capp just left off, and that is you had a startling statistic in your testimony about the number of clinicians who will not recognize the early signs of Alzheimer's. I think perhaps that is what you were going to comment on.

Dr. ATRI. Exactly.

The CHAIRMAN. Go right ahead.

Dr. ATRI. That is exactly right. Part of it is stigma, but part of it, again, is that lack of knowledge and resources. It is remarkable that people get touched by all kinds of clinicians, and yet these things go under the radar.

Years before there is a cognitive issue, it is actually unscrupulous telemarketers and other folks to recognize things. It is not just memory. It could be judgments. These things start manifesting themselves years before.

Sleep issues, anxiety, what appears to be like depression but is really a lack of motivation and withdrawal. We become very, very good as clinicians recognizing those things, but when we think of those things, those are just brain chemicals changing, oftentimes because of neurodegeneration.

If you look at older adults who have those changes and you look forward, it turns out that many of them have neurodegenerative processes, and there is evidence to show that actually if you treat some of those earlier, you can actually change and ward off dementia.

We do not wait for any other disease to say, "You know what? Let us wait for the cancer to metastasize until we treat it" or "Let us make sure you have compression fractures everywhere before we do something about it." Or if you go to see somebody and you say you have chest pain, they do not say, "Oh. You are getting old. Everybody has chest pains," right? Or if you are breathing a little bit heavy, "Oh, you are just older." No, you do something about it, and we have to have the same urgency about this where people come and there is a concern, whether it is a clinician, whether it is a family member, or the patient themselves. We have to do something about it because it turns out those costs that are increasing years before, it is not because suddenly the out-of-control diabetes changed metabolically. It is not because suddenly the heart started pumping the wrong way. It is because people were not managing their medications correctly. The falls, the hospitalizations, those are incredibly costly.

The CHAIRMAN. Thank you, Doctor. I think you are exactly right.

The most important fact that everyone needs to accept is this is not a normal part of aging. It is an illness. It is a disease, but I know when I was growing up, people referred to it as senility, and it was just accepted that that is what happened when you got old. Now we know it is a disease. It is a disease. It is shocking to me that there is still this reluctance to screen for, diagnose, and do whatever we can.

I want to switch to what we can do because although we are doing a lot better in identifying risk factors and also have improved brain research enormously, and, boy, if we could do a blood test to identify biomarkers, that would be terrific as well but we have made big progress in imaging of the brain to identify Alzheimer's too, but just last night on our very long journey to get here because of plan problems, weather problems, I read a story in the Wall Street Journal that talked about the work that is being done on prevention, and I will say, as someone whose family—it is not just my father but two uncles, my grandfather—have died from Alz-

heimer's disease that I always felt there was very little that you could do if you had a bad family history and then you had age, which is obviously a non-controllable risk factor.

This article suggested that studies are now showing that exercise, diet, sleep, meditation, all can play a role. What is your opinion of that? Dr. Brinton, I want you to comment on this as well.

Dr. ATRI. The data for that is strong in a population sense, so you are always trying to—it is like this teeter-totter. You have some of those risk factors, your genes, et cetera, if you have had severe head injury, all the things that take away your reserve.

Then on the side that is giving you cognitive reserve are things like education, cognitive attainment, exercise. I tell my patients, "Gosh, if I had the benefit of that pill to give you growth factors in the brain and increase blood flow and get this garbage out of your brain, I would do it, but I do not have that pill. It is called exercise." What is exercise? It is what you will do.

Isolation, depression, these metabolic risk factors, they have all been shown in a population sense to put on the balance sheet, the part that gives you more reserve, and so those are the things we can do.

The CHAIRMAN. I think that is really encouraging. I must say I am really surprised but heartened by that, because it has felt so uncontrollable, and the clinical trials, many of them have been so disappointing in recent years.

Dr. Brinton, I would like you to comment on prevention also, but before you do, I want to tell you that when we were talking earlier and then your testimony that you also dispelled a myth that despite my 20 years of examining this issue, I held, and that is I thought the reason more women were affected is women lived longer. Whereas, you are suggesting there are different biological reasons that make women more prone to it, so if you could expand a little bit on that as well as the issue of prevention.

Ms. BRINTON. With regard to the sex differences that Senator McSally brought up earlier and is relevant to your question is there a preponderance of women who develop Alzheimer's and multiple sclerosis. Those two disease are more prevalent in women, and men have greater prevalence of Parkinson's and ALS. It is not all or none. It is about a 60–40 split, except for ALS, where it is more like a 70–30 split.

We begin to look at, well, what drives that? Well, we are different. I know. Women have a lipid biology. We are tasked with reproducing the species and feeding it a high-lipid diet called breast milk, so our biology on the whole is a lipid biology.

Then we look at the diseases that are more prevalent in women. They turn out to be diseases of lipid dysregulation and inflammation that targets lipids.

For example, what we see early on in the course in both our discovery science and now in our clinical science is that women can experience following the menopause and the loss of estrogen in the brain, a decline in white matter. The white matter is the lipid of the brain, and it constitutes 60 percent of the brain weight, so what happens is—what we think is happening is that the brain is sending out a starvation signal, "I am starving," because estrogen regulates, promotes glucose utilization in the brain. Now there is

a loss of estrogen, and the brain sends out this starvation signal, “I am starving. Send me fuel.” Well, the starvation response is actually to metabolize lipids into a fuel that the brain can use as an auxiliary backup, which is bodies, so far, so good, except for the fact that 60 percent of the brain is lipid, and now what we see is that the white matter in the brain can actually be a source of those ketone bodies to fuel the energy demand of the brain.

Not a good-news story. However, there is a substantial body of evidence that indicates that in women with symptoms of the menopausal transition that estrogen therapy at the time of the symptoms, not 10, 15, 20 years later, but at the time of the symptoms can actually reduce the risk of developing Alzheimer’s disease.

Again, I come back to kind of the nuances of therapeutic development and therapeutic intervention. Timing matters. One of the things that we did is we understood that women were voting with their feet. There were a lot of reports about the adverse effects of hormone therapy. Women stopped using it for the fear of breast cancer, largely.

We developed an alternative to estrogen therapy that is safe and effective in brain and works like an estrogen in brain but not as an estrogen in the breast or the uterus, so these are aware—and now I come back to this commercialization hurdle. We have that. Now we have to commercialize it and walk through that valley of death looking for commercial partners to actually bring this to—and we have done a clinical trial on this.

Now, you do not need a business opportunity to exercise, although people have made a substantial amount of money on exercise business but what I would say is that I think we can do a better job of communicating about what exercise is. You do not have to go to the gym to exercise.

I exercise pretty much every morning when I race from my house and I walk that aerobic 10, 15 minutes to my office, because I am always racing, as my team will tell you, and then, but wait a minute, I could take some steps and then, oh, I have an elliptical at my desk at work and my desk at home, and I stand at my desk, and I rarely sit during the day. This is the longest I sit, typically.

I think we can, from a clinical perspective, build in that. Exercise does not mean going to a gym. It means get out there and walk, and walk fast. Carry those bags. Do not carry them in the grocery cart. Get yourself some exercise, so there are a lot of ways that we can execute exercise without having to take that out of our day.

Last what I would say, again, coming back to the opportunities for therapeutic development, there is a rich pipeline. There is a rich pipeline. It is a very exciting time. Although there have been 100-plus failures, behind that is 30 years of steadfast work that has been funded by the Federal Government, in large measure, that is coming forward, that because of your funding, because of your financial commitment, the doors are open. Our clinical trial of the first regenerative therapeutic for Alzheimer’s disease would not be possible without that funding. It is too bold. It is too out of the box, and yet in our Phase 1b/2a clinical trial, people said you will never see anything but they did not think about that the brain can actually regenerate.

We have encouraging data, not final data, but encouraging data that the Alzheimer's brain is fighting the good fight. It is trying to survive, and that we can actually rebuild that brain and that life.

The CHAIRMAN. Very interesting.

Ms. Capp, what advice would you give to other caregivers based on your experience?

Ms. CAPP. I spend a lot of time talking to current caregivers because when you enter that tunnel, it is pretty dark, and often there is not a lot of information.

One of the things I would say on this discussion of prevention is it is critically important for caregivers to focus on these prevention messages as well.

Isolation. Caregiving is a very isolating experience. Caregivers have to get help, and asking for help is a very difficult thing for most caregivers to do.

Exercise. Caregivers are so focused on the tasks of caregiving. They have no time even to take a walk.

One of the things that we are seeing a lot of interest in and energy around are programs. Actually, there is a comedian—I cannot think of his name—from “Will and Grace,” the show “Will and Grace,” who is Seth. It escapes me. He has been joining up, as many celebrities have, in this program called TimeOut, and what it provides is data gathering about what caregivers need, so if a caregiver cannot speak their need for time or support from family or friends, they can go into a data bank and they can ask for it. People can commit time to support them because even a little bit of time away from caregiving is going to help caregivers.

Caregivers are giving up opportunity to go to the doctor, to take meds, to do so many things to support their own health, so that is what we focus on is self-health.

The CHAIRMAN. Thank you.

Ms. BRINTON. I wanted to quickly just make mention that we have developed an app. Alzheimer's is personal, and assessment should be too. We developed an app that assesses what is important to that person with Alzheimer's and what is important to the caregiver, so the caregiver gets the app, and the person with Alzheimer's gets the app.

What we are doing is being very mindful that, first of all, maybe what we are measuring in a standardized way in the clinic actually is not detecting, and what we learned from the caregivers is that there is a lot that is being changed during a clinical trial that is not detected on the standardized kind of assessments.

The other is that we want to make sure that the caregiver is not the next Alzheimer's patient.

The CHAIRMAN. Thank you.

Senator MCSALLY. Well, exactly. Actually, I wanted to pick up on that because, as I am thinking about this, we now have women who are more susceptible to be Alzheimer's victims. We have women who are more likely to be the caregivers, which includes being out of the workforce, and the additional stress on them and their lifestyle and their physical and their mental health, which also includes financial instability. They are living longer, but then they will have less paid into Social Security and less paid into any other retirement system, which then makes the cycle of them being

more susceptible just biologically but then for other conditions to be the next victim. This can be a generational issue that is disproportionately impacting women in a very profound way.

How do we break that cycle? We know from the kind of light bulb that came on for us today now that women are impacted more biologically, so we cannot change that. Women are more caregivers. I mean, societally wise, women taking on those responsibilities as a group but how do we break that cycle specifically impacting women in such a profound way?

Dr. BRINTON. Well, I think, frankly, you both exemplify that. Women leaders make a difference.

Senator MCSALLY. Ms. Capp, anything else to share on that?

Ms. CAPP. I absolutely agree. It is about building awareness.

Senator MCSALLY. Yes.

Ms. CAPP. The one thing I am very hopeful for is although women are the vast majority of caregivers in our generation, in the millennial generation we are seeing that shift. It is more split.

Senator MCSALLY. Like the young man I mentioned in my opening statement.

Ms. CAPP. Absolutely.

Senator MCSALLY. It is more split, you are saying?

Ms. CAPP. Yes.

Senator MCSALLY. Dr. Brinton, I wanted to go back to the veterans issues. A veteran myself, we have about 500,000 here in Arizona. You said we are uniquely at risk for Alzheimer's and other cognitive diseases because of our stress, because of our toxic exposure, and traumatic brain injury. I think those are the three you mentioned, right?

Can you talk a little bit more about that and the uniqueness of a veteran's risk? Then I want to know a little bit more about the barriers you mentioned related to information sharing with the Veterans Administration, because we happen to be able to do something about that.

Dr. BRINTON. Wonderful.

With respect to veterans, we had two wonderful ROTC students in the center conducting research, and they were wonderful fellows. Wonderful. Then I was shocked to hear that in their trajectory going on from when they graduated from the University of Arizona, that their job would require them to stay awake for 48 hours. How do you do that? How do you do that? That is disconcerting to someone who understands brain function and the necessity of sleep, so those are some of the issues.

The other is—I know from a perspective is ALS, being in the military is actually a risk factor for ALS.

Senator MCSALLY. Yes.

Dr. BRINTON. The reason is more likely because of the exercise demands through the military, that there is intense exercise requirements, and that exercise does not quite capture carrying how many pounds of weight while you are running in battle.

There is a disproportionate number of veterans who develop ALS, and it is, again, coming back to "Why is that?" Well, our hypothesis is that we are pursuing in the center is that men are at greater risk of developing diseases of motor control of muscle because that is their fuel depot. Women will utilize lipids as a fuel, and men can

utilize muscle as a fuel to generate glucose and ketone bodies from protein, the muscle protein.

Our hypothesis is that across these age-associated neurodegenerative diseases, there is a bioenergetic crisis in the brain that then sends out this alert signal, "I am starving," and now it sends out that signal to female, to the lipids, to men, to muscle, and it begins in the male, not exclusively, but in the male to start basically reducing the real estate that it has to maintain. The brain innervates every muscle with thousands of fibers, axons that regulate muscle control, so imagine now you are withdrawing that real estate that you have to maintain.

These are hypotheses that the American relationship is supporting, but more importantly, it actually gives us two things. It gives us a time window. We know that each of these diseases has a prodromal or preclinical phase, so that is part one, and part two, we can jump in and intervene. If we have the right mechanism for these diseases, we can actually turn that ship around early on.

Senator MCSALLY. Great. What is the barrier, though, with getting access to information?

Dr. BRINTON. The barrier really is—so I will give you a story, so, as scientists, we are pretty good at the science. We are not so good at the business, but what happens now is that in order for our discovery to actually reach the patient, we have to now develop business skills and turn our attention away from this scientific endeavor to now a commercialization endeavor. Some of us are good at that, and most of us are not, right?

Part of what I would really think—I think would really advance is we have now a program that you are funding, Accelerated Medicines Partnership in Alzheimer's Disease. We have other programs in the SBIR, STTR, and the CAP program, the Commercialization Acceleration Program. Imagine we took this kind of accelerated medicine partnership model where we have experts that can come together and advance commercialization, and their job is to make certain that we commercialize.

When you talk to corporate America, they look at this and think, "Neurodegenerative disease? That is a money loser, and it is going to take forever." Whereas, part of what we can do in this space is connect with people who see the opportunities for intellectual property, protection, and development, and can see that way to yes.

Too often we run into no because it does take a different type of support, as you well know. It takes a different type of expertise, and I know that the Federal Government already supports universities through the Bayh-Dole Act. Part of what we now need is a network. We have expanded beyond typically what universities can provide. We need that national network that is devoted to commercialization, and their metric of success is not the no. It is the yes.

Senator MCSALLY. I want to followup maybe—with Dr. Atri. I visited the Critical Path Institute last week.

Dr. BRINTON. Yes. Oh.

Senator MCSALLY. They were talking about such a consortium of trying to bring together, as a nonprofit, industry and universities and other research entities, and they specifically have an area of focus on Alzheimer's. Are you guys interacting?

Dr. BRINTON. Yes.

Senator MCSALLY. Are you participating in that, or no?

Dr. ATRI. Yes. I gave the keynote yesterday to the AAC public conference.

Senator MCSALLY. Oh, perfect.

Dr. ATRI. We were in contact there. I am going to go visit them. I think it is very important what they are doing with integrating big data, actually with clinical trials. This is really, really important. Data sharing is really, really important.

If I may say something about women and what is happening to them?

Senator MCSALLY. Yes.

Dr. ATRI. There is bad news, and I think all of this about sex differences, et cetera, it just really is very complex, and it needs more research.

Some of the good news is that particularly in this era of education, women are getting more education, and they are having more cognitive reserve actually because of it. It turns out that on average, women for different reasons, maybe evolutionary-wise, do very well with their executive function, which is their frontal systems. Multitasking. Those things go along with activities in daily living.

On average, women have performed better than men on those things. With education, et cetera, catching up and women out-performing men, that is actually one good news.

The bad news, I think, is that, yes, they are not only affected more, two-thirds, but also disproportionately both them and minorities get the burden of caregiving a lot more. No one wakes up one morning and says, "Oh, today I have all the knowledge that I need for caregiving. I have all the knowledge of speaking this new language that I need to speak with my family members of how do I change the environment, how do I care about myself," and I think that is really, really important to provide that support.

One of the reasons that actually primary care clinicians and other people do not want to deal with this is that they are overwhelmed. They do not have the resources.

If we could somehow change the codes in some ways for it to be more possible to have social work support, care navigation on that side—and as a clinician, if a mole is removed, what you get paid for that and reimbursement is much more than the hours and hours of time that you actually can spend in giving counseling to people and putting them on a different foundation. I think that is really a big opportunity for us to do that.

Regarding the veterans, I spent 6 years as a social director of the Geriatric Research Education and Clinical Center at the Bedford VA when I was also at Mass General. We had a 100-bed inpatient facility. We called it the Special Dementia Unit. Much of the work actually that we know about end of life was done there, about feeding tubes not working, why people pass, et cetera, and the philosophy of actually hospice. We had clinics all the way through.

What I could tell you is that I think veterans have other risk factors that may mitigate and lessen some of their cognitive reserve. There is a tremendous amount of—again, whether this is traumatic experiences, et cetera, there is alcohol, which is a toxin, supravascular, so they tend to have much more high blood pressure

and lipid problems, heart problems. All these things are bad for the brain, and so that puts them at risk much more.

What I can tell you is that it was difficult to get things done, and there was a lot of no's or nonresponses. We had about 15 percent of people in the system doing 85 percent of the work.

I could tell you at the time—I am involved in clinical trials around the world. I advise companies how to interpret data, how to design clinical trials by using math, and I was at that point a leader in a global trial in 30-something countries, 450 sites, 3,000 patients. It took me years, and I could not get it into our own VA because of local issues with—everything had to go up to a funnel to a certain point, and that is difficulty and that is actually one of the reasons I left.

Senator MCSALLY. Wow.

Senator Collins?

That is awful.

Dr. ATRI. Sorry to bring that up, but it is true.

The CHAIRMAN. No. I am very glad you shared that with us. That is very disturbing, someone of your ability to find it so frustrating, and plus, think of the advances that are being blocked, if that is the case.

Dr. ATRI. Very deserving folks. Yes.

The CHAIRMAN. Thank you for telling us that.

Let me followup with you on a study that you released this past summer on the true economic cost of Alzheimer's, and it created quite a big splash. It garnered a lot of attention because you measured societal costs. You looked at the costs to Federal programs, and you also look at the costs imposed on individuals and families and how insidious they are and how early they start.

I can see Ms. Capp has had this experience and is nodding.

Do you have some specific recommendations on how we can reduce the financial burden on families?

Dr. ATRI. I think part of it, again, comes back all the way—the first recommendation is that early detection. You have to be able to detect it early enough and not blow it off. Then once you detect it, we need these care support systems to be able to provide to folks.

Some of the other recommendations have to do again with really being able to measure in real time these costs, so these are opportunities.

As you were saying, that app is great. Imagine if we can, in real time, be able to integrate the health care cost for the caregivers beforehand. The health care costs for caregivers are twice as much. Someone is paying for that. An employer is paying for that. Medicare is paying for that, so there is an ability in some ways. If we could break down some of those barriers and emerge electronic medical records with insurance data bases and, in real time, get the impact on burden on folks—and it spills on to the children also.

For years—again, 1 day you do not exactly wake up and say, "Today I become a caregiver." It is this partnership where you assume more responsibilities, and family members take on more responsibilities and they miss work. We have to be able to capture those things, and part of that is having realistic cohorts not just for clinical trials but observation in the real world and knowing ac-

tually what—if we are doing interventions, whether diagnosing people early and detecting things, what is the value for that? Where initially you take all the folks in a comprehensive manner and with the social worker, neuropsychologist, and do wrap-around care to prevent falls, how much does that percolate through the system to the end?

I can honestly tell you it makes a difference, but we are not measuring it because we have not had sort of the efforts that are required and some of the collaboration between industry and also the Government, I think. Funding does help.

Dr. BRINTON. I would echo what Dr. Atri said about the VA. The VA has wonderful intentions. There is no question, wonderful intentions.

Too frequently, there are massive numbers of barriers, and you wait years, where you are at this constantly nano-steps to the goal and by the time you get to the goal, you have actually completed the project elsewhere.

I think, in many respects, our veterans are a unique population. We have more women veterans now, and yet most of our care is based on what was developed for the male veteran.

Part of what I would just echo is how do we get to yes, yes in a way that protects patient identity, protects their data, protects their privacy, and at the same time does not lose their opportunity for cures.

The CHAIRMAN. I just have a couple more questions. One is for you, Ms. Capp, and that is you talked very poignantly about the isolation a caregiver can feel and the neglect of the caregiver's own mental and physical health.

I wondered, as you were caring for your mother for so many years, whether there was respite care available to you, because what I found when I was trying to help my mother is living in rural Maine, it just was not available. This is obviously a much more populated area but did you use respite care?

Ms. CAPP. We lived in Vermont when we took care of my mom, and we found the same problems. There was not the support. The Alzheimer's Association was the most significant support we had, so, yes, it is very difficult.

I would like to go back, though, to an earlier comment that was made about the caregiver and getting the right support to the caregiver. There is an explosion of technology and research going on that caregivers, once they figure out they are in the role of the caregiver, have no idea what is available to them.

In the roles that are needed, yes, we need education roles to people who are supporting caregivers in the medical community and other communities. The social work aspect is critical, but another role that is critically important—and a colleague of mine left her role as a physician after caring for her dad to do this—is a navigator role, someone who understands what is available and can bring it to the caregiver so it can be used.

I find so many places I am at where I am hearing about technology that caregivers have absolutely no clue about, so the navigating role is critical.

The CHAIRMAN. Thank you for bringing that up as well.

I want to end my questions on a more positive note. It is to you, Dr. Brinton. I am impressed by listening to all the different avenues of research that you are pursuing, from estrogen to the brain, to looking at regeneration, which if we can repair or replace, turn back on the protein that can regenerate the neurons that have been destroyed by Alzheimer's, how exciting that is.

This really leaves me very hopeful. I have to travel to the Mayo Clinic, to the University of Pennsylvania, NIH, Jackson Labs in my own State, and many other research centers because I am so interested in what is being done. What I see happening is for a long while, researchers were focused just on amyloid plaque and doing research in the latter stages of the disease when the neurons are already killed, have died, and even if they could clear the plaque, function was not being restored.

Now because we have so much more funding invested, we can look at everything from what you have mentioned, which I think is so exciting, to lifestyle factors and start really broadening the projects.

Every year when Dr. Francis Collins, who regrettably is no relation to me, the head of NIH, would come testify before the Senate Health Committee, on which I serve, I would ask him, "How many promising applications do you get that you cannot fund?" and he got to anticipate I was always going to ask him, so he would bring a chart and the good news is that has really changed because of the investment that we have worked so hard to secure.

I mean, when I first started working on this issue more than 20 years ago, it was literally \$400 million for Alzheimer's, and there was no focus at all. It was just not a priority.

For us to now be at \$2.3 billion in the Senate version of the Labor-HHS bill, which includes NIH funding, it has \$2.8 billion, which is another addition, which we fought hard for, it is just so exciting, and it really does give me hope.

I just want to thank all of you for the extraordinary work that you are doing. I think it is so important, and I want to thank Senator McSally for convening such a terrific group of witnesses. It leaves me hopeful—it really does—that as we battle this devastating disease that has claimed the lives of too many and that affects not just the victims but their families almost as much as it affects the victims, that we can make progress, so thank you for the great work that all three of you are doing, and thank you, Senator.

Senator MCSALLY. Absolutely. Thanks, Senator Collins.

I have two general kind of ending-the-hearing questions that I want to hear from each of you on. The first is we have talked about what we can do and what we have done. The first is continuing the strong funding for that research, so we are with you on that, and we are going to continue to advocate for the strong funding.

We have talked about some other legislation related to, again, having the early ability for those under age 60 to get access to the Older Americans Act, so we fully support that, also, the other legislation I mentioned, the CHANGE Act related to allowing individuals in their first assessment with Medicare, annual assessments to be assessed.

There is also the HOPE for Alzheimer's Act, which is related to also caregiving planning and education and all that.

Is there anything else that we can be doing at the Federal level to address these issues?

Dr. ATRI. On the diagnosis and care side, I think years ago, for example, end-stage renal failure because, for some reason, a special sort of a thing of itself. I think when you look at the numbers, what we see, we do not have the workforce to deal with what is happening.

People are not going to want go to geriatric psychiatry or a cognitive neurologist or a geriatrician. This is not sexy and glamorous. It does not pay very well. Even having just the time or in the reimbursement and getting the teams around folks, I think that is really, really important, and to be able to get people to come into our field—because I really do not know. I do a lot of education. I educate something like 20-, 30,000 clinician hours a year, and I have done that for 15 years, and there is just so much knowledge that needs to go there but then the next generation, who is going to take care of them? So we need to somehow be able to invest in that. I think that is really, really important.

Senator MCSALLY. Thanks.

Dr. ATRI. The other part I would say is helping companies with patent life in some ways. Companies want to rush through things. Having been an advisor all the time, people want to rush through because they are worried how much patent life they have, somehow working with them in a partnership, to be able to give them the opportunity for the patents, et cetera, to be longer, so they do not have to rush, so we can actually do this work.

When we think about the funding for Alzheimer's disease, et cetera, we are still in the nascency, honestly. When we look at the other conditions—cardiovascular disease—why are people living longer and coming down with this? It is because we have done better with cancer and cardiovascular disease. I remember when I went to med school, all my patients died when they had HIV but if you look at the funding for those, they have been at levels of 10 times of what was in Alzheimer's disease space for 30 or 40 years.

Thank you so much for advocating for this.

Senator MCSALLY. Absolutely.

Dr. ATRI. I think that is going to help us, but to understand that the brain is very, very complex, and it is going to take a bit of time.

Senator MCSALLY. Great.

Dr. Brinton, anything else we can do?

Dr. BRINTON. Yes. Thank you again for your commitment.

I would say that this catapulting us over the valley of death is part one, and that is—so, for example, there is a translational drug development program at the NIA. They just awarded two major grants, one of which is JAX Labs is participating actually in both of them.

If we could have a center, an initiative like that for commercialization, that would be fantastic, where we get the best minds, and their job is to get to yes.

Thank you for bringing up the patent. The patent on our regenerative therapeutic runs out in 8 years, and that is not good for commercialization, so thank you for bringing that up.

The other aspect is essentially how can we maximize, again, coming back to the education of the next generation. We have a training grant from the National Institute on Aging to train the next generation of translational Alzheimer's researchers, and if we could expand that, that would, I think, be fantastic and bring in the next generation.

We also have a training grant through the NIH with the Navajo Nation to bring those into the neuroscience space.

Thank you.

Senator MCSALLY. Ms. Capp?

Ms. CAPP. I would again thank you for all you have been doing. You are certainly well versed on all of the initiatives the Alzheimer's is interested in having you focus on.

As we have been focusing on the disease, we need more focus on the caregivers, and the one space I would say we have not covered today that I think is critically important is to get companies to recognize the responsibility they have in supporting caregivers. It is a bottom-line equation. If we can help support working caregivers to be healthier, the companies that they work for will have lower cost of medical care, et cetera. It is a business initiative we have to take on.

Senator MCSALLY. Ms. Capp, I am going to give you one last opportunity to kind of close this out, and we have the media here tonight and we will have a platform to speak to Arizonans through the reporting on this hearing today.

As someone who has been through this very personally—I know you have as well—if there is somebody out there in Arizona today that knows something is just not quite right in themselves or in someone that they love, who they love, what is your message to them as to what you would encourage them to do and where they can go?

Ms. CAPP. I would tell them they are not alone. There are so many people going through exactly the same thing, and we find support in recognizing we are not alone.

I would encourage them to reach out. The Alzheimer's Association has a 24/7/365 call line. They can go there.

I have a website. I communicate regularly with caregivers, so find the resource, but start at the Alzheimer's Association.

Senator MCSALLY. Wonderful. Thank you.

I am so grateful for your testimony today and everybody participating in this hearing. This is such an important topic.

Senator Collins, thank you so much for coming here and bringing the Aging Committee to Arizona, and I agree that Arizona has a bold independent spirit and your testimonies today show that we are really on the forefront to breaking through here and addressing these issues, so thank you.

I think I have a few things to say that are official here. The hearing record will be closed on November 8, 2019, so other members of the Committee will have time to submit questions for the record, and we will ask for responses in writing, so I appreciate it.

This concludes this hearing. Thank you.

[Whereupon, at 11:45 a.m., the Committee was adjourned.]

APPENDIX

Prepared Witness Statements

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

By:
Alireza Atri, M.D., Ph.D.,
Cognitive Neurologist/Neuroscientist;
Director, Banner Sun Health Research Institute
Banner Health, Sun City AZ;
and
Lecturer on Neurology, Center for Brain/Mind Medicine
Brigham & Women’s Hospital
Harvard Medical School, Boston, MA

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 anticipated¹⁻⁵. AD is the sixth leading cause of death in the United States, and is the only top-10 cause still significantly increasing¹. 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 2030–2035⁶.

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 technologies¹³⁻¹⁸ 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 2050²⁶. 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 states²⁶. 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 2025²⁶. Almost two-thirds of Americans with AD are women, and the socioeconomic costs and burdens are disproportionately borne by women and minorities²⁷. In 2018, over 16 million caregivers provided over 18.5 billion hours of informal (unpaid) care at a low estimate cost of \$234 billion²⁶.

The socioeconomic costs of AD/ADRD typically begin in the years before a diagnosis is made²⁷. 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 costs²⁷. 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://azaalz.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 worldwide².

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.

References:

1. Association As. 2018 Alzheimer's disease facts and figures. *Alzheimer's & Dementia*. 2018;14(3):367-429.
2. Livingston G, Sommerlad A, Orgeta V, et al. Dementia prevention, intervention, and care. *Lancet*. 2017;390(10113):2673-2734.
3. Prince MJ, Wimo A, Guerchet MM, Ali GC, Wu Y-T, Prina M. *World Alzheimer Report 2015 - The Global Impact of Dementia: An analysis of prevalence, incidence, cost and trends*. London, UK2015.
4. Atri A. The Alzheimer's Disease Clinical Spectrum: Diagnosis and Management. *Med Clin North Am*. 2019;103(2):263-293.
5. Collaborators GBDD. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*. 2019;18(1):88-106.
6. Association As. *Changing the Trajectory of Alzheimer's Disease: How a Treatment by 2025 Saves Lives and Dollars*. 2015.
7. Lang L, Clifford A, Wei L, et al. Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. *BMJ open*. 2017;7(2):e011146.
8. Bradford A, Kunik ME, Schulz P, Williams SP, Singh H. Missed and delayed diagnosis of dementia in primary care: prevalence and contributing factors. *Alzheimer Disease & Associated Disorders* 2009;23(1546-4156 (Electronic)):306-314.
9. Perry-Young L, Owen G, Kelly S, Owens C. How people come to recognise a problem and seek medical help for a person showing early signs of dementia: A systematic review and meta-ethnography. *Dementia (London, England)*. 2018;17(1):34-60.
10. Mitchell AJ, N M, Pentzek M. Clinical recognition of dementia and cognitive impairment in primary care: a meta-analysis of physician accuracy. *Acta Psychiatr Scand*. 2011;124(1600-0447 (Electronic)):165-183.
11. Prince M C-HA, Knapp M, Guerchet M, Karagiannidou M. . *World Alzheimer Report 2016: Improving healthcare for people living with dementia--coverage, quality and costs now and in the future*. September 2016 2016.
12. McCarten JR, Anderson P, Kuskowski MA, McPherson SE, Borson S, Dysken MW. Finding dementia in primary care: the results of a clinical demonstration project. *Journal of the American Geriatrics Society*. 2012;60(2):210-217.
13. Jack CR, Jr., Albert MS, Knopman DS, et al. Introduction to the recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2011;7(3):257-262.
14. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2011;7(3):270-279.

15. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2011;7(3):263-269.
16. Jack CR, Jr., Bennett DA, Blennow K, et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2018;14(4):535-562.
17. Dubois B, Hampel H, Feldman HH, et al. Preclinical Alzheimer's disease: Definition, natural history, and diagnostic criteria. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2016;12(3):292-323.
18. APA. *Diagnostic and Statistical Manual of Mental Disorders - (DSM-V)*. 5th ed. Washington, D.C.: American Psychiatric Publishing; 2013.
19. Dubois B, Padovani A, Scheltens P, Rossi A, Dell'Agnello G. Timely Diagnosis for Alzheimer's Disease: A Literature Review on Benefits and Challenges. *Journal of Alzheimer's disease : JAD*. 2016;49(3):617-631.
20. Weimer DL, Sager MA. Early identification and treatment of Alzheimer's disease: social and fiscal outcomes. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2009;5(3):215-226.
21. Grossberg GT, DD C, Griffith PA, Kerwin DR, Hunt G, Hall EJ. The art of sharing the diagnosis and management of Alzheimer's disease with patients and caregivers: recommendations of an expert consensus panel. *Prim Care Companion J Clin Psychiatry*. 2010;12(1555-211X (Electronic)).
22. Aminzadeh F, Molnar F, Dalziel W, Ayotte D. A review of barriers and enablers to diagnosis and management of persons with dementia in primary care. *Canadian geriatrics journal : CGJ*. 2012;15(1925-8348 (Print)):85-94.
23. Brodaty H, Donkin M. Family caregivers of people with dementia. *Dialogues Clin Neurosci*. 2009;11(1294-8322 (Print)):217-228.
24. Phillips J, Pond CD, Paterson NE, et al. Difficulties in disclosing the diagnosis of dementia: a qualitative study in general practice. *British Journal of General Practice*. 2012;62(601):e546.
25. Pinner G, Bouman WP. Attitudes of patients with mild dementia and their carers towards disclosure of the diagnosis. *International psychogeriatrics / IPA*. 2003;15(3):279-288.
26. Association As. 2019 Alzheimer's disease facts and figures. *Alzheimer's & Dementia*. 2019;15(3):321-387.
27. El-Hayek YH, Wiley RE, Khoury CP, et al. Tip of the Iceberg: Assessing the Global Socioeconomic Costs of Alzheimer's Disease and Related Dementias and Strategic Implications for Stakeholders. *Journal of Alzheimer's disease : JAD*. 2019;70(2):323-341.
28. Prince M, Prina M, Guerchet M. *The World Alzheimer Report 2013 'Journey of Caring: An analysis of long-term care for dementia'*. Alzheimer's Disease International (ADI);2013.
29. Wimo A, Prince M. *The World Alzheimer Report 2010 'The Global Impact of Dementia'*. Alzheimer's Disease International (ADI);2010.
30. Saxena S. *Dementia World Report: A Public Health Priority*. World Health Organization (WHO);2012.

31. Kapasi A, DeCarli C, Schneider JA. Impact of multiple pathologies on the threshold for clinically overt dementia. *Acta Neuropathol.* 2017;134(2):171-186.
32. Power MC, Mormino E, Soldan A, et al. Combined neuropathological pathways account for age-related risk of dementia. *Annals of neurology.* 2018;84(1):10-22.

Senate Special Committee on
Aging: Alzheimer's and Other Cognitive Diseases: An Arizona Perspective
Roberta Diaz Brinton, Ph.D.
Opening Statement
November 1, 2019

Good morning, Senators Collins and McSally, colleagues, and members of the public.

Thank you for the opportunity to address you on the Arizona Perspective on Aging: Alzheimer's and Other Cognitive Diseases. I am Dr. Roberta Diaz Brinton, director of the Center for Innovation in Brain Science at the University of Arizona (<https://www.cibs.uahs.arizona.edu/>) (<https://youtu.be/KQWDXstgXkE>). Our mission is to create innovations in brain science of the future for those who need a cure today. We are an *all brains on deck* translational ecosystem dedicated to addressing the urgent national health crisis of Alzheimer's disease. I am honored to share with you the advances being made in Arizona to prevent and cure Alzheimer's disease.

1. Historical and Future Perspective on Alzheimer's Disease

In 1903, the Wright brothers achieved the first manned flight at Kitty Hawk. Sixty years later, Americans walked on the moon. Three years after the Kitty Hawk flight, in 1906, Dr. Alois Alzheimer first described the pathological hallmarks of the disease. Over a hundred years later, a cure for Alzheimer's remains elusive. By 2025, Arizona will experience a 43% increase in the number of Alzheimer's patients, the largest percentage nationally. Curing Alzheimer's is not rocket science; *it's harder*. That's the bad news. But *I'm here to give you the good news*.

2. The Arizona Advantage

Arizonans have a bold pioneering spirit and innovative culture that is exemplified through the Center for Innovation in Brain Science. Across the state, researchers and clinicians are working together to prevent, delay and cure Alzheimer's Disease through the Arizona Alzheimer's Consortium.

3. The University of Arizona Advantage

The University of Arizona is uniquely positioned to become the epicenter of Precision Aging nationally and globally. The University of Arizona has made strategic investments in our Center for Innovation in Brain Science dedicated to curing age-associated neurodegenerative diseases, the Precision Aging Network which will create a nationwide platform to map the genetic and environmental factors of resilient brain aging, and the Aging for Life strategic initiative that spans the university, Tucson and our state will bring innovations in science, technology, architecture and biomedical engineering to meet the challenges of an aging population world-wide.

4. The University of Arizona Center for Innovation in Brain Science Advantage

The University of Arizona's Center for Innovation in Brain Science (CIBS) was created to address the challenge that in the 21st century there is not a single cure for a single neurodegenerative disease. Operating as a University-Biotech hybrid focused on age-associated neurodegenerative diseases, CIBS is unique in the nation and perhaps globally. CIBS is a mission driven "all brains on deck" translational ecosystem that integrates the discovery prowess of academia with the best-practices of biotech.

Our pipeline of innovative therapeutics for Alzheimer's disease include regenerative therapeutics that activate neural stem cells in the brain, promote energy production in brain, reduce neuro-inflammation and prevent generation of Alzheimer's pathology. A prime example of the success of our efforts, after decades of painstaking research supported by National Institute on Aging, we are conducting a Phase 2 clinical trial of allopregnanolone, the first regenerative therapeutic to regenerate the Alzheimer's brain.

5. Delivering on the National Alzheimer's Project Act (NAPA) Goals

The National Alzheimer's Project Act (NAPA) is an ambitious plan to *Prevent and Effectively Treat Alzheimer's Disease by 2025*. Through the transformative and innovative leadership team at the National Institute on Aging, Dr.s' Richard Hodes, Eliezer Masliah, Suzana Petanceska, Laurie Ryan, Lorenzo Refolo, Zane Martin, Bradley Wise, Nina Silverberg and Molly Wagster, we are closer than ever to delivering on these goals. Federal investments have resulted in discovery of mechanisms and drivers of Alzheimer's and a broad portfolio of therapeutics currently in clinical trial.

To deliver prevention and treatment of Alzheimer's by 2025, two advances are critical.

Big Data Analytics for Precision Prevention:

Electronic medical records held by the federal government hold the key to detecting and preventing Alzheimer's disease in at-risk populations. For example, using existing NIH funded clinical trial data, we were able to identify women at increased risk for Alzheimer's disease when they were still healthy and when they could be treated with currently approved therapeutics to reverse their risk profile. Using Medicare data, we demonstrated that specific statins reduced the risk of Alzheimer's in an ethnically diverse national population. Using insurance claims data, we were able to demonstrate that specific breast cancer therapies reduce the risk of developing Alzheimer's in women later in life. A comparable analysis of prostate cancer treatments is in progress. We are now partnering with VA researchers to determine which therapies for type 2 diabetes reduce or increase the risk of developing Alzheimer's. Through big data analytics, we can inform clinical care to prevent Alzheimer's disease in at-risk populations.

Our veterans face a unique constellation of risk-factors for Alzheimer's including high-stress, sleep deprivation, toxin exposure and traumatic brain injury. The challenges associated with accessing and analyzing veteran health records puts this group at risk when we could prevent Alzheimer's. Through their medical records, our heroic veterans on the battlefield can be heroes again in the fight against Alzheimer's disease.

I urge you to find a way to safely, securely and efficiently expand access to electronic medical records held by the federal government and mandate the sharing of HIPPA compliant patient level data from federally funded clinical trials.

Precision Medicine Cures for Alzheimer's Requires Arizona Commercialization Innovation:

Big pharma and venture capital are abandoning Alzheimer's and other age-associated neurodegenerative diseases. Their departure is Arizona's opportunity to become the new biotech hub for curing Alzheimer's.

A challenge to delivering our discoveries to patients is that commercialization of federally funded therapeutic development ultimately reaches the "valley of death". Universities have limited resources

to fund the expertise and budgets required for intellectual property development and academic start-ups. Critical to delivering precision medicine cures for Alzheimer's is an accessible network of innovation experts to advance intellectual property opportunities, start-up capital, business development and the commitment to find a way to Yes to achieve the goal for the American public.

The National Institutes of Health SBIR, STTR and Commercialization Accelerator Program (CAP) are engines of commercialization that, with modest adjustments, could catapult therapeutic development across the "valley of death".

6. Arizona and Precision Medicine for Alzheimer's

The war against Alzheimer's Disease is being fought on many fronts, from the homes of patients and caregivers to the research laboratories of scientists and clinicians across this great nation. Millions of Americans are counting on us to win this fight. We can, we must, and we will win.

Arizona with its bold pioneering spirit and entrepreneurial culture has a unique opportunity to lead the nation and the world in the science of aging and innovative therapeutic development for Alzheimer's and age-associated neurodegenerative disease. Arizona can deliver precision medicine of the future for those who need a cure today.

Thank you for your commitment to our nation and to Arizona. Through your efforts we are closer than ever to a cure for Alzheimer's.

Testimony of Lisa B Capp (Lisa M. Beilstein)
Surviving dementia & Alzheimer's Caregiving

November 1, 2019

Senator McSally, Senator Collins and distinguished guests, thank you for the opportunity to testify about my experience as my mother's caregiver.

I'm a blogger, an activist and a dementia caregiving survivor after an 18-year journey through the disease with my mother, Vera Cappelletti. After her death in 2015, Chairing the Board of the Vermont Alzheimer's Association and a move to Phoenix, I'm now Co-Chair of the Desert Southwest Alzheimer's Association Board. I write and speak regularly on the subject of dementia caregiving. Why? In 2014 comedian Seth Rogen addressed lawmakers in Congressional testimony about the care of his wife's mother who was diagnosed with young onset Alzheimer's. She was in her mid 50's. Back in 2014 Seth said, "I think until you see Alzheimer's first hand it's kind of hard to conceive how brutal it really is." Today dementia caregiving remains equally brutal around a still stigmatized disease driving family caregivers deeper into emotional, physical and financial hardship.

Mom came to live with us after my dad passed away and at the time I was advancing my career in high-tech. I was lucky, my husband Tom shared fully in my role as caregiver. And without children due to my infertility we didn't count ourselves among those in the sandwich generation of care. My mother's dementia began with whimsical imagining but turned to terrifying delusions and hallucinations. Tom and I continued care in our home until crisis left us with no choice but to involuntarily commit my mom to a psychiatric ward to stabilize her condition. My siblings, although living in other parts of the country, participated in many ways but most notably in the family decision to move our mother not back home from the hospital, but instead to live the remainder of her life in fulltime memory care.

As my mom slid deeper into her dementia, her invisible battle became a struggle I had to watch progress while plaques and tangles took over her brain. We were blessed by a relationship with a skilled geriatric psychiatrist who helped me to understand my mother's world just a little bit better.

Dr. Paul Newhouse asked, "Do you know what *déjà vu* is, Lisa?" "Feeling you've been somewhere before, that it's familiar," I answered. "Yes, *déjà vu* means that the strange is familiar to you. Do you know what *jamais vu* is," I shook my head no. "Jamais vu is what our family and friends experience in dementia – the familiar becomes strange. Imagine every moment of your life struggling with something you know, that you've known for your entire life, but now it's strange to you," the doctor shared.

My life was busy and I didn't understand the nuances of my mom's brain disease. With the stress of having to leave work early to get mom to one of her many doctor appointments, she might pick up a comb and look at it as if she'd never seen it before, confounded by its very function. I'd grab the comb from her hand and smooth her hair as we rushed out the door late to our appointment. Waves of guilt kept building. The emotional web between someone you love living with dementia and you as the unexpected caregiver are made up of strands spun from loss, despair, sadness and intense feelings of inadequacy.

I think about the arc of my mother's life from wife, mother and career; through the hallucinations and delusions; and onto the advanced stages of dementia. Bedridden with her ability to speak gone, I'd lay my iphone on her pillow and play Frank Sinatra's "Fly Me to the Moon". Her beautiful green eyes would open and light would dance in them from a deep and far off place.

Dementia is a set of perpetually evolving diseases requiring the act of caregiving to be both collaborative and yet codependent. As someone living with dementia progresses, so does their caregiver along paths of physical, spiritual and emotional

coping. As one individual declines, the other must advance. And the end of caregiving isn't rewarded with a sense of freedom; it's marked instead by deep and intense grief at yet another loss to this despicable disease.

But I'm hopeful, more hopeful than I have ever been that I will see the first survivor in my lifetime. The unprecedented funding you and your fellow legislators support is leading not only to critically important research discoveries, but a renewed hope among caregivers for earlier detection, prevention and an ultimate cure. I thank you.

I thank you Senator Collins for your leadership as Chair of the Senate Special Committee on Aging and for your support to programs, policies and funding critically important to the Alzheimer's Association and those in our nation requiring their services. I thank you Senator McSally for your support to the younger onset bill (HR 1903/S.901), which passed the House this week. This bill will give access to critical resources for those living with dementia under the age of 60 as part of the Older Americans Act. And I welcome the opportunity to work with you Senator McSally on initiatives that continue to benefit our great state and nation.

There are still so many opportunities yet to exploit. We need to educate and train primary care physicians, first responders, ER and hospital staff, caregivers and administrators in local care facilities, major employers and small business owners for whom caregivers currently work, barbers, lawyers and bankers; all who see the impact of this disease in their day to day lives and work. I applaud Mayor Mitchell and the city of Tempe for their work in becoming a dementia friendly city and to Mayor Gallego for considering similar steps for Phoenix. These actions enabled by your support to The Hope Act (H.R. 1873/S880) go a long way in removing stigma around the disease and make life a bit easier for caregivers.

I'll end my comments by sharing although my legal name is Lisa Beilstein, I write and am active as Lisa B. Capp to honor my mom's memory. Thank you for inviting

me to speak, listening to my story and for all you have done and will do in the fight we share to live in a world without dementia and Alzheimer's disease.