

ALZHEIMER'S DISEASE: THE ONGOING CHALLENGES

HEARING BEFORE THE SUBCOMMITTEE ON HEALTH OF THE COMMITTEE ON ENERGY AND COMMERCE HOUSE OF REPRESENTATIVES ONE HUNDRED ELEVENTH CONGRESS SECOND SESSION

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ALZHEIMER'S DISEASE: THE ONGOING CHALLENGES

THURSDAY, DECEMBER 9, 2010

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 1:47 p.m., in Room 2322, Rayburn House Office Building, Hon. Frank Pallone, Jr., [chairman of the subcommittee] presiding.

Present: Representatives Pallone, Engel, Capps, Barrow, Christensen, Space, Gingrey, and Markey.

Staff Present: Ruth Katz, Chief Public Health Counsel; Sarah Despres, Counsel; Steve Cha, Professional Staff Member; Allison Corr, Special Assistant; Alvin Banks, Special Assistant; Elizabeth Letter, Special Assistant; Ronald Allen, Staff Assistant; Clay Alspach, Minority Counsel, Health; Sean Hayes, Minority Counsel, Oversight and Investigations; and Ryan Long, Minority Chief Counsel, Health.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. The meeting of the House subcommittee is called to order. And today we have a hearing on Alzheimer's disease and its ongoing challenges, and I will recognize myself for an opening statement.

As many of us know, Alzheimer's disease is an irreversible progressive brain disease that slowly destroys memory and thinking skills and, eventually, even the ability to carry out the simplest task. Damage first strikes the areas of the brain that control memory, and problems in memory are the first symptoms to be noticed in early stages of Alzheimer's disease. As deterioration progresses to other areas of the brain, problems with other brain functions develop as well, as severe Alzheimer's disease can affect every part of the brain and rob its victims of their very lives and dignity.

Alzheimer's disease is fatal. It is estimated to be the sixth leading cause of death in our country. NIH estimates that as many as 5.1 million Americans may have Alzheimer's today, and this figure is expected to grow to 13.5 million Americans by 2050.

The truth of the matter, though, is that these figures give an incomplete snapshot of Alzheimer's disease and related dementias. Alzheimer's disease is, at the heart, a family disease, as the intense caretaking that those afflicted with the disease requires places a

heavy financial and emotional burden on the family. The serious medical complications related to Alzheimer's disease mean that caregivers often struggle to maintain work outside their home to earn a living, while balancing a never-ending schedule of monitoring and treatment for family members living with the disease.

For many adults, known as the sandwich generation, they are duly responsible for caring for their aging parents while they are also caring for their children. And Alzheimer's has a devastating impact not just on families but on our national economy. It is projected that the national cost associated with caring for those with Alzheimer's exceeds \$172 billion each year, with the figure expected to rise to \$1 trillion by 2005. And these costs represent the burden on Medicare, Medicaid, private insurance caregiving and out-of-pocket costs for families. Of this figure, \$123 billion can be attributed to Medicare and Medicaid alone.

Until we cure Alzheimer's, it is imperative that our health care system provides stronger support for families caring for loved ones with the disease. The Affordable Care Act, which we passed earlier this year, establishes the Community Living Assistance Services and Support, or CLASS programs, a new national long-term care insurance option. This legislation also provides Medicare beneficiaries with free annual wellness visits, which may increase the detection of early cognitive impairment, enabling patients and families to better plan for care needs. And, finally, the Affordable Care Act will ensure that Americans living with Alzheimer's disease and other preexisting conditions will not have to worry about having their insurance coverage discontinued or denied.

In the future, whether families are subject to the triumph or tragedy of Alzheimer's will be dependent on the innovation and new drugs and therapies being investigated in laboratories across our Nation. And today we are going to hear from the National Institute on Aging at the NIH about the great work their scientists are doing to better understand, diagnose, and treat Alzheimer's disease. NIA's translation objectives have focused on supporting early drug discovery and preclinical drug development of novel compounds for Alzheimer's therapy.

We are also going to hear from the Coalition Against Major Diseases within the Critical Path Institute on its efforts to improve applied regulatory science and how this will strengthen our ability to treat diseases like Alzheimer's.

And, finally, we will hear from the Alzheimer's Association and Alzheimer's Foundation of America about the key research they are supporting, as well as their initiatives and resources that help support day-to-day caretaking of individuals with Alzheimer's.

Now, many of the members of this committee have been touched by Alzheimer's and expressed interest in examining the complex issues related to the disease. I do want to highlight the exemplary leadership and advocacy for Alzheimer's disease by a member of our full committee, Mr. Markey. I think he is going to be able to come today, but he basically has been touched, of course, by his late mother's own struggle with the disease, and because of that and for a lot of reasons he has been an energetic leader in Congress and also chairs the Congressional Caucus on Alzheimer's disease. So he may be joining us later, but I did want to mention him today.

And I will now recognize for an opening statement our ranking member, Mr. Gingrey.

OPENING STATEMENT OF HON. PHIL GINGREY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF GEORGIA

Mr. GINGREY. Mr. Chairman, thank you. And I certainly want to thank our witnesses for their patience with us today. The witnesses will testify, as we hear from them, Alzheimer's disease presents a looming threat to the health of our Nation, and today I think the number is as many as 5 million Americans in the United States have this dreaded disease. And the scientific community is in agreement that these numbers will only increase significantly in the coming years as our society ages.

According to the United States Census Bureau, the number of seniors age 65 and older will actually double to about 72 million in the next 20 years as these baby boomers all reach retirement age. However, as Dr. Morrison-Bogorad will testify, the generation behind them, I think this is what is referred to as Generation X, and these are the folks born between 1965 and 1980, it is a significantly smaller generation than the baby boomers.

So why is this comparison significant for the purposes of the hearing today? As Alzheimer's is a degenerative and, as of yet, incurable disease that requires constant monitoring, the role of the main caregiver often falls to our family members, as we all know. According to a study conducted by the Alzheimer's Association, an estimated 11 million Americans provide 12.5 billion hours of unpaid care annually for people, usually their loved ones, with Alzheimer's and other dementias.

The disease also does require large amounts of medical care in addition to in-home and community-based services. This high use of medical services results in substantial cost to the Federal Government, States, employers, and indeed families.

If the number of Alzheimer's patients does indeed double over the next 20 years as many predict it will, we could be facing a health care crisis if the number of family caregivers declines, and of course the costly care for these patients ultimately shifts to paid health care professionals.

Alzheimer's disease is also a personal issue for me. My wife's mother, Laura Neill Ayers, was a very healthy and vibrant 88-year-old woman. She didn't hear very well. I think she loved that. But she was active. She loved to watch sports, and she spent time in her room every day watching baseball. Her husband, Bill Ayers, actually played baseball for the New York Giants in the 1940s, and Laura picked up her love of the game from her husband. Watching baseball became one of her favorite pastimes and thoughts of spring training I think kept her warm all winter long.

Seemingly overnight, all of that changed. She was diagnosed with dementia and, we suspect, Alzheimer's halfway through her 89th year, and the woman that we know and love was changed forever. Gone was the active woman, 88. In her place was a woman that seemingly was trapped inside her own body, unable to enjoy the comforts of these golden years.

I cannot begin to describe how emotionally destructive this disease was, as many of you I am sure know, not only for my mother-in-law but for my entire family.

There are many stories like this one that help underscore the importance of finding a cure. Today there are no known treatments to prevent, cure, or even delay the onset of Alzheimer's. The five drugs currently approved by the FDA have been shown to be successful in reducing the symptoms of the disease, but much more needs to be done to ultimately find a cure.

And so with that thought in mind, I would like to welcome all of our witnesses here today. Specifically, I am interested in hearing from Dr. Marc Cantillon, the executive director of the Coalition Against Major Diseases for the Critical Path Institute. As Dr. Cantillon will touch on in his testimony, the goal of his organization is to promote a forum for scientists from the FDA, academia, and industry to evaluate innovative testing methods for the use in drug development.

As members of this subcommittee have heard during past hearings, pharmaceutical drug development in the United States can benefit from greater collaboration between industry and the FDA. To the FDA's credit, they have recognized this fact in many areas, including antibiotic drug development, something for which I and a bipartisan group of members on this subcommittee will be advancing pieces of legislation in the 112th Congress.

As a representative of the citizens of the 111th of Georgia, I believe the government works best when its processes are constantly scrutinized and reformed, when necessary, to ensure they work as efficiently as possible. That theory applies not only to Congress and the White House, but government agencies as well. Therefore, I hope to learn more about this phrase, "applied regulatory science," during the question-and-answer portion of the hearing and how it might improve patient access to quality care.

Mr. Chairman, thank you for scheduling this hearing today. And with that, I see my time has expired and I yield back.

Mr. PALLONE. Thank you, Mr. Gingrey.

Mr. GINGREY. Mr. Chairman, I did want to ask for unanimous consent to submit for the record our actual subcommittee ranking member, Mr. Shimkus, a study that comes out of John Hopkins, "Evidence for Neurocognitive Plasticity in At-Risk Older Adults," and the experience of that study.

Mr. PALLONE. Without objection, so ordered.

[The information appears at the conclusion of the hearing.]

Mr. PALLONE. Next for an opening statement, the gentlewoman from California, our vice chair, Mrs. Capps.

OPENING STATEMENT OF HON. LOIS CAPPS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mrs. CAPPS. Thank you, Chairman Pallone, for holding this, the final Health Subcommittee of the 111th Congress. And I want to thank you for your wonderful service as chairman over the last 4 years.

Alzheimer's disease is a very topical subject for this hearing, because the challenges faced by patients and their loved ones are so reflective of the challenges we face throughout our health care sys-

tem. Long term, these are some of the challenges which fit with Alzheimer's so well: long-term care availability and its costs; respite care; an adequate workforce; and research for better treatments and a cure.

Now, that is just touching the surface of the many challenges that we face with this and so many other chronic conditions. And thankfully, the new health care law provides much-needed relief for many of these concerns. One of these is the new long-term care insurance option. There is also Medicare prescription cost relief. And there is opportunities for training the next generation of health professionals; in addition, the Cures Acceleration Network, along with what our chairman mentioned as the CLASS Act. And, of course, we have a lot more that we should undertake now within this framework of the new legislation.

Some of these other steps we can take, such as passage of legislation that I am very proud to cosponsor in the National Alzheimer's Act I know you are going to be addressing today in your testimony, including the National Alzheimer's project, with the goal being that we can provide and develop a comprehensive strategy for how to address Alzheimer's disease, how to continue, as many of you have been doing over these past many years.

So I do look forward to hearing from our witnesses today about the latest in Alzheimer's research. I understand there are some very critical breakthroughs that have been working their way through the clinical trials and so forth, and also what you see for us in guidance in the next Congress as pressing needs that patients and so many of them, increasing numbers of their family members and caregivers, are going to experience.

As has also been mentioned, there is probably not one person in this room who hasn't been touched personally by this devastating disease. And we need to know it is a crisis proportion, really, in our society now, how to best equip ourselves and our communities to cope with it.

So I yield back and look forward to today's hearing.

Mr. PALLONE. Thank you. And I also wanted to thank you also as the vice chair. You have been really tremendously helpful, and so often giving us insight on issues because of your practical experience also as a nurse and your background. So thank you.

Our next member for an opening statement, the gentleman from Georgia, Mr. Barrow.

OPENING STATEMENT OF HON. JOHN BARROW, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF GEORGIA

Mr. BARROW. Thank you, Mr. Chairman. I want to thank you also for your leadership throughout the 111th Congress on this committee.

The poet said that comparisons are odious, and at the personal level no one wants their personal trauma or tragedy compared to someone else's. But at the level of public health and social impact, I think some comparisons are useful. The scourge of cancer has many faces. The scourge of Alzheimer's has a very definite profile, many different impacts on folks, but a very different impact in terms of the family.

I think it is useful to point out that we didn't really begin to marshal the Nation's resources in the war on cancer until folks could say, everybody knows somebody who has been touched by cancer. I think it is fair to say that everybody now knows somebody who has been touched by Alzheimer's. Nobody knows the particular impact it has on family and on the communities of interest around families that is the hallmark of this dreaded disease. So I think we can take inspiration from the fact that so many folks are impacted by this.

I think it is important to point out also in ways that supplement what others have said, the cost of this disease. The uncompensated care and the out-of-pocket expense to our system is staggering and growing exponentially in ways that I think compare very unfavorably to some of the other diseases that we deal with at a social level. Right now, we are spending something like \$170-plus billion a year in compensated and uncompensated care, taking into account the fair market value of the services that folks are being forced to render and not getting any kind of compensation for at all. That is coming out of our gross social product. It is projected to cost our society something on the order of \$1 trillion a year at current growth levels by the time we reach 2050. So it is staggering in its potential for exponential growth and impact on folks.

The point is, this is not only the right thing to do in terms of the quality of the life of folks affected by this. It has never been truer to say that this is not only the right thing to do, but it is the smart thing for us to do, to marshal our resources in more effectively and economically managing and treating and preventing this dreaded disease.

So, with that, I look forward to hearing the testimony of our witnesses and thank them for coming today. And I thank you, Mr. Chairman, for making this, the last hearing of this committee and this Congress, a very large issue that we are going to be dealing with for a very long time.

With that, I yield back.

Mr. PALLONE. Thank you, Mr. Barrow.

Next, the gentlewoman from the Virgin Islands, Mrs. Christensen.

OPENING STATEMENT OF HON. DONNA M. CHRISTENSEN, A REPRESENTATIVE IN CONGRESS FROM THE VIRGIN ISLANDS

Mrs. CHRISTENSEN. Here thank you, Mr. Chairman. And thank you for holding this hearing. And thank you, welcome to the folks who are here to testify. And thank you not only for taking the time to be here but for the work that you all are doing. I really appreciate the approach that is being taken to this devastating disease, a disease that is devastating to not only individuals but families and communities, and potentially to our country, because it is a wholistic approach, looking at prevention, treatment, and research, but also looking at the caregivers who are often forgotten.

I wanted to call attention to several areas.

First, the cost of care. Due to the cost of care, this disease has the potential to bankrupt our health care system unless we invest in all of these aspects today. In fact, by 2050, it is estimated that

13.5 million Americans will be suffering from Alzheimer's, and the cost might be as much as \$1 trillion a year.

Second, there is a grave discrepancy between the funding for research for this sixth leading cause of death compared to other leading causes of death, where billions are being spent compared to just over \$400 million on Alzheimer's.

Third, I want to call attention to the fact that racial and ethnic minorities are disproportionately impacted with Alzheimer's, with African Americans being twice more likely and Hispanic Americans 1.5 more likely to suffer from Alzheimer's and other dementias, despite the fact that they are underdiagnosed compared to their white counterparts.

And I wanted to mention, too, other pieces of legislation just to show that the Congressional Black Caucus has been aware and engaged in this issue for several years. One is H.R. 4123, the Alzheimer's Treatment and Caregivers Support Act, introduced by Representative Maxine Waters, and H.R. 1192, the Alzheimer's Family Assistance Act, introduced by Eddie Bernice Johnson. Both of these bills, like the others that are being mentioned in the testimonies, will help to take the fight against Alzheimer's several steps forward and be a part of this solution to this devastating problem.

So, again, thank you, Mr. Chairman. And thanks, all of you, for being here.

Mr. PALLONE. I thank the gentlewoman.

And next is the gentleman from Ohio, Mr. Space.

**OPENING STATEMENT OF HON. ZACHARY T. SPACE, A
REPRESENTATIVE IN CONGRESS FROM THE STATE OF OHIO**

Mr. SPACE. Thank you, Mr. Chairman. Today is my final hearing in committee, and I wanted to first express my gratitude to Mr. Chairman and to Chairman Waxman, as well as members on both sides of the aisle, for their work in some of the most profound issues of the day and even a generation: issues like energy and health care and the transformational effect that the whole broadband era has brought to this country and to our culture. And while we didn't accomplish everything that I think we had set out to accomplish, we got a lot done. And there is a lot to be done.

My district back in Ohio is a very rural district. It is Appalachian Ohio, where the people are good and they work hard, a lot of good things going for us back there. But there are a lot of challenges that we have, and we share those challenges with the rest of rural America. And one of the things that is unique about this committee, I think, is the effect that it can have on bridging the divide that exists between urban and suburban America and rural America. And certainly the divide does exist when it comes to accessing education, certainly with regards to accessing health care. And I encourage the committee to be every bit as ambitious in tackling some of those challenges in the upcoming session of Congress.

With respect to the issue of today, Alzheimer's, I sympathize with the remarks of my colleague and friend from Georgia, Mr. Barrow; \$172 billion a year, those are war-like numbers. In other words, those are the kind of numbers you spend when you go to war. If you couple the amount of money that we are spending as a society on a disease like Alzheimer's with what we are spending

on diseases like diabetes, cancer, and the list goes on and on, it soon reaches the trillion-dollar level. In fact, Alzheimer's alone, by the year 2050, will reach that level. And we cannot sustain that as an economy.

When John Barrow says it is not only the humane thing to do, it is the right thing to do, what he is saying is if it is not important enough to deal with these issues simply because of the mitigation of human suffering that occurs as a result of these diseases, then certainly we should be able to justify it because of the cost. And like Alzheimer's and diabetes and cancer, the answer, at least from the congressional perspective, is in medical research. We cannot simply rely upon the private sector to tackle these diseases, not simply because it is not the right thing to do but we can't afford it.

For every dime we invest today in research, we will receive a return of dollars in the future. Many dollars. So I urge this committee in future efforts, including its efforts with regards to Alzheimer's, to bear in mind the obligation that we have as an institution, as a government, and the duty we have to our people to conquer these diseases through early diagnosis, advanced diagnosis, advanced treatment, and above all, cure. Let's not forget cure.

With that, Mr. Chairman, again thank you for your leadership, and it has been a pleasure serving on your committee.

Mr. GINGREY. Mr. Chairman, could I have a brief point of personal privilege, a friendly point of personal privilege?

Mr. PALLONE. Absolutely.

Mr. GINGREY. And let me first of all, to my friend from Ohio, Mr. Space—and he truly is my friend and he and I know that—indeed we will miss him. He is a great member with a great heart, and I think the words that he just expressed to this committee indicate the type of person that he is. And, Zack, we will miss you and I really enjoyed serving with you. And I hope we will keep in touch, my friend.

Also, I wanted to say to you, Mr. Chairman, and I say this on behalf of my colleagues who I guess are on airplanes about now, trying to get home to their families, and not the least of which, of course, would be ranking member John Shimkus. We have really enjoyed serving with you, under you, on this Health Subcommittee of Energy and Commerce, not always agreeing on every vote, in fact disagreeing a lot of times. But no one could be more agreeable when he disagrees. Mr. Chairman, We respect you and hold you in high regard and look forward to serving with you in the 112th.

Mr. PALLONE. Well, thank you. I really appreciate that. And I want to say the same about you. Your input not only as a physician, but just in general, has been fantastic. And I kind of wish that Mr. Shimkus was here today, too, because I wanted to say how easy it was to work with him in the last—I guess not 2 years, a little over a year or so. And it is true, I think, that even though we often disagree on a lot of issues, that we have been able to work together on many issues. And it kind of bothers me sometimes when the media, I guess, pays attention to the differences and doesn't highlight how many bills we have actually passed out and worked on together and got signed into law that were very important for the American people. So thank you.

And let me say about Mr. Space. Again, I know that I am really going to miss him. He has really contributed a lot and he has been a friend on so many issues. So thank you. Thank you very much.

So we will get to our panel. Let me welcome you, first of all. We only have one panel today, so I will introduce the members.

Starting on my left is Dr. Marcelle Morrison-Bogorad, who is director of the Division of Neuroscience at the National Institute on Aging, with the National Institutes of Health.

And next is Mr. Harry Johns, who is president and chief executive officer of the Alzheimer's Association.

And then we have Mr. Eric J. Hall, who is president and chief executive officer of the Alzheimer's Foundation of America.

And, finally, Dr. Marc Cantillon, who is executive director of the Coalition Against Major Disease, from the Critical Path Institute, and also happens to be a constituent, so I should know how to pronounce his name, from one of my towns, Kingsbury. So thank you in particular for being here today.

We have 5-minute opening statements that become part of the record, and each of you can also submit additional statements in writing for inclusion if you would like.

STATEMENTS OF MARCELLE MORRISON-BOGORAD, DIRECTOR, DIVISION OF NEUROSCIENCE, NATIONAL INSTITUTE ON AGING, NATIONAL INSTITUTES OF HEALTH; HARRY JOHNS, PRESIDENT AND CHIEF EXECUTIVE OFFICER, ALZHEIMER'S ASSOCIATION; ERIC J. HALL, PRESIDENT AND CHIEF EXECUTIVE OFFICER, ALZHEIMER'S FOUNDATION OF AMERICA; AND MARC CANTILLON, M.D., EXECUTIVE DIRECTOR, COALITION AGAINST MAJOR DISEASE, CRITICAL PATH INSTITUTE

Mr. PALLONE. And I will now recognize Dr. Morrison-Bogorad.

STATEMENT OF MARCELLE MORRISON-BOGORAD

Ms. MORRISON-BOGORAD. Thank you very much, Chairman. And I really thank you for inviting me to appear before you today to discuss the pressing issue of Alzheimer's disease.

The National Institute on Aging is the lead institute for Alzheimer's disease of the NIH. So in this regard I want to tell you that you can now download copies of our 2009 congressionally mandated "NIH Progress Report on Alzheimer's Research" from the NIH Web site.

I am retiring at the end of this year and am truly sad that a cure for Alzheimer's has not been found on my watch. But the momentum is there, and I believe that my successor will have this joy.

Federal researchers, other scientific agencies, the private sector, and not-for-profit are collaborating as never before to try to solve the mysteries of this disease. For example, we have regular meetings with each of the entities that will testify at this hearing. We have partnered with the Alzheimer's Association on many occasions, and ongoing is a joint venture on updating the definition of AD.

The Alzheimer's Foundation of America and other organizations held House and Senate briefings a couple of weeks ago where Richard Hodes, director of NIA, was asked to testify. And we work with

the Coalition Against Major Diseases for the Critical Path Institute on matters related to innovations and marker use on clinical trials.

The NIA plans and manages an extensive program to better treat and ultimately to prevent Alzheimer's. How do we do this? Well, from our Alzheimer's Summit in 2006, the 2010 State of the Science Conference, from numerous specialized workshops, from program review by our NIA Council every 4 years, we get input from all these sources, and from these decide on the best ways to advance Alzheimer's research commensurate with our funding.

For example, at the 2006 Summit, it was recommended that we develop a project focusing on early onset AD families. We have since funded the International Dominantly Inherited Alzheimer's Network to study preclinical disease in these families. Earlier this year, an NIH State of the Science Conference reported that there was, so far, insufficient evidence that any behavioral interventions for AD or age-related cognitive decline were effective, and that we ought to devote more resources to these questions.

Even before the report was finalized, we had stepped up our funding of clinical trials to get definitive evidence whether or not various exercise and cognitive interventions might impact age-related cognitive decline, mild cognitive impairment, and AD. Now we are funding around 20 such trials.

The Alzheimer's Disease Neuroimaging Initiative is another example of our leadership. ADNI is a very successful public-private partnership to identify biological and imaging markers for better ways of monitoring AD clinical trials and also identifying persons at risk for the disease preclinically. Here we initiated the process through a series of meetings where we brought together all interested parties to discuss what initiative would be most useful for them for development in a precompetitive setting, and these discussions led to funding of ADNI in 2004, with substantial financial support from industry and from not-for-profits such as the Alzheimer's Association, coordinated by the Foundation for NIH.

Another aspect of our planning process is to ask our director for funds to specifically target new areas that need to be developed. An example is our Translational Initiative. Partly through these targeted funds, this important and innovative portfolio has grown to over 60 projects, each aimed squarely at bringing a new drug to the stage where it can get FDA approval for performing clinical trials. This is a particularly important area for us to develop, as pharmaceutical companies are often unwilling to put monies into the beginnings of the drug discovery process and translational research.

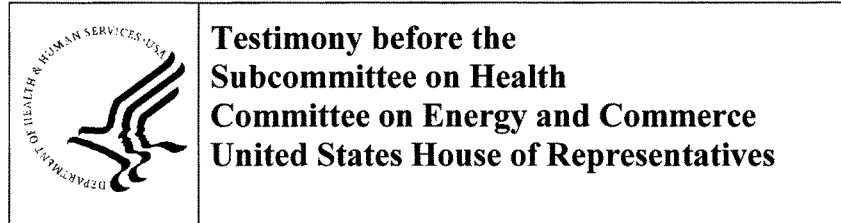
One reason that drug trials have not worked so far may be that the drugs are given too late in the disease to have any effect, but prevention trials to test those possibilities take a lot of money and time under current protocols. We are developing new methodologies, and in the meantime we have been able to fund a number of prevention trials by the simple way of adding cognitive measures on to trials started for other clinical conditions often by other institutes. So it is a cheap way of funding these trials.

But other possible drug therapies for Alzheimer's are directed against unique aspects of the disease, and so for these more specialized interventions NNIA must continue to develop AD-specific trials.

We make difficult decisions all the time about where to put our resources. We do not have a crystal ball to tell us what approach will eventually pay off in relieving suffering from this frightening disease. We are committed to trying every promising avenue, and we will succeed. Thank you.

Mr. PALLONE. Thank you very much.

[The prepared statement of Ms. Morrison-Bogorad follows:]



Alzheimer's Disease: Ongoing Challenges

Statement of
Dr. Marcelle Morrison-Bogorad

*Director
Division of Neuroscience
National Institute on Aging*



For Release on Delivery
Expected at 10:00 a.m.
December 9, 2010

Good morning, Chairman Pallone and Distinguished Members of the Subcommittee:

Thank you for inviting me to appear before you today to discuss Alzheimer's disease, a devastating disorder with a profound impact on individuals, families, the health care system, and society as a whole. I am Dr. Marcelle Morrison-Bogorad, and for fourteen years I have been Director of the Division of Neuroscience at the National Institute on Aging (NIA), a part of the National Institutes of Health and the lead federal agency for Alzheimer's disease research. I am delighted to be here today to tell you about the progress we are making, in partnership with the research and advocacy communities, regulatory bodies and industry, toward understanding, treating, and preventing Alzheimer's disease.

We humans have created our complex societies not because we have bigger hearts or hands, but because we have bigger and more complex brains. Our intelligence has allowed us to create conditions that enable most of us to live longer lives. These added years bring enormous opportunity and richness to our lives. But at the same time, advancing age brings us face to face with a growing burden of chronic, age-related diseases, including Alzheimer's disease.

Alzheimer's disease is a major public health issue for the United States. Today, it is estimated that 2.4 million¹ to 5.1 million² people in the United States have Alzheimer's disease. While estimates vary, depending on how dementia is measured, scientists agree that without breakthroughs in prevention or early treatment, the number of people with Alzheimer's will increase significantly as society ages. Studies suggest that the number of people with the disease doubles for every 5-year age interval beyond age 65, and the U.S. Census Bureau estimates that the 65-and older population will double to about 72 million during the next 20 years, starting with the oldest "baby boomers" who will turn 65 in 2011. The ranks of the very elderly, those 85 years old and older and at the highest risk of developing Alzheimer's disease, will increase even

¹ Plassman BL, Langa KM, Fischer GG, Heeringa SG, Weir DR, Ofstedal MB, Burke JR, Hurd MD, Potter GG, Rodgers WL, Steffens DC, Willis RJ, Wallace RB. Prevalence of dementia in the United States: the Aging, Demographics, and Memory Study. *Neuroepidemiology* 2007;29(1-2):125-132.

² Hebert LE, Scherr PA, Bienias JL, Bennett DA, Evans DA. Alzheimer disease in the US population: prevalence estimates using the 2000 census. *Archives of Neurology* 2003;60(8):1119-1122.

more rapidly, potentially tripling their numbers by 2050. At the same time, the relatively small size of the “Generation X” cohort that follows the baby boomers may lead to a decrease in the number of potential caregivers by 2050, indicating that a higher share of the caregiving burden may need to be assumed by the health care system.

The staggering complexity of the brain and our incomplete understanding of fundamental aging mechanisms have made seeking a cure for Alzheimer’s disease in our older population a difficult task indeed. We know vastly more than we did even five years ago, but, if we have learned one thing, it is just how complex a disease Alzheimer’s is. I can report to you today, however, even amid such challenges, that we have made and are continuing to make dramatic gains in our ability to understand, diagnose, and treat Alzheimer’s disease, progress that offers us the hope of reversing current trends.

What has brought us to this point is a sustained research program employing different approaches to the research challenge. This can involve the support of individual investigators who have a particular research theory or larger scale studies employing the newest technologies to mine extensive data sets to find genes or risk factors related to Alzheimer’s disease. Some research questions, for example, are straightforward and can be pursued with relatively small grants. One recent finding, as a case in point, suggests that a genetic mutation may be involved in impairing the ability of neurons to break down and re-use helpful proteins, as well as compromising efforts to clear away harmful waste proteins and other debris; the insight helps tell us what may underlie the pathology of one of the mutations responsible for early onset Alzheimer’s, and that perhaps also may contribute to late onset disease. Ultimately, this information will allow us to design interventions that may prevent or reverse the processes that underlie disease.

NIA also encourages and engages in partnerships to create synergy and leverage resources within and among scientists, institutions and organizations. NIH-supported investigators often combine their expertise through Program Project Grants, in which a number of collaborators with different skills work together on a common problem. Investigators on one NIA-supported Program Project have worked together to show that around 20 percent of older

adults who are functioning normally have Alzheimer's characteristic amyloid plaques in their brains, and that many have subtle cognitive and brain changes typical of a person with the disease. Today, we are supporting long-term follow up studies of these individuals: How many of them will develop Alzheimer's disease? And when? And how are they able to function with levels of amyloid plaques in their brains that correlate with diagnosis of the disease in other individuals?

In further support of collaborative research, NIA facilitates and participates in a number of strategic partnerships. The largest public-private partnership in Alzheimer's research is the Alzheimer's Disease Neuroimaging Initiative (ADNI), testing whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI), often a precursor condition to Alzheimer's disease, and early onset of the disease, as well as to measure more accurately the effectiveness of potential therapies. NIA's partners in this groundbreaking endeavor include a number of other NIH Institutes (National Institute of Mental Health, National Institute of Neurological Disorders and Stroke, National Institute of Nursing Research, National Institute on Drug Abuse, National Institute for Research Resources, and the National Institute of Biomedical Imaging and Bioengineering), pharmaceutical and diagnostic companies, and manufacturers of imaging equipment, as well as non-profit organizations and foundations, with important participation from the U.S. Food and Drug Administration. The partnership with private sector is managed by the Foundation for NIH, which Congress authorized several years ago to encourage and facilitate such projects.

Using imaging techniques and biomarker measures in blood and cerebrospinal fluid (CSF), ADNI investigators have already established a method and standards for testing the levels of AD's characteristic *tau* and beta-amyloid proteins in the CSF, have correlated levels of these proteins with changes in cognition over time, and have determined that changes in these two protein levels in the CSF may signal the onset of mild Alzheimer's. Last year, funding under the American Recovery and Reinvestment Act expanded the scope of the original ADNI research by allowing enrollment of participants at an even earlier stage of MCI, when symptoms are less severe, and this year the ADNI 2 was funded to enroll a new cohort of participants and expand

on the collection of biological measures. ADNI data are freely available on line, and over 170 papers worldwide have been published using ADNI data. ADNI's success has fueled similar studies in a number of other countries.

A high priority for the NIH is the identification of possible risk and protective factors for cognitive impairment and dementia. One approach encourages and supports use of national surveys of health and well-being to learn more about not only disease risk, but effects on families, use of health care services, and more. For example, investigators with the long-running Health and Retirement Study, the nation's leading source of combined data on health and financial circumstances of Americans over age 50, collect data on the cognitive health of older Americans. NIA also works with the U.S. Census Bureau and the Federal Forum on Aging Related Statistics to coordinate data collection in the area of cognitive impairment and dementia.

In recent years, there has been an explosion of knowledge from large-scale efforts, particularly in providing new clues about risk factor genes and possible environmental and lifestyle factors involved in Alzheimer's disease and cognitive impairment. Identifying risk factor genes pinpoints the brain pathways that are involved in the initiation of disease pathologies, and provides novel avenues for drug targeting. Until recently only one risk factor gene for late-onset Alzheimer's – the $\epsilon 4$ allele of the APOE gene – had been validated. The advent of new technologies to find risk factor genes necessitated the identification of thousands of patients and controls for testing – far too many for any one investigator to assemble – so we asked researchers in the genetics community to form a consortium and pool resources to find the remaining genes. The Alzheimer's Disease Genetics Consortium was funded last year, and in just one year, affiliated researchers have identified and confirmed an astonishing four additional risk factor genes. These investigators have gone on to form an international consortium with members of the European Union, an interaction facilitated by funding from the Alzheimer's Association, which will expand the pool of participants even further and facilitate even more rapid discovery of the remaining Alzheimer's genes. As with all our large studies, the data will be made broadly available to the scientific community.

A related area in which extensive scientific collaboration has been invaluable has been the study of families who are genetically predisposed to develop Alzheimer's disease in early to middle age. Such early-onset disease is rare, and individual investigators usually cannot identify enough individuals to study by themselves. NIA therefore established the Dominantly Inherited Alzheimer's Network (DIAN), a consortium of scientific investigators to identify, recruit, evaluate, and follow up individuals from families beset by early onset dominantly inherited Alzheimer's disease. The scientists involved in this study hope to identify the sequence of brain changes in early-onset Alzheimer's before symptoms appear. Understanding this process could provide insight as well into the more common late-onset form of the disease. Eventually, the investigators intend to conduct a clinical trial in this group. DIAN includes a number of sites in the United States as well as in England, and Australia.

As basic knowledge accumulates, it is critical to apply what we have learned, as quickly as possible, to the ultimate goal – the development of interventions and therapies to treat or prevent Alzheimer's disease. NIA has a longstanding interest and commitment to translational research, and efforts shifted into high gear in 2004 when NIA launched a set of initiatives focused on supporting early drug discovery and preclinical drug development of novel compounds for Alzheimer's therapy. The goal of this translational program is to increase the number of investigational new drugs that can be then clinically developed either by the pharmaceutical industry or through publicly-supported clinical trials. In addition, the program supports the repurposing and reformulation of existing drugs, already approved for other disease conditions such as antihypertensive drugs, as well as the preclinical development of naturally occurring compounds. To date, these translational initiatives have supported more than 60 projects aimed at discovering and developing novel compounds for more than a dozen different therapeutic targets such as amyloid, tau, various neurotransmitter and growth factor receptors, inflammation, ApoE, and more. NIA also co-funds a number of aspects of preclinical development for Alzheimer's disease through the trans-NIH Rapid Access to Interventional Development (NIH-RAID) Program (<http://nihroadmap.nih.gov/raid/>).

To support the extensive research efforts needed to understand the disease process and to test possible interventions, the NIA has organized institutions and studies to facilitate research

and collaboration. The 29 NIA-supported Alzheimer's Disease Centers (ADCs) across the U.S., are an invaluable resource and the source of many fundamental discoveries about Alzheimer's. These Centers combine the expertise of clinicians, pathologists, and many other scientists for studies across the research spectrum, from the longitudinal study of cognitively normal individuals and those in the early stages of disease to the clinicopathological study of their brains after death. The ADCs have provided essential resource and infrastructure support to efforts as diverse as clinical trials and ADNI. To maximize the combined efforts of the ADCs, NIA supports the National Alzheimer's Coordinating Center, which has made possible many new studies incorporating data from tens of thousands of participants seen annually from across the country, and additionally has provided essential infrastructure for DNA collection from Center participants for the Alzheimer's Disease Genetics Initiative. Data and biological samples are shared with scientists not in the Center network.

Many clinical studies collect data on aspects of neurological and behavioral function, but the fact that different studies may not employ the same tests or agree on methodologies can make it difficult to compile data across the full range of normal neurological function, and to compare data across studies. Through the support of the NIH Blueprint for Neuroscience and the NIH Opportunity Network for Research in the Basic Behavioral and Social Sciences, a brief yet comprehensive measurement tool for assessment of cognitive, emotional, sensory and motor function is being developed. Known as the NIH Toolbox for Assessment of Neurological and Behavioral Function, these measures can be used to uniformly assess cognitive performance and to track changes in performance across the lifespan. In addition, NIA is currently partnering with the Alzheimer's Association to update the diagnostic criteria for Alzheimer's disease for the first time in 25 years. The new criteria, to be applied primarily in a research setting where they can be validated, will incorporate knowledge gained over a quarter-century of research, including the role of biomarkers in Alzheimer's dementia diagnosis.

To assess the state of knowledge in developing interventions to prevent Alzheimer's disease the NIH last April convened the collaborative State of the Science Conference on Preventing Alzheimer's Disease and Cognitive Decline. The expert panel – not experts in Alzheimer's research but experts in other aspects of biomedical research and caregiving – noted

that research is providing some important clues, but concluded that no interventions to prevent or delay the onset of age-related cognitive decline or Alzheimer's disease have been scientifically validated. The conference was convened by NIH in collaboration with HHS's Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention, and the Centers for Medicare and Medicaid Services.

NIA already has studies underway in a number of areas highlighted by the panel as areas in need of additional research. Several seek to determine whether behavioral interventions such as exercise or cognitive training might stem the development or progression of age-related cognitive decline or Alzheimer's disease. We know that exercise for example is good for healthy aging in a variety of ways, and observational studies and some short-term clinical trials have suggested that it might be beneficial in delaying the symptoms or preventing dementia or cognitive decline. Testing whether it may have an effect on Alzheimer's is very important. One very large clinical trial, the Lifestyle Interventions and Independence for Elders (LIFE), aims to determine whether a specific regimen of exercise reduces disability in the elderly, and a cognitive component to that study has been designed to determine whether exercise affects cognitive decline or development of Alzheimer's.

The major clinical trial programs sponsored by NIA are the Alzheimer's Disease Cooperative Study (ADCS) and the pilot clinical trials initiative. These programs are in addition to continued support of investigator initiated clinical trials for Alzheimer's, MCI and age-related cognitive decline. The ADCS, a large clinical trials consortium with sites throughout the US and Canada, is a major initiative for Alzheimer's disease clinical trials in the Federal Government, addressing treatments for both cognitive and behavioral symptoms. The ADCS mission is to advance research in the development of clinical trial designs, instruments, and interventions that might be useful for treating patients with Alzheimer's disease, particularly interventions that might not be developed by industry.

NIA currently supports over 60 clinical trials targeting aspects of Alzheimer's disease and cognitive decline, including those being conducted by the ADCS. Both pilot and large scale trials are being undertaken, addressing a wide range of interventions to prevent, slow, or treat

Alzheimer's and/or cognitive decline or to address behavioral problems in person with the disease. Experts in the field are coming to believe it likely that any treatment will be more effective if started before the disease takes hold, and so there is a particular emphasis on prevention trials in presymptomatic individuals using biomarkers identified through ADNI (or elsewhere, as appropriate). However, prevention clinical trials are very expensive. To optimize efficiency and pool resources, we collaborate with other NIH Institutes to incorporate cognitive endpoints into relevant existing and planned trials. One such study is the National Heart, Lung, and Blood Institute's (NHLBI's) Systolic Blood Pressure Intervention Trial (SPRINT), which will evaluate the health effects of lowering systolic blood pressure either to a target level of 140 or to a target level of 120. The add-on study, SPRINT-MIND, is funded by NIA and the National Institute of Neurological Disorders and Stroke (NINDS) and will assess the effect of lowering systolic blood pressure on cognitive decline and development of MCI and Alzheimer's disease. The study will also include brain imaging to measure treatment effects on brain structure, including white matter lesions typical of vascular disease. In partnership with the Food and Drug Administration, NIA also maintains the Alzheimer's Disease Clinical Trials Database, which provides information about Alzheimer's disease clinical trials at sites throughout the U.S.

Finally, a number of studies have demonstrated that the chronic stresses of caring for a family member with dementia can cause lasting psychological and even physical consequences, and NIA works extensively with other agencies on interventions to meet the needs of Alzheimer's caregivers. An initiative with the National Institute of Nursing Research, Resources for Enhancing Alzheimer's Caregiver Health (REACH), has shown that a personalized intervention consisting of home visits, structured telephone support sessions, and telephone "check-ins" can significantly improve the quality of life for caregivers of people with Alzheimer's disease. The REACH intervention is currently being translated more broadly through a partnership between the Veterans Health Administration Geriatrics and Extended Care Unit and the Memphis VA Medical Center, with participating centers in 15 states. The Administration on Aging is also implementing the REACH intervention at centers in Georgia, North Carolina, and Florida.

A core part of NIA's mission is to disseminate information about research, aging and health to a variety of audiences. The NIA-sponsored Alzheimer's Disease Education and Referral Center (ADEAR) is the Federal government's leading source of evidence-based information about Alzheimer's disease and age-related cognitive change, providing resources to older people and their families, health professionals, and the general public. The Institute offers free publications and online materials about the disease and caregiving, a toll free telephone number for seniors and others without web access, details about clinical trials on Alzheimer's disease and a library for experts working with Alzheimer's patients. (ADEAR is located at www.nia.nih.gov/alzheimers and at 1-800-438-4380.)

It is difficult to predict the pace of science or to know with certainty what the future will bring. However, the progress we have already made will help us speed the pace of discovery, unravel the mysteries of Alzheimer's disease's pathology, and develop safe, effective preventions and treatments, to the benefit of older Americans.

Thank you for giving me this opportunity to share with you the challenges and accelerating progress regarding Alzheimer's disease research. I would be happy to answer any questions you may have.

Mr. PALLONE. Next is Mr. Harry Johns.

STATEMENT OF HARRY JOHNS

Mr. JOHNS. Thank you very much, Chairman Pallone, distinguished members of the committee. I want to also thank Ranking Member Shimkus and all of you for holding this hearing this afternoon.

My name is Harry Johns. I am the president and CEO of the Alzheimer's Association. The Alzheimer's Association was created in 1980 and is the leading voluntary health organization in both the provision of Alzheimer's care and support, and in the funding of Alzheimer's research, as the largest nonprofit funder of Alzheimer's research in the world.

To do our job well, we spend a lot of time listening, listening to people with Alzheimer's, their caregivers, their families, to researchers, our many collaborators, and to hundreds of thousands of our advocates. We hear their stories and experiences, and they inspire us to go further, faster, to provide better care, and ultimately the cure that we all seek. We listen to those families in your districts and we listen to our own families.

My mother had Alzheimer's disease herself. Any of us who have seen the disease up close don't want to see it again, for anyone to have the disease or to be a caregiver. Regrettably, we know it is going to happen much more ahead of us.

You know, the effects of Alzheimer's, as it has been stated previously, are truly devastating at the human level. In this country alone, as previously referenced, we estimate actually there are about 5.3 people who have the disease, about 200,000 of them younger onset, younger than 65. And by the middle of the century it could be as high as 13.5, or even as high as 16 million individuals in the United States alone. Today, there are 35 million people worldwide who have the disease.

Today, if you do develop Alzheimer's, we can say with certainty, absolute certainty, that you will either die with the disease or of it. And of the 10 leading causes of death, as previously mentioned, Alzheimer's is now sixth, Alzheimer's is growing by far the most rapidly, a 50 percent increase between 2000 and 2007, the last year that statistics are available. And it is the only one of the top 10 causes of death that has nothing to do to prevent, stop, or even slow it. For perspective, even though Alzheimer's is likely seriously underreported, already today it is killing more people than diabetes and more people than breast cancer and prostate cancer combined.

The 11 million caregivers in the United States, Alzheimer's can literally take everything they have to give: their time, their money, their jobs, and their own good health. And it happens every day, oftentimes never to be recovered. One study at least indicates that people who are caring for a spouse with Alzheimer's can actually predecease the individual with the disease.

The economic impact of Alzheimer's is also devastating, truly staggering numbers. You have already mentioned the \$172 billion in costs today for Alzheimer's going as high as \$1 trillion by the middle of the century, which was reported in the Alzheimer's Association's trajectory report earlier this year. And those are in today's dollars. Those are not inflated dollars. Those are dollars rated in

today's terms. A total of \$20 trillion over the next 40 years just to pay for the care costs, not an additional cent for the research we so badly need. And our country is simply not ready for this onslaught of Alzheimer's that is already upon us.

Let's take the case of research funding. You know, we have made significant progress in other diseases, in fact, in no small part because of the significant investments we have made in those diseases. Research spending at the Federal level for cancer is about \$6 billion today; for a cardiovascular disease about \$4 billion; for HIV/AIDS it is about \$3 billion. Now, all of those are good investments. They have paid off in lives saved, and they are going to continue to pay in that way for our country. But in Alzheimer's, we are only spending \$469 million a year, despite those other huge impacts we have already discussed.

We know that more money invested in research save lives, but we also know that too little money invested in research actually costs lives and ultimately will drive those very huge care costs into the trillions. Today, right now, we spend \$250 in America on care cost for Alzheimer's and dementia compared to \$1 invested in research; 250 to 1.

So to address the underinvestment in Alzheimer's research, the Alzheimer's Association strongly supports the Breakthrough Act. It is a bill that authorizes \$2 billion in Alzheimer's research.

But the Alzheimer's Association will not ask others to do what we won't do ourselves. We play an unparalleled role in the research community in Alzheimer's, globally as well as in the United States, and that certainly includes direct investment in Alzheimer's and effectively investing in science.

Our peer-reviewed research program since its inception has funded \$279 million worth of research to 1,900 investigators, making us the largest funder in the nonprofit world. And through partnerships and our own funding, we have played some kind of a part in every major advance over the past 30 years as a result.

But as I discuss these necessary investments in Alzheimer's research, and more broadly, I certainly recognize that our country is currently engaged in a very appropriate and very necessary conversation about our fiscal situation, our fiscal situation as a country, and we have to address that. But Alzheimer's, unaddressed, is one of our most devastating issues, both human and financial, as we have all discussed. So we must aim at what is the highest return potential we have for investments, Alzheimer's one of them.

So if we can't fix Alzheimer's, I don't think we can fix Medicare. Medicare costs three times more for each individual in the system who has Alzheimer's than it does for a normal individual.

Mr. PALLONE. Mr. Johns, I have been trying not to cut anybody off because we only have the one panel.

Mr. JOHNS. Let me wrap really quickly then, Mr. Chairman.

Certainly I want to mention the National Alzheimer's Project Act, and I want to thank this committee for its leadership. I certainly again want to recognize Congressman Markey who you mentioned for his leadership as the author; certainly recognize Dr. Burgess who has also provided leadership on this. And we know, of course, the Senate passed the bill yesterday. We look forward to the real possibility of the House passing it. We urge you to pass

it. And we look forward to working with this committee and the Congress to realize the ambition of the Alzheimer's Association, its vision, a world without Alzheimer's disease.

Mr. PALLONE. Thank you.

[The prepared statement of Mr. Johns follows:]

U.S. House of Representatives
Energy and Commerce Subcommittee on Health

Testimony of Harry Johns
President and CEO
Alzheimer's Association

December 9, 2010

Alzheimer's: On Course to be the Leading Public Health Crisis of the 21st Century

Today, the effects of Alzheimer's disease are devastating – to the estimated 5.3 million Americans with the disease, to their more than 11 million caregivers, and to the nation as a whole as we all share the tremendous costs of contending with the Alzheimer crisis.

Tomorrow, the devastation of Alzheimer's disease will grow far worse. In fact, it is on course to be our country's leading public health crisis of the 21st century, and the defining disease of the Baby Boom generation. If we don't succeed in changing the trajectory of this disease, by the middle of the century as many as 16 million Americans could have Alzheimer's.¹

We can make highly confident projections about the future growth of Alzheimer cases because these estimates are directly rooted in the broad demographic transformation underway, the graying of America. While Alzheimer's is not a normal part of aging, age is the largest risk factor for the disease. One in eight Americans over 65 have Alzheimer's; age 85 and above almost one in two Americans have the disease.² And so as our nation continues to age rapidly over the coming years – the first Baby Boomer turns 65 in just 23 days – Alzheimer cases will begin to mount at an ever increasing pace. Without the discovery and delivery of effective interventions, ten million American Baby Boomers will develop Alzheimer's disease.³ And the lives of many millions more will be upended by the emotionally, physically and financially draining toll of caring for them.

But how concerned should we be with these trends? The numbers are large, but do they represent a true crisis? To candidly pose a question no doubt on the minds of some, is Alzheimer's really as bad as the diseases many think of most often as public health crises? Those familiar with Alzheimer's know the answer to this question to be a resounding "yes."

Too many Americans are still unaware of the true, devastating impact of this disease. We are changing this, but harmful myths persist, and they must be challenged because they are partly responsible for the fact that our nation has neglected confronting this disease for far too long.

Perhaps the most pernicious of these lingering societal myths is that Alzheimer's is "just a little memory loss." As those of you who, like me, have personally witnessed loved ones suffer the impact of this disease know all too well, nothing could be further from the truth. Alzheimer's is a progressive, degenerative and ultimately fatal disease. It is cruel, and it is a killer. It kills by insidiously clogging and destroying the most vital of organs – the brain. In fact, it is one of the surest killers we know of. If you develop Alzheimer's we can say with absolute certainty that you will either die with it or from it. Alzheimer's is already the sixth

¹ Alzheimer's Association. 2010 Alzheimer's Disease Facts and Figures. Available at: http://www.alz.org/alzheimers_disease_facts_and_figures.asp

² Alzheimer's Association. 2010 Alzheimer's Disease Facts and Figures.

³ Alzheimer's Association. 2008 Alzheimer's Disease Facts and Figures.

leading cause of death in this country and, of the ten leading causes of death, is by far the fastest growing. According to the Centers for Disease Control and Prevention, Alzheimer deaths increased by more than 50% from 2000 to 2007, the most recent year for which data are available. In 2007, Alzheimer's killed more Americans than diabetes, and more than breast cancer and prostate cancer combined.⁴

If you look at the top ten causes of death in America today, you notice something else that is very striking, and very alarming. Alzheimer's is the only one of the top ten causes of death in the United States that remains without effective therapies, treatments, or preventative strategies. This must change. And it will, when we recognize this disease for the threat it is and respond accordingly.

Another aspect of Alzheimer's is its effect on others. It upends the lives of caregivers almost as surely as it does for those with the disease itself. Caregiving for Alzheimer's can literally take everything a caregiver has to give. Many caregivers experience negative health effects associated with caregiving.⁵ The manifestation, the degeneration and the progression of the disease varies with the individual, but the broad outlines are the same. If diagnosed early after symptoms first appear, the individual with the disease often can continue to enjoy a positive and functional (though impaired) life for a time; sometimes even for a few years. However, the individual will progressively lose functions until caregivers must be available 24 hours a day, at home or in a residential care facility.

In one study of family caregivers, 58 percent of caregivers felt as though they were "on duty" 24 hours a day during the last year of life for the person with dementia. 72 percent acknowledged that "they experienced relief when the person died."⁶ A National Alliance for Caregiving and AARP study found two-thirds of employed family caregivers of people with Alzheimer's and other dementia's had to go in late, leave early or take time off because of caregiving. Another study showed that caregivers of people with Alzheimer's or other dementia were 31 percent more likely to reduce hours or quit work altogether when caring for someone without behavioral symptoms when compared to caregivers of other older people. For the similar group of individuals caring for someone with behavioral symptoms of Alzheimer's or another dementia, the comparative likelihood of needing to reduce hours or to quit a job was 68 percent.⁷

America's Economic Toll from Alzheimer's

The economic factors of Alzheimer's rival the human devastation of the disease. According to the Alzheimer's Association's report, *Changing the Trajectory of Alzheimer's Disease: A National Imperative*, we are currently spending \$172 billion annually on Alzheimer's and other dementia care in America. \$88 billion of that is for Medicare alone, which is 17 percent of the total Medicare budget. Medicare beneficiaries with Alzheimer's or another dementia cost the system three times more than otherwise comparable individual in Medicare who does not have a dementia.⁸ For Medicaid, the cost multiplier for someone with dementia is nine times more than a comparable individual.⁹

Alzheimer's also serves as a cost multiplier for other conditions. 95% of Americans with Alzheimer's or another dementia have one or more other serious medical conditions as well. Largely because Alzheimer's strips away an individual's ability to manage other conditions such as diabetes or cardiovascular disease

⁴ "Deaths: Final Data for 2007." National Vital Statistics Report Vol. 58, No. 19. National Center for Health Statistics, 2010 <http://www.cdc.gov/nchs/fastats/deaths.htm>

⁵ Maria Shriver and the Alzheimer's Association. The Shriver Report: A Woman's Nation Takes on Alzheimer's. 2010. <http://alz.org/shriverreport/index.html>

⁶ Alzheimer's Association, 2010 Alzheimer's Disease Facts and Figures

⁷ Alzheimer's Association, 2010 Alzheimer's Disease Facts and Figures

⁸ Alzheimer's Association, *Changing the Trajectory of Alzheimer's Disease: A National Imperative*

⁹ Alzheimer's Association, 2010 Alzheimer's Disease Facts and Figures

successfully, the costs of care for people with these other conditions are far higher when they also have dementia. For instance, average per person Medicare payments for a person with diabetes are \$12,979, but for a person with both diabetes and Alzheimer's or another dementia average annual costs are \$20,655. The same is true for heart disease – those with only heart disease have average Medicare claims of \$14,640, while those that also have Alzheimer's or another dementia have annual costs of \$20,780.¹⁰

The *Trajectory* report estimates that during the next 40 years, the cost of Alzheimer's and other dementias will exceed \$20 trillion. Millions will get Alzheimer's and other dementias, and millions will suffer. Millions more will care for them and will suffer in different ways. So, Alzheimer's is going to cost us \$20 trillion¹¹ and all we will have to show for it are the long list of the dead, personal heartbreak, and the other devastating effects on caregivers and families.

Our country is engaged in a collective and very appropriate conversation about what should be done to address our current fiscal situation. What is notably absent from these discussions – and particularly in conversations about Medicare and Medicaid – is a systematic examination of the cost drivers behind our anticipated out-year liabilities. When we look at how we can take costs out of the system while improving outcomes, much as any successful manager might look to reduce the costs and improve the efficiency of a business operation, we quickly see that Alzheimer's should be a core part of these Medicare discussions.

Alzheimer's Association commissioned research again backs this up. The Association retained a health economics team at Dartmouth University to examine the costs of Alzheimer's and other dementias in Medicare claims data. Then, we commissioned The Lewin Group to build upon this analysis with an economic model that produced not just the future economic costs reported in the *Trajectory Report*, but also the savings our country could expect with incremental research advances. Among other findings, the model demonstrated that a therapeutic intervention that led to even a five year delay in onset would cut the projected cost of Alzheimer's over the coming decades almost in half.¹²

Voluntary Efforts to Overcome the Alzheimer's Crisis

Given the dimensions of this challenge, what's to be done about it? Particularly in these difficult times, no one would propose relying solely on the government to solve this crisis. A core part of the solution must, and should, be the voluntary efforts of Americans across the country.

That is why the Alzheimer's Association exists: to organize and apply this voluntary commitment to overcome this crisis in as compassionate, effective, and strategic a manner as possible. From my vantage point with the leading voluntary health organization in Alzheimer care and support, and the largest nonprofit funder of Alzheimer research, I am pleased to report that the commitment of volunteers is not just alive and well throughout our country, but is making a tremendous contribution to addressing the crisis just described.

The mission of the Alzheimer's Association is to eliminate Alzheimer's disease through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health.

Our vision is a world without Alzheimer's and, since 1980, we have moved toward this goal by advancing research and providing support, information and education to those affected by Alzheimer's and related dementias. We provide information and care consultations at all stages of the disease – and are available to do so every hour of the day, every day of the week, every week of the year. Across the country, we provide

¹⁰ Alzheimer's Association, 2010 Alzheimer's Disease Facts and Figures

¹¹ Alzheimer's Association, *Changing the Trajectory of Alzheimer's Disease: A National Imperative*

¹² Alzheimer's Association, *Changing the Trajectory of Alzheimer's Disease: A National Imperative*

support groups and other community interventions to make a difference in the lives of those who have the disease and those who are affected by it.

To find the ultimate answers to the disease, we fund cutting-edge research in top laboratories around the world. The Alzheimer's Association's peer-reviewed research grant program has awarded more than \$279 million to 1,900 scientists since 1982 – making the Alzheimer's Association the largest non-profit funder of Alzheimer research. Through partnerships and funded projects, the Association has been part of every major research advancement in the field over the past 30 years. We support novel approaches that drive new thinking. We fund science aimed at treatment and diagnosis as well as psychosocial interventions. And, we annually convene the largest research meeting in the world, the Alzheimer's Association International Conference on Alzheimer's Disease (AAICAD), drawing together the global Alzheimer research community to advance the science.

But American volunteers cannot solve this crisis alone. While the best way forward will include public-private partnerships and collaborations with organizations like the Alzheimer's Association, our government must do far more than it does today. It is what the American people clearly expect. According to a report that the Alzheimer's Association recently released with Maria Shriver, *The Shriver Report: A Woman's Nation Takes on Alzheimer's*, 78% of all respondents believe that it is "the responsibility of the government to help find a cure for a way to prevent Alzheimer's." Almost no one—only 7% of the U.S. population—believes a great deal of progress is being made to find a cure. Compared to how much progress they think is being made in heart disease, cancer, diabetes, and strokes, Americans rank Alzheimer's dead last.¹³

And so, in addition to our work in care and research, the Alzheimer's Association is also expanding our efforts in advocacy, fighting for critical Alzheimer research, prevention and care initiatives at the state and federal level, all driven by an aggressive, strategic approach to overcoming this disease as quickly, effectively and efficiently as possible.

How the Government Can Effectively Address this Crisis

Working with Alzheimer champions in the House and Senate, the Alzheimer's Association has collaborated in the drafting of three critical pieces of legislation that together would dramatically transform our national stance toward this disease and generate bold, strategic action. These three bills are the *National Alzheimer's Project Act*, the *Alzheimer's Breakthrough Act*, and the *Health Outcomes, Planning, and Education (HOPE) for Alzheimer's Act*.

Planning: The National Alzheimer's Project Act

We are heartened that the first of these bills, the *National Alzheimer's Project Act* (NAPA), is poised for passage in the remaining days of this Congress. We ask your support for this critical legislation.

Our federal government currently has no systematic plan to overcome Alzheimer's. No plan for investing in research to stop it. No plan to handle the cost of care if it isn't stopped. No plan for having enough residential care facilities for that inevitable point in the disease process when even the most dedicated caregivers can no longer handle the care at home, or a plan for new approaches to homecare. We have no articulation of objectives, timelines, assignment of responsibilities or any of the routine hallmarks of disciplined, effective management. Despite the millions of American lives and the trillions of American dollars at stake, we are drifting into the future rather than marching to a clear destination.

¹³ Maria Shriver and the Alzheimer's Association. *The Shriver Report: A Woman's Nation Takes on Alzheimer's*. 2010.

Building on the recommendations of the Alzheimer's Study Group, an independent, bipartisan panel created to evaluate the government's current efforts to combat the disease, NAPA would create a national strategic plan for the Alzheimer's disease crisis. It would also establish an inter-agency council to work with the Secretary of Health and Human Services to comprehensively assess and address Alzheimer research, care, institutional services, and home and community based programs. NAPA would ensure strategic planning and coordination of the fight against Alzheimer's across the federal government as a whole.

The Alzheimer's Study Group called for this action by 2010, and NAPA would set it in motion. Thanks in part to the leadership and foresight of members of this committee together with other members of the House and Senate, we appear on track to hit this mark.

Research: The Alzheimer's Breakthrough Act

But with what we hope and expect will be the passage of NAPA in this Congress, we must turn to the glaring fact that what's most needed in Alzheimer's is investment in more research to change the course of the disease as soon as possible. The science community is upbeat about the potential for Alzheimer advances, but as the boomer generation ages to the point of what is considered the earliest age of typical onset, 65, we need to act now.

Based on the most recently available data, federal funding for cancer is about \$6 billion, for cardiovascular diseases about \$4 billion, and for HIV/AIDS about \$3 billion. These have all proven to be smart, important investments that should continue based on their high returns in lives saved.¹⁴ By contrast, not counting the one-time stimulus funds, total federal funding for Alzheimer research is currently just \$469 million.

We already spend \$25,000 in care costs for every \$100 we spend on Alzheimer research.¹⁵ By the middle of the century, we will spend more than \$1 trillion annually for care for Alzheimer's and other dementias if we don't change the course of the disease.¹⁶ Those care costs are not due to inflation—the costs are in today's dollars.

The *Alzheimer's Breakthrough Act* would begin to address our woefully shortsighted underinvestment in Alzheimer's research. As investment in other diseases such as cancer, heart disease and HIV/AIDS demonstrates, adequate medical research investment more than pays for itself, not just in improved quality of life for those with Alzheimer's and their caregivers, but for the economic health of the country as well.

Care and Support: The Health Outcomes, Planning and Education (HOPE) for Alzheimer's Act

Yet even if we increase our investments, we cannot simply wait for the breakthroughs that will one day end Alzheimer's. Research takes time to yield results and in the meantime there is much we need to do to improve care and support for those contending with this disease.

Today, our health system does not work well for Alzheimer's care and support. The HOPE for Alzheimer's Act would make immediate contributions to the lives of the more than five million Americans with the disease today and their caregivers.

¹⁴ National Institutes of Health, Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC), 2010. <http://report.nih.gov/rcdc/categories/>

¹⁵ Alzheimer's Association, 2010 Alzheimer's Disease Facts and Figures.

¹⁶ Alzheimer's Association, Changing the Trajectory of Alzheimer's Disease: A National Imperative.

To provide better medical care and outcomes for individuals with Alzheimer's and other dementias, the dementia must first be detected, the disease causing it must then be diagnosed, care must be planned, and the diagnosis must be noted in the patient's medical record.

Figures on diagnosis differ, but it is likely that less than half of people with dementia have been formally diagnosed. Worse, although African-Americans and Hispanics are more likely than whites to have Alzheimer's and dementia¹⁷, studies conducted in physician offices and clinics show that African-Americans and Hispanics are less likely than whites to have a diagnosis of the condition.

If enacted, the HOPE for Alzheimer's Act will increase detection and diagnosis of dementia in primary care settings necessary for the provision of critical information and referrals to support services. It will also insure that Medicare beneficiaries have access to a package of services that will include a diagnostic evaluation, care planning and medical record documentation. Finally, it will help individuals with newly diagnosed dementia and their family caregivers understand the diagnosis, plan for predictable problems, avoid crises, and maintain the best possible quality of life.

The HOPE for Alzheimer's Act will deliver important improvements in outcomes and serve as a strong foundation for subsequent efforts to improve Alzheimer's care and support. We must lay this foundation as quickly as possible.

Hope for the Future – If We Act Quickly and Decisively Today

I get the benefit of exposure to scientists working worldwide to end this disease. I also have the opportunity to see so many others dedicated to providing care and support to those who will have the disease before we finally end it, and all of the volunteers, staff and donors who advance the mission of the Alzheimer's Association each and every day. Because of their collective energy, I remain optimistic about Alzheimer advances. I believe that we will succeed. We *must*.

I'm confident that we will prevail against Alzheimer's. It's not a matter of "if," it's a matter of "when." But "when" needs to be sooner rather than later. It's too late for my mother, and it's too late for the millions more who have died or who have progressed too far in their disease. Until we realize our vision of a world without Alzheimer's, the Alzheimer's Association will keep pursuing every possible approach to support those facing the disease and every possible way to find the answers we need to end it.

On behalf of the millions I represent this morning, I ask for your leadership in securing the success we need to address Alzheimer's, a true public health crisis for America.

Thank you.

¹⁷ Alzheimer's Association, 2010 Alzheimer's Disease Facts and Figures.

Mr. PALLONE. Mr. Hall.

STATEMENT OF ERIC J. HALL

Mr. HALL. Chairman Pallone, members of the committee, thank you so much for convening this hearing and for inviting the Alzheimer's Foundation of America to testify. I am Eric J. Hall. I am the AFA's founding president and chief executive officer, and I am truly honored to be here to testify on behalf of our member organizations and families that we care for across the country.

AFA was formed in February of 2002 to provide optimal care and services to individuals confronting dementia, and to their caregivers and families, through member organizations dedicated to improving quality of life. Today our membership consists of more than 1,400 organizations, including grassroots not-for-profit organizations, government agencies, public safety departments, and long-term care communities.

Our services include a toll-free hotline staffed by licensed social workers, educational materials; Care Advantage, which is a free quarterly family caregiver magazine that right now reaches about 1 million readers; professional training programs; AFA Teens, which is a Web-based support and scholarship program; and our National Memory Screening Date. As a foundation, our money is generated and disbursed by grants to service organizations as well as respite grants to families who are in need.

Recognizing the severe fiscal challenges facing our Nation, it is more important than ever to leverage available private-sector resources in a cost-effective manner to support public-sector initiatives. AFA makes substantial investments in care and services to tackle the enormous challenges associated with Alzheimer's disease and related dementias for both individuals and their family caregivers.

But the needs of the population are going to overwhelm our resources in the years to come. The National Institute on Aging reports that as many as 5.1 million Americans over 65 are, today, dying of Alzheimer's disease, and those numbers are projected to increase dramatically in the coming years. The rapidly rising costs associated with this disease will put an enormously heavy burden on families, businesses, and government economically.

It is our opinion that increased investment in preventing, treating, and/or curing chronic diseases of the aging, such as Alzheimer's disease, is perhaps the single most effective strategy in reducing national spending on health care. Chronic diseases associated with aging account for more than 75 percent of Medicare and other Federal health expenditures. Unprecedented increases in these diseases as the population ages are one reason why the Congressional Budget Office projects that total spending on health care will rise to 25 percent of the U.S. GDP by 2025.

Simply put, our Nation does not have the luxury of time to wait to address the health research needs of this population. Standard & Poors' recent report titled "Global Aging 2010: An Irreversible Truth," stated that no other force, no other force is likely to shape the future of national economic health, public finances, and/or policymaking at the irreversible rate at which the world's population is aging. Standard & Poors believes that the cost of caring for peo-

ple will profoundly affect growth prospects and dominate public finance policy debates worldwide.

As we have learned from the experience that we have all had with polio, heart disease, HIV/AIDS, cardiovascular, and other diseases, medical research and breakthroughs can have a profound impact on reducing health care costs.

As the extension of life expectancy from age 47 in 1900 to almost 80 in 2000 demonstrates, medical advances enormously increase national productivity and prosperity. Yet those benefits can only come about if NIH makes the needed investments and research aimed at preventing, treating, or curing age-related diseases and extending healthy life.

AFA, again, recognizes the serious fiscal challenges facing our Nation, which will require Congress to carefully scrutinize future funding priorities. We believe it is critical to leverage critical resources within the private sector, including not-for-profit organizations such as our own, to support proven, cost effective initiatives, and that is why we will all need Congress to be our partner.

This subcommittee and the full Energy and Commerce Committee have played a critical role in overseeing and supporting the mission of the NIH, and we respectfully urge your support for continued commitment to NIA's important research. AFA is seeking \$1.4 billion, an increase of \$300 million in fiscal year 2012 National Institute on Health budget specifically for the National Institute of Aging. This funding is the minimum essential to sustain the research needed to make progress in attacking the chronic diseases that are driving mass increases in our national health care costs. That level of funding would make the NIA's baseline consistent with comparable research initiatives conducted elsewhere under the auspices of NIH.

If NIA funding is not significantly increased, we stand to lose a generation of more young and emerging investigators in aging and Alzheimer's disease. This would be an enormous waste, since the NIA is poised to accelerate the scientific discoveries that can be translated quickly into effective prevention and efficient health care to reduce the burden of this silver tsunami of age-associated chronic diseases.

Breakthroughs from NIA research can lead to treatments and public health interventions that can delay the onset or slow the progression of costly connections such as heart disease, stroke, diabetes, bone fractures, age-related blindness, Parkinson's, and indeed Alzheimer's disease. From a budgetary perspective alone, such advances could save trillions of dollars by the middle of this current century.

At the Alzheimer's Foundation of America, our incredible strength and our quick success has come from collaboration. AFA looks forward to working with members of the subcommittee to address the important issues raised in today's hearing and, in the long term, to end the devastation caused by Alzheimer's disease.

Mr. PALLONE. Thank you. Thank you, Mr. Hall.

[The prepared statement of Mr. Hall follows:]



Our mission is "to provide optimal care and services to individuals confronting dementia, and to their caregivers and families—through member organizations dedicated to improving quality of life."

Written Statement for the Congressional Record by Eric J. Hall
President and Chief Executive Officer
Alzheimer's Foundation of America

Before the United States House Committee on Energy and Commerce
Subcommittee on Health
"Alzheimer's Disease: The Ongoing Challenges"
December 9, 2010

Chairman Pallone, Ranking Member Shimkus, and members of the Committee, thank you for convening this hearing and for inviting the Alzheimer's Foundation of America (AFA) to testify. I am Eric J. Hall, AFA's founding President and Chief Executive Officer, and I am honored to be here today.

AFA was formed in February 2002 "to provide optimal care and services to individuals confronting dementia, and to their caregivers and families—through member organizations dedicated to improving quality of life." Today, our membership consists of more than 1,400 organizations including grassroots nonprofit organizations, healthcare facilities, government agencies, public safety departments, and long-term care communities. Our services include a toll-free hotline staffed by licensed social workers; educational materials; *care ADvantage*, a free quarterly family caregiver magazine that reaches 1 million readers; professional training programs; AFA Teens support and scholarship program; National Memory Screening Day; and grants to service organizations as well as respite grants to families in need.

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Recognizing the severe fiscal challenges facing our nation, it is more important than ever to leverage available private sector resources in a cost-effective manner to support public sector initiatives. AFA makes substantial investments in care and services to tackle the enormous challenges associated with Alzheimer's disease and related dementias for both individuals and their family caregivers. AFA regularly provides grants to its nonprofit member organizations so that they can develop or enhance educational and support services in their communities. These grants are a critical funding source for these grassroots organizations, which play a pivotal role in their communities as hands-on providers of care and services for individuals with Alzheimer's and related illnesses, and their families. In addition, AFA provides grants to assist families with the cost of respite care, including home care and adult day programs.

AFA has several resources to help train and support family caregivers, including our "Your Time to Care" educational DVD series that addresses specific care issues in the home setting, including:

- Basic Skills for Caring for Individuals with Alzheimer's Disease and Related Dementias at Home
- Wandering...What It Is and What to Do About It
- Medication Management: From Daily Routines to Communicating with Healthcare Providers and Pharmacists; and
- Preventing Falls: Practical Steps to Reduce Fears and Risks

We would be glad to share copies of any of the listed DVDs with members of the Committee or other interested parties.

Another one of our innovative programs is AFA Teens. AFA Teens is aimed at teens with family members affected by the disease and those purely interested in the cause.

The need for the program was demonstrated by AFA's 2008 *ICAN: Investigating Caregivers' Attitudes and Needs* Survey, which found that three in five caregivers say their children aged 8 to 21 are involved in

caring for a loved one with Alzheimer's disease. Children were reported to assist with caregiving responsibilities that range from attending doctors' appointments to feeding and dressing their loved ones.

AFA Teens' dedicated Web site creates an online community for teens, giving them support from experts and the opportunity to share experiences and connect with each other through a bulletin board, blog, and AFA Teens chapters forming across the country. AFA Teens also awards a \$5,000 college scholarship to a college-bound student each year. The scholarship is designed to provide an outlet for teenagers to express their thoughts about Alzheimer's disease and to engage the younger generation in this cause.

AFA offers two national training programs that are specifically designed to raise the bar on dementia care in the United States:

Dementia Care Professionals of America (DCPA) is a division of AFA, and offers membership, training, qualification and other benefits to individual healthcare professionals involved in dementia care. DCPA provides practical training to healthcare professionals, sets standards of excellence through our AFA qualification program, keeps professionals abreast of emerging breakthroughs in treatment and care, and supports professionals as they support those in need.

AFA developed Excellence in Care, www.excellenceincare.org, to partner with care settings in the establishment of a nationwide standard of excellence in care for individuals with Alzheimer's disease or related dementias. The program was created with the Avila Institute of Gerontology and other industry experts and consists of a comprehensive on-site evaluation and consultation on strategies to achieve the established standards and to sustain performance. Key areas of review include environment, education, staff-client interaction and programming.

But the needs of the Alzheimer's population are going to overwhelm our resources in the years to come. The NIA reports that as many as 5.1 million Americans over 65 are today dying with Alzheimer's disease and the

numbers of Americans that will die of this disease are projected to increase dramatically in the coming years. Alzheimer's disease will also cause physical and emotional impairments on more and more families and caregivers. The growing numbers of Alzheimer's victims and the rapidly-rising costs associated with the disease will put a heavy economic burden on families, businesses and government.

Increased investment in preventing, treating or curing chronic diseases of the aging, such as Alzheimer's disease, is perhaps the single most effective strategy in reducing national spending on health care. Chronic diseases associated with aging account for more than 75 percent of Medicare and other federal health expenditures. Unprecedented increases in these diseases as the population ages are one reason the Congressional Budget Office projects that total spending on health care will rise to 25 percent of the U.S. GDP by 2025. Simply put, our nation does not have the luxury of time to wait to address the health research needs of this population.

Standard & Poor's recent Report (titled "Global Aging 2010: An Irreversible Truth") stated that "[n]o other force is likely to shape the future of national economic health, public finances, and policymaking as the irreversible rate at which the world's population is aging. ... Standard & Poor's believes that the cost of caring for these people will profoundly affect growth prospects and dominate public finance policy debates worldwide." As we have learned from the experience with polio, heart disease, HIV/AIDS, cardiovascular and other diseases, medical research and breakthroughs can have a profound impact in reducing health care costs. And the extension of life expectancy from 47 in 1900 to almost 80 in 2000 demonstrates that medical advancements enormously increase national productivity and prosperity. Yet, those benefits can only come about if NIH makes the needed investments in research aimed at preventing, treating or curing aging-related diseases and extending healthy life.

The National Institute on Aging (NIA) leads the national scientific effort to understand the nature of aging in order to promote the health and well-being of older adults. In stark contrast to the rapidly-rising costs of healthcare for the aging, we as a nation are making a miniscule, and declining, investment in the prevention, treatment or cure of aging conditions. Out of each dollar appropriated to NIH, only 3.6 cents goes toward supporting work of the NIA. Between FY 2003 and FY 2010, NIA-funded scientists saw a 14.7 percent reduction in constant dollars. In addition, the success rate of grant applications has declined from approximately 30 percent during the early part of the decade to 17.2 percent in FY 2009, with a payline of 11.8 percent. The announced payline in FY2010 for established researchers is 8 percent (less for larger grants) and is estimated to drop further in FY2011. This can be attributed to several factors—the changing demands on the NIA caused by the slow, progressive character of aging disease and hence the need for larger and longer clinical trials; a decline in the number of small, 2-year grants (i.e., R03, R21) awarded and the corresponding increase in 5-year grants; and the rise in the costs of R01 grants, attributable to documented inflation in the cost of science. Unfortunately, our nation's declining constant-dollar investment in NIA research has not kept pace with the demands of aging research or the health needs of older Americans.

AFA recognizes the serious fiscal challenges facing our nation, which will require Congress to carefully scrutinize future funding priorities. We believe it is critical to leverage available resources within the private sector, including not-for-profit organizations such as AFA, to support proven, cost-effective initiatives.

That's why we need Congress as our partner.

This Subcommittee and the full Energy and Commerce Committee have played a critical role in overseeing and supporting the mission of the NIH, and we respectfully urge your support for a continued commitment to the NIA's important research. **AFA is seeking \$1.4 billion, an increase of \$300 million, in the FY 2012 National Institutes of Health (NIH) Budget for the National Institute on Aging (NIA).** This funding is the minimum essential to sustain the research needed to make progress in attacking the chronic diseases that

are driving massive increases in our national healthcare costs. That level of funding would make the NIA's baseline consistent with comparable research initiatives conducted elsewhere under the auspices of the NIH.

If NIA funding is not significantly increased, we stand to lose a generation or more of young and emerging investigators in aging and Alzheimer's disease. This would be an enormous waste, since the NIA is poised to accelerate the scientific discoveries that can be translated quickly into effective prevention and efficient health care to reduce the burden of a "Silver Tsunami" of age-associated chronic diseases. Breakthroughs from NIA research can lead to treatments and public health interventions that could delay the onset or slow the progression of costly conditions such as heart disease, stroke, diabetes, bone fractures, age-related blindness, Parkinson's and Alzheimer's diseases. **From a budgetary perspective alone, such advances could save trillions of dollars by the middle of the current century.**

At the Alzheimer's Foundation of America, our strength and success come from collaboration. AFA looks forward to working with Members of the Subcommittee to address the important issues raised in today's hearing, and in the longer term, to end the devastation caused by Alzheimer's disease. Thank you again for the opportunity to testify, and I would be glad to answer any questions you may have.

Mr. PALLONE. Dr. Cantillon.

STATEMENT OF MARC CANTILLON, MD

Dr. CANTILLON. Mr. Chairman, members and staff, thank you for the opportunity to present testimony on this very important topic. I am Dr. Marc Cantillon, the executive director of the Coalition Against Major Disease of the Critical Path Institute, also known as C-Path.

I am a practicing physician and a neuroscientist, with 15 years' experience in research and drug development at the NIH, academia, nursing homes, and within the pharmaceutical industry.

C-Path is a nonprofit organization founded in 2005 by the FDA and the Arizona community in order to build collaborations that identify more reliable and efficient methods to test new medicines' applied regulatory science.

As you have heard, in spite of the exciting laboratory discoveries in Alzheimer's research, we lack full translation, we lack new medicines that could significantly alter the course of the disease. And, indeed, we have seen huge Alzheimer's disease drug trials fail. Nevertheless, there is reason for renewed hope.

Across the hall into science is a proverb written up that I would like to quote. "Where there is no vision, the people perish." Proverbs.

Thanks to the work of this subcommittee, the FDA Amendments Act of 2007 included a provision for the FDA to create the Critical Path public-private partnerships. We are extremely grateful to Congresswoman Marsha Blackburn of Tennessee, Congressman Eliot Engel of New York, and Congresswoman Gabrielle Giffords of Arizona for their leadership on this legislation.

The Coalition Against Major Diseases, or CAMD, was one of the first of these partnerships launched by the FDA, and it is already creating and identifying new tools that will speed the safe development of new medicines for Alzheimer's and other neurodegenerative diseases.

CAMD seeks to recreate the sense of urgency and open collaboration that made the unprecedented rapid progress against AIDS possible. Sharing of knowledge was the hallmark and is generally accepted as the reason that the rapid and enduring success was secured against that epidemic. Created by C-Path and the Engelberg Center of the Brookings Institute, CAMD is a consortium that currently includes scientists from 12 major pharmaceutical companies, NIH scientists, as well as experts from patient organizations such as my colleagues here today, the Alzheimer's Association and Alzheimer's Foundation.

The FDA, along with the European Medicines Agency, the EMA, and indeed the Japanese PMDA, provide advisers to our over 250 scientists who participate in CAMD by sharing what they know about Alzheimer's disease and how they can better test new therapies.

CAMD's accomplishments have already changed the way we attack this devastating disease. Firstly, CAMD researchers compare the way that they and other researchers score dementia, scored dementia in a clinical trial, and subsequently corrected over a dozen

inconsistencies. Now it is possible for them and for EMA and FDA to compare results directly from study to study.

This is a great example of applied regulatory science because it improves the quality, the accuracy, and efficiency of decisions made by both the regulators and the regulated industry of the pharmaceutical industry.

A first ever, CAMD was able to pool the data from 11 clinical trials conducted by several different pharmaceutical companies. This has created the largest publicly available Alzheimer's disease database in the world, and it describes the natural course of the disease in over 4,000 patients. Over 200 teams of scientists around the world are already using this.

For example, modeling. In the past, former scientists had to design trials based on their clinical experience or data within the company or what they read in the medical literature. This database allows the individual patient-level data to show progression over time in this number of patients. This is far more precise than their clinical experience or what they can glean from the medical literature.

This database also allows them to more accurately predict the outcome for a particular trial, or how long the trial must be, or how many patients must be included; indeed, how genetic subsets of the population might respond differently, et cetera. CAMD is now working with NIH and with academic centers to pool their data in the same standardized database to further enrich this as a leading-edge tool.

CAMD is also helping define the FDA's new qualification process described in the new guidance. In this work, CAMD submits data and requests that the FDA accept certain brain-imaging tools or cerebral spinal fluid tests as qualified for identifying patients much earlier in their disease when there is still brain function to be saved.

Yes, there are many reasons for hope. The Critical Path public-private partnership is improving the applied regulatory science for Alzheimer's at the FDA. However, we do need your help. Understaffing is a serious problem throughout the FDA and is especially serious for CAMD. The FDA needs your support to be able to dedicate the required number of scientists and staff to participate in CAMD and other Critical Path partnerships. This is the kind of applied critical science that is changing the way drugs are tested and evaluated today, so that Alzheimer's can be prevented, not just slowed.

I thank you for the opportunity to provide this testimony, and everybody in the CAMD thanks you for your leadership and foresight in authorizing the FDA's Critical Path public-private partnerships that are giving new hopes to patients and families at risk for this devastating disease. I would be happy to answer any questions.

[The prepared statement of Dr. Cantillon follows:]

**Testimony before the
Congress of The United States
House of Representatives
Committee on Energy and Commerce
Subcommittee on Health**

***The critical role of public/private partnerships in creating applied regulatory science to
advance the development of new Alzheimer's disease therapies***

December 9, 2010

**Marc Cantillon, MD
Executive Director, Coalition Against Major Diseases
Critical Path Institute**

MCantillon@C-Path.org

Mr. Chairman, Members, and Committee Staff:

Thank you for the opportunity to provide testimony before the Subcommittee on this critically important topic. My name is Marc Cantillon, MD, Executive Director of the Coalition Against Major Diseases (CAMD) for the Critical Path Institute (C-Path). I am a practicing physician and neuroscientist with over 15 years of experience in research at the NIH, academia, and the pharmaceutical industry. C-Path is an independent, non-profit organization founded in 2005 by the U.S. Food and Drug Administration (FDA) and the Arizona community to build public/private partnerships that identify more reliable and efficient methods to test new medicines.

Critical Path Institute

C-Path was created in response to what, we believe, is a crisis in drug development, i.e. the rapidly declining productivity of the biomedical research and development enterprise. Our goal has been to create a forum for scientists from the FDA, academia, biomedical organizations, and the pharmaceutical industry to evaluate innovative testing methods for use in drug development- innovations that will give patients the earliest access to the safest possible medications. We believe that this type of collaboration, a public/private partnership, facilitated by a neutral organization such as C-Path, is essential to bring about needed changes in the way drugs are developed. C-Path focuses on “applied regulatory science”, i.e. the science that improves the quality, accuracy and efficiency of decision-making by scientists in the FDA and in the regulated industry.

In order to serve as a neutral and trusted third party for collaborators, C-Path does not accept funding from the pharmaceutical industry or other companies that develop products regulated by the FDA. Since 2005, over \$30 million in federal and foundation grant awards and \$11 million in contributions from foundations and governments in Arizona have been received to support C-Path's work.

This funding is leveraged by in-kind support from a broad group of stakeholders and enables C-Path to manage five separate consortia with a total of over 750 participating scientists from FDA, NIH, academia and 30 of the largest global pharmaceutical companies. These stakeholders *share pre-competitive knowledge* and *develop consensus* on new drug development tools. These tools will improve the drug development process, make it more efficient and result in new drugs that are safer and more effective. C-Path supports projects that are identified as high priority by the FDA and are in the interest of public health.

CAMD: A Public Private Partnership

Thanks to the work of this Subcommittee, the FDA Amendments Act of 2007 included a provision for the FDA to create Critical Path Public/Private partnerships. Critical Path Institute's Coalition Against Major Diseases was one of the first of these partnerships launched by the FDA, and was formed to tackle brain disease beginning with one of today's most devastating illnesses, Alzheimer's disease (AD).

One of the greatest challenges facing biomedical sciences in the 21st century is the development of better treatments for neurodegenerative diseases. The two most prevalent of these, Alzheimer's disease and Parkinson's disease (PD), exert a heavy and growing human and economic burden on our society. Our lack of knowledge about the specific cause(s) of either disease is a major obstacle to the development of new treatments that have the potential to cure or prevent these devastating and tragic diseases.

In recent years, billions of dollars have been invested to develop new drugs for Alzheimer's disease but so far, all have failed to significantly impact the course of the disease. We firmly believe that new, applied regulatory science created through the public/private partnership of CAMD will result in new tools and methods that will accelerate the development of treatments for Alzheimer's patients that are effective much earlier in the disease.

Why Alzheimer's Disease for CAMD?

As the results of a 2009 study by the Alzheimer's Association make clear, the need for CAMD is compelling. The study revealed that the health care costs for American's over age 65 is three time greater if they have Alzheimer's disease. In the United States, 5.3 million people have Alzheimer's, costing the nation's healthcare system \$148 billion annually. Alzheimer's has become the sixth leading cause of death in the United States. Someone in America develops Alzheimer's every 70 seconds, which means more than 450,000 new patients will be diagnosed next year.

As a practicing neuropsychiatrist, I am proud to serve as the leader of CAMD. I have been frustrated daily by the limited benefits patients receive from our current treatments for Alzheimer's disease. I have spent 15 years conducting clinical trials for Alzheimer's and Parkinson's disease patients at the NIH, in universities and in the pharmaceutical industry where several trials costing \$200-500 million have failed. I am heartened that C-Path's CAMD is developing the needed tools that will help make it possible to find effective drugs quickly for patients.

CAMD seeks to *recreate* the sense of urgency and open collaboration that made unprecedented, rapid progress against HIV/AIDS possible. Sharing of knowledge was a hallmark, and is generally accepted as the reason for early, and continued, successes against that epidemic.

Created jointly by C-Path and the Engelberg Center at the Brookings Institution in February 2008, CAMD is a public/private partnership that currently includes twelve major pharmaceutical companies (listed below), NIH and five organizations that represent patients (including the Alzheimer's Association and the Alzheimer's Foundation here testifying today), with advisors representing the FDA and its European counterpart, the European Medicines Agency (EMA), National Institute of Neurological Disorders and Stroke (NINDS), and National Institute on Aging. CAMD also collaborates with several other organizations, including the Michael J. Fox Foundation, the Metrum Institute, Ephibian, and the Clinical Data Interchange Standards Consortium (CDISC), as well as over 200 academic scientists around the world.

CAMD members are:

Abbott	Alliance for Aging Research	Alzheimer's Association
Alzheimer's Fdn. of America	AstraZeneca Pharmaceuticals LP	
Bristol-Myers Squibb Co.	CHDI Foundation, Inc.	Eli Lilly and Company
F. Hoffmann-La Roche Ltd	Forest Research Institute	Genentech, Inc.
GlaxoSmithKline	Johnson & Johnson	Michael J. Fox Foundation
National Health Council	Novartis Pharmaceuticals	Parkinson's Action Network
Parkinson's Disease Fdn.	Pfizer, Inc.	sanofi-aventis

CAMD's Progress to Date

CAMD's accomplishments have already changed the way we attack this devastating disease.

Several examples are:

- CAMD researchers compared the way they had been scoring a person's dementia in clinical trials and found over a dozen inconsistencies in the way a score was determined for the standard tool, the Alzheimer's Disease Assessment Scale-Cognition or ADAS-cog. With these inconsistencies eliminated, it is possible for these investigators, and the FDA, to compare the results from study to study. This standardization process for ADAS-cog is a great example of "applied regulatory science".
- In CAMD and for the first time ever, pharmaceutical companies are sharing their clinical trial data with one another. CAMD has been able to pool data from 11 clinical trials conducted by seven different pharmaceutical companies. This is now the largest publicly available Alzheimer's disease database and it describes the natural course of the disease in over 4000 patients. Normally to generate new data for this number of patients, it would cost \$300-600 million and take more than six years in new clinical trials. Today, only a few months later, the database has more than 200 users from academia and industry in over 34 countries. More information and how to apply for access to the database can be found at <https://codr.c-path.org>.
- A quantitative disease model that describes the natural progression of Alzheimer's disease has been developed using data from the Alzheimer's Disease Neuroimaging Initiative. This model is now being tested and improved with the larger and regulatory standard database of industry clinical trial data described above. The disease model will be used to help design new clinical trials, and has been submitted to the FDA and EMA for initial review. Scientists around the world are already using the database and models in innovative ways. For example, in the past, scientists designed trials based on their personal experience or what they read in the medical literature. Now, thanks to this database, they have the individual data for exactly how Alzheimer's progressed in each of over 4000 patients. This is far more precise than their personal understanding of the disease or what they have gleaned from text books. This database and mathematical models of the disease allow them to more accurately predict the outcome for a given clinical trial, how long the trial must be conducted, how many patients must

be enrolled, how genetic subsets of the population could respond, etc. CAMD is now working with the NIH and academic investigators to pool their data to further enrich this exciting leading edge tool.

- CAMD is helping define the FDA's new "Qualification" process, described in the new draft guidance released by FDA. (Guidance for Industry: Qualification Process for Drug Development Tools, U.S. Food and Drug Administration, October 2010) In this work, CAMD is submitting data and requesting that the FDA recognize certain imaging tools and cerebrospinal fluid tests as "qualified" for identifying patients much earlier in their disease, when there is still brain function to be saved. In this work, CAMD scientists are identifying imaging, biochemical, genetic, and molecular biomarkers that have the greatest potential to uncover patient populations that are pre-symptomatic and therefore have more potential benefit from new therapies. A research plan was submitted in fourth quarter to FDA and EMA.
- For the first time, we now have mutually agreed upon data standards for Alzheimer's clinical trials. CAMD investigators, working with the standard setting body, CDISC, posted these standards for public comment in an Implementation Guide on Dec 17, 2010. These common data elements will be used by all CAMD members, but are also now published for use by anyone. Having a common data format will enable rapid data sharing and accelerated research and drug development. In the near future, all data submitted to the FDA for this disease should be in a common format greatly accelerating the FDA's ability to quickly evaluate applications.

Having these new tools is allowing drug companies to more quickly evaluate potential therapies and find those that have a beneficial effect on disease progression – and also to more quickly stop working on therapies that show no benefit. This will allow them to optimize resources and bring therapies more quickly to the FDA and, therefore, more quickly to patients.

We need your help

Although CAMD is already improving applied regulatory science for Alzheimer's disease at the FDA, we need your help. Understaffing is a serious problem throughout the FDA and is especially critical for CAMD. The FDA needs your support to be able to dedicate the required number of scientists and staff to participate in CAMD and other critical path partnerships. CAMD's work is the kind of "applied regulatory science" that is changing the way drugs are tested and evaluated today, not ten years from now.

I thank you for the opportunity to provide this testimony and everyone at Critical Path Institute and CAMD thanks you for your leadership and foresight in authorizing the FDA's Critical Path Public/Private Partnerships that are giving new hope to patients and families at risk for this devastating disease.

I respectfully request that my full testimony be accepted to the record. Marc Cantillon, MD

Mr. PALLONE. Thank you, Doctor.

I thank all of you. We will take questions from the members, and I will start with myself, and I will start with Dr. Morrison-Bogorad.

Scientists know Alzheimer's attacks the brain long before people exhibit cognitive decline. But the specifics are crucial because, so far, drug after drug has failed to effectively treat Alzheimer's in people who already show symptoms. I know you suggested that that was part of the problem, that perhaps the answer is earlier treatment before you actually have the signs of the disorder. So what I wanted to ask is why are biological markers, whether gene mutations or pathological brain changes, important to the development of effective treatments for Alzheimer's and what research is NIA conducting to better understand these markers? I am sort of going back to that same issue that you mention, is perhaps we should be starting earlier but then we would have to know if people have the disorder.

Ms. MORRISON-BOGORAD. It is probably one of the items that we are pushing most of our effort into these days, because we do think that understanding the earlier stages of Alzheimer's disease is very important and we have thought that ever since we reissued the request for applications for funding our Alzheimer's disease centers across the country. Because about 8 years ago now we said to them, forget about late stages of disease. We want you to really, really concentrate on the earlier stages.

So we have thought about this for quite a long time; and, obviously, one of the things that held us up is not being able to identify preclinical stages. That is one of the things that is really being addressed by the Alzheimer's disease in your imaging initiative, especially in people who aren't yet showing symptoms or in people who are developing mild cognitive impairment, which is a precursor to Alzheimer's. Researchers working together with industry and people funded by us are identifying markers in the cerebrospinal fluid, and these markers are lowered beta-amyloid and higher levels of protein called tau that signal that a person is approaching the stage of mild cognitive impairment.

The other technology which has been developed by ADNI and by others is actually being able to look at in the brains of individuals cerebral amyloid plaques through positron emission tomography, through imaging. And this is perhaps the most amazing breakthrough over the last several years because that has allowed us to see that in a number of folk, older folk, older than 65 or 70, about 20 percent of these folk who otherwise would have been thought of as normal, who are quite normal cognitively, have levels of amyloid plaques in their brain that in some cases are equivalent to a person with Alzheimer's disease who can't at the moment function for themselves.

So the CSF markers and the brain markers are two ways we have of identifying preclinical disease which we didn't have before, and they could be used to identify people who have got markers in the brain, amyloid in the brain for earlier clinical trials than we are able to do right now. So I agree. It is really, really, really important that we develop these markers and that we use them to do more efficient clinical trials in the preclinical stage.

Mr. PALLONE. I had a second question, but I maybe would prefer if anybody else would want to comment on this issue because I think it is pretty important. Would any of the others like to—

Mr. JOHNS. I simply add that what Marcelle has said is certainly one of the most exciting areas that is occurring in Alzheimer's research today. She has indicated that we have worked together on this at the Alzheimer's Association International Conference on Alzheimer's Disease over the summer. There were significant findings released on this very front. It is potential to go to the point where we can actually identify Alzheimer's presymptomatically in the future. It is not ready for the clinic. That is for the lab at this point. That is a significant set of advances that are very important to us.

What is of course very important is that we have a parallel in treatments. Right now, we are making faster advances on the diagnostic science than we are on treatment side. So what we really need to do is catch that up. And that is one of the most important reasons for the additional funding that is really needed for Alzheimer's disease.

Mr. PALLONE. Thank you.

Mr. GINGREY.

Mr. GINGREY. Mr. Chairman, thank you.

I think I will shift then to the treatment aspect of it and maybe come back to very interesting things that the two of you have just talked about with regard to early diagnosis.

Dr. Cantillon—I hope I did better. I know I botched that up pretty bad the first time—I have a lot of respect that the FDA, the Food and Drug Administration, performs. With that being said, I am interested in exploring how the FDA drug approval process might be improved in the hope it may help spur a greater drug development for diseases such as Alzheimer's.

I think I mentioned in my opening remarks that I have introduced legislation along with my colleagues here on the committee, Energy and Commerce Committee, Health Subcommittee, bipartisan, Mr. Green and Ms. DeGette on the Democratic side and myself and Mr. Rogers from Michigan on this side, the GAIN Act. This is in regard to the shortage of antibiotics. So a different disease, a different category of drugs, but equally as important. Can you tell me, Dr. Cantillon, how applying scientific advances such as the use of biomarkers or drug development tools might aid in drug development in this country?

Dr. CANTILLON. Yes. Thank you for that question.

So, actually, as a medical director of Alzheimer's and other programs with Schering Plough over the last couple of years before CAMD, I did sit on an industry advisory group for this ADNI trial that Dr. Bogorad was speaking about. So I was giving some advice into the choice of the instruments and that these markers were being developed, had my hat on in terms of both drug development and facing the FDA with a package for an approval for a treatment.

The trouble is when you are coming from a drug developer's point of view, this is all very cutting edge. And as I said in my testimony, the science by itself is truly not enough. It is not enough to have exciting markers that may predict something that is going

on in the brain if it can't be harnessed into a path and the development steps to use a new drug and prove that. I will give you an example.

So we talked just now about the cerebrospinal fluid. We know there are certain proteins that can indicate both the disease and perhaps even the type of progression predictive. We would take that and we are taking that and in a collaborative way with the whole field. So we are just one collaboration that I had mentioned. Look at the evidence for that in a critical way, in a scientific manner.

The regulatory science part is having our regulatory scientific colleagues internationally review that in a context of use. Does that allow you to choose a population for a trial who are not yet demented? So to call somebody demented, you don't need to be a doctor. It is very clear that the person does not have their brain functions in the same way for memory and so forth. To find somebody that is very early in the disease or even hasn't fully shown clinical symptoms, you need these markers.

Can we ask for FDA regulatory approval that these are standardized in such a way that they can become a tool, a standard tool publicly available to any company in this country or anywhere else? Can take off the shelf and put into a program such that, by using this tool, they don't have to defend that tool when they go in front of the FDA? That process has already been done in this qualification. And instead they can focus on their own particular drug that then fits into this pattern and can use that patient population, for example, to show progression over time. Do those people who have low tau, high tau, low a-beta or a particular brain picture with amyloid, do they progress faster than others and can you show a difference in the people who were on drug and off drug? That is how the whole development process can make use of this science and translate it into something that the FDA can then approve or not approve.

The FDA did put out a guidance document partially from working with us just 2 months ago, and in that the steps are laid out very clearly. Essentially, it is show us the evidence. Very similar—

Mr. GINGREY. My time is rapidly drawing to a close, but let me quickly ask you, do you think it is important that such drug development tools—biomarkers—that they first receive approval by the FDA before being used by industry and the agency to measure the safety and efficacy of the drug? Do you think that the FDA would have to approve this off-the-shelf kind of testing ahead of time?

Dr. CANTILLON. The FDA has the possibility just to approve for commercial use or other use, but that is not within the context of use that we are talking about. The context of use would help that tool help define a particular population. So, for example, let me give you another—for another consortium. We developed some markers for renal injury, for kidney injury. They were brand new, and they could allow a drug developer or anybody to show if something was happening very early on before the kidney actually was destroyed. These markers went through this qualification process and are being very widely used by all companies, including my former one, to make decisions about drug development. When they

go to the FDA, they don't need to defend those markers for kidney. They have already been approved. So it takes a lot of that work away and you can focus on the drug.

Mr. GINGREY. Doctor, thank you. That does answer my question. And I will yield back, Mr. Chairman.

Mr. PALLONE. Thank you.

The gentlewoman from the Virgin Islands.

Mrs. CHRISTENSEN. Thank you. Thank you, Mr. Chairman.

Dr. Morrison-Bogorad, given the disproportionate impact of Alzheimer's on minorities, is the National Institute of Minority Health and Health Authority Research, which was formally the center among the NIH institutions that you are collaborating with? And, also, how diverse are the participants in the clinical trials?

Ms. MORRISON-BOGORAD. It is again something that we paid particular attention to, especially in our flagship clinical trials, the Alzheimer's disease clinical consortium, and there we have made a rule that a certain number of people in each clinical trial that we run there are minorities. And that has been extraordinarily helpful because it has meant that I think a fifth of the folk who participate in certain of these studies are minorities. So it is amazing what a little rule will do.

And we certainly have got quite a vibrant program in epidemiology looking at Alzheimer's disease in minorities and comparing that with Alzheimer's disease. And I would say at the moment the results are somewhat equivocal because many of the ways in which you define Alzheimer's disease are also very dependent on things like the education of the person who is taking the tests. And many older African Americans, of course, for other reasons haven't had the education that they should have had and so they don't do as well on these tests as they should. It doesn't mean they have Alzheimer's, however.

So this is a very, very thorny issue and we have gotten a number of very good researchers working on that to actually try and tease out what part of the minority burden of Alzheimer's disease is real—and I do believe some of it is because some of the possible things that cause Alzheimer's disease are, as you are aware, much more prevalent in minority communities, things like heart disease. But I do believe that some of the numbers are a little bit over, perhaps larger than they should be because of this issue on how to determine Alzheimer's disease in people with different backgrounds.

Mrs. CHRISTENSEN. That is interesting, because my impression is that it is underdiagnosed rather than overdiagnosed in minorities. And I will let anybody comment on that.

But I wanted to ask Mr. Johns, if I can get this question straight, because I know this hearing is really about getting funding for Alzheimer's. And, Mr. Johns, I heard your argument very clearly about the need for an increased investment in Alzheimer's to reduce the cost of health care eventually and to perhaps even save Medicare. We have been trying to get CBO to score prevention for a while, actually introduced legislation to have them do that when they are asked by the committee. So, without having scoring in place for prevention, how do you foresee getting the funding needed, especially in a Congress that is committed to cutting

spending? And how important do you think scoring prevention is to this particular issue?

Mr. JOHNS. Well, certainly, as you say, the fact is that CBO won't score what I would describe as a game changer. That is a problem I know for all of us when we have interest in what would be effectively R&D for our country. We really have—beyond the immediacy of Alzheimer's, we have what is a potential brain drain in our country as a result of research being attracted overseas. While it isn't specific to Alzheimer's, it is generic and related to Alzheimer's, as well as other medical research.

So we have as a country to face what is, first of all, a significant problem in that larger regard with medical research but very specific in Alzheimer's; and, of course, we have the challenge of facing our economic realities and also then funding something that cannot be scored. We recognize fully the difficulties of this, but we can also see from the projections we have done—and we have gone to outside sources at the Alzheimer's Association to develop what are these data. We have actually used the CMS data on expenditures on Medicare and Medicaid. We have taken those to Dartmouth. We have had the Lewin Group look at all these data and what we have identified is that \$20 trillion cost over the next 40 years.

One of the problems we have as a country, of course, is actually addressing problems that are longitudinal. Those of you sitting across from me know that better than I in terms of how hard it is to make those things work. But we certainly know it, too, the Alzheimer's Association and any of us here sitting on this side who are trying to change the course of Alzheimer's disease. We have to find the national fortitude to address this already enormous problem. Everyone who has the disease today will die with it or of it. We do not have a treatment that stops or even slows it. The devastation of the disease at a human level for all of us who have experienced it personally and for all of those who haven't, we recognize just how bad that is.

I don't have the easy answer to your question, but the scale of the problem, the enormity of the issue begs for us to find a way to answer the question so that we can address this now. We are running out of time.

One of the things that Marcelle mentioned is that the science community believes ever more that we need to intervene sooner, that the plaques entangles of the disease are deposited earlier in life, at least 10 years before the symptoms manifest. If, in fact, we don't make these investments relatively soon, the baby boomers, 10 million of whom will have this disease, will be a lost cause. And the devastation at a human level and the economic toll will be solidified if we don't move relatively soon.

Mrs. CHRISTENSEN. Thank you. Thanks.

Mr. PALLONE. I thank the gentlewoman.

Next, we have our Alzheimer's hero here, who actually sponsored both of the bills that you mentioned, Mr. Johns, the one that I guess is now in the House for action hopefully next week, as well as the larger bill. Mr. Markey.

Mr. MARKEY. Thank you, Mr. Chairman, very much; and I thank our witnesses so much for your participation here today.

Robert Browning wrote, grow old with me, the best is yet to be. But the truth is that for millions of millions of Americans the golden years are now the worst years because of Alzheimer's and the family caregiver who has to help. So this is now at 4 million or 5 million Americans already an epidemic since, as we know, not only does the Alzheimer's patient have the disease, but one family member has it as well as. So about 10 million Americans right now are living with it on a daily basis in their homes or in some facility. And when it goes up to 12 million times 2, 24 million, 25 million people, the caregiver and the patient, it is going to be an incredible moment in American history. So we have an incredible responsibility here to make sure that we put in place a plan.

And, Mr. Chairman, you made reference to it, which is that the National Alzheimer's Project Act, which I introduced on this side along with Christopher Smith, the co-chair of the Alzheimer's Task Force, passed the Senate last night. And Senator Bayh and Senator Collins did an excellent job in framing it up and we will be able to pass that next week on the House floor. And then we will have a plan. We will have something that makes it possible for us to put in place something that is the plan to attack this disease. And it is long overdue, but it is a good beginning.

So let me ask you this, and maybe you could reflect upon it, Mr. Johns, if you could. Last year, the Federal Government spent \$122 billion on helping people with Alzheimer's, but we only invested \$469 million in finding the cure, and we know we are only at the beginning of an explosion of the bills that are going to come in across America for the Federal Government to help families with Alzheimer's. Can you reflect upon that, give us your insight as to how big it is going to become and why it is imperative that we act now?

Mr. JOHNS. Certainly. And let me thank you, Mr. Markey, for your authorship of NAPA and the input and leadership of yours and the committee's in moving that forward.

Certainly Alzheimer's is already costing \$172 billion in total, the \$122 billion you talked about from the Federal Government. Incidentally, at the Medicare level, Alzheimer's is driving 17 percent of the Medicare budget—

Mr. MARKEY. Say that again.

Mr. JOHNS. Seventeen percent of the Medicare budget is driven by Alzheimer's today. The total cost for Alzheimer's again to the country and other dementia is, by the middle of the century, in excess of \$1 trillion per year; and by far the bulk of that will be the Federal Government's cost projected from today's levels with no changes. So that it simply won't be affordable not only on the economic front but again on the human front.

We can't accept what will happen to families. We don't have the ability to deal with the end-of-life considerations of the long-term care. Families at some point, dedicated as they are, with 70 percent of the people who have Alzheimer's living at home and cared for at home, at some point that other percentage as a result of the fact that families, no matter how much time they spend, the 24 hours a day that they often spend as caregivers, especially toward the end of life, is no longer enough or they are simply not capable of handling the difficulty of the care at home so that we are not

equipped at this point. As you indicated, we don't have a plan for any of these things at this point. NAPA will hopefully address that, but we are just not prepared as a country to handle any of these problems at the scale they are going to rise to.

Mr. MARKEY. This is just something that is not as well understood as it should be. My mother had Alzheimer's, and she was a valedictorian. My father was a milkman. And my father always said it was an honor that my mother married him. And he used to say, as well, if the strength of your brain determined who got Alzheimer's that he would have had it and my mother would have been taking care of him. But we know that this is an equal opportunity disease. At age 80, 82, 84, 86, 88, my father kept her in our living room with the arms of a milkman, arms the size of my legs; and he was able to do it.

But for many families it becomes exhausting. You can't do it. There is a point beyond which you need help and that helps comes increasingly from the Federal Government in the form of \$122 billion a year right now.

But I don't think actually we are going to be able to solve the Federal budget deficit if we don't dramatically increase the Federal investment in research. It will be a trillion dollars a year just for Alzheimer's care in another 15 years, and it is just a number that is going to increase exponentially. And despite the efforts of people like my father and other families all across the country, these people are heroes, but heroes need help and they need hope. And only the National Institutes of Health, really the institutes of hope, really give people the courage to keep on going.

So this whole effort is absolutely—I think it should be the number one issue, to be honest with you, just from a budgetary perspective. From a humane perspective, yes. Coupled with the Alzheimer's Breakthrough Act, which I have introduced, and the HOPE Act, the Health Outcomes, Planning and Education Act, which we have to focus on, we have to put in place the kind of ingredients of this plan that make it possible for us to solve this problem. And I commit to you, all of you, that I am going to continue to just work my heart out to make this something that becomes real in people's lives; and I cannot thank you enough all of you for your support.

And, Mr. Chairman, I thank you for conducting this hearing. I don't think there is a more important subject for us to be discussing as Americans.

Mr. PALLONE. Thank you. And thank you for all you do, Mr. Markey, on this and other issues.

Mr. Engel.

Mr. ENGEL. Thank you. Thank you very much, Mr. Chairman. Right in the nick of time.

First of all, I want to thank everyone on the panel. This is certainly a very, very important and—and something I have had a lot of concern about. I think that—what all my colleagues have said—this is what we ought to be spending money on when we talk about some of the other issues. I think we should all agree on issues like this.

Mr. Chairman, I want to ask unanimous consent to insert my opening statement in the record.

[The information was unavailable at the time of printing.]

Mr. ENGEL. Let me ask Dr. Cantillon—first of all, thank you for your comments. I was told the comments you made before, and I deeply appreciate your saying that. The Critical Path Initiative is certainly something that is near and dear to my heart. I have strongly supported public-private partnerships, and I am pleased to learn that this program has been very effective in tackling diseases like Alzheimer's.

You mentioned in your testimony, Doctor, that one way Congress can be helpful is to provide the resources to increasing staffing levels at FDA; and, as I mentioned before, I couldn't agree more. We need to increase resources for the FDA to help them bring drugs to market. But, given the limited resources we are working with, I was wondering if you could address other ways that we might help break down the barriers to translational research and help fill in the gap that has opened up between biomedical researchers and the patients who need their discoveries, which we unfortunately referred to as the valley of death.

Dr. CANTILLON. Indeed, thank you and thank you for your support for these partnerships.

I think that the partnership, the public-private partnerships, are certainly a major part of the answer in this fiscal environment. So we have all said several times that this is about to bankrupt our country and many other aging countries around the world and there aren't unlimited funds either to put into any one particular disease. And maybe we need to look at an innovative science and an innovative way of answering some of these questions that have come up.

So the FDA is going to be faced with a lot of the new science arriving in different ways. Part of what we have been working together with them was to put a process in place to translate this science, not just, let us say, from the test tube to the rat, but all the way through to a new medication at the very end. In other words, to make a process available to be able to gather the evidentiary information.

The FDA doesn't have but a few handful of staff that we deal with on a very regular basis and, as I mentioned, are indeed a part of our consortium; and the Europeans, in fact, are in a similar situation. So what I was referring to is basically stretching the dollar and the people that we have. Part of what we are doing and seek to do more of is in fact build an in-kind work, and there is a lot you can do with that. There is a lot of scientists, just like there was a lot of data, who have been siloed, be it within government—I used to be at NIH—or within companies.

Once a trial has failed, that data is essentially put on the shelf somewhere. Definitely with the kind of tools we are talking about, those data can be re-examined, at the very least, and perhaps there will be some pearls in there. But they also can be mined for the learnings that are there and shared. That is public and belongs to all of us.

So what we put together are these various methods to do that. It is, I would say, an innovative tool to get people to give up their silo thinking, look at a precompetitive space for companies and even for academics, that they actually don't own the data that they

have generated, that it belongs to the people. And if we can set it up that way, have it as a database, for example, as I mentioned, but also the other tools, then that is freed for the best minds in the world to attack and that is actually a very efficient way of doing that.

Mr. ENGEL. Thank you for pointing that out. It certainly is a shame if research is put on the shelf and no one else can get to it or look at it. This has to be a collaborative effort, obviously, and thank you for pointing that out.

I would like to ask a question of Mr. Hall and Mr. Johns. As I am sure you are aware, the Patient Protection and Affordable Care Act, which is referred to as health care reform, that we just passed here, we were doing this for as you know almost 2 years. There was a provision in there that improves access to home and community based care for patients. We know that these services greatly improve the quality of life for Alzheimer's patients.

Health care reform, as we know, strengthens the long-term care system for chronic and other long-term neurological conditions both by eliminating the arbitrary caps on treatment, which we did—that was one of the crowning glories of this bill—and by expanding coverage to include preexisting conditions, which is the second pillar that is so important in this bill.

In an effort to improve upon existing programs that positively impact Alzheimer's patients and help you provide services, can you give us some insight as to how these provisions will improve your ability to provide services for Alzheimer's patients and their families? And can you also address what other Federal programs exist to help you deliver services to more patients?

Mr. JOHNS. Well, I personally think that all of our constituents are in a position, especially, as I mentioned previously, that 70 percent or more of people are cared for at home. All of our constituents who are in a position to be at home need additional assistance. As we see how all this unfolds, we will learn better exactly how it can best serve the individuals who are in those situations. So we certainly always have high hopes for what would help to be a better care at home.

Because we know, as I mentioned a little bit earlier, that we do not have the capability to really accommodate all the folks who would ultimately perhaps need to go to long-term care. So additional ways to find ability to handle people at home is critical to the entirety of the Alzheimer's constituency.

Mr. HALL. Additionally, I think we all agree that the longer we can prolong institutionalization the better it is for the Federal budget, for sure. But families do need an enormous amount of support. The conversation we have had here around research is pivotal. There is no doubt we need to find a cure as quickly as possible, and any amount of money that we can put towards this disease would be an enormous win at this point. But the reality is that a cure does not seem to be coming anytime soon, and so it does rely on care, and it does rely on those families. So any type of provision that supports individuals with the disease and cares for them and provides for them the greatest quality of life for the longest period of time is great.

But also, too, we are recognizing the support that is truly needed for caregivers across the country at this point, at this juncture where we are in relationship to a cure is really the critical step. It is what we need to do.

Mr. ENGEL. Thank you. Thank you, Mr. Chairman.

Mr. GINGREY. Mr. Chairman, just very quickly—and I know the afternoon is getting long, and I appreciate our witnesses who have done a wonderful job. I guess I would direct this to Mr. Hall. Can you talk about the benefits of early detection as it relates to both the financial realities that patients face and for making end-of-life decisions?

Mr. HALL. Sure. The Alzheimer's Foundation of America hosts and is the initiator of National Memory Screening Day, and the reason that we do that is really just to sort of educate the public as a whole and then to allow individuals to participate in memory screenings across the country. That isn't a diagnosis for Alzheimer's, but rather is looking to see if there is an indication of I guess the most common manifestation of Alzheimer's disease, which is memory problems. That initiative to us is really important because of the fact that it points to a possible early diagnosis of this disease. It is really critical because our experience at the Alzheimer's Foundation of America is that our phone calls, our e-mails in the volume that we receive, every single one of those families is in crisis and chaos. So they are really scrambling now to figure out what does Alzheimer's disease care look like? What am I now responsible for as a family? What is required of me legally, financially? What is required of my time?

Early diagnosis in our interpretation is really important because, one, I think some of the treatments that are available right now are able to offset the progression of the symptoms of the disease and therefore the person enjoys—the person with the disease enjoys a higher quality of life for a longer period of time.

And I have to tell you, traveling the country—and I am sure Harry could say the same thing—We have not met one single family anywhere that hasn't said that all they wanted was one more good day with their loved one who is in the grips of Alzheimer's disease. If we can prolong one more day, I think that is a win. That is what we have right now.

But, additionally, planning in this situation is enormous, educating, empowering the family unit so that they understand. It is generally one in four individuals caring for every person with Alzheimer's disease. But also then enabling organizations to surround those families, to hold their hands, to walk with them on the journey and support them, to connect those families at the point of diagnosis with those necessary resources, instilling hope, which is probably the greatest missing link in Alzheimer's disease.

At least by surrounding a family with hope you are doing just that. You are giving them a lifeline, and you are letting them know that they are not going to be alone in the process. That takes care of an enormous emotional toil for a family, which is probably the biggest piece of the picture.

And then if you are able to bring in other resources of financial planning and legal planning and what all this looks like as far as

care in the future, those are enormous wins in alleviating the burden, the stress, depression for caregivers.

Mr. GINGREY. Thank you.

Mr. PALLONE. Thank you. That concludes our questions, but I just want to thank you all of you. It is obvious from listening to the questions and your testimony how important this is both now and in the future. We do plan to move the one bill that passed the Senate on the House floor next week; and, of course, the larger bill will have to wait for another time. But this is—I just want to stress how important really and how we really plan to prioritize this. So thanks a lot.

Let me mention that you may get additional questions from the members to answer in writing. The members are supposed to submit those within the next 10 days or so, but you may get those and the clerk will notify you of that.

But, without objection, this meeting of the subcommittee is adjourned.

[Whereupon, at 3:21 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

**Statement of the Honorable Anna G. Eshoo
Energy and Commerce Committee, Health Subcommittee
Hearing on Alzheimer's Disease
December 9, 2010**

Thank you Mr. Chairman, for calling this hearing on the ongoing challenges of Alzheimer's Disease and the critical healthcare needs of an aging population.

Alzheimer's is a disease all of us know too well. Everyone's had a relative, a friend, a co-worker, or even an acquaintance who's been stricken with this frustrating and painful disease. An Alzheimer's diagnosis can be a long process and lacks a simple test, even as patients lose their memory and ability to connect with others. The causes of Alzheimer's are not well understood and treatments are limited. The annual cost of care in our country for Alzheimer's patients will reach \$172 billion this year.

That's why I'm proud to be a cosponsor of Mr. Markey's *Alzheimer's Breakthrough Act*, which focuses attention and research at the NIH and CDC on early detection, diagnosis and prevention of Alzheimer's and its potential precursors. It will also help us take a close look at interventions designed to help caregivers and improve patient outcomes.

Alzheimer's is not a "Democratic Disease" or a "Republican Disease". It's a disease that can affect anyone, from any walk of life. With the cost of caring for Alzheimer's patients expected to rise to \$1 trillion in 2050, I think we can all see that continuing to fund Alzheimer's research makes common sense *and* fiscal sense.

Thank you again, Mr. Chairman, for holding this hearing, and I look forward to hearing from our witnesses.

The Honorable Joe Barton
Alzheimer's Disease: The Ongoing Challenges
Subcommittee on Health
December 9, 2010

Thank you, Mr. Chairman, for holding this hearing today.

Alzheimer's is a tragic disease affecting millions of Americans and their families and friends. We all must face the reality of death, but Alzheimer's disease forces families and friends to watch as loved ones, once independent and vivacious, suffer personality changes, loss of independence, and severe memory loss, such that they view those close to them as strangers.

As difficult as it must be to watch a loved one struggle with this disease, those afflicted with Alzheimer's face an inevitable

and irreversible process in which they lose many of those things that define them as the person they have become.

While Alzheimer's can affect people as young as in their 30s, most patients are over 60 years old. As this population will double over the next 25 years to around 72 million, the number of people with Alzheimer's will also increase dramatically.

As with other diseases, which also affect large numbers of people and cause profound suffering for patients, families, and friends, we want to do whatever we can to eliminate them or mitigate their impact on people's lives. When Congress reauthorized the NIH in 2006, Congress decided to put the question of which diseases to fund in to the hands of the experts.

While it makes the most sense to let experts determine the best use of scarce resource for research, Congress still has an important role to play in fighting Alzheimer's and other diseases. Specifically, identifying laws and regulations that can be eliminated or streamlined to ensure new research findings are used to develop new treatments and diagnostic tests quickly and safely.

Over the past 2 years, about 10% of the funds for Alzheimer's research came from the 2009 stimulus bill. The stimulus was designed to be spent within 2 years. I hope Dr. Morrison-Bogorad's testimony can also describe not only the type of research funded by the stimulus, but what the long term implications of that research could be for Alzheimer's disease.

I would also be interested to hear about the opportunity costs of the stimulus grants for Alzheimer's disease. Would we have been better served investing those resources in traditional NIH grants rather than the 2 years grants funded by the stimulus?

Thank you Mr. Chairman and I yield back.

Rep. Joseph R. Pitts
Opening Statement
Energy and Commerce Committee Subcommittee on Health
Hearing – “Alzheimer’s Disease: The Ongoing Challenges”
December 9, 2010

- Thank you, Mr. Chairman.
- While estimates vary, as many as 5.3 million Americans may have Alzheimer’s disease.
- According to Alzheimer’s Association estimates from a few years ago, nearly 500,000 people in my home state of Pennsylvania are currently living with Alzheimer’s disease and related dementias.
- And, an additional 24,000 Pennsylvanians have early onset Alzheimer’s.
- Alzheimer’s disease is one of the top ten leading causes of death in the United States. Among American adults, it is the 7th leading cause of death.
- It is the 5th leading cause of death among American adults aged 65 and older.
- It is degenerative and irreversible. And there is no cure.
- The FDA has approved a handful of medications to treat Alzheimer’s, but none of them stops the disease itself. Instead, they help delay or prevent symptoms from becoming worse for a limited amount of time.
- This time period, however short, allows those with Alzheimer’s to live with dignity and independence for as long as possible.
- Millions of Americans, including friends, family members, and health care professionals, serve as devoted caregivers to those suffering from Alzheimer’s, often at great personal cost to themselves.
- And their efforts should be recognized.

- I am proud to be a cosponsor of Mr. Markey's bill, H.R. 4689, the National Alzheimer's Project Act, which seeks to coordinate the federal government's efforts to study, treat, and prevent this disease.
- I look forward to the testimony of our witnesses and their opinions on this bill and others that have been introduced in the 111th Congress.
- Thank you, and I yield back my time.

Congressman Marsha Blackburn
Opening Statement for Energy and Commerce
Health Subcommittee Hearing
“Alzheimer’s Disease: The Ongoing Challenges”
December 9, 2010

I would like to thank the Chairman for holding this hearing today and welcome our witnesses.

Alzheimer’s disease is a devastating illness that affects millions and is of grave concern as the nation’s population ages and lives longer. This is an issue particularly important to me because Tennessee is home to nearly 850,000 residents over the age of 65.

I have personally stood behind the organizations and researchers who are striving to make changes to the treatment and barriers-to-care for those affected. In 2007, I worked with my Committee colleagues – Mr. Engel and Mr. Hall, as well as Ms. Giffords - to establish the Critical Path Public/Private Partnerships

at FDA to improve the process for developing safe medical products, accelerate innovation, and enhance safety. Since the successful passage of this amendment to the FDA Amendments Act of 2007, such partnerships have successfully facilitated collaborations between the FDA and scientists to enhance the safe development of treatments for Alzheimer's disease.

With the increasing number of people living with Alzheimer's, research must delve further into the causes of this disease; a better understanding of the disease will result in improved treatments and outcomes. I commend the work of the Critical Path Initiative and the National Institute of Aging (NIA), within the National Institute for Health, which have the potential to garner the greatest researchers and scientists to do just that.

Support for both the Initiative and NIA are critical to curtailing the continued progression of Alzheimer's, which is quickly becoming one of the costliest and most devastating chronic

conditions of the baby boomer generation. Currently, 5.1 million Americans live with Alzheimer's. The incidence of the disease continues to rise, and I am sure everyone in this room knows someone affected. It is time to solve this problem before the projected 13.5 million potentially-afflicted becomes a reality.

I look forward to hearing testimony from today's witnesses.
Thank you Mr. Chairman and I yield back the balance of my time.

Evidence for Neurocognitive Plasticity in At-Risk Older Adults: The Experience Corps Program

Michelle C. Carlson,¹ Kirk I. Erickson,² Arthur F. Kramer,³ Michelle W. Voss,³ Natalie Bolea,¹ Michelle Mielke,⁴ Sylvia McGill,⁵ George W. Rebok,¹ Teresa Seeman,⁶ and Linda P. Fried⁷

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Objective. To determine whether Experience Corps (EC), a social service program, would improve age-vulnerable executive functions and increase activity in brain regions in a high-risk group through increased cognitive and physical activity.

Methods. Eight community-dwelling, older female volunteers and nine matched wait-list controls were recruited to serve in the ongoing EC Baltimore program in three elementary schools. We employed functional magnetic resonance imaging (fMRI) preintervention and postintervention to examine whether EC volunteers improved executive function and showed increased activity in the prefrontal cortex relative to controls. fMRI volunteers were trained and placed with other volunteers 15 h/wk for 6 months during the academic year to assist teachers in kindergarten through third grade to promote children's literacy and academic achievement.

Results. Participants were African American and had low education, low income, and low Mini-Mental State Examination scores ($M = 24$), indicative of elevated risk for cognitive impairment. Volunteers exhibited intervention-specific increases in brain activity in the left prefrontal cortex and anterior cingulate cortex over the 6-month interval relative to matched controls. Neural gains were matched by behavioral improvements in executive inhibitory ability.

Conclusions. Using fMRI, we demonstrated intervention-specific short-term gains in executive function and in the activity of prefrontal cortical regions in older adults at elevated risk for cognitive impairment. These pilot results provide proof of concept for use-dependent brain plasticity in later life, and, that interventions designed to promote health and function through everyday activity may enhance plasticity in key regions that support executive function.

Key Words: Prefrontal cortex—Executive function—fMRI—Aging—Social engagement.

THE prevalence of one of the most costly and irreversible conditions, Alzheimer's disease (AD), is expected to rise fourfold, to 8.6 million, over the next 50 years (1). In order to be responsive to this potential health crisis, *Healthy People 2010* has emphasized efforts to increase the quality and years of healthy life and eliminate health disparities that magnify with age, particularly among those with low education and low income. Such efforts may include the design of activity programs that improve the health and well-being of our aging population and thus prevent or halt age-vulnerable cognitive and neurological declines.

Epidemiological observational studies have suggested that leisure-time cognitive, physical, and social activities help maintain cognitive and functional health (for reviews, see (2,3)). Executive planning and organizational skills appear to be important to maintaining functional independence (4–7) and appear to be particularly vulnerable to declines at later ages (8–10) along with the prefrontal cortical regions of the brain that support them (11–14). These findings suggest that executive functions may contribute to both

memory and functional difficulties and serve as an important target for preventive interventions.

To date, little is known about the efficacy of community-based cognitive and physical exercise programs to improve a range of cognitive abilities (3). Engaging in complex work and leisure environments has been associated with improved mental flexibility over the long term, particularly among older adults (15). Complex environments impose cognitive challenges through the diversity of stimuli and the number of decisions required. As a result, they exercise organizational, inhibitory, and working memory skills, all components of executive function.

We now describe a new model designed to enhance physical, social, and cognitive activity simultaneously, and how cognitive activity, broadly, and exercise of executive function, in particular, were intentionally embedded within the design of program roles. The Experience Corps (EC) program was designed (16) to train and place volunteers in participating elementary schools for an academic year during which time they assisted teachers in grades kindergarten–third

Table 1. Baseline Demographic and Cognitive Characteristics of Women Participating in the fMRI Pilot Study, Stratified by Intervention and Control Groups

Characteristic	EC, Mean	Control, Mean
N	8	9
Age, in y (SD)	68 (5.0)	67.78 (3.7)
African American, n (%)	8 (100)	9 (100)
Education, in y (SD)	12.4 (1.3)	11.6 (2.5)
Widowed, n (%)	5 (62)	1 (11.1)
MMSE (SD)	24.5 (3.6)	26.4 (1.7)

Note: EC, Experience Corps; fMRI, functional magnetic resonance imaging; MMSE, Mini-Mental State Examination.

grade with literacy and library functions (17). A pilot randomized trial of this program in Baltimore demonstrated program-specific benefits in children's academic achievement (18) and in the physical (17) and cognitive health (8) of senior volunteers. Specifically, we found that those at greatest risk for executive deficits showed substantial and clinically meaningful improvements in these and other functions because of participating in EC. Our promising short-term findings among individuals at risk for cognitive impairment suggest that they have sufficient neurocognitive reserves or plasticity to benefit immediately and substantially from this type of high-impact activity intervention.

We next sought to find preliminary evidence of brain plasticity in age-vulnerable executive functions among these cognitively at-risk older adults through a functional magnetic resonance imaging (fMRI) pilot study of EC in eight volunteers and nine matched controls (see Table 1). We describe results of this pilot study of EC, a program that provides an ideal environment in which to test the potential for a multimodal activity intervention to influence cognitive and brain health. Additionally, practical goals were to determine whether the use of fMRI would be feasible in participants who do not typically comprise volunteer samples for intervention.

METHODS

Participants

All prospective volunteers attended information sessions to describe the EC program and participation requirements, if interested. Eligibility criteria included (a) being 60 years of age or older; (b) English speaking; (c) agreeing to commit to at least 1 year; (d) agreeing to participate at least 15 h/wk for the full school year; (e) meeting minimum criteria for cognitive functioning necessary to function successfully in a school setting via an education-sensitive, two-step process using the Mini-Mental State Examination (MMSE) (19) score = 24 or higher or if scoring 20–23, with a high school education or less, and successful completion of the Trail Making Test (TMT) (20) within the time allotted (420 seconds). The TMT served as a measure of mental flexibility, a

skill presumed key to adaptability in the schools; (f) minimum fifth grade level reading literacy; (g) clearance on the Baltimore city public school's criminal background check; and (h) completing a 2-week training to participate in EC. In addition, to participate in this fMRI pilot study, participants also had to (a) be free of a pacemaker or other ferrous metal objects in the body, (b) have no history of brain cancer or brain aneurysm or stroke in the prior year, and (c) be right-hand dominant to avoid possible confounds due to laterality in left-handed individuals. They were then scheduled for a separate 1-hour fMRI visit at the FM Kirby Center at Johns Hopkins. This study was approved by the Johns Hopkins IRB, and each participant gave informed, written consent. All participants received a \$50 honorarium for each fMRI visit.

Participants were African American, 80% of whom had a high school education and marginally normal global cognitive scores on the MMSE (average = 24.5). Half were trained and integrated with existing teams of experienced EC volunteers in two elementary schools, and half were wait-listed for enrollment the following academic year.

Intervention

This multimodal EC activity program is described in detail elsewhere (21). It was designed to bolster memory and executive functions by exercising working memory skills via reading comprehension activities with children, in literacy and library support, cooperative problem-solving skills with team members, students, and teachers, and through program activities that operated along multiple dimensions of cognitive ability and by exercising mental flexibility through the need to shift across EC roles.

All volunteers were trained on the following modules and provided with a corresponding tool book covering the following:

General Literacy Support: provides a literacy support guide to train adults who are reading with and to children. It aids adults in assessing children's current reading levels to guide level-appropriate book selection, build vocabulary and comprehension, and ask questions about the book.

Library Support: supports library functions, including shelving or cataloguing books, reopening and helping staff school libraries, helping children pick books they will enjoy, and reading to/with children, all under the guidance of a librarian.

Conflict Resolution, entitled "Partners in Play" (18): teaches children conflict resolution through play in a supervised recess program. Volunteers are trained in how to lead, set goals, and play a variety of both quiet group activity games and board games.

Outcome Measure: Flanker Task

This selective attention task measures one's ability to rapidly determine the direction of a central target (arrow)

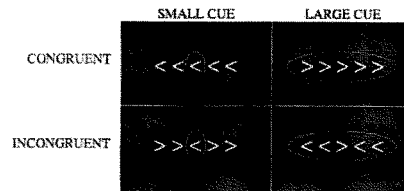


Figure 1. Flanker task conditions in which participants were instructed to respond to the direction of the center arrow. The magnitude of interference from flankers was manipulated by cue size (small and large).

while effectively inhibiting distracting information that flanks the target and may conflict with the target response (e.g., central target points left, whereas flanking arrows point right). Each trial consisted of visual presentation of a central target arrow flanked on either side by two arrows using a magnetic resonance imaging (MRI)-safe back projection system. If the center arrow pointed right, participants were instructed to press the button in their right hand; if the center arrow pointed left, participants were instructed to press the button in their left hand. Speed and accuracy were emphasized. Task difficulty was manipulated across trials by varying the direction of the flankers, which were either *incongruent* (<<<< and >>>>) or *congruent* (<<<< and >>>>) with the central arrow. In the congruent condition, flanking arrows reinforced the target response. In the incongruent condition, flankers conflicted with the target response. The magnitude of interference from flankers was manipulated by cue size on each trial (small and large), which was composed of a red circle that was either drawn only around the central target (small) or around both target and flankers (large; see Figure 1). The small cue helped focus attention on the target and minimize the impact of distracting flankers, whereas the large cue provided no information.

These task manipulations yielded four conditions (small circle incongruent, small circle congruent, large circle incongruent, and large circle congruent), which were each presented 40 times for a total of 160 trials in a rapid event-related paradigm. Each stimulus was displayed for 2 seconds on a black background in the middle of the screen. Baseline consisted of a 3-second presentation of a central fixation cross followed by a 40% interstimulus jitter optimized by optseq2 (<http://surfer.nmr.mgh.harvard.edu/optseq/>).

MRI Parameters and Preprocessing

All MRI data were collected on a 3.0T Phillips scanner (Best, the Netherlands). The functional MRI protocol employed a fast echo-planar imaging sequence with blood oxygenation level-dependent contrast acquiring 20 slices in sequence at a sampling rate of 1000 milliseconds. In addition, for each subject a high-resolution T1-weighted

anatomical image was also collected, stripped of all nonbrain tissue (22), and subsequently used for image registration.

The functional MRI data were preprocessed using FSL version 4.0 (23). Images were slice-time and motion corrected using a rigid-body algorithm (24), temporally filtered with a bandpass filter cutoff at 30 seconds and 1 second, and spatially smoothed with a 7-mm FWHM 3D Gaussian kernel.

Residual noise from excessive head motion was isolated and corrected using MELODIC, an independent components analysis used in FSL. Residual motion artifacts for each participant were signal filtered from her respective time course before the first-level analysis (25).

Data Analysis

A repeated measures analysis of variance (ANOVA) was run on all behavioral data (response times [RTs] and accuracy) with time (baseline, postintervention) and condition (congruent large cue, congruent small cue, incongruent large cue, and incongruent small cue) as within-subjects factors and group (control and treatment) as a between-subjects factor.

The neuroimaging data were convolved using a double-gamma function with temporal derivatives in an event-related analysis. Each condition was added separately to the general linear model. For each participant, a parameter estimate was calculated at each voxel across each of the four conditions. Contrasts of the flanker task conditions were calculated at this level and then forwarded to a higher-level, group-wise analysis in which a mixed-effects ANOVA was carried out. All registration matrices to a standard-space template (Montreal Neurological Institute) were calculated on the individual level and then subsequently applied to the parameter estimates and variance estimates before forwarding to group level analyses. These analyses were conducted separately at each time point. To minimize statistical constraints associated with conducting multiple comparisons, we defined regions of interest (ROIs) based on main effects of congruency (incongruent > congruent collapsed across cue size) at baseline: the anterior cingulate cortex (ACC) and left and right dorsal and ventral prefrontal cortex (dPFC and vPFC, respectively). These ROIs were similar to activated regions found in previous studies of the flanker task (26). The main aim of this study was to examine the effects of the EC intervention; therefore, we used these regions to analyze the follow-up session so that our exploration of the data was restricted to well-defined and theoretically important regions. Data were extracted from these regions and analyzed via a repeated measures analysis in SPSS version 14.0 for Mac (Chicago, IL) to assess effects and interactions of group, time, and condition. We first assessed whether the intervention group exhibited a greater change in activation than the controls over the 6-month interval (Time \times Group interaction). Second, we determined whether such intervention-specific change in activity would

be selective to the most difficult flanker condition (incongruent) compared with the easier congruent conditions (Time \times Group \times Condition interaction).

Analysis of the neuroimaging data was carried out using FEAT (fMRI Expert Analysis Tool) version 5.1 part of FSL. Group level analyses were carried out using FLAME. All Z -statistic images were thresholded using clusters determined by $Z > 3.1$ and a corrected cluster significance threshold of $p = .01$.

RESULTS

As shown in Table 1, both groups were matched on all sociodemographic variables. Participants were African American, with low income, low education levels, and an average MMSE score of 25, a score lower than typically observed in volunteer samples. Only one participant, in the intervention group, dropped out prior to follow-up due to personal health reasons. No adverse events were reported in the intervention or control arms, and the fMRI protocol was well tolerated at baseline and follow-up.

Response Data

The control group and intervention group did not reliably differ for any condition at the baseline assessment (all $p > .05$). Furthermore, at baseline, RTs were slower for the incongruent condition compared with the congruent condition ($F(1,15) = 21.27$; $p < .001$) and for large cues compared with small cues ($F(1,15) = 25.33$; $p < .001$), as expected. At baseline, both groups showed improved performance on the incongruent condition when a small cue was available but showed no similar benefit of cue size on the congruent condition ($F(1,15) = 19.52$; $p < .001$).

In pre-post comparisons, RTs were analyzed using repeated measures ANOVAs with intervention status as a between-subjects factor, time (baseline, postintervention) as a within-subjects factor, and cue size (small circle and large circle) as a within-subjects factor. Percent interference ($((\text{incongruent RT} - \text{congruent RT}) / \text{congruent RT}) \times 100$) was calculated to adjust for general slowing effects related to aging (denominator) and served as the primary dependent variable. We observed a significant Time \times Group interaction ($F(1,13) = 5.28$; $p < .04$) in interference scores such that the intervention group showed a greater reduction in interference over the 6-month interval compared with matched controls (see Figure 2). The percent reduction in interference was equivalent across large and small cue sizes. Similarly, the Time \times Group \times Cue-size interaction was not significant ($F(1,13) = 1.80$; $p < .20$).

Accuracy rates did not reliably differ between the control and the intervention groups at baseline (all $p > .05$). At baseline, accuracy was worse for the incongruent condition compared with the congruent condition ($F(1,15) = 6.32$; $p < .02$) and marginally worse for large cues compared with small cues ($F(1,15) = 2.59$; $p < .06$). In addition, the small cue

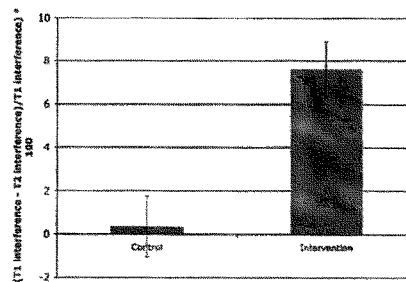


Figure 2. Change in percent interference from baseline to postintervention for both the intervention and the control groups collapsed across both small and large circle cues. *Group \times Time interaction significant at $p < .04$.

improved accuracy more for the incongruent condition than the congruent condition ($F(1,15) = 4.52$; $p < .05$). No other main effects or interactions were significant (all $p > .05$).

Repeated measures ANOVAs were also conducted to examine accuracy rates by intervention status and task difficulty (congruent vs incongruent). Time (baseline and postintervention) and cue size (small circle and large circle) were also within-subjects factors. Compared with RT measures, there was no significant Time \times Group interaction ($F(1,13) = 1.28$; $p < .28$). However, there was a significant Time \times Group \times Congruency interaction ($F(1,13) = 5.77$; $p < .03$). Post hoc comparisons revealed that this three-way interaction was due to a greater intervention-specific improvement in accuracy in the incongruent conditions ($p < .05$) that was independent of cue size ($F(1,13) = 2.160$; $p < .16$).

Neuroimaging

Results are first presented for baseline within- and between-group comparisons and then for intervention-related changes over time. Consistent with prior fMRI studies using the flanker task, we observed significant increases in activity in regions associated with the attentional network, including the left and right dorsal lateral prefrontal cortex, the ventral lateral prefrontal cortex, and the ACC (26). These regions showed elevated levels of activity for the incongruent condition compared with the congruent condition (collapsed across cue size) that met a voxel-wise threshold of $p < .01$ and a cluster-wise threshold of $p < .05$. Prior studies have extensively described these effects in relation to cognitive function, and age-related decline allowing this study to focus on how the EC intervention may impact on processing efficiency and plasticity in these regions. At baseline, both intervention and control groups showed comparable levels of activity across all three ROIs, the ACC, left ventral prefrontal cortex (vLPFC), and left dorsal prefrontal cortex (dLPFC). The effects of the intervention are highlighted subsequently.

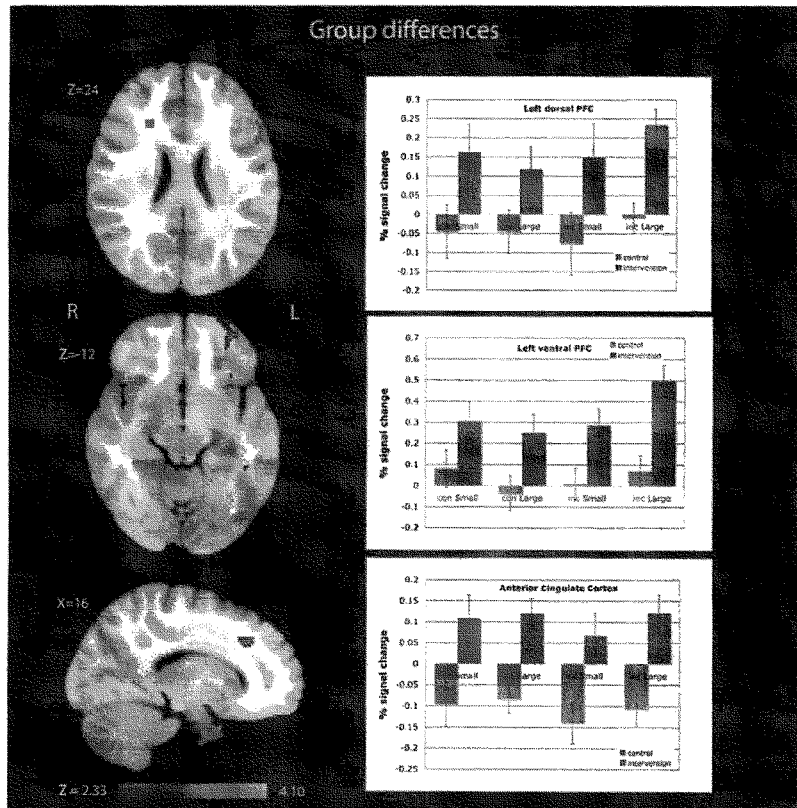


Figure 3. Images and plots showing differences in activity between the Experience Corps (EC) group and the control group for the left dorsolateral prefrontal cortex, the left ventrolateral prefrontal cortex, and the anterior cingulate cortex. These regions were not reliably different between the groups at baseline but showed significant increases in activity at postintervention for the EC group (Time \times Group, $p < .05$). PFC, prefrontal cortex.

In a repeated measures analysis of the ACC (cluster size = 1704 mm³), we observed a significant Time \times Group interaction ($F(1,13) = 13.22$; $p < .003$) that was due to a significant intervention-specific increase in activity over the 6-month follow-up (see Figure 3). There were no interactions with congruency or cue size, suggesting that intervention-specific gains in the ACC were independent of congruency condition or cue size or that there was insufficient power.

Similar analyses of the left dLPFC (cluster size = 2704 mm³) also revealed a significant Time \times Group interaction ($F(1,13) = 5.16$; $p < .04$) with the intervention group showing

a significant increase in activity over time (Figure 2). As with the ACC, there were no significant interactions with congruency or cue size. The left vLPFC (cluster size = 1576 cubic mm) showed a similar Time \times Group interaction ($F(1,13) = 8.99$; $p < .01$) with those in the intervention group showing a significant increase in activity at follow-up. Again, neither congruency nor cue size interacted with time or group, indicating that the intervention group showed increases in this region across all conditions (Figure 2).

No regions showed an intervention-related decrease in activity. The right prefrontal regions, although active at

baseline for both groups, did not show significant changes in activation that met threshold. However, there was a non-significant increase in the right dorsal prefrontal activity for the incongruent condition for both the intervention and the control groups ($p < .16$).

Pre-post comparisons of each group's ability to filter conflicting distracters (incongruent RT-congruent RT) for small and large cues are presented in Figure 3 and show EC-intervention-specific improvements in the ability to selectively attend during the most attention demanding task conditions (incongruent). Corresponding fMRI group comparisons similarly showed increased activity in attentional control regions of the PFC (middle and inferior frontal regions bilaterally) and the parietal regions, suggesting more efficient filtering or inhibiting of target information from distraction (Figure 3).

DISCUSSION

This pilot study provides proof of concept for the feasibility and utility of neuroimaging to begin to understand how a multimodal activity program in the community gets *under the skin* to improve executive functions and supporting brain regions. These at-risk individuals exhibited measurable brain plasticity in direct response to such environmental enrichment, providing initial evidence of this program's potential to reverse cognitive and corresponding neural declines with age. Individuals exhibited use-dependent neural plasticity by exercising and reactivating skills that may have been relatively unused for years or even decades. This finding is best captured by a personal observation from one of the volunteers, who stated that "it [Experience Corps] removed the cobwebs from my brain." Additionally, these previously sedentary at-risk participants were amenable to the fMRI environment on repeated exams, as demonstrated by 100% retention, and those enrolled in the program met the intensive service requirements, which led to unprecedented doses over a relatively short-exposure period.

The results replicate and build on the previous pilot trial of EC and cognition, and on an fMRI trial of physical activity in older adults. First, we replicated the impact of EC on executive functions using a sensitive measure that focuses on the age-vulnerable ability to inhibit distraction in one's environment. Indeed, the present finding suggests generalization of EC improvements over different measures of executive function. These improvements extended to corresponding increases in the activity of supporting prefrontal cortical substrates, further replicate seminal findings on the neurocognitive benefit of physical activity (26–28). The patterns of increased functional activity here differed slightly from the exercise findings in two ways. First, we observed EC-related increases in the ACC during the executive function task, whereas the exercise intervention led to decreased activation in this region. The ACC has been implicated in the efficient filtering or inhibiting of conflicting information

prior to generation of a motor response. Although both studies demonstrated improved inhibitory efficiency (speed), EC participants started with lower baseline inhibitory ability than those in the exercise intervention. Thus, as in a prior pilot trial of EC (21), these individuals were at elevated risk for executive dysfunction and likely exerted more effort to successfully develop inhibitory skills, which may be reflected by increased ACC activity. Second, we observed the lateralized increases in left prefrontal cortical activity in the EC sample while the exercise intervention observed the right prefrontal cortical increases. These laterality differences may be due to the nature of EC volunteer activities, which rely heavily on verbal communication and mediation strategies, and may thus elicit greater improvements in regions associated with communication, such as the left prefrontal and temporo-medial cortices. These hypotheses require replication in a larger sample.

Although the functional significance of the laterality differences is unclear, greater unilateral activation of cortical regions following the EC intervention contributes to discussions in the functional neuroimaging literature (11,29) on the nature of brain plasticity, reserve, and compensatory function. We have yet to determine whether these changes were accompanied by structural changes and changes in supporting white matter tracts that facilitate rapid and efficient communication across regions.

The implications of these findings to the assessment of postretirement lifestyle activity are that a broader range of cognitive activities embedded within social settings may confer great cognitive and brain benefits for older adults. Recent epidemiological evidence in twin pairs suggests that socially engaging cognitive activities in midlife and early late-life may reduce risk for AD and dementia decades later (30) and may be indicative of an enriched environment, which enhances the proliferation of new brain cells and promotes brain repair in animal models (31–33). The implications of these findings to the assessment of postretirement lifestyle activity are that a broader range of cognitive activities may confer great cognitive benefits for older adults and may further confer neurocognitive protection.

Cognitive activity embedded within social settings may further increase task novelty, interactive problem-solving skills, and motivations to sustain these activities. In addition, these activities are generative in giving meaning and purpose to one's life (volunteering, civic organizations, assisting others), which may make them more rewarding and personally enriching than highly stimulating activities performed alone (34). As a result, individuals may place more value on these activities beyond their immediate personal benefit and may sustain interest longer (35). This important developmental need to be generative could provide an important vehicle for enhancing and sustaining behaviors important to successful aging, namely remaining active—socially, physically, and cognitively (34).

Limitations of this pilot study include the small sample size necessarily restricted to women (due to gender differences in brain morphology), which limits generalizability but provides proof of concept for the potential of well-validated parametric fMRI tasks, such as this, to sensitively detect program-related functional brain changes in a larger randomized study of men and women. Second, although the sample represented an important and often under-studied segment of the aging adult population, we have yet to determine whether this program enhances or maintains cognition among more ethnically and socioeconomically diverse individuals. Finally, this study design does not allow us to definitively discern whether the effects of this intervention on cognition function were mediated primarily by cognitive and physical pathways, respectively, or whether benefits represent the synergy of increased activity in all domains. Understanding the mediating source may not be as critical as the observation that a multiple pathway approach set in the community was associated with high doses, good retention, and short-term effects spanning many abilities in the most at risk.

These findings offer next-level questions about the ability of this program, and others like it, to reset one's trajectory of cognitive decline with age, particularly among those at elevated risk for dementia by virtue of impoverished environments over the life course, as marked by low or poor quality (36) education and low income. These individuals require further follow-up in order to determine the potential and boundaries of plasticity in a dose-dependent manner. Questions include whether a lower weekly exposure may confer equivalent benefits and whether continued exposure would lead to accruing benefits, perhaps in other brain regions interacting with these prefrontal circuits, such as parahippocampal and hippocampal regions that support some memory functions. Furthermore, it will be key to determine whether short-term benefits will be sustained after program exposure is discontinued. Overall, these pilot findings hold promise for enhancing functional reserve and neural plasticity among those at great risk.

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**Preliminary Research Shows Promise of Behavioral Interventions in
Improving Cognitive Ability for Older Americans**

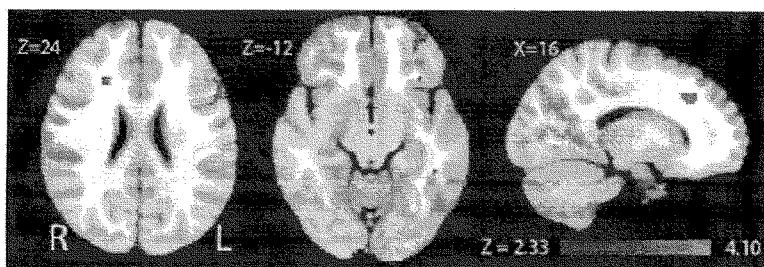
**United States House of Representatives
Committee on Energy and Commerce
Subcommittee on Health
December 9, 2010**

In a study published in the December 2009 issue of the *Journal of Gerontology: Medical Sciences*, volunteer activity in the Baltimore Experience Corps program—a program in which older Americans tutor young children in reading—was found to improve cognitive and brain functions in older women at risk for cognitive impairment. Researchers, led by Michelle C. Carlson, PhD., Associate Professor in the Johns Hopkins Bloomberg School of Public Health and Associate Director of the Johns Hopkins Center on Aging and Health, conducted this six-month case-control study in 17 older adults using brain functional magnetic resonance imaging (fMRI).

The research provides evidence that behavioral interventions, like Experience Corps, designed to promote health and function through volunteer activity may improve the brain's plasticity, or the ability to bounce back, in key regions that support executive function – cognitive abilities associated with planning and organizing one's daily life. These are the same areas critical to maintaining independent function in older age, and areas that are significantly affected by aging related diseases including Alzheimer's disease.

The Experience Corps fMRI pilot study enrolled 17 women aged 65 and older, half of whom were trained and integrated within existing Experience Corps programs in local Baltimore City schools from January-June, and half of whom were evaluated and wait-listed to enroll in the Experience Corps the following academic year. Participants underwent brain scans at baseline and six-months later. The fMRI analyses revealed that Experience Corps volunteers showed a 54% improvement in executive function beyond baseline compared to the control subjects. This is a huge effect by any intervention standard.

"The results of this study hold promise for enhancing and maintaining brain reserve and health in later life," said Dr. Carlson, who is now leading a much larger, multi-year study to confirm these preliminary findings.



Brain areas associated with improved executive function among Experience Corps volunteers.

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