

# A GLOBAL UPDATE ON ALZHEIMER'S DISEASE

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## HEARING

BEFORE THE

SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH,  
GLOBAL HUMAN RIGHTS, AND  
INTERNATIONAL ORGANIZATIONS

OF THE

COMMITTEE ON FOREIGN AFFAIRS  
HOUSE OF REPRESENTATIVES

ONE HUNDRED FIFTEENTH CONGRESS

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## A GLOBAL UPDATE ON ALZHEIMER'S DISEASE

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WEDNESDAY, NOVEMBER 29, 2017

HOUSE OF REPRESENTATIVES,  
SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH,  
GLOBAL HUMAN RIGHTS, AND INTERNATIONAL ORGANIZATIONS,  
COMMITTEE ON FOREIGN AFFAIRS,  
*Washington, DC.*

The subcommittee met, pursuant to notice, at 2:00 p.m., in room 2172 Rayburn House Office Building, Hon. Christopher H. Smith (chairman of the subcommittee) presiding.

Mr. SMITH. The subcommittee will come to order, and good afternoon, everybody. I apologize for the delay. We had a series of votes, and we have one later, too, so I do want to get right to it.

I want to thank you for being here. Today, as we open today's hearing, there are an estimated 47 million people in the world living with Alzheimer's disease and other forms of dementia—more than the entire population of Spain, according to a report by the Alzheimer's Disease International.

The number of victims who have Alzheimer's is projected to double every 20 years. So we are in a race like few other diseases because it is proliferating so fast throughout the globe.

And according to Dr. Marie Bernard, the deputy director of the National Institute on Aging, who we will hear from momentarily, the number is estimated to grow to 115 million by 2050 as populations around the world age.

Although there is early onset but predominantly it is one of the byproducts of all of us aging and there seems to be a higher proclivity the older one gets, and it has been estimated that once somebody reaches 85 the chances of some form of dementia is about one out of two. So it's a very, very serious problem.

The total estimated global cost of addressing this condition today is \$818 billion, but by as early as next year it is estimated that this cost will rise to at least \$1 trillion—that is per year—and then it will go up from there.

As we all know, Alzheimer's is a cruel disease, robbing its victims of their memories and their very identities and robbing their families and friends of the person they know and love.

It is excruciatingly painful for someone to lose themselves gradually, and I have spoken myself to many individuals, especially those who are early onset who have young families and are dealing with the agony that they know it is progressing.

There is no cure. There are drugs, five of them so far, and others that are in the pipeline that treat symptoms but there is no actual cure. And so it is very tough and it takes a very heroic person to cope and manage with that.

We also know that the families have to deal with a very painful ordeal, as well the care givers, the loved ones, the family and the friends.

In 1999, along with then-Congressman, now Senator Ed Markey, I co-founded the Congressional Task Force on Alzheimer's disease, which I still co-chair today with Maxine Waters, to bring this disease to the forefront of the congressional agenda to advance support for Federal research and to increase awareness.

The task force worked in partnership with the Alzheimer's Association to unanimously pass the National Alzheimer's Project Act—or PL 111, which established an advisory committee of private and Federal experts to work with the secretary of HHS to comprehensively assess and address Alzheimer's research, institutional services, and home and community-based care with the goal to identify a cure or disease-modifying therapy for dementia by 2025.

Today, there are over 170 members of the House and Senate in the task force.

This year, we worked very hard in a bipartisan way to get an increase of some \$414 million to the Alzheimer's research funding at NIH.

Under HHS Appropriations Chairman Tom Cole's extraordinary leadership, the fiscal year 2018 omnibus appropriations bill was enacted. It was passed in September of this year.

It included a \$400 million increase for Alzheimer's disease research at the National Institutes of Health. This would bring total funding to \$1.8 billion.

Currently funded at \$1.4 billion, NIH spending on Alzheimer's research has almost tripled since fiscal year 2015 when \$589 million was allocated for such research.

Shockingly, the majority of people with Alzheimer's or other forms of dementia have not received a diagnosis so they are unable to access the care and the treatment of symptoms that they so desperately need. This is true in the developed world but it's even truer in the developing world.

Michael Splaine points out in his testimony today that detection and diagnosis are a stubborn problem everywhere. Research shows that most people currently living with dementia have not received a formal diagnosis, he will testify. In high-income countries, 20 to 50 percent of dementia cases are recognized and documented in primary care.

This treatment gap, as he calls it, is certainly much greater in low and middle income countries. Without a diagnosis, there can't be treatment care or organized support or the opportunity to volunteer for clinical research.

Of course, even when Alzheimer's or other forms of dementia are diagnosed, care is too often fragmented, uncoordinated, and unresponsive to the needs of people living with the condition.

In response, last Congress I introduced the Health Outcomes Planning Education—or HOPE—for Alzheimer's Act of 2015 to provide Medicare coverage for care planning session for patients newly

diagnosed with Alzheimer's disease for family care givers or legal representatives.

In recognition of this great unmet need, the legislation garnered 310 bipartisan co-sponsors. Ultimately, the Medicare adopted an amended version of the HOPE Act—actually an improvement—for final rule for calendar year 2017's positions fee schedule.

Of course, Alzheimer's robs its victims not only of their memories but also of their awareness, but also their lives. In the American Journal of Public Health, a research survey of years of life lost versus the number of deaths between 1995 and 2015, annual deaths due to Alzheimer's complications in the U.S. alone rose from 20,607 in 1995 to 110,568 in 2015.

During that period, Alzheimer's rose from the 14th leading cause of death among ailments in this country in 1995 to number six in 2015.

For the record, this is my fourth hearing I have chaired on Alzheimer's disease. On June 23rd in 2011, we held a hearing on the global strategies to combat the devastating health and economic impacts of Alzheimer's.

On November 21st, we held a hearing on the G8 Dementia Summit and beyond, and then in 2014 on the actual summit report from the G8 and now today's hearing, of course.

Today's hearing is intended to examine the existing potential options for prevention and treatment of this devastating disease and the harrowing statistics cited earlier likely will be much worse in developing countries if they had accurate identification of Alzheimer's and records of victims and of deaths.

As our hearing testimony will demonstrate, there is hope for Alzheimer's patients, their families and friends. There is a surge, particularly for research.

For example, a research team from Columbia University's Medical Center in 2013 said they had finally traced Alzheimer's to its early developmental stages of discovery that they believe could lead to more effective treatments.

In science translational medicine 3 years ago, Australian researchers explained a noninvasive ultrasound technology that clears the brain of neurotoxic amyloid plaques—structures that are responsible for memory loss and a decline in cognitive function in Alzheimer's patients.

By 2016, scientists at the Institute of Regenerative Medicine at the University of Zurich said they were amazed to find that their patients treated with the highest dose of an antibiotic drug experienced an almost complete clearance of the amyloid plaques that prevent brain cells from communicating, leading to reversible memory loss and cognitive decline.

Our witnesses today will tell us more about these and other advances that, again, the United States is walking point in the world in this and we have two tremendous witnesses and experts who are doing their best and their staffs to make sure that we get there sooner rather than later.

I would also just point out for the record this Congress I've joined my colleagues in introducing the BOLD Act, which would establish Centers of Excellence and it is designed to really take this to the

next level—to have congressional support for this effort in a more robust way.

I have also reintroduced Kevin and Avonte’s Law. It passed last year in the House. It deals with the wandering issue.

We know that when Alzheimer’s or autism individuals have the bracelet, they are found usually within 30 minutes. When they don’t and they go wandering, it can be catastrophic if not a cause of death from drowning and a whole host of other reasons if they are not rescued from that wandering.

Next week, I will reintroduce the Global Brain Health Act to increase research on prevention and treatment of autism, hydrocephalic condition and Alzheimer’s and other forms of dementia.

This legislation, which I first introduced in 2015, would encourage the building of treatment capacity for these brain disorders among care givers in developing countries and support increased international cooperation in research and implementation of strategies on prevention and treatment.

I would like to now yield to Dr. Bera for any opening comments he might have.

Mr. BERA. Thank you, Mr. Chairman, and thank you for having this hearing. It, obviously, is incredibly important.

Anytime you can say neurotoxic amyloid plaques in Congress that is a good day, particularly, as a physician.

So I am trained in internal medicine and taking care of many Alzheimer’s patients and, you know, the urgency of addressing this issue and, you know, looking for ways to mitigate the disease but also ultimately looking at ways to reverse and cure disease are, obviously, our ultimate goals.

You know, I think we often focus here domestically on what we need to do to help address this issue. But, you know, I work pretty closely with our Alzheimer’s Association and I think the Alzheimer’s Association has done a wonderful job elevating the level of dialogue but also elevating the dialogue on, you know, why this is a global epidemic.

Often when we think about global health we are thinking about the communicable diseases that are out there. But there really is as—you know, there are more developed nations around the world.

We have got to spend more time thinking about the impact of noncommunicable diseases like Alzheimer’s disease.

You know, as we start to think about those public health approaches, from my public health background, you know, there is a number of things that, you know, are the low-hanging fruit—you know, the lifestyle modifications, the things that you can do to certainly slow down and mitigate disease.

A second step is building the public health infrastructure in the global community to help both families and patients manage and navigate that disease and, again, I do think we are going to see this coming tidal wave as people live longer in the global community, the lack of infrastructure and the lack of readiness to, you know, manage this tidal wave of folks with—with dementia and with Alzheimer’s disease and other noncommunicable diseases, for that matter.

And then, you know, long term this is a global challenge and I look forward to hearing from the witnesses. You know, we can



quantify the direct costs of Alzheimer's but then also the indirect costs of Alzheimer's in terms of, you know, both the patient as well as the impact on families and care givers.

And then, ultimately, you know, part of the reason why I am such a strong advocate for making investments in the NIH and making investments in research is the return on that investment if we are able to find a cure or even better therapies to mitigate disease and slow down disease is going to be, you know, pretty significant, because if we don't we will be spending billions upon billions of dollars on the back end. And this is not just a U.S. challenge. This is a global challenge.

So, Mr. Chairman, I think this is an incredibly timely topic and I look forward to hearing from the panelists. So thank you. I yield back.

Mr. SMITH. Thank you, Dr. Bera.

I would like to now yield to Mr. Donovan for any comments he might have.

Mr. DONOVAN. Thank you very much, Mr. Chairman. Thank you for conducting this very important hearing.

Many of the things that this committee does deals with diseases and things people are suffering from that we don't suffer from in this country.

When I came to Congress, 2 weeks later at 58 years old I had my very first baby. Her mother actually describes her as my very last baby, by the way.

But so all of a sudden, maternal health and infant health, prenatal care became so important to me because it was personal to me. And I always say that Yellow Rose Catherine was—she hit the birth lottery.

She was born on May 19th of 2015 on the same day tens of thousands of other children were born, except she was born on Staten Island in New York City and has had every one of her vaccinations, every one of her well visits, and children born that same day who didn't hit that birth lottery didn't have the same advantages she did. So there's a lot of things this committee has done has been personal to me.

I am also the only son of an Alzheimer's patient. My mother died the year before I was elected after suffering for 4 years.

I was blessed. I had her until she was 89 years old and her mother died when she was 9. So I always say I had my mother for 50 more years than she had her own mother.

But I watched this woman become someone I didn't know—a woman who was always calm who became violent—a woman who would sit and just stare even when you speak to her because she no longer could communicate or understand what you're saying.

And I learned a lot about the disease—not as much as my friend, Dr. Bera, but—about the proteins that grow on people's brains and how advancements in medicine now are finding ways to slow that protein growth down, maybe stop it altogether, maybe at some point actually have medication that could remove the proteins from people's brains that may cure the disease is our hope.

I know that we gave the National Institute of Health in the 21st Century Cures Act billions of dollars to help the advancement of some treatments and cures for things like Alzheimer's.

So I just wanted to tell my personal story just so I could tell you how much I appreciate you being here and how important this is in a global health environment, but how personally it has touched me. So I thank you both for being here today and thank you, Mr. Chairman.

Mr. SMITH. Thank you very much.

At this time, let me introduce our distinguished witnesses and, again, thank them for their tremendous leadership, beginning with Dr. Marie Bernard, who serves as deputy director of the National Institute on Aging at the National Institutes of Health.

Dr. Bernard serves as the principal advisor to the NIA director, working closely with the director in overseeing approximately \$2 billion in aging research conducted and supported annually by the institute.

Dr. Bernard co-chairs two department Health and Human Services Healthy People 2020 objectives—older adults and dementias, including Alzheimer's disease.

We will then hear from Dr. Roger Glass, who I'd point out is also from New Jersey originally—from Summerville, New Jersey. He serves as the director of the Fogarty International Center and associate director for international research at the National Institutes of Health.

Dr. Glass has maintained field studies in India, Bangladesh, Brazil, Mexico, China, and elsewhere in the world. He has received numerous rewards including the prestigious Charles Shepherd Lifetime Scientific Achievement Award presented by the Centers for Disease Control and the Charles—Dr. Charles Merieux Award from the National Foundation for Infectious Diseases for his work on the rotavirus vaccines in the developing world.

Two experts and two very much welcomed witnesses to our subcommittee.

Dr. Bernard?

**STATEMENT OF MARIE BERNARD, M.D., DEPUTY DIRECTOR,  
NATIONAL INSTITUTE ON AGING, NATIONAL INSTITUTES OF  
HEALTH**

Dr. BERNARD. Well, good afternoon, Chairman Smith, Representative Bera, Representative Donovan.

I am happy and honored to represent the National Institute on Aging, one of the 27 institutes and centers at NIH. We, at the NIA, lead NIH's Alzheimer's disease research and as deputy director I bring my experience as an academic geriatrician.

I could very much empathize with the points that were made with regards to the prevalence of this illness and the personal impact that it had on families.

When I saw patients on a daily basis it was heartbreaking to see the impact that this had on those patients and, importantly, on their family members and to recognize that I didn't have much in my armamentarium that I could bring to the care of those individuals at that time.

It's encouraging to be at NIH at this point and to see the blossoming of more and more information that is developed with global partners that will hopefully get us to the point that we will have a prevention or cure for this illness.

We have, in fact, over the decades supported a number of international studies that have led us to a greater understanding of the illness and I will spend what time is allocated to me to briefly highlight three of those.

First, we are making significant advances in our understanding of the course of Alzheimer's disease from our health and retirement study.

This is a 20-year-old national sampling of older adults in the United States—people 50 years of age and older who have followed through to their death—and it has allowed us to see the natural course of aging as well as the natural course of the development of Alzheimer's disease.

This study has recently had a new component added to it that's an international component—the Harmonized Cognitive Assessment Protocol, or HCAP.

We have the hope that if we can get researchers across the globe to harmonize the way that they go about cognitive assessments, we will be able to better understand the course of the illness and to sort out the genetic, social, and environmental influences that impact Alzheimer's disease.

We are supporting the deployment of HCAP and HRS, or Health and Retirement Study, like studies in England, Mexico, China, and India, as well as a smaller scale study in South Africa. This will provide us an unprecedented scientific opportunity.

A second important need is for means to make the diagnosis of Alzheimer's earlier than the current standard, which is when a person has cognitive and functional problems.

There are many promising new findings, particularly as a result of something called the Alzheimer's Disease Neuroimaging Initiative, or ADNI. ADNI is a worldwide collaboration with organizations in Europe, Japan, Australia, Taiwan, Korea, China, and Argentina.

ADNI has led to the identification of biomarkers, proteins, and images of the brain that allow us to measure the onset and progression of this disease.

A decade ago, the only way that you could definitively say that someone likely had Alzheimer's disease or had Alzheimer's disease was by autopsy.

But now we can see in a living brain the deposition of amyloid plaques and tau tangles in an individual and follow its course before they have clinical symptoms.

As we make progress with validating this and other biomarkers, we hope to translate this into useful clinical tools.

Third, NIA-supported investigators are conducting prevention and treatment trials that are globally—or have a global reach.

One such study which has received quite a bit of attention is the Autosomal Dominant Alzheimer's Disease Trial involving the world's largest group of early-onset familial Alzheimer's disease—approximately 300 extended family members in the country of Colombia who share a rare genetic mutation that guarantees that by middle age they are going to have Alzheimer's symptoms.

The trial focuses on whether an anti-amyloid drug, crenezumab, can prevent or delay the onset of cognitive decline.

We are very grateful to this family and all participants in Alzheimer's disease and related trials. They are true heroes who have allowed us to learn and continue to learn about this disease.

Finally, I would say that my patients would tell me every day that they did not want to live—to grow older if they did not have their cognitive capacity because they did not want to become a burden to their families.

We, with global partners, are working diligently to develop answers to their concerns. With the global rise of Alzheimer's prevalence, the situation is urgent, as you well-articulated, and we are using every possible approach to diminish the impact of this disease as rapidly as possible.

Thank you for allowing me to testify, and I look forward to your questions.

Mr. SMITH. Thank you so very much, Dr. Bernard, for your testimony and for your insights.

Dr. Glass?

**STATEMENT OF ROGER GLASS, M.D., DIRECTOR, FOGARTY INTERNATIONAL CENTER, NATIONAL INSTITUTES OF HEALTH**

Dr. GLASS. Thank you, and good afternoon, Chairman Smith, Acting—Ranking Member Bera, and distinguished member Donovan.

I too had a father with Alzheimer's and I sympathize and went through the same experience.

I am Roger Glass. I am the director of the Fogarty International Center at the National Institutes of Health and I am honored to join my colleague, Dr. Bernard, here in discussing how we are confronting the global burden of Alzheimer's disease.

Diseases like Alzheimer's and like flu and ebola know no borders. People throughout the world suffer from this disease and will benefit from treatments and cures.

We need to find the brightest minds everywhere to assist in this endeavor as well as to identify populations with unique environmental or genetic risks because the high quality research that we do doesn't happen only in the United States. It happens elsewhere.

In order to take advantage of these international situations, we need the best trained scientists with high ethical standards, with good data management capabilities, with laboratories capable of conducting the research that's absolutely essential.

Fogarty International Center at NIH facilitates building these research partnerships leading to capacity, building capacity for researchers internationally to create the next generation of scientists who will address the Alzheimer's condition.

These scientists who will address these problems in the future are just being trained today. As Dr. Bernard mentioned in her remarks, NIA is supporting the study in Colombia of an extended family with a genetic mutation for familial Alzheimer's.

This family is now center stage for much of our research on Alzheimer's cures and preventions. This partnership began in the early 1990s when an American investigator, Ken Kosik, then at Harvard, met a Colombian physician, Dr. Francisco Lopera.

Dr. Lopera, as a young neurologist, had a patient with Alzheimer's and found that the patient's father and grandfather had

Alzheimer's, and because of his curiosity as a young physician, not as a researcher, he sought out and ultimately developed a cohort of 5,000 people with this genetic problem and it was from this conversation 6 years later of these American and Colombian investigators that they began a decade-long collaboration to look and see what they could learn about the epidemiology and genetics of Alzheimer's.

This investigation has proved incredibly fruitful beyond our wildest expectations. In the 1990s, these doctors received a grant from Fogarty to work together.

By 2004 and '07, the National Institute of Aging and Fogarty were both engaged in supporting this collaborative research.

And this research involved not only following up on the cohort but training people in laboratory methods, in building capacity so that we could actually conduct quality research under the best ethical standards in the field.

At the same time, it also engendered collaborations between communities that were invested. These were not patients in Colombia. These were community participants in research—a big difference.

Preparing for scientists to conduct high-impact research is critical to the Fogarty agenda and what began as a partnership between these two scientists—individual scientists is now at the cutting edge of what's become a \$100 million clinical trial, the first in the world for early prevention of the progression of Alzheimer's disease.

It is a unique study that couldn't be done anywhere else and this cohort was really an incredible finding and discovery of Dr. Lopera. He's an essential part of the research team as is his laboratory in Colombia—in Medellin, Colombia.

Colombia is not unique in this. While the topic of today's discussion is Alzheimer's disease, the Fogarty Center has also been involved in many other neurological problems such as research on cerebral malaria, neuro HIV, hydrocephalus in Uganda, epilepsy in Zambia, chronic psychotic disorders in Tanzania, and stroke outcomes in Zimbabwe, just to name a few.

Fogarty supports—takes science where the problems are and where the opportunities are for the most rapidly accelerating advances in research. And we also are concerned in developing true partnerships for research and advancing capacity building.

Like Dr. Lopera, who is a unique investigator in a unique setting with a unique population of this familial Alzheimer's disease, it's leading us to, hopefully, more rapid cures.

From this partnership and with NIH support, we are already advancing discovery research. We are already working in basic research in Colombia in collaboration with the U.S.

The group in Colombia is now an integral part and a central part of the U.S. research endeavor on Alzheimer's and the results of this endeavor both for the U.S. population and for the population in Colombia and around the world will all benefit from this activity.

Fogarty is essential for building these international collaborations and we work very closely with NIA and with other institutes at NIH to do this important international collaboration.

Thank you very much.

[The prepared statement of Dr. Bernard and Dr. Glass follows:]

House Foreign Affairs Subcommittee on Africa, Global Health, Global Human Rights and  
International Organizations

Hearing Titled, “A Global Update on Alzheimer’s Disease”

November 29, 2017

Written testimony on behalf of the following witnesses from the  
National Institutes of Health (NIH)

Marie A. Bernard, M.D., Deputy Director, National Institute on  
Aging, NIH

Roger Glass, M.D., Ph.D., Director, Fogarty International Center,  
NIH

Good afternoon, Chairman Smith, Ranking Member Bass, and distinguished members of the Committee. I am Marie A. Bernard, M.D., Deputy Director of the National Institute on Aging (NIA), which is one of the 27 Institutes and Centers of the National Institutes of Health (NIH). I am joined by my colleague, Dr. Roger Glass, the Director of the Fogarty International Center at NIH. It is an honor to be here today to discuss NIH's efforts to stem the rising tide of Alzheimer's disease, a devastating condition and a public health issue of increasing relevance and urgency, both in the United States and globally.

### **An Issue of Mounting Concern**

As all of us are only too well aware, Alzheimer's disease is a currently irreversible, progressive brain disease that slowly destroys memory and thinking skills and eventually even the ability to carry out the simplest tasks of daily living. In most people with Alzheimer's, symptoms first appear after age 60, although a much smaller subset of patients see onset at earlier ages. Although treatment can help manage symptoms in some people, there is currently no cure for this devastating disease. While my focus today will be on Alzheimer's disease, other forms of dementia, including frontotemporal dementia, vascular cognitive impairment/dementia, Lewy body dementia, and mixed dementias, are also important topics of research at the NIH, and I will be sharing some of our activities in these areas with you as well.

Results of a recent meta-analysis<sup>1</sup> indicate that 35.6 million people lived with dementia worldwide in 2010, with numbers expected to double almost every 20 years, to 65.7 million in 2030 and 115.4 million in 2050. Notably, the 2015 World Alzheimer Report estimates that 58% of all people with dementia live in low or middle-income countries.<sup>2</sup> In the United States alone, as many as 5.3 million people age 65 and older are living with Alzheimer's disease. Although several large epidemiological studies suggest that age-specific prevalence rates of dementia,

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<sup>1</sup> Prince M et al., The Global Prevalence of Dementia: A Systematic Review and Metaanalysis. *Alzheimer's and Dementia* 9: 63-75, 2013.

<sup>2</sup> Alzheimer's Disease International. World Alzheimer Report 2015: "The Global Impact of Dementia." <http://www.worldalzheimerreport2015.org/downloads/world-alzheimer-report-2015.pdf>

including Alzheimer’s disease, are declining,<sup>3</sup> it is nevertheless also true that risk for the disease is greatest in the “oldest old” – those over 85. Because this age group is projected to grow substantially in the coming decades – from approximately 5.8 million in 2010 to some 19 million in 2050<sup>4</sup> – it is certain that unless we identify a way to prevent or effectively treat Alzheimer’s, the number of affected Americans will rise significantly within the lifetime of many of us here today.<sup>5</sup>

The NIA-funded Health and Retirement Study (HRS), a 20-year-old nationwide survey of the health, economic, and social status of older Americans, has added a new data resource—the Harmonized Cognitive Assessment Protocol—to help advance population studies of cognitive impairment and dementia. Additional grants are funding harmonized assessments for nationally representative studies in England, Mexico, China, and India, as well as a smaller-scale field study in rural South Africa. These investments will provide unprecedented scientific opportunities for the epidemiological study of Alzheimer’s and related dementias beginning in 2018. NIA also funds other initiatives to study trends in dementia prevalence and incidence around the world. Finally, we support the Integrative Analysis of Longitudinal Studies of Aging and Dementia research network, which is composed of investigators associated with over 100 longitudinal studies on aging and dementia. This initiative facilitates cross-national research on determinants and dynamics of within-person aging-related changes in cognitive and physical capacities.

### Identifying Risk and Protective Factors

Identification of individuals at risk may suggest strategies for disease prevention. NIA supports a number of studies aimed at identifying at-risk individuals, including several with international reach and scope.

For example, NIA supports a study of the biomedical and socio-economic conditions that influence cognition, including susceptibility to dementia, among members of the Survey of

<sup>3</sup> Larson EB, Yaffe K, and Langa KM. New Insights into the Dementia Epidemic. *New England Journal of Medicine* 369: 22-25-2277, 2013.

<sup>4</sup> Vincent, Grayson K. and Victoria A. Velkoff. The Next Four Decades. The Older Population in the United States, 2010-2050. Current Population Reports, P25-1138. U.S. Census Bureau, Washington, D.C., 2010.

<sup>5</sup> Ilbert LI et al. Alzheimer disease in the United States (2010-2050) estimated using 2010 census. *American Academy of Neurology* 80: 1778-1783, (2013).



Health, Aging, and Retirement in Europe (SHARE), a large and population-representative study that is harmonized with the HRS and currently deployed in 27 Continental European countries plus Israel. NIA also supports the COhort Studies of Memory in International Consortium (COSMIC), an international consortium of prospective longitudinal population-based cohorts examining the risk and protective factors for cognitive decline and the development of dementia. Established in 2012, COSMIC has developed into a consortium of 26 studies from 16 countries in five continents, with a combined sample size of >70,000, and is now uniquely placed to address some of the salient questions in relation to the epidemiology and biomarkers of neurocognitive disorders.

Identification of genetic risk factors provides insight about mechanisms that lead to development of Alzheimer's and other forms of dementia. A number of genetic loci – fixed sections of DNA that contain one or more genes – for Alzheimer's have been identified among whites of European ancestry, but the genetics of Alzheimer's among other populations is not as well understood. Investigators with the NIA-supported Alzheimer's Disease Genetics Consortium conducted a large genome-wide association study that included participants of European ancestry, African Americans, Japanese, and Israeli Arabs, and identified several loci of interest, most – but not all – of which appeared to be implicated in the disease in more than one ethnic group. These findings highlight the importance and value of trans ethnic studies for identifying susceptibility loci for Alzheimer's disease.<sup>6</sup>

### **Diagnosing Alzheimer's Disease**

Biomarkers, or changes in the quantities of genes, proteins, or metabolites, whose presence in a living organism can be measured to indicate the presence of disease, are essential to the development of diagnostic techniques and treatments. As recently as 2004, there were no established biomarkers for Alzheimer's. Today, not only can we image both amyloid plaques and tau tangles (the neuropathological hallmarks of Alzheimer's disease) in the living brain, but we have also identified many other potentially promising biomarkers, from blood proteins to early changes in an individual's sense of smell. The NIA-supported Alzheimer's Disease

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<sup>6</sup> Jun GR et al. Transethnic genome-wide scan identifies novel Alzheimer's disease loci. *Alzheimer's and Dementia* 13: 727-738, 2017.

Neuroimaging Initiative (ADNI), which was established in 2004 to identify and validate neuroimaging and fluid biomarkers, has contributed to much of this important progress.

ADNI is a member of the World Wide Alzheimer's Disease Neuroimaging Initiative (WW-ADNI), a global collaboration coordinated by the Alzheimer's Association to help define the rate of progression of mild cognitive impairment and Alzheimer's disease, and to develop improved methods for identifying the appropriate patient populations to participate in clinical trials. WW-ADNI also aims to standardize the methods used for conducting imaging scans and gathering and testing fluid samples so that data from all sites can be readily combined and easily understood by researchers. With participating organizations in Europe, Japan, Australia, Taiwan, Korea, China, and Argentina, WW-ADNI will allow researchers to gain a worldwide picture of the physical changes that lead to Alzheimer's disease.

### **Treatment**

In addition to diagnosis, biomarkers can be used to track response to treatment. The Accelerating Medicines Partnership-Alzheimer's Disease (AMP-AD) Biomarkers Project is exploring the utility of tau PET imaging and novel fluid biomarkers for tracking response to treatment and/or disease progression among anti-amyloid therapies being tested in certain Phase I/II clinical trials. Screening and baseline data from the trials will be made broadly available through the Global Alzheimer's Association Interactive Network collaborative platform. Trial data and biological samples will also be shared after the trials are completed.

NIA-supported investigators are also conducting prevention and treatment trials with global reach. For example, the Autosomal Dominant Alzheimer's Disease Trial involves approximately 300 members of an extended family in Colombia who share a rare genetic mutation that triggers Alzheimer's symptoms in middle age. This family represents the world's largest occurrence of early-onset familial Alzheimer's disease. This trial focuses on whether an antibody treatment, crenezumab, can prevent or delay the appearance of Alzheimer's disease. Notably, Fogarty support enabled the University of Antioquia in Colombia to create a vivarium where rodent models of Alzheimer's have been studied and housed. Another NIA-supported initiative, the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), conducts clinical trials among individuals with the rare early-onset form of the disease. DIAN-TU

currently manages the world's first clinical trial to prevent development of Alzheimer's in families at genetic risk of early-onset disease. This groundbreaking trial is being performed at sites in the United States, Canada, Australia, and across Europe.

DIAN-TU investigators also manage the DIAN Expanded Registry (DIAN EXR), an international research registry for individuals with early-onset Alzheimer's and those known to be at risk. Patients and family members enrolled in DIAN EXR can learn about current research and clinical trials, gain access to genetic counseling and testing, and attend international family conferences that will enable them to connect with scientific and medical experts as well as other families affected by this devastating condition.

### **International Collaboration**

In an interconnected world, it is essential that NIH continue to invest in a research workforce that can respond to evolving challenges that affect us all. As demonstrated in the Colombian trial example, these discoveries are often made by U.S. and foreign scientists working in close collaborations that enable the best and brightest minds to tackle complex health challenges together.

Through its Global Brain Disorders Research program, Fogarty also provides opportunities for investigators to conduct research specifically on nervous system function and impairment, including Alzheimer's disease. In partnership with 10 other NIH Institutes and Centers (including NIA), this program supports international collaborative research relevant to low- and middle-income country settings.

NIA remains committed to speeding the pace of global research by large-scale sharing of data with qualified researchers around the globe. For example, ADNI data have been widely available since the initiative's establishment, and data from AMP-AD and the Alzheimer's Genetics Consortium are also made available to investigators worldwide. Data from the HRS and its sister studies in other countries are likewise freely available without any embargo period.

The International Alzheimer's Disease Research Portfolio (IADRP), developed by the NIA in collaboration with the Alzheimer's Association, enables public and private funders of Alzheimer's research to coordinate research planning, leverage resources, avoid duplication of funding efforts and identify new opportunities in promising areas of growth. Currently, the

database contains information about over 8,300 unique projects representing over 30 funding organizations in 11 countries.

Alzheimer's disease and related forms of dementia devastate families in every corner of the world. At the National Institute on Aging and the Fogarty International Center, it is our hope that through cooperation and coordination with our partners around the globe, we will make much-needed and long-anticipated progress in finding a prevention or a cure.

This concludes my testimony. I welcome the opportunity to answer your questions.

Mr. SMITH. Dr. Glass, thank you very much for your testimony and your leadership as well.

Let me just ask the question with regards to imaging, which you mentioned a moment ago, Doctor. What kind of brain imaging are we talking about? CAT scan? MRI?

Obviously, that is not available in most developing world settings, and since there is such a under—large numbers of people never get a diagnosis—about 50 percent or less in the United States—how quickly is this technology being advanced so more people will get a definitive word earlier on so some of these drugs that, again, only deal with symptoms can be applied to mitigate those symptoms?

Dr. BERNARD. So what I was describing as opportunities with imaging and looking at proteins are meant to be in the research setting currently.

But they are being refined and we are beginning to look at things in the blood—in the peripheral blood. We are looking at things like changes in smell.

We are looking at things like the development of depression symptoms years before a person actually has dementia as things that will help us to be more precise in making that diagnosis clinically.

So it all comes together to help us. We don't quite have something that can be translated directly from the research lab that is anything better than we currently have in terms of looking for symptoms right now.

Mr. SMITH. Just let me ask you, Dr. Glass, about Uganda and the situation with hydrocephalic condition.

I have had five hearings on that. We have a bill that would address that need and we actually had doctors—Dr. Benjamin Warf, who developed a non-shunt intervention to help people who have water on the brain, and it is amazingly effective and not much by way of having to redo it.

You mentioned risk factors. Obviously, genetics is a risk factor. We all know that, and one of those studies you mentioned, that's a big focus.

But when you talk about environmental risk factors, we know that in the area of autism environment does play a very serious role, and NIH has chronicled that in its reports.

I am wondering if other areas of investigation are being pursued including toxic chemicals of various kinds. Lyme disease—I chair the Lyme disease caucus as well and it's a huge problem in my district, in my state, and in our region—is grossly under reported, and there have been studies that found that people with Lyme that dementia was one of the consequences, and I am wondering if that's being looked at.

So maybe if you could speak to the environmental side of it, if you would.

Dr. BERNARD. So I will start off and say that from the environmental perspective, yes, we have a number of studies that are looking at various environmental toxins that may be contributing to problems with the development of Alzheimer's that's particularly assisted by projects that are looking at people in the long term and looking at what has happened to them.

We are also looking at education, looking at diet, looking at geographic location. All of those may contribute. I quite honestly do not know specifically about Lyme disease. We could look back and get back to you on that.

But a variety of things environmentally and socially seem to be associated with differences in the frequency with which various groups have Alzheimer's disease.

Mr. SMITH. Dr. Glass, do you want to add anything?

Dr. GLASS. I don't know of other risk factors for Alzheimer's, although Hispanics have an increased risk and an earlier presentation.

But for other neurological diseases, we know a lot of about infections like malaria and other meningitides. We know about heavy metals and exposures.

We know about foods in Africa, for instance, like manihot, which has a cyanide that leads to poisoning, and alcohol, of course, and fetal alcohol.

So there are other toxins. But for Alzheimer's we don't have those yet and we could look into and provide that information.

Mr. SMITH. I'd appreciate that, for the record.

The international response has become increasingly aggressive and robust. In 2012, the WHO released a document, "Dementia: A Public Health Priority," and I and Greg Simpkins and others on our subcommittee met with Dr. Margaret Chan, a former WHO director general and she had a real heart for this as do so many others at the WHO.

In 2013, the G8—now G7 without Russia—but the G8 committed to more research funding, and that is Canada, France, Germany, Italy, Japan, Russia, the United Kingdom, and, of course, the United States.

And I am wondering if you could tell us that plus the newest 2017 WHO action plan. PAHO—the Pan-American Health Organization—has a plan. People seem to be coming up with action plans, and that's all great, but how well are they being implemented?

Are the other countries, for example, like us—we are tripling our NIH funding. It's a bipartisan effort. Again, I mentioned Tom Cole, the chairman who's doing a wonderful job. He's got a heart for this.

The Alzheimer's Association never lets up in pushing this and having a great impact.

In my own State, Christine Hopkins is the Alzheimer's Ambassador. We all have one. She is constantly in contact with me and I think that is a great way of advocating on behalf of patients and caregivers.

Katie Macklin is the director in our area and I was just at a march for Alzheimer's in Bradley Beach. There was over 1,000 people. So the Alzheimer's Association are here and they will be submitting testimony as well.

We are really pushing for the private sector to come up with money augmented, of course, and leveraged by the public sector money.

Are the others doing it as well? Is Japan, is Germany, the U.K., the other G8—the more affluent countries coming up with the resources so synergistically we'll see a great surge in research?

Dr. BERNARD. So I can certainly say that we track what's happening internationally and something that was developed jointly with the Alzheimer's Association is something called the International Alzheimer's Disease Research Portfolio that allows us to see across the globe what is going on.

It currently has more than 8,000 projects representing 30 funding agencies, 11 different countries. We also work through the department in being responsive to what the World Health Organization is doing to work across the globe in Alzheimer's projects and we are aware that various countries have developed plans as we have. So I will probably defer to my colleague, Dr. Glass, for further elaboration.

Dr. GLASS. The most important risk factor for Alzheimer's is age. We see an aging of the population around the world, which is why this has become such a tremendous problem, as we look forward, and I think it's because of that aging that many groups including the Japanese and the English have invested in this heavily.

I think as new diagnostic methods become available so you can actually make a proper diagnosis, the importance of Alzheimer's globally will be observed in each of the countries that does the surveys.

And so with the improvement of diagnostics that don't require a dead brain, we'll be able to understand the prevalence and increasing incidence over time.

Mr. SMITH. Just two final questions. Is there a best estimate if things don't change where we will be by 2025 and 2050? I gave one estimate and there's highs and lows, of course. They were all guesses.

Do you think we will reach the goal of a disease-modifying therapy by 2025, which was the G8 push, which is the WHO push, which is our push with NAPA, the bill, that we all got behind and pushed a couple of years ago? Do you think we will get there? I mean, is there enough critical mass of resources to get us there, in your opinion?

Dr. BERNARD. I was going to say that we are very grateful for the additional resources that have been provided and, again, as a clinician, I am really excited because there has been the opportunity to invest broadly in basic research that'll help us to better understand what's happening mechanistically with this illness, an explosion of recognition of genes that are related to it.

We went from only knowing four genes a little more than a decade ago to more than 24. Lots of clinical studies, 100 or so, with results coming out in the next many years that'll help us to understand which direction we need to go.

Enhancement of population-based studies that'll help to answer some of the questions that you were asking about toxic exposures, social factors, et cetera.

So I think that there's great momentum going on and we'll have to see.

Dr. GLASS. I would concur. You know, we have more tools to research Alzheimer's today than we've ever had when my dad passed away. We have imaging techniques, which are extraordinary, genetic entrees to the disease, animal models for Alzheimer's that allow us to test out new drugs.

And so we are in a position better today than ever before to accelerate the advances. The fact that we have so many monoclonals in clinical trials and drugs that are being tested could—if any of them delay the progression of the disease they will have a huge impact on the cost of care.

So I think in the short run we have clinical trials that are ongoing now. Also, the trial in Colombia—if it's successful we will all benefit.

If it fails, it will tell us that we are barking up the wrong tree and we need to find other targets that would be more susceptible to—for new drugs. So either way, I think we are on a roll that we've never had before and the opportunities are clearly before us.

Mr. SMITH. As I mentioned in my opening, I will be reintroducing the Global Brain Health bill next week. It deals with three diseases: Autism, Alzheimer's and hydrocephalic condition, referencing what you mentioned about Uganda, Dr. Glass.

Dr. GLASS. Yes.

Mr. SMITH. It concerns me that USAID, and I have had conversations with Mark Green, the new administrator. It's important that we do infectious diseases, communicable diseases, but brain health has been left to CDC and to the diplomacy area, not to the actual assistance at the country level.

So my hope is that we will be able to get this bill passed and begin moving in the direction of funding—those kinds of initiatives as well.

Dr. Bera.

Mr. BERA. Thank you, Mr. Chairman.

Dr. Bernard, you talked about longitudinally following older Americans and so forth.

Is—as you are building this database and looking at that database and now adding in folks from around the world as well in that database, what kind of patterns are—has it been around long enough and what types of patterns, potentially, are emerging?

Dr. BERNARD. Thank you for asking that question, because what we are seeing is, in the United States, at least, that the incidence of Alzheimer's disease may be decreasing in certain segments of the population.

Whether that is because of better education, better blood pressure control, better nutrition, we don't know. But we are seeing other sorts of things like we are being able to determine that if you make it to age 70 without cognitive impairment that you still have, as a man, a almost one out of four chance of developing Alzheimer's, as a woman a one out of three chance of developing Alzheimer's disease, and we are seeing—when we compare across countries that there seems to be a socioeconomic status relationship.

You know, the higher the socioeconomic status, the longer one puts off the likelihood of developing an Alzheimer's type dementia. So there is, clearly, a social component to this and we are looking forward to further disentangling that.

Mr. BERA. Do you see a pattern with level of educational attainment? So, you know, lower rates of Alzheimer's disease in folks with higher educational attainment?



Dr. BERNARD. It appears that that there is such a correlation—that the rate of the development of the disease, the age at which one develops the disease is—the rate is lower.

The age at which you develop is older. So there seems to perhaps be some sort of protective or beneficial effect of education.

Mr. BERA. So when I used to practice medicine, I would tell my patients to do crossword puzzles every day. It wasn't—just something that I was telling them to do in terms of exercising your brain and go into distant memories and—

Dr. BERNARD. Yes. Yes. We have a number of studies where we are trying to really disentangle exactly what makes the difference. Whether it's doing crossword puzzles or the brain games are out there, et cetera, we don't have definitive evidence that that's truly impactful.

We do have one study, something called the Active Study, that demonstrated that if you trained people in a particular component of cognition that that was beneficial for that component like speed of processing of information or memory or things like that.

But it's not clear that it truly can put off dementia. In fact, we had the Agency of Health Research and Quality and the National Academy of Science, Engineering, and Medicine to look at that very carefully for us recently and they—their assessment was that we are not yet at the point that we can say definitively that those things that we recommended for patients are going to make a difference.

But it certainly can't be harmful and particularly if they're enjoying those sorts of things. I do the same sort of thing as well.

Mr. BERA. Dr. Glass, do you want to add anything in addition to that?

Again, you know, as we—as we do when we do medical research we are creating this huge database and we are looking for patterns.

In terms of risk stratification now and, you know, as, you know, we try to come up with better diagnostic tools, what are some of the, you know, outside of family history of Alzheimer's what are some of the risk factors that we ought to be thinking about and educating the public on and, certainly, educating our physicians on as well in our workforce?

Dr. BERNARD. So, certainly, it appears that people who are likely to develop an Alzheimer's type dementia are the people who live for a longer period of time, the people who may not have as high a level of education, people who have had problems with high blood pressure and diabetes and that's the reason some of the populations that are considered to be under represented populations in the United States may have a higher prevalence, as Dr. Glass alluded to.

There may be some role for past significant head trauma—things of that sort. But, you know—

Mr. BERA. We are not—we still haven't quite seen definitely those patterns emerge out of the—out of the database?

Dr. BERNARD. There are risk factors that we've seen. Whether they are modifiable risk factors is the—is the question.

Dr. GLASS. Let me just add, Congressman Bera—Dr. Bera—even with in the Colombia cohort, which comes from a single founder, there are genetic mutations that have been introduced over the last

200 years so that the age of onset, the speed of progression, are all idiosyncrasies—differences that we can understand by linking the genetics with the phenotype and with the progression.

So we can actually learn a lot about the genetics by plotting those individuals. So I think there's—when we deal with the melting pot of the United States with genes that have been mixed from all over, much more difficult to do and I think that we'll learn a lot more from this cohort and perhaps from others, which have these familial modifications.

Mr. BERA. Dr. Bernard, with a family history of Alzheimer's disease, what is the risk of developing Alzheimer's disease? Can we say definitively or—

Dr. BERNARD. What we can say is that if you have an APOE 4 gene or two versions of the APOE 4 gene that you have a very high risk. We can't say there's 100 percent likelihood but a very high risk of developing Alzheimer's disease.

If you have an amyloid precursor protein mutation presenilin one or presenilin two, those are associated with early onset Alzheimer's disease.

They tend to be autosomal dominant, meaning that very likely you are going to develop Alzheimer's disease associated with that. That's with the Colombian cohort. And then just simply a family history, yes.

I mean, if you have family members who've had an Alzheimer's type dementia you may be at greater risk as well. Whether it's related to one of those other genes that we've discovered of late or a combination of the genes or environmental factors or social factors, not totally clear at this point.

Mr. BERA. And in terms of risk stratification, so patient presents with a family history of Alzheimer's disease, how readily available are the genetic testing and, you know, again, just to try to think about risk stratify?

Dr. BERNARD. So I think that there are private entities that are available that can do the genetic testing. We certainly have a system—Alzheimer's disease centers that are set up to bring people in to participate in research programs and some of these centers are focusing on people who have genetic risk.

And I would again put a plug in for people to be involved with such things because we need lots of different people—a diversity of people involved in these studies to really understand what—how is it going to present in different groups.

Mr. BERA. And do we know, are there any prospective studies going on right now where you are taking folks with a confirmed diagnosis of Alzheimer's type dementia, taking—taking their family members and prospectively following those family members, looking for patterns? Are those studies ongoing?

Dr. BERNARD. So we have a number of studies that are looking at people who, by biomarkers—you know, they have the changes in the brain, they may have a genetic abnormality but they are not yet symptomatic—and we are looking at various interventions to try to make a difference in their outcomes. So to that degree, yes.

Mr. BERA. Now, and at this stage with what we do know, there's nothing that prevents us from educating our health care workforce.

If someone has that family history of Alzheimer's disease, you know, they ought to look at those other mitigating factors—manage their diabetes a little bit better, you know, look at those other lifestyle changes, you know, look at alcohol consumption and, you know, again, those other mitigating factors that may not prevent them from developing Alzheimer's but may slow down the evolution of the disease, look at maintaining brain activity through, you know, whether it is, you know, brain games or crossword puzzles or, you know, maintaining physical well-being—those are all reasonable interventions that we can do at—probably have a cost benefit but also, you know—is that an accurate statement?

Dr. BERNARD. I think that's a fair statement—that National Academies and Agency Research and Quality Study that I referenced they said that we do not yet have definitive evidence but there's encouraging though inconclusive evidence that controlling blood pressure and hypertension, physical activity can make a difference and inconclusive but possibility of cognitive engagement.

So yes, I would hope that my colleagues, your colleagues, would do all of the things that you'd mentioned as well as encourage those patients to think about getting involved in a clinical study.

Mr. BERA. Great. I could ask 100 more questions but I will yield back. Thank you.

Mr. SMITH. Mr. Donovan.

Mr. DONOVAN. Well, now that Dr. Bera has made Dr. Glass and myself feel real comfortable about asking about family history of two people who have Alzheimer's patients as parents—no, thank you, Doc. This entire process is an education for me.

And I wanted to ask about—we are talking about studies and being able to diagnose, and Dr. Bernard, I remember when they'd say you needed an autopsy to actually do a diagnosis. I remember that.

Are we advancing also in how we are treating patients now with Alzheimer's as we are waiting for the studies to conclude and how advanced have we gone?

I can't believe what you said in your testimony about, I think, identifying four genes 10 years ago or so. Now we could identify 24. That's an incredible advancement for the person on the panel who's not a physician.

So has our treatment gotten better as your studies have advanced and developed?

Dr. BERNARD. So we, unfortunately, do not have a true treatment. We have drugs that can slow down symptoms for a period of time but it really doesn't change the course of the illness.

So at the same time that we are vigorously looking for that prevention or a cure, we are also supporting research that's looking at being more effective at caring for the individual with Alzheimer's disease and for their caregiver.

In fact, on the NIH campus just last month there was a summit on Alzheimer's caregiving with some 500-plus researchers, advocates, people living with dementia, and it was really edifying to hear them reviewing what's there and noting that we have a lot of interventions that are effective and can be generalized.

There are opportunities for further enhancements there. Some 450 recommendations came from that study. So we are sifting through that and seeing what we can do to further enhance things.

But I would like to think that we are further down the road in terms of paying attention to issues of caring for individuals with Alzheimer's and for their caregivers. There is still room for further improvement.

Mr. DONOVAN. Anything to add, Doctor? I am sorry.

Dr. GLASS. Not really.

Mr. DONOVAN. Okay.

Dr. GLASS. It would be nice that we had a cure. There are certainly cultural differences in giving care and keeping people at home versus in institutions—definitions that people use.

And we have supported research on caregivers in the Spanish language because the way you make a clinical diagnosis based on history is linked to the terms that are used for dementia and for acceptance of the disease and I think that's an area where we are learning.

But not breakthroughs as such, just in the care giving—quality of care giving.

Mr. DONOVAN. I certainly understand that. I mean, my mother suffered for 4 years, as I said. A woman from Trinidad and a woman from Ghana treated my mother like she was their own mother for 4 years.

These people became part of our family. We still have Thanksgiving with these two women and my mother passed 2 years ago. And the toll that takes on people—it was almost like at some point my mother had this innocence about her.

She didn't understand what was going on with her body and her mind. It was everybody around her who were suffering. So the emphasis, and Dr. Bera said it too—the recognition and focus on some of the caregivers of Alzheimer's patients I think is just as important as caring for the patient.

When you are successful and we do develop a treatment or a cure, another one of my fears is that as we—I spoke earlier about global health with maternal health and child health or even prenatal health, is that we are not getting those things that we actually do have now here for our children to some of those developing countries—those folks who are—don't have the resources we have, and I suspect we'll probably have the same problem after your success in finding treatments and cures for Alzheimer's of getting whatever is developed to folks in less developed areas of our world and do you see that as something that—I know we have to concentrate on first finding the treatment and the cure but once we do, getting it to folks outside of our own country I suspect the folks in our own country for the most part anyhow will—this will be more readily available to them than places in other parts of our world.

So as we see with immunizations for children or prenatal care from mom, my fear is that after you are successful we might have the same problem getting the resources to the folks who need them outside of our own country. Do you see that as an issue?

Dr. GLASS. I will make two comments. I thought it was very thoughtful about your mother and I think part of the issue in care

giving is how do we train caregivers to give the quality of care that your mother got from these two women.

My father was in exactly the same situation and that quality of care and how we train people to provide this is essential. Some of this we can learn through global collaborations.

On the other part of your question, can the interventions that we develop in the United States be carried abroad? We have a whole agenda at Fogarty on implementation science—of taking what we've learned and implementing it in developing countries.

We have learned, for instance, how to prevent mother-to-child transmission of HIV. But in many countries this has not reached all the pregnancies and mothers, and if you miss a pregnancy, you'll have a child born with HIV who will need treatment for life.

So in the area of implementation strategies, that has really become a priority for our research of taking what we've learned and implementing in developing countries.

I think, Chairman Smith, one other thought I—since you mentioned Dr. Warf, one of the values of global health research from his research is that he developed methods to treat hydrocephalus without needing to revise shunts every few years in children in developing countries because you can't take them in for repeat surgery.

So through two procedures that he's adapted that were known but mixed together, one to open the outflow of cerebral spinal fluid, the other to cauterize the choroid plexus that produces CSF—the spinal fluid—he could decrease the flow, increase the outflow, decrease the input, and so he could do a single operation without the revision.

That operation is now being used in the United States to treat our children with hydrocephalus. So it's through that research done in Uganda by an outstanding American neurosurgeon, seeing the need in that country to bring that technology home to our own children, it is another benefit of, I would say, reverse technology transfer—learning from the developing world these kinds of lessons.

It will make American children survive better with hydrocephalus as well.

Mr. DONOVAN. Since everyone mentioned a doctor, and you are the only two doctors that I know besides Dr. Bera, Tony Fauci is a friend and I remember him saying at one of our conferences that if you are successful finding a cure for Alzheimer's, the amount of money that we gave NIH in the 21st Century Cures Act it will pay for itself, the amount of money we spend on treating this disease.

I thank you both for your work. Besides being here today, I thank you both for your work—the people who will benefit once you are successful.

Thank you all.

Mr. SMITH. Thank you, Dan.

Let me just conclude and ask you, if you could—the 2017 WHO Action Plan—on November 13th we know the Bill and Melinda Gates Foundation and now it's \$100 million for Alzheimer's research—the U.N. itself has established a Global Dementia Observatory to collate and disseminate key dementia data from member states to support evidence-based service planning and strengthening of policies as well as health and social care systems.

What is your opinion of the WHO Action Plan? The steps, obviously, are a whole of government approach for ourselves. Are you happy with it? Do you feel that this is really going to be transformational?

Dr. GLASS. First of all, we were delighted to hear about the Gates contribution to Alzheimer's, and I think as Bill and Melinda Gates age, they realize that this is a risk that's before them as well.

So their investment is really appreciated and shows a broadening of global interest in this—in this endeavor. I think the fact that the U.N. has a Global Action Plan is also wonderful recognition of the importance of this problem globally and it remains to be seen how this will be rolled out.

But the fact that it's there and it's recognized and it's recognized by so many international partners is an awakening to the—to the importance of the burden of this disease for all of us globally.

Mr. SMITH. Thank you.

Dr. BERNARD. I would just support what my colleague has said. We think that this is something that needs all the best and brightest minds put toward it and what we have observed is that as other countries are putting resources toward it, there are more and more scientists with whom we can collaborate and that's only to the good of all.

Mr. SMITH. Thank you for your leadership. Thank you for being here today. Is there anything else you'd like to add before we go to panel two?

Thank you so very much.

I would like to now welcome to the witness table our second panel, beginning with Dr. Mary Mittelman, who serves as research professor at the Department of Psychiatry and Rehabilitative Medicine, and director at NYU Alzheimer's Disease and Related Dementias Family Support Program at NYU's School of Medicine and the Langone Health at NYU.

Dr. Mittelman was principal investigator of a randomized controlled trial of the NYU caregiver intervention funded for 20 years by the National Institutes of Health, the results of which have been published widely.

Dr. Mittelman has expanded her research focus to interventions that include the person with dementia as well as the caregiver. She's the founder of the Unforgettables, a chorus of people with dementia and their family members, which rehearses and gives regular concerts in New York City.

We will then hear from Dr. Richard Mohs, who is the chief scientific officer for the Global Alzheimer's Platform—GAP—Foundation, a patient-centered nonprofit organization devoted to enhancing the speed and quality with which new treatments for Alzheimer's disease are developed.

He retired in 2015 from Eli Lilly and Company where he held several leadership positions including VP for neuroscience early clinical development and leader of the Global Alzheimer's Drug Development Team.

He also serves as a member of the Board of Governors for the Alzheimer's Drug Discovery Foundation, a member of the board of directors of Cogstate Limited based in Melbourne, Australia, and

senior associate editor for *Alzheimer's and Dementia*, the journal of the Alzheimer's Association.

Then we will hear from Michael Splaine, who is owner and principal at Splaine Consulting, a small advocacy and government affairs consulting firm with a very big impact based in Washington, DC.

Immediately prior to starting the company he was Director of State Government Affairs in the Public Policy Division of the Alzheimer's Association, leading its grassroots network to accomplish State policy priorities including comprehensive State Alzheimer's plans.

Well known as an advocacy trainer and grassroots organizer, Mr. Splaine has also been faculty for Alzheimer's Disease International University public policy and is active in ADI's World Health Organization's Strategy Group and is now advancing its policy agenda with U.N.-based opportunities in New York and Geneva.

Thank you all for being here and please, Dr. Mittelman, if you would begin.

**STATEMENT OF MARY MITTELMAN, DR.P.H., RESEARCH PROFESSOR, ALZHEIMER'S DISEASE AND RELATED DEMENTIAS FAMILY SUPPORT PROGRAM, NEW YORK UNIVERSITY**

Ms. MITTELMAN. Thank you. I got into this field because my mother had dementia. I am trained as a psychiatric epidemiologist and when my mother had dementia my family really did not cope very well. In fact, the dementia probably drove us apart rather than bringing us together.

And after she died, I decided to try to figure out whether there was a way to help families like mine to cope better with the illness.

And I was lucky enough to meet four women who were working at NYU, helping caregivers as volunteers and I—and I saw what they were doing and I decided to try to write a—to run a clinical trial of what they were doing.

So I wrote a grant proposal to the NIMH and was funded from 1987 to 2010, ultimately, by the NIMH and the NIA to study an intervention that was based on what these women had been doing at NYU.

The intervention, which we subsequently named the NYU Caregiver Intervention, is a multi-component intervention and it is individualized to the needs of every caregiver. It starts with a comprehensive assessment of the primary caregiver and then there is an individual counselling session, the point of which is to help the caregiver to understand the need—her need or his need for support from other family members, friends, and formal support.

And then there are four family counselling sessions with family members that the caregiver nominates as important to him or her and a final individual session.

So there are six counselling sessions in a period of 4 months. But since Alzheimer's disease can last as long as 20 years in an otherwise healthy person, we thought it was important to provide ongoing support.

So other parts of the intervention that provide ongoing support are recommendations that the caregiver join a support group that's

run by the Alzheimer's Association or other organizations like it and also we were available for what we named ad hoc counselling.

So any caregiver or family member who participated in our study was able to call the counselor at any time for as long as they stayed in the study and some caregivers actually stayed in the study for more than 18 years.

So in that time I was—in the time I was funded and because people stayed in the study for so long, I was able to demonstrate incredible benefits of this intervention compared to the usual care that people were able to get at NYU at the time.

And, basically, the most important component that was not available to the control group in our original randomized control trial was the family counselling.

So we think the family counselling was the key and most important ingredient in this package in the multi-component intervention.

So what were some of the benefits that we were able to demonstrate? We were able to show that family—the first thing that happened was that the primary caregiver was more satisfied with the support that he or she got from family members and friends.

This then led to significantly reduced symptoms of depression, significantly reduced symptoms of stress, improved caregiver physical health, and by those—by those changes all through improving family support for the primary caregiver we were able to keep the person with dementia at home on average a year and a half longer than the people who got our usual care.

So this is a really powerful intervention and its—and its power is through social support. More recently, we were able to show that this intervention could save huge costs to the health care system in a study that we published in *Health Affairs* in 2014.

We showed that the State of Minnesota with a population of about 5.5 million people could, if every caregiver got the NYU caregiver intervention, save \$996 million in 15 years.

That factoid, not all the other things I told you about—depression and stress and physical health—but that fact was brought to the attention of the governor of the State of New York who, because of it, allocated \$75 million to family support programs of which now I am running one.

And I think—and our program is really, while we would have to do what is mandated by the State, is really—the core of it is improving social support for the family caregiver.

And I think that everything that we've done has been about social support and that is something which doesn't cost necessarily a lot of money and I think in any country that could—that would want to learn how to would want health care providers to learn how to do this intervention.

It could be done at a relatively low cost and in developing costs often labor is cheap and pharmaceutical interventions may be very expensive.

So because of our—of our success, even before the *Health Affairs* article, people in other countries were interested in doing the study.

We did the three-country study in the U.S., the U.K., and Australia, which replicated our findings of reduced depression in care-



givers even though all of the people in the study—all the patients in the study were getting Donepezil, which was an approved drug for dementia.

We have done a study in Israel that showed similar findings and we did a study in—we are currently doing a—finishing a study in Spanish Harlem, which is showing the effects, again, of this intervention.

So I am here to say that there is something right now that works—that it isn't a drug and it won't cure the disease but I can help people to live better with the disease, and I think that while we are waiting for an intervention—a pharmaceutical intervention, it is incumbent upon all societies to do the best they can to improve the quality of life of family caregivers and people with dementia.

So some of the more recent interventions that I am involved with you mentioned the chorus, which I founded in 2011, is a very relatively inexpensive intervention. People with dementia sing with their family members.

They rehearse for concerts and they give concerts. They learn new songs, which is something nobody believed could happen. So people with dementia are learning 18 new songs for every concert, not only giving pleasure to themselves, not only finding support with other people like themselves, but giving pleasure to the community.

So I think that what we can do right now is to improve social support for family caregivers and for people with dementia.

Thank you.

[The prepared statement of Ms. Mittelman follows:]

**Counseling and Support Can Reduce Emotional, Physical and Financial Costs of Dementia  
A Vision for International Expansion of an Evidence-Based Intervention**



*“Everyone is interested in research on drug trials and how drugs can improve cognitive function. I think that we should be equally concerned with well-being and quality-of-life for those with dementia, their caregivers, and their families.”*

Mary Mittelman, DrPH  
Developer of the NYU Caregiver Intervention  
Research Professor, Psychiatry and Rehabilitative Medicine  
NYU School of Medicine, NYU Langone Health

**The Problem**

Alzheimer’s disease has devastating effects on both patients and on the families who care for them. Drugs produce only modest improvements and the possibility of curing or preventing Alzheimer’s disease remains far in the future. In the meantime, as the population continues to age, the financial and emotional cost to patients and families as well as the cost to the federal health care budget continues to grow. This problem is growing more quickly in developing countries than in industrialized countries. While new pharmaceutical interventions may provide more benefits than those that are currently available, they are likely to be expensive, and may be unaffordable by many families dealing with dementia. In addition, migration of young adults to cities or from other countries to the United States while older family members have remained behind, means that family caregivers are often widely dispersed

**A Potential Solution**

The NYU Caregiver Intervention (NYUCI) can be provided to caregivers at relatively low cost, particularly in countries where wages are relatively low. The intervention has demonstrated multiple benefits over the past 30 years. Online training in how to conduct the NYUCI both in person and via videoconferencing is available. The NYUCI can be used in combination with pharmaceutical intervention, and provides additional benefits. The nihilism among physicians, who avoid diagnosing dementia because there is currently no drug that can slow or reverse the progression of dementia could be counteracted by more widespread knowledge of the power of psychosocial interventions like the NYUCI. If there are more patients diagnosed, there are more patients potentially available for clinical trials of drugs to treat AD.

**The Goal of the NYUCI**

The goal of the NYUCI is to improve the well-being of family caregivers, and thereby to enable them to keep the person with dementia at home longer than would otherwise have been possible. The main mechanism for improving caregiver well-being is improving social support, largely through helping the caregiver and other family members to interact in positive ways, but also by

providing referrals to appropriate resources in the community. Because every family has different needs, the intervention is individualized. counseling. Because most caregivers would benefit from more understanding and help from their families, the intervention includes family counseling. Because Alzheimer's disease can last for many years and its effects change over time, the intervention is not time-limited.

#### What is the NYUCI?

The NYUCI, developed at the NYU School of Medicine, in New York, USA, is an evidence-based multicomponent intervention that provides counseling, education and support to family caregivers of relatives living with dementia, either in person or via video teleconferencing. It includes individual consultation, family consultation, and 'ad-hoc'—additional phone or video telecounseling as needed—for primary caregivers and other family members.

#### The Components of the NYUCI

When they enroll, , caregivers receive a comprehensive assessment of their needs, strengths and resources, the support they receive and would like to receive from family members and friends, and their emotional and physical health. They then have six consultations over a four month period. First, they have an individual consultation with a trained counselor, to further explore their needs and encourage them to think about the family members they would like to include in the following sessions. There are then four consultations with family members selected by the caregiver. Then there is an individual session to discuss what has been achieved, and what issues still remain and how to potentially address them. A vital component of the intervention is that counselors continue to provide what we call ad hoc counseling, which is consultation and support for caregivers and their families for as long as needed usually on the telephone or by email. Thus, counselors are available to help caregivers and their families deal with crises and with the changing nature of the patient's symptoms, to provide information and referrals for additional help, and help them understand and manage their reactions to the patient's behavior. Caregivers are also encouraged to join support groups that met regularly, as an additional source of ongoing information and support from their peers. The NYUCI received the first global award for psychosocial interventions from Alzheimer's Disease International/Foundation Mederic Alzheimer.

#### The Initial Study of the NYUCI

The NYUCI was first evaluated in a randomized controlled trial, which began in 1987 and lasted for more than 20 years, with funding from the National Institute of Mental Health and the National Institute on Aging (NIA). More than 400 husbands and wives of patients with Alzheimer's disease enrolled in the original study over a 10 year period, beginning in 1987. Some stayed in the study for as long as 18 years. The exceptionally long duration of the study made it possible for us to assess both the short and the long term effects of the intervention. The study was a randomized controlled trial, in which participants either received the NYUCI, or the usual care available to caregivers at NYU at the time.

#### Evidence of Benefits

The beneficial effects of the NYUCI have been well documented in peer-reviewed journals. The initial 20-year randomized controlled trial demonstrated that the NYUCI had long lasting benefits; caregivers were more satisfied with the support they received from family and friends<sup>1</sup>, experienced fewer symptom of depression<sup>2</sup>, were less reactive to dementia-related behaviors<sup>3</sup> and

were physically healthier than those who received usual care<sup>4</sup>. As a result, caregivers who received the NYUCI were able to keep the person with dementia at home for an average of a year and a half longer than those who received usual services<sup>5</sup>. These benefits were largely achieved through improving social support – the number of people to whom the caregiver felt close, and the caregiver’s satisfaction with emotional support and with assistance from family and friends<sup>6</sup>. Many additional randomized controlled trials and successful community implementations of the NYUCI in the United States and abroad, in England, Israel, and Australia have achieved similar results.

#### **The Benefit of the NYUCI for Caregivers of People Receiving a Drug for Dementia**

In the Three Country Study (US, UK and Australia), all participants with dementia received donepezil, one of the drugs that are currently available to mitigate some of the symptoms of dementia, while half the caregivers in each country received the NYUCI. We demonstrated that the caregivers who received the NYUCI became less depressed over the two year period in which they participated in the study.<sup>7</sup> This suggests the potential greater power of a combination of drug plus psychosocial intervention for maximum positive effect.

#### **An Example of a Community Implementation of the NYUCI**

Evidence of the effectiveness of the NYUCI led the Administration on Aging to fund translations of the NYUCI in six states—Minnesota, Florida, Georgia, California, Wisconsin, and Utah—through the Alzheimer’s Disease Supportive Services Program. Minnesota was the earliest, and the longest-running, implementation and included 228 caregivers. The implementation of the NYUCI in Minnesota was associated with improved outcomes in multiple key domains for caregivers of people with dementia that have critical clinical and public health implications. Consistent with the original study of the NYUCI, assessments showed decreased depression and distress among caregivers. Participating in a greater number of caregiver counseling sessions was also associated with longer time to nursing home placement for the person with dementia. Given the challenges faced in the community setting, web-based training for providers and video-conferencing for caregivers may be a cost-effective way to realize the maximum benefits of the intervention for vulnerable adults with dementia and their families.<sup>8</sup>

#### **The NYUCI in Israel**

A recently completed randomized controlled trial in Israel was the first to confirm the effectiveness of the NYUCI in a non-English speaking country, especially its long-term effects in reducing depression. As a consequence of the study’s positive results the NYUCI is now being implemented by many municipalities across Israel.

#### **The Cost Savings**

The potential cost savings from keeping people with dementia out of expensive institutional care for a year and a half are substantial. A model of the economic impact of the NYUCI estimated that the state of Minnesota (with a population of only 5.5 million) could save as much as \$996,000,000 in direct healthcare costs in 15 years if all caregivers for those with dementia participated, solely due to lower rates of institutionalization.<sup>9</sup> Potential direct cost savings to Medicaid were also substantial.<sup>10</sup> By improving the physical and emotional well-being of caregivers, the NYUCI undoubtedly achieves additional healthcare cost savings.

#### Issues in Expansion to Developing Countries and Potential Solutions

- Not every health professional has access to telemedicine capabilities for training in providing the NYUCI, but some will and can transmit the information they receive to others. Furthermore, the content of the training can be put on DVDs, which could be distributed to those who do not have internet access.
- Many people in developing countries are poor, and many of them work at home, which makes it difficult to provide care for a person with Alzheimer's disease at home. Others leave the person with dementia alone at home in order to go to work. There are very few, if any, institutions to provide patient care outside the home. A program of training for home care workers could be developed in tandem with training of professionals to provide the NYUCI. Thus paid help (which could be other relatives) could supplement the efforts of the primary caregiver. This could provide jobs as well as help to meet caregivers' needs.
- Traditional healers provide ongoing health care in many in rural areas using "home remedies," and are respected by their clients. Unless they are made part of the process of disseminating and providing the intervention, they may interfere and oppose new treatment strategies such as the NYUCI. They should be given the opportunity to learn about dementia and its effects on caregivers, and about the potential effectiveness of interventions like the NYUCI. Perhaps they should also be trained to provide the intervention. Traditional healers in Africa have a continental association that could be worked with on this.

#### Vision for International Partnerships to Make the NYUCI Widely Available

International availability of the NYUCI will have a global impact on the cost and care of people affected by Alzheimer's disease, helping families with the proven benefits of counseling and support. We have developed and tested an online NYUCI training and certification program for professionals that can be translated into any language. The online training in providing the NYUCI in person and via video teleconferencing can further be embedded, in whole or in part, in educational courses to make this effective psychosocial intervention culturally relevant, scalable and widely available. The NYUCI has been implemented by mental health providers such as social workers, nurses and psychologists. We recognize the importance of the context of caregiving, health care policy and service delivery and therefore would want to partner with stakeholders in developing a linguistically and culturally specific training program based upon local needs. Our 30 years of experience in providing, studying and creating training materials for the NYUCI has given us unique expertise in how to operationalize its essential core concepts and yet remain flexible to specific culturally appropriate realities in each setting.

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Mr. SMITH. Thank you, Dr. Mittelman. That is so encouraging, and thank you for your leadership and for providing this subcommittee with those insights.

I would like to put that article, if you would. We could find it and make it a part of the record because that would——

Ms. MITTELMAN. The Health Affairs article?

Mr. SMITH. Yes.

Ms. MITTELMAN. Okay. Yes, I have the list—there is a list in my testimony of all the articles but I am happy to send it to you.

Mr. SMITH. Great. Thank you. We will look it up and download it and put it in. Thank you.

Dr. Mohs.

**STATEMENT OF RICHARD MOHS, PH.D., CHIEF SCIENTIFIC OFFICER, GLOBAL ALZHEIMER'S PLATFORM FOUNDATION**

Mr. MOHS. Thank you, Chairman Smith. Thank you for inviting me. It's a real pleasure especially to follow Dr. Mittelman.

Most of my career has been devoted to trying to develop new medicines for Alzheimer's disease and I wish I could report that we had been more successful up to now.

But I can tell you what we've been trying to do and give you some thoughts about how we could maybe make that happen faster. But medicine alone is not the answer and so the programs that Dr. Mittelman and people like her are developing are going to be an integral part of the management program for dementia forever, essentially.

So the Global Alzheimer's Platform Foundation for which I now work is a not for profit organization, was founded by patient advocates to help speed the completion of high-quality clinical trials of potential new therapies for treating and preventing Alzheimer's disease.

It is the belief of GAP's founders, primarily George and Trish Vradenburg, along with John Dwyer, that only through rapid and rigorous testing of potential new treatments we will be—will we be able to make progress in alleviating the suffering caused by Alzheimer's disease.

The foundation has worked with academic investigators, government agencies, pharmaceutical companies, and other organizations similar to GAP outside the United States to develop networks of clinical trial sites that conduct—that can conduct studies quickly and with high quality.

GAP has found eager partners for our efforts in the European Union where there is something called the EPAD Network for the European Prodromal Alzheimer's Disease network, and Japan has a JPAD network, Australia has an APAD network, and we have partnerships developing in other regions around the globe.

Before joining GAP, I was for 14 years, as was mentioned, at Eli Lilly and Company where I was responsible for clinical testing of several potential new medicines for Alzheimer's disease including two that reach large global late phase studies.

Before Lilly, of course, I had an academic career in New York at Mount Sinai School of Medicine where we also did smaller scale studies.

Both of the compounds at Lilly that reached late phase testing were very promising scientifically. They actually did address some aspects of what is called the amyloid cascade hypothesis. But neither showed sufficient efficacy to enable registration as actual medicines for prescription.

The four-phase three trials that we did—there is usually two phase three trials for each new potential medicine—included a total of 4,694 patients with mild to moderate Alzheimer’s disease and these were conducted in 31 countries simultaneously.

Approximately 40 percent of those seen were seen at clinical sites in North America, 21 percent at sites in western Europe, 10 percent at sites in Japan, 9 percent at sites in Mexico and South America, 8 percent at sites in eastern Europe including Russia, 7 percent at Asian countries outside of Japan, and 5 percent in South Africa and Australia.

From these experiences with GAP and Lilly and a lot of years trying to develop new medicines, I’d like to share the following observations about the global burden of disease and give you some thoughts about how I think the process of medicine development might be made a little better.

First of all, in all the countries where GAP and Lilly have worked we found a high degree of interest in cooperation from clinicians, health authorities, regulators, patients, and families.

It is not difficult if you go into any of these countries to find people who are concerned about Alzheimer’s disease and who are eager to contribute in some way to try and develop a treatment. It is just a matter of trying to show them what it is they can do.

I would say that in spite of their limited efficacy, the currently approved medicines for Alzheimer’s disease are pretty widely used globally.

We were, of course, testing our therapies as add-on to standard of care—standard of care, which in most countries did include the already approved medicines, even though they have limited efficacy, and what we found was that in North America, western Europe, and Japan over 90 percent of all the study patients that we found who had a diagnosis of Alzheimer’s disease were already receiving an AD medication.

But in every country where we went it was over 70 percent. I don’t say that this is typical of everybody in that country because there are a lot of undiagnosed people. But they are available and they are used.

It was interesting relative to Dr. Mittelman’s presentation that the primary care givers assisting patients with AD as they navigated through the clinical trials process varied by region.

That is required because these people have some impairment that every study participant has to have a care giver or somebody who comes with them to participate in the study.

In North America, western Europe, South Africa, Australia, and Japan, it was usually primary care givers were spouses—about 70 percent in all those regions—while in the other regions—eastern Europe, other Asian countries, and Mexico/South America, the primary care givers were much more likely to be adult children or some other neighbor or person involved with the patient.



Now I move on to some issues and I think it's clear from what we heard earlier from the first panel we have learned a lot about Alzheimer's disease. There are a lot of opportunities, but this is a tough nut to crack, scientifically.

I have spent 40 years at it and there are a lot of smart people out there working at it very hard every day. But it's proved to be hard. So I'd like to just give you a couple observations about how the system I think could be a little bit better.

I think developing drug candidate molecules for clinical testing based on new biological findings about AD could be faster. Basically, when you find some new bit of biology, the therapeutic implications are not always obvious and it takes somebody who knows about what a medicine has to look like to make that translation.

I think policies that facilitate communication and collaboration of academic scientists with those in the biopharmaceutical industry could be helpful to enable more rapid discovery of high-quality clinical candidate molecules accompanied by the biomarkers and other kinds of technology that's necessary to do clinical testing.

If you just take the history of our drugs to date, the cholinergic deficiency in Alzheimer's disease was found in 1976.

The first cholinergic therapy was not approved until 20 years later and that was a well-known area of biology. What we know about A beta or amyloid, the structure of that protein was originally discovered in 1986. We still do not have an A beta-related therapy, although we have tried but it's a tough nut.

I think also the conduct of clinical trials could be faster. Streamlining processes of study review, contracting with sites, review by ethics committees, and site certification could reduce time to completing clinical testing.

It is often a bureaucratic nightmare to get these studies up and running. Granted, this is a human endeavor that will always have some human elements in it. But I think some of these are partly manmade problems.

Many current clinical trials are designed for patients who are not yet demented but have subtle clinical signs or biomarker evidence that they are at risk for AD. This is a lot of the current work that's going on on either primary or secondary prevention.

The problem is those people are not diagnosed in the current clinical care environment. We have heard that earlier. Such patients are not regularly identified in clinical practice and are very difficult to find for clinical trials.

So if you go out to find them, the epidemiology tells me there is lots of them out there. We just can't find them readily for trials, and I think that policies that would encourage early diagnosis of at-risk patients would speed the completion of trials as well as provide drug benefit to patients.

So those are my observations. Thank you very much for your attention.

[The prepared statement of Mr. Mohs follows:]

**Name:** Richard C. Mohs, Ph.D.  
**Title:** Chief Science Officer  
**Organization:** Global Alzheimer's Platform Foundation  
**Committee:** Committee on Foreign Affairs  
**Subcommittee:** Africa, Global Health, Global Human Rights, and International Organizations  
**Date:** November 29, 2017  
**Hearing:** A Global Update on Alzheimer's Disease

Thank you to the subcommittee for inviting me. I am Richard Mohs, Chief Science Officer for the Global Alzheimer's Platform (GAP) Foundation a not-for-profit organization founded by patient advocates to help speed the completion of high quality clinical trials of potential new therapies for treating and preventing Alzheimer's disease. It is the belief of our founders, primarily George and Trish Vradenburg along with John Dwyer that only thru rapid and rigorous testing of potential new treatments will we be able to make progress in alleviating the suffering caused by Alzheimer's disease. The foundation has worked with academic investigators, government agencies, pharmaceutical companies and, very importantly, other similar groups outside the United States, to develop networks of clinical trial sites that can conduct studies quickly and with high quality. GAP has found eager partners for our efforts in the European Union with its EPAD network, Japan with it's JPAD Network, Australia with APAD and we have partnerships developing in other regions of the globe.

Before joining GAP I was, for 14 years, at Eli Lilly and Company where, for 5 years I led the Global Alzheimer's Development team. In that role I was responsible for clinical testing of two potential new medicines for AD, semagacestat and solanezumab. While both compounds were very promising scientifically, neither showed sufficient efficacy in global phase 3 studies to enable registration. Conducting the trials, however, gave me considerable insight into the impact AD has around the globe and the ways patients, families, and health care systems cope with the epidemic. The four phase 3 clinical trials for these compounds included a total of 4,694 patients with mild to moderate Alzheimer's disease from 31 countries. Of the total approximately 40% were seen at clinical sites in North America, 21% at sites in Western Europe, 10% at sites in Japan, 9% at sites in Mexico and South America, 8% at sites in Eastern Europe including Russia, 7% in Asian countries outside of Japan, and 5% in South Africa and Australia. From these experiences with the GAP Foundation and Eli Lilly and Company I'd like to share the following observations about the global burden of this disease and the prospects for developing new treatments.

1. In all of the countries and regions where GAP and Lilly have worked we have found a high degree of interest and cooperation from clinicians, health authorities, regulators, patients and families It was not difficult anywhere to

find people concerned about the disease and eager to work toward better treatments.

2. The clinical presentation and care burden of patients is quite similar across geographies, countries and health systems. Memory problems, difficulty in communication and progressively greater need for assistance in activities of daily living are found in all patients regardless of country.
3. In spite of their limited efficacy, the currently approved medicines for AD are widely used and are an integral part of medical management. The highest use is in North America, Western Europe and Japan where over 90% of enrolled patients with AD were receiving one or more medications for AD, but over 70% of study patients with AD in every region were taking at least one AD medicine.
4. The primary caregivers for patients with AD varied by region. Patients with AD enrolled in clinical trials are required to have a caregiver or study partner who knows them well and will assist in monitoring adherence to medication along with the patient's symptoms, daily functioning, and changes in health status. In North America, Western Europe, South Africa/Australia and Japan approximately 70% of primary caregivers were spouses while in other regions primary caregivers were more likely to be adult children or other study partner. These differences may be relevant to the integration of behavior management plans with medication.
5. There is a need to improve the efficiency of the drug discovery and development process. Novel ideas about how to treat and prevent AD are slow to get from basic science laboratories to clinical testing. Policies that facilitate communication and collaboration of academic scientists with those in the biopharmaceutical industry are necessary to enable rapid discovery of high quality clinical candidate molecules accompanied by biomarkers and other tools needed for clinical testing.
6. The conduct of clinical trials could be faster. The process of starting clinical studies, identifying clinical trial sites and enrolling patients is slower than it needs to be if we are to test all of the promising compounds available. Streamlining processes of study review, contracting with sites, review by ethics committees and site certification could reduce time to complete clinical testing.
7. There is a need for more global collaboration on the discovery, development and testing of potential new treatments for Alzheimer's disease. Active participation by US agencies with international groups such as the World Health Organization (WHO), Organization for Economic Cooperation and Development (OECD) and the World Development Council (WDC) is needed to insure faster development and more efficient use of resources globally to meet this global challenge.
8. There is a growing discrepancy between the way patients with AD are diagnosed in ordinary clinical practice and the way they are enrolled in clinical trials. In clinical practice patients are usually diagnosed fairly late in disease when symptoms are unequivocal and cannot be ignored. Many clinical trials are now designed to test prevention therapies in patients who

are at high risk because of biomarkers but with few or no disease symptoms. Finding appropriate patients for these prevention studies is very difficult.

9. To develop truly effective ways to treat, manage and delay the onset of AD will require many studies of potential medicines, behavioral interventions, patient assistance technologies and combination approaches. These studies should be done quickly, with rigorous methodology and with results communicated quickly to investigators, patients and clinicians so that we can, collectively develop and disseminate the best treatment approaches.

Thank you very much for your attention.

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Mr. SMITH. Thank you so much for your testimony and, again, for your leadership as well. Thank you.

Mr. Splaine.

**STATEMENT OF MR. MICHAEL SPLAINE, PRINCIPAL, SPLAINE CONSULTING**

Mr. SPLAINE. Good to see you. Thanks for the opportunity to appear before the subcommittee today. I've been working with people with Alzheimer's and their families since 1986.

Currently, I am a consultant and since 2011 our consultancy has served as the policy and advocacy advisor to Alzheimer's Disease International.

ADI is the global umbrella for over 90 national Alzheimer's Associations including the U.S. Alzheimer's Association.

Of historical note—and I am a little bit of a historian because I've been around—this whole panel has been around—it is worth noting that the U.S. Alzheimer's Association and ADI share common founders.

In fact, 4 years after the Alzheimer's Association was established by Jerome Stone and others, they established Alzheimer's Disease International. So some sense of this being a global issue was there even in the very beginning in the early 1980s.

Our current work with Alzheimer's Disease International has put my associate, Kate Gordon, and myself in the middle of a burst of international energy and work streams that are moving on the issue of dementia and moving it closer to a public health priority that experts believe it needs to be.

My plan with limited time is to hit the high points on what I think are key developments that have not been covered by other witnesses.

The facts are stark, and in the introduction to the hearing, Mr. Smith kindly cited the facts that I have on record as well.

One possible fact that was not cited by the chairman that might be of special interest to this subcommittee is the publication of a report on Alzheimer's disease in sub-Saharan Africa that is less than 6 weeks old. It was published by ADI.

It estimates that there are 2.13 million persons with dementia in that region, a number that is expected to roughly double every 20 years.

Sometimes there's a belief that Alzheimer's can't and dementia issues can't really be truly global. But with the publication of that report and the facts therein, I think that has been put to bed.

Well, let me review some key global developments. First of all—and there's a graphic in my testimony that kind of tries to demonstrate this—dementia is increasingly understood to be a life course disease by policy makers, not merely a disease of older persons, not merely a condition of complete and utter disability, although the public perception that a person with Alzheimer's disease must necessarily be older and quite disabled and the latter stages of the disease persists.

This opportunity to diagnose early and having early stage persons involved in many facets of the work is putting a different face on what it means to live with dementia.

Even further to the left in that curve that you have in your packet is a representation of what the Lancet Commission and others have recently found that there is action to be taken by public health authorities on modifiable risk factors for dementia.

Keep in mind that population health personal results may vary. We are talking about the health of the entire population. But it's pretty clear it can be summarized simply as what's good for your heart is good for your brain—is actionable today by public health authorities and in fact there are many examples of that going on around the world.

A second important trend or a second important global development is that we continue to have detection and diagnosis as a stubborn problem everywhere.

Although cited earlier, let me just repeat what you cited earlier, which is that without diagnosis there can't be treatment care and organized support or the opportunity to participate in research.

I think some of our gap in research is the diagnostic gap and I think this gap should also be of interest to any health system as persons with impaired thinking and another chronic disease are expensive because thinking is important to navigating complex health decisions and treatment regimens that are only frequently seen in deep crisis.

Third, I want to mention and in fact already mentioned before the committee that in the Americas in 2015, PAHO/OPS adopted a regional dementia action plan and in 2017 just a few months ago, the World Health Assembly adopted a global dementia aging plan.

Taking a right spaced approach, these action plans call on and will provide technical support for national government plans and policies over the next 5 years to take advantage of our newer understandings of dementia and to plan nation by nation a response across the spectrum of the disease.

I note that 30 countries have published national plans and nearly 100 subnational governments, States, or regional governments have taken action.

But I will also note that in our view only one country has taken serious action on dementia without a strong civil society push. It is almost as if we have a three-legged stool where the advocacy as well as the knowledge of the issues and advocacy capacity are important to move forward.

On rights, another subject of great interest to this committee, let me note that persons with Alzheimer's disease are in some cases using the Convention on Rights of Persons with Disabilities as a platform for action on care and support.

Dementia has been a special issue in the Organization for American States Regional Convention on the rights of older persons, now out for ratification, and in a regional declaration on older person's rights by the African Union.

Dementia and its consequences has also been a major topic in the ongoing work of the U.N. Open Ended Working Group on the rights of older persons.

Last, and I'll leave the rest to my written testimony, a broader community of interest in dementia as a social issue is emerging.

It is taking many forms such as the organizing of nearly 20,000 young professionals in Indonesia around the issue of Alzheimer's

who don't have family experience, as well as issues being an agenda item at the World Economic Forum in Davos or this week at the Salzburg Global Seminar

Also in the wake of the Japanese tsunamis we saw for the first time disaster authorities paying attention to the problem of Alzheimer's disease.

Multiple international organizations helped raise awareness during Alzheimer's Awareness Month, and even Pope Francis made a major address on World Alzheimer's Day last fall.

It is fair to mention that myriad scientific meetings and cooperation are increasingly becoming the norm. The world's largest scientific meeting on Alzheimer's disease is hosted and will be hosted in our country by the Alzheimer's Association in Chicago in July.

It will be followed this year immediately by the Annual Conference of Alzheimer's Disease International, truly a global gathering.

As I was preparing this testimony, my last thought is faces come to mind—faces of families such as my sisters, my Aunt Lee, my Aunt Marilyn—all Alzheimer's care givers—my mother-in-law, but also faces of people like Lucien and Lee Yu and even two women from Yemen who started an Alzheimer's Association—its fate unknown at this moment—in Yemen.

I also think about researchers in Poland, in the Czech Republic, all over eastern Europe that I've met and enjoyed their company. There truly is a global view in my head.

I also can't not mention that I am here today principally because 13½ years ago my brother gave me a kidney. So thank you again, Dan.

I am done.

[The prepared statement of Mr. Splaine follows:]

Statement of Michael Splaine

Owner and Principal, Splaine Consulting, Policy Advisor Alzheimer's Disease International

**COMMITTEE ON FOREIGN AFFAIRS**

**Subcommittee on Africa, Global Health, Global Human Rights and International Organizations**

**November 29, 2017**

**"A Global Update on Alzheimer's Disease"**

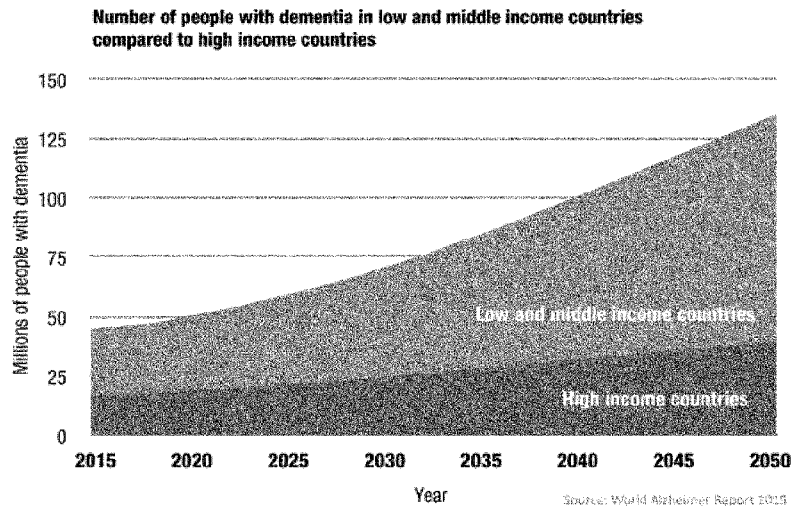
Thank you for the opportunity to appear before the subcommittee today and offer a global view update on dementia. I have been working with persons with Alzheimer's disease and related disorders and their families since 1986. Since 2011 our consultancy has served as policy and advocacy advisers to Alzheimer's Disease International ([www.alz.co.uk](http://www.alz.co.uk)) the umbrella organization of over 90 national Alzheimer associations around the world, including the US Alzheimer's Association ([www.alz.org](http://www.alz.org)).

It is worth noting that the US Association and ADI share a common founder--the late Jerome Stone--thus there was some sense of dementia being more than a domestic issue was present in the early 1980's even as we saw initial organizing around the problem.

Our work with ADI has put my associate Kate Gordon and I in the middle of a burst of international energy and work streams that are moving the issue of dementia closer to the public health priority experts believe it needs to be. My plan with my limited time today is first review a few key facts and then highlight on key developments that other witnesses have not covered.

**The facts are stark.** Globally 47.5 million people live with some form of irreversible dementia, (<https://www.alz.co.uk/research/world-report-2015>) a number that will grow to 130 million by 2050 with most of the new cases and burden of disease falling on lower and middle income countries. Global cost of AD is estimated at just above 1% of global GDP (\$818 billion USD)



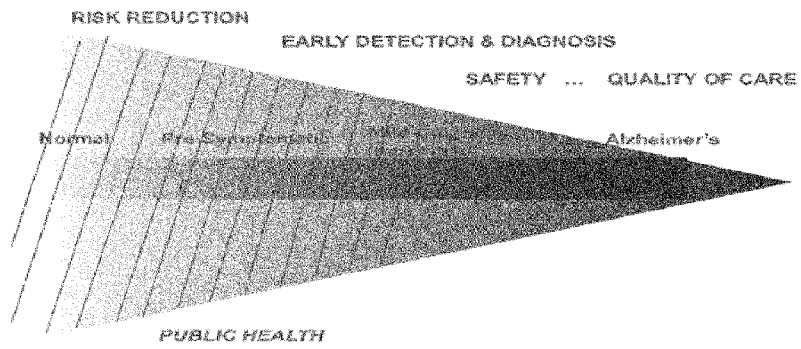


Of possible special interest to this subcommittee has been the publication of a report on AD in Sub Saharan Africa (<https://www.alz.co.uk/research/dementia-sub-saharan-africa.pdf>) which estimates 2.13 million persons with dementia now live in the region, a number that is expected to roughly double every 20 years.

Let me now review seven key global developments.

1. **Dementia is increasingly understood to be a life course disease by key policy-makers, not merely a disease of older persons.** Population aging is driving the numbers but slowly the general public perception of dementia that it must necessarily be an older person quite disabled in the latter stages of the disease is changing, as some persons diagnosed early in the disease have put a different face on what it means to live with dementia. Perceptions are also changing in countries rich in scientific resources we can image changes in the brain before symptoms develop, and anywhere in the world we can begin to use the tools of public health to reduce population risk of dementia in late life.

True, awareness raising activities have a more complicated story to tell with a 30 year disease process to describe as illustrated below, and everywhere in the world there is constant messaging needed that dementia is not a normal part of aging, but the life course view is taking hold increasingly in policy circles.



2. **Detection and diagnosis are a stubborn problem everywhere.** Research shows that most people currently living with dementia have not received a formal diagnosis. In high income countries, only 20-50% of dementia cases are recognized and documented in primary care. This 'treatment gap' is certainly much greater in low and middle income countries. Without a **diagnosis**, there can't be treatment, care and organized support or opportunity to volunteer for clinical research. This gap should be of interest to health systems as persons with impaired thinking and other chronic disease are expensive and have difficult lives navigating complex health decisions and treatment regimens and are frequently only seen in deep crisis.

United States figures suggest that only about 50% get a formal diagnosis, and more troubling is the fact that as many as 30% of persons with a diagnosis in their medical record have not been informed of their diagnosis.

3. **In the Americas, in 2015 PAHO/OPS adopted a regional dementia action plan and in 2017 the World Health Assembly adopted a global dementia action plan.**

Taking a right based approach, these action plans call on and will provide technical support for national government plans and policies over the next 5 years to take advantage of this newer understanding of dementia and to plan response across the spectrum of disease.

30 countries have published national plans, but I would note that only one country has taken serious action on dementia without a strong civil society push. (with its deeper and more personal knowledge of the issues and its advocacy capacity.)

On rights let me note that persons with ADRD are in some cases using the Convention on Rights of Persons with Disabilities as a platform for action on care and support and that dementia has been a special issue in the OAS regional convention on the Rights of Older Persons (now out for ratification) a regional declaration on older persons rights by the African Union and a major topic in the ongoing work of the UN Open Ended Working Group on Aging and its special rapporteur.

4. **A broader community of interest in dementia as a social issue is emerging.**

This is taking many forms, such as social media awareness raising and organizing by young students and workers in Indonesia, myriad dementia friendly community programs unique to place and culture or dementia being an agenda item at the World Economic Forum in Davos or as it is this week at the Salzburg Global Seminar. In the wake of the Japanese tsunamis, natural disaster authorities have begun better planning for persons with dementia in those circumstances. Multiple international NGO's help raise awareness during World Alzheimer's Month (<https://www.worldalzmonth.org>) Even Pope Francis made a major address on World Alzheimer's Day!

**5. Dementia is gaining recognition in the non-communicable disease movement.**

Beginning with the UN Political Summit and Declaration on NCD's in 2011 through the present moment, dementia issues have been raised in two ways—from a public health perspective dealing with shared risk factors for NCD's in late life with brain health messaging integrated into a smoking cessation campaign and from the perspective of the challenges of self-managing chronic disease when one is seriously cognitively impaired. It is important to note that this is promising but that the community has yet to see the declaration intent on dementia implemented in NCD plans generally.

**6. (Some) political leadership has embraced action on dementia (some of the time).**

In December 2013 the G-8 (now G-7) held a major summit <https://www.gov.uk/government/publications/g8-dementia-summit-agreement> and then convened several follow on high level meetings and activities that set in motion action to increase commitments to government backed research funding and greater international cooperation on science and policy, including care policy. Of special note is the stimulus to the Organization for Economic Co-operation and Development (OECD) to consider what changes could be made to promote and accelerate discovery and research **and** the transformation of innovative and efficient care and services. The subsequent formation of a World Dementia Council <https://worlddementiacouncil.org/> which has been an advocate for innovative and global finance models, integrated drug development and the encouragement of open science collaborative research, including big data.

**7. Myriad strong scientific meetings and cooperation are now the norm.**

The world's largest scientific meeting on Alzheimer's is the Alzheimer's Association International Conference (<https://www.alz.org/aaic/>) to be held this July in Chicago, followed immediately by the annual conference of Alzheimer's Disease International (<https://www.alz.co.uk/ADI-conference>) Dozens of smaller regional and specialty meetings are harnessing scientific interest, opening new theories of the disease and supporting thousands of active scientists, especially younger professionals.

Mr. SMITH. Mr. Splaine, thank you very much. Thank you to your brother.

Let me just ask a couple of questions. Again, you are leaders. You have made all the difference in the world and I think your point, Mr. Splaine, about the importance of advocacy, when people have a message that is well-founded and they back it up with empirical data it gets action on Capitol Hill.

As dysfunctional as people think Congress is these days, we are getting some very important things done, and I mentioned earlier a tripling of the NIH funding for Alzheimer's and I do believe we will get to there with the 2018 HHS appropriations bill.

It is no small achievement. I introduced the Ronald Reagan Breakthrough Act for years and working alongside of you and others, and we couldn't get even a markup, and now we are at the point where the money is actually flowing and we are talking about a tripling—I should underscore a tripling—since 2015.

So that burst that you talked about needs to become a sustainable surge for the sake of the patients, the families, the care givers and so thank you for your advocacy, all three of you, and others who have been instrumental in making all the difference.

I think we don't focus enough on how health systems could implode over the next 30 years or so. I mean, care givers deflect a lot of those costs that would be borne, and Dr. Mittelman, you know better than anyone with your work so often it's the spouse or it's a daughter or a daughter-in-law that steps up to the plate to take care of the Alzheimer's patient.

I hope you are going to be able to answer this—whether or not the WHO new agenda item, the surge that they are making—the new seven point, which includes in its seven points providing support for care makers, those living with dementia care givers, and it's one of their seven points.

Hopefully, they are listening to you and the breakthrough and landmark work you've done so that they don't have to reinvent the wheel.

So—yes, please. Could you put on your mic, too?

Ms. MITTELMAN. I neglected to mention earlier that because we were so successful in these randomized control trials of which there had been more than one, we were being asked to provide training for providers, mostly social workers but also nurses and people in allied professions, and we were going all around the world to provide this training, as far as Israel, France, Australia.

Sometimes it was fun but eventually it got to be too much so we got a grant from the NIH to develop online training. So now people can receive training on how to provide the intervention online when they wish.

Only in English and in Australian at the moment but—American English and Australian—but easily—one could easily imagine how this training, which includes videos of both role plays and real cases of family care givers being given the counseling, could be incredibly valuable, even if people didn't do the actual NYU care giver intervention as we developed it, to have the training and to understand how to work with families to help them to support the primary care giver.

Mr. SMITH. How hard is it to access? I mean, can you give the web address or—

Ms. MITTELMAN. Well, at the moment it has a cost because it was developed with an SBIR grant.

Mr. SMITH. Okay.

Ms. MITTELMAN. But it is available and I'd be delighted to talk to you about it more online or offline. But in addition to that, we encountered another issue that we thought was worth developing a solution for, which is the that very often families are dispersed and there could be a primary care giver in Miami, Florida and the daughter in New York and the daughter can't participate—couldn't participate in personal counseling or—and felt left out of the care. So we developed video—a video conferencing version of our intervention, which we are doing a randomized control trial of right now.

But I think of that as a potential for people who live in other—who have family members who live in other countries. Perhaps the adult child is living in New York and the parents are living in China or wherever.

One could use video conferencing potentially in countries where—and for people who have access to the internet to bring families together and to provide them and the primary care giver with the kind of support that they need. So—

Mr. SMITH. Is WHO accessing your work?

Ms. MITTELMAN. Not that I know of but, I mean—

Mr. SPLAINE. Well, that—I know a little bit about that work stream at WHO and I think they are not just looking at made in America programs. I mean, they are the global health organization and there are many to the level that we accept in the United States—random clinical trial, peer-reviewed journal, evidence-based programs that were not invented in the United States.

So I think the task of the very small staff working on dementia at the World Health Organization—did I say that clearly enough?

Mr. SMITH. How small?

Mr. SPLAINE. That—four, six. I mean, a place where this—where the United States Government could, frankly, make a real difference, with a couple of secondments of key people from the United States to either PAHO or to WHO, which is minuscule dollars compared to what kind of rich resources we have could make a huge difference.

But they are compiling and evaluating and not reinventing the wheel. But the wheel goes both ways. One of the things we get asked all the time by ADI—representing ADI is can you help us access evidence-based Portuguese language, Spanish language programs that were—or Chinese language programs that were invented and validated in other cultures because that is who we are dealing with as America ages and changes demographically.

So I think, you know, it's bidirectional. It's multi directional. I also think that this—you mentioned health system.

Let me just say the population aging is global and it's really an opportunity for, from a noncommunicable disease as well as an aging point of view, it may be a real opportunity for this committee to insist on or take its own top to bottom look at how we make investments as a government, as a people, in global health and

take—start to factor in not just the disease by disease approach but really maybe this whole theme of noncommunicable diseases, going back again to my testimony about the linkages between risk factors between brain health and other health. It might be a real opportunity for the committee.

Mr. SMITH. I appreciate that. And the idea of secunding U.S. personnel, that is a great idea. We will follow up with you on that one.

Mr. SPLAINE. Thank you.

Mr. SMITH. And please take a look again at our global brain initiative bill because the idea is that infectious diseases are horrifyingly prevalent in Africa. But, frankly, with Bush's PEPFAR program, which is about \$5 billion a year, mother to child transmission ARVs—the pandemic—certainly have been mitigated, and other diseases such as malaria are being attacked as they should be. But we leave out brain health, except for diplomacy at WHO and elsewhere.

You mentioned African countries, \$2.1 million—has the AU—the African Union—been responsive at all, as far as you know?

Mr. SPLAINE. From a rights perspective, the African Union is one of only two regions in the world that actually has an explicit rights policy for older persons and Alzheimer's has been part of that story because, unfortunately, in some pockets in Africa, people with Alzheimer's disease are perceived as witches, demonic, and governments like the Government of Ghana literally have disrupted these witch camps that were developed as a way of stashing people who are, clearly disabled from severe cognitive issues from Alzheimer's disease or other dementia.

So I think that there is some visibility. You know, they've got a lot on their plate. But I think population aging is becoming better known.

There have been two regional meetings inside of a year of people interested in doing more about Alzheimer's disease on the African continent that have included African Union representatives.

There is also country by country but also as a region—I hesitate to say but I think it's one of the most active regions in organizing around noncommunicable diseases by the Noncommunicable Disease Alliance and other interested parties because that is becoming part of the reality of health in the region as well.

Mr. SMITH. Just two final questions. Let me ask, do you believe that we are on track to, by 2525, get a disease-modifying treatment or maybe even a cure?

Are other countries like Japan and China, the U.K., coming forward with sufficient moneys? Particularly on the research side to have that critical mass Manhattan Project type of focus?

Mr. MOHS. There is no doubt that in the countries that have a large number of older people, particularly Japan and certainly China and western Europe, you'll find a lot of money being devoted to Alzheimer's research.

So I don't think that that is the issue. I think there is a certain amount of discouragement that comes with lack of more tangible success.

But it would help if we have these existing international organizations like WHO and OECD and so forth actually make this a priority because it gives some credibility to these national organiza-

tions that are trying to do something about this to go ahead with international cooperation and the perception that this is really a high priority globally.

Ms. MITTELMAN. Can I make a comment?

Mr. SMITH. Yes, please.

Ms. MITTELMAN. Well, I think that when there are—when we are trying to find people to participate in clinical trials of new drugs, if we have psycho social interventions as well as we did in the three-country study, there may be more—these trials may seem more attractive to participants.

Mr. MOHS. I think that is quite true, and it's interesting that for a brain disease to not more fully recognize the interplay between psycho social and medical interventions is a little odd.

I mean, it's hard for me to imagine in cardiology that they would think that medicine without exercise and weight control is going to solve the problem.

But we just have to get an understanding that all these things have to work together and I think from a patient acceptability standpoint the psycho social interventions are much more tangible and immediate and provide a more immediate benefit for people who participate in these trials.

Mr. SMITH. And just the final question—I do have others that I would like to submit to you—the issue of brain imaging that we discussed in panel number one, you say there is a viable diagnostic tool, going forward, particularly for early onset?

Mr. MOHS. Well, we were involved in the development of some of those early amyloid imaging technologies when I was back in the pharmaceutical industry and I think it has assisted a lot in getting more biologically uniform people entering into clinical trials.

Its role in ordinary clinical practice in the absence of directly related therapies is much more limited. But there has been discussions about that.

But it's, clearly, a great advance to have a brain disease where you can actually see the pathology in life. That's something we have almost never had for any brain disease in the past.

Mr. SMITH. Mr. Garrett.

Mr. GARRETT. Thank you, Chairman Smith, and thank you, members of the panel. And my apologies—I was in another committee and we got here as quickly as I could.

I did not imagine that I would have the opportunity in the Foreign Affairs Committee to discuss Alzheimer's and so I am delighted that that opportunity has presented itself and I thank the chairman again.

Now, having said that, I will tell you that you probably didn't imagine the direction that I am about to go here. I think it's fair to say that a rising tide lifts all ships. I know that is a cliché and I would ask rhetorically, because I don't want to waste your time, whether or not we do medical research well here in the United States.

I think the answer is yes. Relative to the world, we do a pretty good job, right?

But the next rhetorical question would be, would the designation of a particular item as a Schedule One controlled substance stymie the ability of entities whether government or private to research



said Schedule One controlled substance as it related to medical uses.

And I think the answer—and if anybody disagrees with me you are welcome to—you are welcome to chime in. You can interrupt. But I think the answer has to be yes.

And so, obviously, some of you are probably miles ahead of me because I am a lawyer, not a doctor, which means you all are smarter.

But as I look through a list of medications derived from plants, I find medications that help with blood pressure, with malaria, with pain, with dysentery, anti-tumor agents, diuretics, anti-fungal, sedatives, anesthetics, muscle relaxants—watch me mispronounce—cholinesterase inhibitors, right. I mean, and when you look up medical plants you'll find a list that is literally in the hundreds.

So the question that I have for members of the panel is—and I am not arguing in the favor of any panacea or any overarching wonderful solution—but might we be well served to review in the United States our scheduling of cannabinoids, whether it's CBD oils extracted from hemp, to allow the research to be done?

Because as I look for studies that relate to CBD oil and Alzheimer's specifically I find a lot of them and they all come from the Netherlands and Australia and Great Britain, et cetera, and we have essentially tied our own hands behind our back with what I would argue is an archaic legal structure that denies the opportunity to find potential cures or at least aiding elements by virtue of the stigmatization of a particular plant.

So the question is, could we further potentially better outcomes and at least addressing symptoms if we were to free the circumstances that currently stymie the private sector and even public moneys from being used to research cannabinoids?

Mr. MOHS. I don't know that I can give you a complete answer to that questions. Couple of comments, though. You're quite correct that many current medicines are—were originally discovered as extracts from the natural world—from plants or someplace else—and that has been the case throughout the history of the development of medicines.

My own view, and I just speak from a couple of companies that I've worked with, yes, it would be a—certainly a consideration if a—if you were talking about trying to develop a scheduled substance as a new medicine. That means you got to do other studies, allowed use liability and potential harm.

But, you know, we used to have a saying—no side effect, no drug. So usually medicines have some unwanted effects along with the desired effects and the important part about any medicine development program is that you fully understand both of those so that in the end if the judgement is that their benefits outweigh the risks that at least that can be approved with an appropriate labeling of all the benefits and the risks and it's the nature of a development program that it should investigate both of those things.

But if your point is that it would be a—weigh kind of negatively on a company thinking about developing something where you have this whole other side path of trying to mitigate the risk, I think the answer is probably yes.

Mr. GARRETT. And there is an inherent cost, right, to that legal sort of—

Mr. MOHS. Sure. There is a cost—more studies, more time, more potential that you are going to find something. I mean, you don't want to start out with a—with a potential new medicine where you know right off the bat that it's got down sides. I mean, that is—

Mr. GARRETT. And there is no arguing, certainly, that there are down sides. But I think if I am correct—and, again, I am going to let each one of the members of the panel speak to this—that CBD oil, particularly hemp extracted, you don't get high. I mean, it's not even a side effect as it's administered therapeutically, right? I mean, that is—

Mr. MOHS. I think there are cannabinoid derivatives that actually do not make you high. That's correct.

Mr. GARRETT. Yes, sir. And certainly there are some that you could—that you could, right? I mean, I am not trying to tell one side of the story.

But anyway, I'll open the floor to either of you fine folks to just comment on whether or not it might be easier and cheaper and more cost effective to study potential positives if the scheduling regime in the United States were relaxed to allow more efficient and cheaper and more ready studying.

Ms. MITTELMAN. Oh, I actually think that one of the benefits of psycho social interventions is that they have absolutely no negative side effects. So I would go in the other direction.

If I were going to try to do things that were unusual I would try to figure out what nonpharmacologic interventions could have major impact.

For example, to go back to the chorus that we founded, nobody believed when I started it that people with dementia could learn new songs, and they are learning new songs.

So this is a medicine that has no potential side effects. In fact, we did a video of the original chorus and one of the caregivers said, "Forget about pills. Just give me this."

Now, imagine if singing could have a major impact on learning new songs—could have a major impact on neurologic function and we don't think about those kinds of interventions.

Mr. GARRETT. No, I think what you are saying is brilliant and I appreciate it. But I am an all-of-the-above kind of guy, and what might work well for one individual or entity might not work as well for another.

But what you are doing is commendable and I admire you. I simply submit that because one thing works doesn't mean another doesn't and I believe we have a regulatory scheme here that is draconian at best and—

Ms. MITTELMAN. I agree with you on that, but I think that what you are talking about is thinking out of the box.

Mr. GARRETT. Yes, ma'am. No, again, we are not arguing. We are agreeing.

Mr. Splaine, am I pronouncing it correctly?

Mr. SPLAINE. Well, I am not a doctor. Don't play one on television. So a couple of thoughts.

I wonder whether it's—you know, is it Schedule One or are there other things that prevent this kind of imaginative thinking about experimenting with these substances.

So a couple of thoughts on that. One is we do have a pretty strong not invented here ethos in the scientific community and I think that is made a little bit more challenged because there is a prevailing theory of Alzheimer's disease in the United States and in the United States science establishment that although respected in other countries they are investigating along different lines.

For example, Mr. Smith, I don't want to correct you except I will—I will add the Republic of Korea to your list of very engaged countries about Alzheimer's also from a research point of view.

Their drug mechanisms of action—remember, Alzheimer's has three parts. It has plaques, tangles, and inflammation. They are almost completely zeroed in on inflammation and it's something that is almost completely not ignored but it's not a mainstream in the United States.

It's attacking the amyloid. So I think that is just something to think about is the prevailing theory keeping this out of consideration rather than Schedule One.

Last, our language about Alzheimer's treatments is most unfortunate in that somewhere in the 1980s we started talking about disease-modifying drugs and mere symptomatic treatments and we have minimized social interventions.

We have minimized the drugs we have by calling them mere symptomatic treatments. I would submit what is insulin? A mere symptomatic treatment? Yes, but it also—I mean, what do people want when they live with a disease?

I can tell you first hand as somebody who has lived with disease, we want treatments that allow us to get on with our lives.

So I think sometimes the language and holding out for—this is why I get really uncomfortable about will we have a cure by 2025. We have this language we have developed in Alzheimer's about symptomatic treatment versus disease-modifying treatment and I think that too is a barrier to people thinking outside the box.

Mr. GARRETT. So let me—

Mr. SPLAINE. So I think it's those other things that are going on in the Alzheimer's scientific thinking, not so much that it's a Schedule One problem.

Mr. GARRETT. Well, let me—let me—at the indulgence of the chair very quickly—submit that while we search for a cure in the interim we should also be searching for treatments, right? That it's an all-of-the-above, not a—one or the other.

And so while we hope one day to move away from fossil fuels, in the interim we are burning oil as we develop wind and solar, right. I mean, it's getting from point A to point B.

But let me ask you this, and I am leading intentionally because I can here—would you not agree that Schedule One designation inhibits research and makes that more tedious and costly for those who might be interested in engaging in it? I was actually—

Mr. MOHS. I can't—

Mr. GARRETT. I was actually addressing that—

Mr. MOHS [continuing]. I have never had—I have never had any clinical candidate that I was responsible for impeding in its development by scheduling.

That doesn't mean somebody else might have and, honestly, in my time in the pharmaceutical industry most of our interactions with FDA were actually quite helpful. They were leaning forward.

Now, there may be some areas that I didn't get into where there is some adjustments that need to be made. But I will tell you, they were—they were actually quite forward thinking in their treatment about approval processes for Alzheimer's disease.

I think they knew quite well that it was a very bad disease and were willing to work with any sponsor that came to them with any reasonable proposal about how to develop a treatment.

Mr. GARRETT. But if you want to work with willow bark you don't need to get Federal Government permission to get the precursor.

If you want to work with quinine, you don't need to write—I mean, anyway, thank you for being here and, again, I am not suggesting this is a panacea, just that we should get out of our own way, and thank you all for thinking outside the proverbial box.

But, again, the tact to win this fight I think it's an all of the above and open minds and look at what works and what doesn't.

So thank you, Mr. Chairman.

Mr. SMITH. Thank you, Mr. Garrett.

I'll just conclude, and any comments you might want to make, any questions that went unasked please, if you could provide those answers or just speak to it.

The idea of a goal that we developed with the NAPA bill and also with the G7 and the WHO Assembly, isn't that it's—it's to sharpen the mind and to marshal resources, as you know.

That's why I've asked are we on the right path to either achieve it or come close? Even coming close will be an achievement.

I do—Dr. Richard Mohs, you make the point that to develop truly effective ways to treat, manage, and delay the onset of Alzheimer's disease will require many studies of potential medicines, behavioral interventions, patient assistive technologies, and the combination approaches.

We are doing that, right? Or are we lagging in any of those areas?

Mr. MOHS. We are—we are doing it. I think it could be—as I mentioned, I think it could be done a little faster. The scientific uncertainty is still great and so the only way to tackle that is to accumulate knowledge as fast as you can and that requires a lot of—

Mr. SMITH. Well, how many compounds are being tested as unique?

Mr. MOHS. I think the last we checked there were about 30 something in phase three and in the 60 range in phase two, and usually companies don't report earlier than that because it's so iffy back there that it's hardly worth reporting.

But there is a lot, and that doesn't even take into account all the little labs and so forth around the world. But on problems like this you need a lot of ideas.

You need a lot of studies to help resolve the uncertainty about those ideas and the communication from different laboratories to

each other so that they don't repeat and follow up on unpromising areas is very important.

Mr. SMITH. I want to thank you again for your leadership and for being here today and helping to inform this subcommittee and, by extension, the U.S. Congress.

And I thank you again. The hearing is adjourned.

[Whereupon, at 4:16 p.m., the subcommittee was adjourned.]



## A P P E N D I X

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MATERIAL SUBMITTED FOR THE RECORD

**SUBCOMMITTEE HEARING NOTICE  
COMMITTEE ON FOREIGN AFFAIRS  
U.S. HOUSE OF REPRESENTATIVES  
WASHINGTON, DC 20515-6128**

**Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations  
Christopher H. Smith (R-NJ), Chairman**

November 22, 2017

**TO: MEMBERS OF THE COMMITTEE ON FOREIGN AFFAIRS**

You are respectfully requested to attend an OPEN hearing of the Committee on Foreign Affairs, to be held by the Subcommittee Africa, Global Health, Global Human Rights, and International Organizations in Room 2172 of the Rayburn House Office Building (and available live on the Committee website at <http://www.ForeignAffairs.house.gov>):

**DATE:** Wednesday, November 29, 2017  
**TIME:** 2:00 p.m.  
**SUBJECT:** A Global Update on Alzheimer's Disease

**WITNESSES:** Panel I  
Marie Bernard, M.D.  
Deputy Director  
National Institute on Aging  
National Institutes of Health

Roger Glass, M.D.  
Director  
Fogarty International Center  
National Institutes of Health


Panel II  
Mary Mittelman, Dr.P.H.  
Research Professor  
Alzheimer's Disease and Related Dementias Family Support Program  
New York University

Richard Mohs, Ph.D.  
Chief Scientific Officer  
Global Alzheimer's Platform Foundation

Mr. Michael Splaine  
Principal  
Splaine Consulting

**By Direction of the Chairman**

*The Committee on Foreign Affairs seeks to make its facilities accessible to persons with disabilities. If you are in need of special accommodations, please call 202/225-5021 at least four business days in advance of the event, whenever practicable. Questions with regard to special accommodations in general (including availability of Committee materials in alternative formats and assistive listening devices) may be directed to the Committee.*





# COMMITTEE ON FOREIGN AFFAIRS

MINUTES OF SUBCOMMITTEE ON Africa, Global Health, Global Human Rights, and International Organizations HEARING

Day Wednesday Date November 29, 2017 Room 2172

Starting Time 2:22pm Ending Time 4:16pm

Recesses ☐ (to to) (to to) (to to) (to to) (to to) (to to)

Presiding Member(s)

*Smith*

Check all of the following that apply:

Open Session ☒

Executive (closed) Session ☐

Televised ☐

Electronically Recorded (taped) ☐

Stenographic Record ☒

TITLE OF HEARING:

*A Global Update on Alzheimer's Disease*

SUBCOMMITTEE MEMBERS PRESENT:

*Smith, Bera, Donovan, Garrett*

NON-SUBCOMMITTEE MEMBERS PRESENT: (Mark with an \* if they are not members of full committee.)

HEARING WITNESSES: Same as meeting notice attached? Yes ☒ No ☐

(If "no", please list below and include title, agency, department, or organization.)

STATEMENTS FOR THE RECORD: (List any statements submitted for the record.)

*-Smith: Joint Testimony of Alzheimer's Association and Alzheimer's Impact Movement*

*-Smith: External Validity of the New York University Caregiver Intervention: Key Caregiver Outcomes Across Multiple Demonstration Projects*

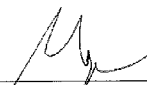
*-Smith: The Minnesota Economic Model of Dementia: Demonstrating Healthcare Cost Savings with the New York University Caregiver Support Intervention*

*-Smith: Estimating The Potential Cost Savings From The New York University Caregiver Intervention In Minnesota (Health Affairs)*

TIME SCHEDULED TO RECONVENE \_\_\_\_\_

or

TIME ADJOURNED \_\_\_\_\_

  
Subcommittee Staff Associate

MATERIAL SUBMITTED FOR THE RECORD BY THE HONORABLE CHRISTOPHER H. SMITH,  
A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY, AND CHAIRMAN,  
SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, GLOBAL HUMAN RIGHTS, AND INTER-  
NATIONAL ORGANIZATIONS



U.S. House Foreign Affairs Committee  
Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations  
A Global Update on Alzheimer's Disease

Joint Testimony of Alzheimer's Association and Alzheimer's Impact Movement

November 29, 2017

Good afternoon, Chairman Smith, Ranking Member Bass, and members of the Subcommittee. Thank you for addressing the global challenge of Alzheimer's disease. Dementia is a condition fast becoming one of the world's largest and most expensive health issues. It is affecting lives and decimating health and social care systems across the world. Forty-seven and a half million people worldwide have dementia and these numbers will double within a generation. Research must be a global priority if we are to improve care, find preventions and treatments, and ultimately cure dementia.

Founded in 1980, the Alzheimer's Association is the world's leading voluntary health organization in Alzheimer's care, support, and research. Our mission is to eliminate Alzheimer's disease and other dementias through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health. As the world's largest nonprofit funder of Alzheimer's research, the Association is committed to accelerating progress of new treatments, preventions, and ultimately, a cure. Through our funded projects and partnerships, we have been part of every major research advancement over the past 30 years. Likewise, the Association works to enhance care and provide support for all those affected by Alzheimer's and reaches millions of people affected by Alzheimer's and their caregivers. The Alzheimer's Impact Movement (AIM), the sister organization of the Alzheimer's Association, is a nonpartisan, nonprofit advocacy organization and works in strategic partnership with the Alzheimer's Association to make Alzheimer's a national priority.

#### **The Global Impact of Alzheimer's and the Global Policy Response**

Alzheimer's disease is a global crisis. This crisis is placing – and will increasingly place – an enormous strain on the health care system, families, and government budgets of nations around the world. Current estimates indicate that about 47.5 million people worldwide are living with dementia, and when we reach the middle of the 21st century, there will be 130 million people living with dementia on this planet.

In 2015, Alzheimer's Disease International (ADI) released the *World Alzheimer Report 2015: The Global Impact of Dementia*, which explores the global prevalence, incidence, and costs of dementia. ADI is the international federation of Alzheimer's associations around the world; the Alzheimer's Association is the sole United States member of ADI.

According to the 2015 Report, the global cost of dementia consumes over one percent of global Gross Domestic Product (GDP) and cost the world \$818 billion in 2015, with 65 percent of the costs incurred by North America and Western Europe. As we all live longer, dementia is spiraling out of control, holding healthcare systems ransom. This cost trajectory can only be fundamentally altered through prevention and effective treatments.

Research shows that most people currently living with dementia have not received a formal diagnosis. In the United States, as many as a half of the over 5 million individuals with Alzheimer's have not been

diagnosed, while a study of India found nearly 90 percent remain unidentified. Individuals living with dementia who have not been diagnosed do not have access to treatment, care, and organized support that getting a formal diagnosis can provide.

While the statistics are dire and the outlook may seem bleak, the crisis is forcing governments around the world to take action. The G8 Summit on Dementia, held in London in December 2013, as well as the constant work of ADI have set this progress in motion. In May of this year, the World Health Assembly -- the voting body of the member countries of the World Health Organization (WHO) -- approved a global action plan on dementia. It lays out a comprehensive effort by the WHO, working with individual countries around the world, to address the dementia crisis, especially the care and support needs of those living with dementia and their families. This effort is of crucial importance in low- and moderate-income countries, which will see the greatest growth in dementia cases by mid-century. The WHO is also in the process of creating a Global Dementia Observatory, so we have better data on the impact of dementia in individual countries and can better monitor global progress in addressing the crisis.

During the 2013 G8 Dementia Summit, the member countries created what is now known as the World Dementia Council (WDC). The President and CEO of the Alzheimer's Association and the Alzheimer's Impact Movement (AIM), Harry Johns, is a member of the WDC and leads its Global Care Team. From the work of the Global Care Team, the WDC last spring released eight principles of high-quality care and support to which governments around the world should strive for all those living with dementia and their care partners.

Finally, it is worth noting that over two dozen nations now have national plans, thanks to a decade-long effort by ADI and Alzheimer's associations in individual countries throughout the world. ADI was also the driving force behind the adoption of the first regional plan on dementia by the Pan-American Health Organization (PAHO) in 2015.

This is truly significant progress on a policy level. But, we are far from conquering this disease and far from providing the care and support needed. The work must continue, and support from governments is key.

#### **Global Research Efforts**

The Alzheimer's Association and Alzheimer's Impact Movement (AIM) are committed to accelerating the global effort to eliminate Alzheimer's disease. No single organization can surmount a challenge as great as Alzheimer's. To help achieve our vision of a world without Alzheimer's, the Association partners with key government, industry, and academic stakeholders in the global race to end Alzheimer's.

The Association formula for progress rests on four pillars: funding, increasing collaborations with investigators, sharing data, and overcoming barriers to progress. The first pillar is the Alzheimer's Association International Grant Program. Typically 10 to 15 percent of our grant funds are expended outside the US. Currently, we fund active grants in 18 countries, and have funded research in 28 overall.

We fund across the total spectrum of Alzheimer's research from molecular biology to medical systems investigation. Our funding is peer-reviewed by a vast international network of volunteer scientists and quality-assured by our Medical and Scientific Advisory Council, a group of distinguished professionals who represent a range of dementia research, including bench research, clinical care, community health, and support services. In addition to funding research directly, we work to ensure the federal investment in Alzheimer's research is comparable with the public threat of the disease.

The second pillar of the Alzheimer's Association program is encouraging increased cooperation between scientists. The Association is responsible for the largest meeting of Alzheimer's scientists every year. This year, the Alzheimer's Association International Conference (AAIC), attracted over 5,600 scientists in London to compare, reveal progress, and develop new working collaborations to advance treatments for the disease. AAIC provides a platform for presentation and discussion of all aspects of Alzheimer's research from genetics to animal models, pathology, biomarkers, interventions, and social and behavioral issues. By encouraging the attendance of researchers from around the world, the Alzheimer's Association is able to bring new innovations in Alzheimer's research to a single thought forum designed to accelerate the understanding of Alzheimer's and related dementias. The Association is also the home of the International Society for the Advancement of Alzheimer's Research and Treatment, a collegial professional society that encourages focus groups for increased cooperation.

The third pillar of our program is sharing of information. We publish *Alzheimer's & Dementia*, the official journal of the Alzheimer's Association. This journal allows important progress to be collected in one place to increase the efficiency of Alzheimer's research. In 2011, the latest criteria defining Alzheimer's disease were published in *Alzheimer's & Dementia*. We partnered closely with the National Institute on Aging (NIA) of the National Institutes of Health to develop the first new criteria and guidelines to diagnose Alzheimer's disease in 27 years. The new criteria and guidelines were the result of a two-year effort by three expert workgroups. Consisting of a total of more than 40 Alzheimer's researchers and clinicians from around the globe, the workgroups began the in-depth process of reviewing the original criteria and deciding how they might be improved by incorporating research advances from the last three decades. These criteria are now reshaping our approach to Alzheimer's treatment. Currently, the NIA and the Alzheimer's Association are leading an effort to develop a new framework to define Alzheimer's disease in the context of biomarkers to help accelerate research. This new research framework will be published in 2018.

The fourth and final pillar of our program is selectively investing in projects to overcome common barriers in the field of Alzheimer's. Projects include TrialMatch™, World Wide Alzheimer's Disease Neuroimaging Initiative (WW-ADNI), and the Global Biomarkers Standardization Consortium (GBSC) focused on cerebrospinal fluid (CSF) biomarkers of Alzheimer's disease.

TrialMatch™ is a confidential, free, and interactive tool that provides comprehensive clinical trial information and an individualized trial matching service for people with Alzheimer's disease and related dementias. Recruiting and retaining trial participants is now the greatest obstacle, other than funding, to developing the next generation of Alzheimer's treatments.

WW-ADNI, of which the Alzheimer's Association is the administrative home, is a collaborative effort of scientists from around the world and is the umbrella organization for neuroimaging initiatives being carried out through the North American ADNI, European ADNI (E-ADNI), Japan ADNI, Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL), Argentina ADNI, India ADNI, China ADNI and two new initiatives in Brazil and Mexico. The Initiative unites leading international investigators in a common effort to:

- Help predict and monitor the onset and progression of Alzheimer's disease
- Establish globally recognized standards to identify and diagnose Alzheimer's disease
- Document cognitive changes linked to physical changes

- Share data across the international research community

Ultimately, we aim to better understand the physical changes that occur in healthy individuals compared with individuals with mild cognitive impairment (MCI) and Alzheimer's disease. WW-ADNI focuses both on changes in the brain that can be identified with tools such as positron emission tomography (PET) and magnetic resonance imaging (MRI) and changes in fluids such as blood and CSF. As its name suggests, another area of focus is to involve individuals from multiple sites around the world and to follow their progress over several years to gain a worldwide picture of the physical changes that lead to Alzheimer's disease.

Data from WW-ADNI are expected to play a key role in identifying effective treatments for Alzheimer's, as well as methods that may prevent the disease or slow its progression. Each WW-ADNI site collects participant data on physical changes related to the onset and progression of MCI and Alzheimer's (called biomarkers). WW-ADNI is unique in that most of the clinical, neuropsychological, imaging, and biological data gathered is quickly made available to the scientific community at no cost so researchers can use the information when designing or evaluating their own research.

The Global Biomarkers Standardization Consortium (GBSC) is an international group consisting of academic, industry, and government scientists who are brought together by the Alzheimer's Association to standardize the methods and materials used to measure key Alzheimer's biomarkers found in CSF. Several studies, including studies involving data from the ADNI have shown that levels of biomarkers in CSF are often accurate predictors of which individuals will go on to develop Alzheimer's disease. CSF biomarkers may be useful not only in aiding early detection of Alzheimer's and improving diagnostic accuracy, but also in identifying and monitoring the effects of drugs in clinical trials, understanding the molecular changes that lead to Alzheimer's, and helping to ensure that individuals recruited into Alzheimer's clinical trials are on a path toward developing the disease. To date, the GBSC has produced two globally-recognized standard methods for the measurement of amyloid  $\beta_{1-42}$  protein, a key Alzheimer's biomarker, in the CSF.

#### **Changing the Trajectory of Alzheimer's**

Until recently, there was no federal government strategy to address this looming crisis. In 2010, thanks to bipartisan support in Congress, the National Alzheimer's Project Act (NAPA) (P.L. 111-375) passed unanimously, requiring the creation of an annually-updated strategic National Alzheimer's Plan (Plan) to help those with the disease and their families today and to change the trajectory of the disease for the future. The Plan is required to include an evaluation of all federally-funded efforts in Alzheimer's research, care, and services -- along with their outcomes. NAPA allows Congress to assess whether the nation is meeting the challenges of this disease for families, communities, and the economy. As mandated by NAPA, the Secretary of Health and Human Services, in collaboration with the Advisory Council on Alzheimer's Research, Care, and Services, released the first-ever *National Plan to Address Alzheimer's Disease* in 2012. The Advisory Council, composed of both federal members and expert non-federal members, is an integral part of the planning process as it advises the Secretary in evaluating and updating the annual Plan, makes recommendations to the Secretary and Congress, and assists in coordinating the work of federal agencies involved in Alzheimer's research, care, and services.

In addition to improving health outcomes for people living with Alzheimer's and to reducing the financial impact of Alzheimer's on families and our federally-funded programs, NAPA requires the Secretary of Health and Human Services to coordinate with international bodies to integrate and inform the fight against Alzheimer's globally. The specific dedication of two ongoing strategies within the Plan to

international collaboration—one to coordinating research efforts and one to enhancing public awareness and engagement—underscore its importance in creating a world without Alzheimer's.

Having this Plan with measurable outcomes is important. But unless there are resources to implement the Plan and the will to abide by it, we cannot hope to make much progress. If we are going to succeed in the fight against Alzheimer's, Congress must provide the resources the scientists need. A disease-modifying or preventive therapy would not only save millions of lives but would save billions of dollars in health care costs. Specifically, a treatment that delayed the onset of Alzheimer's by five years (a treatment similar to anti-cholesterol drugs), would reduce Medicare and Medicaid spending nearly in half in 2050.

Today, despite the federal investment in Alzheimer's research, we are only just beginning to understand what causes the disease. Americans are growing increasingly concerned that we still lack effective treatments that will slow, stop, or cure the disease, and that the pace of progress in developing breakthrough discoveries is much too slow to significantly impact this growing crisis. Scientists fundamentally believe that we have the ideas, the technology, and the will to develop new Alzheimer's interventions, but that progress depends on a prioritized scientific agenda and on the resources necessary to carry out the scientific strategy for both discovery and translation for therapeutic development.

#### **Moving Forward**

It will take concerted and sustained action from world leaders to tackle dementia. They must commit to meaningful, shared steps to drive forward dementia research, agree to a collaborative global action plan, and make significant investment in dementia research to attract, develop and retain the best scientists, clinicians, and care professionals.

Research has transformed the lives of millions living with heart disease, stroke, HIV/AIDS, and cancer. Now is the time to make dementia a priority. Countries must commit to increased investment and improved coordination in research that will transform the lives of people with dementia across the globe.

Thank you again for holding this hearing about the global impact of Alzheimer's disease. The Alzheimer's Association and AIM commend the committee and look forward to continued work together to do all we can to improve the lives of those with Alzheimer's, as well as for those who care for them.



MATERIAL SUBMITTED FOR THE RECORD BY THE HONORABLE CHRISTOPHER H. SMITH,  
A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY, AND CHAIRMAN,  
SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, GLOBAL HUMAN RIGHTS, AND INTER-  
NATIONAL ORGANIZATIONS

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# External Validity of the New York University Caregiver Intervention: Key Caregiver Outcomes Across Multiple Demonstration Projects

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Donna K. Walberg<sup>2</sup>, Nancy E. Lee<sup>2</sup>,  
Leisa R. Easom<sup>3</sup>, Gayle Alston<sup>3</sup>, Angel Ramos<sup>3</sup>,  
Kristen Felten<sup>4</sup>, Asenath LaRue<sup>5</sup>,  
and Mary Mittelman<sup>6</sup>

## Abstract

**Purpose of the Study:** The Administration on Aging funded six New York University Caregiver Intervention (NYUCI) demonstration projects, a counseling/support intervention targeting dementia caregivers and families. Three sites (Georgia, Utah, Wisconsin) pooled data to inform external validity in nonresearch settings. This study (a) assesses collective changes over time, and (b) compares outcomes across sites on caregiver burden, depressive symptoms, satisfaction with social support, family conflict, and quality of life.

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**Design and Methods:** Data included baseline/preintervention ( $N = 294$ ) and follow-up visits (approximately 4, 8, 12 months). **Results:** Linear mixed models showed that social support satisfaction increased ( $p < .05$ ) and family conflict decreased ( $p < .05$ ; Cohen's  $d = 0.49$  and  $0.35$ , respectively). Marginally significant findings emerged for quality of life increases ( $p = .05$ ) and burden decreases ( $p < .10$ ). Depressive symptoms remained stable. Slopes did not differ much by site. **Implications:** NYUCI demonstrated external validity in nonresearch settings across diverse caregiver samples.

### **Keywords**

caregiving, dementia, intervention

Caregiving for family members with dementia can be rewarding (Carbonneau, Caron, & Desrosiers, 2010; Kramer, 1997) but is also associated with stress that affects caregivers' physical and mental health (Pearlin, Mullan, Semple, & Skaff, 1990; Pinquart & Sörensen, 2003). Meta-analyses of 78 articles suggest that interventions are effective at improving caregiver outcomes such as burden, depressive symptoms, and overall life satisfaction, particularly if the interventions include both psychotherapeutic (i.e., counseling) and educational components (Sörensen, Pinquart, & Duberstein, 2002). Interventions that reduce caregiver stress can affect caregiver physical health directly and/or indirectly via these improved mental health processes (Basu, Hochhalter, & Stevens, 2015). Zarit and Femia (2008) discuss characteristics of successful interventions with examples drawn from specific interventions in the literature. Interventions that are multidimensional and target the heterogeneous goals and needs of caregivers, offer flexibility and adaptability to the curriculum or approach, pay attention to the dosage of the intervention, and match their research design to effectively document the desired outcomes are noted as particularly successful approaches.

Between 2008 and 2013, the Administration on Aging (AoA) Supportive Services Program (ADSSP) provided funding to replicate empirically validated caregiver interventions, including the Savvy Caregiver (Hepburn, Lewis, Sherman, & Tornatore, 2003), REACH II (Elliott, Burgio, & Decoster, 2010; Nichols et al., 2008), and the New York University Caregiver Intervention (NYUCI; Mittelman, Epstein, & Pierzchala, 2003). Caregiver support services in California, Florida, Georgia, Minnesota, Utah, and Wisconsin were awarded funding to translate the NYUCI in their areas. Translation projects were awarded from independent applications, and although each site was required to empirically assess program effectiveness,



sites were not, a priori, required to participate in a coordinated cross-site research comparison. In a post hoc decision, however, three sites (Georgia, Utah, and Wisconsin) agreed to pool data for the purposes of (a) assessing collective changes over time and (b) comparing outcomes across sites.

The current article provides a unique opportunity to describe how an intervention program that was originally embedded within a structured randomized control trial in an urban setting (the original NYUCI) translates to multiple real-world settings, where there is more “noise” (variability) introduced both within and between sites. When state or regional service providers across the United States (e.g., Divisions of Aging Services, Area Agencies on Aging) seek to implement empirically validated programs, they will need to be aware of results from highly controlled studies with high levels of internal validity (as is presented below, from the original NYUCI). They should also be aware, however, of program outcomes from settings that might be more similar to their own, for example, when the target population of caregivers is rural, include nonspouses, or vary in ethnicity from the original NYUCI. Describing outcomes from these pooled data across participating demonstration projects addresses external validity of NYUCI.

### **The NYUCI Program: Description of the Program and Prior Research**

The NYUCI began in 1987 and enrolled 406 participants over a 10-year time frame with high retention rates. The study involved only spousal caregivers of persons with dementia living in the New York City metropolitan area. Participants were randomly assigned to the NYUCI treatment group or to a usual-care control group (who received advice, information about resources, and support services as needed). Details of the NYUCI protocol are published (Mittelman et al., 2003), with a brief overview of the research design and intervention included here.

The program includes identical assessment of caregivers preintervention (baseline) and at 4, 8, 12 months follow-up (and for the original study, every 6 months thereafter, continuing after nursing home placement and up until 2 years after the death of the person with dementia). The assessment battery includes demographic characteristics, physical health of the caregiver and care recipient, sources of caregiver assistance, behavioral symptoms and dementia severity of the care recipient, caregiver burden, depressive symptoms, family conflict, satisfaction with social support, and quality of life (QoL). These interviews are conducted face to face by trained NYUCI interventionists/counselors, and they inform both program evaluation and caregiver needs.

Over 4 to 6 months with the same counselor, caregivers receive one individual counseling session, followed by four family counseling sessions (caregivers choose who it is that they invite), and one final individual session. Sessions occur in caregivers' homes or at counselors' service delivery centers based on the preference of the caregiver. In the first individual session, the caregiver and counselor discuss expectations, the importance of including family members in support of the caregiver and person with dementia, decide on family members to be invited to participate, and review the intervention timeline. During family sessions, the caregivers and their family members discuss the impact of the disease and the experiences of caregiving, and the family focuses on building a support network for the caregiver and care receiver. In the final individual session, the counselor and caregiver review the family sessions and focus on integrating the experiences into a plan for the future. Caregivers are encouraged to join a support group after the first follow-up evaluation and receive ad hoc counseling as needed, generally via telephone calls to their assigned counselor if they have specific questions or concerns. Follow-up evaluations provide opportunities to assess change and have further counseling.

Randomized control trials of the original NYUCI identified that the intervention was associated with (a) improved caregiver satisfaction with social support (Drentea, Clay, Roth, & Mittelman, 2006; Roth, Mittelman, Clay, Madan, & Haley, 2005), (b) reduced depressive symptoms (Mittelman et al., 1995; Mittelman, Roth, Coon, & Haley, 2004) both before and after institutionalization (Gaugler, Roth, Haley, & Mittelman, 2008), and (c) decreased distress ratings of behavioral symptoms of the person with dementia (Mittelman, Roth, Haley, & Zarit, 2004). Participating caregivers reported better health and fewer illnesses longitudinally (Mittelman, Roth, Clay, & Haley, 2007) and delayed institutional placement of care recipients (Mittelman, Ferris, Shulman, Steinberg, & Levin, 1996; Mittelman, Haley, Clay, & Roth, 2006). Long, Moriarty, Mittelman, and Foldes (2014) used NYUCI data for economic projections of dollars saved, associated with prevented or delayed institutionalization.

The Three Country Study—a randomized control study testing NYUCI in the United States, England, and Australia—replicated the decrease in depressive symptoms over 2 years for the NYUCI treatment group and found increases in symptoms for the control group (Mittelman, Brodaty, Wallen, & Burns, 2008). A modified version of the intervention in Minnesota with adult-child caregivers (NYU-AC) found similar results. Caregivers receiving NYU-AC were less reactive to behavioral symptoms in the person with dementia (Gaugler, Reese, & Mittelman, 2016), showed a 3-year reduction in depressive symptoms, and showed increased QoL compared with control

group caregivers (Gaugler, Reese, & Mittelman, 2015). These caregivers also kept their parents at home significantly longer than caregivers in the control group (Gaugler, Reese, & Mittelman, 2013). Collectively, these studies support the effectiveness of NYUCI in randomized control studies with high levels of internal validity.

### **AoA Demonstration Projects: NYUCI Across Multiple Sites**

The AoA funded six NYUCI demonstration projects; awardees were California (CA Dept. of Aging), Florida (FL Dept. of Elder Affairs), Georgia (Rosalynn Carter Institute for Caregiving and GA Southwestern State University), Minnesota (MN Board on Aging), Utah (UT Division of Aging and Adult Services), and Wisconsin (WI Department of Health Services). Funding for these projects was purposefully focused on service delivery. The assessment component in the demonstration projects was intended to document program effectiveness within each site and inform the individualized counseling, and the studies were *not* designed with the original intention of conducting comparative analyses. However, discussions among participating sites during the period of implementation led to a collaboration and pooled data, the purpose of which is to report information helpful in discerning external validity across diverse locations and samples. To do so, we report the extent to which outcomes changed over time (across all available sites) and/or if significant differences emerged in outcomes between sites.

The California site did not share data for pooled analyses, as their data management agreement did not permit pooling with external collaborators. Despite requests to amend the original approved protocols, the Institutional Review Board (IRB) overseeing the Florida data collection restricted the agencies from pooling the data because consent from participants had not been collected for these purposes. Minnesota used measures of caregiver outcomes that were different from those used by the other sites, prohibiting the pooling of Minnesota data. Thus, the current manuscript includes data from Georgia, Utah, and Wisconsin. We note, however, that outcomes from the Minnesota translation project are published elsewhere. The Minnesota translation project reported decreased depressive symptoms and distress. The project also identified that attending a greater number of counseling sessions was associated with delayed institutionalization of the person with dementia (Mittelman & Bartels, 2014).

The three demonstration sites using the NYUCI protocol and pooling data for the current analyses differed from the original study design/protocol in a number of ways: First, although the original NYUCI utilized spousal

caregivers, in the current study only Wisconsin utilized a spousal sample, while the other sites include spouses and adult-offspring caregivers (see Table 1). Second, the sample in the original NYUCI was drawn from a largely White, urban population; however, all subsamples in our investigation were more likely to include rural caregivers, and Georgia specifically targeted service delivery to a sample subset of African American caregivers. Finally, the original study with high levels of internal validity included a randomized control design with a usual-care comparison group. As AoA demonstration funding focused on service delivery, it would not support the assessment of a control group. Thus, while we compare NYUCI outcomes collectively and across sites, we cannot determine how these pooled data compare with a control or usual-care group.

## **Method**

### *Participants*

Recruitment of caregivers took place through state and local aging agencies, public resource centers, and the Alzheimer's Association state/regional chapters, although the sites varied to some extent in their recruitment approaches. Most caregivers in Georgia were recruited when they contacted participating Area Agencies on Aging. Utah identified caregivers in a similar way and via caregivers' phone calls to the Alzheimer's Association. Wisconsin followed similar procedures and added outreach to health care facilities, senior services programs, and community organizations.

Inclusion criteria varied only slightly by site. All sites required the care recipient to have a diagnosis of Alzheimer's disease or other dementia, and excluded caregivers who were not primary caregivers, or those with a serious mental illness that would prevent participation in counseling sessions, or those that did not have at least one family member available to attend family counseling sessions. All sites also required the care dyad to live in the community (not be institutionalized) at baseline but not necessarily in the same home. Utah and Wisconsin also explicitly stated that they limited participation to English-speaking participants. Wisconsin was the only state to require that caregivers were spouses. Georgia required that caregivers endorsed having some burden in their role and the need for assistance.

Baseline preintervention data come from a total sample of 294 caregivers. Table 1 provides rates of attrition and sample characteristics. Georgia had the highest rates of attrition. The counselors/interventionists in Georgia could not identify one or more particular reasons for lack of interest in follow-up, but speculated that with service delivery as their main focus there was a low level

**Table 1.** Sample Demographic Characteristics of Caregiver (CG) and Person with Dementia (PWD).

	All sites	Utah	Georgia	Wisconsin
Baseline <i>N</i>	294 (100.0%)	88 (100.0%)	132 (100.0%)	74 (100.0%)
Follow-Up 1 <i>n</i> (% retention from baseline)	152 (51.7)	55 (62.5)	54 (40.9)	43 (58.1)
Follow-Up 2 <i>n</i> (% retention from baseline)	74 (25.2)	36 (40.9)	11 (8.3)	27 (36.5)
Follow-Up 3 <i>n</i> (% retention from baseline)	44 (15.0)	24 (27.3)	5 (3.8)	15 (20.3)
CG kin relationship (%)*				
Adult child	9.6	13.6	12.1	0
Spouse	89.8	83.0	87.9	100.0
Other	0.7	2.3	0	0
CG married (%)*	90.2	90.0	84.8	100.0
CG female (%)	66.9	68.2	63.1	71.6
CG age ( <i>M</i> )*	70.8 ( <i>SD</i> = 11.5)	69.1 ( <i>SD</i> = 11.8)	69.2 ( <i>SD</i> = 12.3)	75.2 ( <i>SD</i> = 8.3)
PWD female (%)	38.4	35.2	45.9	29.7
PWD age ( <i>M</i> )	76.1 ( <i>SD</i> = 9.7)	75.5 ( <i>SD</i> = 7.9)	75.6 ( <i>SD</i> = 11.6)	77.7 ( <i>SD</i> = 7.9)
CG ethnicity: % identifying as Hispanic	2.6	5.7	1.5	0
CG race (%)*				
White	88.4	96.6	76.5	100
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Black/African American	8.5	0	18.9	0
Native Hawaiian/Pacific Islander	1.0	1.1	1.5	0
Other	2.0	2.3	3	0
CG education (%)*				
Graduate school	14.5	21.6	11.7	10.8

(continued)

**Table 1. (continued)**

	All sites	Utah	Georgia	Wisconsin
Completed college	21.4	28.4	15.6	23
Some college	24.8	35.2	15.6	28.4
Completed high school	25.9	13.6	32.0	29.7
Some high school	7.6	1.1	12.5	6.8
Junior high school	3.8	0	7.8	1.4
<7 years of school	2.1	0	4.7	0
CG %working*	17.2	23.9	18.6	6.8
PWD global deterioration (M)	4.8 (SD = 1.12)	4.6 (SD = 1.3)	4.9 (SD = 1.1)	4.8 (SD = 0.9)
CG clinically depressed <sup>a</sup> (%)	31.6	38.6	24.2	36.5
Reasons for attrition				
Lack of interest from CG or family members in attending family counseling	25 (17%)	7 (21%)	11 (14%)	7 (22%)
Closure of service provider or other scheduling difficulties for follow-up assessments <sup>b</sup>	23 (16%)	9 (27%)	—	14 (45%)
Institutionalization of PWD	9 (6%)	6 (18%)	3 (4%)	—
Death of PWD	9 (6%)	4 (12%)	5 (6%)	—
CG or PWD declining health	17 (12%)	5 (15%)	5 (6%)	7 (22%)
CG death or moved from area	3 (2%)	—	2 (3%)	1 (3%)
Other/unknown/lost to follow-up	58 (41%)	2 (6%)	52 (67%)	2 (7%)

Note. All values except attrition information are baseline (preintervention) data. CG = caregivers; PWD = persons with dementia.

<sup>a</sup>Clinical depression cutoff scores are 10 for Geriatric Depression Scale, based on Lyness, et al., 1997

<sup>b</sup>A UT Alzheimer's Association branch office closure forced these participants to leave the study, as the remote geographic location did not allow for counselors in other areas to continue working with these participants.

\*Indicates that chi-square (categorical variable) or ANOVA (continuous variable) differed by site at a level of  $p < .05$ .

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NATIONAL ORGANIZATIONS



**The Minnesota Economic Model of Dementia:  
Demonstrating Healthcare Cost Savings with the  
New York University Caregiver Support Intervention**

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May, 2014

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## Executive Summary

No therapies are known to substantially alter the course of dementia and associated treatment costs. However, enhanced support services for caregivers for people with dementia have been shown to improve caregivers' capabilities and well-being and delay patients' institutionalization.

Using a model that simulated disease progression, place of residence, and costs of care, we estimated the economic impact to Minnesota from offering the New York University Caregiver Intervention (NYUCI), an enhanced support services program for adult caregivers of community-dwelling people with dementia. We estimated the impact of the NYUCI on:

1. the potential healthcare savings to all eligible people in the state, assuming all current and future caregivers participate in the NYUCI from 2010 to 2025;
2. the net healthcare cost savings, inclusive of program costs, to eligible caregivers, assuming three less-than-complete levels of participation in the NYUCI from 2010 to 2025 (5% of all caregivers, 10% and 30%);
3. the potential indirect cost savings to all eligible people in the state, assuming all current and future caregivers participate in the NYUCI from 2010 to 2025.

Results indicate that approximately 5 percent more people with dementia would remain in the community from year 3 (2013) on, and that 19.3 percent fewer people with dementia would die in institutions over fifteen years. During those years, Minnesota could potentially save as much as \$1.24 billion (\$996 million in discounted dollars) in direct healthcare costs. The estimated savings in net healthcare costs during those years, including all program costs except for program marketing, were \$61.8 million, \$103.7 million, and \$250.6 million, assuming 5, 10, and 30% of caregivers participate in the NYUCI, respectively. Estimated potential indirect cost savings are also substantial, well exceeding the estimated direct healthcare cost savings.

These findings suggest that broader access to enhanced caregiver supports is a promising way to moderate the growing economic burden of dementia. Substantial long-term savings are possible even without a breakthrough in the pharmacologic treatment of the disease. These direct healthcare cost savings would benefit taxpayers (through reduced expenditures for the Medicaid program) and people with dementia and their families, who largely pay the medical and facility fees for those in residential care settings. Other payers who would benefit include the Medicare program, commercial health plans and long term care insurers, to the extent that they fund these formal care services. The substantial indirect cost savings with enhanced support services would benefit caregivers and likely their employers through improved quality of life and increased productivity. Enhanced support services programs for dementia caregivers, such as the NYUCI, are cost-effective ways to manage dementia while researchers continue to seek effective treatments for the disease.



## Background

ACT on Alzheimer's (ACT) is a voluntary collaborative in Minnesota convened in 2011, with the goal of implementing legislative recommendations to prepare the state for the personal, social and budgetary impacts of dementia. One of ACT on Alzheimer's five leadership groups set out to identify and encourage investment in promising approaches that reduce costs and improve care. The leadership group decided to develop a model useful both now and in the future to provide Minnesota policy makers and health care leaders with relevant estimates of potential cost savings associated with varying dementia care approaches to help guide the investment of resources in the future. To this end, the group engaged healthcare researchers to develop an economic model to estimate the cost-saving potential of proven interventions.

Given multiple and diverse stakeholders, the leadership group sought to estimate the impact of one or more care interventions from varying perspectives, including the state-wide Minnesota societal and health system perspectives as well as from the perspective of the Minnesota Department of Human Services, the state's public payer who serves low-income Minnesotans with dementia. At this time the model has been configured to estimate potential and net cost savings from specific perspectives of interest. The same approaches can be used to estimate results from other perspectives and interventions as well as simulate other economic outcomes (such as return on investment or cost-effectiveness) with structural and parameter changes as appropriate.

This paper describes the development of the model, including the initial choice of intervention and modeling approach, and provides a high-level overview of the study methods and results. Further methodologic details and more detailed results can be found in Long et al. 2014 as well as in forthcoming peer-reviewed publications<sup>1</sup>.

## Clinical and Economic Burden of Dementia

The burden of dementia is widely documented and increasingly recognized in policy settings. Although estimates of the prevalence of dementia in the United States vary, few doubt that the number of people affected is large and increasing with the aging of the population<sup>2</sup>. One recent estimate yielded a prevalence of 14.7% in people older than 70 years of age, approximately 4.1 million individuals in 2010<sup>3</sup>. More than 15 million family members provide unpaid care for these individuals, often at their own physical and emotional expense<sup>4</sup>.

Annual dementia-attributable direct costs in this population were estimated at \$109 billion; total cost estimates were \$159 to \$215 billion, depending on how the monetary value of informal caregiving was calculated<sup>5</sup>. The direct cost of care alone ranks expenditures for dementia similar to expenditures for heart disease and substantially higher than expenditures for cancer. These costs are projected to more than double by 2040<sup>3</sup>. Additionally, since nursing home costs are a primary driver of dementia-related expenditures, the high rate of institutionalization contributes substantially to state and federal expenditures<sup>5-7</sup>.

Recognition of this burden led Congress to pass and President Barack Obama to sign the National Alzheimer's Project Act in 2011. The act required the creation of a national strategic

plan to address the escalating crisis of Alzheimer's disease and to coordinate efforts to combat the disease across the federal government<sup>8</sup>. And, even in an era of limited research resources, the National Institutes of Health distributed \$45 million in new funding in 2013 to support innovative studies of Alzheimer's disease<sup>9</sup>. Furthermore, the fiscal year 2014 budget included an increase of \$122 million for Alzheimer's research, education, outreach, and caregiver support<sup>10</sup>.

### **ACT on Alzheimer's Collaborative**

In 2009, to tackle the mounting Alzheimer's crisis in Minnesota, the Minnesota Legislature charged the Minnesota Board on Aging to establish the Alzheimer's Disease Working Group (ADWG) and make recommendations for policies and programs that would prepare Minnesota for the future. The ADWG developed a set of recommendations for the Legislature in January 2011. A voluntary coalition, now named ACT on Alzheimer's, was subsequently formed to focus on implementing the recommendations (see <http://www.ACTonALZ.org>). As a statewide collaboration, ACT on Alzheimer's fosters collective ownership and accountability in preparing Minnesota for the clinical and economic impacts of Alzheimer's disease and related dementias. The collaboration has more than 300 participants and 60+ nonprofit, governmental and private organizations.

A goal of ACT on Alzheimer's was to develop a model useful both now and in the future to provide Minnesota policymakers and healthcare leaders with relevant estimates of potential cost savings that could be achieved by investing in evidence-based dementia care interventions. The Minnesota Economic Model of Dementia was developed as a vehicle for influencing care delivery and payment policy to ensure that persons with dementia and their caregivers receive optimal care and support in a manner that both improves their quality of life and is likely to reduce the State's and other payers' burden.

### **Choice of Intervention**

The ACT on Alzheimer's leadership group, focusing on identifying and investing in promising care interventions, convened a number of times to discuss the evidence on interventions that had the potential to moderate the economic burden of dementia. The group considered evidence surrounding early identification of disease, pharmacologic treatments, and models to improve continuity of care for persons with dementia.

#### ***Early Identification***

Being able to identify dementia earlier in the course of the disease clearly has clinical advantages, including improved coordination and continuity of care around dementia progression. Research has demonstrated that early identification alone is possible through screening, although whether this approach has any economic benefits is currently

undetermined due to limited research in this area and the absence of therapies that prevent, cure or significantly delay symptoms<sup>11</sup>.

#### ***Pharmacologic Treatment***

Currently there are five therapies approved by the United States Federal Drug Administration for management of Alzheimer's disease. Most of these medications are classified together as cholinesterase inhibitors, which are approved for mild-to-moderate Alzheimer's disease. The additional medication option, memantine, is approved for the treatment of moderate-to-severe disease. While initially these medication options held great promise to delay disease progression, systematic literature reviews have been less favorable and currently the effectiveness of drug treatment remains controversial<sup>12</sup>. Even if clinical benefits exist with pharmacologic treatment, they come at substantial cost and it is unlikely that drug treatment is cost-saving or even cost-effective<sup>13-17</sup>. For these reasons access to these medications is currently limited in some countries, given the limited value of drug treatment<sup>12</sup>. Following extensive discussion, the ACT on Alzheimer's leadership group decided that the research on pharmacologic treatment is inconclusive regarding clinical effectiveness and the potential for cost savings and it was not chosen to be a focus of economic model simulations at this time.

#### ***Improved Continuity of Care***

Several types of interventions may be grouped under the concept of improved continuity of care or care coordination. The National Coalition on Care Coordination defines care coordination as "...a client-centered, assessment-based interdisciplinary approach to integrating health care and social support services in which an individual's needs and preferences are assessed, a comprehensive care plan is developed, and services are managed and monitored by an identified care coordinator following evidence-based standards of care".

An expanding body of literature demonstrates that improved coordination of care practices are effective in ameliorating behavioral and psychological symptoms in persons with dementia and reducing distress in caregivers<sup>18-20</sup>. Positive results have been observed in multiple controlled and translational studies in clinical and community settings<sup>18,20</sup>. Formal evaluations have been conducted of several primary-care based coordinated care models for persons with dementia<sup>21-23</sup>. These studies suggest substantial benefits for both caregivers and people with dementia, including improvement in the quality of care and in behavioral and psychological symptoms, without significantly increasing the use of pharmaceutical interventions. A recent study of a primary care based collaborative care model documented nearly \$3,000 in annual savings per patient, largely attributable to reduced rates of hospitalization<sup>24</sup>. However, the literature to date is limited and conflicting as to whether economic benefits to these models exist, such as reduced emergency room visits, hospitalization, or delayed nursing home admission.

From an economic perspective, a more promising form of improved continuity of care may be the transitional care model that focuses on improving the multiple transfers of persons with chronic conditions between hospitals, nursing homes, and community settings, where evidence has shown that continuity of care often falters<sup>25</sup>. Naylor and colleagues at the University of Pennsylvania have shown through a randomized controlled trial that a transitional

care model can reduce repeat hospitalizations in a general elderly population<sup>26</sup>. This model has been studied with favorable results in a dementia population but results are still pending academic publication. Currently the evidence in the literature remains limited regarding cost savings associated with either primary care-based coordinated care models or transitional care models for persons with dementia.

#### ***Enhanced Caregiver Supports***

Nationally, 44% of community-dwelling persons with dementia live with an adult caregiver, most often a spouse or adult child<sup>27</sup>. In 2012, an estimated 15 million dementia caregivers provided 17.5 billion hours of unpaid care<sup>28</sup>. These caregivers provide a wide range of unpaid services, including helping with activities of daily living (ADLs), instrumental activities of daily living (IADLs), and managing behavioral symptoms of the disease. Caregivers frequently provide this care at the expense of their own wellbeing and productivity<sup>29-31</sup>. Caregiver stressors in conjunction with care recipient characteristics have been shown to predict nursing home admission<sup>32</sup>. Institutionalization has multiple consequences, not the least economic, because nursing home costs can greatly exceed the cost of community-based care.

Education and support programs for dementia caregivers have been demonstrated to have multiple benefits. Studied programs have multiple components and may combine individual counseling, family sessions and support, and ongoing assistance to help the caregiver cope with the behavioral symptoms that often accompany the progression of disease. Program benefits include reduced levels of caregiver stress and depression, reduced time spent caregiving, and delayed nursing home placement<sup>33-35</sup>.

### **Initial Focus for the Economic Model: The New York University Caregiver Intervention**

Based on this review of the evidence regarding possible cost saving interventions, the ACT on Alzheimer's leadership group reasoned that without a clinical breakthrough that can substantially alter the course of disease, the best current evidence-based approach to reducing the costs for persons with dementia may be through provision of enhanced caregiver support. The Minnesota Economic Model of Dementia was initially used to project the healthcare cost savings in Minnesota associated with participation in the New York University Caregiver Intervention (NYUCI), a well-studied enhanced caregiver support program.

The NYUCI was developed in the 1980s to educate caregivers about dementia, involve the family to support the primary caregiver, and provide the caregiver with tools to cope with the behavioral symptoms of the disease. This program consists of two individual and four family counseling sessions, encouragement to participate in weekly support groups, and ongoing ad hoc telephone counseling. Counseling sessions are tailored to meet the needs of the caregiver and family. Previously documented benefits, identified through randomized controlled trials, include improved levels of caregiver wellbeing and capabilities, and an estimated median delay of 557 days before permanent residential placement of the person with dementia<sup>33</sup>.

## Minnesota Economic Model of Dementia

The Minnesota Economic Model of Dementia is the first formal economic evaluation of the cost savings associated with implementing the NYUCI program. It is a population-based microsimulation Markov model to simulate disease progression and place of residence of Minnesotans with Alzheimer's disease and other related dementias. The model tracks individuals as they move through discrete health states and accumulate costs over 15 years under two scenarios: (1) no enhanced caregiver supportive services, in which adult caregivers of community-dwelling persons with dementia do not receive specialized supportive services in addition to usual care; and (2) enhanced caregiver supportive services, in which adult caregivers participate in the NYUCI. The model is informed by primary data collection as well as the literature on the epidemiology, natural history, costs, and evidence-based management of the disease<sup>27,33,35-43</sup>. A full discussion of the research methods, model specifications, additional results and limitations can be found in Long et al. 2014 and the accompanying online Appendix<sup>1</sup> (see <http://www.actonalz.org/economic-impact>).

### Model Results

#### *Potential Healthcare Cost Savings*

The Minnesota Economic Model of Dementia was used first to estimate the maximum potential cost savings associated with the NYUCI, without incorporating variable implementation factors such as program and marketing costs and less-than-complete participation rates. These results appeared in Health Affairs in April, 2014<sup>1</sup>. Results suggest that significant direct healthcare savings and other benefits are possible.

- Approximately 5 percent more people with dementia would be able to remain in their homes each year rather than moving to a residential facility, after 3 years of program implementation.
- Approximately 19 percent fewer people with dementia would likely die in institutional settings after 15 years of implementation.
- Minnesota could save as much as \$1.24 billion (\$996 million in discounted dollars) in direct healthcare cost savings over 15 years of program implementation.

These results do not include program and marketing costs. They also assume that all unpaid adult caregivers living at home with the estimated 30,872 Minnesotans with dementia in 2010, and all caregivers of newly diagnosed future cases, were to participate in the NYUCI. While this assumption is unrealistic, these initial results indicated the strong probability that enhanced caregiver support is a promising way to moderate the growing economic burden of dementia. Accordingly, the ACT on Alzheimer's leadership group decided to extend the analysis

to investigate cost savings under three different “real world” participation scenarios as well as account for program costs.

***Net direct healthcare cost savings***

The Minnesota Economic Model of Dementia was extended to project the likely net cost savings associated with the NYUCI by incorporating estimated program costs and varying participation rates of caregivers of people with dementia in Minnesota. Results suggest that, in addition to allowing more people with dementia to live and die at home, as noted above, net direct healthcare savings are achievable within a few years of program implementation. The following table summarizes the net direct healthcare savings at three possible levels of program participation by caregivers.

<b>Projected Cumulative Net Direct Healthcare Cost Savings for Minnesota</b>			
<b>Proportion of 36,786 Eligible Caregivers in 2011</b>			
<b>Participating in the NYUCI/</b>			
<b>Initial Number of Caregiver Participants</b>			
	<b>5% / 1,840</b>	<b>10% / 3,678</b>	<b>30% / 11,035</b>
<b>Net Savings:</b>			
After 3 Years	\$ 281,000	\$ 2,500,000	\$ 795,000
After 5 Years	\$ 6,000,000	\$ 17,200,000	\$ 38,300,000
After 10 Years	\$ 33,000,000	\$ 60,800,000	\$ 145,800,000
After 15 Years	\$ 61,800,000	\$ 103,700,000	\$ 250,600,000

These estimated direct healthcare cost savings account for all program costs but do not include costs to increase awareness of the program and encourage participation. These marketing costs could not be credibly incorporated into the model because the approaches to marketing the program have not been determined and may vary substantially based on methods used. However, the estimated net savings suggest broad latitude to conduct outreach and awareness while still providing overall net savings after three or four years of program implementation.

**Indirect Costs Associated with Caregiver Burden**

The dementia caregiver burden is substantial. As noted earlier, an estimated 15 million caregivers provided 17.5 billion hours of unpaid care nationally in 2012<sup>28</sup>. The indirect costs associated with this time spent caregiving have been estimated between \$50 to \$106 billion, depending on how the monetary value of informal caregiving was calculated<sup>3</sup>. The ACT on Alzheimer’s leadership group was interested in determining whether enhanced caregiver support might reduce this economic burden for caregivers, in addition to the direct healthcare savings for patients, families, and payers. The Minnesota Economic Model of Dementia, therefore, was extended to include indirect costs associated with time spent caregiving.

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## CAREGIVER SUPPORT MODELS

By Kirsten Hall Long, James P. Moriarty, Mary S. Mittelman, and Steven S. Foldes

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## Estimating The Potential Cost Savings From The New York University Caregiver Intervention In Minnesota

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**ABSTRACT** No therapies are known to substantially alter the course of dementia and associated treatment costs. However, enhanced support services for caregivers of people with dementia have been shown to improve caregivers' capabilities and well-being and delay patients' institutionalization. Using a model that simulated disease progression, place of residence, and direct costs of care, we estimated the potential savings to Minnesota from offering the New York University Caregiver Intervention, a program of enhanced support services for spouse and adult child caregivers of community-dwelling people with dementia, to all eligible people in the state from 2010 to 2025. Results indicate that approximately 5 percent more people with dementia would remain in the community from year 3 (2013) on and that 19.3 percent fewer people with dementia would die in institutions over fifteen years. During those years Minnesota could save \$996 million in direct care costs (with a range of nearly \$100 million to \$2.64 billion under worst- and best-case scenarios, respectively). These findings suggest that broader access to enhanced caregiver supports could produce a positive return on investment or be cost-effective—assuming widespread implementation, reasonable program costs, and substantial caregiver participation.

**T**he burden of dementia is widely documented and increasingly recognized by policy makers. Estimates of the prevalence of dementia in the United States vary. However, few researchers and policy makers doubt that the number of people affected is already large and is increasing as the population ages.<sup>1</sup> One estimate is that 14.7 percent of people ages seventy and older, or approximately 4.1 million people nationwide, had dementia in 2010.<sup>2</sup> Annual direct health care costs for this population that were attributable to dementia have been estimated at \$109 billion.<sup>3</sup> Thus, expenditures for dementia are near those for heart disease and much higher than expenditures for cancer. Expenditures for dementia are projected to

more than double by 2040.<sup>2</sup>

Recognition of this burden led Congress to pass and President Barack Obama to sign the National Alzheimer's Project Act of 2011. The act required the creation of a national strategic plan to address the escalating crisis of Alzheimer's disease and to coordinate efforts to combat the disease across the federal government.<sup>3</sup>

Even in an era of limited research resources, the National Institutes of Health distributed \$45 million in new funding in 2013 to support innovative studies of Alzheimer's disease.<sup>4</sup> Furthermore, the fiscal year 2014 budget included an increase of \$122 million for Alzheimer's research, education, outreach, and caregiver support.<sup>5</sup>



More than forty states are developing their own Alzheimer's disease plans, which are in various stages of implementation.<sup>6</sup> The ACT on Alzheimer's Collaborative was founded in Minnesota in 2011 with the goal of implementing legislative recommendations to prepare the state for the personal, social, and budgetary impacts of dementia.

One of the collaborative's five leadership groups seeks to identify and encourage investment in promising approaches to reduce the costs and improve the quality of care for Alzheimer's patients. This leadership group commissioned an economic model to estimate the cost-saving potential of proven interventions in Minnesota.

The group convened several times to discuss the evidence, based on a systematic literature review, about tested interventions. Pharmacologic options initially held great promise to delay the disease's progression and manage patients' behavioral symptoms. However, more recent reviews have suggested that such options are more likely to be supportive or palliative than capable of altering disease progression and can have adverse effects. Thus, their use remains somewhat controversial.<sup>7-10</sup> Even if pharmacologic options are effective, they have a substantial cost and are not likely to be cost-saving or even cost-effective.<sup>7,8</sup>

A growing body of literature demonstrates that nonpharmacologic treatments are effective in ameliorating behavioral and psychological symptoms in people with dementia and reducing distress in their caregivers.<sup>9,11,12</sup> Positive results have been observed in multiple controlled and translational studies in clinical and community settings.<sup>11,12</sup>

The primary care setting, where many people with dementia are diagnosed, has been the focus of collaborative care models designed to integrate dementia treatment guidelines more effectively into clinical care. These models have been shown to improve the quality of care, and research suggests that they reduced the use of acute care in the short term.<sup>13-15</sup> However, the short durations of the studies make it difficult to know whether the models would have sustained economic benefits. And, as Laura Gitlin commented in a recent meta-analysis of non-pharmacologic treatments, "cost analyses for almost all of the included interventions are woefully missing."<sup>16(piv-5)</sup>

Models of community-based caregiver support that include education and support programs for informal—that is, unpaid—caregivers for people with dementia have demonstrated multiple benefits. Some of the programs that have been studied have multiple components, combining indi-

vidual counseling, family sessions and support, and ongoing ad hoc assistance to the caregiver. These programs aim to educate caregivers about dementia, involve the family to support the primary caregiver, and provide the caregiver with tools to cope with the behavioral symptoms that often accompany the progression of disease. Repeatedly documented benefits include reduced levels of caregiver stress and depression, reduced time spent caregiving, and delayed residential placement of the person with dementia.<sup>16-20</sup>

Formal economic evaluations of enhanced caregiver support interventions were not available. However, the ACT on Alzheimer's Collaborative leadership group reasoned that because the cost of residential care can greatly exceed the cost of community-based care, these interventions currently offer the greatest chance for savings in the long term.

#### New York University Caregiver Intervention

Delayed residential care placement as a result of enhanced caregiver support was repeatedly observed in the New York University Caregiver Intervention (NYUCI), which was originally implemented at the NYU Langone Medical Center.<sup>16,21,22</sup> In the final analysis of the NYUCI randomized controlled trial, 406 spouse and adult child caregivers of people with dementia living in the New York metropolitan area were randomly assigned to receive either enhanced support services or usual services and were followed for up to eighteen years.<sup>16</sup> Of the spouse and adult child caregivers, 60 percent were female, and their average age was seventy-one. Few of the caregivers had minority ethnic backgrounds.

Enhanced support services consisted of six sessions of individual and family counseling within four months of enrollment in the NYUCI, encouragement to participate in an ongoing weekly support group, and ad hoc telephone counseling as needed for an indefinite period. Counseling sessions were tailored to meet the needs of the spouse caregiver and family. The trial demonstrated improved caregiver well-being and capabilities and an estimated median delay of 557 days before the person with dementia was placed in a residential facility.<sup>16</sup>

A recent adaptation of the NYUCI to adult child caregivers in Minnesota also demonstrated substantial delays in residential placement.<sup>17</sup> The NYUCI model has been implemented in multiple demonstration projects, including the Family Memory Care Program in fourteen urban and rural sites in Minnesota.<sup>12,23</sup> This made the

## CAREGIVER SUPPORT MODELS

NYUCI model of care familiar to the leadership group of the ACT on Alzheimer's Collaborative and a likely candidate for statewide implementation.

Another randomized trial, Resources for Enhancing Alzheimer's Caregiver Health II, or REACH II, failed to confirm delayed residential placement with a similar program of enhanced caregiver support.<sup>30</sup> However, the limited follow-up period in that trial made it difficult to detect a longer-term effect. Thus, the leadership group requested that the economic model it commissioned estimate the potential for savings in care costs of the NYUCI for all Minnesota adult caregivers of people with dementia living in communities throughout the state. ACT leaders asked what the health system could save during fifteen years—not taking program costs into account—if this model of enhanced caregiver services were widely available to caregivers of people with dementia and used statewide.

#### Study Data And Methods

We developed a population-based Markov model to simulate disease progression and place of residence of Minnesotans ages 65–100 with Alzheimer's disease or other dementias. The model tracked people as they moved through discrete health states and accumulated costs during a period of fifteen years under two scenarios: with enhanced caregiver supports, in which their spouse or adult child caregivers participated in the NYUCI; and with usual services only—that is, without enhanced caregiver supports in the form of the NYUCI.

The model was designed to assess the potential cost savings associated with the NYUCI without incorporating variable implementation factors such as program and marketing costs and less-than-complete participation rates. The model's development was informed by the literature on the epidemiology, natural history, costs, and evidence-based management of dementia.<sup>24–31</sup> The online Appendix provides further details on the model's specifications.<sup>32</sup>

**HEALTH STATES** Our model included three discrete Markov health states: living in the community, being institutionalized in a residential care facility (a nursing home or assisted living facility), and dead. The eligible population included people with dementia who all initially lived in the community with a spouse or adult child caregiver. Based on severity-specific annual probabilities of transitions between health states, the model projected and tracked from 2010 to 2025 the number of people who remained in the community and their associated costs of care; the number who required residential placement,

## Enhanced caregiver support is a promising way to moderate the growing economic burden of dementia.

thereby incurring additional facility fees; and the number who died.

**PREVALENCE AND INCIDENCE OF DEMENTIA IN MINNESOTA** To estimate the number of people with dementia, we applied to state population trends the prevalence and incidence rates that the Rochester Epidemiology Project observed in Rochester, Minnesota.<sup>34–36</sup> We adjusted rates upward to account for Rochester's educational level, which is higher than the state average, because that level is known to be inversely correlated with the risk of dementia.<sup>27</sup>

We also adjusted the rates upward to account for a documented bias that might be associated with improved recognition of dementia in clinical practice since the early 1990s, when the Rochester Epidemiology Project's rates were estimated, for cases that might have been missed because of the project's reliance on medical records alone to identify people with dementia, or both.<sup>28</sup> An additional discussion of prevalence rates can be found in the online Appendix.<sup>32</sup>

We distributed the estimated prevalence across disease severity (mild, moderate, severe) as observed in the Canadian Study of Health and Aging, and we assumed that incident—that is, newly diagnosed—cases were of mild severity.<sup>29</sup> Exhibit 1 shows the estimated numbers of community-dwelling Minnesotans with dementia living with an adult caregiver by severity used in the primary-case (standard model assumptions) and alternative-case (alternative model assumptions) analyses. The model assumed that incidence rates remained constant over time; the increase in the number of incident cases reflected the projected demographic changes in the state's population.<sup>33</sup>

**TRANSITION PROBABILITIES** Minnesota residents with dementia in our model had an annual likelihood of moving among the defined health states based on the estimated probabilities of disease progression, residential placement, or dying. We based the likelihood of disease progression and residential placement on analyses of the Consortium to Establish a Registry for

**EXHIBIT 3**

**Estimated Prevalence Of People With Dementia Living In The Community With A Spouse Or Adult Child Caregiver In Minnesota Who Were Eligible For The New York University Caregiver Intervention (NYUCI), 2010, And Incidence Of Dementia In Selected Years 2011–2025**

	Primary-case analysis (20% upward adjustment)	Alternative-case analyses, with adjustments of:		
		15% upward	25% upward	50% downward
PEOPLE ELIGIBLE FOR NYUCI, 2010				
Mild dementia	14,359	13,761	14,958	7,180
Moderate dementia	13,641	13,073	14,210	6,821
Severe dementia	2,872	2,752	2,992	1,436
Total	30,872	29,586	32,160	15,437
ANNUAL INCIDENCE OF DEMENTIA IN MINNESOTA, SELECTED YEARS				
1 (2011)	5,913	5,667	6,160	2,957
5 (2015)	6,496	6,226	6,767	3,248
10 (2020)	7,493	7,090	7,706	3,699
15 (2025)	8,711	8,348	9,074	4,356

**SOURCE** Authors' analysis of data from the following sources: (1) Kokmen E, et al. Time trends in the prevalence of dementia and Alzheimer's disease in Rochester, Minnesota [Note 24 in text]; (2) Knopman DS, et al. Incidence and causes of nondegenerative nonvascular dementia [Note 25 in text]; (3) Minnesota Department of Administration. Dataset [Note 26 in text]; (4) Meng X, D'Arcy C. Education and dementia in the context of the cognitive reserve hypothesis [Note 27 in text]; (5) Minnesota Population Center. National Historical Geographic Information System, version 2.0. Minneapolis, MN: University of Minnesota; 2011; (6) Knopman DS, et al. Passive case-finding for Alzheimer's disease and dementia in two U.S. communities [Note 28 in text]; (7) Graham JE, et al. Prevalence and severity of cognitive impairment with and without dementia in an elderly population [Note 29 in text]. **NOTES** People eligible for the NYUCI were ages 65–100 living in the community with a spouse or adult child caregiver. All incident cases were assumed to be of mild severity. The primary-case analysis assumed that all eligible caregivers participated in the NYUCI, and it reflected a 20 percent upward adjustment for potentially improved recognition of dementia in clinical practice since rates of disease were assessed in the 1990s. The alternative-case analyses with upward adjustments used different percentages to reflect potentially improved recognition of dementia. The alternative-case analysis with a 50 percent reduction, relative to the primary-case analysis, reflected a lower prevalence of dementia recognized in primary care settings.

Alzheimer's Disease (CERAD) database.<sup>30,34</sup>

CERAD enrolled 1,145 patients with Alzheimer's disease from twenty-two academic medical centers between 1986 and 1995, and its data have been widely used in health economic evaluations of dementia care.<sup>35–37</sup> The members of this relatively large and fairly diverse enrolled population receive annual assessments. CERAD data enable reliable estimates of severity-specific transition probabilities before enhanced caregiver interventions became widely available.

We assumed, as has been observed in CERAD and other Alzheimer's disease registries, that residential placement rates increased by disease severity but did not differ by duration within a given disease stage.<sup>30,38</sup> No data similar to those in the CERAD database were available for patients with dementias other than Alzheimer's disease. Thus, we assumed that the rates of transitions as observed in the CERAD data applied to all people with dementia.

We reduced the probability of permanent residential placement for people whose caregivers received enhanced services, according to the results observed in the NYUCI randomized trial that was conducted at the NYU Langone Medical Center. This trial is by far the largest and longest application of enhanced caregiver support to date.<sup>16</sup>

We adjusted the CERAD-based probabilities of residential placement for the 28.3 percent reduced risk of placement compared with usual-care controls reported for the NYUCI. We varied this effect size based on the variability in estimated risks in the alternative-case analyses (Exhibit 2).

We based the annual probability of death on statewide mortality rates calculated by the Center for Health Statistics, Minnesota Department of Health, to conform to the model's specifications. In our primary-case analyses we assumed a differential mortality of 1.5 for moderate dementia and adjusted for mild and severe disease based on the estimated likelihood of death by severity in the CERAD data.<sup>39</sup> We assumed that mortality was unaffected by the NYUCI.

**COSTS** We estimated direct costs for people with dementia by residence (community versus residential facility) based on analyses of the Medicare Current Beneficiary Survey (MCBS).<sup>34</sup> The costs were those for medical care and the use of nursing homes and assisted living facilities across payer types (including out-of-pocket expenses). We adjusted these costs to reflect prices in Minnesota and stratified them by disease severity.<sup>39,40</sup>

The estimated annual direct costs for people with dementia living in the community were

## CAREGIVER SUPPORT MODELS

## EXHIBIT 2

Estimated Annual Probabilities Of Residential Placement For People With Dementia In The Community, With And Without The New York University Caregiver Intervention (NYUCI)

Level of dementia		Probability of transition			
		With NYUCI			
		Without NYUCI	Primary-case analysis	Alternative-case analyses	
In community (starting status)	In residential facility* (transitioned status)			Larger NYUCI effect	Smaller NYUCI effect
Mild	Mild	2.33%	1.68%	1.26%	2.24%
	Moderate	1.22	0.88	0.66	1.17
Moderate	Severe	0.16	0.12	0.09	0.15
	Moderate	6.22	4.53	3.53	5.97
Severe	Severe	3.73	2.72	2.06	3.58
	Severe	21.90	16.38	12.59	21.14

**SOURCE** Authors' analysis of data from the following sources: (1) Mittelman MS, et al. Improving caregiver well-being delays nursing home placement of patients with Alzheimer disease (Note 1.6 in text); (2) Neumann PJ, et al. Measuring Alzheimer's disease progression with transition probabilities (Note 3.0 in text). **NOTES** The alternative-case analyses reflected larger and smaller effects of the NYUCI based on the 95% confidence interval for the adjusted risk of residential placement observed in the NYUCI (see Note 1.6 in text). \*Assisted living facility or nursing home.

\$16,177 for mild dementia, \$20,643 for moderate dementia, and \$32,213 for severe disease. The corresponding estimates for people with dementia in residential facilities were \$43,299, \$55,253, and \$86,221. The NYUCI did not assess direct health care costs. Therefore, we assumed that these MCBS-based annual costs per person with dementia were not affected by the NYUCI.

**ANALYSIS** In our model, people with dementia progressed through the three health states—incurring costs over a period of fifteen years—under the two scenarios described above. Our analyses projected and compared population-level direct costs by year of follow-up, discounted 3 percent annually.

The model tracked outcomes by sex and age group for subgroup analyses. In addition, we performed several alternative-case analyses to test the strength of the results.

**LIMITATIONS** Assembling the multiple parameters required for our model entailed making several assumptions and therefore imposed limitations on our results. Rates of dementia prevalence and incidence show considerable variation, likely based on trends in clinical diagnosis, methods of ascertainment, sampling strategies, and varying access to health care.<sup>1,28</sup>

We performed adjustments and analyses using alternative rates of disease detection. However, the current and future rates of clinically diagnosed cases of dementia (as opposed to cases identified by proactive screening) in Minnesota remain uncertain.

Furthermore, rates of dementia increase with age but are generally considered to be unchanging over time. Our model followed this consen-

sus. Recent studies from Europe have raised the possibility that rates are declining.<sup>41</sup> No recent US studies exist, but if rates are decreasing, our estimated savings are exaggerated.

Residential placement rates based on CERAD data may not apply across Minnesota, even though CERAD enrolled patients from national academic medical centers. Nonetheless, we assumed that transitions to nursing homes for patients with Alzheimer's disease found in CERAD data applied to all people with dementia and to other institutional settings. The impact of these assumptions on our results is unclear.

For estimated direct costs, our model assumed that future patterns of care would remain similar to current ones. If the relative difference in costs between community- and facility-based care changed, our results would differ.

People with dementia who remain in the community with the NYUCI might incur marginally greater costs for support services than the average community-dwelling person with dementia as assessed in the MCBS. If that were the case, our estimated savings would be overstated. However, our results might be conservative since the NYUCI (and therefore our model) did not assess the potentially cost-saving impact of reduced use of emergency departments, hospitals, and pharmaceuticals that might occur with enhanced caregiver support.<sup>44</sup>

The NYUCI did not assess the impact of enhanced caregiver supports on the hours spent by informal caregivers. Furthermore, no consensus exists regarding methods to value this caregiver burden. Thus, we chose to focus only on direct costs and omitted the substantial indirect costs

associated with care provided by informal caregivers.<sup>7</sup> If time spent caregiving was greatly reduced in the NYUCI, as was observed in REACH II, then inclusion of these indirect costs would increase our estimated cost savings.<sup>18</sup>

We also did not consider the indirect effects on caregivers of reduced depression and associated health care costs.<sup>12</sup> Nor did we perform a cost-effectiveness analysis that incorporated the potential effects on mortality and quality of life associated with delayed residential placement. Including these additional caregiver outcomes, as well as mortality and quality-of-life effects for the person with dementia, might demonstrate different types of NYUCI benefits.

### Study Results

Our model predicted a 38.6 percent increase in the prevalence of people with dementia in Minnesota from 2010 to 2025 who initially lived in the community with a spouse or adult child caregiver. Exhibit 3 shows the proportion of our population in each health state with and without the NYUCI for selected years of follow-up.

With the NYUCI, the proportion of people with dementia remaining in the community increased by approximately 5 percent at year 3, compared to the results without the NYUCI, and that difference persisted in years 5, 10, and 15. For instance, the proportion of people remaining in the community increased from 60.5 percent to 65.4 percent, from 58.4 percent to 63.3 percent, and from 59.4 percent to 64.0 percent in years 5, 10, and 15, respectively (Exhibit 3). In addition, the number of people who died in an institution from 2010 to 2025 decreased from 32,897 to 26,557 a 19.3 percent reduction with the NYUCI. However, the number of people who died in the community during these fifteen years increased from 64,137 to 70,286, a 9.6 percent increase with the NYUCI (data not shown).

The estimated cumulative population-level potential cost savings associated with the NYUCI were substantial. They increased from \$289 million after five years to \$996 million after fifteen years (Exhibit 4). At the population level, estimated savings with the NYUCI in residential placement costs after fifteen years were partially offset by the higher costs estimated for the care of people with dementia in the community, because of the higher proportion of community-dwelling patients and no assumed savings in per person costs with the NYUCI.

Analyses by age group suggested that the cumulative savings would be highest for people with dementia ages 75–84 (\$432 million), reflecting projected population trends for Minnesota. In addition, cumulative savings would be

higher for women than for men (\$616 million versus \$380 million).

We performed alternative-case analyses on the variables and methods of greatest uncertainty. The variability in estimated cost savings was most affected by the NYUCI's effect size and the assumed prevalence and incidence of eligible people with dementia.

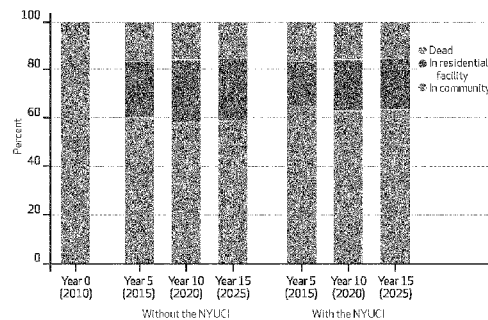
For instance, we varied the NYUCI effect based on the estimated 95% confidence interval for the risk of residential placement.<sup>16</sup> The potential (undiscounted) savings with the NYUCI differed from \$135 million to \$2.3 billion, compared to the primary-case analysis (undiscounted) result of \$1.24 billion. Similarly, we assumed a 50 percent reduction in the prevalence and incidence of dementia, to reflect a lower prevalence of dementia recognized in primary care settings—where most people with dementia would be offered a chance to participate in the NYUCI. In that case, the estimated (undiscounted) savings were reduced to \$608 million.

We constructed best- and worst-case scenarios by varying several model inputs simultaneously. The best-case scenario assumed higher numbers of people with dementia, a lower mortality rate, and a larger intervention effect, and it did not discount costs. In contrast, the worst-case scenario assumed lower numbers of people with dementia, a higher mortality rate, a smaller intervention effect, and a higher discount rate for costs, compared with the primary-case analysis.

Potential savings in these best- and worst-case

EXHIBIT 3

Distribution Of Three Health States Among People With Dementia In Minnesota Eligible For The New York University Caregiver Intervention (NYUCI), By Year



SOURCE: Authors' analysis of model results. NOTE: People eligible for the NYUCI were ages 65–100 who initially were living in the community with a spouse or adult child caregiver.

# CAREGIVER SUPPORT MODELS

## EXHIBIT 4

### Potential Cumulative Direct Cost Savings With New York University Caregiver Intervention (NYUCI) For People With Dementia In Minnesota, By Year

Year	Cumulative savings for people with dementia (\$)		
	All	In residential facility*	In community
5 (2015)	288,954,986	461,172,862	-172,207,876
10 (2020)	673,127,779	1,072,761,818	-399,634,039
15 (2025)	996,033,190	1,618,120,046	-622,086,856

**sources** Authors' analysis of model results. **notes** Direct costs (in discounted 2011 dollars) are medical and facility costs. Positive dollar values indicate potential population-level savings with NYUCI compared to without NYUCI. Negative dollar values for people living in the community indicate higher population-level costs with NYUCI compared to without NYUCI because more people with dementia remained in the community. \*Assisted living facility or nursing home.

scenarios were estimated at \$2.64 billion and at nearly \$100 million, respectively, driven largely by the variation in the assumed NYUCI effect. (See the online Appendix for further details and complete results from the alternative-case analyses.)<sup>21</sup>

#### Discussion

A key question for policy makers is how to reduce the massive increase in dementia-related expenditures that is anticipated as the US population ages. Our study demonstrates that if a program providing multicomponent support for informal caregivers of community-dwelling patients with dementia were widely available and used, it could lead to substantial savings in direct health care spending. That would be the case even if there were no major breakthrough in the prevention or treatment of dementia.

Our model projected \$996 million in cumulative savings in direct costs over fifteen years in Minnesota. This estimate was highly sensitive to alternative assumptions. Nonetheless, the savings remained substantial in alternative-case analyses, ranging from \$100 million to \$2.6 billion.

The estimated savings were driven by the demonstrated effectiveness of the NYUCI in delaying residential placement. In addition to offering a potential financial benefit for payers and society at large, that delay is concordant with the wishes of most people with dementia and their caregivers to avoid or delay residential placement. Consistent with this scenario, our model projected that after fifteen years of having the NYUCI available statewide, 19.3 percent fewer people with dementia would die in institutions.

Several studies have estimated the expenses attributable to dementia, but estimates of the economic impact of nonpharmacologic interventions are rare. David Weimer and Mark Sager simulated the early identification of Alzheimer's

disease combined with pharmaceutical treatment and caregiver support in Wisconsin and found the approach fiscally attractive.<sup>41</sup> However, the efficacy of drug treatment remains controversial, and Weimer and Sager assumed that caregiver support was equally effective in cases identified by proactive screening—which is not the standard of practice in most clinical settings—and in clinically diagnosed cases. To our knowledge, ours is the only model to estimate the population-level cost savings of enhanced caregiver support under current practices of identifying patients with dementia.

The observed sensitivity of our results to the assumed NYUCI effect size raises the issue of the NYUCI's generalizability. Treatment in an urban university hospital setting among caregivers of limited ethnic diversity may differ in effectiveness from treatment applied statewide. Cultural, demographic, and socioeconomic factors such as interest in counseling and levels of education and income may alter rates of program completion and, ultimately, residential placement.<sup>23</sup>

However, substantially delayed residential placement with the NYUCI was observed not just in the New York metropolitan area with spouse caregivers, but also in Minnesota with adult child caregivers. This suggests that the NYUCI may be generalizable to other populations.<sup>17</sup>

We designed our model to investigate savings under the assumption of widespread program availability and complete participation, without factoring in program costs, so we could determine whether sufficient economic potential existed to warrant analyses of return on investment. The sensitivity of our estimated savings to the assumed NYUCI effect size and number of participants suggests that actual savings in Minnesota could differ greatly depending on the fidelity with which the NYUCI was implemented, program costs, and caregiver participation rates. In fact, these important factors varied greatly across sites in the Minnesota NYUCI demonstration project, which indicates the need for further research on the effective statewide replication of the NYUCI.<sup>14</sup>

#### Conclusion

Our results indicate that enhanced caregiver support is a promising way to moderate the growing economic burden of dementia. By quantifying the potential savings for a single state, we demonstrated that substantial long-term savings in direct costs would be possible even without a breakthrough in the pharmacologic treatment of dementia. Our findings are relevant to the larger policy question of where resources should be directed in the fight against dementia. Multi-