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TAKING A TOLL ON FAMILIES AND THE ECONOMY: THE RISING COST OF ALZHEIMER'S IN AMERICA

HEARING

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS

UNITED STATES SENATE

ONE HUNDRED THIRTEENTH CONGRESS

SECOND SESSION

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FEBRUARY 26, 2014—WASHINGTON, DC

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TAKING A TOLL ON FAMILIES AND THE ECONOMY: THE RISING COST OF ALZHEIMER'S IN AMERICA

WEDNESDAY, FEBRUARY 26, 2014

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 2:03 p.m., in room SD–106, Dirksen Senate Office Building, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin, Mikulski, Moran, Cochran, Shelby, Alexander, and Kirk.

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. The Senate Appropriations Subcommittee on Labor, Health, Human Services, Education, and Related Agencies will please come to order.

Today's hearing is the sixth that this subcommittee has held since 2000 focusing on Alzheimer's disease, the burden of the disease, the state of the research, and the challenges faced by caregivers. Going back many years, we have heard predictions from experts about the far-reaching consequences this disease will have on the quality of life for American families and the burden it will place on our economy in the years ahead.

Last April, a major study predicted that these consequences will be far greater than anyone even previously imagined. We will hear from the author of that study today on our second panel. I won't steal his thunder, but I do note that this study commanded the attention of the Nation and particularly this subcommittee.

There are few Americans whose life hasn't been touched in some way by Alzheimer's disease, whether through a family member or a friend. It is the most common form of dementia among older Americans, and its risk increases with increasing age. For those living with the disease, its ravages get worse over time, as does the burden on their families and on society.

The number of Americans living with Alzheimer's has doubled since 1980, and the growth will almost certainly accelerate as the baby boom generation continues to retire in the future.

The Federal Government's involvement in Alzheimer's disease research began in 1976 when three institutes at the National Institutes of Health (NIH) invested a total of $3.8 million in research

into the cause of this disease. We now spend approximately $0.5 billion each year on research into Alzheimer's disease.

We have had some successes along the way. But the harsh reality is that we still do not know how to prevent, reverse, or definitively diagnose Alzheimer's disease. More research is desperately and urgently needed.

This subcommittee has always adhered to a strict policy of not earmarking money for particular diseases, or definitively saying what diseases the money has to go to—a good policy. Instead, we allow the peer-review process to support the most promising science. However, we were able to provide a $131 million increase for the National Institute on Aging in the recent fiscal year 2014 Omnibus, again with the expectation that promising science in Alzheimer's disease will be supported.

We have a distinguished panel of experts here today: Scientists, economists, patients, family members. We also have quite an audience. Let me welcome representatives of the Alzheimer's Association, some of you came a long way to be here today. We thank you for your tireless work to educate Members of Congress and the press about the need to do more to help you and your loved ones.

Also in the audience are students from the University of Virginia. These young people are spending a day here learning about budget and appropriations, and we welcome all of you here also.

[The information follows:]

These students were brought here by one of our retired Senate Appropriators, Galan Fountain, he was the clerk on Agriculture Subcommittee for a long time. The students with him today are: Abraham Axler, Andrew Boyer, Luke Handley, William Henagan, Ian Van Der Hoven, Drew Ricciardone, and Blake Sinyard. I hope you will learn something today.

Senator HARKIN. On our first panel, of course, we'll hear from Dr. Francis Collins, the distinguished Director of the National Institutes of Health, who will discuss the current state of science and what kinds of research are most likely to benefit from our appropriations. I would note we are also very fortunate to have both Dr. Story Landis of the National Institute of Neurological Disorders and Stroke, and Dr. Richard Hodes of the National Institute on Aging, also here to answer questions.

On the second panel, we'll hear from Dr. Michael Hurd, the researcher who wrote the landmark RAND study that I mentioned earlier. And we'll be joined by two individuals personally impacted by this devastating disease.

PREPARED STATEMENT

Finally, former Congressmen Dennis Moore of Kansas is here today. As a long-time colleague and friend of his, I was saddened to learn of his Alzheimer's diagnosis so soon after his retirement from the House of Representatives. It's no surprise to anyone who knows him, though, that his first instinct was to educate others and continue serving the public through advocacy and education.

So I look forward to hearing from each of our distinguished experts.

[The statement follows:]

PREPARED STATEMENT OF SENATOR TOM HARKIN

Today's hearing is the sixth this subcommittee has held since 2000 focusing on Alzheimer's disease—the burden of this disease, the state of research, and the challenges faced by caregivers.

Going back many years, we have heard predictions from experts about the far-reaching consequences this disease will have on the quality of life for American families and the burden it will place on our economy in the years ahead. Last April, a major study predicted that those consequences will be far greater than anyone previously imagined. We will hear from the author of that study today, so I won't steal his thunder now. But I note that this study commanded the attention of the Nation and, in particular, this subcommittee.

There are few Americans whose life hasn't been touched in some way by Alzheimer's disease—whether through a family member or a friend. It is the most common form of dementia among older Americans, and its risk increases with increasing age. For those living with the disease, its ravages get worse over time—as does the burden on society. The number of Americans living with Alzheimer's has doubled since 1980, and the growth will almost certainly accelerate as the Baby Boom generation continues to enter its senior years.

The Federal Government's involvement in Alzheimer's disease research began in 1976 when three Institutes at the National Institutes of Health invested a total of $3.8 million in research into the cause of the disease. We now spend approximately half a billion dollars each year on research into Alzheimer's disease.

We've had successes along the way. But the harsh reality is that we still do not know how to prevent, reverse, or definitively diagnose Alzheimer's disease. More research is desperately and urgently needed.

This subcommittee has always adhered to a strict policy of not earmarking money for particular diseases, instead allowing the peer-review process to support the most promising science. However, we were able to provide $131 million increase for the National Institute on Aging in the recent fiscal year 2014 Omnibus, with the expectation that promising science in Alzheimer's disease will be supported.

We have a distinguished panel of experts here today: Scientists, economists, patients, and family members. We also have quite an audience. Let me welcome representatives of the Alzheimer's Association, some of whom came a long way to be here today. We thank you all for your tireless work to educate members of Congress and the press about the need to do more to help you and your loved ones. Also in the audience are students from the University of Virginia. These young people are spending a day here learning about budget and appropriations. We welcome all of you.

First, we'll hear from Dr. Francis Collins, the distinguished director of the National Institutes of Health, who will discuss the current state of science and what kinds of research are the most likely to benefit from the fiscal year 2014 appropriation.

I would also note that we are very fortunate to have both Dr. Story Landis of the National Institute for Neurological Disorders and Stroke, and Dr. Richard Hodes of the National Institute on Aging, here to answer questions.

On the second panel, we'll hear from Dr. Michael Hurd, the researcher who wrote the landmark Rand study that I mentioned earlier. He will explain the projected growth in the disease and the impact on our economy.

We are also joined by two individuals who are personally impacted by this devastating disease. Mr. Seth Rogen is an accomplished actor, writer, and producer who is known for his talent in dealing with some very serious topics through humor, including non-Hodgkin's lymphoma in the film "50/50," and the challenges of suddenly and unexpectedly becoming a father in the movie "Knocked Up." And, yes, for the record, I believe this is the first time the words "knocked up" have been uttered in a congressional hearing! More importantly for our purposes today, Mr. Rogen is a tireless and effective champion for the Alzheimer's Association. He will speak about his experience marrying into a family with a history of Alzheimer's disease, and supporting a spouse in caregiving.

Finally, former Congressman Dennis Moore of Kansas is here, today. As a longtime colleague and friend of the Congressman, I was saddened to learn of his Alzheimer's diagnosis so soon after his retirement from the House of Representatives. It is no surprise to anyone who knows him, though, that his first instinct was to educate others and continue serving the public through advocacy and education. He is an inspiration.

I look forward to hearing from each of these distinguished experts. Before we turn to the first panel, I'll yield the microphone to Senator Moran for his opening statement.

Senator HARKIN. Before we turn to the first panel, I'll yield to Senator Moran for his opening statement.

STATEMENT OF SENATOR JERRY MORAN

Senator MORAN. Mr. Chairman, thank you very much. I'll make my remarks relatively brief because I would not want to detain or delay the testimony of our distinguished experts. But I very much appreciate what you just said, and I appreciate your willingness to conduct this hearing on Alzheimer's disease. In my view, this could be the defining disease of our generation.

I'm pleased, as you indicated, to have former Congressman, Kansas Congressman Dennis Moore testify on his experience with living with Alzheimer's. I appreciate Dennis as a friend, and I also appreciate his desire to take his own difficult challenges and focus them in helping other individuals and families struggling with this horrific disease. He has used the years since his diagnosis to advocate for those living with the disease. And in Dennis's words, "We need to find a cure, like next week." I could not agree more.

Mr. Chairman, every 68 seconds, someone in America develops Alzheimer's disease, a devastating, irreversible brain disease that slowly destroys an individual's cognitive functioning, including memory and thought. Alzheimer's currently affects more than 5.2 million people in the United States and more than 44 million worldwide, according to the Alzheimer's Disease International.

As our population ages, the number of people diagnosed with Alzheimer's after the age of 65 will double every 5 years, while the number of individuals 85 years and older with the disease will triple by 2050. Already, Alzheimer's is the sixth leading cause of death in the United States, and there is currently no cure, no diagnostic test, no treatment. With the baby boomer generation aging, Alzheimer's disease becomes more prevalent and the need to confront the pending healthcare crisis has become ever more urgent.

As you indicated, the study by RAND Corporation stated the cost of dementia is projected to double over the next 30 years, surpassing healthcare expenses for both heart disease and cancer. Alzheimer's disease has become a disease to define a generation, but if we focus our priorities on our research capacity, it does not need to continue to be an inevitable part of the aging process.

For every $270 that Medicare and Medicaid spends caring for individuals with Alzheimer's, the Federal Government only spends $1 on Alzheimer's research. In fiscal year 2014, the Omnibus Appropriation Bill provided for an increase of $100 million for Alzheimer's research. And I appreciate working with you to accomplish that goal.

But without a way to prevent, cure, or effectively treat Alzheimer's, it will be difficult, if not impossible, to rein in our Nation's healthcare costs. In this subcommittee and in the full committee, you've often heard me say that I really appreciate dealing with the issue of healthcare and health research.

Health research is an opportunity for those who are the most fiscally conservative and those who are the most caring and compassionate to come together, because we can save tremendous amounts of money and we can improve people's lives by doing so. It's an opportunity for all of us to work together to find a solution.

One study has found that a breakthrough against Alzheimer's that delays the onset of the disease by 5 years would mean a total savings of $447 billion by 2050. Now is the time that, as a nation, that we fully commit to defeating one of the greatest threats to our health of Americans and the financial wellbeing of our country.

1962, President Kennedy called the Nation to action to reach the moon by the end of that decade. We need to commit ourselves to the goal of advancing Alzheimer's research with the same ambition and urgency. Over the next decade, we must strive to achieve not only an effective treatment, but a cure for Alzheimer's. Alzheimer's is, as I say, the defining challenge of our generation. We need to find a cure, like next week.

The gift that we all could provide, every American and every American family, is a special gift. It's called the gift of hope.

Mr. Chairman, thank you very much.

Senator HARKIN. Thank you, Senator Moran.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Senator HARKIN. Now we welcome our first panel. Dr. Francis Collins, the Director of the National Institutes of Health, overseeing the work of the largest biomedical research entity in the world that spans the spectrum from basic to clinical research.

Dr. Collins is a physician geneticist noted for his landmark discoveries of disease genes, his leadership of the Human Genome Project, which he started in 1993, culminated in April 2003. He continued on in that capacity until 2008, and is now the Director of the National Institutes of Health.

He is an elected member of the Institute of Medicine and the National Academy of Sciences. He was awarded the Presidential Medal of Freedom in November 2007, and received the National Medal of Science in 2009.

I also want to welcome Dr. Richard Hodes, the Director of the National Institute of Aging. He has held this position since 1993. This is our primary Federal agency supporting and conducting Alzheimer's disease research. As director, Dr. Hodes oversees studies of the basic, clinical, epidemiological, and social aspects of aging.

And Dr. Story Landis, the Director of the National Institute of Neurological Disorders and Stroke (NINDS); she has served as its director since 2003. NINDS, as we call it, supports and conducts basic translational and clinical research on the normal and diseased brain system.

So we welcome you all here. Dr. Collins, again, thank you for your leadership through all these years, both first for the human genome project and now for the entire National Institutes of Health. Dr. Collins, welcome, and please proceed.

STATEMENT OF FRANCIS S. COLLINS, M.D., Ph.D., DIRECTOR

ACCOMPANIED BY:

RICHARD J. HODES, M.D., DIRECTOR, NATIONAL INSTITUTE ON AGING

STORY C. LANDIS, Ph.D., DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Dr. COLLINS. Thank you. Good afternoon, Mr. Chairman, and members of the subcommittee. As always, it's a great honor to appear before you, along with my two distinguished colleagues. We're here to discuss the latest research into Alzheimer's disease and related dementias. Before getting into the science, I would like to thank you for the recent fiscal year 2014 Omnibus appropriation for NIH.

This subcommittee came together in a bipartisan way to reverse the deeply troubling downward spiral of support that NIH has found costing us about 25 percent of our purchasing power for research over the last 10 years. While difficult tradeoffs did not ultimately make it possible in fiscal year 2014 to completely reverse the devastating effects of the fiscal year 2013 sequester, we are gratified that NIH was at least able to turn that corner.

THE GROWING PUBLIC HEALTH CRISIS

Let me begin my report on the scientific challenges and promises that we face in Alzheimer's by underscoring that all of the work that I'm going to discuss is really about helping patients and their loved ones. That's what we are committed to, and we know you are, too.

One of the most famous of those patients is country music star Glenn Campbell. Along with a number of you, I was thrilled to be on hand last spring when Glenn was honored at the Alzheimer's Association gala. There's a photo of him and me with an autographed guitar pick that he gave me, which is my prized possession, since I'm a musician also. To see his great talents, a national treasure, really, so compromised by this devastating disease is a reminder of just how much is at stake.

We've heard the sobering statistics, and they've been already cited in opening statements by Senator Harkin and Senator Moran, about the wave of diseases that will break over the United States as the baby boom generation ages. Already about 5 million Americans have been diagnosed with Alzheimer's disease, and hundreds of thousands more affected with other types of dementia.

Without new scientific breakthroughs, those numbers will continue to rise, along with the terrible toll on our Nation's health and its economy that this disease creates. As you've mentioned already, the Alzheimer's Association estimates that our Nation is currently spending more than $200 billion a year on care of people with Alzheimer's. And those costs are projected to soar to $1.2 trillion annually by 2050.

To put this into context, consider how much our Nation is spending on medical research. NIH's budget was $29.1 billion in fiscal year 2013, with $504 million of that devoted to Alzheimer's disease research. We are thrilled that the fiscal year 2014 Omnibus includes an additional $100 million for research on diseases of aging, including Alzheimer's disease. But as you can see, the investment pales in comparisons to the cost.

REVVING UP RESEARCH

In our effort to find ways to prevent, delay, or treat Alzheimer's and other dementias, we are bringing to bear all possible technologies, from genomics to imaging to big data tools. But this task is immense. There are a great many things we still don't know about how the normal brain functions, let alone a brain with Alzheimer's.

In fact, this month's National Geographic provides a glimpse at what NIH-funded researchers are doing to explore what's been called biology's last frontier, the human brain. And I couldn't help but notice Scientific American, just on the newsstands, has the brain on its cover also for the current issue.

As you know, NIH is leading the initiative called Brain Research Through Advancing Innovative Neurotechnologies. That's an acronym, B–R–A–I–N. And we are grateful for the subcommittee's support for this pioneering venture in the fiscal year 2014 Omnibus. The BRAIN initiative, which the President has called "the next great American project," will create tools capable of examining the

activity of the brain's billions of nerve cells, networks, and pathways, in real time. That's sure to be of tremendous value to researchers who are working on autism, schizophrenia, epilepsy, traumatic brain injury, depression, Parkinson's disease, and, yes, all forms of dementia, including Alzheimer's.

Let me tell you of one recent finding in brain science that's generated a lot of excitement. It involves a protein called tau, T–A–U. This is one of the major culprits in Alzheimer's disease. The other one is amyloid. To give you a better idea about how tau affects the brain, I'd like to show you this short video, and I'll explain what you're looking at.

In normal brain cells, this tau protein that you see here stabilizes structures that are called microtubules and that are involved in internal transport. That's what you see happening here with this amazing machine inside the cell. But in Alzheimer's, the tau separates from those microtubules, causing them to fall apart. Strands of this tau protein then combine to form tangles within the neuron, disabling the transport system and destroying the cell, ultimately, as you see in this animation. Neurons in certain parts of the brain disconnect from each other, and eventually they die, causing memory loss.

The effect on the brain? The brain shrinks and begins to lose function, showing you here what happens in advanced Alzheimer's disease, as the brain's substance is gradually shrunken away by the loss of brain cells.

Now, one of the exciting findings recently is we've discovered that this tau protein, which we used to think was just inside cells, and therefore kind of inaccessible, that it's actually transferred from neuron to neuron, almost like an infection inside the brain. That may sound a little scary, but for us it means opportunities for therapy. Proteins that spend their whole existence inside cells, they're hard to attack. But if we can find a way to prevent that cell-to-cell transmission, perhaps by blocking tau with an antibody, we might be able to stop Alzheimer's in its tracks.

Still, new drugs won't do a whole lot of good unless we can identify accurately those who might benefit from them. To do that, we need better ways to diagnose Alzheimer's disease and to do so as early as possible. Until recently, we could only conclusively diagnose Alzheimer's after someone had died. This involved examining slides of brain tissue, like you see here, for the classic signs of Alzheimer's disease, amyloid plaques and tangles, neurofibrillary tangles made up of tau.

BRAIN IMAGING

But now, thanks to recent advances in imaging technology, we can detect signs of Alzheimer's inside living brains. What you see here are PET scans of two living people. On the top, an Alzheimer's patient whose brain lights up with markers for both tau on the left and amyloid on the right. And on the bottom, you see a normal brain. Quite a difference.

Importantly, these scans are able to detect deposits of tau and amyloid years before the onset of symptoms. That should improve our ability to diagnose and, hopefully, treat Alzheimer's at a much earlier stage before so many brain cells have been lost.

It may also be possible to use these scans or other biochemical measures in blood or spinal fluid to see if a new therapy is working even before it has an impact on the course of memory loss. Those kinds of predictive measures are called biomarkers, and one of our top priorities is to find and validate those kinds of biomarkers for clinical use so we'll know if treatments are working, as quickly as possible.

This leads me to the crucial issue of clinical trials. Until a couple of years ago, we focused primarily on trying to treat people with unmistakable symptoms of advanced Alzheimer's, those who had already lost many of their brain cells. The results, I'm sorry to say, have been almost entirely discouraging. But today, we are focused on earlier interventions. So many of our newest clinical trials are actually looking at pre-symptomatic patients who are at high risk, but don't yet show symptoms.

One of these is a 5-year clinical trial to see if an antibody treatment aimed at amyloid can prevent cognitive decline by starting a treatment before any symptoms appear. In a unique situation, we're testing this among members of a very large family in Colombia, as well as some U.S. patients, who share a dominantly inherited genetic mutation that causes Alzheimer's at about age 45 and places those individuals at extremely high risk.

A second study, the Anti-Amyloid Treatment in Asymptomatic Alzheimer's, also just called A4 because that's easier to say, this will test another antibody in 1,000 volunteers aged 65 to 85. These individuals do not yet have any symptoms of Alzheimer's, but by PET scans they're found to have sufficient amyloid in their brain to be considered at risk, like the person in the middle here. This is somebody with completely normal function, but there's a lot of amyloid there. Is that somebody who will go on to Alzheimer's? Is this the moment to intervene? This is a great opportunity, again, to try therapeutics before there has been major damage done to the brain.

All of these studies will hinge upon validated biomarkers, as I mentioned a minute ago, which is why I'm especially excited to announce the Accelerating Medicines Partnership, or A–M–P, AMP, earlier this month. AMP is an unprecedented collaboration between NIH and 10 pharmaceutical firms and will accelerate identification and testing of drug targets for Alzheimer's disease, diabetes, rheumatoid arthritis, and Lupus.

About $230 million will be invested over 5 years, with NIH and industry contributing equally; we both have skin in the game. For Alzheimer's disease, AMP will incorporate an expanded set of biomarkers into four ongoing trials designed to delay or prevent disease, and then evaluate those for effectiveness. Another part of the project will develop detailed maps of molecular networks in the Alzheimer's brain, potentially pointing to new therapeutic targets.

EXPANDED FUNDING, EXPANDED DISCOVERY

And empowered by the $100 million fiscal year 2014 budget increase for research on diseases of aging, NIH will be able to make major investments in four cutting-edge areas of dementia research that we would otherwise not have been able to pursue: Genetic analysis, optogenetics, stem cells, and translational centers.

Similarly, we will now be able to fund a significant number of investigator-initiated research grants, or RO1s, that otherwise would not have made the pay line and would have gone unsupported.

So, Mr. Chairman and members of the subcommittee, I began talking about people with Alzheimer's disease. I'd like to close with a tribute to another deeply affected group, and represented, I'm sure, by many in this room: The people who care for their loved ones as they slip into those deepening shadows of Alzheimer's and dementia.

One such caregiver is Meryl Comer, friend of mine, a former TV newscaster, who has cared full time for her husband, Harvey Gralnick, in their home for nearly 20 years. Harvey was a leading investigator at NIH until he began showing signs of confusion in his late 50s.

Just last week, Meryl shared with me these lines from a book that she's working on about her experience, entitled, poignantly, Slow Dancing with a Stranger. Her words: "As I write these words, a faint glow of light fills the room I share with Harvey. He's always present even though he is absent. The person I knew is lost, but not gone." So heartbreaking and so true.

PREPARED STATEMENT

What Harvey has suffered, what Meryl has suffered is what inspires all of us in Alzheimer's research to fight back against this insidious disease as vigorously and swiftly as possible. That is our commitment, and there is no time to waste.

On behalf of my colleagues, thank you for this opportunity. We look forward to your questions.

[The statement follows:]

PREPARED STATEMENT OF DR. FRANCIS S. COLLINS, DR. RICHARD J. HODES, AND DR. STORY C. LANDIS

Good afternoon, Mr. Chairman and distinguished members of the committee. I am Francis S. Collins, M.D., Ph.D., the Director of the National Institutes of Health (NIH). I have with me Story C. Landis, Ph.D., Director of the National Institute of Neurological Disorders and Stroke (NINDS), and Richard J. Hodes, M.D., Director of the National Institute on Aging (NIA). 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.

First, however, I would like to thank you, Mr. Chairman, and Ranking Member Moran, as well as your colleagues on the committee, for your unflagging championship of NIH's research mission, especially our research on Alzheimer's disease. I would particularly like to acknowledge the significant increase in funding that you have provided to NIH for fiscal year 2014, in order to bolster our support for research on aging. I am happy to share with you some of our plans for these additional funds, as well as some exciting recent scientific discoveries and new initiatives.

THE GROWING PUBLIC HEALTH CRISIS

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. While Alzheimer's disease is the most common cause of dementia among older people, other forms exist, including frontotemporal dementia, Lewy body dementia, and mixed and vascular dementias. Although treatment can help manage symptoms in some people, there is currently no cure for these devastating diseases.

As many as 5 million people age 65 and older suffer from Alzheimer's disease in the United States alone, and we expect these numbers to increase exponentially as the U.S. population continues to age. Globally, the statistics are truly dire: Results of a recent meta-analysis suggest 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.

This disease is not just a burden on our health; it is also a burden on our economy. Recently, NIH-supported economists calculated that the costs in 2010 to the U.S. healthcare and long-term care systems for caring for people with Alzheimer's disease were between $159 billion and $215 billion, depending on how caregiver costs were assessed. The researchers estimated direct costs of dementia care purchased in the market in 2010 at $109 billion. To place that figure in context, that same year, direct health costs for heart disease and cancer were estimated at $102 billion and $77 billion, respectively. And again, unless effective interventions are developed, those costs will rise dramatically with the increase in the numbers of senior citizens in coming decades.

AN EXPLOSION OF KNOWLEDGE

The good news, in the face of these grim statistics, is that we have made tremendous strides in our understanding of the basic mechanisms of Alzheimer's disease within the last 5 years, and this new understanding has led to entirely new research paradigms: Both for studying the disease in the laboratory and managing it in the clinic.

The first set of discoveries I'd like to discuss have to do with the genetics of Alzheimer's disease. Until 2009, only one genetic variant, APOE e4, had been shown to increase the risk of late-onset Alzheimer's disease. However, with the advent of genome wide association studies (GWAS) and other high throughput technologies, the list of known gene risk factors grew substantially over the next few years, and in 2013, the largest GWAS ever conducted identified a total of 11 genetic risk factors. The research conducted by the International Genomic Alzheimer's Project—a collaborative, international study supported in part by the NIH—strengthens evidence about the involvement of particular pathways in the disease, such as inflammation, lipid metabolism, and amyloid deposition, and also points to entirely new molecular pathways that were not known to be involved.

In the clinical arena, researchers—supported by a compelling body of NIH-supported research—have realized that the most effective way to treat and prevent Alzheimer's disease is to attack it early, before symptoms begin. Investigators discovered that higher amounts of brain beta-amyloid, the toxic protein that clogs the brains of Alzheimer's patients and is associated with memory loss and other symptoms, is related to an increased risk of developing dementia over time and to loss of brain volume and subtle declines in cognitive abilities. These findings suggest that brain beta-amyloid may in fact be a preclinical sign of disease even among individuals who appear cognitively normal.

In parallel, NIH-supported investigators with the Alzheimer's Disease Neuroimaging Initiative (ADNI) established a method and standards for testing levels of beta-amyloid and tau, another known biomarker for Alzheimer's disease, in the cerebrospinal fluid (CSF). They correlated levels of these proteins in the CSF with changes in cognition over time and determined that changes in these two protein levels in the CSF may precede the onset of the disease.

In 2011, these findings made possible the first revision of the clinical diagnostic criteria for Alzheimer's disease in 27 years through a joint effort of the NIA and the Alzheimer's Association. Unlike the previous criteria, the updated criteria cover the disease as it gradually progresses over many years, from the earliest preclinical, pre-symptomatic phase through mild cognitive impairment (MCI) to advanced dementia. The new guidelines also address the use of imaging and biomarkers to determine whether changes in the brain and body fluids are due to Alzheimer's. A separate update addresses diagnosis at autopsy, to help neuropathologists characterize Alzheimer's-related brain changes at death in people who have been diagnosed with dementia and those who have not yet shown clinical symptoms, taking into account that the disease process may begin a decade or two before outward signs like memory loss appear.

Recognizing the devastating impact of Alzheimer's disease and Alzheimer's Disease-Related Dementias, or ADRDs, on patients and families, and also recognizing that the time is right—from both a scientific and a public health standpoint—to move aggressively toward the development of new and effective treatments for Alzheimer's and ADRDs, President Obama signed the National Alzheimer's Project Act (NAPA) into law on January 4, 2011. NAPA requires the HHS Secretary to:

—Create and maintain an integrated national plan to overcome Alzheimer's disease and related dementias;
—Coordinate research and services across all Federal agencies;
—Accelerate the development of treatments that prevent, halt, or reverse the disease;
—Improve early diagnosis and coordination of care and treatment of the disease;
—Improve outcomes for ethnic and racial minority populations at higher risk;
—Create an Advisory Council to review and comment on the national plan and its implementation;
—Coordinate with international bodies to fight Alzheimer's disease globally.

Under NAPA, the first National Plan to Address Alzheimer's Disease (National Plan) was released on May 15, 2012, was subsequently updated in June 2013, and will continue to be updated annually.

In response to guidance from NAPA and the National Plan, NIA convened the Alzheimer's Research Summit 2012: Path to Treatment and Prevention. An international group of some 500 researchers, clinicians and members of the broader Alzheimer's community contributed actively to the Summit process through extensive input and discussion during the course of the meeting. As a result of recommendations from the Summit, NIH issued several solicitations for research on topics including the discovery of basic molecular processes underlying Alzheimer's disease and drug development and testing. Seven groundbreaking studies, ranging from research on the most basic underpinnings of the disease to early-stage clinical trials of promising agents, are now underway.

In addition, in May 2013, as part of the National Plan, NINDS together with NIA held the workshop "Alzheimer's Disease-Related Dementias: Research Challenges and Opportunities." An international group of experts developed prioritized research recommendations to address ADRDs, including frontotemporal, Lewy body, mixed, and vascular dementias, as well as clinical diagnosis and health disparities in ADRDs. These recommendations were revised based upon public discussion during the lively two-day conference, and in February, the Advisory Council on Alzheimer's Research, Care, and Services created under NAPA recommended that they be added to the National Plan. NINDS has already begun implementing these recommendations by using a high program priority funding process to support investigator-initiated grants on frontotemporal dementia and the vascular contributions to dementia.

REVVING UP RESEARCH

Research in Alzheimer's disease at NIH today runs the gamut from very basic neuroscience research to cutting-edge clinical trials designed to prevent or treat the disease. In the basic science arena, a major new program that has just begun this year is the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative—referred to by President Obama as the "next Great American Project". NIH is a leading member of this pioneering new venture, and has issued several research solicitations in the past 2 months that will enable us to develop a deeper understanding of brain function through the creation of new tools capable of examining the activity of millions of nerve cells, networks, and pathways in real time. By measuring activity at the scale of circuits and networks in living organisms, we can begin to translate data into models that will decode sensory experience, motor planning, and, potentially, even memory, emotion, and thought. We believe that successful completion of the BRAIN Initiative will revolutionize the field of neuroscience, providing a foundational platform for major advances in Alzheimer's and other brain diseases.

Another major current opportunity lies in the work of the Alzheimer's Disease Sequencing Project (ADSP), a program supporting large scale DNA analysis for the Alzheimer's disease research community. The ADSP is a collaboration between NIA-funded geneticists and the National Human Genome Research Institute Large-Scale Sequencing Program. Goals of the program are to identify new genes contributing to increased risk of and protection from the disease; to provide insight as to why individuals with known genetic risk factors escape the disease; and to identify potential avenues for therapeutic and preventive approaches. Last December, NIH announced the availability of the first batch of genome sequence data from the ADSP, including whole genome sequence (WGS) data from 410 individuals in 89 families. Researchers can access the sequence data at dbGaP (http://www.ncbi.nlm.nih.gov/gap) or the National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS), https://www.niagads.org/.

Still another example of how NIH-supported research is accelerating scientific discovery, with the potential for tremendous gains in the area of Alzheimer's disease, is in the area of stem cells. Induced pluripotent stem (iPS) cell technology is revolu-

tionizing the way we study disease, and holds the promise of dramatic advances in treatment. iPS cells are patient-derived cells, typically from skin or blood, that scientists can reprogram back to an embryonic stem cell-like state. These cells can then be induced to turn on specific sets of genes to differentiate into a variety of cell types, including neurons. For Alzheimer's disease, it has been possible to show abnormalities in amyloid metabolism in this "disease in a dish" model, opening the door to a new method to screen drug compounds for possible efficacy.

A seminal finding that has recently generated a lot of excitement is the discovery that the protein, tau, which appears to be in part responsible for the cognitive decline in Alzheimer's patients, may spread from neuron to neuron. This means that if researchers could find a way to prevent cell-to-cell transmission, perhaps by blocking tau with an antibody, the disease process could be halted. The problem was that until recently we had no way of visualizing what was happening with tau inside the living brain, making it difficult to assess the efficacy of treatment on that particular molecule. However, last fall researchers reported that they had developed a new class of imaging agents, termed PBBs, that bind to tau deposits in transgenic mice and in human subjects with normal cognition, Alzheimer's disease, or a corticobasal syndrome. The ability to visualize both beta-amyloid and tau in the living organism will enable us to evaluate the effect of new treatments more rapidly and efficiently than ever before.

With respect to new treatments for Alzheimer's disease, as I noted before, the paradigm has really shifted in recent years, from an emphasis on treatment of individuals with symptomatic disease to primary prevention among individuals at risk. This is not to say that we have forgotten those patients whose disease has advanced; NIH currently supports clinical trials of interventions for agitation, disruption, depression, and other troubling symptoms of Alzheimer's in affected individuals.

Vascular contributions to dementia are especially common and highlight the complex relationships among various types of dementia. The 7 million U.S. stroke survivors and 13 million people who have had "silent strokes" have an increased likelihood of cognitive problems. Brain vascular problems that cause stroke are associated with Alzheimer's disease in multiple ways. For example, signs that a stroke has occurred are often found in the brains of Alzheimer's patients, and beta-amyloid, a key protein in Alzheimer's pathology, may stimulate the formation of blood clots, which can cause stroke. The Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, which is following more than 30,000 people, is one of several epidemiological studies that demonstrate that high blood pressure and other known risk factors for stroke increase the risk of cognitive problems, even among people who have never had a stroke. Because reducing blood pressure and other cardiovascular risk factors might have an immediate impact on dementia, NINDS and NIA are funding a study to test whether an aggressive treatment program to reduce systolic blood pressure lower than the currently recommended goal also reduces age-related cognitive decline. This is part of a large, multi-center trial funded by NHLBI and NIDDK on the effects of this treatment on cardiovascular and kidney disease.

However, many of our newest clinical trials focus on presymptomatic, at-risk patients. New studies include:

—A 5-year clinical trial to determine if an antibody treatment, crenezumab, designed to bind to and possibly clear away abnormal amounts of amyloid protein in the brains of people with Alzheimer's, can prevent decline in cognitive function. Crenezumab will be tested among members of a unique and large family population in Colombia sharing a genetic mutation known to cause observable signs of Alzheimer's disease at around age 45, along with a smaller number of U.S. participants ages 30 and older.

—The A4 (Anti-Amyloid Treatment in Asymptomatic Alzheimer's) Trial which will test the drug solanezumab in 1,000 cognitively normal volunteers, age 65 to 85, who have enough of the amyloid protein in the brain to put them at risk for developing Alzheimer's, but do not show clinical symptoms of the disease.

—The Dominantly Inherited Alzheimer's Network Therapeutic Trials Unit, which will study the effects of different treatments among individuals who are at high genetic risk for developing the disease. In 2014, the first DIAN-TU trial, a comparison of two monoclonal antibodies—gantenerumab and solanezumab—with placebo will begin.

Each of these studies will rely on the availability of validated biomarkers of disease. Identification and characterization of biomarkers and targets for intervention are the primary goals of the Accelerating Medicines Partnership (AMP), just announced in February 2014. With project management by the Foundation for NIH (FNIH), ten pharmaceutical companies will collaborate with NIH. All data will be

made publicly available, and NIH and industry will share in the $230 million cost over 5 years for the first projects: Alzheimer's disease, type 2 diabetes, and the autoimmune disorders rheumatoid arthritis and systemic lupus erythematosus. For Alzheimer's disease, AMP resources will be used to incorporate an expanded set of biomarkers into four ongoing trials designed to delay or prevent disease, and then evaluate which ones are most effective. AMP resources will also support large-scale, systems biology analyses of brain tissue samples from people with Alzheimer's disease to validate biological targets that play key roles in disease progression, in order to increase understanding of molecular networks involved in the disease and identify new potential therapeutic targets. AMP represents an unprecedented model for pre-competitive collaboration that should substantially accelerate the ability to identify the next generation of drug targets and biomarkers.

EXPANDED FUNDING, EXPANDED DISCOVERY

On behalf the biomedical research community, whose scientists have been under stress as NIH purchasing power over the last decade has declined due to inflationary effects, I would like to acknowledge the fiscal year 2014 funding increase with which NIH has been entrusted for supporting new research on aging, including Alzheimer's disease. The addition of these new funds to our base appropriation will enable us to plan carefully for their use, consistent with funding the best peer-reviewed science and the priorities established at the Alzheimer's Summit and 2013 ADRD Workshop.

Several fiscal year 2014 initiatives can be mentioned that we plan to support with this increased base. First, these funds will facilitate analysis of the DNA sequences generated through the ADSP. Second, we are soliciting research on the use of iPS and other reprogrammed human cells specifically for aging and Alzheimer's disease. Also, researchers will study the function and activity of individual cells in the brain in animal models by turning functions of those cells on and off using—simply—light. Remarkably, the technology has advanced to the point where we can safely introduce tiny lasers and light-sensitive proteins into the brains of mice and rats. When the laser is remotely activated, the proteins respond by turning cells on and off, enabling us to track the cell's function. This technology—known as optogenetics—is being used in animal models of Alzheimer's disease to provide information that will help us to understand functions of the normal as well as the Alzheimer's brain.

This concludes my testimony. I am happy to respond to your questions.

Senator HARKIN. Thank you very much, Dr. Collins, for a very lucid presentation. I must say when you were talking about that BRAIN initiative, I was driving in to work late one day. It must have been a Friday or a Monday if I was coming late. And I heard you on the Diane Rehm Show talking about that. And once again, I say this with all respect, you're one of the unique individuals who can take very complicated and hard-to-understand scientific processes and research and put it in language that people understand. And I want to thank you for that. Because I thought what you said on that show just brought it home to the average person who just doesn't understand a lot of what this research is involved with.

So thank you very much for that. And again I compliment you for that ability.

We'll start a round of 5-minute questions.

CAN WE PREVENT DEMENTIA?

Dr. Collins, this may be a simplistic question after your presentation. But I see all kinds of claims about what people can do to prevent Alzheimer's. Well, let's see. There are brain games for sale. There are articles telling seniors to do a crossword puzzle every day, Sudoku also. There are Web sites suggesting supplements of Ginkgo Biloba or Vitamin E or B12. There may be others, too.

What does the research community know about these claims? What are the best things that individuals can do right now to lower their risk of dementia or Alzheimer's disease?

Dr. COLLINS. Well, you're right that those are questions on many people's minds, and NIH has funded a lot of research in that area. I'm going to turn to my colleague Dr. Hodes to summarize what we have learned.

Dr. HODES. Thank you for the very important question. You know, all of us have to make lifestyle choices every day. There's no such thing as not making a choice. We do by our actions. And there's no question that general issues of health, that exercise, diet are important in many aspects and they correlate to risk factors for Alzheimer's disease.

So we know that having high blood pressure or inactivity or overweight are associated with increased risk of Alzheimer's disease. But the critical question you asked—Do we know with certainty what activity, what exercise, what diet will decrease the probability of developing Alzheimer's disease?—is a question being addressed by ongoing research for which we do not currently have a definitive answer.

I would emphasize again there's important research going on in this area. So there were studies looking at the effect of exercise intervention on individuals before they developed Alzheimer's, who were at early stages of Alzheimer's. In years to come, we will have the results of those studies. There's a major study called LIFE that is looking at exercising folks and then looking at the impact on their ability to maintain mobility and also cognitive function.

There are two studies currently funded by investigators at the University of Kansas that are looking at either pre-symptomatic or early symptomatic disease to determine whether exercise actually changes the course of disease or changes these brain alterations that we have seen.

We have the ability now, and Dr. Collins emphasized it, as we never did before to look at the ability of interventions to make a difference, not just once people have developed disease. And then we follow for years to see if their symptoms become worse. We can look before there's any evidence of clinical disease, we can use biomarkers, and we can determine whether exercise or cognitive exercises will affect the course of those processes.

We're in the midst of those studies now. In these next years, we should have the answers. In the meantime, although we say that research does not have a definitive answer, there are so many good reasons to be practicing the positive aspects of lifestyle and choices that you mentioned that we have no hesitation in recommending those.

AFRICAN AMERICAN PARTICIPATION IN CLINICAL TRIALS

Senator HARKIN. Thank you, Dr. Hodes.

Our former Surgeon General, David Satcher, brought up a very important issue in this past Sunday's Washington Post. He noted that African Americans are two to three times more likely to develop Alzheimer's disease than non-Hispanic whites, but they participate in clinical trials at far lower rates than other ethnic groups.

[The information follows:]

The Washington Post article can be found at: http://www.washingtonpost.com/opinions/more-african-americans-need-to-participate-in-clinical-trials/2014/02/21/65c89742-9983-11e3-b931-0204122c514b_story.html

Senator HARKIN. Now, we all know the shameful history of the Tuskegee experiments. So the community's level of distrust is natural, and Dr. Satcher referred to that. Is there anything NIH can do to inspire more participation by minorities in this research?

Dr. COLLINS. Yes, I read that editorial by Dr. Satcher. It was indeed compelling and moving, a reminder of how important it is to focus on health disparities. And that's certainly an issue for Alzheimer's disease.

I'll say one thing and then ask Dr. Hodes to say a bit more about what we're doing now. One of the greatest opportunities in terms of encouraging minority participation in clinical trials is if the researchers themselves represent the diversity of our country. You can see that over and over again. This is a strong reason why we need to focus on improving and expanding the diversity of our own biomedical research workforce.

We have a number of new programs that are quite bold. And this is a high personal priority for me, to try to see if we could do a better job of recruiting and maintaining and mentoring and supporting individuals from under-represented groups in order to populate those clinical trial workforces with people who represent our country and would, therefore, perhaps be more welcoming to the groups that, tentatively right now, are unsure about whether they want to join up or not.

Dr. Hodes can tell you what we're already doing in terms of Alzheimer's trials because all of our centers are engaged in that.

Dr. HODES. We are indeed making great efforts to correct what you point out, an under-representation of minorities in clinical studies, in particular, clinical trials. All the Alzheimer's disease research centers, for example, have outreach cores. Some of them, for example, one in the city of Chicago, happen to serve an area where some 90 percent of individuals are African American. But in all cases, these outreaches are intended to maximize recruitment.

We're working actively with CDC (Centers for Disease Control and Prevention) and former AOA (Administration on Aging), ACL (Administration for Community Living), the partners in an exercise that's called ROAR (Recruiting Older Adults for Research), which overall has attempted to increase the recruitment of older adults into clinical studies and trials with a very concrete emphasis on minorities. We have a program of centers that are particularly focused on minority aging research and developing methods for enhancing the right liaison and communication with minority communities to increase their level of comfort, confidence, and stability as a means to recruiting them to clinical research.

Senator HARKIN. I appreciate that. I hope you'll do it very aggressively. The chair of our distinguished appropriations committee and a distinguished member of this subcommittee was the first person to bring to this subcommittee's attention, a long time ago, the disparity in women in terms of research trials at NIH. So I hope that we've taken a lesson from that and from what Dr. Satcher said and we really become more aggressive in including these minorities in these clinical trials.

So I thank you very much, and I'll now turn to Senator Moran.

PROGRESS IN THE PAST 5 YEARS

Senator MORAN. Mr. Chairman, thank you. Dr. Collins, thank you for your testimony. We're honored to have you here.

You indicated in your testimony several developments and promising opportunities in research in Alzheimer's. Let me ask you to put this in kind of a chart as an answer. Where were we 5 years ago compared to today? And are the increases in knowledge: Are they growing at a faster rate all the time? How does this look in the progress that's being made or not being made?

Dr. COLLINS. Well, I love the question. Thank you, Senator.

I think if you go back 10 years, people working in Alzheimer's disease were pretty darn frustrated. The ability to understand what are the molecular pathways that have gone awry in the brain to cause this condition was limited. Our tools, our technologies were not very good at making that kind of comprehensive assessment.

Our clinical trials, largely based upon hunches, were turning out badly. We had a limited number of ideas about where to go next.

In my view, and I've been at NIH for 20 years, the last 5 years have been really quite a dramatic change in that environment. We have learned, through a variety of approaches, things that we probably didn't expect would be now in front of us this soon.

For instance, what are the hereditary factors that are involved in this disease? It clearly runs in families. We have gone from knowing sort of one risk factor for the late onset type of Alzheimer's disease to now, depending on who you ask, 19 or 20 that we have. And that number is growing. In fact, it will be growing rapidly this coming year, in part because of the fiscal year 2014 appropriation, because we're expanding our ability to do that kind of genetic analysis.

We have gone from understanding that amyloid was a player to now understanding a lot more about tau, and to be able to look at pathways in the brain that are really quite complex, and point to other sort of nodes in those pathways that are really important and might be drug-able.

We have gone from having a few clinical trials focused largely on advanced cases of Alzheimer's to what you heard about today, where we, now because we can make the prediction about high risk, start the treatment earlier. Just like people have often said, and I'll say it now: If you try to test statins by waiting until somebody had far-advanced congestive heart failure, you would assume they don't work because you're too late.

Well, likewise, if we want to have a successful treatment for Alzheimer's, start while there are still lots of brain cells and see if you can protect them.

So there's a sense in this community of momentum. And it's coming from imaging and genomics and clinical studies and biochemistry and behavior studies. Everything is sort of coalescing here. So it is the right moment to really try to provide that extra push. And that's why what's happened in fiscal year 2014 could not come at a better time. It's momentum we hope can be sustained.

As you know, this kind of science is not a 100-yard dash. We're engaged in a marathon.

The other thing about that trajectory you're asking about, it's on an upward course. But I guarantee you it won't be a smooth and steady one. It will be herky-jerky, because we'll have big moments of realization that we've learned something we didn't expect. And then we'll have big disappointments where a clinical trial that looked really good, somehow it didn't work. We've got to go back to the drawing board. It's going to be jumping around a bit. But it's headed upward.

And it is my hope and my commitment that, with your help and with the amazing talent that we have in our U.S. and worldwide scientific workforce, we are going to tackle and win this disease battle.

Senator MORAN. I appreciate that answer, and again you used the word "hope." I always use the word "hope" when it comes to medical research. And what you're suggesting is that there are reasons to be hopeful.

Dr. COLLINS. Yes. I totally support that statement 100 percent.

DOWN SYNDROME AND ALZHEIMER'S DISEASE

Senator MORAN. Let me ask about a particular set of people that we care greatly about. Scientists have discovered that people with Down syndrome are at increased risk for developing Alzheimer's disease. By the age of 40, as I understand, almost everyone with Down syndrome has beta-amyloid deposits in their brain. Yet only about half of those people who have Down syndrome ever develop dementia. And even if they do, they develop plaque.

So my question is: Is NIH exploring the question of why 50 percent have a different outcome, a different result than the other 50 percent?

Dr. COLLINS. A wonderful question, Senator. I just spoke this morning to Dr. Guttmacher, who is the Director of the Child Health Institute, about this very issue. This is another opportunity perhaps to try to understand this disease in a group that has such a high risk. And both in terms of understanding why some develop and some do not, what are the other modifiers? But also, this could be a great opportunity to try new therapeutics at the earliest stage before the dementia has begun to actually take its toll on function.

There was a workshop which was held specifically on this topic about Alzheimer's and other dementias in Down syndrome kids. There's a challenge here in terms of things like the informed consent. We would want to do whatever we were doing in a way that's absolutely recognizing the difference in carrying out research in individuals who may themselves not be in the best position to give consent. We will depend on their parents.

But there is intense interest in this, and I would predict, based on that workshop, that in the course of the next year or two, there will be in fact new initiatives focused on that very special population to see what we can learn and see how we can help.

Senator HARKIN. Thank you. In order, I have here Senator Mikulski, then Senator Shelby, Cochran, Kirk, and Alexander.

Senator Mikulski.

Senator MIKULSKI. Thank you very much, Mr. Chairman. Thank you and also Ranking Member Moran for organizing this hearing on this topic of Alzheimer's. It is very special to me because my own very dear father died of the consequences of Alzheimer's, now 25 years ago. So I've been at this a long time.

And for many of us, we've had it either in our own families or people near and dear to us. And of course, there are marquee names that talk about this—Mrs. Reagan, Justice Sandra Day O'Connor, and others.

But really, this is an equal opportunity epidemic. It hits people at all income levels. And whether you are the President of the United States, like President Reagan, or a small grocer businessman like my father, or like the men and women out here in the audience who wear the purple sash, they know this tremendous impact on family life, the family budget, and ultimately on our budget.

So I think we all do need a sense of urgency about how we can come to grips with this and accelerate what we're going to do.

I want to welcome the witnesses here, Dr. Collins, Dr. Landis, Dr. Hodes. I was just at NIH on Monday. I'm so proud of the fact that it's in Maryland. I call it the National Institutes of Hope. The National Institutes of Hope. And I think that's what brings all the men and women and family members here.

HOW BEST TO ACCELERATE BREAKTHROUGHS IN ALZHEIMER'S DISEASE

My question, because we've been able to do something in this year's appropriations—and I might add, every single Senator up here is also a member of the appropriations committee—and we can feel proud of the fact that we put close to $30 billion into NIH, a billion more than last year. We've increased the National Institutes of Aging by $100 million. We've included money for the BRAIN initiative. So we think we're making that progress. And that comes to me, Dr. Collins, and other esteemed witnesses.

We would like to be able to accelerate these breakthroughs which you just testified seem so promising. But I feel that we also need a sense of urgency, because we are facing an epidemic in this country and the impact, again, on family budgets and on our Medicaid budget, of course, ultimately the impact of people being in long-term care. I remember what Senator Harkin and Senator Specter did when they doubled it.

Is it that we need more money? Do we need more people going into science? What do we need to put this on the fast track so that these promising breakthroughs, following all the rubrics of the scientific method? How can we? Because the clock is ticking, and the numbers are growing. The poignancy is there. Could you share how we can help move this along?

Dr. COLLINS. I appreciate the question, Senator, and it was great hosting you at NIH on Monday.

I think we are not at the moment limited by ideas. We're not limited by scientific opportunities. We're not limited by talent. We are, unfortunately, limited by resources to be able to move this enterprise forward at the pace that it could take. And it would be, of course, great to see that achieved. And it would actually, even setting aside the pressing need for the benefits to health, it would also

be a nice investment in our economy since, as many of you know, the way in which we put dollars into medical research pays back more than twofold in just a single year.

At the moment, people who have great ideas about Alzheimer's disease who come to NIH with those—and again, we have some ideas about areas that we think are exciting, but we also count on our community to come up with ideas that we, the three of us, couldn't necessarily have thought about, and to send us those. And we put them through the most rigorous peer review process. But their chance of getting funded right now is about one in six.

IMPACT ON LOW SUCCESS RATE ON INVESTIGATORS

Senator MIKULSKI. One in six?

Dr. COLLINS. So, five out of six are going away with nothing. The community is incredibly struggling and demoralized about that. You and I looked at this survey from the Chronicle of Higher Education on Monday—that just came out on Monday, indicating what's happening to investigators in laboratories all over the country.

[The information follows:]

The restricted link for the Chronicle of Higher Education article can be found at: http://chronicle.com/article/Strapped-Scientists-Abandon/144921/.

Dr. COLLINS. Remember, NIH is not just in Bethesda; most of our money goes out to all 50 States where this research is going on. And more than half of those investigators are saying they've basically had to let somebody go or they can't take on a student that they wanted to, or they're not going to start a project that they're excited about but they don't think they have the resources to do it. We are constraining the energy, the innovation, the creativity of the most amazing engine for discovery the world has seen, which is America's science.

Senator MIKULSKI. Well, Dr. Collins, what you're saying is that young people are discouraged from coming forth because they don't think that there's going to be the money there to fund their project. I see Dr. Hodes and Landis shaking their head.

Dr. COLLINS. Yes.

Senator MIKULSKI. Is that right? So we have promising ideas and people in our own country—in our own country—with these ideas ready to roll.

WHERE WOULD WE BE IF WE HAD STAYED ON 3-PERCENT GROWTH RATE

Well, let me ask you this. The whole idea of doubling: I don't know if it was in our fiscal cards, but I understand we shared an idea here that if we had stayed on the 3-percent growth initiated by Arlen Specter, where would we be now? At about $40 billion?

Dr. COLLINS. If you look at that curve of what the trajectory was prior to the 1998 doubling, it was about a 3-percent growth rate, and that's accounting for inflation, so real growth in terms of purchasing power. If we had stayed on that curve, we would now be just at about $40 billion.

Senator MIKULSKI. So it's $10 billion less than where we are for both not only at the National Institute of Aging, but as you pointed

out, this could be in a variety of other institutes, from Dr. Landis's on neurological behavior, everything.

INFLATION PLUS 5 PERCENT

So here's my question. I understand you have an idea that if we took inflation plus 5 percent for about 4 years, we could get to where we are today.

Dr. COLLINS. That would, if you do the math, carry NIH back up to that $40 billion number, if it were possible to do that. And again, that's a decision that is up to the Congress, the administration, the American people. But I must say, from my perspective, the best thing we could do for science would be to get on that kind of a stable, predictable trajectory so we can plan more than 3 months at a time, so we can actually tell young people who are coming into the field, "There's a career for you." "America is going to invest in this." "You can count on, if you have a great idea, you're going to be able to be part of an adventure that is going to be exciting and world-changing."

Right now, people aren't quite sure. This up and down and uncertainty has really done quite a lot of damage to the momentum.

Senator MIKULSKI. Well, thank you, Dr. Collins, and also the wonderful people there. My time is up. But I look forward to—really, this seems to be an achievable goal if we put our minds to it.

Dr. COLLINS. Thank you, Senator.

Senator HARKIN. Thank you, Senator Mikulski.

And Senator Shelby.

ALZHEIMER'S DISEASE NOT CURRENTLY PREVENTABLE

Senator SHELBY. Thank you.

Dr. Collins, I just want to share some statistics I have and see if you agree with them. I bet you would, but I don't know. That Alzheimer's is the only cause of death among the top 10 causes in America without a way to prevent it, cure it, or even slow its progressions. Is that true here in America? And what about in some of the European countries like Germany and England, France, Switzerland, more industrialized countries? Are these statistics prevalent there, too?

Dr. COLLINS. Yes, sir, they would be. I mean, the Alzheimer's epidemic is not just the U.S., it's worldwide. And it's a function of the aging of our population, which is, by the way, a good problem that medical research has contributed to. One hundred years ago, Alzheimer's was barely known because people didn't live long enough to get it. Now we've created a wonderful possibility of longer life, but with it has come this new responsibility to do something about Alzheimer's.

RISK OF ALZHEIMER'S DISEASE INCREASES WITH AGE

Senator SHELBY. So some of us that hope to be in our 90s someday, and there's a good chance we might have symptoms of Alzheimer's or even have it or have acute cases of it; is that correct?

Dr. COLLINS. Well, Dr. Hurd, who is in the second panel, in the study he published in The New England Journal kind of went through those. And as I recall, people in their 90s, the incidence

of Alzheimer's or some form of dementia is up there in about 30 percent.

ALZHEIMER'S DISEASE TRANSLATIONAL RESEARCH AT NATIONAL INSTITUTES OF HEALTH

Senator SHELBY. Tell us about how some of the translational research that's going on at NIH hopefully will affect maybe a slowdown or cure for this.

Dr. COLLINS. Well, translation is the process of going from basic science discoveries, translating those into clinical benefit. And that is a major focus of all of the parts of NIH. All 27 institutes have an investment in that. I think I'll ask Dr. Hodes for Alzheimer's to give a quick snapshot of some of the most of exciting areas of translation we're pursuing right now.

Dr. HODES. Thank you. I can really organize thoughts along the lines of Dr. Collins's response to the areas of hope and progress over the past 5 or 10 years because they really do range from basic discovery through their translation.

The level of basic discovery, he noted, for example, the number of new genetic risk factors and protective factors that we're finding. With funding that was made available this year, we're going to be able to expand new analyses that will look at not just single genes or proteins, but the way they interact in very complex ways, contrasting what goes on in a normal brain, in a diseased brain.

And these were already identifying critical points that seem to be central to disease. That means we can test that hypothesis by tracking and interventions such as a drug or small molecule to that specific process. Find out in a single cell or in an animal model if that has the right effect, and then translate those into clinical studies.

For translation, again to emphasize what Dr. Collins has noted, we now have the capability of beginning interventions at a stage at which we can track disease long before extensive cell death and damage has occurred in the brain. We can also track the effectiveness of treatment through biomarkers.

The biomarkers will be the ones that we know now, and new markers that will develop as we learn more about the progress of disease. So everything is about translation. And in fact, in the planning in process now for 2015 and years beyond, with the benefit of this increased funding by appropriation, we will be looking at precisely the right balance of initiatives across this whole spectrum, from discovery, translation, to clinical trials for the most promising of initiatives.

And this is an ongoing effort. We'll meet periodically with the best minds in the Nation and internationally to revise those plans. But translation is what is primarily in line for this whole effort. And I think progress at each of these levels, from basic science through clinical trials, is going to support acceleration with full utilization of the resources that are made available to us.

STEM CELLS AND ALZHEIMER'S DISEASE TRANSLATIONAL RESEARCH

Dr. COLLINS. Let me add one other translational thing that's pretty exciting. And that is based on stem cells. The ability now to be able to take a skin biopsy or a blood sample from somebody with

Alzheimer's disease and, by adding just four genes, convince those cells to go back in time and become what you'd called pluripotent. Then having achieved that, add a certain number of growth factors and convince those cells to become neurons.

So you can take somebody with Alzheimer's disease with a skin biopsy and a blood cell and study their neurons, sort of the disease in a dish. And already that's been done. And it's clear that you can tell the difference in those neurons if they came from somebody with Alzheimer's versus somebody who doesn't.

That is an incredibly exciting opportunity, to be able to understand the disease in a system where you can really work closely with it, and even use it as a drug screen because you could then take 1,000 or 100,000 drugs and say, "Which of these make the Alzheimer's cells look like the normal neurons? How could you do that?"

LONGEVITY RESEARCH

Senator SHELBY. Dr. Collins, one last question. My time is up. In your research, do you do research into animals that live longer than others and see if there are some corresponding problems with their aging process? And if so, could you speak to that?

Dr. COLLINS. Well, this is the central role of the National Institute on Aging—is to look at the whole question of longevity.

Senator SHELBY. I need to visit with Dr. Hodes.

Go ahead, Dr. Hodes.

Dr. HODES. Yes. Looking at varied species with different lifespans and expectancies is a very important part of the research that's ongoing and is still a mystery, the solution to which is unraveling.

So, for example, we know that examples that have been given for different kinds of clams that live in the same environment, some species of clams will have a life expectancy of no more than a year or two, others 500 years, the longest life expectancy of any animals. Trying to understand the reason for that so-called comparative genetics is an important area.

We know that if one takes certain species, flies and worms happen to be those which are very easily manipulated, with single or multiple genetic changes in those animals, we can extend their lifespan several-fold, maybe three-, four-, six-, or tenfold.

Now, that obviously reveals something about the basic pathways that determine health and life expectancy. And now the real promise and the excitement currently is translating that to the equivalent pathways in humans to understand whether manipulating those pathways will improve health and lifespan. So a very informative area of research.

Senator SHELBY. Thank you both.

Thank you, Mr. Chairman.

Senator HARKIN. Thank you, Senator Shelby.

Senator Cochran.

SHOULD THERE BE CRASH COURSE ENDEAVOR FOR ALZHEIMER'S DISEASE

Senator COCHRAN. Mr. Chairman, thank you. Thank you all for joining us today to discuss this situation.

I'm reminded that at the University of Mississippi, Dr. Arthur Guyton embarked upon a study of the heart. And flowing from the research that he managed and was in charge of at the university, a textbook was written and great strides were made in understanding and prescribing changes in lifestyles and medications that could have this effect or that effect on the human heart.

Is it time now for us to encourage and identify someone or someplace where a crash course in research and emphasis on this horrendous disease called Alzheimer's can be undertaken, maybe with the hope of marshalling the best minds and the greatest techniques of research that we have, and take one step into the future, where your name might be on a textbook?

What's your reaction to that? Do we have the capacity to do that? What amount of funding should we urge the Senate to consider appropriating for such a crash course endeavor?

Dr. COLLINS. That's an interesting question. To think back about Dr. Guyton and the incredible impact that he had and reverberates down through the decades on what we understand about the heart.

Over the course of those decades, we have moved more and more into a realization that for the current challenges, it's bringing disciplines together that seems to be the most promising way to make progress. And certainly in Alzheimer's disease, the idea that you can bring together people who know something about neuroscience, people who know something about clinical medicine, people who know about imaging technologies, people who study genomics, people who are engineers, robotics experts, big data is a big part of this now—that's where a lot of the excitement is.

And so, increasingly, what we need to do, sort of the modern version of Dr. Guyton, is to come up with teams that are made of many brains sort of working together. And that is very much the way science is now proceeding.

The BRAIN initiative, which Dr. Landis co-leads for us, is a great example of how to achieve that. I don't know. Maybe you could say a word about how that is coming together in a way that reflects this change in the dynamics.

Dr. LANDIS. So it's very clear that we've made excellent advances in understanding brain structure. We know we have crude wiring diagrams for the brain. But we don't know how information is processed along those wires, how the vision of a rose actually gets translated through many, many different way stations in the brain to recognition that this is a rose and the expectation that it will smell sweet.

And what we need to do to really understand how the circuits work—that's the organization of the brain, brain cells—is to bring together neuroscientists, computational people, physicists, chemists, engineers, to work to develop tools that we then can apply to answer those questions about how brain circuits really function. And that obviously starts with normal brain circuits.

But what we learn from understanding normal brain function will have significant implications for diseases like Alzheimer's, other kinds of dementia, Parkinson's disease, epilepsy. And so we hope to build those kinds of teams that Dr. Collins spoke about to really unravel the language of the brain.

Dr. HODES. Yes. First I have to agree with the appreciation for the remarkable Guyton family. One of the Drs. Guyton was a classmate of mine in medical school, and they are clearly remarkable folks.

But in line with your suggestion of a new kind of center that will allow a translation from basic observations through at least preclinical stages, in fact, the very existence of the additional appropriation this year has led us to begin a set-aside of funds for planning grants for a translational center. In fact, the concept just approved this morning by our advisory council, the concept developed and now implemented in the context of funds available.

So it's intended to do just the sort of thing you were mentioning, I think, will bring together, as Dr. Collins mentioned, individuals from multiple disciplines to look at new ways to integrate and, hopefully, accelerate progress in this area.

Senator COCHRAN. Thank you very much.

Thank you, Mr. Chairman, for calling this hearing.

Senator HARKIN. Thank you very much, Senator Cochran.

Senator Kirk.

NATIONAL INSTITUTES OF HEALTH ACCELERATING MEDICINES PARTNERSHIP INITIATIVE

Senator KIRK. Mr. Chairman, I just wanted to highlight and praise Dr. Collins for the AMP effort that brings together 10 pharmaceutical companies. I'll mention them: ABBVie, I will note, headquartered in Illinois, Biogen, Bristol-Myers Squibb GlaxoSmithKline and Johnson & Johnson, and Lilly and Merck and Pfizer and Sanofi, Takeda, all part of AMP.

I would say that, institutionally, these are all shareholder-sponsored entities who all are going to be very interested in bringing something to market eventually, which actually means actual patients will be helped, and not a 25-year research pact where, with all these institutions coming into play, they're only interested in the clinical application of what they find.

And for a lot of the people who are in the sessions here, I am sure that that's what they're most focused on.

Dr. COLLINS. Senator, I appreciate your raising AMP, because I'm personally very excited about this and have put close to 3 years into trying to build the momentum and was thrilled that it was possible to announce this just a couple of weeks ago.

It is unprecedented to have NIH and academic researchers getting together around the same table with equal financial contributions with these 10 pharmaceutical companies, to say, "This is a hard problem. Let's work on it together," and with an agreement that all the data is going to be publically accessible.

So we're calling this no longer a competitive part of the process. This is pre-competitive. But the opportunities now, because of the proliferation of discoveries about basic science that's involved in Alzheimer's and in diabetes and in rheumatoid arthritis and in Lupus, to try to move those to the clinic has never been greater. But it's a little overwhelming to see how exactly to do that. And those 10 companies kind of came to the conclusion no single one of them could do this in the kind of timeframe that is necessary.

So let's just get together and do it as a team and recognize that, once we've done this pre-competitive part, the companies are going to jump in, and they're going to race each other to try to get to the end point of having an FDA-approved drug. And we want them to. That part of competition is how we get to ultimately the treatments that people are waiting for.

But it's a very exciting model. It's been never tried like this. Watch us closely now. We put ourselves in a position of having to deliver on some very ambitious milestones. But I think we'll get there. And it's going to be great also to mix these cultures together, the culture of the academic scientists and the private sector scientists with different kinds of ideas, but agreeing as deep as their DNA that what they're really at here is to try to solve problems and help patients. Thank you.

Senator KIRK. And I just want to make it clear. This information is shared across all the companies and the public and everybody?

Dr. COLLINS. Absolutely. Absolutely. Yes. Some of the companies initially were like, you know, "Why should we join, because if we sort of sit on the outside and watch, we're still going to see the data." Right?

Senator KIRK. That's right.

Dr. COLLINS. Yeah, they'll sit on the outside. But if you're on the outside, you're not actually able to steer the project. You're not able to say, "Oh, why don't we try that?" So being part of the team here is going to be significant and useful and, I think, very exciting for the participants.

ACCELERATING AND ALZHEIMER'S DISEASE

I should have said Alzheimer's is one of the projects that was chosen. We had to figure out which of these various disease opportunities were the companies excited enough about to put money on the table. And Alzheimer's was one of those. In Alzheimer's, the goal is going to be very much to see what we could do about these biomarkers that relate to identifying whether a therapy is working or not, and also to study these brain networks that Dr. Hodes was talking about to identify new targets for drug treatment that we don't know about already. It's going to be very interesting.

Senator HARKIN. Again, thank you and congratulations for pulling this group together. Quite a feat.

Senator Alexander.

"MOONSHOT" FOR ALZHEIMER'S DISEASE

Senator ALEXANDER. Thanks, Mr. Chairman. Thanks, Dr. Collins, and to all of you. Of course, we greatly admire what you've done. I think we've all asked you about the same question, so let me ask you again and make sure I understand it.

A moon shot had a very specific goal, and all the incredible human activity, was organized around that specific goal. I suppose mapping the human genome was a very specific goal. And all this activity was organized around that goal. So you knew when you got to the moon, and you knew when you'd finished mapping the sequence that you worked on.

What is the AMP? The equivalent of those big crash courses that Senator Cochran called them, or goals? Or is there a better goal?

I think what I'm asking, I think every one of us may have asked, is: What would be the equivalent here in terms of brain research or in terms of Alzheimer's? What should the goal be? And then how much money should a great country put behind that to reach the goal?

In my work in public life, it's always seemed to me that the money was not the problem; the goal, defining the goal usually was the problem. If the goal was compelling enough, usually the resources would follow the goal.

So tell me again what the equivalent of the moon shot or the Human Genome Project is here so I understand it clearly. And then remind me again, if you know, what it would cost to do it.

Dr. COLLINS. That's the hardest part because we don't know what the trajectory is going to be. But let me try and see if I can address your very thoughtful question.

You're right. The moon shot, the Human Genome Project, those were unique situations where you could define a very precise endpoint and everybody would know whether you got there or not. You've got a man on the moon. Okay, you did it. You read out 3 billion letters of the DNA instruction book. Okay, you did it.

For Alzheimer's disease, what would be an appropriate goal? There's going to be lots of goals in there. Getting diagnosis so that it is accurate and can be done early, before symptoms. We're coming along pretty well on that one. I wouldn't say we're there. But of course, the big goal is prevention, treatment, so that nobody gets this disease anymore. That is far enough out in the future that I think it's hard for us, with the uncertainties about how we will get there, to be able to put a timetable on that. But people are trying.

NATIONAL PLAN FOR ALZHEIMER'S DISEASE

I'm going to ask Dr. Hodes to say something about the national plan.

Senator ALEXANDER. Before you do, is the goal to prevent anyone from getting Alzheimer's just like we say today polio's gone from the United States?

Dr. COLLINS. That would be my goal. That would be my goal. That's very bold, very ambitious. But that's got to be the place to try for.

Now, I'm going to ask Hodes to say something about Alzheimer's plan, the national plan. But we also have this BRAIN project. And it's holding itself accountable. Kind of like a genome project, it's going to stretch out over a decade or so. But it needs to have clear indications of whether it's succeeding or not, milestones.

I think maybe that's the difference, that even with the moon shot, you had to have milestones about whether you're going to get there. Can you put a man in orbit? Can you actually go around the moon and come back? And then, ultimately, can you put somebody on the moon?

Maybe Dr. Landis could say just a word about BRAIN in terms of how we are trying to set those specific milestones so that we can say we're getting there. And then you can perhaps say something about the Alzheimer's plan.

Dr. LANDIS. So, as I said, we have maps of the connections in the human brain. But what we don't have is a way to record from the

86 billion neurons and the 1,000 connections that each of them has in order to understand how the brain actually functions.

So, what we need to do is to be able to record, not just from 1 neuron or 10 neurons or 100 neurons, but thousands or tens of thousands of neurons at the same time as a person, or an animal to start with, is performing a behavior, and then to reconstruct how those circuits, those brain cells, actually directed that behavior.

And if we could do that, it would give us a much better understanding of this amazing computational machine that accomplishes actions and thoughts that no computer could ever replicate.

Dr. COLLINS. And there are milestones.

Dr. LANDIS. And there are milestones. In fact, those milestones are being developed and will be presented to the Advisory Committee to the Director. We have requests for applications out on the street now that have discrete pieces of that problem that we will fund projects to answer, different steps in that process.

Dr. COLLINS. Richard, maybe you can say just a quick word about the national plan because it's all about milestones.

Dr. HODES. Yes. The national plan establishes and has established long-term goals including the very ambitious goal by 2025 of generating an effective means of treatment or prevention. What we then did is to ask: What would be necessary in order to reach that success by that date, and from there, set a series of specific research objectives and milestones so that in 2013 and 2014 there are investments in certain areas of research, which as projected, if successful, will lead in 2025 to ultimate success?

We don't know which of the approaches we take are going to succeed, which are going to fail. But the milestones are designed to set out an approach that has the potential for that success. Ambitious as it is, we have no choice, given the urgency, but to move towards just that accelerated a course.

Senator ALEXANDER. Thank you, Mr. Chairman.

Senator HARKIN. Thank you, Senator Alexander.

I thank you again, Dr. Collins, Dr. Landis, Dr. Hodes, for being here today. Again, congratulations on bringing together the drug companies on this AMP (Accelerating Medicines Partnership) project. I think it's just a milestone. And again, hopefully, we'll be able to continue our funding in the next fiscal year like we did in the last fiscal year.

And again, I would be remiss if I didn't thank the chairman of our full committee for giving us the allocation with which to do that.

Thank you all very much.

And we'll now turn to our second panel.

"MANHATTAN PROJECT" FOR ALZHEIMER'S DISEASE

Senator MIKULSKI. But, Mr. Chairman, if I could, really I'd also raise kind of Manhattan-like project, the genome, landing on the moon, the Manhattan Project. Wasn't one of the biggest concerns, the fact that would be discouragement to or an impediment, two things, the shutdown of our Government and the other is sequester? So that there is the lack of certainty, as you have to not only sequence the human genome, but you've got to sequence what

you're going to do when, in terms of research, recruitment, retention and so on.

Don't you need certainty as well as resources?

Dr. COLLINS. Absolutely. People say that the worst thing you can do to the business community is uncertainty. Well, that's true for science even more so. Our cycle time for projects runs about 4 years in order to come up with an idea, put it into practice, work really hard, and see if it works.

When your cycle time for support sometimes is 3 months, and we've been there for some of these continuing resolutions. And certainly, when you lose $1.5 billion halfway through the fiscal, as we did with sequester, it's very damaging to the ability for people to pursue momentum and to be innovative and to take risks. We want them out there taking risks, not worrying about whether somehow they're just going to miss the pay line because it's so tight.

If we can find our path forward, Madam Chairwoman, to that kind of a stable support for medical research in the United States, it would make a huge difference.

Senator HARKIN. I can't help, then, but add here that years ago Mark Hatfield, Senator Hatfield came up with an idea.

Senator MIKULSKI. Yes.

Senator HARKIN. And I joined with him on it, and so did others. He pointed out that every time you buy a drug at a drugstore, every time you buy an off-the-shelf drug or even a prescription drug, some of that money goes for research. When you buy a health insurance policy, none of it goes for research.

Think of the amount of money we spend every year on our health insurance policies to treat and to take care of illnesses. But none of it goes for research. So, Senator Hatfield came up with the idea, it was a long time ago, about having, I think it was 2 or 3 cents if I'm not mistaken, out of every healthcare dollar appropriated would go to NIH for research.

And of course, the argument was made, well, that would just supplant the money that we were doing. So he said no. What you do is, as long as this committee funded NIH, or the Congress funded NIH at a minimum of inflation, then that money would flow on top of it and be a supplement to it. I've been preaching this for 25 years, that some of this health insurance money that we spend ought to go for research. And I'm sorry that the health insurance industry has always opposed it. But it seemed to me that this is one way of getting some amount of money that you know every year is going to be there.

With that, thank you very much, Dr. Collins. We'll turn to our second panel.

Dr. COLLINS. Thank you.

NONDEPARTMENTAL WITNESSES

Senator HARKIN. Now we'll call our second panel, Dr. Michael Hurd, Congressman Dennis Moore, and Mr. Seth Rogen. And while they're coming to the table, I will go ahead and introduce them.

First, Dr. Michael Hurd, a senior principal researcher at the RAND Corporation, where he directs the RAND Center for the Study of Aging. He is also a professor at the Pardee RAND Graduate School in Santa Monica, California. Dr. Hurd's research focuses on the economics of retirement, Social Security and social welfare systems, and other topics related to aging and the elderly.

We have Congressman Dennis Moore, who represented the Third District of Kansas in the U.S. House of Representatives for 12 years. First elected in 1998, Congressman Moore served on the Budget and Financial Services Committees. In 2010, he announced he would not seek re-election. Prior to his time in office, Congressman Moore served in the U.S. Army and the U.S. Army Reserve, was an assistant attorney general for the State of Kansas, Johnson County District Attorney, as well as a private practice lawyer.

In February 2012, he and his wife Stephene announced that he, Congressman Moore, had been diagnosed with Alzheimer's disease.

Mr. Seth Rogen, a stand-up comedian, actor, producer, director, screenwriter, and voice actor. Originally from Vancouver, British Columbia, Mr. Rogen began his career performing stand-up comedy, moved to Los Angeles to pursue acting in the late 1990s. Since that time, Mr. Rogen has acted in and co-written major movies, as well as done voice-over work for animated films.

Mr. Rogen raises awareness of Alzheimer's disease as a celebrity champion for the National Alzheimer's Association. Alzheimer's has greatly affected his wife's family, and he will talk about that.

We welcome you all here. I read your testimonies last night. They are great. All your testimonies will be made a part of the record in their entirety. And I would ask if you would give a short 5-minute summation of that so we can engage you in questions and answers and conversation.

First, we'll recognize our former colleague from the House side, Congressman Dennis Moore. Good to see an old friend back again from the Midwest.

Dennis, thanks for being here, and please proceed.

STATEMENT OF DENNIS MOORE, FORMER U.S. CONGRESSMAN FROM THE THIRD DISTRICT OF KANSAS

Mr. MOORE. Thank you. Good afternoon, Chairman Harkin, Ranking Member Moran, and members of the subcommittee. As an individual living with Alzheimer's disease, I thank you for the opportunity to testify here before this subcommittee.

Alzheimer's is a devastating progressively and ultimately fatal disease. It currently impacts more than 5 million Americans. These men and women are husbands and wives, mothers and fathers, sisters and brothers, Republicans and Democrats. I should know; I'm a former member of the United States House of Representatives, and I'm one of them.

I was diagnosed with Alzheimer's disease almost 3 years ago on June 1, 2011. I had become concerned when I noticed I was having

some difficulty remembering random events and difficulty managing our household finances.

Since then, I've learned coping skills, but still recognise the issue I have with my short-term memory loss. I'm now an Alzheimer's advocate for the Alzheimer's Association because I know personally how this disease affects an individual and family.

There is a great need for educating the general public and funding research for a cure. Not only does Alzheimer's steal our memories, independence, and eventually our ability to function, but it demands increasing amounts of care. Beyond the exhaustion and stress, there's the financial burden. The direct cost of Alzheimer's and related dementia is greater than any other condition in the United States, including heart disease and cancer, according to a recent study in The New England Journal of Medicine.

[The information follows:]

The link for The New England Journal of Medicine article can be found at: http://www.nejm.org/doi/full/10.1056/NEJMsa1204629.

Mr. MOORE. Over the next 40 years, caring for people with Alzheimer's and related dementias will cost $20 trillion—trillion. However, even with this information, for every $27,000 Medicare and Medicaid spend on caring for individuals with Alzheimer's, the National Institutes of Health spends only $100 on Alzheimer's research—$100 on Alzheimer's research.

Fortunately, Alzheimer's is a bipartisan issue. In 2010, Congress unanimously passed the National Alzheimer's Project Act.

[The information follows:]

Public Law 111–375—January 4, 2011—Legislative History: S. 3036:
December 8, considered and passed the Senate.
December 15, considered and passed the House.

Mr. MOORE. The act mandated the creation of the first-ever National Alzheimer's Plan, which was released in May 2012 with the goal of preventing and effectively treating Alzheimer's by 2025. Recently updated, the plan now includes important milestones and a timeline to facilitate achieving that goal.

However, goals of this magnitude, goals aimed at changing the trajectory of a national health crisis require significant investments if we hope to realize success. Recognizing this, we commend Congress, through their leadership of you, Chairman Harkin and Ranking Member Moran, for providing an historic increase for Alzheimer's in the Consolidated Appropriations Act of 2014. This is an important down payment and step in implementing the National Alzheimer's Plan so we can reach the goal of effectively treating and preventing Alzheimer's by 2025.

This critical funding will allow scientists to pursue innovative research that will lead to new treatments, interventions, and diagnostics. Continued funding of these programs will encourage a greater investment in the academic and private sector and ultimately lead to a game-changing diagnostic or treatment.

For all of these reasons, it's vital that we continue to make investments in Alzheimer's disease research, education, outreach, and support activities to implement the National Alzheimer's Plan as we look to fiscal year 2015.

In order to take full advantage of the potential of the National Alzheimer's Plan, Congress must see to it that the necessary resources are committed to accelerate and prioritize the Government's efforts on Alzheimer's. The infusion of funding for fiscal year 2014 took the next step in recognizing the correlation between investments in Alzheimer's research today and a much healthier and sounder financial future for our Nation.

It is now incumbent upon our Nation's leaders to ensure the promise of the National Alzheimer's Plan. My fellow Alzheimer's advocates and I thank you again for your support in fiscal year 2014 and urge you to stay committed to Alzheimer's as you start discussions for fiscal year 2015.

PREPARED STATEMENT

An epidemic is upon us, and too many families are in situations like mine, facing a fatal disease that currently has no way to prevent, cure, or even slow its progression. As a nation, we cannot afford to wait until Alzheimer's bankrupts us. We must make the smart investment now to realize a better, healthier future for our families and our country. Thank you very much.

[The statement follows:]

PREPARED STATEMENT OF HON. DENNIS MOORE

Good afternoon Chairman Harkin, Ranking Member Moran and members of the subcommittee. As an individual living with Alzheimer's disease, thank you for the opportunity to testify before the subcommittee.

Alzheimer's is a devastating, progressive and ultimately fatal disease. It currently impacts more than 5 million Americans living with the disease and their 15.4 million caregivers. These men and women are husbands and wives, mothers and fathers, sisters and brothers, business leaders, medical professionals, Republicans and Democrats. I should know. I, a former member of the U.S. House of Representatives, am one of them.

I was diagnosed with Alzheimer's disease just 2 years ago on June 1, 2011. I had become concerned when I noticed I was having some difficulty remembering random events and difficulty managing our household finances. Since then, I have learned coping skills but still recognize the issue I have with my short-term memory loss. I am now an Alzheimer's advocate for the Alzheimer's Association and serve on the Advisory Council on Alzheimer's Research, Care, and Services because I know personally how this disease affects an individual and family. There is a great need for educating the general public and funding research for a cure.

ALZHEIMER'S IMPACT ON THE AMERICAN PEOPLE AND THE ECONOMY

In addition to Alzheimer's stealing our memories, independence and eventually our ability to function, it demands increasing amounts of care. Beyond the exhaustion and stress, there is the financial burden. Alzheimer's is creating an enormous strain on the healthcare system, families and the Federal budget. Alzheimer's is a progressive brain disorder that damages and eventually destroys brain cells, leading to a loss of memory, thinking and other brain functions. Ultimately, Alzheimer's is fatal. Currently, Alzheimer's is the sixth leading cause of death in the United States and the only one of the top 10 without a means to prevent, cure or slow its progression. Over 5 million Americans are living with Alzheimer's, with 200,000 under the age of 65.

A Federal commitment can lower costs and improve health outcomes for people living with Alzheimer's today and in the future. By making Alzheimer's a national priority, we can create the same successes that we have been able to achieve in other diseases that have been prioritized by the Federal Government. Leadership from the Federal government has helped to lower the number of deaths from other major diseases like heart disease, HIV/AIDS, many cancers, heart disease and stroke. While those deaths have declined, deaths from Alzheimer's have increased 68 percent between 2000 and 2010.

Alzheimer's is the most expensive disease in America. In fact, an NIH-funded study in the New England Journal of Medicine confirmed that Alzheimer's is the most costly disease in America, with costs set to skyrocket at unprecedented rates. In 2013, America is estimated to have spent $203 billion in direct costs for those with Alzheimer's, including $142 billion in costs to Medicare and Medicaid. Average per person Medicare costs for those with Alzheimer's and other dementias are three times higher than those without these conditions. Average per senior Medicaid spending is 19 times higher. A primary reason for these high costs is that Alzheimer's makes treating other diseases more expensive, as most individuals with Alzheimer's have one or more co-morbidities that complicate the management of the condition(s) and increases costs. For example, a senior with diabetes and Alzheimer's costs Medicare 81 percent more than a senior who only has diabetes.

If nothing is done, as many as 16 million Americans will have Alzheimer's disease by 2050 and costs will exceed $1.2 trillion (not adjusted for inflation), creating an enormous strain on the healthcare system, families and the Federal budget. The expense involved in caring for those with Alzheimer's is not just a long-term problem. As the current generation of baby boomers age, near-term costs for caring for those with Alzheimer's will balloon, as Medicare and Medicaid will cover more than two-thirds of the costs for their care.

With Alzheimer's, it is not just those with the disease who suffer—it is also their caregivers and families. In 2012, 15.4 million family members and friends provided unpaid care valued at over $216 billion. Caring for a person with Alzheimer's takes longer, lasts longer, is more personal and intrusive, and takes a heavy toll on the health of the caregivers themselves. More than 60 percent of Alzheimer's and dementia caregivers rate the emotional stress of caregiving as high or very high, with one-third reporting symptoms of depression. Caregiving also has a negative impact on health, employment, income and finances for countless American families. Due to the physical and emotional toll of caregiving on their own health, Alzheimer's and dementia caregivers had $9.1 billion in additional health costs in 2012.

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) (Public Law 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. In addition, the Plan must outline priority actions to reduce the financial impact of Alzheimer's on Federal programs and on families; improve health outcomes for all Americans living with Alzheimer's; and improve the prevention, diagnosis, treatment, care, institutional-, home-, and community-based Alzheimer's programs for individuals with Alzheimer's and their caregivers.

As mandated by NAPA, the Secretary of Health and Human Services, in collaboration with the Advisory Council on Alzheimer's Research, Care and Services, developed the first-ever National Plan to Address Alzheimer's Disease in May of 2012. The Advisory Council, of which I am a member, is composed of both Federal members and expert non-Federal members. It is an integral part of the planning process as it advises the Secretary in developing and evaluating 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.

NAPA, and the Plan it has yielded, finally provides a framework for Congress to assess whether the Nation is meeting the challenges of this disease for families, communities and the economy. The Plan sets important goals. The first of these aims squarely at changing the trajectory of Alzheimer's by setting the goal to, "[p]revent and effectively treat Alzheimer's disease by 2025." Further, to the great credit of the National Institutes of Health and the National Institute on Aging, our Nation's leading scientists have specified the annual research milestones they have concluded they must achieve to remain on track to accomplish this transformative goal. With these milestones in hand, a direct product of NAPA, this subcommittee now has a tool to constructively assess whether we remain on track toward 2025, whether Congress is providing the necessary resources, and whether available resources are yielding the anticipated progress from year to year. Until this past year, such engagement between Congress and the National Institutes of Health simply was not possible for lack of this framework. We ought to recognize what a significant achievement this is in the service of disciplined, priority-driven science, and I urge you to take full advantage of it.

Having this Plan with measurable milestones and outcomes is important. But unless there are resources to implement the Plan and the will to abide by it, we cannot hope to make sufficient progress. If we are going to succeed in the fight against Alzheimer's, Congress must provide the resources the scientists need. These funds are critically needed for research and services for Alzheimer's patients and their families.

The potential in reach could scarcely be greater. A disease-modifying or preventive therapy would not only save millions of lives but would save billions of dollars in healthcare costs. Specifically, a treatment that delayed the onset of Alzheimer's by 5 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 still must do much more to understand what causes the disease and to capitalize on it. 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. For every $27,000 Medicare and Medicaid spend caring for individuals with Alzheimer's, the National Institutes of Health (NIH) spends only $100 on Alzheimer's research. Scientists fundamentally believe that we have the ideas, the technology and the will to develop new Alzheimer's interventions. But that progress depends on implementing NIH's prioritized Alzheimer's research agenda, and on having the resources necessary to carry out the scientific strategy for both discovery and translation for therapeutic development.

Additional funding has been requested in the NIH budget over the past several years because their scientists have determined that additional research on Alzheimer's is a priority. These budget requests reflect the changing needs of the Alzheimer's community, the scientific opportunity, and the results of disciplined analysis and planning. It is vital that Congress support the research projects the scientists at NIH deem necessary.

However, Congress does have a responsibility to direct resources to solve the most serious problems. By every objective standard (whether cost to Medicare/Medicaid, families caring for individuals with Alzheimer's, or mortality rate), Alzheimer's is one of our most serious health problems—and it will only get worse as the Baby Boomer generation ages.

While pursuing effective treatments for tomorrow, deliver better care and support today Alzheimer's is the most expensive disease in the country not just because of the lack of adequate treatments, but also because our care systems do not effectively address dementia and its consequences. For too many individuals with Alzheimer's and their families, the system has failed them, and today we are unnecessarily losing the battle against this devastating disease. Despite the fact that an early and documented formal diagnosis allows individuals to participate in their own care planning, manage other chronic conditions, participate in clinical trials, and ultimately alleviate the burden on themselves and their loved ones, as many as half of the more than 5 million Americans with Alzheimer's have never received a formal diagnosis.

Unless we create an effective, dementia-capable system that finds new solutions to providing high-quality care, provides community support services and programs, and addresses Alzheimer's health disparities, Alzheimer's will overwhelm the healthcare system in the coming years. For example, people with Alzheimer's and other dementias have more than three times as many hospital stays as other older people. Furthermore, one out of seven individuals with Alzheimer's or another dementia lives alone and up to half of them do not have an identifiable caregiver. These individuals are more likely to need emergency medical services because of self-neglect or injury, and are found to be placed into nursing homes earlier, on average, than others with dementia. Ultimately, supporting individuals with Alzheimer's disease and their families and caregivers requires giving them the tools they need to plan for the future and ensuring the best quality of life for individuals and families affected by the disease.

Recognizing this, President Obama's budget request for fiscal year 2014 included an increase of $80 million for Alzheimer's research at NIA and an increase of $20 million for education, outreach and support services. Congress, through the leadership of Chairman Harkin and Ranking Member Moran, provided much needed resources in the Consolidated Appropriations Act of 2014 that are allowing the pursuit of the goal of effectively treating and preventing Alzheimer's by 2025 to continue into the next immediate steps without faltering.

The funding provided in the Omnibus will allow scientists to pursue innovative research that will lead to new treatments, interventions and diagnostics. Continued funding of these programs will encourage a greater investment in the academic and

private sector and ultimately lead to a game-changing diagnostic or treatment. For all these reasons, it is vital that we continue to make investments in Alzheimer's disease research, education, outreach and support activities to implement the National Alzheimer's Plan as we look to fiscal year 2015.

CONCLUSION

Thank you again for the opportunity to testify today. I appreciate the steadfast support of the subcommittee and its priority setting activities. I look forward to continuing to work with Congress in order to address the Alzheimer's crisis. Alzheimer's is the costliest disease in the country and these costs are set to increase like for none other. I ask Congress to address Alzheimer's with the same bipartisan collaboration demonstrated in the passage of the National Alzheimer's Project Act (Public Law 111–375) and this subcommittee's deliberations on Alzheimer's, and with a commitment equal to the scale of the crisis. An epidemic is well upon us, and too many families are in situations like mine—facing a fatal disease that currently has no way to prevent, cure or even slow its progression. As a nation, we cannot afford to wait until Alzheimer's bankrupts the Nation, just as it already has so many hardworking families in Iowa, Kansas, and all across this country. We must make the smart investment now to realize a better, healthier future for our families and our Nation. Thank you.

Senator HARKIN. I appreciate your being here and your advocacy.

Next, we'll turn to Dr. Hurd, the author of this famous study that came out last year, I think, that really shook us all up.

STATEMENT OF DR. MICHAEL HURD, DIRECTOR, RAND CENTER FOR THE STUDY OF AGING

Dr. HURD. Thank you for the kind words about that study. It was challenging, as I'll outline now. Chairman Harkin and Ranking Member Moran, thank you for the opportunity to testify about the monetary costs of dementia in the United States.

My testimony will be based upon research that co-authors and I did at the RAND Corporation and the University of Michigan, and it was published last year in The New England Journal of Medicine. Emotional costs of dementia are immeasurable. Our more modest goal was to measure the monetary costs of dementia, but even so, there were a number of challenges.

[The information follows:]

The link for the RAND study can be found at: http://www.rand.org/pubs/external__publications/EP50247.html.

Dr. HURD. First, most people with dementia have co-existing health problems, such as a history of stroke or a heart condition, which by themselves would lead to higher costs. We wanted to find the cost attributable to dementia itself, not the healthcare costs of people with dementia.

A second difficulty concerns informal care, that is, unpaid care most often performed by a family member. We had to develop a method of placing a monetary value on that care, knowing it could have a large effect on our estimates.

These are other challenges made it difficult to find valid and reliable data that were adequate for the needs of this research.

Fortunately, the National Institute on Aging, NIA, under the leadership of Dr. Hodes and Dr. Richard Suzman, had the foresight many years ago to invest in a data infrastructure, the Health and Retirement Study, without which this research could not have been accomplished. The HRS has become the preeminent data source for general population representative studies of aging. It provides a

wide range of data, including cognition, healthcare use, costs, and informal caregiving.

However, the HRS lacked a measure of the dementia status of its respondents. In 1998, a multidisciplinary team, including myself, proposed and then fielded a small sub-study to diagnose a sample of HRS respondents for dementia status. In our study we used these diagnoses to estimate the dementia status of a much larger HRS sample, around 6,000 persons.

According to our results, in 2010, the prevalence of dementia in the population aged 71 or older was 14.7 percent. The annual healthcare spending attributable to dementia was about $29,000 per person. The great majority of these excess costs were for nursing home stays and paid in-home care. Adding in the costs of unpaid or informal care increased total annual cost per person to between $42,000 and $56,000, where the range depends on the method of valuing informal care.

We were not able to allocate costs between Alzheimer's and other dementias, but we know that the great majority would be due to Alzheimer's.

We used census estimates of the population to estimate the annual cost of dementia in the United States. We found that actual spending attributable to dementia was $109 billion in 2010. This cost places dementia as the most costly disease in the United States in terms of actual spending. Adding in costs for informal care increased this estimate to a range of $160 billion to $250 billion per year.

Because the prevalence of dementia sharply increases with age, the aging of the population in itself, particularly when the baby boom generation reaches an advanced age, will increase future costs. The cost for care purchased in the marketplace will increase in real terms from the 2010 value of $109 billion to $260 billion in 2040. That's in real terms. Adding in the costs of informal care increases the cost estimate to the range of $380 billion to $510 billion per year in 2040.

We are extending this research in two directions. Dementia is very costly on average, but these costs are unequally distributed. Some households spend nothing, while others might spend more than $100,000 per year. In new research, we find that the costs are even more skewed when accumulated over many years, because some people with dementia can be in a nursing home for 5 years or even longer. The accumulated costs can be financially devastating to some families.

In a second extension, because of the great importance of long-term care in the total cost of dementia, RAND is developing a report to be released this year that aims to help providers, payers, and policy makers efficiently improve long-term care for dementia.

PREPARED STATEMENT

In summary, dementia is already very costly and will grow even more costly. Clearly, medical breakthroughs that would prevent or delay onset are urgently needed, but even in the absence of such breakthroughs, innovations and policies that can reduce costs should be pursued.

Thank you, Mr. Chairman, and Ranking Member. Thank you for your attention, and I look forward to your questions.

[The statement follows:]

PREPARED STATEMENT OF MICHAEL D. HURD

Chairman Harkin, Ranking Member Moran, and members of the subcommittee, thank you for the opportunity to testify before you today about the monetary costs of dementia in the United States. My testimony will be based upon research performed at the RAND Corporation and the University of Michigan by me, and Professors Paco Martorell, Adeline Delavande, Kathleen Mullen, and Kenneth Langa. It was published in April, 2013 in the New England Journal of Medicine last year.

INTRODUCTION: DEMENTIA AND ITS COSTS

Dementia, a chronic disease of aging characterized by progressive cognitive decline that interferes with independent functioning, affects a large and growing number of older adults. The National Alzheimer's Project Act seeks to improve the ability of the Federal Government to track monetary costs incurred by individuals and public programs, such as Medicare and Medicaid, that result from dementia. We believe that our research will contribute to that effort.

Our goal in this research was to estimate the monetary costs due to dementia, not the monetary costs of people with dementia. Accurately identifying the costs attributable to dementia is challenging for many reasons but two stand out: First, persons with dementia are likely to have co-existing health problems: Insulating the costs attributable to dementia requires that they be separated from other concurrent healthcare costs. Second, informal caregiving, the unpaid care provided by family and friends for assistance with activities of daily living, is an important component of the support required by persons with dementia, yet it is unclear how to attribute a monetary cost to an informal caregiver's time.

DATA AVAILABLE FOR ESTIMATION

The complexities of the research made it difficult to find valid and reliable data that were adequate for our needs. Fortunately the National Institute on Aging, under the leadership of Dr. Richard Hodes and Dr. Richard Suzman, had the foresight many years ago to invest in a data infrastructure, the Health and Retirement Study (HRS), without which this research could not have been accomplished. The HRS is a longitudinal survey; that is, it interviews repeatedly the same individuals over time, about 20,000 persons over the age of 50 every 2 years in the case of the HRS. The HRS was first fielded in 1992 and since then has become the pre-eminent data source for population-representative studies of aging. Funded by the National Institute on Aging and the Social Security Administration, it provides a wide variety of longitudinal data on persons, including cognitive assessments and data on the need for assistance in activities of daily living as well as on healthcare and other costs. However, the HRS does not have a direct measure of dementia, but such a measure is available through the Aging, Demographics, and Memory Study, or ADAMS. The ADAMS is study of a nationally representative sub-sample of 856 HRS respondents who underwent a detailed in-home clinical assessment for dementia. Using the diagnoses of the ADAMS subjects, we constructed a statistical model to identify the probability that some 6,000 HRS respondents over the age of 70 had dementia.

We assessed several categories of healthcare spending: Out-of-pocket spending, spending by Medicare, net nursing-home spending, and formal and informal healthcare spending. Out-of-pocket spending includes any out-of-pocket healthcare expenses for nursing-home or hospital stays, medical visits, outpatient surgery, home healthcare, special services such as outpatient rehabilitation, prescription drugs, and dental services. Medicare spending is available for HRS respondents who agreed to the linkage of their Medicare records and who were enrolled in fee-for-service plans, or approximately 70 percent of persons in our study population. Net nursing-home spending distinguished between rates paid by Medicaid and those paid by third parties. Formal healthcare includes paid care in home. Informal care includes unpaid care in home, most often provided by family members.

INDIVIDUAL PREVALENCE AND COSTS OF DEMENTIA

Overall, we found 14.7 percent of the population 71 years of age or older had dementia in 2010. Nonwhite, female, single, less-educated, and lower-income persons have an elevated probability of dementia, as do persons with a history of stroke,

heart disease, or psychiatric conditions. Those who did not graduate from high school were more than twice as likely as those who graduated from college to have dementia, and those with household income of less than $15,000 were more than four times likely to have dementia as those with household income more than $75,000.

We distinguish between costs that flow through the marketplace such as spending for hospital stays, doctor visits, nursing homes, hired caregiving at home and so forth, and implicit additional costs that are due to informal care and result from caregivers withdrawing from the labor market. We found that persons with dementia had $33,329 more in annual healthcare costs that flow through the marketplace than persons without dementia. Adjusting for coexisting conditions and demographic characteristics reduced this estimate to $28,501. This is the average annual market cost attributable to dementia. Of the $28,501 in costs attributable to dementia, $13,900 is for nursing-home care, $6,200 is for out-of-pocket expenditure, $5,700 is for formal home care; Medicare spent $2,700 of the total.

We were not able to distinguish costs due to Alzheimer's disease from costs due to other types of dementia, but we know from other research that Alzheimer's disease is responsible for a large majority of dementia cases.

Adding the cost of informal care to the cost of market-based care increases the total annual costs due to dementia to $41,685 per person with dementia when based on the value of foregone wages. These costs would be $56,290 per person with dementia when based on the valuation of replacement cost for the informal care. Put another way, the value of informal home care represents 31 percent to 49 percent of the costs attributable to dementia, depending on how such care is valuated.

POPULATION-WIDE COSTS AND PROJECTIONS

To estimate the total cost of dementia to the U.S. economy now and in the future, we combined the adjusted cost per person with dementia with prevalence rates from the ADAMS and population estimates and projections from the U.S. Census. Multiplying the per-person costs for dementia by the estimated number of persons with dementia who were 71 years of age or older in 2010 indicates an annual population cost of $109 billion for care purchased in the market. Including the estimated value of informal home care boosts this estimate to a range of $159 billion to $215 billion. The cost for care purchased in the market place ($109 billion) places dementia as the most costly disease in terms of actual spending in the United States: According to tables based on the Medical Expenditure Panel Survey published by the Agency for Healthcare Research and Quality, heart disease cost $102 billion in 2010 (adjusted from $96 billion in 2008) and cancer cost $77 billion in 2010 (adjusted from $72 billion in 2008). Because neither heart disease nor cancer is likely to require the large amount of informal care that is required by dementia, accounting for informal care would increase the cost difference between dementia and those diseases even further.

Because of the aging of the population, the fraction of the population at advanced old age where the risk of dementia is greatest will increase. By 2040, assuming that prevalence rates of dementia at each age remain the same, our estimates suggest that the costs for care purchased in the market place will more than double from $109 billion to $259 billion in real terms. Adding in the cost of informal care places the cost in 2040 from $379 billion to $511 billion, depending on the method for valuing informal care.

DIFFERENCES FROM OTHER ESTIMATES AND POSSIBLE BIAS

A critical assumption in our estimates was that real costs per case will remain constant. This may be likely for care-giving, because wages of workers likely to provide care have remained stable or even decreased in real terms. It is less likely, however, for healthcare spending such as that for hospital costs or medication costs. To the extent such costs continue to rise we may be underestimating future costs of dementia. However, the amount of bias may be relatively small because between 75 percent and 84 percent of attributable costs are for care-giving, which has not been subject to the large increases in prices of healthcare services.

Our cost estimates are considerably lower than those reported by the Alzheimer's Association, which estimated that annual monetary costs alone were $172 billion in 2010, compared with our estimate of $109 billion. There are several reasons for this difference. The Alzheimer's Association estimate of cost per case was higher than ours, but it was based on a more severely impaired population. Its estimated prevalence of dementia, which was higher than ours, was derived from a different population than the population that produced the cost per case. Prevalence came from a study of three Chicago neighborhoods. In that study the diagnostic criteria for de-

mentia did not require the presence of a limitation in activities of daily living, as the ADAMS does, likely explaining why prevalence was higher. Finally, its cost estimate was not adjusted for coexisting conditions, as ours was.

FUTURE RESEARCH

Considerable future research remains to be done on this topic. We did not address the distribution of costs, that is, who is likely to pay the costs of dementia, particularly at the household level. Most households will not incur large costs for dementia care: many patients will have their care covered by Medicaid or private long-term care insurance. Their nursing-home or hospitalization stays may be short and relatively affordable, or households will avoid serious hardship for some other reason. However, other households may face great costs because of nursing-home stays of 5 years or more. In new, ongoing research we found that when out-of-pocket spending for nursing homes is aggregated over time, the distribution of costs is highly skewed because of those very long nursing home stays. Thus, a minority of families may face financially devastating costs. Research is needed to quantify the distribution of costs so that families will have a better understanding of the risks.

Such research will also clarify the role of long-term care insurance. This situation in which many families incur minor costs but a few incur very large costs ought to call for an insurance solution, one in which the costs of long-term care could be spread across the entire population rather than being concentrated on the unlucky few. At the moment the long-term care insurance products that are available apparently do not meet the needs of the older population as evidenced by the very low take-up rates, about 13 percent in the population age 55 or older. Better designed products to reduce the risk of very large out-of-pocket spending for long-term care would help reduce a significant cause for concern of the older population.

Because a large majority of costs due to dementia are for long-term care, supported by a grant from a private donor, RAND is developing a report to be released this year that aims to help providers, payers and policy makers efficiently improve dementia long-term care.

RESEARCH FUNDING

This research on the costs of dementia was funded by a peer-reviewed grant from the National Institute on Aging.

Senator HARKIN. Thank you very much, Dr. Hurd.

Now we'll turn to Mr. Seth Rogen.

Mr. Rogen, welcome, and please proceed.

STATEMENT OF SETH ROGEN, STAND-UP COMEDIAN, ACTOR, PRODUCER, DIRECTOR, SCREENWRITER, VOICE ACTOR

Mr. ROGEN. Thank you very much for having me, Mr. Chairman, Ranking Member Moran, and the members of the subcommittee. Thank you for the opportunity to testify today and for the opportunity for me to be called an expert at something, because that's cool.

I don't know if you know who I am at all. You told me you never saw "Knocked Up," Chairman.

So, it's a little insulting.

It's very important, guys.

Senator HARKIN. I want the record to note this is the first—I will wager this is the first time in any congressional hearing in history, that the words "knocked up" have ever been uttered.

Mr. ROGEN. Oy. You're not going to like the rest of this, then.

First, I should answer the question I assume many of you are asking. Yes, I'm aware this has nothing to do with the legalization of marijuana.

In fact, if you can believe it, this concerns something that I find even more important.

I started dating my wife Lauren 9 years ago when her mother was almost 54 years old. The first time I met her parents, being the mensch that I am, I was excited to spend time with them and make Lauren think I was the type of guy she should continue dating.

It was this trip, the first time I met my now-mother-in-law, that Lauren first admitted to herself, and then to me, that something was off with her mother. I guess the clues were, unfortunately, easy to spot since both of Lauren's mother's parents had Alzheimer's disease. Soon after this trip, at 55 years old, Lauren's mother was diagnosed with early onset Alzheimer's.

Now, at this point, my impression of Alzheimer's was probably what I assume most people's impression is. I thought it was something only like really, really old people got, and I thought the way the disease primarily showed itself was in the form of forgotten keys, wearing mismatched shoes, and being asked the same question over and over. This period, which was the only way I'd seen Alzheimer's displayed on movies or television, lasted a few years for Lauren's mom.

After that, however, is when I saw the real ugly truth of the disease. After forgetting who she and her loved ones were, my mother-in-law, a teacher for 35 years, then forgot how to speak, feed herself, dress herself, and go to the bathroom herself, all by the age of 60. Lauren's father and a team of caregivers dedicate their lives to letting my mother-in-law be as comfortable as she can be. They would love to do more, but can't, because, as you've heard, unlike any of the other top 10 causes of death in America, there is no way to prevent, cure, or even slow the progression of Alzheimer's disease.

Another thing I didn't realize until I was personally affected was the shame and stigma associated with the disease. It was before I was born, but I'm told of a time when cancer had a stigma that people were ashamed by. Celebrities and other public figures that were stricken would hide rather than be voices of hope for people in similar situations. And although it's turning, this is currently where we are largely at with Alzheimer's disease, it seems like.

And it's because of this lack of hope and shameful stigma that my wife, some friends, and myself decided to actually try and do something to change the situation. We started Hilarity for Charity. Hilarity for Charity is a fund we have as a part of the Alzheimer's Association to raise money to help families struggling with Alzheimer's and support cutting-edge research.

That's right. The situation is so dire that it caused me, a lazy, self-involved, generally self-medicated man-child to start an entire charity organization. It was through this that we felt we weren't

just complaining there was nothing to be done, but actively taking steps to do something. Instead of being disappointed that young people were so misinformed about the reality of the disease, we've started to educate them.

We recently started a college program that allows university students to hold their own Hilarity for Charity events, and in the months since it's started, 18 schools nationwide had signed up to hold events. The fact that we actually got college students to stop playing videogames and volunteer their time is a huge accomplishment, especially considering both Xbox One and PlayStation 4 came out this year. I'm sure these people know what I'm talking about.

I came here today for a few reasons. One, I'm a huge "House of Cards" fan. Just marathoned the whole thing, had to be here.

Two is to say people need more help. I've personally seen the massive amount of financial strain this disease causes, and if the American people ever decide to reject genitalia-driven comedy, I will no longer be able to afford it. Please don't. Therefore, I can't begin to imagine how people with more limited incomes are dealing with this.

As you've also heard, studies show that Alzheimer's and related dementia is the most costly condition in the United States. Yes, it's more costly than heart disease in a country where, for a $1.29, you can get a taco made out of Doritos. They're delicious, but they're not healthy.

While death from other major diseases like heart disease, HIV, and strokes continue to decline, deaths from Alzheimer's have increased almost 70 percent in the last 15 years. Over 5 million Americans have Alzheimer's, and at this rate, in 35 years as many as 16 million will have the disease.

The third reason I'm here simply is to show people that they're not alone. So few people share their personal stories, so few people have something to relate to. I know that if me and my wife saw someone like me talking about this, it would probably make us feel a little less alone.

Americans whisper the word "Alzheimer's" because their Government whispers the word "Alzheimer's." And although a whisper is better than the silence that the Alzheimer's community has been facing for decades, it's still not enough. It needs to be yelled and screamed to the point that it finally gets the attention and the funding that it deserves and needs.

I dream of a day when my charity is no longer necessary and I can go back to being the lazy, self-involved man-child I was meant to be. People look to their Government for hope, and I ask that when it comes to Alzheimer's disease, you continue to take more steps to provide some more.

PREPARED STATEMENT

I would like to thank the committee again for the opportunity to share my story and to voice my wholehearted support for the continuing work that pursues a cure for Alzheimer's disease. Thank you very much.

[The statement follows:]

PREPARED STATEMENT OF SETH ROGEN

Mr. Chairman, Ranking Member Moran, and members of the subcommittee, thank you for the opportunity to testify today, and for the opportunity for me to be called an "expert" at something, because it makes me feel smart.

I should first answer a question I assume many of you are asking: Yes, I'm aware this has nothing to do with the legalization of marijuana. In fact, if you can believe it, this concerns something that I find even more important.

I started dating my wife, Lauren, 9 years ago, when her mother was almost 54 years old. The first time I met her parents, being the mensch I am, I was excited to spend time with them and make Lauren think I was the type of guy she should continue dating.

It was this trip, the first time I met my now mother-in-law, that Lauren first admitted to herself, and then to me, that something was off with her mother. I guess the clues were unfortunately easy to spot since both of Lauren's mother's parents, had Alzheimer's disease. Soon after this trip, at 55 years old, Lauren's mother was diagnosed with early onset Alzheimer's.

Now, I think at this point, my impression of Alzheimer's was probably what I assume most people's impression is. It was something I thought only really old people got, and I thought that the way the disease primarily showed itself was in the form of forgotten keys, wearing mismatching shoes, and being asked the same question over and over. This period, which was similar to how I'd seen Alzheimer's displayed movies and TV, lasted a few years for Lauren's mom. After that, however, is when I saw the real ugly truth of the disease. A side I literally had never been exposed to even by hearsay or dramatization.

After forgetting who she and her loved ones were, my mother in law, a teacher for 35 years, then forgot how to speak, feed herself, dress herself, and go the bathroom herself. All by the age of 60.

Lauren's father and a team of caregivers dedicate their lives to letting my mother in law be as comfortable as she can. They would love to do more, but can't, because unlike any of the top 10 causes of death in America, there's currently absolutely no way to prevent, cure, or even slow the progression of Alzheimer's Disease.

Another thing I didn't realize until I was personally effected, was the shame and stigma associated with Alzheimer's. It was before I was born, but I'm told of a time when cancer had a stigma that people were embarrassed by. Celebrities and other public figures that were stricken would hide rather than be voices of hope for people in similar situations. This seems to be where Alzheimer's is today. And it's because of this lack of hope and shameful stigma that my wife, some friends, and myself decided to actually try to do something to change the situation.

We started Hilarity for Charity. Hilarity for Charity is a fund we have as part of the Alzheimer's Association to raise money to help families struggling with Alzheimer's and support cutting edge research.

That's right. The situation is so dire that it caused me, a lazy, self involved, generally self-medicated man-child to start an entire charity organization. It was through this we felt that we weren't just complaining there was nothing to be done, but actively taking steps to do something. Instead of being disappointed that young people were so misinformed about the reality of the disease, we've started to educate them.

We recently started a college program that allows university students to hold their own Hilarity For Charity events, and in the month since it started, 18 schools nationwide have signed up to hold events. The fact that we got students to volunteer their time is a huge accomplishment; especially considering both Xbox One and PlayStation 4 both came out this year.

I came here today for a few reasons:

One: this is a super cool story, and I'm a huge House of Cards fan.

Two is to say, people need more help. I've personally seen the massive amount of financial strain this disease causes, and if the American people ever decide to reject genitalia driven comedy, I would no longer be able to afford it. Therefore, I can't begin to imagine how people with more limited incomes are dealing with this. Studies show that Alzheimer's and related dementia is the most costly condition in the United States. Yes. It's more costly than heart disease in a country where for a $1.29, you can get a taco made out of Doritos.

While deaths from other major diseases like Heart disease, HIV, and Strokes continue to decline, deaths from Alzheimer's have increased almost 70 percent in the last 15 years. Over 5 million Americans have Alzheimer's and at this rate, in 35 years, as many as 16 million will have the disease.

The third reason I'm here, simply, is to show people they're not alone. So few people share their personal stories, so few people have something to relate to, I know

that if me and my wife saw somebody like me talking about this, we would feel less alone.

Americans whisper the word Alzheimer's because their Government whispers the word Alzheimer's. And although a whisper is better than the silence that the Alzheimer's community has been facing for decades, it's still not enough. It needs to be yelled and screamed to the point that it finally gets the attention and the funding it deserves and needs, if for no other reason than to get some peace and quiet.

People look to their Government for hope, and I ask that when it comes to Alzheimer's disease, you continue to take more steps to provide even more.

I would like to thank the committee again for the opportunity to share my story and to voice my wholehearted support for continuing the work that pursues a cure for Alzheimer's disease.

Senator HARKIN. Thank you, Mr. Rogen. That was great. That was very, very good. Thank you, thank you.

Although I'm sorry you had to unmask me; I'm really Kevin Spacey in disguise. Not too many people knew that.

Thank you all very much.

I'll start out with Dr. Hurd. I'm pleased to see your research was funded by the National Institute on Aging. You may be aware, all of you, or maybe you're not aware, that some of my colleagues in the House of Representatives hold a different view of the role of NIH in health economic research.

In fact, the House draft of last year's appropriations bill, our counterpart, which they released but did not pass, included language that would have precluded NIH from supporting any health economics research such as what Dr. Hurd did.

So, Dr. Hurd, as an economist researcher, how important is NIH's support to your work? Are there other Federal grants you could have applied for to get this study off the ground?

Dr. HURD. It's extremely important, I would say all-important to my work. I'm the holder of several investor investigator initiative RO1s and program projects, as well as a center grant.

The importance of NIH funding comes from its long-term, I would say primarily from its long-term reach and also from its multidisciplinary aspect. Our study involved cognitive scientists, economists, gerontologists, and similar. That kind of assembling of a team is not easy outside of the NIH umbrella.

The long-term reach, however, is extremely important. I mentioned the HRS was the foundation for this study. It would not have been possible without the HRS. The HRS began in 1992. I was part of the original team assembling HRS. That kind of sustained funding over many years, I think, does not happen outside of NIH for this type of research. I mentioned the 1998 study, a similar example, where we laid the foundations for the study that we published in The New England Journal, really in 1998 and pursued over many years.

So I just don't think the kind of study that we did would be feasible outside of the NIH. I don't know of an agency that would support that kind of long-term study, as well as the multidisciplinary aspects.

Senator HARKIN. I appreciate that. Now, we didn't do that on this side. Bipartisanly, we didn't. But I just want to get that out just so that people understand that and that, hopefully, the House won't repeat that again this year.

Representative Moore, as a former policy maker, and a patient, is there anything you've personally experienced that would change?

Is there anything we need to better educate primary care physicians on, number one? I'll ask two questions. That was number one, Dennis.

Secondly, you've spent a lot of time on this side of the dias. Is there—if you were up here, what questions would you ask of NIH? Is there anything that we didn't ask or something that we didn't cover?

Mr. MOORE. I really think you have asked the appropriate questions of NIH. I just think it's important that people in this country understand that this is a disease that's affecting more and more people. I had it in my family with my dad. So I wasn't terribly surprised when I was diagnosed. I understand there are some genetics involved. It's something you wouldn't wish on anybody, but it happens.

And I hope someday they will find a cure. But right now, I just think as a nation we need to deal with this disease as best we can, and I really, really, really appreciate the fact that you're holding this hearing and trying to get more information so you can do the right thing.

Senator HARKIN. Thank you very much, Dennis.

Mr. MOORE. Thank you.

Senator HARKIN. Mr. Rogen, I got to be honest.

I was reading this last night very quickly. I was reading through it, and I said, "Hillary for Charity? Hillary?"

Mr. ROGEN. Yeah. I forgot the T, I think, yeah.

Senator HARKIN. I had to stop and go back and read that again.

Mr. ROGEN. Exactly. It's a progressive program.

Senator HARKIN. So, tell us more about Hilarity for Charity and why focus on young people?

Mr. ROGEN. We chose to focus on young people because they are the ones who will be affected by this very soon. And there seems to be almost zero acknowledgement of it in the world of these young people. It seems to be something that's not of a high priority.

It seems to be something that people, again, think only happens kind of naturally when people enter their 90s. And I don't think people understand that it's not their grandparents being affected, it's their parents being affected. And soon enough, it's them being affected.

I really just saw that firsthand and really felt that there was a massive hole missing when it came to, you know, informing young people about the reality of this disease. And it didn't seem like a high priority anywhere globally to inform young people about the disease. So we decided we should do it because no one else seemed like they were going to.

Senator HARKIN. Good for you.

Senator Moran.

Senator MORAN. Mr. Chairman, thank you very much. I don't know that I'll ask Mr. Rogen any questions. I'm a dull, boring person.

And I would certainly be reticent to have a conversation with you as a comedian. I was fully prepared to be shown up by you, but it really bothers me that Senator Harkin is even funnier.

Mr. ROGEN. That Kevin Spacey line was great, yeah.

Senator MORAN. So, I don't know whether I'll ask you a question or not. I'll start it with Dr. Hurd.

And this really probably is a question, perhaps for Dr. Collins and his crew at NIH. As I was listening to Dr. Hurd's testimony, it occurred to me that it would be useful for me to understand whether the prevalence of Alzheimer's is increasing, or is that just a factor of us living longer?

I don't know the answer to that. But I assume that has significant cost consequences. So do the costs—are you expecting greater costs in the future as a result of longevity? And then scientifically, on a research basis, has Alzheimer's been with us to the degree that it is today into the past? It's just that we now live longer and therefore—it's not that we're physiologically changing, it's just that we lived longer and therefore the evidence exists?

I don't know whether that's a question for you, Dr. Hurd, or not. But before I've forgotten my question, I wanted to make certain that I got it in front of Dr. Collins.

Dr. HURD. I can say something about that in two ways. We looked in our data to see if we saw any trend in prevalence adjusted for age. So you're exactly right. One needs to be quite careful about increased dementia due to increases in aging of the population, from changes in dementia prevalence holding age constant.

The latter would be a very important finding because then that would suggest that, as the population ages, we may see less prevalence than had been forecast. Our forecasts are based upon constant prevalence holding age constant.

So, the question came up earlier about over the age of 90. We estimate around 38.5 percent of those over the age of 90 are suffering from dementia. We assumed that rate remained constant to 2040 until it's the aging of the population, more people reaching those ages, that caused the increase in overall population prevalence and the increases in cost.

We studied our data quite carefully whether we could see any change in age-specific rates of dementia over time. We saw a slight suggestion of that, but we're not ready to write a paper on that until we really are quite certain about that.

There was a recent study in The Lancet in England that suggested a decline in age-specific prevalence of dementia, quite a large decline in prevalence. I think before we would want to take that and put that into a forecast, we would want to have more examples of that from a wider range of populations.

But right now, I think, at least from our perspective, we do not see any change in age-specific prevalence.

Senator MORAN. Doctor, we generally have been using the word "Alzheimer's," and you've been using the word "dementia." Is there a distinction to be drawn here?

Dr. HURD. Yes. We used—our study was about dementia because that's what our data would support. We had sub-diagnoses of Alzheimer's, but the data, we didn't have enough observations really to distinguish those.

This is somewhat outside my area of expertise, but my understanding is that there is somewhat of a blurring line between many forms of dementia and Alzheimer's. The majority of dementia is

Alzheimer's, the great majority. But typically, there will be vascular dementia in addition to Alzheimer's at the same time.

Senator MORAN. Should we expect an announcement, another study, or the results of another study from you related to these topics?

Dr. HURD. We're working right now. We have an RO1 from NIA to look at long-term care, the costs of long-term care and the role of health insurance for long-term care, long-term care insurance. Why do we not have a functioning long-term care insurance market? It's very clear that the costs are highly skewed, and this should be an insurable situation. But we don't yet have a well-functioning market for that. And we've produced one paper on that and will produce further papers.

Senator MORAN. Thank you very much.

Mr. Rogen, I appreciate your work, Hilarity for Charity. And so my comments are dull and boring, but it's really an expression of gratitude. I appreciate your efforts to educate and to communicate with young people.

One of the things that I might suggest in that regard, and in talking to young people, is we need to instill in American young men and women the desire to pursue careers, degrees, and education in science, research, and medicine. We need the next generation of the doctors that were in the preceding panel. And I just would encourage you, and maybe you have comments in that regard, but to do everything that you can to instill in people the desire that this is a noble calling worthy of a career.

Mr. ROGEN. Yeah. I would love to do that. But actually, I think one of the most distressing things, honestly, I learned today was talking to Dr. Hodes before the panel, just in the little waiting room area.

And he was explaining to me something that he touched on here as he was talking, was how the funding for the research in this area is so sporadic and inconsistent that people—and I relate to it as just a young person who is pursuing a career—people are discouraged from entering this pursuit because it's not as financially stable as many of the other diseases that are having great strides taken in, you know, conquering them.

And I will do my best to encourage it. But again, I ask the Government to create a situation financially where there's the means for the people with ideas to actually do something with them. I mean, what he told me, again backstage, was there's people that come to us with ideas that could literally be the thing that cures this disease. And what we have to tell them is, "There's a one in six chance of that getting funding."

And they probably take from that, "Man, if I go focus on heart disease, I'll make more money and I'll also save lives." But it's a more glamorous situation financially. Alzheimer's just isn't a cool disease, unfortunately.

And it's something that I think, you know, that was honestly one of the most distressing things I heard today was, even people whose natural instinct would be to pursue curing this disease are discouraged from the financial landscape of this profession.

Senator MORAN. Well, while you earn a living as a comedian, you are a very effective lobbyist.

Mr. ROGEN. I'll do it. You give the means, I'll give you the people.

Senator MORAN. I certainly noticed that although you will find that it's, this request, this plea for constant increasing of funding is one that we've made for a number of reasons. But included in those reasons is the understanding that people who are making decisions about what to do in their careers need to know, whether it's Alzheimer's or any other disease, that NIH funding is going to be there and there's an opportunity for them.

The uncertainty that Congress and the administration can create in budgets and spending creates a real challenge as we try to recruit young people to the professions.

Mr. ROGEN. And I think that mentality trickles down to people my age, and just honestly, shows them that it's not that high of a priority on a national level. And that's what we're trying to change.

Senator MORAN. Thank you very much.

Let me now visit with my former colleague from Kansas.

Dennis, thank you very much for being here. I appreciate you reminding me that I was at your father's funeral. I remember his condition and the reminder of heredity in Alzheimer's disease. My question to you is this: What is the state of knowledge? What is it that we know? When you've been diagnosed with Alzheimer's, what is it that they can tell you to do to make the quality of your life better, to slow the process?

In other words, my impression would be that you would be a typical patient who learns of a diagnosis and you've pursued, I assume, all the opportunities to try to find things that make life better over the course of your remaining life. What is it that's out there that people can tell you, our healthcare professionals and others that can tell you what you can do? What does the Alzheimer's Association tell you to do to accomplish that in your life?

Mr. MOORE. Basically, to take the medication that they've diagnosed for me, and others, I think. And also to get some exercise, which I try to do on a daily basis. And my wife very much encourages me to do that. And I'm a smart husband: I say, "Yes, dear."

Senator MORAN. Very good. Some things we won't forget. It's a good thing.

Mr. MOORE. Right, right.

Senator MORAN. Well, Dennis, again, I appreciate you and your public service.

Mr. MOORE. Thank you.

Senator MORAN. The chairman had a long list of things that you've done in our State. And I wish you and Stephene absolutely all the very best. And it's very pleasing to me to see you here not on your behalf, but on behalf of all the people who sit in this audience and the thousands of Americans and people around the world who have encountered the same circumstance that you encounter.

And the way that you're living your life, I believe, gives others courage and hope. And I commend you and Stephene for that tremendous addition to your life, another role to play, and you're playing it very well.

Mr. MOORE. I thank you very, very much for those comments. And I also thank you for conducting this hearing and learning more about this and what we as a nation can do to better deal with this situation of Alzheimer's, because millions and millions of

Americans, as you well know, are being affected by this. Thank you very much.

Senator MORAN. You're very welcome.

Mr. Chairman, thank you.

Mr. MOORE. Thank you, Mr. Chairman.

Senator HARKIN. Dr. Hurd, and maybe I need to get Dr. Hodes in on this, too. I'm a little confused here a little bit, listening to your response on this.

In other words, is dementia getting more aggressive, affecting more percent of the population? Or is there just an increase in the number of people over 65 that were living longer, so the incidence is more? Another way I guess I might say that is, is there any data that we have from the past about the prevalence of dementia, let us say, in someone who is 50 or 55, compared with what it is now? So, do we have a higher percentage of our population affected by dementia?

Dr. Hodes, maybe this is for you. I don't——

Dr. HODES. There is no evidence of an increase in the risk of dementia at a given age. I think, as you were alluding to, in past years there was so little awareness and specificity of diagnosis and so relatively few people reaching an age that we don't have accurate figures for that point. Certainly, longitudinal studies are ongoing now. But there is at present no evidence that there's an increase in the incidence of Alzheimer's at a given age.

Senator HARKIN. So, the percent of the population, say at age 55 or 60, that were diagnosed with dementia, say 50 years ago, is about the same as it is right now?

Dr. HODES. Well, really, I think all I can really say is there's no evidence of a change. Fifty years ago, we simply didn't have the statistics to answer your question.

Senator HARKIN. But you said that—I thought you told me, though, that it is about the same, that there hasn't been an increase in prevalence.

Dr. HODES. I'm trying to be careful. We have no evidence that there has been any change.

Senator HARKIN. Oh.

Dr. HODES. And I think if you were asking people, asking us to speculate, we don't—we don't know of reasons for change.

Now, there are, for example, vascular components to dementia that are affected by hypertension. And since hypertension is better controlled, we might have expected it to made a difference.

But the straightforward answer: Do we have statistics 50 years ago and now, comparable diagnostic means that would allow us to answer your question? The answer is: We don't know.

The studies that have been referred to, the population-based studies in Health and Retirement Survey that were—as an example—that are beginning now or began 10 years ago will tell us in the future, 10 years, 20 years from now.

Senator HARKIN. I see.

Dr. HODES. We'll be able to answer your question when you're here 20 years from now better than we can right now.

Senator HARKIN. I'm retiring next year, by the way.

Thank you very much.

Senator MORAN. I do have a question for Dr. Hodes.

Senator HARKIN. Dr. Hodes.

Senator MORAN. Dr. Hodes, thank you. I just saw the word "doctor" in front of "Hurd" and just started asking medical questions.

Senator Harkin has asked the question that I was trying to pursue better than I did. And if you took the 50 years away and said 5 or 10, is there evidence that the disease is more prevalent, the incident is changing, either increasing or decreasing in a shorter period of time? Or again, we just don't yet have the evidence, we've got to wait another 20 years?

Dr. HODES. We don't have sufficient evidence over time.

Senator MORAN. Now, do you want to comment in the longitudinal study, HRS?

Dr. HURD. Yes. So in the HRS, we again looked at that. This is the time period from about 2000 up to 2008, which is a very short time period, and maybe saw a slight suggestion of improvement in age-specific rate of dementia. But we want to pursue that further because of some technical reasons. As I mentioned, there was the study in Lancet that suggested an improvement. But I would say right now that we don't know.

But you have to have very consistent methods over a long period of time. We have that in the HRS, but not a long enough time period to be able to answer your question.

Senator MORAN. I think why I think this is important is that part of it is the cost. When you analyze what the costs are going to be, you need to know what the trend is. But also, from the diagnosis or the cause, are there environmental factors? I hadn't thought about high blood pressure. But that, the increase of stress in life and higher blood pressure, what's the consequence? And again, does that then have a consequence on the disease we're trying to eradicate?

Dr. HURD. Absolutely. And as a part of the priorities through the national plan is having in place means to do just this sort of surveillance. So, the longest term success we mentioned, preventing, delaying Alzheimer's disease, will need to be reflected by monitoring these kinds of population effects. To do that, we have to have such surveillance. Those studies are now in place, and it's important we maintain them.

So we see whatever our interventions, whether it's on blood pressure or any other more specific approaches to treat or prevent dementias, we can monitor the impact on the prevalence of the disease, the risk of the disease in the general population.

Senator MORAN. Thank you very much, Dr. Hurd. Thank you for piquing my interest.

And, Dr. Hodes, thank you for answering the question.

Senator HARKIN. I have a follow-up question for Dr. Hurd. Let me find your testimony here again. Just a second. What did I do with it? Here it is. On this study, something leaped out at me. It was this: "Those who did not graduate from high school were more than twice as likely as those who graduated from college to have dementia. And those with household incomes of less than $15,000 were more than four times likely to have dementia as those with household income more than $75,000."

What does that tell us? Four times?

Dr. HURD. So these are raw statistics in the population over the age of 70.

Senator HARKIN. Okay. But why would income have any bearing on whether someone gets dementia or not?

Dr. HURD. It has to do with the correlation between age and income. Very old people have much lower incomes than younger people. So within the age 70 and above, the poorest people are the oldest people. And age is so highly correlated with dementia status.

Senator HARKIN. What do you mean the poorest people are the oldest people? Rich people live to be old, too.

Dr. HURD. Yes.

Senator HARKIN. They probably live longer because they are better able to get help.

Dr. HURD. Yes, that's certainly the case. More wealthy people live longer than poor people. It's a cohort difference. People who are age 90 live through a period where their earnings are substantially less than people who are age 70. So when the 90-year-olds were 70, they were poorer than today's 70-year-olds. And so there's a relationship between income and age that brings the relationship between income and dementia into the quantitative aspect that you mentioned.

Senator HARKIN. But when I read that, when you say household income less than $15,000 more than four times likely to have dementia as household income more than $75,000, I would assume that's at every stage, at 70, 72, 75, 80, 90. No? That's not right?

Dr. HURD. That's not what is in that table. It's not corrected for anything. For age in particular is the main aspect that it's not corrected for. And of course, in our research, we do correct for that. But in that particular table, there is not that correction.

Senator HARKIN. I'm having trouble with this.

Dr. HURD. Ask Mr. Rogen.

Mr. ROGEN. I actually get it, I think.

Senator HARKIN. You get it?

Mr. ROGEN. I think I do, right?

Senator HARKIN. And Kevin Spacey doesn't.

Mr. ROGEN. Yeah, exactly. I know.

Senator HARKIN. All right. Tell me. Tell me what you think.

Mr. ROGEN. I think what he's saying is that older people have less of an income, and therefore, if you're older, by default you'll have less of an income. And therefore, if you have dementia, odds are you're old. Which, odds are, means you don't have much of an income, which supports those statistics.

Senator HARKIN. Thanks. Thank you, Dr. Rogen.

Dr. HURD. It's easier to see in education, where the older population is much less educated. And so 90-year-olds have, on average, education of less than high school. And so in that table, education is highly related to dementia status simply because the much-older population is much less educated.

Senator HARKIN. Okay. My mistake is thinking that this was true at every level of age.

Dr. HURD. No. No.

Senator HARKIN. I understand now. I got that. I just wondered why there would be that difference, and there's not. I understand that.

Well, thanks for clearing that up, again, Dr. Rogen.

Mr. ROGEN. Any time.

Senator HARKIN. You have a future at NIH.

Or the RAND Corporation. I don't know which.

Did you have anything else?

Senator MORAN. Only this, Mr. Chairman. Thank you very much to these witnesses. Thank you to the earlier panel from NIH. We're very grateful for you allowing us to have this hearing today. And I found it very useful. I appreciate the folks here in the audience and across the country who are observing this hearing. We understand how important this issue is in a human, very direct way. And we want to continue our efforts to work together to find the cure and provide hope to the American people.

On a much more pedestrian matter, Senator Collins asks that she have a statement be made part of our record. And I would ask unanimous consent to accomplish her request.

Senator HARKIN. Without objection. So ordered. Also, I have received a statement from Senator Durbin. His statement will be inserted at this point as well.

[The statement follows:]

PREPARED STATEMENT OF SENATOR SUSAN M. COLLINS

Mr. Chairman, Ranking Member Moran, thank you for calling this hearing to examine the tremendous personal and economic toll that Alzheimer's disease takes on the individual, the family, and our Nation.

Like many families, mine has experienced the pain of Alzheimer's many times. There is no more helpless feeling than to watch the progression of this devastating disease. It is equally painful to witness the emotional and physical damage inflicted on family caregivers, exhausted by an endless series of "36 hour" days.

In addition to the human suffering it causes, Alzheimer's costs the United States more than $200 billion a year, including $142 billion in costs to Medicare and Medicaid. This price tag will increase exponentially as the baby boom generation ages. If nothing is done to slow or stop the disease, the Alzheimer's Association estimates that Alzheimer's will cost the United States an astonishing $20 trillion over the next 40 years.

It is estimated that nearly one in two of the baby boomers reaching 85 will develop Alzheimer's. As a consequence, chances are that the members of the baby boom generation will either be spending their golden years with Alzheimer's or caring for someone who has it. In many ways, Alzheimer's has become the defining disease of this generation. If we are to prevent Alzheimer's from becoming the defining disease of the next generation, it is imperative that we dramatically increase our investment in Alzheimer's disease research.

Alzheimer's is costing the United States more than $200 billion a year, yet we are spending less than three tenths of 1 percent of that amount—an estimated $584 million in fiscal year 2013—on research. We currently spend about $6 billion a year for cancer research, $3 billion a year for research on HIV/AIDS, and $2 billion for cardiovascular research, all worthy investments. Surely we can do more for Alzheimer's given the tremendous human and economic price of this devastating disease.

Investments in research for other diseases have yielded tremendous results: patients have access to new treatments, and death rates for some diseases are decreasing. At the same time, mortality due to Alzheimer's is escalating dramatically, and it stands alone among the top ten causes of death in the United States without an effective way to prevent it, cure it, or even slow its progression.

There is promising research in the pipeline that holds great hope for Alzheimer's patients and their families. The research community is poised to make important contributions toward the treatment of this disease through clinical trials and by investigating new therapeutic targets.

The Omnibus Appropriations bill for fiscal year 2014 takes an important step forward by providing for a $100 million increase for Alzheimer's disease research at the National Institute of Aging. I believe, however, that we need to do more.

The National Plan to Address Alzheimer's Disease, which was authorized by the 2010 National Alzheimer's Project Act which I co-authored with then-Senator Evan Bayh, has as its primary goal, to "prevent and effectively treat Alzheimer's disease by 2025." To meet that goal, the Chairman of the Advisory Council created by the legislation says that we will need to devote $2 billion a year to Alzheimer's research.

I believe that increasing our Nation's spending on Alzheimer's research to just 1 percent of what we are currently spending to care for Alzheimer's patients is a wise investment. I have therefore joined with my colleague from Minnesota, Senator Klobuchar, in introducing a resolution declaring that the goal of preventing and effectively treating Alzheimer's by 2025 is an urgent national priority. Our resolution calls for a doubling of our investment in Alzheimer's research in fiscal year 2015 and resolves that the Senate will develop a plan to meet our ultimate goal of a $2 billion annual investment within the next 5 years.

Mr. Chairman, Ranking Member Moran, I know that you share my commitment to finding a way to prevent and effectively treat Alzheimer's by 2025. Thank you for all of your efforts, and I look forward to working with you to meet that goal.

PREPARED STATEMENT OF SENATOR RICHARD J. DURBIN

Thank you Chairman Harkin for convening this hearing to raise awareness around the health and economic impact of Alzheimer's disease and the importance of biomedical research to prevent and treat Alzheimer's.

Alzheimer's is so much more than just memory loss. It is a debilitating disease that only gets worse as it progresses. People living with the disease often forget conversations, appointments, and eventually forget the names of close friends and may no longer recognize their spouse or their children. They struggle to recall the words to identify objects, and eventually lose the ability to read and write. Alzheimer's makes everyday activities like keeping track of bills and cooking a meal extremely challenging and frustrating. Although the disease develops differently for every person, it eventually leads to loss of memory, thinking, and reasoning skills.

Last year, approximately 450,000 people in the United States died from Alzheimer's disease. Today, more than 5 million Americans are living with the disease. And with a new person being diagnosed with Alzheimer's every 68 seconds, the number of people with Alzheimer's will rise to 16 million by 2050. If nothing is done to change the trajectory of the disease, more people and families will suffer and Federal spending on care will soar.

In 2013, the Medicaid and Medicare costs for caring for those with Alzheimer's disease was $203 billion. If we stay on this path, total medical costs associated with Alzheimer's disease are expected to rise to $1.2 trillion by 2050, an increase of more than 500 percent.

The promise of conquering Alzheimer's disease will only be fulfilled through sustained Federal investment into biomedical research. After several years of flat funding and spending cuts, NIH isn't able to fund all of the critical research that needs to be done. The number of research grants NIH funds has declined every year since 2004. In 2012, NIH funded 3,100 fewer grants than in 2004. Currently, less than 1 in every 5 qualified grant proposals to the NIH is awarded funding.

Disinvestment in NIH has a far reaching ripple effect that hurts economic growth and local economies in every State. Every dollar in NIH funding stimulates $2.21 in business activity that develops around research, such as biotech companies that provide supplies, food services and restaurants, building construction, and hiring support staff. Stagnant funding for biomedical research is short-sighted. It undermines everything we are trying to do for this country and delays the medical discoveries that will lower medical costs and improve the lives of people with Alzheimer's. But the true cost of inadequate support for Alzheimer's disease research is the toll that it takes on our loved ones.

Janet Dever is 73 years old and was diagnosed with Alzheimer's disease 5 years ago. She does her best to not dwell on the negatives or sink into depression. But she says that the hardest part of the disease is watching her family and friends suffer along with her. The part of the disease that upsets her the most is that many people don't know how to interact with her anymore, so they have stayed away. Janet and her husband Bill aren't giving up. And we shouldn't give up either.

Over the past few years, Congress and the Administration have stepped up the Federal investment in Alzheimer's research. In 2010, Congress unanimously passed the National Alzheimer's Project Act, which created a national strategic plan, establishing goals and action steps to combat the disease in the areas of research, care, support, and public awareness. In 2012, the NIH dedicated an additional $50 mil-

lion for Alzheimer's research. I will continue to work to bolster our national commitment to ensure investments are made in Alzheimer's research.

Last summer, I met with a research scientist in St. Louis, who was confident that biomedical research is on the cusp of making transformative discoveries for diseases like Alzheimer's, but he fears that what will keep us from making those discoveries will not be lack of knowledge, but lack of Federal funding.

Now is not the time for stagnant support for biomedical research. Now is the time to invest in NIH and promising research to develop cures and treatments for Alzheimer's. The Federal Government can and should play a leading role to ensure our Nation remains the leader in biomedical research, supports economic growth rooted in research, and saving lives and improving lives through medical innovations. I look forward to working with my colleagues to ensure continued and strong support for biomedical research and to improve the lives of people impacted by Alzheimer's.

Senator HARKIN. And again, I just join with my friend and my colleague, Senator Moran, in thanking you all. Again, thanks for our great leadership at NIH.

Dr. Collins, Dr. Hodes, Dr. Landis were here. Thank you for your great leadership.

And all of you who are here today, I know a lot of you came a great distance. I just want you to know this is an issue that we are serious about. And we've got to find the funding for it. And we've got to make sure we have a steady stream of funding. This up-and-down just can't continue.

I was very happy that I was able to join years ago with Senator Spector to double over 5 years the funding for NIH. But since then, it's gone downhill. We can't do that. We got it up in that plateau to think that's where we were going to go up from there. And it didn't work out that way.

So we need your presence here, but we need your presence back in your home States and back in your congressional districts, talking to your Members of Congress on both sides of the aisle to let them know the importance of this and the importance of the steady funding that we need for the National Institutes of Health.

So if you'll do that, I hope that our funding level this year will reflect again the kind of increases that we had last year. We'll do everything in our power to make that happen.

Again, I thank all of you for your advocacy, and I encourage you to keep strong in that advocacy.

ADDITIONAL COMMITTEE QUESTIONS

This place, this Senate, this Congress, however much you may read to the contrary in the newspapers and the media, it does respond to you. It responds to our constituents. It responds to the pressure. It responds to what people want us to do. And so, if you want this to happen, if you want us to make sure we get this good funding stream for NIH, you've got to keep the pressure up.

And if you'll do that, then I think that we will see the way clear for great strides in getting to that point where we can actually prevent, treat, and cure Alzheimer's. That's our goal. We're going to get there.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED TO DR. FRANCIS S. COLLINS

QUESTIONS SUBMITTED BY SENATOR TOM HARKIN

Question. As you know, I fought hard to overturn the Bush Administration limitation on stem cell research. At the time, there were a lot of high expectations for stem cell therapies that we have not yet seen come to fruition. Can you elaborate, for the record, on the role and the importance of stem cells on Alzheimer's research today?

Answer. The study of human embryonic stem cells has been essential in aiding researchers in the development of many of the methods, technologies and molecular tools that subsequently enabled them to generate induced pluripotent stem cells (iPSCs). iPSCs are adult skin cells that have been genetically reprogrammed to an embryonic stem cell-like state and are one of the most exciting areas of stem cell research in Alzheimer's and other neurodegenerative diseases. NIH-funded researchers have developed methods for turning iPSCs into different types of neurons, and are using these neurons to study disease mechanisms and test potential therapeutic drugs—all in a dish.

Recognizing the potential of iPSCs as a tool to enhance drug discovery and provide further insights into the cell biology behind neurodegenerative diseases, NIH is supporting several groundbreaking initiatives relevant to the application of iPSC technologies to Alzheimer's and related dementias. For example, six studies are currently active under a 2012 solicitation for research supporting development of human iPSCs and other reprogrammed cells for aging and Alzheimer's disease modeling. These include a study to generate and characterize iPSCs and neurons from individuals with both familial and non-familial forms of Alzheimer's; development of an in vitro model of inherited Alzheimer's disease; and a study using iPSCs to study Alzheimer's epigenomics. In a separate initiative, announced in 2013, investigators will use iPSCs to determine the function of candidate risk genes and genetic variants in order to identify new gene or cellular networks and molecular targets underlying the etiology of the disease. Applications have been received in response to this solicitation and are in review. In addition, NINDS has established consortia to develop and study iPSCs derived from patients with neurodegenerative diseases, including frontotemporal degeneration, a type of dementia related to Alzheimer's disease. Cell lines developed by these consortia as well as several Alzheimer's disease cell lines developed by other scientists are stored in the NINDS Repository at Coriell and are being distributed to academic and industry scientists all over the world.

The therapeutic potential of iPSCs remains undetermined, and considerable research is needed before these cells can be considered for testing as experimental treatments of Alzheimer's or other diseases. Currently, researchers must use viruses to introduce the reprogramming factors into adult cells, and this process must be carefully controlled and tested before the technique can be applied to clinical studies in humans. In animal studies, the virus used to introduce the stem cell factors sometimes causes cancers. Researchers are currently investigating non-viral delivery strategies.

Question. I have read about a new method of aging stem cells rapidly so that late-onset diseases can be better understood. Prior to this technique, we could create cells, but we would have to grow them for 60 or more years to see what happens in age-induced diseases. I read that a recently identified protein can age a cell in a matter of weeks. Can you explain for the record this Sloan Kettering study and give us an idea of what it might mean for research into spontaneous Alzheimer's disease?

Answer. In this study,[1] investigators introduced a protein called progerin, which is associated with premature aging syndromes (e.g., progeria), into induced pluripotent stem cells from Parkinson's disease (PD) patients. The progerin accelerated the aging process of neurons differentiated from the iPSCs, and the induced neurons manifested PD-like pathology within several weeks—considerably more rapidly than they otherwise would have.

If this technique can be replicated with cells from Alzheimer's patients, it could speed the pace of discovery by providing a renewable source of neurons within a very short period of time. This could facilitate basic discovery and provide a platform for rapid preclinical testing of Alzheimer's drugs.

Question. I am pleased to hear that genetic sequencing has become so rapid that in just 4 years we've moved from identifying one genetic marker to identifying elev-

[1] Miller et al. Human iPSC-based Modeling of Late-Onset Disease via Progerin-induced Aging. Cell Stem Cell, December 2013.

en. We could not have imagined this even 10 years ago. Are there similar high throughput testing mechanisms for compounds that could be identified as drug targets?

Answer. NIH is continually working to develop new mechanisms and techniques to speed preclinical testing of compounds for Alzheimer's disease. For example, NIH-supported investigators recently used a yeast model that produces toxic amounts of amyloid-beta, one of the disease's pathological hallmarks, to screen approximately 140,000 compounds. They found that a class of compounds related to the drug clioquinol, which alleviates amyloid toxicity in a mouse model, also reduced toxicity in the yeast model, suggesting that this strain of yeast may prove to be an effective, efficient, and relatively inexpensive model for rapidly testing potential interventions.

In addition, NIH is currently soliciting research applications to develop assays for high-throughput screening for potential therapeutic small molecule compounds. Although this new initiative is not specific to Alzheimer's disease, the National Institute on Aging—the lead Federal program for Alzheimer's disease research—is participating, and applications on Alzheimer's disease are encouraged.

NIH also supports drug discovery and development through programs such as the Blueprint Neurotherapeutics Program, which identifies investigators who have promising small molecule compounds but lack outside drug development expertise and infrastructure support and allows them access to a virtual pharma network of contract research organizations, technical and regulatory experts and project managers, with extensive biopharma-industry experience. The long-term goal of this program is to advance projects from medicinal chemistry optimization through Phase I clinical trials and facilitate industry partnership for their further development.

Identification of drug targets for Alzheimer's disease is also a high priority for NIH. For example, in response to input from the international research community at the May 2012 *Alzheimer's Disease Research Summit 2012: Path to Treatment and Prevention*, the NIH released four Funding Opportunity Announcements (FOAs) for new projects aimed at speeding up drug development and testing of new therapies, including one FOA intended to stimulate interdisciplinary research focused on the identification and preclinical validation of novel therapeutic targets within molecular networks involved in different stages of Alzheimer's disease pathogenesis. Three large projects have been funded under this initiative, including a study to identify and characterize therapeutic targets within the innate immune system; a study to discover, characterize and validate complex molecular networks and candidate genes that influence susceptibility to cognitive decline and Alzheimer's disease; and a study in which investigators will apply innovative analytical methods to large-scale molecular, cellular and clinical data from Alzheimer's patients to construct biological network models and gain new insights into the complex mechanisms of the disease.

Finally, identification and characterization of biomarkers and targets for intervention are the primary goals of the Accelerating Medicines Partnership (AMP). Through the Foundation for the NIH, AMP partners will invest more than $230 million over 5 years in the first projects, which focus on Alzheimer's disease, type 2 diabetes, and the autoimmune disorders rheumatoid arthritis and systemic lupus erythematosus. For Alzheimer's disease, AMP resources will be used to incorporate an expanded set of biomarkers into four ongoing trials designed to delay or prevent disease, and to then evaluate which of these biomarkers are most effective in reflecting the process of disease and its response to intervention. AMP resources will also support large-scale, systems biology analyses of brain tissue samples from people with Alzheimer's disease to validate biological targets that play key roles in disease progression in order to increase understanding of molecular networks involved in the disease and identify new potential therapeutic targets.

Question. We talked a little about the BRAIN initiative, which the recent Omnibus supported. As Dr. Collins mentioned, researchers have made great strides in imaging techniques for Alzheimer's disease. Can you explain how the BRAIN initiative is different than brain imaging research NINDS has been doing in the past few years?

Answer. The information from brain imaging research and from the BRAIN Initiative are different, but they complement each other and will ultimately come together to provide a more complete picture of how the brain works and what goes wrong in diseases like Alzheimer's. Brain imaging research has developed a powerful suite of non-invasive methods for clinicians to diagnose and therefore treat brain disorders and for researchers to study the living human brain in action. The various types of imaging can reveal brain structure, activity, and even biochemistry—for example, the accumulation of amyloid plaques that characterize Alzheimer's disease or the loss of the signaling molecule dopamine in Parkinson's disease. Brain imag-

ing, however, is currently limited in its resolution, both in space and time. At present, imaging methods look at areas of the brain or nerve pathways that include thousands or even millions of nerve cells, rather than at individual cells, and average activity over seconds, while brain cells exchange signals in milliseconds (thousandths of a second). The BRAIN Initiative, in contrast, will develop methods that can resolve the structure of individual nerve cells, nerve fibers, and synapses, that is, the connections between cells, and can monitor activity of tens of thousands of individual cells at the millisecond scale. This level of detail is essential to understanding how nerve cells, precisely connected in functional circuits, perform the computations that enable us to perceive, think, and act.

Another difference from brain imaging is that methods developed through the BRAIN Initiative will not only allow investigators and potentially clinicians to observe brain activity, but also to control the activity of individual nerve cells. We have learned from years of study in the simpler nervous systems of laboratory animals that manipulating nerve cells' activity is essential to analyze how circuits of nerve cells work. Optogenetics, for example, is a technology that enables researchers to control cells' activity with light pulses in experimental animals. As with brain imaging, methods now available to stimulate the human brain affect large populations of cells. Even so these methods can provide significant benefit for some diseases, such as deep brain stimulation for Parkinson's. As understanding of brain circuits advances and better methods become available to adjust their activity, the application of these new tools and technologies should provide better treatments for a much larger number of disorders.

One of the six funding opportunity announcements that NIH released for the BRAIN Initiative focuses on proposals for "next generation" human brain imaging that will go beyond incremental improvements in existing technologies. This has the potential to have as transformative an impact on brain science as next generation sequencing has had on understanding the genome.

Background.—Baby boomers are the offspring of a generation where we saw the first group of long surviving family members with Alzheimer's. Most baby boomers have, or will have, some exposure to this illness, and they are concerned about their futures. They do not want their children to have to take this on, and in some cases they are aware that their children cannot take it on—financially or emotionally.

Question. Early-onset Alzheimer's has become a bigger issue now that the baby boomers are contracting this illness in the prime of their lives. Would you elaborate on the difference between early-onset Alzheimer's and Alzheimer's or dementia? What are the symptoms and long-term effects of having early-onset Alzheimer's vs. showing signs later in life (55 vs. 80)? What are the survival rate differences? I know I hear that some people that are diagnosed at 75 can live for another 15–20 years.

Answer. Early- and late-onset Alzheimer's disease share the same characteristic pathologies (i.e., development of amyloid plaques and tau tangles in the brain), and symptoms and disease course for early-onset and late-onset patients are largely the same. For most patients, memory problems are the earliest and most prominent symptom. However, a subset of patients with early-onset disease will first experience non-memory symptoms, including difficulties with language, visuospatial skills, or executive function. These individuals also show distinctive patterns of brain atrophy that are not seen in patients with late-onset disease, and are less likely to carry the APOE-E4 genotype, which is associated with Alzheimer's-related memory loss.

Both early- and late-onset forms of Alzheimer's are associated with a reduced life expectancy. Life expectancy after a diagnosis of Alzheimer's disease can vary widely; some people live 20 years or more, although this is unusual. In a recent NIH-supported study, among participants over age 65 without dementia at baseline, individuals who were diagnosed with the disease lived an average of about 4 years post-diagnosis. Other sources place the average life expectancy for a newly diagnosed patient at 8–10 years. Life expectancy is influenced by a number of factors, including the patient's age at diagnosis, severity of disease at diagnosis, and overall health.

NIH-supported investigators have developed a tool physicians can use to predict length of time from diagnosis to the need for full-time care and to death. See http://www.cumc.columbia.edu/dept/sergievsky/predictor.html.

Question. We have entire generation of baby boomers that will eventually face Alzheimer's or regular dementia. While the actual, out-of-pocket, cost (not fees covered by insurance, Medicare or long-term care insurance) of both of these illnesses will be expected to be taken care of by the individuals and their families, how well will our Country be prepared to handle these cases? Let's assume that baby boomers, for the most part, are willing to assume the biggest costs—over 55 housing, assisted living facilities, 24-hour caregivers, how prepared will communities be? Will there be adequate facilities available? Do we have the proper training and reg-

ulations in place for their nursing care? (A concern I always hear is the turnover of caretakers in private and public run facilities.) Are you finding that young people want to pursue these kinds of careers? Are these factors considered when you and your labs are researching Alzheimer's disease and those affected?

Answer. As you know, there is a growing demand for a health workforce that is sufficiently prepared to meet the specialized needs of an aging population. Within HHS, several agencies are charged with ensuring that needs of this often vulnerable, underserved population are met, including the Health Resources and Services Administration, which focuses on bolstering the healthcare workforce to ensure that adults living with Alzheimer's disease and dementia have access to the care they need. HRSA supports several programs whose primary goal is to improve access to quality healthcare for America's elderly by addressing both the supply and education of geriatric specialties, including Alzheimer's disease and dementia.

We have found these programs to be successful in preparing our communities to meet the needs of our aging population. For example, in Academic Year 2012–2013, HRSA's Geriatrics Education Centers partnered with over 650 healthcare delivery sites, including nursing homes, chronic and acute disease hospitals, ambulatory care centers and senior centers, across the country to provide clinical and experiential training to over 25,000 student trainees. In addition, over 17,500 faculty-level trainees were trained on geriatric-related topics as a result of these types of activities.

Further, HRSA's National Center for Health Workforce Analysis continues to analyze long-term care across the country. This analysis will ultimately support a better understanding of how the Nation's healthcare workforce can best meet the needs of our aging population and inform the work of HRSA, NIH, and other agencies across the Department that focus on geriatric and elder care.

Question. Some independent labs are offering testing for individuals that think they may be susceptible to Alzheimer's in their future (due to family members, etc.), and there is talk concerning the fact if Alzheimer's if treated early, possibly before the disease really gasps the brain, that early drug treatment could help these particular individuals. What do you say about that? Would you recommend that people seek this kind of advance information? And, is it true that early treatment might slow down the effects?

Answer. The realization that the most effective way to treat and prevent Alzheimer's disease may be to attack it early, before symptoms begin, represents a watershed moment in the history of the disease. Investigators have discovered that higher amounts of brain beta-amyloid, the toxic protein that clogs the brains of Alzheimer's patients and is associated with memory loss and other symptoms, is related to an increased risk of developing dementia over time and to loss of brain volume and subtle declines in cognitive abilities. These findings suggest that brain beta-amyloid may in fact be a preclinical sign of disease even among individuals who appear cognitively normal. Other studies have shown that beta-amyloid may be present in the brain for years—even decades—before clinical symptoms are evident, raising the possibility that a "window of opportunity" exists to stop the disease in its tracks before it has the opportunity to cause obvious outward effects.

However, we are just beginning to test preventive strategies, including anti-amyloid therapies, in at-risk, pre-symptomatic patients, and results from these studies will not be available for several years. One very exciting such study is a 5-year clinical trial to determine if an antibody treatment, crenezumab, designed to bind to and possibly clear away abnormal amounts of amyloid protein in the brains of people with Alzheimer's, can prevent decline in cognitive function. Crenezumab will be tested among members of a unique and large family population in Colombia sharing a genetic mutation known to cause observable signs of Alzheimer's disease at around age 45. These individuals will be treated at a time when abnormalities have appeared in brain images, but before appearance of symptoms, when it may be possible to have an effect before irreversible damage has occurred in neurons and their connections. In another study, investigators are employing a similar strategy of early intervention in testing an anti-amyloid drug in cognitively normal older volunteers who are at increased risk of developing late-onset Alzheimer's because they inherited two copies of the APOE-E4 allele, the best known genetic risk for late-onset disease. In addition, researchers on the Dominantly Inherited Alzheimer's Network Trials Unit trial are testing new anti-amyloid-beta drug treatments in volunteers who have an inherited form of Alzheimer's disease. We anticipate results from the DIAN trial in 2016.

The question of whether an individual should undergo testing to assess risk for Alzheimer's disease is complex and highly personal, and is best made in close consultation with that individual's healthcare provider.

QUESTIONS SUBMITTED BY SENATOR JERRY MORAN

BARRIERS TO A CURE

Question. Alzheimer's disease currently has no cure, no diagnostic test, and only symptomatic treatments. The Alzheimer's Disease Summit mentioned several impediments to finding an Alzheimer's cure, including the cost of bringing a potential treatment to market. Can you explain the barriers preventing us from finding a cure for Alzheimer's disease?

Answer. Alzheimer's disease is highly complex, with an imperfectly understood etiology and an often complex underlying pathology. These are some issues that have slowed our search for a cure.

—A significant percentage of dementias is considered "mixed," i.e., it may combine Alzheimer's characteristic amyloid plaques and tau tangles, vascular pathologies, and other issues. This makes it difficult to know what, specifically, to target in the brain—or how to target it.

—A major issue, and one that we are now addressing, is that previous trials may have been intervening too late in the disease process to be effective. Biomarker studies have shown that Alzheimer's pathology may be present in the brain literally for decades before symptoms occur, and we're finding that by the time symptoms appear in the clinic, it may be too late to intervene. For this reason, we've begun several major trials in individuals who are either asymptomatic but show Alzheimer's lesions on imaging, or who are at very high genetic risk. We have high hopes for this research and will report promptly and regularly on results.

Question. Are you meeting the milestones set forth in the National Plan to Address Alzheimer's Disease?

Answer. NIH has been successful in meeting the initial milestones established in the National Plan, and is well positioned to continue meeting milestones in the immediate future.

For example, the National Plan calls for the identification of research priorities and milestones. NIH has taken the following steps:

—Conducted the first Alzheimer's Disease Research Summit in May 2012. The Summit was attended by an international group of some 500 researchers, clinicians and members of the broader Alzheimer's community who worked together to identify research priorities and strategies needed to accelerate the development of successful therapies. A follow-up Summit is planned for 2015.

—Collected feedback on research needs and priorities through a 2012 Request for Information.

—Held the "Alzheimer's Disease-Related Dementias: Research Challenges and Opportunities" conference in May 2013 by NINDS, in collaboration with NIA and with support from several foundations (http://www.ninds.nih.gov/ADRD2013). This conference included an international group of experts that developed prioritized research recommendations to address AD-related dementias including frontotemporal degeneration, Lewy body disease, vascular and mixed dementias, as well as clinical diagnosis and health disparities in AD-related dementias.

—Regularly updated the Plan to reflect evolving scientific opportunities and needs.

Elsewhere, the Plan calls for the expansion of research aimed at preventing and treating the disease. NIH activities in this area include:

Strategy: Expand research to identify the molecular and cellular mechanisms underlying Alzheimer's disease, and translate this information into potential targets for intervention.

Under several funding opportunity announcement (FOAs) issued in response to the 2012 Summit, NIA has recently funded several major projects responsive to this strategy:

—*Pathway Discovery, Validation, and Compound Identification for Alzheimer's Disease,* a study to discover, characterize and validate complex molecular networks and candidate genes that influence susceptibility to cognitive decline and Alzheimer's disease.

—*Integrative Biology Approach to Complexity of Alzheimer's Disease,* through which investigators will apply innovative analytical methods to large-scale molecular, cellular and clinical data from Alzheimer's patients to construct biological network models and gain new insights into the complex mechanisms of the disease. Several cellular and animal models will be used to validate the actions of individual genes, as well as entire molecular networks predicted to drive the disease.

—*A Systems Approach to Targeting Innate Immunity in Alzheimer's,* which will use a systems biology approach to integrate genomic, gene expression, and pathological data from Alzheimer's patients and Alzheimer's mouse models and analyze them in novel ways with the goal of identifying and characterizing therapeutic targets within the innate immune system. The study builds on the genetic and pathological evidence that the innate immune system, which provides immediate defense against infection, and brain inflammation have a significant role in Alzheimer's disease.

Strategy: Expand genetic epidemiologic research to identify risk and protective factors for Alzheimer's disease.

NIA is accelerating the search for genes involved in late onset Alzheimer's disease (AD) through the AD Genetics Initiative. NIA is stepping up the collection of a large bank of genetic material, cell lines, and data from families with multiple members with late-onset AD at the http://www.ncrad.org/. A case-control series also is being developed. Qualified scientists will use the bank to search for the remaining risk factor genes that contribute to late-onset AD, the most common form of the disease. Scientists will share genetic data developed from their research on an NIH-approved Web site, usually the NIA Genetics of Alzheimer's Disease Data Storage Site or dbGaP. Discovery of risk factor genes will help illuminate the underlying disease processes of AD, open up novel areas of research, and identify new targets for drug therapy.

For a complete update on activities related to the National Plan, please see http://aspe.hhs.gov/daltcp/napa/NatlPlan2014.shtml

Question. A working draft of a report presented at the Alzheimer's Disease Summit in November 2013 mentioned several impediments to finding an Alzheimer's cure. The barriers include a lack of biomarkers, finding appropriate people for clinical trials, and the lack of partnerships with the private sector. How would you prioritize these barriers and what is being done to overcome them?

Answer. Each of these issues is significant, and NIH is taking steps to address them. For example:

Biomarkers.—NIH supports a number of initiatives aimed at identifying and validating biomarkers for Alzheimer's disease. These include:

—*The Alzheimer's Disease Neuroimaging Initiative (ADNI)*. This ambitious study began in October 2004 and was designed to find more sensitive and accurate methods to detect Alzheimer's disease at earlier stages and mark its progress through biomarkers. The study gathered and analyzed thousands of brain scans, genetic profiles, and biomarkers in blood and cerebrospinal fluid that are used to measure the progress of disease or the effects of treatment. In 2011–2012, data from ADNI facilitated the development of new diagnostic and neuropathologic criteria for mild cognitive impairment and Alzheimer's disease. Phase II of ADNI is currently underway to define changes in brain structure and function as people transition from normal cognitive aging to mild cognitive impairment (MCI—often a precursor to Alzheimer's) to AD.

—*The Biomarkers for Older Controls at Risk for Dementia (BIOCARD) study*.—This longitudinal study was initiated in 1995 and uses repeated clinical evaluations, neuropsychological testing, neuroimaging, and fluid biomarkers to understand and predict progression from normal cognition to mild cognitive impairment (MCI) and to dementia, particularly Alzheimer's disease. Participants are cognitively normal individuals who were first degree relatives of patients with dementia.

Encouraging Participation in Clinical Trials.—Insufficient participant recruitment for research can delay or cause research study cancellation, a substantial waste of resources. The need for Alzheimer's clinical research study participants is particularly urgent: Tens of thousands of volunteers are needed for research studies focused on delaying, treating or preventing this growing public health problem. To address this need, NIH has established several programs and initiatives.

—*Recruiting Older Adults into Research (ROAR) Project*.—Through this initiative, the Administration for Community Living, and the Centers for Disease Control and Prevention, the NIH, and their networks of state and community-based health and social service providers collaborated with researchers and private organizations to raise awareness, enhance knowledge and connect gatekeepers and older adults with easy, actionable opportunities for research participation. The cross-agency team established partnerships with existing government-funded resources and registries such as ResearchMatch, a free, national recruitment registry funded in part by NIH; the Alzheimer's Prevention Registry; and the Alzheimer's Association's TrialMatch service. The goal of the ROAR project is

to significantly increase older adult enrollment in these registries, allowing for more targeted invitations to enroll in current and future research studies.

—*NIH Request for Information*.—In 2012, the National Institute on Aging issued a Request for Information seeking input regarding strategies for increasing enrollment in Alzheimer's and related clinical trials. The Institute received approximately 20 responses, which will inform recruitment activities going forward.

—*Outreach activities*.—To help the public learn more about participating in clinical research, NIH created the resource "NIH Clinical Research Trials and You". The Web site includes personal stories from study participants, information about how to find a clinical trial, and educational resources for healthcare providers and the public. Among the materials included on the NIH Web site, as well as directly from the NIA, is the NIA fact sheet "Participating in Alzheimer's Disease Clinical Trials and Studies", which describes Alzheimer's disease clinical trials and studies, explains their scientific design, and offers key facts and questions to consider about volunteering for clinical research.

Partnerships with the Private Sector.—NIH has successfully teamed with private-sector partners on several initiatives, most notably the Alzheimer's Disease Neuroimaging Initiative (see above). More recently, NIH has established the Accelerating Medicines Partnership (AMP), a bold new venture between the NIH, 10 biopharmaceutical companies and several non-profit organizations to transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets of disease. The ultimate goal is to increase the number of new diagnostics and therapies for patients and reduce the time and cost of developing them. Alzheimer's disease is one of the first disease areas to be addressed through AMP. By optimizing the process for identifying and validating clinically relevant disease targets for drug design, AMP aims to increase efficiency, improve the drug development process, and increase the number and effectiveness of new targeted therapies.

Question. Are these barriers specific to Alzheimer's?

Answer. These barriers, while significant, are not specific to Alzheimer's disease, and many of NIH's ongoing programs and initiatives reflect this. For example, AMP will facilitate partnerships related to type 2 diabetes, rheumatoid arthritis, and systemic lupus erythematosus, in addition to Alzheimer's. The NIH Clinical Trials Resource (discussed above) is not specific to Alzheimer's disease, and in fact NIH supports a thriving communications and outreach infrastructure that provides information and support to patients with hundreds of diseases and conditions. Finally, identification of disease-specific biomarkers is an important priority in a number of disease areas, including neurological diseases and cancer.

PHYSICAL ACTIVITY'S EFFECT ON PREVENTION/TREATMENT

Question. As we continue to search for a cure, there is promising evidence physical activity may prevent or delay Alzheimer's disease. However, it is my understanding that we are just scratching the surface on how lifestyle factors such as diet and exercise can influence the risk of developing the disease. At the University of Kansas Alzheimer's Disease Center, research is ongoing related to the role of exercise in preventing Alzheimer's disease. Could you explain the potential behind this research path?

Answer. The effect of exercise and physical activity on cognition, including Alzheimer's disease, remains an area of intense scientific study. Exercise benefits every organ of the body, improves sleep, and promotes a sense of well-being. While the effects of exercise and physical activity on cognitive health, including Alzheimer's disease, have not been established in controlled studies, we do know that exercise can help with weight control, which can be associated with a decreased risk of cardiovascular disease and diabetes—both of which are associated with a higher risk of Alzheimer's. Aerobic exercise also improves oxygen consumption, which benefits brain function; aerobic fitness has been found to reduce brain cell loss in older subjects. People who have had overt strokes or "silent" strokes with no apparent symptoms have an increased risk of developing dementia, and it is therefore possible that exercise and other lifestyle interventions that improve cardiovascular risk factors can reduce the risk of dementia.

Work continues in this important area. NIH-supported Alzheimer's Disease Cooperative Study, a 70-member consortium of academic medical centers and clinics that collaborate on the development of Alzheimer's treatments and diagnostic tools, has recently initiated a randomized, controlled trial to find out if supervised aerobic exercise can influence cognitive decline, slow brain atrophy, or mitigate Alzheimer's pathology in older adults with mild cognitive impairment (MCI), a condition that

often leads to Alzheimer's disease. Also, the ongoing Lifestyle Interventions and Independence for Elders (LIFE) study, a Phase 3 multi-center randomized controlled trial comparing a moderate-intensity physical activity program to a successful aging health education program in prevention of mobility disability among sedentary older adults, will measure cognitive function as an outcome.

Question. What are the strategies for the Alzheimer's Disease Center network to continue building this type of research?

Answer. The Alzheimer's Disease Center (ADC) Clinical cores enroll subjects with normal cognition, mild cognitive impairment, and Alzheimer's dementia. These subjects are then available to researchers who may wish to study life-style factors such as exercise and nutrition to investigate what role these factors may have in preventing cognitive decline leading to MCI and AD. The life style studies are usually funded by sources other than the Centers themselves but the Centers are very useful because they provide research subjects and a rich environment to support such research. A good example is the University of Kansas ADC, where recruitment of subjects occurs through the center and the exercise and nutrition studies are supported by R01 grants.

Question. Do you plan to devote more resources towards this type of research activity?

Answer. The effects of exercise on cognitive decline and Alzheimer's disease remains an important area of research, and NIH will continue to support meritorious projects in this area as appropriate.

BRAIN INITIATIVE

Question. How have new technologies, for example brain imaging and scans, helped identify people who may have Alzheimer's disease before the actual symptoms occur?

Answer. As recently as 10 years ago, definitive diagnosis of Alzheimer's disease could only be made at autopsy. However, in 2004, NIH-supported investigators developed the tracer compound Pittsburgh Compound B (PiB) and demonstrated that it binds to amyloid-beta in the brain, where it can be imaged using positron emission tomography (PET). Several years later, investigators with the Alzheimer's Disease Neuroimaging Initiative found that higher amounts of the protein deposits in dementia-free people were associated with an increased risk of developing dementia over time and with loss of brain volume and subtle declines in cognitive abilities. These findings suggest that brain beta-amyloid may in fact be a preclinical sign of disease even among individuals who appear cognitively normal. Subsequent research indicated that Alzheimer's pathology may be present in the brain years—even decades—prior to diagnosis.

In addition to imaging technologies, the use of fluid biomarkers to diagnose disease and track treatment response has gained considerable traction. ADNI investigators have also established a method and standard of testing levels of both tau and amyloid-beta proteins in the cerebrospinal fluid (CSF). They correlated levels of these proteins in the CSF with changes in cognition over time and determined that changes in these two protein levels in the CSF may signal the onset of mild Alzheimer's disease.

Scientists now are beginning to explore the combined use of biomarkers and brain imaging to predict disease risk. A growing body of research is devoted to looking for blood proteins whose levels change during the early stages of Alzheimer's, which could lead to the development of routine blood tests for risk assessment.

Most of these early diagnostic tools and techniques are currently only used in research and are not yet validated for use in clinical practice. However, they may eventually facilitate clinical diagnosis of the disease. Importantly, imaging and fluid biomarkers are increasingly being incorporated into clinical trials as a means to track treatment response.

Question. How will the BRAIN Initiative help move research in Alzheimer's forward?

Answer. To find better treatments for Alzheimer's and other intractable neurological disorders, we first need to gain a deeper understanding into how normal circuits function and how the changes wrought by these diseases impair the function of those circuits. For example, in Alzheimer's disease, circuits reorganize as neurons die off. Understanding how the circuits reorganize and how we might intervene to optimize their function could help us develop new and effective interventions for patients with Alzheimer's and related dementias.

Under the BRAIN Initiative, NIH has issued several research solicitations that will enable us to develop a deeper understanding of brain function through the creation of new tools capable of examining the activity of millions of nerve cells, net-

works, and pathways in real time. By measuring activity at the scale of circuits and networks in living organisms, we can begin to translate data into models that will elucidate how the brain encodes sensory experience, motor planning, and, potentially, even memory, emotion, and thought.

We believe that successful completion of the BRAIN Initiative will revolutionize the field of neuroscience and set the stage for major advances in Alzheimer's and other brain diseases.

FISCAL YEAR 2014 FUNDING

Question. The fiscal year 2014 Omnibus appropriations bill provided a $100 million increase for research funding at the National Institute on Aging. Can you please provide specific details on what research activities this funding will go towards?

Answer. In fiscal year 2014, the overall NIH appropriation was increased to $30.15 billion (a 3.4 percent increase), while Congress provided approximately $100 million in additional funding for the National Institute on Aging (NIA), resulting in a budget increase of 12.5 percent for that Institute. In the Conference Report accompanying the 2014 Consolidated Appropriations Act, legislators stated, "Recognizing that Alzheimer's disease poses a unique and serious threat to the Nation's long-term health and economic stability, the Committee expects that a significant portion of the recommended increase for NIA should be directed to research on Alzheimer's . . . The Committee encourages NIA to continue addressing the research goals set forth in the National Plan to Address Alzheimer's Disease, as well as the recommendations from the Alzheimer's Disease Research Summit 2012."

Consistent with this language, NIA plans to use these additional funds to support Alzheimer's research in areas of strategic priority and scientific priority. Specifically, in fiscal year 2014, NIA will fund additional awards to applications received from Funding Opportunity Announcements issued in fiscal year 2013 (the President's Alzheimer's initiative) and fiscal year 2014.

These additional appropriated funds are added to our base (unlike the one-time funds added by the NIH Director in fiscal year 2012 and fiscal year 2013), so the NIA's fiscal year 2014 budget will be estimated from this increased base. NIA is distributing these funds among single-year and multi-year projects to maintain a stream of new competing dollars to support high quality, peer-reviewed research on aging and Alzheimer's disease in future years.

Question. What types of research on Alzheimer's do you want to fund in fiscal year 2015?

Answer. The ongoing Alzheimer's disease (AD) research supported by the National Institute on Aging (NIA) will continue in 2015, along with several recently launched efforts made possible with increased funding. These include:

—Whole genome sequencing to identify new genetic variants that either increase risk (risk factors) or reduce risk (protective factors) for AD (in collaboration with the National Human Genome Research Institute).

—A treatment trial to test the effectiveness of intranasal insulin in individuals with mild cognitive impairment or mild Alzheimer's dementia on cognition and daily functioning.

—A 5-year prevention trial to test the ability of an antibody called crenezumab to bind to and clear away abnormal amounts of amyloid protein in the brain and prevent cognitive decline in people with early-onset AD.

—Research to be funded in fiscal year 2013 and fiscal year 2014 under four 2012 Funding Opportunity Announcements supporting drug discovery, development, and preclinical and clinical testing.

We anticipate supporting new and ongoing activities in the following areas in fiscal year 2015:

—*Additional Drug Development and Testing*.—This will include support for drug repurposing and combination therapy, phase 2 (proof of concept) drug trials for agents against currently known therapeutic targets, and studies of possible agents against not-yet-known therapeutic targets for AD.

—*Non-Pharmacological Intervention Development*.—We will focus on advancing non-pharmacological interventions for the cognitive and behavioral symptoms of AD and the design of approaches that combine pharmacological and non-pharmacological treatments.

—*Biomarkers of Disease Progression to Measure the Effects of Potential Treatments*.—We will test imaging and fluid biomarkers for the assessment of disease-related pathology, work to develop and validate sensitive measures to detect and track the earliest clinical changes of AD, and develop and test methods for the standardization of neuroimaging procedures and data collection.

Question. If funding were unlimited, how much would you commit to Alzheimer's research?

Answer. The infusion of new Federal funds to Alzheimer's research in the past several years has accelerated the pace of discovery and facilitated the support of research projects that may not otherwise have been funded. It is also true that key findings in Alzheimer's may come from unrelated (or loosely related) scientific areas, including the new BRAIN initiative. Much of the research that we would support in any year would be investigator-initiated that is, proposals from the best scientists across the country, and budgeting for the creativity of Alzheimer's researchers is, as I'm sure you can appreciate, an inexact science, and not necessarily amenable to exacting cost estimates. It is our expectation that as the field is stimulated by the additional funds in fiscal year 2014 for NIA, there will be increased interest by both investigators already involved in AD and related fields to apply for support. In order to further stimulate the field, NIH has been through an intensive planning process that has generated five priority RFAs, which will be presented to NIA's Council for concept clearance in May. While we cannot discuss the nature of the planned RFAs and their costs until after concept clearance at NIA's May Council, we will do so for the record after NIH Council Meeting.

VASCULAR CONTRIBUTIONS TO DEMENTIA

Question. Studies have indicated that most people who die with dementia have a combination of Alzheimer's and vascular disease (stroke) and that vascular disease is the second leading cause of dementia. What is the interplay between stroke and dementia?

Answer. A recent article in the journal Neurology that highlighted the burden of mortality from Alzheimer's disease pointed out that the research community has embraced the concept of mixed dementia. In other words, as you say, dementia most often arises from an interplay of Alzheimer's disease and vascular causes. Brain vascular disease can contribute to dementia not only through overt strokes, but also through "silent strokes," which are not recognized from symptoms but are apparent on brain imaging or examination of autopsied brains. Silent strokes are very common—about 13 million people in the United States have had silent strokes; twice as many have MRI scan evidence of diffuse damage to the connecting fibers (diffuse white matter disease). Studies show that these common consequences of chronic hypertensive vascular disease are associated with dementia risk. Most importantly these are modifiable by current treatments and recent reports of decreased annual dementia risk from Europe may be related to better vascular health. Therefore control of vascular risk throughout the lifespan should be aggressively pursued not only to reduce heart attack and stroke but also dementia.

Brain vascular disease and dementia intersect at every level from risk factors to molecular mechanisms. People who have had a stroke are about nine times as likely to have cognitive impairment, and signs that a stroke has occurred are often found in the brains of Alzheimer's patients. Conversely, brain imaging studies suggest that people who have brain protein aggregations characteristic of Alzheimer's disease but have healthy brain vasculature are less likely to suffer dementia. The Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, which is following more than 30,000 people, is one of several epidemiological studies that have reported that high blood pressure and other known risk factors for stroke increase the risk of cognitive problems, even among people who have never had a stroke. At the cellular and molecular level of analysis we are just beginning to recognize the interrelationships between the mechanisms that underlie Alzheimer's pathology and vascular problems. For example, beta-amyloid, a key protein in Alzheimer's pathology, may stimulate the formation of blood clots, which can cause stroke, and may have direct effects on the integrity of blood vessels in the brain.

The National Alzheimer's Disease Project Act recognized the importance of Alzheimer's Disease Related Dementias, including vascular dementia. In keeping with that, NINDS led a major planning effort, in collaboration with the NIA and private groups, on these other contributions to dementia. The NAPA Council has approved the recommendations from that group.

ACCELERATING MEDICINES PARTNERSHIP

Question. Which NIH Institutes and Centers will provide funding?

Answer. National Institute on Aging (NIA), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS)

Question. How much?

Answer. NIA will contribute $67.6 million; NIDDK will contribute $30.4 million; and NIAMS will contribute $20.9 million. These numbers are over 5 years.

Question. What research projects do you plan to fund with the $129.5 million in total funding provided in this program for Alzheimer's?

Answer. The Alzheimer's disease proposal seeks to fund three major clinical trials designed to delay or prevent disease onset. Additionally, funds will go toward conducting a large scale analysis of human Alzheimer's disease patient brain tissue samples to validate biological targets previously shown to play key roles in disease progression.

Question. What is the 5-year budget plan for these funds?

Answer. $4.4 million from industry x 5 companies = $22 million + $67.6 million from NIH + $40 million in-kind contributions from industry = $129.6 total.

Question. How much funding will be expended in each year?

Answer. Costs will be spread out approximately equally across the 5 years

Question. Press reports indicate that other pharmaceutical companies may be interested in the program in the future. Do you have the ability to expand the pilot to include other companies?

Answer. Yes. The partnership is fully formed and ready to get started but organizations will likely keep joining and we hope and expect there will be others. There is always a critical momentum effect generated once a partnership like this is established.

Question. Dr. Collins, could you please share with us the origin of the idea for the Accelerating Medicines Partnership? Do you believe drug discovery to be one of the most important investments for helping control the rising costs of Alzheimer's care?

Answer. It has become very clear in recent years that the therapeutics development process is not efficient enough. We are seeing extremely high attrition rates of safe, but ineffective therapeutics in late phase clinical trials. In fact, failures due to insufficient efficacy are responsible for 51 percent of Phase II failures and 66 percent of Phase III failures. This is costly in time and money and is preventing the sector from focusing resources on the most promising drugs. A major factor implicated in these failures is inadequate target validation—the scientific process of identifying and verifying that a specific molecule, if targeted by the right compound or drug, will modulate disease progression. If the best targets were chosen earlier, the late stage failure rate would decrease. And yet, despite the challenges there is a great opportunity in science right now—our knowledge of human biology is growing, DNA sequencing is getting cheaper, and there is a real drive in the private sector to consider target identification and validation pre-competitive and to work together.

Observing the challenges and the opportunity for a robust solution, the NIH and industry began discussing these issues beginning in the spring of 2011. In late 2011 NIH hosted a workshop with scientists from all sectors to identify how the sectors could work together on this problem. Following this workshop NIH and the industry partners undertook a thoughtful planning process to understand the needs in this area and how to design a partnership that could answer those needs. The final characteristics of the program, with committed partners took shape in the summer and fall of 2013, just months before the public announcement on February 4, 2014.

Question. Given your work in helping to promote genetic testing technology, do you believe that consumers should have to wait until the science is settled on the relationships between diseases, such as Alzheimer's, and genetic or molecular markers before having access to that information? Can the links ever truly be settled, or is better to get patients genetic information to them when the patients want the information? Could patients better informed on their own genetic information be a link to help enable further research and education even if what that information may mean is not fully understood?

Answer. Your question is an important one. As you point out, in some cases, the technology for genetic testing is out in front of the evidence for the validity of a genetic test, that is, whether the test accurately detects the presence of, or predicts the risk for, a particular health condition. The best approach to genetic testing for tests that predict the risk of a complex disease such as cancer or Alzheimer disease is to consult with a genetics professional (e.g., a genetic counselor, a physician who is board-certified in medical genetics, or a nurse with specialized genetics training) before and after testing. Before testing, a genetics professional can explain the benefits, risks, and limitations of genetic testing. After testing, a genetics professional can interpret the test results in the context of a person's medical history, family history, the type of genetic test (e.g., predictive vs. diagnostic), and the level of evidence for the test's validity. Professional practice guidelines are also an important resource to assess the validity of genetic tests.

The NIH Genetic Testing Registry (http://www.ncbi.nlm.nih.gov/gtr/), which provides detailed information about tests for more than 4,000 genetic conditions, links to practice guidelines that have been developed for certain diseases and disorders. For example, tests for Alzheimer disease link to practice guidelines from the American College of Medical Genetics, the Agency for Healthcare Research and Quality, and the European Federation of the Neurological Societies (see http://www.ncbi.nlm.nih.gov/gtr/conditions/C0002395/). A list of practice guidelines is available at https://www.ncbi.nlm.nih.gov/medgen/docs/guideline/. NIH is committed to supporting research that establishes the genetic contribution to health and disease and providing resources that help patients and consumers make informed decisions about genetic testing.

QUESTIONS SUBMITTED BY SENATOR RICHARD C. SHELBY

FUTURE OF ALZHEIMER'S RESEARCH

Question. The National Alzheimer's Plan set forth an ambitious and worthy goal of curing Alzheimer's disease by 2025. Do you think we will reach this goal?

Answer. The identification and development of interventions that will prevent or treat Alzheimer's disease have proven to be extremely challenging, and it is still not possible to predict with certainty when an effective treatment or preventive intervention will be available. However, we have greater reason than ever before to be optimistic.

Our efforts have been significantly advanced by recent breakthroughs in biomedical imaging that are enabling us to identify and track the earliest pathological stages of the disease process, long before clinical symptoms are apparent. These discoveries, in addition to discovery of other early biomarkers of the Alzheimer's disease process, have opened a "window of opportunity" for us to target and potentially reverse the disease's underlying pathology before cognitive, behavioral, and emotional symptoms appear.

NIH has begun to launch its first such clinical trials in presymptomatic individuals. For example, in one study, investigators are studying whether an antibody treatment, crenezumab, which is designed to bind to and possibly clear away abnormal amounts of amyloid protein in the brains of people with Alzheimer's, can prevent decline in cognitive function among members a unique and large family population in Colombia sharing a genetic mutation known to early-onset disease. We anticipate initial results from this groundbreaking study by 2017. In another study, the A4 Trial, will test an amyloid-clearing drug in the pre-symptomatic stage of the disease, in symptom-free older volunteers who have had positron emission tomography brain images that show abnormal levels of amyloid accumulation. Positive results from these or similar studies would provide important "proof of concept" that targeting preclinical disease is an effective strategy, and would represent a major step forward in our efforts against Alzheimer's disease.

NIH also supports over 35 Alzheimer's disease clinical trials, including a number of studies of interventions to slow disease progression among individuals who are already showing symptoms. Over 40 compounds are currently under study to stimulate and advance research on the discovery and development of new preventive and therapeutic interventions for AD, mild cognitive impairment, and age-related cognitive decline.

Question. The Plan also set forth specific milestones. Are you meeting them?

Answer. NIH has been successful in meeting the initial milestones established in the National Plan, and is well positioned to continue meeting milestones in the immediate future.

For example, the National Plan calls for the identification of research priorities and milestones. NIH has taken the following steps:

—Conducted the first Alzheimer's Disease Research Summit in May 2012. The Summit was attended by an international group of some 500 researchers, clinicians and members of the broader Alzheimer's community who worked together to identify research priorities and strategies needed to accelerate the development of successful therapies. A follow-up Summit is planned for 2015.

—Collected feedback on research needs and priorities through a 2012 Request for Information.

—Held the *Alzheimer's Disease-Related Dementias: Research Challenges and Opportunities* conference in May 2013 by NINDS, in collaboration with NIA and with support from several foundations (http://www.ninds.nih.gov/ADRD2013). This conference included an international group of experts that developed prioritized research recommendations to address AD-related dementias includ-

ing frontotemporal degeneration, Lewy body disease, vascular and mixed dementias, as well as clinical diagnosis and health disparities in AD-related dementias.

—Regularly updated the Plan to reflect evolving scientific opportunities and needs.

Elsewhere, the Plan calls for the expansion of research aimed at preventing and treating the disease. NIH activities in this area include:

Strategy: Expand research to identify the molecular and cellular mechanisms underlying Alzheimer's disease, and translate this information into potential targets for intervention.

Under several FOAs issued in response to the 2012 Summit, NIA has recently funded several major projects responsive to this strategy:

—*Pathway Discovery, Validation, and Compound Identification for Alzheimer's Disease*, a study to discover, characterize and validate complex molecular networks and candidate genes that influence susceptibility to cognitive decline and Alzheimer's disease.

—*Integrative Biology Approach to Complexity of Alzheimer's Disease*, through which investigators will apply innovative analytical methods to large-scale molecular, cellular and clinical data from Alzheimer's patients to construct biological network models and gain new insights into the complex mechanisms of the disease. Several cellular and animal models will be used to validate the actions of individual genes, as well as entire molecular networks predicted to drive the disease.

—*A Systems Approach to Targeting Innate Immunity in Alzheimer's*, which will use a systems biology approach to integrate genomic, gene expression, and pathological data from Alzheimer's patients and Alzheimer's mouse models and analyze them in novel ways with the goal of identifying and characterizing therapeutic targets within the innate immune system. The study builds on the genetic and pathological evidence that the innate immune system, which provides immediate defense against infection, and brain inflammation have a significant role in Alzheimer's disease.

Strategy: Expand genetic epidemiologic research to identify risk and protective factors for Alzheimer's disease.

NIA is accelerating the search for genes involved in late onset Alzheimer's disease (AD) through the AD Genetics Initiative, and is stepping up the collection of a large bank of genetic material, cell lines, and data from families with multiple members with late-onset AD at the National Cell Repository for Alzheimer's Disease. A case-control series also is being developed. Qualified scientists will use the bank to search for the remaining risk factor genes that contribute to late-onset AD, the most common form of the disease. Scientists will share genetic data developed from their research on an NIA-approved Web site, usually the NIA Genetics of Alzheimer's Disease Data Storage Site. Discovery of risk factor genes will help illuminate the underlying disease processes of AD, open up novel areas of research, and identify new targets for drug therapy.

For a complete update on activities with respect to the National Plan, please see http://aspe.hhs.gov/daltcp/napa/NatlPlan2014.shtml

Question. What advances in Alzheimer's research can we expect to see in the next 5–10 years?

Answer. The field is moving more rapidly than ever. In 5–10 years, we would expect to see a much more comprehensive understanding of the basic pathology of Alzheimer's disease and how it moves throughout the brain. We should have a number of new therapeutic targets, as well as new clinical trials in the pipeline. And, of course, we have every hope that we'll have found something that delays, prevents, or slows the progression of the disease.

TRAUMATIC BRAIN INJURY

Question. Repetitive concussions have been known to cause dementia and, in particular, that Traumatic Brain Injury may increase a person's risk for dementia. How common is this occurrence and what is the connection with brain injury and dementia, particularly Alzheimer's?

Answer. There is compelling evidence that frequently repeated blows to the head can lead to dementia. First recognized in boxers as early as the 1920s, this disorder, now called chronic traumatic encephalopathy, or CTE, has been identified in the autopsied brains of athletes from other sports, including football and hockey, and in the brains of military veterans exposed to multiple head trauma. Although we know that CTE occurs, and have begun to learn about its underlying mechanisms

in the brain, there are many unanswered questions, including the important public health issue of how common CTE is and the connection of less frequent mild traumatic brain injury (TBI) with dementia in general.

NIH is addressing these gaps in our knowledge. In September 2012, the Foundation for NIH established the Sports and Health Research Program with a generous donation from the National Football League. NIH convened scientific workshops in December 2012 and July 2013 with experts in CTE, Alzheimer's disease, and other dementias to discuss the best pathways forward. Based on that guidance, NIH funded two cooperative agreements, led by investigators at Boston University and at Mount Sinai Hospital in New York City, that are focused on defining the scope of long-term changes that occur in the brain years after a single TBI or after multiple concussions. Among their activities, the teams will also examine brain tissue for signs of CTE from elderly participants of the NIA-funded "Adult Changes in Thought" study who had a history of TBI at some time prior to death and brain tissues collected by the NIH Neurobiobank from individuals who have died years after a variety of TBI exposures. Neuropathologists in these projects will also submit brain tissue with evidence of CTE to advanced brain imaging teams who will attempt to identify a signature of CTE that could be used to recognize CTE in brain scans of living people, complementing promising developments in TBI brain imaging that are already underway.

To date, there is conflicting evidence and much uncertainty about the important question, outside the extreme cases of professional and high level amateur sports, of whether single or multiple TBIs increase the likelihood that a person will develop Alzheimer's disease in later life. Published reports have indicated that TBI can provoke changes in tau and other proteins that have been associated with Alzheimer's disease. For example, a recent article found that even a single TBI can increase tau and amyloid beta, another protein characteristic of Alzheimer's disease, many years later. Furthermore, any insult that decreases "cognitive reserve" might be expected to affect cognitive functioning in later life. Some epidemiological studies have found evidence that there is indeed increased likelihood of developing Alzheimer's disease among people who have a prior history of TBI. However, other large epidemiological studies have not detected such an association, so we do not yet have a definitive answer. Individual differences in susceptibility, now under investigation for TBI, may be part of the answer.

Question. How are you collaborating with the Department of Defense on this type of research?

Answer. For many years, NIH has collaborated with the Department of Defense, and also Veterans Affairs, on issues related to traumatic brain injury (TBI), including long term consequences such as cognitive problems. For example, NIH intramural investigators led a major long-term study that followed the outcomes of TBI in Vietnam veterans. Over the last several years, with the increasing concern about TBI in the military, NIH and the Department of Defense have greatly enhanced their interactions. NIH and the Department of Defense have held several joint scientific workshops on topics including the neurological effects of blast injury, emergency medicine for trauma, mild TBI diagnostics, combination therapies for TBI, and TBI classification. The Department of Defense was one of several agencies that came together with the research community through the NINDS Common Data Elements (CDE) program to agree upon standards for data collection that will allow meaningful comparison across TBI studies in the United States and internationally. The Department of Defense and NIH together led development of the Federal Interagency TBI Informatics System (FITBIR), which provides a common database for sharing of information among qualified researchers. The Center for Neuroscience and Regenerative Medicine (CNRM) is a major collaborative program that brings together Intramural NIH researchers with those from the Uniformed Services University and Walter Reed Medical Center. NIH leadership and program staff also participate on grant and programmatic review panels and on advisory boards for the Department of Defense and VA on research for TBI, and Departments of Defense and of Veterans Affairs representatives are ad hoc members of the NINDS Council. In 2013, as directed by an August 31st 2012, White House Executive Order the Departments of Defense, HHS, VA, and Education with OSTP developed a National Research Action Plan on PTSD and TBI. The report presents strategies for enhancing the already extensive inter-agency coordination and collaboration on TBI. Workgroups across agencies are now implementing the research plan.

Question. Have the brains of service members who have died from Traumatic Brain Injury been part of any Alzheimer's disease research studies to date?

Answer. No. Not that we are aware. The Department of Defense has not permitted examination of the brains of service members who have died from blast injury, or who have died from suicide or other causes after suffering blast injury. Cur-

rently there is no published information on the effects of blast injury on the brains of service members. In 2013, the Department of Defense funded the Chronic Effects of Neurotrauma Consortium, which is designed to develop better understanding of the linkage between combat-related TBI exposure and later problems, including neurodegeneration. The Department of Defense is also extending the NIH-led public-private partnership Alzheimer's Disease Neuroimaging Initiative (ADNI) to include Vietnam veterans. This project will examine the effects of TBI and PTSD on veterans using brain imaging methods and biomarkers that the ADNI project developed and validated. The Militarily-Relevant, Peer Reviewed Alzheimer's Disease Program (MRPRA) has also focused on understanding the relationship between TBI and Alzheimer's disease and on reducing that burden. NIA and NINDS scientific experts have served as advisors on these DOD programs, as appropriate.

DRUG APPROVAL

Question. There are several FDA-approved drugs for Alzheimer's disease, however none address the underlying disease itself. If we can delay the progression of some of the symptoms and help memory and cognitive thinking with treatment, why have we not found a cure? What are the major obstacles?

Answer. Alzheimer's disease is highly complex, with an imperfectly-understood etiology and an often complex underlying pathology. Some issues that have slowed our search for a cure include:

—Presence of multiple pathologies—a significant percentage of dementias is considered "mixed," i.e., it may combine Alzheimer's characteristic amyloid plaques and tau tangles, vascular pathologies, and other issues. This makes it difficult to know what, specifically, to target in the brain—or how to target it.

—A major issue, and one that we are now addressing, is that may have been intervening too late in the disease process to be effective. Biomarker studies have shown that Alzheimer's pathology may be present in the brain literally for decades before symptoms occur, and we're finding that by the time symptoms appear in the clinic, it may be too late to intervene. For this reason, we've begun several major trials in individuals who are either asymptomatic but show Alzheimer's lesions on imaging, or who are at very high genetic risk. We have high hopes for this research and will report promptly and regularly on results.

Question. I recently read about two breakthrough Alzheimer's clinical trials funded by the National Institute on Aging and conducted by the Alzheimer's Disease Cooperative Study. These two promising drugs aim to prevent the disease itself. Can you discuss these two trials, the Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease Trial (A4) and the Study of Nasal Insulin to Fight Forgetfulness (SNIFF)?

Answer. The A4 (Anti-amyloid treatment in asymptomatic Alzheimer's disease) secondary prevention trial will test an amyloid-clearing drug in the pre-symptomatic stage of the disease, in 1,000 symptom-free older volunteers who have had positron emission tomography brain images that show abnormal levels of amyloid accumulation. Cognitive tests over 3 years are designed to determine if the drug is effective in maintaining cognitive health, and imaging tests will track structural and functional brain changes. The trial, which will also be supported by private sector contributions, will provide important information about the effectiveness of clearing amyloid from the brain in the early stages of the disease and inform future prevention studies.

The purpose of the SNIFF study is to find out whether a type of insulin, when administered as a nasal spray, improves memory in adults with a mild memory impairment or Alzheimer's disease. The rationale behind the study is growing evidence that insulin carries out multiple functions in the brain and that poor regulation of insulin may contribute to the development of Alzheimer's disease. Insulin resistance, reduced cerebrospinal fluid insulin levels, and reduced brain insulin signals have been found in Alzheimer's patients, suggesting that a therapy aimed at correcting these deficiencies may be beneficial.

Both studies are being carried out under the auspices of the Alzheimer's Disease Cooperative Study, and both will be active in 2014.

DOWN SYNDROME AND ALZHEIMER'S DISEASE

Question. Research has indicated that studying individuals with Down syndrome may help progress research on Alzheimer's disease. The majority of Down syndrome individuals develop plaque in the brain and over half of those with Down syndrome will suffer from the early onset of Alzheimer's disease. But conversely, only half of those with plaque—the hallmark of Alzheimer's—develop the Alzheimer's. Is NIH researching this phenomenon?

Answer. Researchers funded by the National Institutes of Health are working on many fronts to explore the nexus of Alzheimer's and Down syndrome (DS). Basic research aims to better understand the two disorders' common genetic and biological underpinnings. Observational studies are looking at young adults with DS to see if and how they develop Alzheimer's. In addition, basic studies or epidemiological or observational studies that help define risk factors or measure the course of the disease are underway. Some studies seek to uncover the specific molecular and genetic processes at work, while others follow study volunteers with DS as they age to look for correlations between brain changes and changes in cognition. An ongoing study funded by the National Institute on Aging (NIA) is documenting amyloid deposition in asymptomatic adults with DS and following these individuals to understand the course of amyloid deposition and its effect on functioning over time, while the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) is currently supporting a five-year study to identify how dementia develops in adults with DS over age 35 by looking at cognitive-test results, certain proteins in blood, and connections between brain regions measured by a type of magnetic resonance imaging (MRI) called diffusion tensor imaging.

A few clinical trials are testing potential treatments; these include a study of low-dose transdermal nicotine to slow cognitive decline in DS patients with mild cognitive impairment and a study of epigallocatechin-3-gallate, a compound found in green tea, to improve cognitive performance and slow disease progression in DS patients with Alzheimer's.

In April 2013, the NIA co-sponsored a conference to help set a research agenda aimed at speeding the development of possible therapies to treat Alzheimer's in DS. Representatives from academia, industry, Federal agencies, and private foundations explored topics such as the Alzheimer's disease pathway, animal models, biomarkers, and cognitive assessments. In September, NICHD launched the Down Syndrome Consortium Registry, called DS ConnectTM. Through this dynamic resource, people with DS, their family members, and others will be able to enter highly secure profiles to access information about DS and, with their permission, be contacted about opportunities to participate in research.

QUESTIONS SUBMITTED BY SENATOR THAD COCHRAN

ALZHEIMER'S RESEARCH FOR MINORITY POPULATIONS

Question. Recognizing the devastating impact of Alzheimer's disease and Alzheimer's Disease-Related Dementias on patients and families, and also recognizing that the time was right—from both a scientific and a public health standpoint—to move aggressively toward the development of new and effective treatments for Alzheimer's, Congress passed the National Alzheimer's Project Act (NAPA) in December 2010 and it became public law on January 4, 2011. NAPA requires the HHS Secretary to improve outcomes for ethnic and racial minority populations at higher risk, among other requirements. The value of the diversity of Mississippi's population for research is commonly unrecognized.

Dr. Collins, your testimony indicates that one of requirements of the National Alzheimer's Project Act is to improve outcomes for ethnic and racial minority populations who may be at higher risk. How important is it to ensure that we are expanding Alzheimer's research to these unique and diverse populations, including in my home state of Mississippi?

Answer. Addressing disparities in Alzheimer's disease risk and outcomes is a major priority for NIH, and a number of studies are ongoing in this area. For example, research supported by the National Institute on Aging aimed at elucidating risk and protective factors among vulnerable populations includes the following:

—In an ongoing study, researchers are working to identify genetic risk factors for Alzheimer's disease (AD) in a cohort of Hispanics of Caribbean descent.

—The Chicago Health and Aging project is exploring several genetic and other risk factors for cognitive decline and AD in African American and non-Hispanic white participants, including the intersection of markers of inflammation, blood pressure, and other vascular factors with cognitive function.

—A recently-completed study, initiated with funding from the American Recovery and Reinvestment Act, assessed the associations of over 900,000 genetic markers with cognitive decline among 7750 older African Americans and Africans.

—Support from the American Reinvestment and Recovery Act has enabled the Health and Retirement Study (HRS) to conduct genotyping on approximately 20,000 participants and use these data to elucidate genetic influence on a number of parameters, including cognition. ARRA funds also facilitated the recruit-

ment of additional minority participants, further strengthening the study's utility in identifying risk and protective factors in these populations.

—The Alzheimer's Disease Genetics Consortium (ADGC) collaborates with the NIA-supported Alzheimer's Disease Centers to conduct large-scale genome wide association studies (GWAS) in search of risk factor genes for the disease. To provide insights into genetic risk and protective factors related to cognitive decline and dementia, the ADGC has leveraged a variety of existing epidemiologic, case-control, and family based data and sample sets, including African American and Hispanic cohorts.

Minority populations, including African Americans and Hispanics, have a higher risk than whites of both strokes and "silent strokes," placing them at a particularly high risk for cognitive decline and dementia. Recognizing the urgent need to address health disparities in dementia, an entire session of our recent conference on Alzheimer's Disease-Related Dementias (ADRDs) was devoted to health disparities. This conference, which was convened as part of National Plan to Address Alzheimer's, brought together internationally recognized experts to develop a set of prioritized recommendations to guide scientific research on AD-related dementias for the next 5 to 10 years, including recommendations focused on increasing recruitment in clinical studies and advancing treatment and prevention strategies among diverse populations. The NAPA Council has approved these recommendations and proposed that they should be included in the next version of the National Plan to Address Alzheimer's.

In another ongoing study, supported by the National Institute of Neurologic Disorders and Stroke, investigators are studying the hypothesis that Vitamin D deficiency may partially explain some of the excess risk of cerebrovascular disease and cognitive decline in African Americans compared to whites. This study, led by researchers at Johns Hopkins University, has a performance site at the University of Mississippi. A study to elucidate the relationship between depression and cognitive decline, including Alzheimer's disease, is likewise ongoing in Mississippi; this study is funded by the National Institute of Mental Health. Finally, the National Heart, Lung, and Blood Institute is supporting a number of studies in Mississippi dealing with hypertension, diabetes, and cardiovascular disease, all of which disproportionately affect underserved populations and all of which are associated with an increased risk of Alzheimer's.

ACCELERATING MEDICINES PARTNERSHIP

Question. Identification and characterization of targets for intervention are the primary goals of the Accelerating Medicines Partnership (AMP), just announced in February 2014. With project management by the Foundation for NIH, ten pharmaceutical companies will collaborate with NIH. All data will be made publicly available, and NIH and industry will share in the $230 million cost over 5 years for the first projects including Alzheimer's disease. For Alzheimer's disease, AMP resources will be used to incorporate biomarkers into four ongoing trials designed to delay or prevent disease, and then evaluate which ones are most effective. AMP resources will also support analyses of brain tissue samples from people with Alzheimer's disease in order to increase understanding of the disease and identify new potential therapeutic targets. AMP represents an unprecedented model for pre-competitive collaboration that should accelerate the ability to identify the next generation of drug targets and biomarkers.

Dr. Collins, could you please share with us the origin of the idea for the Accelerating Medicines Partnership? Do you believe drug discovery to be one of the most important investments for helping control the rising costs of Alzheimer's care?

Answer. It has become very clear in recent years that the therapeutics development process is not efficient enough. We are seeing extremely high attrition rates of safe, but ineffective therapeutics in late phase clinical trials. In fact, failures due to insufficient efficacy are responsible for 51 percent of Phase II failures and 66 percent of Phase III failures. This is costly in time and money and is preventing the sector from focusing resources on the most promising drugs. A major factor implicated in these failures is inadequate target validation—the scientific process of identifying and verifying that a specific molecule, if targeted by the right compound or drug, will modulate disease progression. If the best targets were chosen earlier, the late stage failure rate would decrease. And yet, despite the challenges there is a great opportunity in science right now—our knowledge of human biology is growing, DNA sequencing is getting cheaper, and there is a real drive in the private sector to consider target identification and validation pre-competitive and to work together.

Observing the challenges and the opportunity for a robust solution, the NIH and industry began discussing these issues beginning in the spring of 2011. In late 2011

NIH hosted a workshop with scientists from all sectors to identify how the sectors could work together on this problem. Following this workshop NIH and the industry partners undertook a thoughtful planning process to understand the needs in this area and how to design a partnership that could answer those needs. The final characteristics of the program, with committed partners took shape in the summer and fall of 2013, just months before the public announcement on February 4, 2014.

ESTABLISHED RESEARCH PROGRAMS

Question. Language was included in the fiscal year 14 Omnibus Appropriations bill by the Committee urging NIH to take advantage of existing, well-characterized, longitudinal, population-based cohort studies in order to build upon the strong body of work already being done in NIH-funded Alzheimer's Disease Research Centers. Mississippi researchers currently participate in several already established studies and we believe that it is worthwhile to continue this support.

Dr. Collins, I was pleased my state of Mississippi was able to host you at the University of Mississippi Medical Center in 2012 where we recognized the Mississippi recipients of NIH's Institutional Development Awards. Is it a priority for NIH to leverage previously established research studies where significant Federal investments have already been made in order to propel Alzheimer's research forward?

Answer. NIH places a high priority on leveraging previously established research, where appropriate. For example, hundreds of studies have been initiated based on data from the NIH-supported Alzheimer's Disease Neuroimaging Institute. In fact, ADNI's data-sharing policy—data are freely available to any qualified researcher—has stimulated the development of a worldwide Alzheimer's collaboration among academia, government and industry researchers by making study data publicly accessible and has resulted in over 350 published papers. To date, nearly 2,500 researchers have signed up for ADNI database access.

Other NIH initiatives share ADNI's approach to data-sharing. In fact, data from the Brain Research through Advancing Innovative Technologies (BRAIN) initiative,, the Accelerating Medicines Partnership (AMP), the National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS), and the Database of Genotypes and Phenotypes (dbGaP) are available to investigators worldwide.

QUESTIONS SUBMITTED BY SENATOR LAMAR ALEXANDER

Question. You mentioned that the Alzheimer's Disease Neuroimaging Initiative established methods and standards for testing biomarkers in cerebrospinal fluid, and the Accelerating Medicines Partnership is focused on incorporating an expanded set of biomarkers into four ongoing trials. One concern I have is that some of the innovative breakthroughs happening in this and other fields are not translating into drug evaluation by the FDA.

Have you worked with FDA on how these exciting biomarker breakthroughs could be used as the basis of or evidence for drug approvals? What barriers, if any, are there to working with FDA on some of the advancements you have made with biomarkers and testing and using that to shorten drug development?

Answer. Through our involvement with the National Alzheimer's Project Act (NAPA) Council and elsewhere, NIH is working closely with the FDA to facilitate approval of drugs for Alzheimer's disease. In February 2013, FDA released draft guidance for industry on developing drugs for the treatment of early stage Alzheimer's; this draft guidance specifically addresses the approval of drugs for Alzheimer's disease based on the use of biomarkers. The draft guidance indicates that a positive biomarker result in combination with a positive finding on a clinical outcome measure may be used as evidence of drug efficacy. However, the draft guidance also indicates that FDA will not be able to consider an approval based on the use of biomarkers until there is widespread evidence-based agreement in the research community that an effect on a particular biomarker is reasonably likely to predict clinical benefit. FDA's involvement in the Accelerating Medicines Partnership also signals their commitment to work with NIH and others on this important issue.

Question. Given your work in helping to promote genetic testing technology, do you believe that consumers should have to wait until the science is settled on the relationships between diseases, such as Alzheimer's, and genetic or molecular markers before having access to that information? Can the links ever truly be settled, or is better to get patients genetic information to them when the patients want the information? Could patients better informed on their own genetic information be a link to help enable further research and education even if what that information may mean is not fully understood?

Answer. Your question is an important one. As you point out, in some cases, the technology for genetic testing is out in front of the evidence for the validity of a genetic test, that is, whether the test accurately detects the presence of, or predicts the risk for, a particular health condition. The best approach to genetic testing for tests that predict the risk of a complex disease such as cancer or Alzheimer disease is to consult with a genetics professional (e.g., a genetic counselor, a physician who is board-certified in medical genetics, or a nurse with specialized genetics training) before and after testing. Before testing, a genetics professional can explain the benefits, risks, and limitations of genetic testing. After testing, a genetics professional can interpret the test results in the context of a person's medical history, family history, the type of genetic test (e.g., predictive vs. diagnostic), and the level of evidence for the test's validity. Professional practice guidelines are also an important resource to assess the validity of genetic tests.

The NIH Genetic Testing Registry (http://www.ncbi.nlm.nih.gov/gtr/), which provides detailed information about tests for more than 4,000 genetic conditions, links to practice guidelines that have been developed for certain diseases and disorders. For example, tests for Alzheimer disease link to practice guidelines from the American College of Medical Genetics, the Agency for Healthcare Research and Quality, and the European Federation of the Neurological Societies (see http://www.ncbi.nlm.nih.gov/gtr/conditions/C0002395/). A list of practice guidelines is available at https://www.ncbi.nlm.nih.gov/medgen/docs/guideline/. NIH is committed to supporting research that establishes the genetic contribution to health and disease and providing resources that help patients and consumers make informed decisions about genetic testing.

Question. The National Plan to Address Alzheimer's laid out a series of actions that must be implemented in order to reach the overarching goals. For example, NIH has laid out short, medium and long-term research milestones. In your opinion, are we on schedule to meet those milestones? Are your current and projected resources adequate to meet those goals?

Answer. NIH has been successful in meeting the initial milestones established in the National Plan, and is well positioned to continue meeting milestones in the immediate future.

For example, the National Plan calls for the identification of research priorities and milestones. NIH has taken the following steps:

—Conducted the first Alzheimer's Disease Research Summit in May 2012. The Summit was attended by an international group of some 500 researchers, clinicians and members of the broader Alzheimer's community who worked together to identify research priorities and strategies needed to accelerate the development of successful therapies. A follow-up Summit is planned for 2015.

—Collected feedback on research needs and priorities through a 2012 Request for Information.

—Held the Alzheimer's Disease-Related Dementias: Research Challenges and Opportunities conference in May 2013 by NINDS, in collaboration with NIA and with support from several foundations (http://www.ninds.nih.gov/ADRD2013). This conference included an international group of experts that developed prioritized research recommendations to address AD-related dementias including frontotemporal degeneration, Lewy body disease, vascular and mixed dementias, as well as clinical diagnosis and health disparities in AD-related dementias.

—Regularly updated the Plan to reflect evolving scientific opportunities and needs.

Elsewhere, the Plan calls for the expansion of research aimed at preventing and treating the disease. NIH activities in this area include:

Strategy: Expand research to identify the molecular and cellular mechanisms underlying Alzheimer's disease, and translate this information into potential targets for intervention.

Under several FOAs issued in response to the 2012 Summit, NIA has recently funded several major projects responsive to this strategy:

—Pathway Discovery, Validation, and Compound Identification for Alzheimer's Disease, a study to discover, characterize and validate complex molecular networks and candidate genes that influence susceptibility to cognitive decline and Alzheimer's disease.

—Integrative Biology Approach to Complexity of Alzheimer's Disease, through which investigators will apply innovative analytical methods to large-scale molecular, cellular and clinical data from Alzheimer's patients to construct biological network models and gain new insights into the complex mechanisms of the disease. Several cellular and animal models will be used to validate the actions

of individual genes, as well as entire molecular networks predicted to drive the disease.

—A Systems Approach to Targeting Innate Immunity in Alzheimer's, which will use a systems biology approach to integrate genomic, gene expression, and pathological data from Alzheimer's patients and Alzheimer's mouse models and analyze them in novel ways with the goal of identifying and characterizing therapeutic targets within the innate immune system. The study builds on the genetic and pathological evidence that the innate immune system, which provides immediate defense against infection, and brain inflammation have a significant role in Alzheimer's disease.

Strategy: Expand genetic epidemiologic research to identify risk and protective factors for Alzheimer's disease.

NIA is accelerating the search for genes involved in late onset Alzheimer's disease (AD) through the AD Genetics Initiative. NIA is stepping up the collection of a large bank of genetic material, cell lines, and data from families with multiple members with late-onset AD at the http://www.ncrad.org/. A case-control series also is being developed. Qualified scientists will use the bank to search for the remaining risk factor genes that contribute to late-onset AD, the most common form of the disease. Scientists will share genetic data developed from their research on an NIA-approved Web site, usually the NIA Genetics of Alzheimer's Disease Data Storage Site. Discovery of risk factor genes will help illuminate the underlying disease processes of AD, open up novel areas of research, and identify new targets for drug therapy.

For a complete update on activities related to the National Plan, please see http://aspe.hhs.gov/daltcp/napa/NatlPlan2014.shtml

Consistent with the priorities established at the Alzheimer's Summit and 2013 ADRD Workshop, NIH will strategically use appropriated funding to support these priorities. We are currently working diligently to plan new initiatives for fiscal year 2015 that will enable us to support additional high priority and high quality Alzheimer's-related research projects.

Question. What are the specific breakthroughs in science and technology that you are targeting to put our understanding of the brain on the path towards dramatic breakthroughs for diseases like Alzheimer's, Parkinson's? What are the specific deliverables and milestones that will get us to this point? Will the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative achieve this or will more need to be done? What is the optimum investment from both the public and private sector that could be made in brain research in order to achieve specific deliverables?

Answer. Many of the symptoms of brain diseases like Alzheimer's, Parkinson's, autism, and epilepsy, are due to disruption of the complex neuronal circuits that produce human behavior. To find better treatments for these diseases, we first need to gain a deeper understanding into how normal circuits operate and how the changes wrought by these diseases impair the function of those circuits.

Currently, we have the technology and computational sophistication to record and analyze the activity of pairs or small networks of neurons; however, brain research on neuronal circuits has been limited because of the difficulty of monitoring activity in many cells at once. Through the BRAIN initiative, researchers will build on emerging insights from multiple disciplines to develop, disseminate, and apply new tools and technologies that will allow scientists to generate a dynamic, real time picture of entire functioning brain circuits. Investments in tool development for neuroscience research will empower investigators beyond those receiving direct funds through the BRAIN initiative, because a more complete understanding of how brain circuits function is the necessary foundation for developing new breakthroughs in how we treat brain disorders like Alzheimer's and Parkinson.

To develop the BRAIN Initiative's scientific plan, NIH established a group of 15 highly qualified external scientific advisors, with additional input from 4 ex officio members from NIH, the National Science Foundation (NSF), the Defense Advanced Research Projects Agency (DARPA), and FDA. In September of 2014, this working group of the Advisory Committee to the NIH Director released an interim report identifying high priority research areas that are the critical first steps in supporting the mission of the BRAIN Initiative. Using the recommendations contained in this report as a guide, NIH released six funding opportunity announcements that represent the initial steps towards creating a new arsenal of tools and technologies for revolutionizing our understanding of the complex interactions within neuronal circuits. The Working Group's final report, to be released in June 2014, will contain a multi-year scientific plan, including recommendations for timelines, milestones, and cost estimates for the overall initiative.

In the launch of the BRAIN Initiative, the President recognized that the next generation of neuroscience breakthroughs will emerge not only from collaboration across disciplines, but collaboration across sectors. For this reason, he called for an "all hands on deck effort" and has asked the nation to leverage the vast expertise residing within both the public and private sectors.

Question. What innovations in computing will be required to advance brain science? How will we "mine" the enormous data that comes from brain-related simulations to drive discovery, especially in our understanding of diseases like Parkinson's and Alzheimer's? Are you currently collaborating with the National Science Foundation on this initiative? What other agencies are necessary to collaborate with because of their expertise and strength in high performance computing in order to achieve the benefits of advanced brain-related simulations?

Answer. The BRAIN Initiative, and neuroscience in general, present enormous challenges for computing. The most obvious challenge is the sheer quantity of data from millions of cells with thousands of interconnections operating on timescales of thousandths of a second. But that is just the beginning. Integrating the qualitatively multi-dimensional data on structure, activity, genes, and other aspects of nerve cells adds to the complexity, as does the plasticity of the brain as it continuously adapts. Further, the methods for generating data are not yet up to computational intensive tasks such as analyzing the intricacies of brain anatomy. Finally, turning data into understanding is perhaps the biggest challenge. Unlike the Human Genome Project, for which the fundamental rules of the genetic code were known at the start, we have only the faintest glimmers of how information is coded in the structure and activity of brain circuits.

Fortunately, there is a long and successful history of applying computational approaches in neuroscience, from the early days when scientists determined how nerve cells generate electrical currents and how signals flow within and between cells, to the more recent advances in brain imaging, genetics, and protein structure determination, among many other aspects of modern neuroscience that rely on computational methods. For this reason, NIH has long supported research at the interface of computation and neuroscience. One example is a collaborative program with the NSF begun more than 10 years ago to encourage interdisciplinary research in computational neuroscience. Meeting computational challenges has also been a major theme in the BRAIN Initiative since its inception, including a scientific meeting last year focused on that topic, and the Initiative is collaborating closely with the European Union Human Brain Project, whose goal is to pull together existing knowledge about the human brain via a supercomputer-based simulation. The broader NIH Big Data to Knowledge program and the recent appointment of the NIH's first Associate Director for Data Science will also help meet these challenges.

Confronting the challenges of brain science is likely to spur innovations in computer science that have benefits beyond neuroscience, or even science in general. And there may be a virtuous circle—learning how the three pound, energy efficient, human brain, which is composed of cells that act thousands of times more slowly than electronic circuits, outperforms room size, energy intensive, electronic supercomputers on some tasks may inspire scientists to improve the design and programming of tomorrow's computers.

Question. Seven years ago when the Senate passed the America COMPETES Act, we committed to steadily increasing basic Federal research funding over the next 7 years. Today those investments are paying off at facilities like the High Flux Isotope Reactor (HFIR) at Oak Ridge National Laboratory.

Scientists at HFIR have access to some of the most advanced neutron imaging in the world, which could lead to breakthroughs in brain related diseases, including Alzheimer's. Recent studies with neutrons at HFIR have revealed the earliest structural formation of Huntington's disease, and that research is moving forward to study protein malformation responsible for Alzheimer's and Parkinson's diseases.

The problem is that HFIR is the only facility in the world capable of this type of research, and is primarily dependent on funding from the Department of Energy. If we want to make substantial breakthroughs in Alzheimer's, and related diseases, we need to continue to invest in basic research facilities that can provide scientists with cutting edge technology, like those found in our national laboratory system.

Is NIH funding neutron scattering research related to Alzheimer's, and what additional resources are needed to ensure that researchers have access to these types of advanced research facilities?

Answer. NIH is not currently funding neutron scattering research related to Alzheimer's disease, although we have supported such research in the past. For example, NIH-supported researchers have used neutron scattering to determine beta-amyloid's structure and function.

NIH frequently collaborates with other Federal agencies on programs, projects, and initiatives related to neuroscience and Alzheimer's and related dementias. For example, the National Alzheimer's Project Act Advisory Council includes members from NIH and other HHS agencies as well as participation from the Department of Defense, the National Science Foundation, and the Department of Veterans Affairs. NIA, NINDS, and several other NIH Institutes participate in the Interagency Working Group on Neuroscience, which was created to foster collaboration across agencies and to coordinate Federal investments in neuroscience research. Other members of this group include the Departments of Agriculture, Defense, Education, Energy, Health and Human Services, Homeland Security, Justice, and Veterans Affairs, as well as the CIA, Environmental Protection Agency, NASA, the National Science Foundation, and the Office of the Director of National Intelligence. NIH program staff also lend their expertise to committees and working groups on Alzheimer's and other dementias at the Department of Defense and the Department of Veterans Affairs.

Trans-agency coordination efforts will be facilitated by the recent launch of the International Alzheimer's Disease Research Portfolio (IADRP), a new, publicly available database to capture the full spectrum of current Alzheimer's disease research investments and resources, both in the U.S. and internationally. Developed by NIA in collaboration with the Alzheimer's Association, the IADRP will enable 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. Along with NIA, over 20 NIH Institutes and Centers and a number of other Federal and non-Federal agencies contribute to the database. Research organizations from the UK, Canada, and Australia have also joined the collaboration.

We anticipate that further collaboration with other Federal agencies, including those with advanced research facilities such as those supported by the Department of Energy and the National Science Foundation, will be a natural outcome of these activities, and we look forward to continuing to work with these groups to facilitate additional efforts in Alzheimer's and related dementias.

ADDITIONAL STATEMENTS

The following statements were received subsequent to the hearing for inclusion in the record.

[The statements follow:]

PREPARED STATEMENT OF ALZHEIMER'S FOUNDATION OF AMERICA

On behalf of the Alzheimer's Foundation of America (AFA), a national nonprofit organization that unites more than 1,600 member organizations with the goal of providing optimal care and services to individuals confronting dementia, and to their caregivers and families, I want to express my gratitude to the Senate Appropriations Committee for recognizing the growing crisis surrounding Alzheimer's disease and taking concrete steps to mitigate the impact of this devastating brain disorder.

Specifically, we thank the Committee for instructing the National Institutes of Health (NIH) to increase funding for Alzheimer's disease research by at least $80 million in the fiscal year 2014 budget. In addition, this hearing will allow for greater awareness of the negative impact Alzheimer's disease has on American families and our society.

COSTS OF ALZHEIMER'S DISEASE

As the incidences of Alzheimer's disease grow, costs are skyrocketing. A recent RAND study of adults aged 70 and older found that the total economic cost of dementia in 2010 was estimated to be $109 billion for direct care—higher than heart disease and cancer; and $159 billion to $215 billion when cost of informal care is included.[1] The per-person cost of dementia was $56,290 or $41,689. Medicare paid about $11 billion of dementia-related costs. In 2012, the direct costs of caring for people with Alzheimer's disease or other dementias to American society will total an estimated $200 billion, including $140 billion in costs to Medicare and Medicaid.[2]

[1] Monetary Costs of Dementia in the US, www.rand.org/pubs/external__publications/EP50247.html.

[2] Ibid.

These costs will soar to a projected $1.1 trillion (in today's dollars) by 2050.[3] This dramatic rise includes a 500-percent increase in combined Medicare and Medicaid spending.

Complicating this condition, people with Alzheimer's disease tend to have multiple co-existing medical conditions, such as coronary artery disease, diabetes, congestive heart failure, and chronic obstructive pulmonary disease. Thus, they tend to have higher rates of healthcare use than others without the disease. For example, hospital stays are more frequent among people with Alzheimer's disease than among those without this brain disorder.[4] In addition, avoidable hospitalizations are more common among Medicare beneficiaries with Alzheimer's disease than for diabetes (short-term and long-term complications of diabetes) and hypertension, COPD or asthma, and heart failure.[5] These results suggest that Alzheimer's disease creates additional challenges in managing certain comorbidities, resulting in higher costs.

Facing this crisis, strides are being made. Congress and the Administration passed the National Alzheimer's Project Act (NAPA)[6] that resulted in the historic "National Plan to Address Alzheimer's Disease" (national Alzheimer's plan), which calls for a cure or effective treatment by 2025. To reinforce commitment to this goal, Congress appropriated at least an additional $80 million investment for Alzheimer's disease research at NIH in the fiscal year 2014 budget, along with funding for the BRAIN Initiative, which will help researchers unlock the mysteries of the brain. In addition, international efforts to confront Alzheimer's disease are developing, as leaders at the recent G–8 Summit announced that G–8 countries have committed to identifying a cure or a disease modifying therapy by 2025 and to increase worldwide funding for dementia research.[7]

AFA RECOMMENDATIONS

"Double Down" on Alzheimer's disease research funding at the National Institutes of Health (NIH).

AFA is asking Congress for $500 million in additional resources, for a total over $1 billion, for Alzheimer's disease research and enhanced investments for caregiver supports in the fiscal year 2015 budget.

Efforts are already underway in the Senate to ramp up funding for Alzheimer's disease research and caregiver services. Senators Collins and Klobuchar have introduced S. Res. 303, a resolution calling on the U.S. Senate to make fighting Alzheimer's disease an urgent national priority and to increase funding to $2 billion by fiscal year 2019. We urge all Senators to support this bipartisan effort and pass S. Res. 303.

Adopt a direct home care coordination model that targets people with dementia.

Several dementia care coordination demonstration projects are currently being conducted by the Centers for Medicare and Medicaid Innovation (CMMI).[8] We urge Congress to instruct the Centers for Medicare and Medicaid Services (CMS) to build upon these efforts and expand these successful care coordination delivery models nationwide.

Develop a new Medicare Alzheimer's disease benefit that extends home care and case management services to individuals with Alzheimer's disease.

Congress should instruct the CMS to allow greater case management for beneficiaries diagnosed with Alzheimer's disease who have difficulty with one or more activities of daily living (ADLs), as well as access to home- and community-based services, despite not falling into the current statutory definition of "skilled need" and, therefore, not "homebound" for the purpose of qualifying for the Medicare home health benefit.

Establish a Medicare palliative care benefit for people with chronic conditions, including Alzheimer's disease and related dementias.

We urge Congress to reform the palliative care benefit under Medicare to make it a viable end-of-life option for individuals with dementia.

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[3] Ibid.

[4] Zhanlian Feng, PhD, et.al., Hospital and Emergency Department Use by People with Alzheimer's Disease and Related Disorders: Final Report (August 2013) (http://aspe.hhs.gov/daltcp/reports/2013/ADRDhed.shtml#execsum).

[5] Ibid.

[6] National Alzheimer's Project Act (Public Law 111–375), passed unanimously by Congress in December 2010 and signed into law by President Barack Obama in January 2011.

[7] See, G–8 Dementia Summit Declaration (December 2013) (www.gov.uk/government/publications/g8-dementia-summit-agreements/g8-dementia-summit-declaration).

[8] See, http://innovation.cms.gov/index.html.

Support expansion and funding Older Americans' Act (OAA) programs.

Congress needs to pass OAA Reauthorization legislation that has been introduced in both the Senate and House (S. 3562, H.R. 3850). Absent these vital OAA supports, the dementia population and their families would face increased hardships, greater challenges and higher costs.

Pass the HOPE Act.

S. 709, the Health Outcomes, Planning and Education (HOPE) for Alzheimer's Act, provides for Medicare reimbursement to help increase the detection and diagnosis of Alzheimer's disease and other dementias. Specifically, the HOPE Act would establish a new benefit for Medicare beneficiaries for diagnostic and care planning services for people with Alzheimer's diseases and related dementias. It would also ensure that a diagnosis of Alzheimer's disease or dementia is included in the individual's medical record.

AFA calls on Congress to pass the HOPE Act (S. 709, and its companion in the House H.R. 1507).

Adopt the Veterans' Administration REACH II program to support family caregivers of individuals with Alzheimer's disease.

Resources for Enhancing Alzheimer's Caregiver Health II (REACH II) is a multicomponent psychosocial and behavioral training intervention for caregivers of individuals with Alzheimer's disease or a related dementia. The intervention is designed to reduce caregiver burden and depression, improve caregivers' ability to provide self-care, provide caregivers with social support, and help caregivers learn how to manage difficult behaviors in care recipients.[9]

AFA calls on Congress to encourage nationwide adoption of the REACH II program for all Medicare/Medicaid beneficiaries who have dementia and one ADL limitation.

Establish an adult day program benefit under Medicare and mandate adult day program as a State Medicaid benefit.

Adult day services provide socialization and stimulation to people with Alzheimer's disease and provide respite to family caregivers. They also provide family caregivers an avenue to maintain a worker/caregiver balance, which may enable them to stay economically productive in the workforce while serving as primary caregivers. AFA recommends Congress make adult day services a benefit under both the Medicare and Medicaid programs. Representative Sanchez has introduced legislation in the House (H.R. 3334), that would establish an adult day care option under Medicare.

Pass the ABLE Act.

Introduced by Senator Casey S. 313, the Achieving a Better Life Experience (ABLE) Act will help families and individuals defray costs associated with caring for a person with Alzheimer's disease or other dementias. Under the legislation, family caregivers will be able to tap into new ABLE accounts, modeled after the popular 529 college education saving program, that will allow contributions to grow tax free and would be easy and inexpensive to create. We urge Congress to pass S. 313 and its companion bill in the House (H.R. 647).

Provide interventions for family caregivers of individuals with Alzheimer's disease and related dementia to delay nursing home placement.

AFA recommends Congress to instruct CMS to develop and implement caregiver intervention strategies for family caregivers of individuals with Alzheimer's disease. Greater access to effective programs of education, counseling and support could yield considerable benefits for caregivers and cost savings to Federal health programs through deferred nursing home placements.

Increase geriatric and dementia care training to direct care workers who participate in Federal health programs.

AFA urges Congress to require direct care workers in Federal health programs to meet specific training standards in geriatrics and dementia to ensure that individuals with Alzheimer's disease and their family caregivers have access to high quality long term services and supports (LTSS) that can specifically address behavior modifications that result from dementia.

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[9] Resources for Enhancing Alzheimer's Caregiver Health II, National Registry of Evidence-based Programs and Practices, (http://nrepp.samhsa.gov/Index.aspx).

Establish tax credits for people with Alzheimer's disease and their family caregivers.

Congress, through the tax code, should provide greater incentives for family members who help shoulder the enormous and typically lengthy responsibilities of providing care for a loved one with Alzheimer's disease.

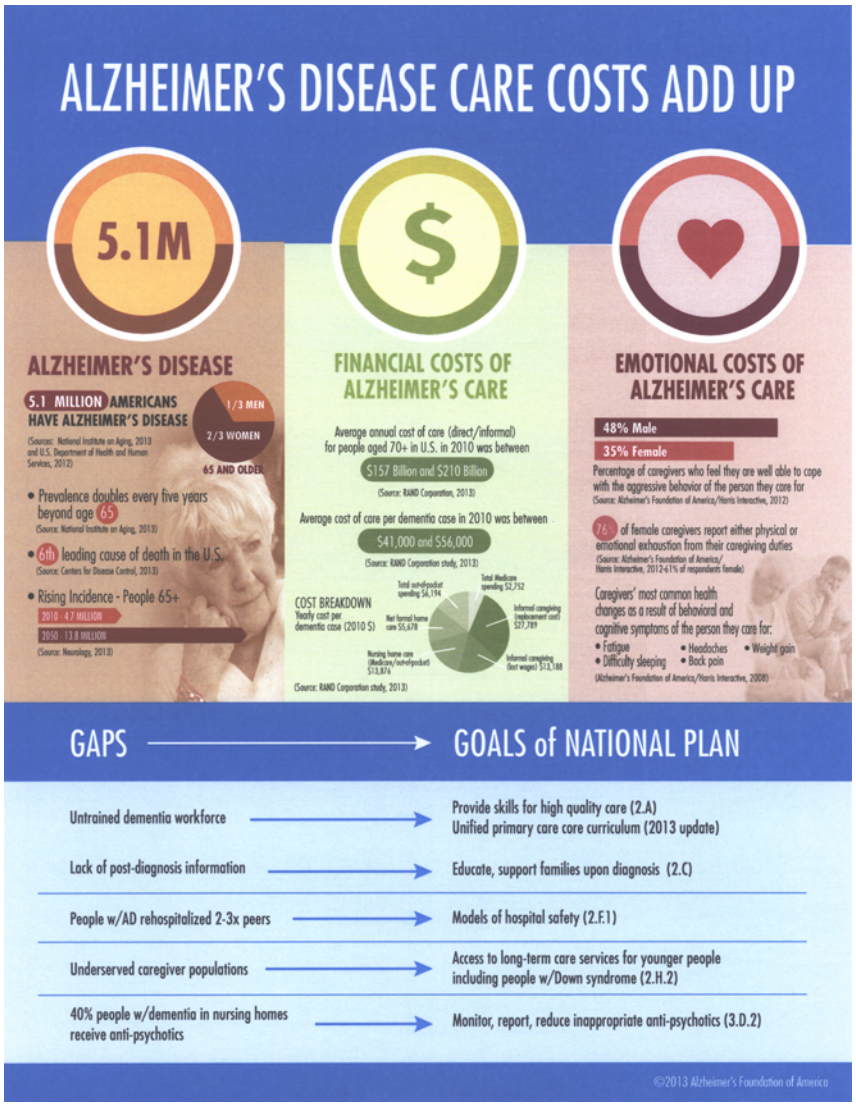
Develop transitional housing for individuals with Alzheimer's disease and their family caregivers based on the Housing Opportunities for People with AIDS (HOPWA) model.

AFA recommends Congress address the transitional housing needs of individuals with Alzheimer's disease and their families. The Department of Housing and Urban Development (HUD) has developed a successful transition housing model, Housing Opportunities for People with AIDS (HOPWA), for low-income Americans living with HIV/AIDS and their families. AFA urges adopting the HOPWA model for low-income persons with Alzheimer's disease or related dementias.

CONCLUSION

The status quo is inadequate to meet the growing needs anticipated by the "silver tsunami" as our population ages and incidence of people with Alzheimer's disease and their family caregiver multiplies. AFA's recommendations will help advance promising research while strengthening the safety net for individuals with LTSS needs, as well as support family members and other unpaid caregivers, whose participation in providing LTSS will continue to be essential. In addition, new delivery models that increase care management and care coordination will lower overall healthcare costs while allowing for more healthy outcomes for both the increasing number of people with Alzheimer's disease and their family caregivers.

AFA looks forward to working with Congress, the Administration and Alzheimer's disease stakeholders to ensure that a meaningful increase in Alzheimer's disease funding becomes a reality in fiscal year 2015 and moves us closer to attaining the ambitious, yet essential, care- and research-related goals of the national Alzheimer's plan.



This statement was submitted by the Honorable Charles J. Fuschillo, Jr., Chief Executive Officer, Alzheimer's Foundation of America.

PREPARED STATEMENT OF UNITED DOMESTIC WORKERS OF AMERICA, AMERICAN FEDERATION OF STATE, COUNTY AND MUNICIPAL EMPLOYEES (AFSCME), LOCAL 3930

The United Domestic Workers of America (UDW), AFSCME Local 3930, is a union for homecare workers, by homecare workers. We look after loved ones in our families, or we care for community members who need our assistance through California's In-Home Supportive Services (IHSS) program. Many of us left paid, full-time jobs to do this work, and we frequently work more hours than we are paid for. And while our work is incredibly rewarding, it is also extremely hard. This is why we have come together to offer each other a community of support. Through our union

we connect with each other, advocate for our clients, and we also advocate for each other.

Many UDW members are experts on Alzheimer's. They see how the disease progresses. They know how it steals memories. They know how it can change proud and strong people by taking away their ability to perform basic activities of daily life. UDW members are authorities on what those changes mean to individuals, caregivers and families. They see what Alzheimer's and dementia mean economically, emotionally, physically and socially. This disease may change a person but it can never take away a person's humanity because UDW homecare providers are heroes. They help people keep their dignity. They help people remain in their own home even as the disease takes its toll.

Sylvia Peralta is 62. For the last decade she has been taking care of her parents, who both have dementia. Her father and mother were born in the United States. They worked hand in hand in fields and canneries to build a better life for their children. When her father's medical condition deteriorated he could no longer safely remain at home. For Sylvia and her mother, the toughest times are when her mother cries because she does not understand why her husband of 64 years has left. It is Sylvia's compassionate and repeated reminders that make it possible for her mother to get through those hours.

Carolyn Haines's 18-month-old daughter tragically fell in a swimming pool and sustained traumatic injuries. She is now middle-aged and unable to speak, feed herself or hold things in her hands. But because of Carolyn's care for her at home, she is very social, attempts to speak and lights up a room with her laughter. When Carolyn's husband started to say inappropriate things, Carolyn knew something was different. It was Alzheimer's. In addition to taking care of her daughter, Carolyn took care of her husband as he went through the progressive decline from the disease for 11 years. She wasn't prepared for all the changes, particularly when he became combative. A month before he died, he said "I love you." It was the first clear thing he said to her in 6 months. She clung to that through his last days.

The stories of Sylvia and Carolyn and tens of thousands of UDW members are proof of the true value of homecare providers. Unfortunately, Federal and State spending on homecare can tell a different story.

Research to prevent and treat Alzheimer's disease is important for a better future, but in the absence of a cure, it would be wrong for Federal spending decisions to overlook the need to respect and value homecare providers. Families dealing with Alzheimer's today ask, "Who will care for my loved one today and tomorrow and the next day?" For too many families the answers boil down to unacceptable choices.

Federal dollars must fuel a caring revolution to help homecare providers and those whose independence depends on in-home services and supports. Targeting Federal funds to encourage States to increase spending for homecare providers is the right thing to do and makes economic sense. Homecare work cannot be outsourced and this workforce spends its income in their communities. To meet the growing demand for services and to stabilize this workforce, we need our State and national spending policies to provide increased dollars to sustain quality homecare through better homecare jobs.

Sylvia, Carolyn and the tens of thousands of homecare providers who get up early and go to bed late caring for others are courageous. Courage does not mean being fearless. They have more than their share of fears and heartache. They have courage because they are brave to do what they do every day and keep on doing it.

We call upon Congress to have the courage to do right by these workers and those who depend on their care. We urge Congress to increase Federal spending for homecare and to make sure States increase their funding for homecare providers like Sylvia and Carolyn.

PREPARED STATEMENT OF USAGAINSTALZHEIMER

Chairman Harkin, Ranking Member Moran, Chairwoman Mikulski and members of the committee. I applaud you for convening this hearing to focus on the urgent health and financial crisis that is Alzheimer's disease. Given the magnitude of this issue, it is quite fitting that Alzheimer's is the topic of the committee's first hearing of the fiscal year 2015 appropriations cycle. It is also apt that you have chosen to focus on the economic impact of Alzheimer's on American families and the economy as a whole.

In Washington, the term crisis is often overused to the point where it becomes an empty modifier devoid of its true meaning. However, the term crisis is quite accurate when it comes to Alzheimer's, particularly considering the looming health and financial burdens if the current trajectory remains unchanged.

Thankfully, our Government has stepped up in a significant way to recognize the enormity of this threat. A little more than 3 years ago, Congress passed and the President signed into law legislation establishing the National Plan to Address Alzheimer's Disease. Two years ago, the first iteration of that plan was released, setting as goal one the prevention and effective treatment of Alzheimer's disease by 2025. 2025. Think about that. It may seem far off but it is just a little more than a decade away or less than two terms in the Senate. We all know how quickly this date will be upon us and that we must, therefore, do everything in our power to maximize our chances of achieving this goal.

We are making progress, thanks in large part to the work of this committee. Just last month, Congress increased the budget for the National Institute on Aging (NIA) in a way that can provide for about $100 million in increased Alzheimer's research in fiscal year 2014. According to the National Institutes of Health (NIH), about $562 million will be spent on Alzheimer's. While this is a laudable increase during a time of flat or declining funding, I fear it remains insufficient to satisfy the task at hand.

Leading Alzheimer's scientists, as well as the Advisory Council on Alzheimer's Research, Care and Services, have estimated that an annual U.S. Government commitment of $2 billion to Alzheimer's research is needed if we are serious about achieving the 2025 goal. The current level of appropriated funding, even with some recent increases, is a little more than one-quarter of the amount recommended by leading experts.

At the recent meeting of the Advisory Council, leading Government officials noted that the current level of funding is simply inadequate to achieve the 2025 goal given the immense scientific challenges—and the opportunities—before us today. While we recognize the fiscal challenges impacting the Nation and the need for substantive and lasting debt, deficit, entitlement and tax reform, the reality is that we simply do not have a choice as to whether or not we will pay for Alzheimer's. We are already paying, quite dearly I might add, in the form of nearly $150 billion in Medicare and Medicaid costs to care for these patients. And we will pay even more money—both public and private—over the coming years and decades absent breakthroughs in research that lead to the development of therapies able to slow, modify, stop and ultimately reverse the effects of Alzheimer's.

I urge this committee to do all you can to continue building on these recent gains and to capitalize on the possibilities by committing to double—to about $1 billion—the amount of NIH funds available for high-quality and meritorious Alzheimer's research. Just as you did in the past year, you can do so without breaking longstanding policy and directing the dollars to a specific disease. Rather, just as NIH funds institutes focused on cancer, diabetes, heart disease and HIV/AIDS, you can allocate the funding to the NIA so it can be used assuming enough meritorious applications are submitted.

I also urge you to look beyond the 1 year funding cycles of the Federal budget and appropriations process to envision this as part of an effort to achieve the $2 billion target over the coming 4 to 5 years. Such a multi-year commitment—similar to what Congress bravely did a decade ago to double the overall NIH budget—will provide the level of resources deemed necessary to achieve our national goal. This action would send an important signal to non-government entities—academia, industry, venture capital, and philanthropists—that the U.S. Government is firmly committed to Alzheimer's research and that they should make similar financial commitments. And it would also send a message to global governments—some of which are already calling for a similar commitment—that the U.S. is ready and willing to lead this effort, just as we have led on so many other critical health issues over the decades.

Preventing and effectively treating Alzheimer's disease by 2025 is not an easy goal. In fact, it is a daunting goal, and the outcome is far from guaranteed. The U.S. has a long history of setting and achieving ambitious goals when we commit our minds, our hearts and our resources to the task. In the fall of 1962, the idea of landing a man on the moon in less than a decade was fantastical to many, yet we were able to achieve the goal with time to spare. Stopping Alzheimer's within 11 years can seem just as daunting given the state of the science and the spate of recent setbacks. However, I remain convinced that we can—and we will—achieve this goal if our resolve remains steadfast and if the appropriate level of resources is allocated.

This statement was submitted by George Vradenburg, Chairman.

2012–2013 ALZHEIMER'S DISEASE PROGRESS REPORT: SEEKING THE EARLIEST INTERVENTIONS

The report "2012–2013 Alzheimer's Disease Progress Report: Seeking the Earliest Interventions, Preview Copy, December 2013" from the National Institute on Aging, National Institutes of Health is available at the following link: www.nia.nih.gov/alzheimers/publication/2012-2013-alzheimers-disease-progress-report/.

CONCLUSION OF HEARING

Senator HARKIN. Thank you very much.

Housekeeping. The record will remain open until March 5 for other statements and comments from other Senators.

Thank you all very much. Safe travels home, everybody. Safe travels home.

[Whereupon, at 4:02 p.m., Wednesday, February 26, the hearing was concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

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