

**GLOBAL STRATEGIES TO COMBAT THE  
DEVASTATING HEALTH AND ECONOMIC IMPACTS  
OF ALZHEIMER'S DISEASE**

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**HEARING**  
BEFORE THE  
SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH,  
AND HUMAN RIGHTS  
OF THE  
COMMITTEE ON FOREIGN AFFAIRS  
HOUSE OF REPRESENTATIVES  
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# GLOBAL STRATEGIES TO COMBAT THE DEVASTATING HEALTH AND ECONOMIC IMPACTS OF ALZHEIMER'S DISEASE

THURSDAY, JUNE 23, 2011

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

The subcommittee met, pursuant to notice, at 2:10 p.m., in room 2200, Rayburn House Office Building, Hon. Christopher H. Smith (chairman of the subcommittee) presiding.

Mr. SMITH. The subcommittee will come to order. I want to apologize for the lateness in starting. We are just completing a vote. But I do thank you all for being here and for joining us at this first ever congressional hearing examining the global strategies to combat the devastating health and economic impacts of Alzheimer's disease. This is the first in what will be a series of hearings. And hopefully over the course of the next 1½ years, this will be an opportunity to really refocus congressional efforts on the fact that this is not just a domestic problem, but also an international one that needs additional congressional engagement.

Alzheimer's disease is the most common form of dementia, and it is a degenerative, irreversible, and terminal disease. Alzheimer's disease is most prevalent in people over 65 years of age, but early-onset Alzheimer's can occur at a much younger age, as we all know, even decades earlier. Alzheimer's progressively destroys remembering, thinking and reasoning skills, and eventually even the ability to carry out the simplest of tasks.

While the cause and progression of Alzheimer's disease are not well understood, research indicates that the disease is associated with plaques and tangles in the brain that begin to develop 10 to 20 years before any problems are evident. As plaques and tangles form, neurons lose their ability to function, and eventually die. As more neurons expire, affected brain regions begin to contract. In the final stages of Alzheimer's, there is widespread damage and tissue shortage.

Current treatments provide modest symptomatic benefits, but there are no therapies available that can halt or even delay the progress of the disease. The effects and duration of the disease vary from patient to patient, but it is invariably fatal.

According to the Alzheimer's Disease International there were some 35.6 million people living with Alzheimer's and other demen-

tias in 2010, and the number of people living with dementia is expected to nearly double every 20 years to 65.7 million in 2030, to 115.4 million in 2050. However, the increase is greater for low and middle income countries, as some 57 percent of all people with dementia are currently living in low and middle income countries. And that will rise to 63.4 percent in 2030, and a whopping 70 percent in 2050.

Here in the United States, up to 5.4 million people have Alzheimer's disease, and the number is expected to increase to up to 16 million by 2050 unless something is done to reverse the trajectory. The elderly population as a whole is growing, but the oldest elderly are the fastest growing age bracket.

According to Alzheimer's Disease International, the total worldwide estimated cost of dementia is \$604 billion, with 89 percent of the costs occurring in high income countries and about 70 percent of those costs occurring in just two regions, Western Europe and North America. In low and middle income countries, the costs of informal care, in other words unpaid care provided by families and others, accounts for some 64 percent of all care, while in high income countries the informal care accounts for 40 percent of the costs.

Even in countries that have high health care expenditures and that provide government-funded support for long-term care, a vast amount of that care occurs informally within families. Not only will the increase in the population with Alzheimer's and other dementias result in skyrocketing costs of health care, but changing family dynamics will further exacerbate the economic stress on families, societies, and governments.

As an example, on Monday of this week I chaired a hearing of the Commission on Security and Cooperation in Europe, also known as the U.S. Helsinki Commission, on the implications of demographic trends in the OSCE region, and we looked at some other parts of the world as well. Dr. Richard Jackson, Director of Global Aging Initiative at the Center for Strategic and International Studies, testified in that hearing that in certain European countries by 2020 the extended family will essentially be nonexistent. Half of young adults don't have any brothers or sisters or uncles or aunts or cousins. Another projection during the same hearing was that Japan could potentially experience an explosion of Alzheimer's prevalence of up to 1 in 25 as a result of the aging of the population, coupled with some 40 percent of the Japanese being childless. So the number of caregivers available will rapidly decline in Japan and elsewhere.

When we look more closely at projected demographics for some countries, the pool of family caregivers is shrinking as the number of individuals with Alzheimer's is correspondingly exploding, which will significantly shift the costs of care away from unpaid, informal care to institutional and direct medical care.

Poor recognition, under-diagnosis, and lack of public awareness are all causes of significant problems for afflicted individuals and their caregivers, especially in low and middle income countries.

In those developing countries, it is often incorrectly assumed that dementia, such as Alzheimer's, is a normal part of aging and that nothing can be done to address it. Because of lack of recognition

of the nature of the problem, there is a lack of pressure on government bodies to respond to the crisis. As a result, there is a lack of effort to devote resources toward finding a cure to help those with Alzheimer's by providing assistance or seeking a diagnosis and caring for those potentially afflicted.

International cooperation and collaboration to find solutions for Alzheimer's is not new, as clearly demonstrated by the fact that the Alzheimer's Disease International began in 1984, 27 years ago, with four members, and has grown now through the years to over 75 members. Similarly, I look forward to receiving testimony outlining past, present, and future international research collaborations.

However, we do seem to be at a precipice now of making great strides on several different fronts. First, there is the greater recognition, including in low and middle income countries, of the need to address Alzheimer's as a major public health crisis. I agree with you, those who will testify, that we need to pressure international institutions responsible for health issues to recognize dementia as a global health problem. That is why Congressman Markey and I, and we do cochair the Alzheimer's Caucus here in the House, and we have done so for over a decade, we have coordinated a letter signed by 28 Members of Congress to the U.N. General Assembly President Deiss to include Alzheimer's disease in the September U.N. Summit on Noncommunicable Diseases. Involvement of international organizations such as the United Nations and WHO are necessary to make substantial inroads toward raising awareness of dementia and beginning to address it in national health care policies and action plans. I plan on sending today's hearing record to all relevant U.N. officials, PAHO officials, and officials in the EU, and especially to heads of country delegations at the United Nations.

Second, there is a significant momentum toward broader sharing and an increasing number of proposals for major intergovernmental research projects that will take advantage of emerging research opportunities and new computing platforms and communications technologies. Also, in response to two of our witnesses, Eric Hall and George Vradenburg, who made recommendations in their testimony for a government-sponsored international conference, I will soon introduce legislation to convene in the first quarter of calendar year 2012, or at a date thought to be more appropriate, an international conference to include at a minimum countries that have or are in the process of developing national Alzheimer's plans.

Third, it is significant that the NIH funded the first intensive caregiver support intervention proven to be effective, through rigorous testing, in an ethnically diverse population, and that they are beginning to export the program. I do look forward to Dr. Hodes' testimony on this and other outstanding initiatives that he is leading at the NIA.

Finally, since 2005, several countries have developed national Alzheimer's plans or strategies, which have already begun to accelerate changes in health care systems. I was honored to have introduced with Congressman Markey legislation to create a national strategic Alzheimer's plan for the United States. The National Alzheimer's Project Act, or S. 3036, which was passed first by the Sen-

ate and then by the House and signed in December by the President—or in January I should say, January 4th; it was a large, huge legislative victory for the cause of Alzheimer's here in the United States. The National Alzheimer's Project Act, NAPA, is designed to help turn the tide by creating a national strategic plan to address the rapidly growing crisis of Alzheimer's disease. NAPA provides for the coordination of all Alzheimer's disease efforts across the Federal Government. It also establishes an advisory council on Alzheimer's research, care, and services that would allow participation by patient advocates, health care providers, researchers, and State health departments in the evaluation of Federal Alzheimer's plans and the formulation of a strategic plan to reduce costs and improve health services. Recognizing the importance of international collaboration, the law requires coordination with international bodies to make the United States Government a committed partner in the global fight against Alzheimer's.

Like many of you, I will be following closely the implementation of NAPA. And if Dr. Hodes would like to share any information on HHS activities on implementing NAPA, we would certainly appreciate any insights he could provide.

While the national Alzheimer's strategic plan is being developed, Congressman Markey and I have also introduced additional legislation designed to bolster programs for Alzheimer's research and diagnosis.

In May, we introduced the Alzheimer's Breakthrough Act, H.R. 1897, designed to accelerate treatments that prevent, cure, hopefully, or slow the progression of Alzheimer's disease and reduce the financial burden of Alzheimer's on federally funded programs and families. The Director of NIH will develop a strategic research plan, including budget estimates, for Alzheimer's disease, focused on targeting scientific opportunities and priorities, developing public-private partnerships, and improving coordination of Alzheimer's disease research across 27 institutes and centers at the NIH.

Instead of prescribing a funding level for Alzheimer's research at NIH, as we attempted to do in previous bills, which sadly did not pass, this bill requires the experts at NIH to tell Congress and the administration what Alzheimer's research is needed to develop treatment breakthroughs and what level of funding is needed to accomplish that goal.

In addition, I have joined Congressman Markey in introducing H.R. 1386, the Health Outcomes, Planning and Education for Alzheimer's Act, or HOPE, which will provide Medicare coverage for a comprehensive diagnosis of Alzheimer's disease and help improve care and reduce costs by providing information and resources to newly diagnosed patients and their families.

I am very pleased to now yield to my good friend and colleague Mr. Payne, fellow New Jerseyan, for any comments he might have.

Mr. PAYNE. Thank you very much. And let me commend my colleague, Chairman Smith, for calling this very important hearing: Global Strategies to Combat the Devastating Health and Economic Impact of Alzheimer's Disease. You, Mr. Chairman, along with Congressman Markey, Congresswoman Waters, and others, have been important drivers on this issue of Alzheimer's and other forms of dementia.



I would also like to thank our witnesses. I look forward to hearing each of you and your testimonies on how Congress can best tackle Alzheimer's globally, specifically in Africa and developing nations that lack infrastructure to provide basic needs or are engaged in conflicts that displace large portions of their population and whose health care centers are overwhelmed with those suffering from HIV/AIDS, malaria, tuberculosis, and neglected tropical diseases.

Alzheimer's disease, or AD, is the most common form of dementia. Symptoms include difficulty with speech, memory loss, depression or anxiety, and a decrease in mental ability. The disease often begins to show signs after the age of 65, and its likelihood of onset and severity increases as one ages. There is no cure, and symptoms are irreversible.

According to Alzheimer's Disease International's 2009 World Alzheimer's Report in 2010, there were an estimated 35.6 million people suffering from dementia. This same report cites that 58 percent of these people lived in low and middle income countries. It is projected that in 2050 the total number of those with dementia will be close to 110 million, with 71 percent in those low and middle income countries.

This growth, however, is likely to be less dramatic in sub-Saharan Africa, where life expectancy is below that of the usual age of onset. There may be additional reasons for a lower prevalence of dementia in developing countries outside of lower life expectancy. Part of this may simply be diagnosis. There is no set approach or test to diagnose Alzheimer's, as we all know, nor can the disease be labeled conclusively until postmortem. Given that mild dementia can be subtle and a strain on health care centers in these countries due to diseases such as HIV and others, as I mentioned, it is often severe. It is reasonable to assume that in many of these countries this is being overlooked, and therefore, as we would know, under-reported.

I am interested to hear the panel's thoughts on these issues, as well as the potential causes of Alzheimer's. It is thought by many that genetics play a role. However, environmental factors may also contribute. In New Jersey, we have had a tremendous increase in Alzheimer's, in a State that has had environmental problems throughout the years, and we feel that that may be one of the possible causes. However, there is no conclusive evidence to that fact. These include high blood pressure, cholesterol, illiteracy, lower education levels, and stress.

I am also interested in learning how these factors are being taken into consideration when both diagnosing and treating Alzheimer's. Additionally, I would like to know how these factors are taken into account when looking at Alzheimer's from a global perspective.

Though a cure does not yet exist, both drugs and nondrug treatments are available for sufferers here in the United States and other developed countries. I hope to learn from our witnesses today about the best practices in combating Alzheimer's and how these practices can be applied to developing nations.

I also hope to hear how those with Alzheimer's and other forms of dementia are being treated in conflict zones. Disabled people are

often faced with increased challenges when displaced due to violence, and I am interested in learning about specific challenges Alzheimer's sufferers face in these crisis situations.

Again, I look forward to the testimony of our witnesses, and I yield back the remainder of my time.

Mr. SMITH. Thank you, Don. I would like to now yield to a good friend and colleague, Ed Markey, who is the cochair of the Alzheimer's Caucus, and has been a true leader in that issue for a long, long time.

Mr. MARKEY. Thank you, Mr. Chairman, very much. You and I created the Alzheimer's Task Force 13 years ago, and I think we are really making progress on the issue. But at the same time, 5.4 million Americans now have Alzheimer's, 15 million baby boomers will have Alzheimer's. If we don't find a cure for Alzheimer's, that one disease will equal and exceed the entire defense budget of the United States in Medicare and Medicaid payments for those families. Last year it was \$132 billion in Medicare and Medicaid that went just to Alzheimer's.

So the numbers are absolutely staggering. Within a generation, there will be more people over the age of 60 than under the age of 15. So, you know, we are in a race against time here in terms of our ability—that is across the whole planet. And so this isn't just a national, but an international issue because you can multiply the consequences, you know, for America across the whole rest of the population of the world, and it is imperative for us to have action plan that does work because failure is not an option here. We, like the Apollo astronauts coming back, we have to fabricate some way of finding the clues that will make it possible for us to make it possible for children to have to look to the history books to find that there ever was such a disease as Alzheimer's.

But it is something that I think has to be bipartisan. And your leadership and Congressman Payne's leadership helps to demonstrate that. And thank you for inviting me here today. Thank you, Doctor, for all of your incredible work on this issue.

Mr. SMITH. Mr. Markey, thank you very much for your leadership over all these years. In a place where bipartisanship seems to be diminished, there are some issues where that is simply not the case, and this is one of those. It has been great to work with you those 13 years on this issue, and may it continue.

Mr. MARKEY. Thank you.

Mr. SMITH. I would like to now introduce our first very distinguished witness, Dr. Richard Hodes, who has been director of the research program at the National Institute on Aging at the National Institutes of Health since 1993. Dr. Hodes has devoted his tenure to the development of a strong, diverse, and balanced research program. He focuses on the genetics and biology of aging, basic and clinical studies aimed at reducing disease and disability, including Alzheimer's disease, and investigation on the behavioral and social aspects of aging. He is the author of many research papers, and is an active scientist in and contributor to the field of immunology. His full, very, very impressive resume will be made a part of the record. I would like to ask Dr. Hodes to proceed as he would like.

**STATEMENT OF RICHARD HODES, M.D., DIRECTOR, NATIONAL  
INSTITUTE ON AGING, NATIONAL INSTITUTES OF HEALTH**

Dr. HODES. Thank you, Congressman Smith, Congressman Payne, Congressman Markey, for the opportunity to be here and talk with you about international aspects of Alzheimer's disease, in particular Alzheimer's research. All of you have very effectively introduced the magnitude of the problem at an individual, personal, and social level, and the international nature of it. The projections for future increases in Alzheimer's, moreover, are predicted to affect disproportionately the less developed parts of the world, again emphasizing the international aspects of what is yet to come.

Overall, the science and pursuit of solutions to Alzheimer's research is international. It is marked by some of the events that have been discussed already. International scientific colloquia, such as the International Conference on Alzheimer's Disease, which will be held next month in France, typify the opportunities for scientists from around the world to share information in the goal of constructing the most efficient and effective plans for attacking the problems.

In addition, also referred to after passage of NAPA, the National Alzheimer's Project Act, there has been institution at DHHS of an interagency committee that is charged with coordinating efforts, including most notably, as read from that bill, efforts at an international level to consolidate and coordinate levels, and those are very much underway already.

I would like to present in the next few minutes some of the examples in which the international approach has been particularly important in pursuit of Alzheimer's research in three areas that I will typify, one of them being the area of basic research, the attempt to identify the underlying pathogenesis, the processes that lead to Alzheimer's; second, the translation of this to early diagnosis, the ability to track disease and to facilitate the testing of interventions; and then finally, also alluded to, research aimed at addressing the great burden of caregivers, who currently constitute the major force for care of individuals with Alzheimer's disease.

Over the last years, we have instituted, for example, through NIH support a project called DIAN. It is a Dominantly Inherited Alzheimer's Disease Network. As alluded to, Alzheimer's is typically a disease of older individuals, but there is a relatively rare, though particularly tragic inherited form that can occur in individuals in their 30s and 40s and 50s. The disease is rare, but presents an unusual opportunity to study the features of Alzheimer's disease with perceived clinical manifestations because it is so predictable in these individuals that sadly 100 percent assurance that over subsequent years they will develop Alzheimer's.

An initial collaboration between the United States, the United Kingdom, and Australia, soon to be joined by other nations, will look at the individuals from these families who are rare but exist in many parts of the world, to achieve a number of them to allow meaningful studies to better understand the processes that exist many years or even decades before Alzheimer's disease, and in turn to address them before irreversible symptoms and damages occur.

Also important has been the discovery of genetic risk factors for the more common form of adult onset, late onset Alzheimer's dis-

ease. Here, the techniques of GWAS, or genome-wide association studies, have been particularly important. And the international aspects here again I once more emphasize, because of the need to study large numbers of individuals, including individuals in diverse environmental contexts in order to understand the genetic risk factors, in the past years a number of new genes have been discovered through collaborations of investigators in the United States, Canada, and Europe. And just this year a new consortium worldwide will collect approximately 40,000 individuals with Alzheimer's disease, allowing a still greater sensitivity in understanding the genetic factors that affect the disease, and in doing this to find targets for potential intervention.

Another approach that has been critical is the identification of early changes in Alzheimer's that allows not only for early diagnosis, but the means to track progression of disease. This is most important so we become more efficient in testing whether products are or are not effective. Currently, these trials generally mean treating several hundreds of individuals and waiting the years it takes to determine whether clinical course has been varied. New research looking at biomarkers that involve neuroimaging and spinal fluid chemistries have made enormous breakthroughs in past years.

In particular, an initiative called ADNI, the Alzheimer's Disease Neuroimaging Initiative, is really a remarkable precedent in which private sector, public sector, Federal, and not-for-profit and academic representatives have converged on a project which has made available now new means in the research setting for tracking disease through changes in structure and function years and even decades before the appearance of any symptomatology, and now promise to find the same predictive value in tests of cerebrospinal fluid.

In order to increase the power and again the international scope of this, there have now been ADNI-like initiatives that are already in place in Europe, in Australia, and in Japan. There are additional efforts that are in progress now being established in China, in Taiwan and Korea, once again exemplifying the power that will come with coordinating efforts across nations to understand the factors which are in common and as well the factors which are independent and may vary from country to country.

So specific examples in which comparison of effects in different countries is important and can be outlined as well. One, which you will hear about subsequently this afternoon from Hugh Hendrie, has been a remarkable study, the Ibadan-Indianapolis study, in which Nigerians living in Ibadan and those of Nigerian descent living in Indianapolis are compared for the factors which determine Alzheimer's and other forms of dementia, again allowing a real and powerful opportunity to dissect genetic and environmental influences.

Similarly, there are collaborations with Israel studying the way in which diabetes is a risk factor for development of Alzheimer's disease; and recently, with assistance through U.S., institution of a study in China that is looking at the potential effects of exposure to trace elements on development of cognitive loss and dementia.

Finally, I would turn to the emphasis that was placed here now, so long as we still have individuals suffering with Alzheimer's and

have to provide the best care we can to them and their care providers, NIH has also supported research aimed particularly at the well-being of care providers. The study REACH, Resources to Enhance Caregiver Health, has identified through clinical trials just as rigorous as those for drugs, interventions which are capable of decreasing the stress, depression, other health, adverse health outcomes in those individuals who are caring for patients with Alzheimer's, and has also been effective in delaying the time of institutionalization so individuals with Alzheimer's are able to spend more time at home with their families and loved ones.

This study has been disseminated in the U.S. now very effectively through the Department of Veterans Affairs and the Administration on Aging, and we are looking similarly to extend this to an international level. Most recently, the very first of these efforts has been put into place in Hong Kong, where again in consultation U.S. studies of the outcomes of these clinical trials, we will have an opportunity to begin the process of international dissemination of these effective interventions.

Just as has been described, the problem of Alzheimer's is international, and will remain so, and for that very reason the research approach to it has to remain an international effort, and we at NIH and across the HHS are committed to this with many powerful beginnings and the prospect of much more to come.

And I thank you for this opportunity to speak with you and look forward to addressing any questions you may have.

[The prepared statement of Dr. Hodes follows:]

Testimony of Richard J. Hodes, M.D.  
Director, National Institute on Aging

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

June 23, 2011

Good afternoon. I am Dr. Richard Hodes, Director of the National Institute on Aging (NIA), one of the 27 Institutes and Centers of the U.S. National Institutes of Health and the lead federal agency for research on Alzheimer's disease (AD). It is a pleasure to be here today to discuss our work with partners around the world to understand, prevent, and treat AD.

Alzheimer's disease – the most common form of dementia – and related dementias represent a considerable global health burden. In the United States alone, as many as 5.1 million individuals may have AD.<sup>1</sup> Worldwide, an international team of researchers recently estimated that over 24 million people suffer from dementia, with approximately 4.6 million new cases every year; approximately 70 percent of these cases are likely AD. The number of people affected is expected to double every 20 years and will reach 81.1 million by 2040. Most people with dementia live in developing countries (60% in 2001, rising to 71% by 2040), and the projected increase in prevalence is expected to be particularly dramatic in low and middle income nations.<sup>2</sup> Among individuals ages 65 and older with dementia, experts estimate that just over half have AD, 16 percent have vascular dementia, and 30 percent have another form of dementia.<sup>3</sup>

As part of our comprehensive program of basic, clinical, and translational research on AD, NIH collaborates with a number of international partners to broaden understanding of the disease, to identify potential risk and protective factors, and to support the family members and others who care for patients with AD. We are also engaged in the broad coordination of research efforts around the world, including the exchange of cutting-edge information at influential global forums such as the International Conference on Alzheimer's Disease. In addition, NIA is a member of the Department of Health and Human Services Interagency Group on Alzheimer's Disease and Related Dementias, which was established this year to support the goals articulated in the National Alzheimer's Project Act (PL 111-175). This group is charged with "coordinat[ing] with international bodies to integrate and inform the fight against Alzheimer's

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<sup>1</sup> Hebert LE, Scherr PA, Bienias JL et al. Alzheimer disease in the U.S. population: prevalence estimates using the 2000 census. *Arch Neurol* 60: 1119-1122, 2003.

<sup>2</sup> Ferri CP, Prince M, Brayne C et al. Global prevalence of dementia: a Delphi consensus study. *Lancet* 366: 2112-2117, 2005.

<sup>3</sup> Kester MI and Scheltens P. Dementia: The Bare Essentials. *Pract Neurol* 9: 241-251-, 2009.

globally.” HHS has already begun reaching out to other countries to discuss the best way to carry out this coordination.

I’d like to focus on three critical areas today that have particular importance in the international context – understanding the roots of AD, seeking ways to better detect and diagnose it, and supporting for the caregivers that are the backbone of our care system for AD patients.

### **Understanding Alzheimer’s Disease**

Ongoing studies to elucidate the basic underpinnings of AD will suggest pathways for the development of preventive and treatment interventions. NIH has established the Dominantly Inherited Alzheimer’s Network (DIAN), a consortium of scientific investigators from the United States, England, and Australia who will identify, recruit, evaluate, and follow up individuals from families with early onset dominantly inherited AD, a rare form of the disease. The scientists involved in this study hope to identify the sequence of brain changes in early-onset AD, before symptoms appear, and by understanding this process to also gain insight into the more common late-onset form of the disease.

Identification of genes that influence risk is an active and productive area of study. Until recently, only one gene variant, Apolipoprotein E-e4 (APOE-e4), had been confirmed as a significant risk factor gene for late-onset AD, the more common form of the disease. In the last several years, however, researchers have confirmed additional gene variants as possible risk factors for late-onset Alzheimer’s, including SORL1, CR1, CLU, and PICALM – the latter two of which were identified in a study pooling DNA samples from a number of U.S. and European research groups. More recently, the NIH-supported Alzheimer’s Disease Genetics Consortium (ADGC) coordinated a team of American, British, and Canadian researchers in a study that confirmed yet another gene variant, BIN1, and identified four others that may be risk factors.

Earlier this year, ADGC investigators joined with other research groups around the world to establish the International Genomics of Alzheimer’s Project (IGAP), a global collaborative effort to identify additional genes that contribute to AD risk and influence progression of the



disease. IGAP researchers have created a shared resource database that includes genetic data for more than 40,000 individuals. This large, multinational data set will enable the researchers to identify rare genetic variants that would be impossible to find in smaller study populations, as well as find population-specific differences in genetic risk.

The identification of other risk and protective factors for cognitive impairment and dementia is a high priority for NIH. Ongoing studies are providing a wealth of information about the relationship between an array of economic, demographic, and lifestyle variables and cognitive health at the national and international levels. The long-running Health and Retirement Study (HRS), the U.S.'s leading source of combined data on health and financial circumstances of Americans over age 50, collects data on the cognitive health of older Americans, and similar surveys are ongoing in Europe, Mexico, Asia, and Africa. Efforts are currently underway to enhance cross-comparability of these surveys, which will facilitate innovative cross-national research. NIH also supports and encourages the inclusion of questions about cognitive health in other international data collection efforts, including surveys in Brazil, Ireland, and Japan.

These studies have already generated intriguing findings about interventions and lifestyle factors that may protect cognitive health. For example, NIH-supported investigators studying older populations in the U.S., England, and 11 European countries recently found that early retirement (prior to age 65) was associated with a significant decline in cognitive performance. The investigators suggest that this may be in part because for many people retirement leads to a less stimulating daily environment, and the prospect of retirement reduces the incentive to engage in mentally stimulating activities on the job. Although further study is needed, these findings suggest that the recent trend of American workers delaying retirement may eventually lead to improved cognitive performance in this group.

Another important effort is the Indianapolis-Ibadan Dementia Project compares the risk of dementia among community-dwelling African American elders in Indianapolis with the risk among their counterparts in the city of Ibadan, Nigeria. This study was one of the first to underscore the importance of vascular risk factors to AD pathogenesis. Further, a collaborative study between American and Israeli investigators is examining long-term characteristics of type

2 diabetes and inflammation and how they affect the development of cognitive decline among cognitively normal diabetic individuals 65 years and older living in Tel Aviv. A third project is exploring the possible association between exposure to certain trace elements and cognitive decline and dementia among elderly individuals in rural China.

### **Detection, Diagnosis, and Biomarker Identification**

The NIH-supported Alzheimer's Disease Neuroimaging Initiative, a public-private partnership involving collaboration among government, academic, and industry partners, is the most comprehensive effort to date to find neuroimaging and other biomarkers for the progressive changes associated with AD and mild cognitive impairment (MCI is often a precursor condition to AD). ADNI investigators are testing whether serial imaging and other biomarkers and clinical and neuropsychological assessment can be combined to measure the progression of MCI and early AD. They made a significant step forward recently in developing an experimental test to diagnose the early stages of AD more accurately by measuring two biomarkers—tau and beta-amyloid proteins—in cerebrospinal fluid. These findings facilitated the first revision in 27 years of the clinical diagnostic criteria for AD, which characterize – for the first time – preclinical stages of the disease and address the use of imaging and fluid biomarkers to detect AD's onset and track its progression and (potentially) response to treatment.

An extension of the original ADNI, ADNI2, began last year. The overall goal is to determine the relationships among the clinical, cognitive, imaging, genetic and biochemical biomarker characteristics of the entire spectrum of AD, as the pathology evolves from normal aging through very mild symptoms, to MCI, to dementia. ADNI2 includes several Canadian sites which receive some funding from the Canadian Institute of Health Research.

Importantly, clinical, imaging, and biological data from ADNI are immediately made available to all qualified scientific investigators in public and private sectors worldwide, whether they are part of the study or not. Many of the tools and methods developed by the study have fueled similar efforts in Japan, the European Union, and Australia; Chinese, Korean, and Taiwanese versions of ADNI are also being established.

### **Helping Alzheimer's Caregivers**

People with AD are frequently cared for in the home, and the physical and emotional toll AD exacts on family, caregivers, and friends can be significant. REACH II (Resources for Enhancing Alzheimer's Caregiver Health), an NIH-funded study, was the first intensive caregiver support intervention to be proven effective, through rigorous testing, in an ethnically diverse population. The REACH intervention is currently being translated more broadly through the U.S. Department of Veterans Affairs, which is now offering the program to veterans and their families and is beginning to test the intervention with caregivers of patients with other devastating chronic conditions. The Administration on Aging also is implementing the REACH intervention at centers in several states.

Recently, researchers at the University of Hong Kong have begun to adopt REACH through the Reaching Out Dementia Caregiver Support Program. This program, which is coordinated by the Hong Kong Council of Social Service, is the first international adaptation of the REACH intervention, and we are delighted to help foster this promising collaboration between Hong Kong and the American investigators involved in REACH.

Although geographic, language, and cultural differences exist within the international research community, we share an important goal: the reduction, and eventual elimination, of the devastation brought on by Alzheimer's disease. We look forward to continuing to work together with our international partners to reduce the burden of AD not just in the United States but throughout the world.

Thank you. I welcome your questions.

Mr. SMITH. Thank you very much, Dr. Hodes, for your testimony, and for the tremendous leadership you provide. Let me ask just a couple questions with regards to the sharing of data among scientists around the world.

How robust is it? Is there a stovepipe mentality, or are scientists funded by your shop and others more than willing to share findings and to collaborate?

Dr. HODES. Although there is always room for improvement, I think that there is an enormously positive attitude of data sharing in the area of Alzheimer's research. To cite a couple examples or expand upon those that I mentioned, for example in the field of genetics, as we have studied the power that is needed to carry out genetic evaluations, we have quickly learned that the number of individuals studied by any one laboratory or even any one nation are often insufficient to make the discoveries that are needed. So some of the great discoveries the past years have come through voluntary participation, collaborations from investigators in many nations studying populations of these nations to accumulate the power needed for clinical trials and these clinical evaluations.

The ADNI study, as I mentioned, is particularly informative because it stresses not only the willingness to collaborate, but sometimes the technical advances that are necessary in order to achieve collaboration. So what ADNI did in terms of its neuroimaging capacity was to establish the methodologies that allow individuals to be scanned by different machines, brain scans, in different parts of the country and in different parts of the world, and to make those compatible so that one could translate them into a common language, compare one subject or patient to another. With this enormous benefit, it is now possible to share the neuroimaging and other data from ADNI nationally and internationally.

The international efforts that I mentioned are being taken with great care to harmonize so there will be a common language to allow translation. And I think with these technical issues addressed, we generally are finding very gratifying collaboration across nations.

Mr. SMITH. Let me ask you, you mentioned the caregiver issue. I know that the veterans, because I used to be chairman of the Veterans' Affairs Committee, we had a very important, I think, Alzheimer's project, the REACH program: Resources for Enhancing Alzheimer's Caregiver Health. Have you gleaned lessons from them? And what are you finding with regards to caregivers? And secondly, in planning, the United States doesn't seem to be as poorly off as some countries in Europe. And again having just had this hearing, and without objection, I would like to make all four of the demographers' testimonies from Monday's hearing part of this hearing, because the impact of not having children and caregivers is going to be enormous both in terms of the patients themselves and on health care delivery systems worldwide.

As I mentioned in my opening comments, it is catastrophic. It is a demographic winter that is just around the corner all over the world. And I mean one statistic that I found troubling in Russia, this was Nicholas Eberstadt provided this to our commission on Monday, for every 2 million births there are 3 million deaths in Russia. So I mean they are rapidly losing the ability to—plus an

aging population—to have a caregiver available for an Alzheimer's patient. Your thoughts on that? Do you collaborate, for example, with CMS or with HHS about projections of what costs really will be as the caregiver pool dries up even here in the United States and people then have to go into an institutionalized setting?

Dr. HODES. There are a number of extremely important and good points made. The first of them, the question of how the Department of Veterans Affairs, and again I would add, the Administration on Aging, have been effective in translating the programs of research are a very important illustration of the way in which Federal agencies can collaborate. So the discovery, the demonstration in an experimental setting, a clinical trial that something is effective now needs to be followed up by these organizations, which in effect are doing demonstration projects, translating them into the real world. We work very closely, in fact our last meeting with the Department of Veterans Affairs was just last week, to monitor these outcomes. And as I mentioned, their translation internationally is beginning to occur as well.

The demographics you described are indeed imposing and are a part of all our projections. So that even as we expressed optimism about a program such as REACH, which allows caregivers to take better care of those with Alzheimer's, which is critically important in the present, as your remarks explain, we in the future may not have sufficient numbers of caregivers even with the best of circumstances to support, to care for those with Alzheimer's, meaning that institutionalization may become an undesirable but only alternative, which all turns to emphasize yet once again the urgency of our finding a way to decrease the burden of Alzheimer's, to prevent and treat it, because even the best of caregiving circumstances is going to be compromised by the very demographics that you described.

Mr. SMITH. Let me ask you, is the 115 million Alzheimer's patients by 2050, as provided by Alzheimer's Disease International, is that order of magnitude what you think is accurate?

Dr. HODES. I think it is very appropriate you asked about order of magnitude. And the answer is yes. You will see and hear and read many differences that have to do with projections based on different numbers of individuals currently affected. And that has to do with diagnostic criteria, with different predictions of birth rates, death rates, and longevity in populations. With so many unknowns there, it is unavoidable there is going to be a range of uncertainty in projections. But for order of magnitude, that seems to be precisely within the range of multiple proposals and projections.

Mr. SMITH. A couple of final questions. In your opinion, are we on the verge of a chemical compound therapy intervention that might lead to at least arresting the progression of the disease? And can you make any kind of prediction that a cure might be found in the not too distant future?

And secondly, George Vradenburg and Eric Hall both make a very strong appeal for an international meeting to share best practices. I would hope that it would be at the very highest of levels, presidents; secretaries or ministers of health, or Secretary of Health and Human Services in our case; and then an NGO inclusion, not just a side event, but something where they would really,

the NGOs around the world, including here in the U.S., could really participate and be a part of it so that we could all share best practices.

Eric Hall talks about the extraordinary work being done in Israel, for example, and how we might learn from that. You mentioned the Nigerian diaspora here and those in Nigeria, what we could learn from that. I mean, there are huge lessons learned. And if we were to push for this, which I am going to introduce a bill, or try to get some funding for it, I know my colleagues will all work collaboratively for that, off the top of your head do you think it would be a good time, 2012, as recommended by the Alzheimer's Foundation, or could it be done sooner?

Dr. HODES. So to the first question, of course I wish that I could estimate the time in which we will finally achieve the kind of effective interventions that we want. But what I can express for myself is the shared enthusiasm about scientists in the field for the undeniable and enormous pace of discovery. The amount we understand about the basic underlying processes, the degree to which we can now in individuals who are alive and either with or without symptoms, the underlying brain changes that are occurring enable an efficiency of clinical trials and tests on newly identified targets that is unprecedented. And so the pace of discovery will enhance. Just when that will converge on a final successful solution is certainly beyond my ability to predict.

Your question about convening an international meeting, again I would emphasize that at the scientific level these meetings occur and need to occur, such as the ICAF that is coming up. What you are talking about, what has been proposed is a meeting at a larger level that goes beyond research to the application of research, the societal implications, the best practices. And here I can only express the great enthusiasm that we at NIH and others would have to make sure that we contribute to the evidence base and learn from such an exercise more about what the priorities need to be so that we can direct our research to best serve the process. So we would be certainly enthusiastic participants in such an activity.

Mr. SMITH. And I think the political buy-in of having at the highest level Prime Ministers and Presidents, if that could be arranged, would make an enormous difference. You know, G-8, G-20 and the rest of the world. Thank you very much. And I do hope that is something that the administration could support very strongly as well, because it would take planning now to make that happen in the very near future.

Mr. Payne.

Mr. PAYNE. Thank you very much. Thank you for your testimony.

As we know, we are in a new economic era here as we proceed to deal with the debt and the deficit, and as we are embarking on having a broader approach to the problem of Alzheimer's here in the United States, but also abroad. I just wonder what, in your opinion, you know, have you seen as effective in the U.S. support of global dementia? And in your opinion, what steps could the U.S. Government take in order to improve our support of this global health issue? As I mentioned, we are sort of moving in the other direction, but this is such a devastating health issue, I just wonder if you have any advice that we might be able to use.

Dr. HODES. Well, again I think from the perspective of an agency committed to research to identify best practices and means for intervention, it certainly is the translation of research findings as they currently exist, such as in areas of REACH that are likely to be effective.

You touch upon another area where there has been a good bit of controversy of late, that is in terms of what we know about how to translate apparent risk factors for Alzheimer's disease into recommendations for interventions that are likely to decrease the probability of developing Alzheimer's. And there was a state of the science conference that was carried out by bringing in experts who reported about 1 year ago to NIH. They concluded, in language that really requires clarification, that there was no high quality evidence indicating that any intervention, for example, based on control of behavioral factors or blood pressure was proven to prevent Alzheimer's disease development. This created I think an unfortunate perhaps over-interpretation of the fact that we don't know what we can reasonably recommend. The clarity of evidence will continue to increase as we do more clinical research.

But there is certainly strong associative evidence that suggests that people with high blood pressure, as you alluded to, with diabetes, people who don't exercise, people who don't have social connectivity are at higher risk for Alzheimer's disease. And even as we continue to develop better research, the ability to support appropriate treatment of these cardiovascular risk factors and environmental factors is I think a very reasonable recommendation at this point in time.

So disseminating that nationally and internationally I think is an appropriate use of the evidence base that we were able to generate and we continue to generate at the present state of knowledge.

Mr. PAYNE. That sort of leads into another thought that I had that, as I mentioned in my testimony, that figures indicate that the majority of dementia cases are located in low to middle income countries throughout the world. Additionally, the World Health Organization estimates that currently 58 percent of the worldwide dementia is in moderate income countries. But of course the dilemma is the future, where it is estimated that 71 percent by 2050 will be in countries in that category. So I am just wondering what, in your opinion, do you think can be done in order to halt the growth of dementia cases? And additionally, what capacity building is being done in low and middle income countries so that they are better prepared to handle dementia cases, and much more of them as they will be coming in the coming years? Are they willing to listen? Do they feel it is an issue that, with all their other problems, that should be raised to a higher level? What has been, in your opinion, the response from countries in this category?

Dr. HODES. I think one very important aspect of what you raise is the fact that as we have increasing proportions of individuals affected with dementia in less developed countries, we have to take great care to be sure that what we identify as causes and interventions that are effective for preventing or delaying Alzheimer's are solutions that will be relevant to many parts of the world. And for example, the relative importance of risk factors such as hyper-

tension or diet versus genetics may well vary from one part of the world to another. Whether dementia caused by what we identify pathologically as Alzheimer's disease versus that which has more important components of vascular disease is a critical determinant.

I think you will hear more again from Dr. Hugh Hendrie as he talks, for example, about the informative comparison of Nigerians in Ibadan versus those of Nigerian descent in the U.S. is an example. We see changes in what the risk factors appear to be for these presumably genetically similar populations. And this itself is informative. But it suggests that to the future, as we develop effective interventions, we are going to have to pay attention to the likelihood that there will not be a single intervention that may be first shown to be effective in Bethesda or New Jersey or in Boston, and to assume that it will be universally applicable.

So the research again has to continue internationally. Right now it is doing so in terms of risk factors. As we become better able to translate into interventions, we are going to have to similarly keep in mind that interventions are going to have to be tailored to the genetic, environmental, and socioeconomic conditions of the various nations of the world.

Mr. PAYNE. Just finally, have we been able to determine whether there may be a correlation between diet or say weight factors, obesity? Have we seen any kind of correlation in your studies to those issues?

Dr. HODES. Well, there is some very strong correlations between high blood pressure and risk of developing Alzheimer's disease or dementia, between diabetes and the risk of developing Alzheimer's disease or dementia. Now what is important is to move from those correlations to asking whether if we address blood pressure or control of diabetes we can make a difference in terms of cognitive function. And those very studies are currently underway. So that for example in the studies carried out with support from the Heart, Lung and Blood Institute or the Diabetes Institute, which are looking at various interventions to treat various levels of control of blood pressure or of blood sugar, NIA and other components of NIH have added to that measures of cognitive function and even of neuroimaging so we will learn in the format of a clinical trial whether we can establish evidence that indeed preventing high blood pressure or high blood sugar in addition to the very likely impact these are going to have on stroke, cardiovascular disease, and other complications of diabetes may also have a direct impact on cognitive function and risk of dementia.

So your question directly, yes, there are strong correlations. Now even more important, testing to see if we intervene on those variables we can translate the correlation to find out whether it is causal and leads to a preventive intervention is the state that we are at currently.

Mr. PAYNE. Thank you very much. I yield back.

Mr. SMITH. Thank you very much, Mr. Payne. I just do have one final question. With regards to early-onset, are the risk factors the same, similar, or different? And what is the earliest onset that has been recorded thus far of Alzheimer's?

Dr. HODES. Well, in the category of dominantly inherited early-onset Alzheimer's disease, these cases around the world are caused



by a number of mutations, but in one of only three genes. It is essentially 100 percent certain, tragically, that someone with this mutation will develop Alzheimer's disease. The age ranges have been 50s, 40s, even 30s. They vary somewhat with the identity of the population and the genetic mutation.

In terms of identifying risk factors other than the gene, in those cases of course, since the gene is essentially determinant, there has been very little opportunity to ask whether that genetic predisposition or predestination, sadly, is influenced by other factors. So there isn't so much known.

Now, if we set aside those and ask about the cases of Alzheimer's in which there is not a dominantly inherited mutation, but nonetheless are recurring not at the more common 80s or 70s, but occurring in the 60s or 50s, we are currently through population studies monitoring onset and prevalence of cognitive decline and even Alzheimer's in populations that range in age from 50s through the 80s and 90s. For example, the Health and Retirement Study puts us in a position to better understand whether the risk factors vary with age. An important factor in studies currently in progress ought to be able to address this.

Mr. PAYNE. Just one additional question also. The increase in the percentage or the number of people that are being diagnosed with Alzheimer's, in your opinion do you think it is an increase that is happening or do you think that it has simply been underreported in the past and just called something else?

Dr. HODES. I am not aware of any conclusive evidence that the risk of developing Alzheimer's disease at a given age, other variables essentially being similar, has changed. There is room for this to occur. For example, if the epidemic we are seeing in obesity and associated diabetes were to continue, it is possible that due to an increase in diabetes and the associated risk in Alzheimer's there might be such a change. But the short answer to your question, to date I think it is likely that the increase in what we are seeing is due to two principal factors, overwhelmingly the increase in the number of people who are reaching an age at which they are at higher risk, and in addition the greater awareness and diagnosis.

Mr. SMITH. Finally, Dr. Hodes, could you give us a sense of how many laudable research proposals go unfunded because of inadequate funding?

Dr. HODES. I can give you an answer which I think shows the magnitude of that category. Currently, the pay line, that is the percentile at which applications are being funded at NIA, and it is not so different across other components of NIH, this year for example for the bulk of grants is at the 11th percentile. I think there would be little disagreement, if any, that grants that receive percentile scores at least twice that level, into the 20s, are deemed by peer review to be outstanding. By that criterion, I would say that we could fund twice as much research as we are currently able to fund, and still be funding uniformly outstanding research, if that is responsive to the question.

Mr. SMITH. That is very helpful. Thank you so much, Dr. Hodes. Thank you so much for your testimony. We look forward to working with you. Did you say if you would personally, or on behalf of the administration, be able to support an international conference?

Dr. HODES. Of course I can't speak for the administration. I can certainly say if there is such a conference, then I would be enthusiastic about there being a presence of agencies such as NIA and NIH to lend their perspective on evidence and to learn from such a conference about where research ought to be conducted. But beyond that—

Mr. SMITH. Clear it with OMB. Thank you very much, Dr. Hodes.

I would like to now introduce our second panel. And without objection, I would like to make part of the record, as I indicated earlier, the four demographics experts who testified on Monday at the Commission on Security and Cooperation in Europe. And that is Dr. Nicholas Eberstadt, Dr. Jack Goldstone, Richard Jackson, and Steven Mosher. Without objection, it will be part of record.

I would like to now introduce our second panel, beginning with Dr. Daisy Acosta, who is Alzheimer's Disease International, chairman of ADI, which seeks to empower the 75 national Alzheimer's associations around the world to promote and offer care and support for people with dementia and their caregivers, while maintaining a global focus. She is certified by the American Board of Psychiatry and Neurology, and Dr. Acosta specializes in geriatric psychiatry. She has a large clinical practice in the Dominican Republic, and is in charge of organizing and teaching at the university psychogeriatric unit in that country. Welcome, Dr. Acosta.

We will then hear from Mr. Eric Hall, who is the President and founding CEO of the Alzheimer's Foundation of America, and President and CEO of Alzheimer's Foundation International, an outgrowth of AFA. Mr. Hall spearheaded the development of AFA to improve the quality of care for individuals with Alzheimer's disease and related dementias and their families. During that goal, he has initiated major national initiatives related to early detection, training of health care professionals, and standards for dementia care settings. Mr. Hall has spoken at numerous conferences on Alzheimer's disease and caregivers, and sits on leading advisory councils.

We will then hear from Mr. Bill Thies, who is Chief Medical and Scientific Officer at the Alzheimer's Association, which is dedicated to eliminating Alzheimer's disease through the advancing of research, providing care and support for all affected by the disorder, and reducing the risk of dementia through the promotion of brain health. Mr. Thies oversees a research grants program at the Alzheimer's Association. He launched Alzheimer's & Dementia, the journal of the Alzheimer's Association, and established the Research Roundtable, a consortium for industry, academia, and government, who meet regularly to explore topics of mutual interest in drug discovery and common barriers to progress.

We will then hear from Mr. George Vradenburg, who is the founder of USAgainstAlzheimer's, a national disease advocacy network, and chair of the Geoffrey Beene Foundation-Alzheimer's Initiative on Early Diagnosis. Mr. Vradenburg also directs Leaders Engaged on Alzheimer's Disease, a tri-sector coalition of Alzheimer's-serving organizations. The USAgainstAlzheimer's co-convenes with the Alzheimer's Foundation of America. Mr. Vradenburg was drawn to Alzheimer's advocacy through the death of his mother-in-law, Bea Lerner, from the disease. Prior to 2003,

Mr. Vradenburg held several executive positions in large media companies.

We will then hear from Dr. Giovanni Frisoni, who is currently with the Scientific Institute for Research and Care at Brescia, Italy, where he oversees research on Alzheimer's and other neurological diseases. In addition, Dr. Frisoni is part of several international groups that are focused on Alzheimer's research and treatment. His work is widely published in medical journals and books. In the past 6 years, Dr. Frisoni's work has become more expansive, focusing on developing infrastructure for storing and processing brain imaging data to increasing the understanding of Alzheimer's in Europe and in the United States. He will be joining us live from Italy in the order that I am announcing.

We will then hear from Dr. Jeffrey Cummings, of the Cleveland Clinic Lou Ruvo Center for Brain Health. Dr. Jeffrey Cummings is director of that clinic for brain health in Las Vegas, Nevada, and Cleveland, Ohio. In addition to many articles and books, Dr. Cummings is the author of the Neuropsychiatric Inventory, which is the most commonly used tool for characterizing behavioral disturbances in dementia syndromes, and for measuring the effect of therapies on neuropsychiatric symptoms in Alzheimer's disease. Dr. Cummings has served as president of the Behavioral Neurology Society and the American Neuropsychiatric Association.

We will then hear from Dr. Hugh Hendrie, Professor of Psychiatry at Indiana University, where he directs the IU Center on Aging Research. Dr. Hendrie served as chairman of the Department of Psychiatry, a position he held for 25 years, until 2000. While in that position, Dr. Hendrie developed and directed a section focused on geriatric psychiatry. He served as the President of the American Association of Geriatric Psychiatry and The Geriatric Psychiatry Alliance. Dr. Hendrie is well known internationally for his research and published works on psychiatry. He is currently serving on the National Advisory Council on Aging.

And that is it. Dr. Acosta, if you could begin, please.

**STATEMENT OF DAISY ACOSTA, M.D., CHAIR OF THE  
EXECUTIVE BOARD, ALZHEIMER'S DISEASE INTERNATIONAL**

Dr. ACOSTA. Thank you, Chairman Smith, Ranking Member Payne, for this opportunity to testify before you today. My name, as you said, is Daisy Acosta, and I come from the Dominican Republic. I am a caregiver, a doctor, and a researcher, and I am the chairperson of Alzheimer's Disease International, the worldwide federation of Alzheimer's associations around the world. Our 76-member associations represent the people with dementia and their families in their countries. Alzheimer's Disease International was founded here in this country in 1984, being the U.S. Alzheimer's Association one of our founding members. Today, 27 years later, for the first time ADI has a chair from a developing country. So you can be sure that I am very proud of that.

Alzheimer's disease and other dementias, as you have been saying, is a global problem, and are the single most important health and social crisis of the 21st century. The impact of this disease today is massive, and will accelerate with the years to come. You have already said how many people live with dementia at this

point, 37 million people. And this is going to increase due to global aging by more than 1 million per year, as you said before, to 115 million by 2050.

Alzheimer's disease is devastating not only to the victims, but also to the families and to society at large, and there is something really that cannot be put in papers about the devastation of this illness. It is the human fiber of this illness. You really have to live with a person with dementia, with a family with dementia at least for 24 hours to understand the urgent need that we need to solve this problem.

Alzheimer's disease in developing countries, the burden of this disease falls completely on the families. And as you said before, again, these countries will see the largest increase in numbers in the next decades. So I want to stress again that this is a global problem, and that we have to find global solutions.

The global cost of this illness, as you said, is \$604 billion. This equals 1 percent of the global GDP. If Alzheimer's disease were a country, it would be the 18th largest economy based on GDP. And it exceeds that annual turnover of any company in the world. And as you said, because I am glad to see that you really have all the facts with you and all the statistics with you, which is really great, but Alzheimer's Disease International put together all this data in our two reports, the 2009 and 2010 reports, not just to sit in those reports. The aim to gather all this data was really to serve as a wakeup call for governments, leaders in the community, health care professionals, to really put this data into action.

We have made great progress with many other diseases like cancer, HIV/AIDS, but we have done so because there has been a political commitment to act, and because of national planning and substantial investment in research and care options. And this is exactly what is needed to solve this problem.

There is increasing awareness about Alzheimer's disease and other dementias in the world. Several countries have launched a national plan or strategy, starting with Australia in 2005, and then France and South Korea in 2008. These plans have started creating significant changes in health care systems. More and earlier diagnoses are being made, better disease management, and increased research are key issues in this strategic planning. All of these governments are aware that investments made now will reduce future health-care costs.

At our annual international conference in March 2011 in Toronto, we hosted for the first time a symposium looking at the results of these national plans. And we will do the same thing in 2012. And I certainly hope to see the national plan for Alzheimer's disease and other dementia in this great country being included in this symposium next year.

The United States has shown global leadership in the past and was one of the first countries to create a dementia research budget in the 1990s. Having said that, as I understand, that budget has not followed the increase in number of people with dementia that has doubled in the last 20 years. And that budget has not been adjusted for inflation, as I understand.

Your Congress has now taken an important step by passing the National Alzheimer's Project Act. I congratulate the USA on this

decision because it is a great opportunity to improve the ways that your health care system deals with dementia: Earlier diagnosis and intervention; giving more people access to medical and nonmedical treatment; and last, but not least, and I think it is extremely important, support for caregivers.

This should be accompanied, of course, by increased budgets for research into the cause of the disease and possible prevention.

If the USA takes these steps, it will encourage governments in other parts of the world, as well, to do so. And I am sure of that; at least, that will be so in my region where I live.

ADI—and this is very important—and its members have empowered people with dementia to have a voice. I commend you to continue the productive work with the Alzheimer's Association as a champion in advocacy and encouraging research efforts in your country.

Finally, we need the help of the U.S. Government in an international issue. The United Nations are going to hold a high-level meeting on the 19th and 20th of September in New York City. It is a meeting about noncommunicable diseases. This summit currently does not include Alzheimer's disease as one of the noncommunicable diseases—only cancer, diabetes, and heart and lung diseases—although these illnesses share the same risk factors and often coincide together. It would be great if a USA representative at the United Nations could raise this in the discussion on the outcome document that has already started.

I think we really can win this fight against dementia, but only if governments get committed to do so. And we have no time to waste. The time to do it is now. It is time, really, for global action.

Thank you very much.

[The prepared statement of Dr. Acosta follows:]

**Dr Daisy Acosta**  
**Alzheimer's Disease International Chairman**  
**U.S. House Committee on Foreign Affairs**  
**Subcommittee on Africa, Global Health, and Human Rights**  
**23 June 2011**

Thank you, Chairman Smith, Ranking Member Payne, and members of the subcommittee, for this opportunity to testify before you today.

My name is Daisy Acosta and I come from the Dominican Republic. I am a caregiver, doctor and researcher. I am the Chairman of Alzheimer's Disease International, the worldwide federation of Alzheimer associations. Our 76 member associations represent people with dementia and their families in their countries. Alzheimer's Disease International, known as ADI, was formed in 1984 in this city with the Alzheimer's Association being one of the founding members. 27 years later, I am the first Chair of ADI from a developing country.

Alzheimer's disease and other dementias are a global problem. We estimate that there are currently 37 million people with this disease in the world and, due to global ageing, the number will increase by more than one million a year to 66 million by 2030 and 115 million by 2050. Alzheimer's disease is devastating not only to the people who have it, but also to their families and to society at large. Many people have to stop working because they are caring for a relative.

In developing countries, the burden of the disease falls almost completely on the families and these countries will see the largest increase in numbers in the next decades. So I want to stress again: this is a global problem. The global cost of the disease was calculated last year at 604 billion dollars, which is around 1% of global GDP. This is more than the annual turnover of any company in the world. If dementia were a country, it would be the 18<sup>th</sup> largest based on GDP. One third of these costs are in the USA.

There is increasing awareness about Alzheimer's disease and other dementias in the world. Several countries have launched a national plan or strategy, starting with Australia in 2005 and then France and South Korea in 2008. These plans have started creating significant changes in health care systems: more and earlier diagnosis of the disease, better disease management and increased research efforts are the key issues. All of these governments are aware that investments made now will reduce future health care costs.

At our annual International Conference in March 2011 in Toronto, we hosted our first symposium on the results of the current national plans and we will follow this up in 2012.

The United States has shown global leadership in the past and was one of the first countries to create a dementia research budget in the 1990s. Having said that, this budget has not followed the increase in the number of people with dementia, which has doubled in the last 20 years. It has not even been adjusted for inflation. Your Congress has now taken an important step by passing the National Alzheimer's Project Act. I congratulate the USA on this decision. It is a great opportunity to improve the ways that your health system deals with dementia, by providing information to the public, educating health care professionals, stimulating earlier diagnosis and intervention, giving more people access to medical and non-medical treatment and last, but not least, improving caregiver support. This should be accompanied by increased budgets for research into the cause of the disease and possible

prevention. If the USA takes these steps, it will encourage governments in other parts of the world as well.

ADI and its members have enabled people with Alzheimer's disease and other dementias to have a voice. I commend you for your continued, productive work with the Alzheimer's Association as a champion in advocacy and encouraging research efforts in your country.

Finally, we need the help of the US Government for an international issue. Alzheimer's disease and other dementias are the single most significant health and social crisis of the 21<sup>st</sup> century. The impact today is massive and will accelerate in the years to come. We must prepare now for the social and economic disruptions that this disease will cause. We have made great progress with other major diseases, such as cancer and HIV/AIDS, through national planning and political commitment to act and with substantial investment on research and care options. The United Nations are going to hold a High Level Meeting on 19 and 20 September this year in New York on Non Communicable Diseases (NCD). This NCD Summit currently does not include Alzheimer's disease and other dementias, only cancer, diabetes, heart and lung diseases, although they share the same risk factors and often coincide. It would be great if USA representatives at the UN could raise this in the discussion on the outcome document that has already started.

We can win this fight against dementia if governments make the commitment. Now is the time for global action!

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Mr. SMITH. Dr. Acosta, thank you much for your testimony and your leadership.

Mr. Hall?

**STATEMENT OF MR. ERIC HALL, PRESIDENT AND CHIEF EXECUTIVE OFFICER, ALZHEIMER'S FOUNDATION OF AMERICA**

Mr. HALL. Chairman Smith, Ranking Member Payne, thank you for convening this hearing and for inviting the Alzheimer's Foundation of America to testify. I am Eric Hall, AFA's founding president and CEO, and I am honored and privileged to be here today.

My involvement in this cause is not simply a career endeavor, and it is more than simply my family history, as if that would not be enough, but it is a painful result of the many stories that I hear from struggling families across our country. I need to do something, we need to do something, and I beg you to make the most of the present opportunity and to make it happen now.

The National Alzheimer's Project Act passed by Congress last year was a groundbreaking first step toward the creation of a National Alzheimer's Disease Plan in the United States. However, it is no secret that the U.S. is behind the curve of several other countries that already have national Alzheimer's disease plans in place or in process. We have a lot of homework to do, but we can learn a lot from what has already been done overseas, both in planning and in political commitment.

The next crucial step is an international meeting of countries with plans in place or in process in the first quarter of 2012. AFA would be honored to serve as an NGO supporting partner in such an effort and would be glad to work with ADI and others. AFA applauds ADI for its financial support of the 10/66 Dementia Research Group and its commitment to international collaboration.

In AFA's view, the international meeting would ideally consolidate how other countries have approached their plans and would produce a compendium with common threads. Such a meeting would help us develop our plan and help us to begin to develop a global approach to this pandemic.

The meeting would also include a day or more of panel discussions on established policies, as well as innovative care programs abroad as well as those here in the United States, of which there are many. There is little doubt we can get there faster by reviewing what has already been done, what has been successful, and what to avoid.

One example that the U.S. can learn from is the award-winning dementia care available in Israel through an organization called Melabev. Melabev is a founding member organization of the Alzheimer's Foundation of Israel. And, together, they share a combined commitment to serve the Alzheimer's population in that country. The Alzheimer's Foundation of Israel is a not-for-profit organization that I established in January of this year through the Alzheimer's Foundation International, which has been an outgrowth of the Alzheimer's Foundation of America.

Melabev has spent the last 30 years developing therapeutic activities that give people with dementia and Alzheimer's disease a reason to get up in the morning. In addition to its day centers, Melabev also brings services and activities right into the family



home. Each individual with dementia is given a geriatric assessment, and a range of health-care professionals are available for working with the individual and the family members under their roof.

Not only does Melabev care for the person with dementia, but it also cares for the family caregivers. It provides palliative care for individuals in the end stages of the disease, as well as guidance on end-of-life issues for the whole family. In between regularly scheduled house calls, the members of this team are accessible by phone whenever needed. Melabev, quite simply, gives families a shoulder to lean on.

Israel also has groundbreaking geriatric programs at Herzog Hospital in Jerusalem. Their motto is, "Restoring dignity to all." Herzog Hospital is currently the only facility in Israel to combine neurological, behavioral, and social approaches in treating the full range of geriatric illnesses, including Alzheimer's disease. Most uniquely, Herzog also has a specialized emergency room for behavioral and psychiatric issues. And all of its staff members, from physicians to social workers, are trained in geriatric approaches to care.

Melabev and Herzog Hospital in Israel are just two quick examples of the many innovative programs available throughout the world. A congressional call for an international meeting is how we will learn more. And if we do things right, an international movement will follow.

I would like to end with a quote from Peter Drucker, a writer who was awarded the Presidential Medal of Freedom in 2002. He said, "Unless commitment is made, there are only promises and hopes; but no plans."

AFA looks forward to working with members of the subcommittee to address the important issues raised in today's hearing. And, of course, I would be honored to answer any questions you may have.

[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 Foreign Affairs  
Subcommittee on Africa, Global Health, and Human Rights  
"Global Strategies to Combat the Devastating Health and  
Economic Impacts of Alzheimer's Disease"  
June 23, 2011

Chairman Smith, Ranking Member Payne, and members of the Subcommittee, 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.

My involvement in this cause is not simply a career endeavor and it is more than my family history—as if that would not be enough—but it is a painful result of the many stories I hear from struggling families across our country. I need to do something, we need to do something—and I beg you to make the most of the present opportunity and make it happen now.

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 1,600 organizations across the country. Our services include a toll-free hotline staffed by licensed social workers; *care ADvantage*, a free quarterly magazine for caregivers 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.

The Alzheimer's Foundation International (AFI) was founded in 2009, and is expanding worldwide by forming member organizations in various countries. AFI is an outgrowth of the Alzheimer's Foundation of America (AFA), and its member organizations include AFA; Alzheimer's Foundation for Caregiving in Canada; and Alzheimer's Foundation of Israel. I serve as the president and CEO of the Alzheimer's Foundation International.

AFI is working toward collaboratively setting a paradigm of quality care for individuals with the disease and their families by raising awareness of Alzheimer's disease and related dementias, providing education, and establishing programs and services that can be replicated in countries around the globe.

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AFI's goals include: advocating to make Alzheimer's disease and related dementias a national priority in a country; working in partnership to advance this disease state as a global health crisis that requires worldwide attention; promoting public awareness and understanding of Alzheimer's disease and related illnesses; improving quality of life for individuals with dementia and their families; and raising the bar on dementia care, provided by informal and formal caregivers.

Accomplishing these goals include: educating families and professionals about diagnosis, treatment and care, including the importance of early detection; providing education, social services and community resources for individuals with Alzheimer's disease and related dementias, their caregivers and families; advancing programs and services that meet the educational, emotional, financial, practical and social needs of individuals with dementia and their families; providing education and training, and promoting best practices for healthcare professionals; and minimizing informal and formal social care and medical costs on families.

The National Alzheimer's Project Act passed by Congress last year was a groundbreaking first step toward the creation of a National Alzheimer's Disease Plan in the United States. However, it's no secret that the U.S. is behind the curve of several other countries that already have National Alzheimer's Disease Plans in place or in process. We have a lot of homework to do but we can learn a lot from what has already been done overseas—both in planning and in political commitment.

The next crucial step is for an international meeting of those countries by the first quarter of 2012. AFA would be honored to serve as an NGO supporting partner in such an effort and would be glad to work with ADI and others. AFA applauds ADI for its financial support of the 10/66 Dementia Research Group and its commitment to international collaboration.

In AFA's view, the international meeting would ideally consolidate how other countries have approached their plans and would produce a compendium with common threads. Such a meeting would help us develop our plan and help us begin to develop a global approach to this pandemic. The meeting would also include a day or more of panel discussions on established policies as well as innovative care programs abroad as well as those in the U.S., of which there are many. There is little doubt we can get there faster by reviewing what has already been done, what has been successful, and what to avoid.

One example that the U.S. can learn from is the award-winning dementia care available in Israel through Melabev. Melabev is the founding member of the Alzheimer's Foundation of Israel and together they share a combined commitment to serve the Alzheimer's population in Israel. The Alzheimer's Foundation of Israel is a nonprofit organization founded in January 2011 by the Alzheimer's Foundation International (AFI)—an outgrowth of the Alzheimer's Foundation of America.

Melabev has spent the past 30 years developing therapeutic activities that restore the dignity and joy of men and women who suffer from the symptoms of Alzheimer's disease. Its mission is to help elders function at their maximum ability. Melabev does not look at what these older adults have lost but instead focuses on how to bring out and strengthen the incredible person that is inside each of them.

The Melabev network of centers gives people with dementia and Alzheimer's disease a reason to get up in the morning. Melabev Memory Clubs offer memory exercises, stimulating cognitive activities and word games in a friendly social environment for the mild memory and cognitively impaired. Memory Clubs are sub-divided by language: English, Hebrew and Russian (especially for those who forget and revert to their mother tongue). Other Melabev day care centers are multi-lingual. The empathic professional staff conducts a range of innovative age-appropriate, dignified activities for people with Alzheimer's symptoms, such as: dance, art, music gardening, pet therapy, and mental stimulation with computers.

A Melabev team of multi-professionals brings Melabev services and activities right into the family home. Each individual with dementia is given a geriatric assessment and a range of healthcare professionals are available for working with the individual and the family members under their roof.

Not only does Melabev care for the person with dementia, but also for the family caregivers to help cope with their burden of care. This is done through support groups and family meetings with the social workers from the day care centers or home care. Melabev also believes that giving the family knowledge empowers them in their task so they provide a library and resource center, Web site, and lectures with the latest updated information on care of people with dementia.

It provides palliative care for individuals in the end stages of the disease as well as guidance on end of life issues for the whole family. In between regularly scheduled house calls the members of team are accessible by phone whenever needed. Melabev gives families a shoulder to lean on. No other organization in Israel provides home care or home hospice care that is specific to the needs of individuals with Alzheimer's disease and related dementias and their families. The Home Hospice program—and related end-of-life courses in the Institute for the Study of Aging—are funded by the UJA-Federation of New York.

The Institute of Studies on Aging at Shaare Zedek offers courses, seminars and workshops for in-service training that are accredited by the Ministries of Health, Education and Social Welfare. Professionals who work with the elderly, such as nurses, social workers and therapists, come from all over the country to attend. The Institute keeps them updated on the latest findings in the field. There are courses on Alzheimer's disease and dementia and specialized therapies for working with the elderly such as art therapy. The Institute has educated a generation of geriatric professionals.

Israel also has groundbreaking geriatric programs at Herzog Hospital in Jerusalem, whose motto is "Restoring dignity for all." Herzog Hospital is currently the only facility in Israel to combine neurological, behavioral and social approaches in treating the full range of geriatric illnesses—including Alzheimer's disease. Its Center for Neurobehavioral and Neurogeriatric Disorders integrates clinical, research and public education activities in geriatric neurology, psychology, and psychiatry. The In-Patient Division includes a neurobehavioral and psycho-geriatric unit; rehabilitation; a 24-hour hotline, including real-time emergency response; and family and social services that offer family therapy, home visits, support groups and individual consultation. Most uniquely, Herzog also has a specialized emergency room for behavioral and psychiatric issues; and all staff persons—from physicians to social workers—are trained in geriatric approaches to care.

Melabev and Herzog hospital in Israel are just two examples of the many innovative programs available throughout the world. A Congressional call for an international meeting is how we'll learn more. And if we do things right, an international movement will follow.

I'm going to end with a quote from Peter Drucker, a writer who was awarded the Presidential Medal of Freedom, in 2002. He said, "Unless commitment is made, there are only promises and hopes; but no plans." AFA looks forward to working with Members of the Subcommittee to address the important issues raised in today's hearing. Thank you again for the opportunity to testify, and I would be glad to answer any questions.

Mr. SMITH. Mr. Hall, thank you very much. And as you heard from my opening, I think we would be in one accord to try to push the very idea that you and others have espoused. I thank you so much for that.

Mr. Thies?

**STATEMENT OF BILL THIES, PH.D., CHIEF MEDICAL AND  
SCIENTIFIC OFFICER, ALZHEIMER'S ASSOCIATION**

Mr. THIES. Chairman Smith, Ranking Member Payne, I appreciate your giving me the opportunity to speak to you today. My name is Bill Thies. I am the chief medical and scientific officer of the Alzheimer's Association.

I spent most of the time I sat in the back of the room crossing out parts of my presentation because other people were already giving that.

And I think the numbers are really clear. This is an epidemic now. It is big. It is only going to get bigger. I think one of the things that we miss if we focus too much on the numbers is that this is a truly awful disease. It robs you of your memories and abilities, it robs you of your resources, and at the end it robs you of your dignity.

There really is only one way out from under the burden of the Alzheimer's epidemic, and that is by having new and better treatments to either slow the progression of the disease or actually prevent the disease from becoming symptomatic. Those sorts of efforts will, in fact, not only have to be done at a global level, but they also will benefit the whole world.

I think that the Alzheimer's Association has had an international science program for many years. Some of our particular activities have been mentioned. The Alzheimer's Association International Conference on Alzheimer's Disease that is coming up in Paris brings all of the researchers in Alzheimer's from around the world. The international consortium, bringing the biggest sort of collections of genetics studies together, is one where the Alzheimer's Association has been able to step in and fund at the last stage.

I mean, basically, the Association is small by governmental standards, certainly. We do have the ability to convene, catalyze, and then promote the results of various studies. And we will continue to do that as frequently as we can.

We do believe in collaboration with the scientists. Certainly, the Alzheimer's Disease Neuroimaging Initiative (ADNI) study that has already been mentioned by Dr. Hodes has grown to be Worldwide ADNI, which is hosted by the Association. It is particularly important to have those studies grow in an orderly way so they really can be used complementary.

We also have started projects like a European ADNI where we can invest a small amount of money. And you will hear from Dr. Frisoni later. And we particularly believe in trying to identify barriers to progress that actually we can have an impact with with our limited budget. So we do things like a cerebral spinal fluid standardization project in Europe and the United States, which is really designed to make measurements of CSF biomarkers really practical in a clinical sense. We look for those kinds of projects.

And the future is clearly going to be determined by some legislation that has already been passed. National Alzheimer's Project Act (NAPA), I would like to compliment the Members for having voted for that. But we not only have to pass NAPA, we actually have to implement it, and then we have to devote appropriate resources to that implementation. If we don't do that, we simply will have a wasted exercise.

And, finally, I would just like to conclude that I don't think I have to tell those of you up at the panel that activities of the government are not always appreciated for the boons that they are. Some people will tend to disagree with you. But, in fact, efforts that increase the longevity and the quality of the life of the citizen is probably the finest public service that you can do.

We just recently had the national conference of oncologists in Chicago, where they announced a variety of highly specific, terrifically effective new therapies for cancer. Heart disease, over the last 50 years or so, has reduced the number of deaths from heart disease by 1 million a year—1 million people a year that don't die from heart disease from new science. HIV/AIDS has gone from being a virtual immediate death sentence to now a chronic manageable disease.

There is no secret for why that happens. We invest \$6 billion a year for cancer, \$4 billion a year for heart disease, and \$2 billion a year for AIDS. We are at about \$450 million for Alzheimer's disease. Without increasing that significantly, we are going to see the peak of this epidemic and we are going to see the worst possibilities of it.

And what I would challenge the panel to recognize is that this is a place where the United States is going to have to lead. It is going to have to lead the world, because the rest of the world is going to suffer from exactly the same disease without the resources to do anything about it.

Thank you for your attention.

[The prepared statement of Mr. Thies follows:]

U.S. House Foreign Affairs Committee  
Subcommittee on Africa, Global Health, and Human Rights  
Global Strategies to Combat the Devastating Health and Economic Impacts of Alzheimer's Disease

Testimony of William H. Thies, Ph.D.,  
Chief Medical and Scientific Officer  
Alzheimer's Association

June 23, 2011

Good afternoon Chairman Smith, Ranking Member Payne and members of the Subcommittee. Thank you for the opportunity to join you in this discussion about the global impacts of Alzheimer's disease.

I am Bill Thies, Chief Medical and Scientific Officer for the Alzheimer's Association.

**About Alzheimer's Disease**

Since its inception in 1980, the Alzheimer's Association has led the Alzheimer's movement: promoting and funding innovative research; speaking out for greater public awareness and the need for increased research, prevention, and care; and working on a global, national and local level to enhance care and support for all those affected by Alzheimer's and related dementias.

The urgency of the Alzheimer's Association's work is driven by the millions now affected by Alzheimer's. Today, an estimated 5.4 million people suffer from Alzheimer's in the United States<sup>1</sup> and approximately 36 million are affected worldwide.<sup>2</sup> By 2050, there will be as many as 16 million Americans suffering from Alzheimer's, with a projected global total of more than 115 million. Alzheimer's disease is an escalating global epidemic. In almost every country, the proportion of people aged over 60 years is growing faster than any other age group as a result of both longer life expectancy and declining fertility rates.

Alzheimer's is the most common type of dementia that causes problems with memory, thinking and behavior. While research has revealed a great deal about Alzheimer's, with the exception of certain inherited forms of the disease, the cause or causes of Alzheimer's disease remain unknown. The greatest risk factor for Alzheimer's disease is advancing age, but scientists have come to understand that Alzheimer's is not a normal part of aging. In its early stages, memory loss is mild, but with late-stage Alzheimer's, individuals lose the ability to carry on a conversation and respond to their environment, requiring caretakers to provide constant supervision and attentive care.

No treatment is available today to slow or stop the deterioration of brain cells in Alzheimer's disease. Approximately 75 to 100 experimental therapies aimed at slowing or stopping the progression of Alzheimer's are in clinical testing in human volunteers. The Alzheimer's Association applauds the Chairman's leadership on Alzheimer's issues by authoring the Alzheimer's Breakthrough Act, a bill that requires the Director of NIH to accelerate the development of treatments that prevent, cure, or slow the progression of Alzheimer's disease.

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<sup>1</sup> Alzheimer's Association, *2011 Alzheimer's Disease Facts and Figures*.

<sup>2</sup> Alzheimer's Disease International, *World Alzheimer Report 2010*

### **The Global Cost of Alzheimer's**

Alzheimer's disease is a global crisis. Current estimates indicate that about 36 million people worldwide are living with dementia, and that is expected to more than triple by 2050.

Last year on World Alzheimer's Day, the Alzheimer's Disease International (ADI) released the *World Alzheimer Report 2010: The Global Economic Impact of Dementia*, which explores the cost of dementia to our societies. ADI is a London-based, nonprofit, international federation of 73 national Alzheimer's organizations, including the Alzheimer's Association (U.S. member), which was a founding member.

According to the 2010 Report, the global cost of dementia consumes one percent of global Gross Domestic Product (GDP) and is estimated to cost \$604 billion by 2010. About 70% of the costs occur in Western Europe and North America. The Report finds that costs in low and middle income countries are likely to rise much faster than in high income countries, because, with economic development, costs will increase towards levels seen in high income countries, and because increases in numbers of people with dementia will be much sharper in those regions. In the United States, the aging of the population will result in the direct costs to American society of an estimated \$183 billion this year to \$1.1 trillion in 2050. This does not include the \$202 billion in unpaid care provided by nearly 15 million family and friends.

Costs were attributed to the direct costs of medical care (the costs of treating dementia and other conditions in primary and secondary care), direct costs of social care (provided in residential care settings and by community care professionals), and informal care (unpaid care provided by family caregivers and others).

Recently, the Alzheimer's Association called on the World Health Organization (WHO) to make Alzheimer's disease and other dementias a Non-Communicable Disease (NCD) priority. As the costs and prevalence show, the global Alzheimer's crisis demands the attention of the WHO, who can assist in implementing programs to increase the early detection and diagnosis of Alzheimer's; ensure access to medical and non-medical care and support services; promote comprehensive and coordinate care approach to treatment and disease management of those with NDCs; and support the unpaid Alzheimer's caregivers.

This crisis is placing – and will increasingly place – an enormous strain on the health care system, families, and government budgets of nations around the world.

### **Global Research Efforts**

The Alzheimer's Association is committed to accelerating the global effort to eliminate Alzheimer's disease. No single organization can surmount a challenge as great as Alzheimer's. To help achieve our vision of a world without Alzheimer's, the Association partners with key government, industry and academic stakeholders in the global race to end Alzheimer's. We believe in the value of collaboration and are a catalyst toward the time when we will have disease-modifying treatments, preventive strategies and gold-standard care for all people affected by Alzheimer's disease.

The Association formula for progress rests on four pillars. Funding, increasing collaborations with investigators, sharing data, and overcoming barriers to progress. The first pillar is the Alzheimer's Association International Grant Program. Typically 10 to 15 % of our grant funds are expended outside the US. Currently, we fund grants in 24 countries. We fund across the total spectrum of Alzheimer's research from molecular biology to medical systems investigation. Our funding is peer



reviewed by a vast international network of volunteer scientists and quality-assured by our Medical and Scientific Advisory Council, a group of distinguished professionals who represent a range of dementia research, including bench research, clinical care, community health and support services. In addition to funding research directly, we work to ensure the Federal investment in Alzheimer's research is comparable with the public threat of the disease.

The second pillar of the Alzheimer's Association program is encouraging increased cooperation between scientists. The Association is responsible for the largest meeting of Alzheimer's scientists every year. This meeting, The Alzheimer's Association International Conference (AAIC), will attract 5,000 scientists to Paris in July to compare, reveal progress, and develop new working collaborations to advance the disease. AAIC provides a platform for presentation and discussion of all aspects of Alzheimer's research from genetics to animal models, pathology, biomarkers, interventions, and social and behavioral issues. By encouraging the attendance of researchers from around the world, the Alzheimer's Association is able to bring new innovations in Alzheimer's research to a single thought forum designed to accelerate the understanding of Alzheimer's and related dementias. The Association is also the home of the International Society for the Advancement of Alzheimer's Research and Treatment, a collegial society that encourages focus groups for increased cooperation.

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

The fourth and final pillar of our program is selectively investing in projects to overcome common barriers in the field of Alzheimer's. Projects included in this effort, that I will discuss in detail, include TrialMatch™, World Wide Alzheimer's Disease Neuroimaging Initiative (WW-ADNI), and the Cerebrospinal Fluid (CSF) Quality Control Program.

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

WW-ADNI, which the Alzheimer's Association is a major sponsor, is a collaborative effort of scientists from around the world and is the umbrella organization for neuroimaging initiatives being carried out through the North American ADNI, European ADNI (E-ADNI), Japanese ADNI, Australian ADNI (AIBL), and Taiwan ADNI. The Initiative unites leading international investigators in a common effort to:

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

- Document cognitive changes linked to physical changes
- Share data across the international research community

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

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

The Alzheimer's Association Cerebrospinal Fluid (CSF) Quality Control Program, which brings together laboratories across the globe with the aim of standardizing the measurement of potential Alzheimer's biomarkers. Several studies, including studies involving data from the ADNI have shown that levels of biomarkers in CSF are often accurate predictors of which individuals will go on to develop Alzheimer's disease. CSF biomarkers may be useful not only in aiding early detection of Alzheimer's and improving diagnostic accuracy, but also in identifying and monitoring the effects of drugs in clinical trials, understanding the molecular changes that lead to Alzheimer's, and helping to ensure that individuals recruited into Alzheimer's clinical trials are on a path toward developing the disease. More than 60 labs in North and South America, Asia, Australia and Europe are participating in the program.

#### **A Plan for the Alzheimer's Crisis**

The *World Alzheimer Report 2010* contained seven recommendations, one of which called on governments to make dementia a health priority and develop national plans to deal with the disease. Thanks to your support, this year the United States joined the growing list of countries across the world taking an important step towards tackling Alzheimer's disease — the creation of a national plan.

The National Alzheimer's Project Act (NAPA) passed unanimously in both the U.S. House and Senate last December and was signed into law by President Obama in January 2011. The National Alzheimer's Project requires creation of an annually-updated national strategic plan to address the rapidly escalating Alzheimer's disease crisis and will ensure the coordination and evaluation of all national efforts in Alzheimer's research, clinical care, institutional, and home- and community-based programs and their outcomes.

By requiring the government to make Alzheimer's a national priority, create a strategic plan for Alzheimer's, and coordinate its activities, the National Alzheimer's Project has the potential to create the same success that has been demonstrated in the fights against other diseases. Leadership by the Federal government has helped lower the number of deaths from other major diseases such as HIV/AIDS, Influenza and Pneumonia, and stroke. We can and must do the same for the millions of Americans living with Alzheimer's disease.

In addition to improving health outcomes for people living with Alzheimer's and for reducing the financial impact of Alzheimer's on families and our Federally funded programs, NAPA requires the Secretary of Health and Human Services to coordinate with international bodies to integrate and inform the fight against Alzheimer's globally. We hope that the Secretary will work with her global partners to improve the treatment and care of the millions of people living with Alzheimer's.

The Alzheimer's Association is working with the Administration to ensure swift implementation of the National Alzheimer's Project and looks forward to working with Congress once the first annual plan is reported early next year.

**Conclusion**

Thank you for inviting me to participate in this important discussion about the global impact of Alzheimer's disease. The Alzheimer's Association commends the committee for today's hearing and looks forward to continued work together to do all we can to improve the lives of those contending with Alzheimer's, as well as for those who care for them.

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Mr. SMITH. Mr. Thies, thank you so much for your testimony and your extraordinary leadership, as well.

Mr. Vradenburg?

**STATEMENT OF MR. GEORGE VRADENBURG, FOUNDER,  
USAGAINSTALZHEIMER'S**

Mr. VRADENBURG. Thank you, Mr. Chairman, Ranking Member Payne, Mr. Marino, and Mr. Markey. My name is George Vradenburg. I founded USAgainstAlzheimer's last year to try and commit this country to solving Alzheimer's, addressing Alzheimer's, by 2020.

You, Mr. Chairman, have already responded to the three things that I was urging upon you in your opening comments, so I am going to take off in a different direction.

You talked most eloquently and persuasively about the public health crisis that Alzheimer's is and will be becoming. I would like to try and take some of what you have said and build on it, and say that this is not just a public health crisis; it is potentially a fiscal crisis and an economic crisis.

And let me build on that by saying this: There are two major demographic changes—two major demographic changes affecting the world right now.

Number one, we are living longer. For thousands of years, we used to live to age 30, you know, and then by 1900 it was age 50, now it is age 80. That trend isn't going to stop. We are continuing to invest in the extension of life. We are continuing to do what we have been able to do in overcoming infectious diseases and, as Bill just pointed out, what we are doing to achieve better results in terms of heart and cancer, HIV/AIDS, and others. So we are going to extend life well into the 90s, into the 100s. My grandchildren, aging experts tell me, will live to 110 to 120. That is number one.

That particular ability to extend human life has driven American economic growth and the growth of the developed world since World War II. We have increased our population, we have increased our labor participation, we have increased our workforce, and, in fact, we have driven economic growth. And economists will tell us that, because of that extension of life, we probably have doubled or tripled what the GDP would have been had we stayed at a life expectancy of 50 to 60 years old. That is one demographic change. So there is an economic impact to the extension of life.

The second is the changing role of women in the world. In the developed nations, women are increasingly regarded as equals. They are increasingly entering the workforce as equals. And, as a consequence, they are having fewer children. And that means lower fertility rates, and that means that, not only in the developed world are we seeing aging and life extension, but we are seeing fewer people on the younger end of the scale.

Now, what does that mean? In Europe, Western Europe, Russia, United States to a lesser extent, but in the Asian Rim countries, there are declining populations, fewer workers, and more people dependent upon public health systems for their support. That is producing fiscal stress on health systems around the world. And it is producing the risk that the developed world, particularly the Asian Rim and particularly Western Europe, are going to be declin-

ing in their relative economic growth and prosperity in the coming years.

So how is Alzheimer's relevant to all this?

Number one, as we age physically, as we get to 90 or 100 years old—after 85, one in two has Alzheimer's—we are going to see, increasingly, a physically able population but a cognitively disabled population. We are going to be in a situation where we are going to be able—some countries are going to be able to productively employ their older workforce through new technologies and techniques—a physically frail but still physically able population—but we cannot engage those people because of their cognitive disabilities.

So we are going to see Alzheimer's actually having an adverse effect on economic growth in some nations. And those nations that get it right and figure out how to support their aging populations, keeping them healthy and keeping them productive, are going to be winners in the 21st century. And those countries that do not figure out how to solve cognitive disability and how to address aging populations are going to be losers.

And, secondly, on the fiscal stuff, Alzheimer's is particularly costly. A 10-year duration of the disease. The cognitive disability basically means that people forget to take their meds for other purposes. So you are going to see complications of Alzheimer's—Alzheimer's is going to cause complications for diabetes and other diseases. And in the later stages of the disease, you will see greater institutionalization because of the total dependence of the victim.

As a consequence, there are major fiscal impacts as a consequence, particularly, of Alzheimer's. So it is economic growth issue, and it is a fiscal issue. So as we focus on what to do with our aging populations, we need to change our aging populations from people who are taking public benefits through our health-care systems, pension systems, and the like and turn them into productive taxpayers who are participants in the workforce. And that means keeping them healthy. That means not just physical health; that means cognitive health.

And I would suggest, as you have written already, to the United Nations on the NCD conference, it is critical for the world to begin to recognize this not just as a health issue but as a fiscal issue. So, Mr. Chairman, as you were emphasizing the importance you attach to the potential of a government-led but NGO- and corporate-involved international conference among nations that have Alzheimer's plans in place or in process, I would urge that the Treasury Department and the finance ministers be there as well as the health ministers.

Because this is an issue that is confronting the developed world now. And, indeed, in the developing world, where this is going to become a bigger problem, like China, where their population will start shrinking in 20 years, this is going to have major shifts in the relative economic power, economic relationships, and, obviously, the fiscal stability of these sovereign budgets.

So I thank you for the opportunity to be here today. And I applaud your leadership and that of Mr. Markey and the other members of the committee who are here on this subject.

[The prepared statement of Mr. Vradenburg follows:]

**Testimony of George Vradenburg  
Co-Founder and Chairman  
USAgainstAlzheimer's**

**Before the House Committee on Foreign Affairs  
Subcommittee on Africa, Global Health, and Human Rights**

**"Global Strategies to Combat the Devastating Health  
and Economic Impacts of Alzheimer's Disease"**

**June 23, 2011  
Washington, DC**

Good afternoon Chairman Smith, Ranking Member Payne, and members of the Subcommittee. Chairman Smith, you are to be commended for not only calling this hearing but for your steadfast leadership on Alzheimer's disease policy in the U.S. Congress, including your co-founding and co-leading, with Congressman Ed Markey, the Bipartisan Congressional Task Force on Alzheimer's Disease.

Alzheimer's disease and related dementias is a global public health, fiscal and economic crisis that acknowledges no national boundaries. With the aging of global populations, it will inevitably worsen with each passing year. Public health experts may debate the merits of whether or not this is an epidemic, but it is abundantly clear that we are facing a worldwide health and fiscal crisis of major consequence unless the world unites to stop it. If the prospect of over 100 million people, including over 20 million Americans, dying with Alzheimer's in fewer than 40 years – plus a population two to three times that size serving as family caregivers of those terminal victims – is not frightening enough to spur immediate global action, what will be?

It is this frightening specter that spurred my wife and me to join with other like-minded friends and colleagues to form USAgainstAlzheimer's, which has a clear and simple mission – stopping Alzheimer's by 2020. We are well aware of the enormity of this challenge. Yet time and again, America and the world have taken on and conquered enormous challenges, and we strongly believe controlling Alzheimer's within the decade can be achieved if we bring the right focus and resources to bear.

To begin with, we must accept two basic facts about Alzheimer's disease:

- 1) There is no treatment or therapy available today to prevent, modify, stop, or reverse Alzheimer's disease; and
- 2) Because of this dynamic, no one survives Alzheimer's disease. There is no remission. There is no cure. There is no “living with Alzheimer's”, there is only “dying with Alzheimer's”. In the end, Alzheimer's is 100 percent effective in killing its victims.

The research community believes that it is possible to prevent or control Alzheimer's within the decade with a disciplined and adequately funded strategy. As some of my fellow witnesses have already mentioned, the United States is – thanks to the work of Congress and President Obama in enacting the National Alzheimer's Project Act or NAPA earlier this year – working to develop its own National Alzheimer's Plan. But I will submit to you that more must be done – and done more quickly – if we as a nation and world are to be successful in addressing the grave public health and fiscal burdens of Alzheimer's and dementia.

### **Call to Action**

I join my fellow witnesses in calling for immediate actions to achieve the goal of stopping Alzheimer's. Specifically, I offer the following three recommendations:

- 1) **Lead by Example.** The United States has a long and storied legacy of leading the way to address significant health crises. Nearly 60 years ago, we led the effort to eradicate polio. Forty years ago, we declared a war on cancer, a bold statement that resulted in bold action including the establishment of the National Cancer Institute. Thanks in large part to this legacy, many cancers have moved from near-certain death sentences to treatable diseases. More recently, thanks in large part to the work of this very committee, the United States recognized the global threat of HIV/AIDS and enacted the successful President's Emergency Plan for AIDS Relief or PEPFAR. Because of the one-two punch of PEPFAR and the Global Fund to Fight AIDS, Tuberculosis, and Malaria, millions of lives have been saved. I propose to you that through similar leadership – both domestic and international – we can achieve a similar impact against Alzheimer's and dementia.

So what does this leadership look like? First, we must articulate, with urgency, a robust and comprehensive National Alzheimer's Plan, one that accounts for the impact caring for an aging population will have on the healthcare system. We should have in hand by the end of this year a statement of our national goal and a set of initial recommendations. I know Dr. Hodes and many other departments and agencies are working to move the plan process forward.

USA against Alzheimer's and the large tri-sector coalition of Alzheimer's-serving organizations we co-convene with the Alzheimer's Foundation of America (called LEAD, or Leaders Engaged in Alzheimer's Disease), stand at the ready to assist however possible. Yet, we do not yet see a timeline for plan deliverables that matches the urgency of the challenge. We must also include candid yet realistic action items, assign responsibilities for tasks to specific agencies and departments, and hold all parties accountable. We all know any plan is worth little more than the paper on which it is written, absent a clear national goal that can mobilize needed resources, catalyze private and public innovation and lay out an execution plan with defined metrics of progress and mechanisms of accountability.

While the rapid development of the National Alzheimer's Plan is critical, we must not wait patiently for the bureaucracy to do its work or for the ink to dry on a plan document. Rather, we must aggressively seek out and advance all legislative,

administrative, and regulatory opportunities to accelerate high-tempo Alzheimer's outcomes-oriented research and innovative regulatory reforms needed to reduce the time and cost to market of safe and effective treatments for this and other diseases driving up our healthcare costs of the Medicare beneficiary population.

- 2) **Ensure Alzheimer's and dementia are included on the agenda of global institutions responsible for fiscal and health issues, most urgently the upcoming United Nations Summit on Non-Communicable Diseases (NCDs).** I commend Congressmen Markey and Smith for leading a Congressional letter to the United Nations General Assembly advocating for the inclusion of Alzheimer's disease on the agenda of this upcoming landmark summit. USAgainstAlzheimer's and many of the other witnesses here today have taken similar actions, and I am hopeful the UN will heed this call and not miss this important opportunity to address this grave threat. Beyond the UN Summit, we must pursue ways to place Alzheimer's on the agendas of the G8 and G20 groups of nations, the WHO, the OECD and other global institutions charged with health and fiscal issues of global dimension.
- 3) **Convene an international conference of the countries that have or are in the process of developing National Alzheimer's Plans.** In addition to existing multi-lateral mechanisms – such as the Asia-Pacific Economic Cooperation (APEC) and the North Atlantic Dialogue – an innovative tri-sector gathering of international experts in Alzheimer's from government, NGO's and the private sector, would inform the development of the U.S. plan and enable us to contribute to the larger global effort. To be impactful, such a gathering must be outcomes oriented and produce a comprehensive set of recommended global actions in all major categories including:
- Biomedical research and discovery;
  - Diagnostics and early detection;
  - Best practices in clinical care;
  - Evidence-based preventative measures;
  - Access to affordable and quality long-term healthcare support services; and
  - Caregiver support.

This effort must also explore other international collaborations that have successfully addressed global health challenges, notably the Global Fund – and determine if similar public-private mechanisms could be developed and deployed in the global battle against Alzheimer's disease and related dementias.

Mr. Chairman, it is time for meaningful national and global strategies and actions to stop Alzheimer's disease before it devastates our domestic and international economies and hundreds of millions of families. Alzheimer's disease is already forcing our nation and world to spend hundreds of billions of dollars, money we simply don't have. Of the estimated \$183 billion spent last year to care for more than 5 million Americans with the disease, about 70 percent – nearly \$130 billion – is public money through Medicare, Medicaid and other programs.



The question is not will we spend money on Alzheimer's but rather how will we spend it. Do we want to invest in cutting-edge research to discover and develop effective Alzheimer's treatments and therapies and innovative technologies and services to allow greater care at home? Or, do we want to spend our money on lengthy nursing home stays and lengthy hospitalizations, the equivalent of the iron lung and leg brace industries of a half-century ago?

The challenge ahead will not be easy, but America has never shied away from the tough challenges. I submit to you that with the right plan and leadership, commitment of resources, and global cooperation, we can stop Alzheimer's by 2020.

Thank you, again, for calling this hearing. I would be pleased to answer any questions you may have.

Mr. SMITH. Mr. Vradenburg, thank you very much for your testimony. And your full statement and that of all of our distinguished panel—and this is truly a tremendous panel of experts.

My hope is—and, again, as I said this, before I go to Dr. Frisoni, we will share this hearing record with policymakers throughout the entire world. I actually chair the Helsinki Commission, and we meet three times a year, at least. And heads of delegations, usually speakers—speaker of the Duma, for example—head of the Duma—we will be handing this out, because there is a tsunami of disability that is predictable unless drastic action is taken. So, again, I thank you all.

I will now go to Dr. Frisoni, who is coming in from Italy.

Dr. Frisoni, please proceed.

**STATEMENT OF GIOVANNI FRISONI, M.D. (VIA TELECONFERENCE), DEPUTY SCIENTIFIC DIRECTOR, IRCCS-FBF ALZHEIMER'S CENTER**

Dr. FRISONI. Chairman Smith, Senator Markey, honorable Senators of the U.S. Congress, it is an honor to give this testimony to the U.S. Congress.

The aim of my testimony is to stimulate greater coordination of large research efforts in the field of Alzheimer's disease that will be undertaken in Europe and the U.S. In the coming years. As has been already underlined, much has been understood about how Alzheimer's disease develops in the brain, thanks to research carried out in Europe, the U.S., and elsewhere in the past decades.

We currently believe that Alzheimer's develops due to the accumulation in the brain of at least two toxic proteins, amyloid and tau, that, with the variable contribution of the factors that have been mentioned, lead to progressive synaptic and neuronal damage. This has allowed us to design drugs that, administered sufficiently early in the 30-odd-year-long process, should delay or altogether arrest its progression.

Enthusiasm on these achievements is reflected by a number of large research efforts with an innovative approach. While such efforts see active cooperation of scientists across the Atlantic, unfortunately these are not coordinated at the funding level. And I will give you the two most glaring examples, one in the U.S. and one in Europe.

In the U.S., the Alzheimer's Disease Neuroimaging Initiative, which has also already been mentioned by Dr. Hodes, the ADNI, is probably the largest ever single effort in Alzheimer's, entailing 150 million U.S. dollars for 10 years, coming from NIA and industry. ADNI aims to describe the natural history of the disease at the clinical and biological level with a number of highly sophisticated imaging and biochemical techniques. In all medical disciplines, ADNI has pioneered the paradigm of open access to research data, such that any scientist in the world can download an unprecedentedly wealthy database and do science on it.

In Europe, 85 percent of the public research budget of European countries are fully controlled at a national level, and less than 1 percent is reoriented to collaboration or coordination between countries through a number of community programs. This may change in the near future with the advent of joint programming funding

schemes. These are led at the central level by the European Commission and aim to support and catalyze that 85 percent of research funded by national states by establishing closer and robust collaborations. The forerunner of all joint programs is the Joint Programming on Neurodegenerative Diseases, an effort just recently started and focusing mainly on Alzheimer's disease.

Remarkably, a European ADNI is currently active in Europe, thanks to close cooperation between U.S. and EU scientists, and the first JPND, Joint Programming on Neurodegenerative Diseases, is on a topic, standardization of biomarkers, where U.S. and EU scientists of the European Alzheimer's Disease Consortium are working closely together, as Bill Thies was reminding everyone earlier on.

The key role of the Alzheimer's Association, to foster the transatlantic cooperation among scientists, should be here underlined and acknowledged. However, the funding of ADNI in the U.S. and JPND in Europe are not coordinated, such that scientists very closely aligned at the scientific level in the two areas of the world are completely detached when they run for grants. Transatlantic coordination might have the obvious positive fallout of maximizing the effectiveness and cost-effectiveness of research.

Early initiatives, however, are being developed aiming to synergize research efforts across the Atlantic. A scientific infrastructure is under development, funded by the European Commission with overall 9 million euros, that will allow to bring the concept and benefits of cloud computing to imaging neuroscientists working on Alzheimer's. The neuGRID electronic infrastructure will allow global scientists to exploit the enormous amount of scientific information conveyed by large public datasets such as the ADNIs.



The Laboratory of NeuroImaging at the University of California at Los Angeles is full partner in the NeuGRID efforts. Works are under way, led by the Alzheimer's Association, to develop the U.S. chapter of neuGRID, the Cloud Network of the Alzheimer's Association, CNAA, where EU partners will be symmetrically represented.

The neuGRID/CNAA example is just a drop in the vast sea of Alzheimer's research. Funding bodies may wish to borrow this model of cooperation to inform the largest initiatives on Alzheimer's in the EU and U.S. If this will happen and be effective, more funding bodies, from China, Japan, Australia, and elsewhere, may wish to join in.

In conclusion, global research on Alzheimer's is benefiting from enthusiasm of recent scientific discoveries and prospect of an effective cure. Decision makers in the U.S. and EU should capitalize on scientific enthusiasm by developing more effective funding strategies that will allow scientists to progress at greater speed. This will increasingly feed the fire of enthusiasm of scientists with the logs of knowledge and may ultimately lead to find an effective cure for this devastating disease.

And I thank you for your attention.

[The prepared statement of Dr. Frisoni follows:]

<b>NAME</b>	<b>Giovanni B Frisoni</b>
<b>TITLE</b>	<b>Coordination of Research on Alzheimer's Disease Across the Atlantic: This Might be the Right Time</b>
<b>ORGANIZATION AFFILIATION</b>	 <b>The neuGRID Consortium</b>  <b>European Alzheimer's Disease Consortium</b>
<b>DATE OF THE HEARING</b>	<b>June 23, 2011</b>
<b>CONGRESSIONAL COMMITTEE AND SUBCOMMITTEE</b>	<b>House Committee on Foreign Affairs, Subcommittee on Africa, Global Health, and Human Rights</b>

Honorable Senators of the US Congress,

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Much has been understood about how Alzheimer's disease develops in the brain, thanks to research carried out in Europe, the US, and elsewhere in the past decades. We currently believe that Alzheimer's develops due to the accumulation in the brain of at least two toxic proteins (amyloid and tau), that lead to progressive synaptic and neuronal damage. This has allowed to design drugs that, administered sufficiently early in the 30-odd year long process, should delay or altogether arrest its progression. Enthusiasm on these achievements is reflected by a number of large research efforts with an innovative approach. While such efforts see active cooperation of scientists across the Atlantic, unfortunately these are not coordinated at the funding level. I will give the two most glaring examples.

In the US, the Alzheimer's Disease Neuroimaging Initiative (ADNI) is the largest ever single effort in Alzheimer's, entailing US\$ 150M for 10 years coming from NIA (65%) and industry (35%). It aims to describe the natural history of the disease at the clinical and biological level with a number of highly sophisticated imaging and biochemical techniques. In all medical disciplines, ADNI has pioneered the paradigm of open access to research data, such that any scientist in the world can download an unprecedentedly wealthy database and do science on it.

In Europe, 85% of the public research budgets of European countries are fully controlled at a national level, and less than 1% is reoriented to collaboration or coordination between countries through a number of community programs. This may change in the near future with the advent of Joint Programming funding schemes. These are led at the central level by the European Commission and aim to support and catalyse that 85% of research funded by national states by establishing closer and robust collaborations. The forerunner of all Joint Programs is the Joint Programming

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Initiatives are being developed aiming to synergize research efforts across the Atlantic. A scientific infrastructure is under development funded by the European Commission with overall € 9M that will allow to bring the concept and benefits of cloud computing to imaging neuroscientists working on Alzheimer's. The neuGRID electronic infrastructure ([www.neuGRID.eu](http://www.neuGRID.eu)) will allow global scientists to exploit the enormous amount of scientific information conveyed by large public datasets such as the ADNIs. The Laboratory of Neuroimaging at the University of California at Los Angeles is full partner in the neuGRID efforts, and works are under way led by the Alzheimer's Association to develop neuGRID's US chapter (the Cloud Network of the Alzheimer's Association – CNAA), where EU partners will be symmetrically represented. The neuGRID/CNAA example is just a drop in the vast sea of Alzheimer's research, and funding bodies may wish to borrow this model to inform the largest initiatives on Alzheimer's in the EU and US. If this will happen and be effective, more funding bodies from China, Japan, Australia, and elsewhere, may wish to join in.

In conclusion, global research on Alzheimer's is benefiting from enthusiasm of recent scientific discoveries and prospect of an effective cure. Decision makers in the US and EU should capitalize on scientific enthusiasm by developing more effective funding strategies that will allow scientists to progress at greater speed. This will increasingly feed the fire of enthusiasm of scientists with the logs of knowledge, and may ultimately lead to find an effective cure for this devastating disease.

Thank you for your attention.

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Mr. SMITH. Dr. Frisoni, thank you so very much. I know it is very late there. I hope you can hang on a little bit longer for, perhaps, a question or two from the members or, perhaps, our panel, who might want to pose a question to you.

Dr. Cummings?

**STATEMENT OF JEFFREY CUMMINGS, M.D., DIRECTOR,  
CLEVELAND CLINIC LOU RUVO CENTER FOR BRAIN HEALTH**

Dr. CUMMINGS. Thank you, Chairman Smith, Mr. Payne, Mr. Marino. It is a pleasure to be here, and I am grateful for your willingness to call attention to this tremendous problem that we face.

We haven't heard too much about Africa so far, so I am going to say a few things about Africa. And then I am going to tell you about a couple of experiments that we are doing at the Cleveland Clinic Lou Ruvo Center that we think could be exported and could be influential in terms of the way patients are cared for.

So, as you have heard, Alzheimer's disease is age-related, and I would like to make the point that the African continent is aging, just as every continent is. So there are 36 million people in the sub-Saharan African region that are over the age of 60. And that predicts a cognitive impairment number, population, of around 9 million—Alzheimer's disease, plus mild cognitive impairment of various sorts. Dr. Hendrie has done terrific work in Nigeria. There are recent reports from the Congo and from other republics that suggest that the numbers are becoming more comparable to Western numbers over time—that is, high.

For every patient with Alzheimer's disease, there are at least two caregivers. So if we say there are 9 million victims, then we have to say that there are at least 18 million caregivers on the African continent who are involved with Alzheimer's disease. That is a tremendous number, a tremendous burden.

The cost of Alzheimer's disease, of course, is terrific. It is estimated at \$172 billion annually in the United States now. Africa is spending \$2.9 billion annually on its dementia population. And these economies are ill-suited to absorb very much more, in terms of care of elderly and demented individuals. So they are going to have trouble responding meaningfully to the burden, and the increasing burden, that this represents.

Risk factors are very important. And I take Dr. Hodes' admonishment that we don't have the kind of data that we would like, and it is going to be hard to get. We understand, for example, that hypertension in mid-life contributes to dementia in late life. Well, that is a long-term experiment, right, for you to decide whether reducing hypertension in mid-life is going to have an effect 20 or 30 years later.

So we are not going to have the kind of data that we would like to have for intervention. And we are going to have to accept some of the correlative data that we have now, such as there is an association between Alzheimer's disease and high blood pressure, with diabetes, with low educational level, and with head trauma. All of those things are overrepresented in Africa in the population, and they represent very substantial risk factors for cognitive impairment in the African population.

Stroke is a risk factor for Alzheimer's disease. There are twice as many strokes in African blacks compared to African whites. So stroke is playing a substantial role in Alzheimer's disease in Africa.

Nutritional status is compromised in much of sub-Saharan Africa. And we hear a lot about nutrition in children and nutrition in lactating women, but we hear very little about nutrition in the elderly, and yet it is a risk factor for Alzheimer's disease and cognitive impairment.

Stress is a risk factor for Alzheimer's disease. So think of war and famine and refugee status and what that must do to the incidence and prevalence of cognitive impairment in the African population.

Behavioral problems—and I am quoting here Dr. Acosta's work and the tremendous work of the 10/66 Group—behavioral problems such as agitation and depression and sleep disturbances are common in Alzheimer's disease. They have been shown to be present in 70 percent of dementia patients in developing countries—so, very high.

Dementia has largely been under-prioritized, I think for financial and simple educational reasons, in Africa. The policies that could be supported would be: Increasing awareness; they would be social protection. Mr. Payne, you mentioned that when there is displacement of populations, the last protected are the elderly. So social protection programs would go a long way toward helping this. Access to good-quality, age-appropriate health care would be very important. And reducing disability could make a tremendous impact in the lives of these patients.

Now, I will just tell you about two things we doing at the Cleveland Clinic that I think are important.

One is our patients first philosophy. You have the choice of taking the science to the patient or taking the patient to the science. So we said, let's put the patient in the middle, let's make them the focus, let's try to understand the experience they are having. So we took away waiting rooms, for example, because we don't think a patient with mild disease should be in a waiting room with a patient with severe disease. So there are no waiting rooms in our clinics.

We changed the geography so that there is a circle of flow of patients through the clinic and out, so that the only chance of one patient encountering another is in the elevator lobby.

We give a patient a flower when they leave our clinic, because we are trying to make this an experience that, if they can remember it, they will remember it as a pleasant experience, and certainly the caregiver will remember it.

We have built our caregiver programs around the experience of the patients. So we have dance programs, where patients and caregivers come together to dance. We have music programs. We have weekly "lunch and learn" programs. These are the things that we draw people into to help make their lives better.

Finally, we said to ourselves, our interest is in clinical trials. I am basically a person committed to new therapeutics in Alzheimer's disease. And we have way too few Alzheimer's patients coming into clinical trials. A tiny minority of patients with Alzheimer's disease are participating in trials, and yet trials are the only way to get new drugs approved for Alzheimer's disease.

So we said, let's give the patient the message that they can help solve this problem; that doctors and scientists, without the help of the patient, cannot solve Alzheimer's disease; that patients have to be part of the Alzheimer's disease solution. So we empower them to be part of the solution for Alzheimer's disease by participating in clinical trials. And we have some of the highest participation rates in the country for our patient population in clinical trials.

Now, a final point about clinical trials and an experiment we are trying. By and large, clinical trials are conducted at individual sites throughout the country. And they recruit slowly; it is the slowest part of every drug-development program. And almost no drug-development program finishes on time. So we are literally slowing our ability to get to new drugs because we cannot conduct the clinical trials fast enough.

In Cleveland Clinic, what we have decided to do is to make all of the sites of the Cleveland Clinic clinical trial sites. In Nevada, in Ohio, in Florida, everybody is participating in clinical trials. It is all controlled by one IRB, because regulatory hurdles are a major reason for slowing clinical trials. This is one of the barriers that can be solved.

I will tell you a final point, which is that we recently reviewed the 269 Alzheimer's trials being conducted in the world now. Only 28 percent of them are being done in the United States. So trials have been exported outside of the country because we are not able to adequately recruit for them in the United States.

We are very concerned about the quality of some of those trials conducted at international sites. We need to solve the problem of recruitment. We do not have a national Alzheimer's disease clinical trials recruitment program. We need to solve that problem so that we can get more patients into trials in the United States. And we need better collaboration internationally, because most of the trials are being done outside of the United States. Our growth in getting new drugs for Alzheimer's disease depends on international collaboration.

I will stop there. Thank you very much for the opportunity to speak with you.

[The prepared statement of Dr. Cummings follows:]



**House of Representatives  
Committee on Foreign Affairs  
Subcommittee on Africa, Global Health, and Human Rights  
June 23, 2011  
Global Strategies to Combat the Devastating  
Health and Economic Impacts of Alzheimer's Disease**

**Congressional Testimony by Jeffrey Cummings, MD, DSc**

Director, Cleveland Clinic Lou Ruvo Center for Brain Health

Andrea and Joseph Hahn Chair of Neurotherapeutics

Cleveland Clinic Neurological Institute

Las Vegas, Nevada; Cleveland, Ohio; Weston, Florida

**Key points:**

- Alzheimer's disease is an age-related disease and becomes more common when there are more elderly persons
- The number of elderly in the African population is increasing rapidly and the number of persons with Alzheimer's disease is rising
- The approximately 36 million elderly persons in sub-Saharan Africa predicts approximately 9 million persons with Alzheimer's disease now, rising to nearly 15 million by 2030.
- Most of the care of Alzheimer patients is provided by family caregivers who bear much of the emotional and financial toll of the disease; the increase in the number of Alzheimer patients in Africa will greatly increase the demands made on families
- The care of patients with cognitive impairment is costly (\$172 billion annually in the US now); African economies will be strained to provide proper care for African elderly with Alzheimer's disease (current expenditure\$2.9 million USD annually).
- Risk factors for Alzheimer's disease (high blood pressure, diabetes, head trauma, low educational level) are common in African countries and will increase the number of Alzheimer's disease patients beyond that associated with healthy brain aging
- Stroke is a risk factor for Alzheimer's disease; stroke is two-fold more common in Black Africans than in White Africans.
- Nutritional status is poor in much of Sub-Saharan Africa and nutrition of the elderly has received little attention. Poor nutrition is a risk factor for dementia and Alzheimer's disease.
- Stress is a risk factor for cognitive impairment and Alzheimer's disease; famine, war, and refugee status are sources of extreme stress and contribute to an elevated risk of cognitive impairment among Africans
- Behavioral problems such as agitation, depression, and sleep disturbances are common complications of Alzheimer's disease and significantly increase the burden of the disease for patients and caregivers. These symptoms have been reported in 70% of persons with dementia in developing countries.
- Dementia has been under-prioritized; policies to be supported include increasing awareness, social protection, access to good quality age- appropriate healthcare and addressing problems of disability.

### **Aging in Africa**

Between 2005 and 2030, the population of Sub-Saharan Africa over age 60 will approximately double from 36,594,000 to 71,033,000. The population over age 80 will almost triple during this same time period from 2,626,000 to 6,550,000 (Cohen and Menken, 2006; Velkoff et al, 2007). Between 2030 and 2050 the number of older people in this region is projected to double again to over 139 million (Velkoff et al, 2007).

The average annual growth rate of those over age 60 in Sub-Saharan Africa is 2% and will increase to 4% in the next 45 years. This contrasts with growth rate of older persons in developed countries of 2% and a projected decrease to less than 1% (Velkoff et al, 2007).

### **Prevalence of cognitive impairment in Africa**

Rates of cognitive impairment are high in elderly African populations varying among surveyed populations from 24 to 37% (Guerchet et al, 2010). This would translate to approximately 9 million affected persons now and 20 million by 2030.

Surveys of communities in Central Africa reveal prevalence rates of dementia similar to those observed in higher-income countries with approximately 10% of those over age 65 affected (Guerchet et al, 2010). This will translate into 3.6 million persons with dementia now and over 7 million by 2030.

Studies in Nigeria suggested a somewhat lower prevalence of Dementia (2.3%) among elderly (Kalaria et al, 2008).

The current cost of caring for dementia patients in Africa is estimated at 2.9 billion (Kalaria et al, 2008).

### **Aging and dementia in developing countries**

WHO projects that by 2025  $\frac{3}{4}$  of the estimated 1.2 billion people aged 60 years and older will reside in developing countries. By 2040, there will be 81.1 million cases of dementia in the developing world. The largest number will reside in China and India (Kalaria et al, 2008).

Behavioral problems such as agitation, depression, and sleep disturbances increase the burden of the disease for patients and caregivers. These symptoms have been reported in 70% of persons with dementia in developing countries (10/66 Dementia Research Group, 2004; Kalaria et al, 2008).

Dementia has been under-prioritized; policy guidelines include social protection, access to good quality age-appropriate healthcare and addressing problems of disability (Prince et al, 2008).

Incontinence, hearing impairment, and mobility impairment are consistently associated with dementia in developing countries (Prince et al, 2011). These contribute importantly to the disability associated with dementia.

### **Risk factors for Alzheimer's disease and vascular dementia in Africa**

Hypertension is present in 24.4% of Black South Africans; 31.8% of Black South African women are obese; the prevalence of diabetes is at least 8%; the African diet is becoming Westernized with increased fat intake (Bourne et al, 2002).

Stroke is twice as common in Black than White South Africans (Opie and Seedat, 2005).

The rapid urbanization of the Black African population is associated with more diabetes, hypertension and obesity – risk factors for Alzheimer's disease (Opie and Seedat, 2005).

Nutrition attention in Africa has been directed to infants, children, and pregnant and lactating women. Malnutrition is common in the elderly and is under treated. Folate deficiency is common and is associated with cognitive impairment (Charlton and Rose, 2001).

Smoking is a risk factor for stroke and stroke contributes to the occurrence of Alzheimer's disease. 28.1% of adult African males smoke (Akinboboye et al, 2003).

#### **General points:**

- The world's population is rapidly aging and with the increase in older persons all diseases of the elderly are increasing.
- Alzheimer's dementia affects 10% of those over the age of 65 and the diseases is progressing in the brain in twice that number
- Currently there are 35 million Alzheimer's dementia victims in the world; this will grow to 65 million in 2030 and 117 million by 2050.
- Alzheimer's disease strikes a family; not an individual. A minimum of 2 family members are impacted by each person with Alzheimer's dementia
- There are no therapies that prevent or slow the progression of Alzheimer's disease.
- New technologies and new diagnostic criteria are allowing earlier diagnosis of Alzheimer's disease.

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Mr. SMITH. Thank you very much, Dr. Cummings.  
Dr. Hendrie?

**STATEMENT OF HUGH HENDRIE, M.D., PROFESSOR, INDIANA  
UNIVERSITY**

Dr. HENDRIE. Chairman Smith, Ranking Member Payne, and other members of the subcommittee, I am just delighted to be here, to be invited to this really remarkable conference and understanding, again, all of these initiatives that, honest to goodness, Congressman, I wasn't very well aware of, so maybe you need to do more education to your republic. And it is wonderful to hear.

I also would like to thank everyone very much for the comments that people have made before over our study, the Indianapolis-Ibadan Dementia Project, which I have been principal investigator of originally, but I am not now the principal investigator, but still involved. And that is what I wanted to talk about today. I thought maybe my best contribution will be to try to bring you through some of the evolution of this particular project. It will show you how these comparative global studies can be very influential in identifying, potentially modifying risk factors, the surprises we sometimes come up with, and the challenges that you have to make them.

Now, I did put with the testimony the outline of the project. Alas, when we went through all of the various iterations, it became very tiny and it required a great effort to read the little comments. So your staff member kindly put it on up on the screen. And if that is okay with Chairman Smith, I could go ahead and very quickly go over the findings.

So, again, you have heard about all of this before. Comparing rates of illness between countries or communities can be very informative. You can compare risk factors then for the illness. And the benefits of the international studies developing in developed countries is it produces huge diversity. So you can look at much, much different environments than you can if you are just concentrating on one country.

Our first venture actually was not in Africa but with the Cree, elderly Cree, in Manitoba, a place where I practiced before. But during the course of this study, we met a very remarkable man, and that was Professor Ben Osuntokun, who was from the University of Ibadan in Nigeria. And he came over to study with us for a year, in the process of this study. And the Indianapolis-Ibadan project is his idea. And I wish I could take credit for it, but it was his.

And so, what he said was—now I can't even read it on there. Oh, well, we tried our best. There are versions of it that are bigger on the table.

But what he said was, he had information from his population in Nigeria, Yoruba, from autopsy studies he had done, that he didn't think Alzheimer's disease occurred in the Yoruba because of a lack of plaques and tangles in the brain and so on.

So what he proposed was a kind of unique thing. He said, why don't we do a classical migrant study? We will look at the Africans living in Ibadan, Nigeria, which is in West Africa, and we will look at the migrant population. That is where most of the African-Amer-

icans came from as part of the slave trade, of course, that came over from West Africa—not all were Yoruba—and were in the various communities.

So we sat down and we wrote the Indianapolis-Ibadan project. We would look at large numbers of community-dwelling elderly people in Ibadan and large numbers of elderly African-Americans living in Indianapolis. And that is what we have been following for the past 20 years. And over that period of time, we have seen over 4,000 people at each side over a long period of time.

So what did we find? Well, the first thing we found was Dr. Osuntokun was wrong, that Alzheimer's disease was, indeed, present in Yoruba, and Alzheimer's disease was producing serious, significant defects for the families. The families were in great distress because of the behavioral symptoms that have been described before by Daisy Acosta. But the rates were lower in Yoruba at that time than the rates in African-Americans.

I should be very cautious about this. When we compare them with all of the rates of all the different countries in the world that have been published, they weren't out of the boundaries. So that the Yoruba were at the lower level of rates, the African-Americans were at the higher level, but they were all within the ballpark. There was nothing new.

But the other thing that was surprising about this or was interesting about this was, it wasn't just rates of Alzheimer's disease that were lower; rates of diseases which are considered risk factors for heart disease were also lower, so lower rates of hypertension, lower rates of diabetes, lower rates of stroke. Actually, at that time, they were skinnier, their BMI was lower. The few studies we did of cholesterol levels showed that cholesterol levels were also lower. And there are a lot of different lifestyle factors involved with that, particularly diet. And we can talk about the diet issues later.

So we were excited about that, and we thought there was clearly a connection between the heart and brain. That was relatively new at the time we talked about it, but now it is, as you see, pretty well-established. In fact, I think Bill Thies once said, "What is good for the heart is good for the brain," which was a nice way to summarize the information.

So what we planned to do at that stage was we would increase the intensity of looking at risk factors for heart disease in our populations. So we would do biomarkers, diseases, and so on, biomarkers of lipids and inflammatory markers and so on.

But then what we were confronted with was the genetic explosion. All of a sudden, a huge amount of information became available in genetics. First of all, they found this remarkable finding that this form of a gene, APoE-e4, increased the risk dramatically for Alzheimer's disease. Not just in the United States but in almost any other country that we measured, there was almost no exceptions to the rule that e4 increased the disease.

And then, for us, even maybe a more exciting finding from the population geneticists, the population geneticists then said, maybe the anthropologists are right, that it looks as if modern human beings arose in Africa and migrated not terribly long ago, about 150,000, 200,000 years ago. So that if you want to study chronic illness, the likelihood is that all of the genes for chronic illness

were present in the African population, and you should try to incorporate the African population when you are studying the genesis of chronic illness throughout the world, including Alzheimer's disease, which made us, of course, very happy. And we incorporated, then, into our study a large genetic component, as well as the biomarker component that we talked about before in the risk factors.

So, building upon that, we said, well, we are going to look at the biomarkers for cardiovascular disease, and we are going to look at the genetics of Alzheimer's disease, and we are going to look particularly at those genes that people had picked out, the APOE-e4 and so on, that were big risk factors. And this is the model we were going to use.

If you really want to understand Alzheimer's disease rates in any community, you would have to look at both. You look at genetics, look at environmental factors, and, even more importantly, see how they interact with each other. And if I had to bet what is going to happen in research in the next 10, 15 years—it is already happening—is how do genes and the environmental factor interact and alter gene function in the process and may produce illness.

So what did we find? Very quickly, well, with the biomarkers, some surprises, but some not. So when we looked at all of the cholesterol levels, the lipid levels, and so on, they were lower in Yoruba than they were in the African-Americans—not surprising because of their diet. Surprising that one-quarter of African-Americans were now on statins. Even with the statins, there were still lower levels in Yoruba.

And, by the way, in 1991 when we started, the number of African-Americans on statins was almost zero. In 2001, when we did that, a quarter of the population were now taking statins—a very dramatic increase.

But some surprises, like we would have thought oxidative stress would be lower in the Yoruba than it is in African-Americans because of the diet again. It wasn't. The measures of oxidatives were higher in the Yoruba. So it is sometimes very puzzling. Inflammatory markers were just as common in the Yoruba as the African-Americans. So one of the nice things to think about research and this kind of research is it often gives you unusual results that allow you to explore it further.

So the big finding when you put everything together was APOE-e4, the big risk factor for almost the rest of the world, was not a risk factor for the Yoruba—not a risk factor for dementia, not a risk factor for Alzheimer's disease, not a risk familiar for cognitive decline, not a risk factor for mortality—whereas it was in the African-American population and most of the other populations.

And some of the other findings—you mentioned hypertension, for instance. That is one of the nice things I think you can do when you look at different populations—a little sad, in a way, because the Yoruba population, alas, doesn't get the treatment for hypertension that we get in our country. And, in fact, now it looks as if hypertension in old people is definitely a risk for dementia in Nigerians, and once they get above systolic levels of 160 or so on, they ought to be treated. And that information is now being conveyed to the faculty and group at the university hospital.

But, again, a surprise was, when we looked at the lipids, there was an interaction between lipids and—you couldn't understand the effects of the lipids without taking into consideration APoE-e4. So there was some interaction between the both of them. If you added APoE-e4, lipid levels didn't make any difference in the two communities. If you didn't add APoE-e4, lipid levels when they rose increased the risk for dementia. So that made us puzzle, is there some sort of link between e4 and lipid levels, and could this explain some of the differences in the communities?

So one of the things we are going to now look at is we are trying to figure out what is going on. And one of the things going on is that there may be—if e4 is not a risk, there may be other genes that are present that are much more easily identifiable in Nigerians because they are not overwhelmed by the e4 risk. There may be gene clusters that protect against e4 that is particularly seen in the Nigerian population but it would also be seen in others. And, again, as we said, the environmental factors may result in alterations in gene function.

And at the moment what we are doing is we are now expanding the GWAS studies that Dr. Hodes talked about before, both for the African-Americans and for the Nigerians, looking at their generic structure to make new associations. We hope, by combining that genetic information with all of the information we have available at the moment, we will be able to come up with better models of the disease.

Thank you.

[The prepared statement of Dr. Hendrie follows:]



U.S. House Committee on Foreign Affairs  
Subcommittee on Africa, Global Health and Human Rights  
Global Strategies to Combat the Devastating Health & Economic Impacts of Alzheimer's  
Disease

Testimony of Hugh C. Hendrie, MB, ChB, DSc  
Professor, Department of Psychiatry  
Indiana University School of Medicine  
Scientist, Indiana University Center for Aging Research  
Scientist, Regenstrief Institute, Inc.

Good afternoon Chairman Smith, Ranking Member Payne and members of the Subcommittee. I appreciate very much being given the opportunity to testify before this committee on the global impact of Alzheimer's disease.

I am Hugh Hendrie, Professor of Psychiatry and Research Scientist at the Center for Aging Research at Indiana University and the original principal investigator for the Indianapolis-Ibadan Dementia project.

Studies that compare the rate of disease in one country to the rate in another country can help us understand the causes of the diseases. The value of these studies is greatly enhanced if they include comparisons from countries with very different environments such as those from the developed and developing worlds where the greater diversity of environmental exposure may make risk factors more identifiable. Alzheimer's disease is likely to be caused by a complicated interaction of genes, environment and toxic exposures. The recent explosion of knowledge about the genetics of Alzheimer's disease and the genetics of human populations now allows for the incorporation of both genetic and environmental information into these comparative studies. The promise of these studies would be to increase our understanding of Alzheimer's disease causation that is applicable to countries throughout the world and to identify risk factors in these countries that are modifiable. Currently there are few such international comparative projects exploring the risk for Alzheimer's disease and fewer still involving African nations. Currently about 70% of all the elderly worldwide are living in developing countries. The burden of caring for Alzheimer Disease patients in these countries is likely to be staggering.

The National Institute on Aging supported Indianapolis-Ibadan dementia project, which is now 20 years old, exemplifies this approach. The project is a longitudinal comparative study of the incidence and prevalence of dementia and Alzheimer's disease and their associated risk factors in 2 elderly community dwelling residents, African Americans residing in Indianapolis Indiana and Yoruba living in Ibadan Nigeria. Over 4000 residents in each community have been evaluated and followed over this period.

An outline of the evolution of the project and its major findings is included below and will be summarized in this brief presentation.

6/22/2011

**The Evolutionary Path of the  
Indianapolis-Ibadan Dementia Project**

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INDIANAPOLIS-IBADAN COMPARATIVE EPIDEMIOLOGICAL  
STUDY OF ALZHEIMER'S DISEASE

Supported by National Institute of Aging Grant AG02956  
and  
Alzheimer's Association Grant IIRG-04-25464  
Pilot Research Grant IU-95-064

**Goals of Comparative  
Epidemiological Studies**

- Compare rates of illness between communities
- Analyze and compare risk factors for the illness
- Benefits of international studies- increase diversity

**The First Venture – Dementia Screening  
Methods: Indian/Non-Indian Manitoba**

*Supported by the  
National Institute of Aging*

6/22/2011

**Hypothesis/Objectives for Indian/Non-Indian Study – The Influence of Culture**

- Preliminary evidence suggested Alzheimer's Disease prevalence is low in Canadian Native Americans
- This pilot consisted of a comparative study between elderly Cree (treaty Indian) living on two reserves and non-Indian Winnipeg residents (pilot study)
- Eventual goal to conduct a survey of all elderly treaty Indians primarily Cree and Ojibwa living in Manitoba within and outside reserves

**The Role of Ben Osuntokun in the Development of the African Project**

The advantages of studying a migrant population

**INDIANAPOLIS – IBADAN  
COMPARATIVE EPIDEMIOLOGICAL  
STUDY OF ALZHEIMER'S DISEASE**

Supported by National Institute of Aging Grant AG09956  
and  
Alzheimer's Association/F.M. Kirby Foundation Pilot Research  
Grant IRG-95-084

6/22/2011

### Phase I – Epidemiology of Dementia/AD 1992 - 2001

- Objective
  - Comparative study of Migrant Populations – African Americans and Hispanics with similar geographic origins now living in very different environments
  - Compare incidence rates of AD and dementia and their associated risk factors in Hispanic and African Americans
- Risk Factors – Classical Epidemiological
  - Demographics
  - Lifestyle/Factors
  - Cognitive Function
- Outcomes
  - Cognitive Decline
  - Cognitive Impairment/Dementia (multi-domain MC)
  - Dementia
  - Alzheimer Disease
  - Mortality

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### Phase I – Results

- AD was indeed present in Hispanic/Latino migrant populations for the Alzheimer's Disease Center (ADC)
  - Population-based study (1992-2001) – Dementia: African Americans 1.24 (1.1-1.4), Hispanic 1.13 (1.1-1.2), AD: African Americans 1.24 (1.1-1.4), Hispanic 1.13 (1.1-1.2) – lower in migrant populations
  - Rates were within the expected range for educational levels. No comparative studies in Africa / Hispanic risk factors: "African American/Hispanic, Type 2 Diabetes" – lower in Hispanic
- Lifestyle Differ for Population

Risk Factor	African Americans	Hispanic
Uneducated Age	↑	↑
Gender (female)	ns	↑
Low Education	↑	ns
Low Educational Years/Proficiency	↑	ns
High Educational attainment	↓	↓
Alcoholism	↓	ns
Anti-hypertensive	↓	ns

NOTE: ns = not significant; ↑ = risk indicator

↓ = protective factor

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### The Genetic Explosion

- Background
  - Population Genetics – Out of Africa
    - Modern humans originated in Africa and spread throughout the world in a series of migratory waves
    - Risk alleles for chronic illnesses distributed throughout the world across populations are likely to have originated in Africa
  - Studies of genetic risk in AD
    - APOE ε4 is a major risk factor for AD in most populations.

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6/22/2011

### Phase II – Explore Mechanisms of Dementia/AD - 2001

#### Objective / Hypothesis

- To build upon our initial findings and intensify our exploration of potential risk factors for dementia/AD by:
- Adding biomarker measurements from blood samples to assess cardiovascular risk and recording vital signs including BP at all visits
  - Expanding the genetic studies to include DNA from all consenting participants and analyzing APOE and related genes
  - More sophisticated lifestyle assessment
  - Enrich population

AD Center for Aging Research

### Modeling the Contribution of Genes & Environment

Observed Phenotypic Variation = Genes + Environment +

Genes \* Environment + Genes \* Genes + Environment \* Environment

Models for the nature-nurture construct

DeFries and Kuznetsov, 1998

AD Center for Aging Research

### Biomarker Means and Standard Deviations

	Indianapolis (n=1516)	Ibadan (n=1254)	P-value
	Mean ± SD	Mean ± SD	
Cholesterol (mg/dL)	185.66 ± 40.11	174.61 ± 40.88	<.0001
HDL (mg/dL)	51.23 ± 16.53	50.02 ± 13.73	0.0307
LDL (mg/dL)	112.75 ± 34.81	108.70 ± 33.33	<.0001
Triglycerides (mg/dL)	113.40 ± 55.58	89.47 ± 36.44	<.0001

In 2001 22.3% in Indianapolis on statins  
 NB Ibadan had higher levels of a measure of oxidative stress

AD Center for Aging Research



Mr. SMITH. Dr. Hendrie, thank you very much.

I would just say to my colleagues that I have been advised that we will have a series of votes that will last for well over an hour, beginning around 4:10, 4:20. We would need to leave here by about 4:20 or so. So I thought what we might all do, if it is okay, is just, we will all ask our questions, and if you don't just mind then responding just so that everyone gets an opportunity to pose.

I will ask just a couple. Dr. Frisoni talked about the research not being coordinated. It is detached, to use his words. If you could maybe speak to what kind of prioritization you think other countries are doing. You know, if any of you would want to—perhaps, Dr. Acosta, you would be the one.

What countries are doing the best? Is it the U.K.? Is it some other country? You know, a list of, perhaps, some of those countries. Have WHO, PAHO, and other regional health bodies prioritized Alzheimer's sufficiently well, or are we in the beginning stages of getting them to embrace it?

Mr. Vradenburg, you talked very eloquently about bringing members of the Treasury Department and others. Maybe others might want to respond to that, because I think the fiscal crisis parallels the health crisis. And if we underestimate CBO, CMS, and all the other agencies that do numbers-crunching, they will miss by a mile the impact, the devastating impact, that Alzheimer's will have.

And, Dr. Cummings, when you talked about all of the risk factors, since Africa has disproportionately suffered so much trauma—you mentioned DR Congo, 4 million dead due to its wars, ongoing violence against women and all people—is there any indication that that is now manifesting in additional cases of Alzheimer's going forward?

I do have a lot of other questions, like about effective drugs, but in the interest of my colleagues, I would like to yield to Mr. Payne, Mr. Marino, who was here and I am sure will be back, Mr. Connolly, and certainly a good friend and colleague, Mr. Markey. Please.

Mr. CONNOLLY. Mr. Markey has switched sides, obviously.

Mr. SMITH. He has seen the light.

Mr. PAYNE. When I was listening to your comments, Dr. Vradenburg, about the people living to be 110, 120, I was cringing when I thought maybe Mr. Ryan would hear about these numbers and we would be in pretty bad shape.

Let me just ask regarding the studies, Dr. Hendrie—very interesting. And the majority of studies on dementia were conducted in the developed world, but, as you mentioned, estimates of the prevalence of dementia in sub-Saharan Africa are based on limited and dated studies. Your research was a few years ago, and conducted involving Nigeria—still a key source of information.

And do you know, actually, about the prevalence of Alzheimer's in Africa? Has it increased?

In your opinion, what are the greatest challenges in conducting Alzheimer's prevalence studies in the developing world? And what might you expect? I expect that we can focus more attention on these studies that were conducted before we can sort of rev it up again.

I have a number of questions, but let me just stop there. If there is time left, then we could ask another question. But I will just end there, and we can just let other members——

Mr. SMITH. Mr. Markey?

Mr. MARKEY. Thank you so much.

And thank you all for your excellent testimony.

Dr. Cummings, you have worked to expand the use of brain imaging and biomarker technologies to allow Alzheimer's to be diagnosed earlier than before. How do we get more people in the United States and abroad involved in these modern scans to detect plaques and tangles in the brain before they show up as symptoms?

Mr. SMITH. And Mr. Connolly?

Mr. CONNOLLY. Thank you, Mr. Chairman.

And thank you for letting me participate in the subcommittee. I am here because I bumped into Daisy Acosta and my friend George Vradenburg in the cafeteria, and I was not aware of the fact you were having this hearing. And I think it is a very important hearing. Sooner or later, Alzheimer's touches everybody's life.

And maybe I could put a question to Mr. Vradenburg, and that is if you might comment on, where are we from USAgainstAlzheimer's point of view and other advocates in terms of research dollars in the United States? And are they going to the right kinds of research, in terms of efficacy?

Thank you, Mr. Chairman.

Mr. SMITH. Please proceed.

And, Dr. Frisoni, if you wanted to chime in and answer any of the questions, please jump in.

Mr. VRADENBURG. Let me quickly respond to a couple of those.

Has WHO prioritized Alzheimer's? The answer is no. They have one person who has a—John Beard, you mentioned him—a Life Course and Ageing portfolio. They do not have any resource applied to studying the incidence or prevalence of this disease or how to treat it at WHO. And, indeed, they have reached out for private resources, including mine, to help them finance a study at WHO. If my mother were alive and I told her that the World Health Organization at the United Nations was coming to me for finance on how to figure out a study on this problem, she would be surprised.

CBO and OMB will miss this by a mile, you are absolutely right. We do think short term in this country. If, in fact, you talk the word "investment" right now, if you can't show a return within a year, you are having a hard time crossing any of the hurdle rates.

So, in fact, you know, arguing for additional resource to NIH, or to NIA in particular, is a very hard lift, even though you could say, just by looking at historic examples, investment makes a difference. As Dr. Thies pointed out, \$6 billion for cancer and \$4 billion for heart and \$3 billion for AIDS and \$450 million for Alzheimer's.

The death rates: Cancer going down, generally, not across the board, but generally; heart death rates going down. Indeed, heart used to be the highest cost to Medicare; it is now 14th in cost. HIV/AIDS has gone from 60,000, 70,000, 80,000 people dying a year to 10,000. Its cost is now not even in the top 15—or the mortality is not even in the top 15. A hundred billion dollars invested



in HIV/AIDS research saved us \$1.4 trillion in terms of costs. But those things would not have been scored by CBO or OMB.

To your point, Mr. Connolly, there is absolutely no question that this aging phenomenon has overcome us, in terms of our research portfolio. We invested in a lot of the diseases that were—the war on cancer was 1971, the efforts against heart were in the 1980s–1970s, HIV/AIDS was 1980s to 1990s. Alzheimer's has sort of come too late in the public and political consciousness to catch up to those diseases, in terms of our investment. As a consequence, we are way underinvested in terms of the aging agenda and the Alzheimer's agenda.

Mr. HALL. If I may with some of these other disease states that we talked about, the funding came about because there was a cry from the people who were impacted by these diseases and thereby really sort of forced everyone's hand to sort of move.

The problem we have with our population is that the people with the disease are unable to speak for themselves, so you are not going to have a rally of the 5 million here in DC, of them gathering. And, additionally, you are not going to have even their families who are impacted rallying, as well, with such enormous numbers to really push the agenda, because they are engaged 24/7 in the care of the population, the care of their loved one with the disease.

With these other countries that have designed their own Alzheimer's project acts and have put together a plan and moved it forward, the ones that have been most successful, in my estimation, are the ones that have really strong political resolve to get it done.

And it really takes leadership, enormous leadership, to push this disease, especially when you are not going to have that large of a cry from constituents, you know, to say that this needs to get done, because they are not able to rally. But, at the same time, based on everything that you have heard here and things that we have heard for years before this meeting, as well, about the growing population, it really does take enormous political resolve to get this done.

Dr. ACOSTA. I think that by history the World Health Organization and most health systems in all governments in all countries pay more attention to illnesses who have a higher burden on mortality than on disability. But that is definitely changing, because now the most common cause of ill health are chronic illnesses. The WHO had launched the MHA guide last October, and they developed packages of cure for different chronic illnesses. Dementia was one of those seven illnesses.

So I really do encourage all of you to take a look at all of those packages of care when you are developing your national plan because they are set for different countries, a different level according to the budget of each country. I think it is very important.

Dr. CUMMINGS. You asked about other countries and were other countries getting it right. A few examples that I think are important. President Sarkozy will come to the ICAD meeting in July and address us, and he really gets it about Alzheimer's disease. I think he understands the importance. He has championed that in the European Commission as well as in France.

The Queen Sofia Alzheimer's Disease Center in Madrid I think is a centerpiece for Alzheimer's disease care, and she is trying to proliferate that in other cities in Spain. Both Italy and Germany have made new recent progress in terms of creating Alzheimer's disease centers throughout their countries.

So I think we have done a lot, and the NIA program, the other programs you have heard about are terrific. There is more to be done, and there is a lot to be learned from other countries.

Dr. HENDRIE. I would like to respond to Congressman Payne's questions about frequency of Alzheimer's disease in Africa. Just a couple of things about our own study. When we do studies here, we like to get what we call representative samples. So we will look over the population, like our African-Americans in Indianapolis, who are representative of African-Americans throughout our State of Indiana. You can't do that in Africa because we don't have a good enough census. So what you do is you take one particular district or area, and then you try to make sure you see every person in the area, which is a very good way to do it, but it means you can't generalize. So we can't say from our study what it would be like in other parts of Africa or even other Yoruba communities. There hasn't been any really—one other thing about our study is that we saw this link between hypertension and diabetes. In 20 years since we started the study, our data and the data from other studies looking at hypertension in middle-aged people all come to the same conclusion. It is increasing dramatically in Nigeria and increasing dramatically probably in Africa. And if it is increasing dramatically, then I would bet a lot of money that Alzheimer's disease and other dementing disorders are also going to increase rapidly.

There have been a few other pilot studies. There was one very big study done in Egypt which came up with results very similar to the Europeans. Pilot studies in Kenya that we did and in Benin, and so on, came up with rates roughly comparable with ours, but relatively small populations. So rates that we had are the low estimate. And in the near future they are going to go up.

Mr. SMITH. Yes.

Dr. FRISONI. Mr. Chairman, may I add a comment?

Mr. SMITH. Please do, Dr. Frisoni.

Dr. FRISONI. Okay. Thank you. It seems to me that clearly Alzheimer's is a global challenge that requires a global answer. These are times when funding agencies are short of money, and things may not improve dramatically in the foreseeable future. It seems to me from what has been said by a number of speakers that there are three levels of coordination that we can envision, coordination at the level of funding research, coordination at the level of doing research, and coordination at the level of applying the results of research.

Now, the second level, the level of doing research, is the coordination among scientists, and is very good. The AAIC, the international meeting on Alzheimer's has been repeatedly mentioned. And that is a place where scientists from all over the world align their ideas, align their minds.

Coordination at the level of applying the results of research has been mentioned as an area that requires more coordination. What

I have tried to advocate with my testimony is the increased coordination at the level of funding research. In Europe, there is awareness that countries, member countries, so-called member countries of the European Union, must fully join forces. But that will not be enough. Joined forces among European members will not be enough. I suspect, I strongly believe that it will be necessary to join forces between all Europe and the U.S.—at least to start with—at the level of funding agencies, with coordination.

There is an initiative of the European Parliament to develop a directorate to coordinate research across the Atlantic. I believe that this is definitely a big challenge. It is a huge challenge. But it is something that is worth trying.

Mr. SMITH. Dr. Frisoni, thank you so much. We only have about 13 or 14 minutes left. We do have to report for a vote. But Dr. Thies.

Mr. THIES. I would like to say there are two major barriers to progress in Alzheimer's disease. There is clearly not enough money for basic research, and probably we could improve that by coordinating it with other countries.

The second biggest barrier is not enough people in clinical trials. And while I am very unwilling to correct Dr. Cummings, there is a national recruiting program for Alzheimer's trials called TrialMatch. You can access it at ALZ.org or at our 800 number.

Mr. SMITH. Dr. Cummings and then Dr. Acosta.

Dr. ACOSTA. I wanted to address Congressman Markey's question, even though he is not here. He asked how could we get more people into these scans? And I think that is a real problem. I think many doctors in the United States still believe that cognitive decline is normal in aging. We have an enormous educational hurdle ahead of us. One of the things we are trying to do is to develop an electronic medical record that will actually guide people through the dementia workup so that if they don't understand how to do this they could open up an application, maybe it could even be a phone app, and it would guide them through what a good mental status examination and diagnostic workup would be.

So I think we can look to technology to advance us in some of these fields. But again we are still at a relatively primitive level, and we have an enormous hurdle ahead of us for detection of Alzheimer's disease.

Mr. SMITH. Thank you. Dr. Acosta.

Dr. ACOSTA. I don't want you to think of people with dementia as people who cannot have an input in helping you do what you want do. So it is important for you get the consumers' perspective, to include them into their opinions. We have a board member with dementia, and they are excellent in giving us and leading our work.

Mr. SMITH. Dr. Vradenburg?

Mr. VRADENBURG. Mr. Chairman, I would urge you to consider the creation of a national goal to stop—by stop I mean prevent or control Alzheimer's—by 2020. By setting a national goal, you will mobilize the resources necessary to do it. You will force a reexamination of the systems which are impeding the speed at which these developments occur, whether it is basic research, translational research, clinical trial development, or regulatory processes that themselves are sluggish. Capital is leaving this mar-

ket because of the length and time of the cost and time to get to market. And researchers are not going to cure this disease. They may find pathways, but it will be companies that will invest in the drug treatments and other treatments necessary to cure this disease. By setting a national goal, you will mobilize the resources and you will examine the processes that are slowing or making sluggish our path to a solution.

Right now we are building more nursing homes and we are building more care facilities, which is the equivalent of building an iron lung and leg brace industry. And we can think of that as jobs, jobs, jobs, but cures will drive economic growth.

So I would urge your consideration, Mr. Smith, of adopting a national goal in this area.

Mr. SMITH. Excellent idea. Thank you very much, Mr. Vradenburg.

Dr. Acosta, could I just ask you briefly, Dr. Hodes said earlier that with adequate funding, twice as many outstanding research proposals could be resourced. What is the sense of what is happening in other countries? And anyone who would like to address this as well. Are they getting laudable proposals that are falling off the table? And we have not spoken at any length about what is happening in Central and South America. How prioritized is combating Alzheimer's disease south of the border?

Dr. ACOSTA. Definitely not prioritized at all. I think you should set the example. And I am not kidding about this. I will just give you an anecdote. It was very hard for me to get an appointment with our first lady in the Dominican Republic in order for me to propose to them a national plan. The first thing I was asked was what is the United States doing? I said they are working on it. I was never called back again.

So I think you have an enormous duty not only with the United States, but also with other developing countries.

Mr. SMITH. Thank you.

Mr. THIES. I would just comment on the grant question. We just finished our funding for this year, and we will be at about the same stage as NIA. We probably will fund a little over 10 percent of the grants that come to us. I think Dr. Hodes is being characteristically conservative when he says double. I think it is three or four times, with really meritorious projects, and projects that would contribute significantly.

And as a follow-on to George's comment about the development of real medications, those do depend on the corporate sector. And we don't really have any representatives of that sector here.

Actually, I came from another meeting which is going on on the other side of Washington, which is academic scientists, corporate scientists, and regulators that are talking about particular barriers for making progress. We have an interest in investing in Alzheimer's disease treatments from the corporate sector. They don't have enough new ideas, and they don't have certain types of technical ideas, and the reason they don't is that we just don't have the money to fund those.

Mr. HALL. It is quite appropriate that the conversation here goes toward a discussion about research for treatments and a cure. Ultimately, that is what we all want. I would simply ask in the con-

versation going forward that we really need to stay also focused on families and their needs. The care giving burden is left to the family. There are needs for programs and services and some level of support. All the families I have met from coast to coast are not asking for anyone to do their work or their job for them. They fully accept their responsibility. They are simply asking for some help along the way. And so as much as we are focusing on research and cure, I would really like to focus on the role of the caregiver and supporting care giving as well.

Mr. SMITH. Mr. Payne.

Mr. PAYNE. Yeah, and actually in the 1960s and 1970s, when cancer started to be noticed, they had all kind of assistance for families, if you lived in the right place, to help pay your mortgage, et cetera, and so forth.

It seems to me that Alzheimer's, you know, if we could get a goal, it seems like it is a disease that impacts many people. And if there can be a profit. You know, we never saw much work on malaria because, well, even if they found the cure, the people that get it can't pay for it, so no incentive for a company to go look at a cure for malaria. But it seems like Alzheimer's, since it is so predominant across all countries, it seems like that would be financial incentive to these companies to do research.

And the other thing too, Dr. Hendrie, and I probably won't even have time for an answer, but what about the Western diet that has been introduced into say Africa, for example, or probably even China? You know, people were eating what was available, grains, maybe soy stuff, things that were more healthy I guess. Well, now they have become Westernized, and a lot of advertisement about eating what we eat, and so things like diabetes, or seems like those kinds of Western diseases are going to be introduced. Do you think that is a possibility?

Dr. HENDRIE. Just very quickly, I do think that. It is very hard to know the extent in the relatively poor people we are studying just now. But I think there are more processed foods than were available before. You know, it used to be called the Nigerian paradox that in our country hypertension occurs most commonly in poorer people. In Nigeria, it occurred most commonly in richer people. And why was that? Because they were able to buy processed foods and foods that were heavily salted and so on. Now, whether that is true or not now, I don't know. But the change in diet I think is certainly going to be significant.

Mr. SMITH. Sadly, we are out of time. There are nine votes pending on the House floor. I do want to thank our august panel. You have been extraordinary. Your recommendations are all actionable. And I can assure you this subcommittee will do everything possible, and, with Mr. Markey joining on the Energy and Commerce Committee and others, I think we can be very successful. At least we will try.

Without objection, I would like to include a report on a high level seminar at the European Parliament from January 26, 2011. A couple weeks ago I met with a member of the European Parliament, Mario Mauro. I will meet him next week in Brussels and talk further about how we can collaborate with our friends in the European Parliament as well as at the OSCE and other bodies

where we can all work together on combating Alzheimer's. Dr. Frisoni, thank you so much for joining us. And without further adieu, the hearing is adjourned.

[Whereupon, at 4:30 p.m., the subcommittee was adjourned.]

## A P P E N D I X

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MATERIAL SUBMITTED FOR THE HEARING RECORD

**SUBCOMMITTEE HEARING NOTICE**  
**COMMITTEE ON FOREIGN AFFAIRS**  
 U.S. HOUSE OF REPRESENTATIVES  
 WASHINGTON, D.C. 20515-0128

**SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, AND HUMAN RIGHTS**  
**Christopher H. Smith (R-NJ), Chairman**

June 23, 2011

You are respectfully requested to attend an OPEN hearing of the Committee on Foreign Affairs, Subcommittee on Africa, Global Health, and Human Rights, to be held in **Room 2200 of the Rayburn House Office Building (and available live, via the WEBCAST link on the Committee website at <http://www.hcfa.house.gov>)**:

**DATE:** Thursday, June 23, 2011

**TIME:** 2:00 p.m.

**SUBJECT:** Global Strategies to Combat the Devastating Health and Economic Impacts of Alzheimer's Disease

**WITNESSES:** Panel I  
 Dr. Richard Hodges  
 Director  
 National Institute on Aging  
 National Institutes of Health

Panel II  
 Mr. Eric Hall  
 President and Chief Executive Officer  
 Alzheimer's Foundation of America

Bill Thies, Ph.D.  
 Chief Medical and Scientific Officer  
 Alzheimer's Association

Dr. Daisy Acosta  
 Chair of the Executive Board  
 Alzheimer's Disease International

Mr. George Vradenburg  
 Founder  
 USAgainstAlzheimer's

Dr. Giovanni Frisoni (via teleconference)  
 Deputy Scientific Director  
 IRCCS-FBF Alzheimer's Center

Dr. Jeffrey Cummings  
 Director  
 Cleveland Clinic Lou Ruvo Center for Brain Health

Dr. Hugh Hendrie  
 Professor  
 Indiana University

**By Direction of the Chairman**

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



## COMMITTEE ON FOREIGN AFFAIRS

MINUTES OF SUBCOMMITTEE ON Africa, Global Health, and, Human Rights HEARINGDay Thursday Date June 23, 2011 Room 2200 RayburnStarting Time 2:10 p.m. Ending Time 4:27 p.m.Recesses 0 ( to ) ( to ) ( to ) ( to ) ( to ) ( to )

Presiding Member(s)

*Rep. Chris Smith*

Check all of the following that apply:

Open Session ☒Executive (closed) Session ☐Televised ☒Electronically Recorded (taped) ☒Stenographic Record ☒

TITLE OF HEARING:

*Global Strategies to Combat the Devastating Health and Economic Impacts of Alzheimer's Disease*

SUBCOMMITTEE MEMBERS PRESENT:

*Rep. Chris Smith, Rep. Donald Payne, Rep. Tom Marino*

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

*Rep. Ed Markey\*, Rep. Gerry Connolly*HEARING WITNESSES: Same as meeting notice attached? Yes ☒ No ☐

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

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

*Dr. Richard Hodes: Prepared statement**Dr. Jack Goldstone: Prepared statement from Helsinki Commission hearing, submitted by Mr. Smith**Dr. Nicholas Eberstadt: Prepared statement from Helsinki Commission hearing, submitted by Mr. Smith**Dr. Richard Jackson: Prepared statement from Helsinki Commission hearing, submitted by Mr. Smith**Mr. Steven Mosher: Prepared statement from Helsinki Commission hearing, submitted by Mr. Smith**Mr. Eric Hall: Prepared statement**Mr. Bill Thies: Prepared statement**Dr. Daisy Acosta: Prepared statement**Mr. George Vradenburg: Prepared statement**Dr. Giovanni Frisoni: Prepared statement**Dr. Jeffrey Cummings: Prepared statement**Dr. Hugh Hendrie: Prepared statement**The Honorable Russ Carnahan: Prepared statement**newGRID fact sheet*

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

or

TIME ADJOURNED 4:27 p.m.*Sheri A. Pickett*  
Subcommittee Staff Director

**OPENING STATEMENT OF  
THE HONORABLE RUSS CARNAHAN (MO-03)  
SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, AND HUMAN RIGHTS  
U.S. HOUSE COMMITTEE ON FOREIGN AFFAIRS**

**Hearing on  
*Global Strategies to Combat the Devastating Health and Economic Impacts of Alzheimer's  
Disease***

**Thursday, June 23, 2011, 2:00 P.M.  
2200 Rayburn House Office Building**

Chairman Smith and Ranking Member Payne, thank you for holding this hearing on Alzheimer's disease, an increasingly pressing global health issue. Today, I hope our dialogue sheds light on ways to combat Alzheimer's and other global health crises.

Mental and neurological disorders are common in all regions of the world, affecting a broad range of communities. With an aging global population, Alzheimer's disease presents us with a difficult public health challenge, particularly in developed and developing nations. In lower-income countries impacted by Alzheimer's disease or other forms of dementia, diagnosis often comes too little too late, with a staggering 75% of affected people lacking access to the treatment they need.

As Founder and Co-Chair of the Multiple Sclerosis Caucus, I am keenly aware of the need to further our research and treatment of neurological disorders. My district is home to the Charles F. and Joanne Knight Center, one of the world's leading Alzheimer's research facilities. At Washington University in St. Louis, this center has worked for over 25 years to promote collaborative Alzheimer's research and medical training. The center has developed a diagnostic scale that pinpoints dementia severity. This innovation has benefited clinicians across the world. With the global dementia burden expected to nearly double every 20 years, these are the kinds of research facilities we must continue to support.

Healthy aging is an important public health goal. Unfortunately, in Sub-Saharan Africa, life expectancies average only about 45 years. From malaria and neglected tropical diseases to HIV/AIDS, the continent is facing dire public health challenges. Despite significant strides that PEPFAR, other U.S. programs, and efforts of the international community have made in recent years, an estimated 22.4 million are infected and AIDS is still likely to remain the leading cause of death in Sub-Saharan Africa for the next several decades. We must continue to working with our international partners to improve weak health systems, poor infrastructure, and powerful social stigmas that continue to perpetuate HIV/AIDS and other epidemics in Africa.

It is clear that the world faces very stark health challenges—from Alzheimer's disease, multiple sclerosis, and other debilitating neurological disorders to malaria, neglected tropical diseases, and HIV/AIDS among the world's most poor. I thank the witnesses for their presence here today, and I look forward to hearing their testimony.

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

**Testimony of Jack A. Goldstone**

**Hazel Professor of Public Policy**

**George Mason University**

**HEARING CONVENED BY THE COMMISSION ON SECURITY AND  
COOPERATION IN EUROPE**

**“2050: Implications of Demographic Trends in the OSCE Region.”**

**A CHANGING WORLD MAP**

The OSCE nations came together to realize the principles of openness, cooperation, and mutual security, grounded in the protection of basic human rights for all of its member nations and their citizens. At the closing of the cold war, it was clear that these principles were necessary to overcome the legacies of racism, nationalism, and abuses of state power that had caused so many deaths and so much suffering over much of the twentieth century.

Unfortunately, the specters of racism, nationalism, and state power trumping human rights are again being raised in regard to immigration issues in the OSCE region. While most countries in the region have been open to immigration to varying degrees, and many have generous asylum policies for refugees from violence elsewhere, we are seeing calls by some politicians that say ‘enough.’ A new wave of demographic changes, with birth rates plummeting while immigration rises, has raised fears that some European nations are committing slow suicide, or that foreign cultures and legal practices will somehow displace core European legal and cultural values.

It is difficult to overstate the degree to which such fears, while understandable – especially in times of economic crisis – are misplaced. Indeed, they are not only based on misunderstandings, they are positively destructive for the future prosperity of Europe as well as for the OSCE region and even the Old World as a whole.

Simple arithmetic, applied to current demographic trends, shows unambiguously that the OSCE nations will need more immigration in the future. While many of the labor needs in the OSCE region are currently being satisfied by migration within and among OSCE countries, mainly from the eastern portion of the region to the west, this will not suffice in the future. Rather, the OSCE region will need immigrants from outside, including not only the adjacent regions of northern Africa, but also parts of Asia and sub-Saharan Africa.

This statement of course raises fears of an imminent “Eurabia” or “Londinistan” that will be foreign to its own historic inhabitants. But these fears should be recognized to be similar to

those fears of the “yellow peril” and other xenophobic creeds. These fears are based on racism and the worst form of hostile nationalism, and imply nothing less than the belief that non-European peoples are unable to appreciate and acquire the benefits of freedom, equality, and liberty under the law.

Let us grant two truths that make the absorption of immigrants difficult in Europe. First, for most of the last five hundred years, Europe has been a country that sent immigrants OUT, to the rest of the world. From the 1500s up through the 20<sup>th</sup> century, Spanish and Portuguese, English, Irish and Scots, Germans and Swedes, Italians and Poles, even Dutch and French colonists, spread out and established communities in the Americas, Africa, and Asia. However, we may feel today about the mixed results of these imperialist and colonial efforts, it is difficult to imagine what Europe would have looked like – overrun, impoverished, deprived of skills and products gained abroad – if the rest of the world had been able to close its doors and prevent Europeans from leaving their own countries. It has thus been difficult for Europeans to readjust their mental map and realize the world has changed, so that their numbers are stagnating rather than expanding, while the rest of the world has become more numerous, richer, and better able itself to undertake large-scale migration. Some Europeans react to this change, as many people react to any change from past patterns, as a threat, as if reversing the past patterns of global population movement will inevitably bring them harm.

Second, precisely because they have not been able to conceive of foreign immigration as a permanent, long-term shift in their very circumstances, European countries have treated foreign immigrants as temporary guests, often relegated to roles in unskilled labor and housed in neighborhoods separate and often poorly served in regard to social services. Rather than aggressively working to seek integration and assimilation of their migrants, many countries have left them to fend for themselves, so of course they turn inward to their own communities, reinforcing impressions of being closed-off and separate. It is often the very resistance to immigration that breeds the segregation, mutual hostility, and behavioral problems that are blamed on immigration itself.

The best way to overcome the hostility toward migrants within the OSCE region is two-fold. First, the U.S. should lead the way as a country where welcoming and absorption of migrants has been a way of life, and where every economic study shows the benefits of immigration outweighing its costs. Of course, the U.S. still must work on its own misconceptions – for example, the false belief that illegal immigrants ‘pay no taxes.’ This is simply untrue, as anyone in the U.S who pays rent is indirectly paying property taxes, anyone who purchases products pays sales taxes, and anyone on a legal payroll is paying social security taxes. However, the U.S. can show the way forward as a country where immigrants from every region of the world have made crucial contributions to science, sport, business, the arts, and politics.

Second, the OSCE should strive for standards for the active integration of legal migrants into societies. This includes provisions that make it easier to acquire language training, formal education, job training, health care, and quality housing. These investments, as I shall show in a moment, are simply vital to the self-interest of OSCE countries to sustain their own economies and finances. These must also include legal protections against discrimination and defamation

of migrants and their cultures.

At the same time, the OSCE countries must make it clear that immigration is not intended to create enclaves of foreign culture and distinct legal practice – rather all immigrants are expected to follow the existing laws and respect the public practices of the countries to which they have come. Where issues of minority rights and religious practice are concerned, boards of minority and religious leaders must work with local governments to arrive at clear understandings of the limits of separate and distinct immigrant practices. Just as Mormons cannot claim polygamy as a right in the United States, certain religious practices from abroad that contravene prevailing laws and practices in destination countries will also be denied by host countries. However, the presumption in the OSCE countries should always be that the values of equality, freedom, liberty, and protection of basic human rights will prevail, and forms a foundation that immigrants themselves are eager to accept as a reasonable price for the privilege of immigration.

#### THE ARITHMETIC OF DEMOGRAPHIC CHANGE

Demographic projections can often seem to produce a wall of numbers, and be subject to a wide range of uncertainty and dispute. But this need not be the case. The number of people who will be over 60 years old in forty years is pretty clear, because all of them are already alive today.

The number of people who will be born in the next twenty years is more subject to dispute; but patterns of births have been fairly stable for the last few decades, and so reasonable projections based on recent patterns can be made.

To show why immigration patterns are changing, and will change in the future, let us focus on one simple number – how many people in a country are of prime working age, from 15 to 59, compared to how many who are 60 years and older. In the United States today, that number is just over 3. That is, there are just over 3 people of prime working age for every person 60 and older. That is a reasonable ratio to sustain pension and health care costs for the seniors, by taxing the work of those who are still in the prime working years.

However, the U.S. today faces a fiscal crisis in the future because that number is set to decline to about 2 over the next forty years. At a level of only two workers for every older person who still needs income and health care support, taxation and state debt become a problem. Rising health care costs, and shifts in the population toward a larger number of elderly persons, threaten to overwhelm and bankrupt state pension and health care systems. This is why reforms of the US system are needed to avert problems in the future.

But things can get worse. At levels below 2, as one approaches a situation where there is almost one person over 60 for every person aged 15-59, the relationship indicates a crisis in the shortage of prime workers. And that is precisely where many OSCE countries are headed.

Let me ask you to examine Figure 1. This shows that even today, a few countries in Europe have already dipped well below the US level of 3 workers for every senior – some

countries such as Germany and Italy are already approaching the problematic level of only 2 workers per senior. By contrast, countries such as Romania, Russia, Poland, and the US are still at a reasonable 3 workers per senior, and countries further East, such as Turkey and Kazakhstan, have plentiful workers. Their ratio of workers to seniors is 6 to 7 or higher! Thus, it is not surprising that at the present, the major trend of migration within the OSCE nations is from the eastern part of the OSCE region to the west.

However, by 2050, things will change dramatically. Over the next four decades, almost all the countries of Europe will see their senior populations soar while their working age populations remain stable or decline. As a result, their numbers will drop. Italy, Germany, Spain, Romania, and Poland will ALL be coming close to a level of only 1 working age person per senior; even the U.K., France, Hungary, and Russia will drop well below 2. Thus there will be a widespread shortage of workers needed to support the senior population and contribute to keeping economies growing. Even Turkey, alongside the U.S., will drop to around 2 workers per senior, and even Kazakhstan, where birth rates are converging toward those in Europe, will have dropped from labor-rich condition to a reasonable level of 3 workers per senior. Thus by 2050, no regions of the OSCE will be nearly as rich in young workers as they are today. To keep its population growing, and to cope with need to support an older population, OSCE countries, especially those in western Europe, will need to draw on more immigrants from outside the OSCE nations.

Some have pointed to a slight rise in recent births in Russia, France, and the U.K. as evidence that the recent 'birth dearth' is ending. That may be true. But the gains are very small. Moreover, for the next twenty years, any increase in births only results in dependent children who will themselves pose a burden on state and personal finances for health and education, so that they will only begin to contribute to the labor force in significant numbers after 2030.

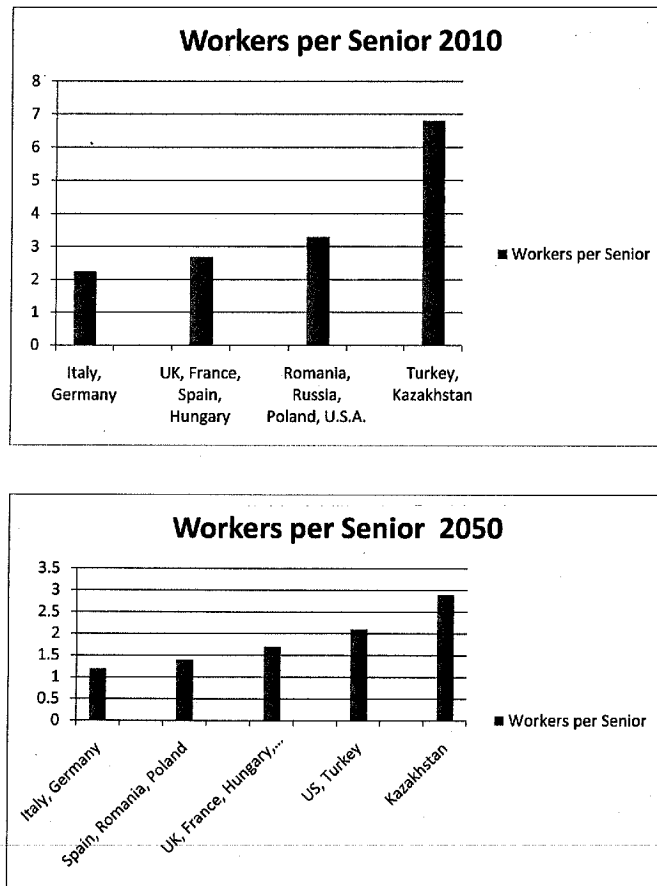
In short, there is no alternative for Europe but to accept that the world has changed, and increased immigration will be part of the mix of policies needed to cope with demographic patterns that will prevail in the future.

But that should be a cause for celebration, not alarm. Throughout history, the most fruitful and innovative societies have been those that mixed peoples from varied culture, and held to pluralist and open societies. This was true of the United States, but also of the periods of greatness in India, the Ottoman Empire, and China. During the Roman Empire – when Europeans were arguably the most powerful nation in the world – the peoples of north Africa and Europe from Scotland to the Danube were united under one set of laws, despite their varied religions and languages. The foundational values of the OSCE, if applied with regard to immigration, can offer an era of continued growth, innovation, variety, and prosperity for Europe and the OSCE nations as a whole. The alternative – nationalist closure, hostility, covert racism – by contrast offers only a return to the horrors of the early 20<sup>th</sup> century. The choice should be clear.

There should be no illusions that the assimilation and integration of migrants from outside the OSCE to its member nations will be simple or without effort. Many complex issues will need to be addressed with energy and dedication, and much effort will be needed to

implement policies designed to manage and smooth immigration. But what projects and gains of great value are achieved without some effort? The gains from a more open and welcoming system of immigration in OSCE countries will be so great, and so necessary, as to more than justify the efforts required to achieve them.

Figure 1. Workers per Senior in selected OSCE countries 2010 and 2050



Dr. Nicholas Eberstadt  
 “2050: Implications of Demographic Trends in the OSCE Region”  
 Hearing before the Commission on Security and Cooperation in Europe  
 Monday, June 20, 2011

Uncorrected remarks

I'm going to talk in the next few minutes about the demographic circumstances and outlook for the OSCE's most populous country, the Russian Federation. Demographers are often chided for seeming to be excessively gloomy for finding the cloud around any sort of silver lining. But when we look at the situation in Russia today, we have to see the makings and prospect for a real demographic crisis, and the most peculiar sort of crisis, because it is a peacetime crisis for an educated and urbanized society. It has humanitarian implications, but I believe it also has economic and security implications.

And with your indulgence, I will run through some slides, which I hope can illustrate what I mean more vividly than my few words. Since the end of the communist era, Russia has seen 13 million more deaths than births. There have been three deaths for every two births in Russia over the past roughly 20 years. If this is all one knew about that society, one would think this was a place in the midst of a prolonged famine or total war; yet, as I mentioned, this is a peacetime, educated, urbanized society.

Thanks to net in-migration, Russia's population decline has been cushioned somewhat but only somewhat. Russia's absolute numbers have dropped by at least 6 million over the last two decades, probably the largest peacetime decline in any human population since the catastrophic consequences and aftermath of China's Great Leap Forward.

So what exactly is going on? The problem – the driver of this situation in Russia is not in particular a collapse in births, although births have dropped in Russia. Russia's fertility patterns look quite European when put in a larger context. Russia is a sub-replacement European society, but its fertility levels, absolute levels, do not look so different from other developed societies.

What we see in Russia is that births have been – childbearing has been at a below-replacement level for a very long time, for perhaps two generations at least, since – for the women born in the 1930s and since.

And fertility levels throughout Russia's ethnicities are perhaps surprisingly low. Chechens are seen in Russia as being famously prolific, but even in Chechnya, birth levels are apparently only at about three births per woman per lifetime, somewhat similar to perhaps less than Mexican-Americans in our own society. The dramatic finding, I think, that one sees is that almost all groups within Russia including, quote, “Muslim heritage groups,” have below-replacement fertility. And Russian ethnics within Russia have one of the very lowest levels of fertility.

There's a great deal of interest within Russia and outside Russia about the population of Islamic or Muslim heritage. These numbers are very difficult to specify with any precision. One study



which has attempted to do this suggests that maybe 10 percent of Russia's population comes from groups that have traditional Muslim cultural heritages, which does not necessarily mean that all the people are believers or practicing if they are adherents.

So this means that Russia's population of people with Muslim backgrounds would be somewhat higher than any in Western Europe, but the comparisons are somewhat difficult to make for historical reasons – the, quote, “Muslim population” in Russia, having been there for hundreds and hundreds of years; Europe's – Western Europe's, quote, “Muslim population” being newcomers or second-, third-generation populations.

It's impossible to make accurate forecasts in the future for a country's population. That being said, there are factors which are pushing fertility prospects down for Russia in the future. One of these is a change in marital patterns. Divorce is coming to Russia with a – with a – with alacrity, let's say. And as in Western Europe we can see that the proportion of children born outside of marriages is increasing quite vigorously. Both of these factors tend to press down on average childbearing levels, especially in places where welfare states are very poorly developed for child support.

So in those ways, Russia looks quite European. When one looks at Russia's health situation, one might say there's a big difference. The outlook and prospect is – might be considered third world. And in some ways, you'll see that that sort of a comparison is unfair to third-world countries.

Unlike any Western European countries, Russia has had a health catastrophe. There's no other word for it. Russia's life expectancy level is a little bit lower now than it was 50 years ago. And if we look at the actual trends that have evolved per capita – I mean, excuse me, age-standardized death levels are over twice as high as in Western Europe. They're 50 percent higher than in the former Soviet bloc countries of the new EU, which were similar to Russia only a generation ago.

There are two drivers behind this health catastrophe.

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There are two drivers behind this health catastrophe. One is cardiovascular deaths. And Russia's level of death from heart disease is over twice as high as would be predicted by the country's income level – difficult, but apparently not impossible.

The other is injury from – is deaths from injury and so-called external causes – homicide, suicide, things like that, poisonings. Russia's level is five times as high as Western Europe's in this regard.

And if all one knew about Russia were its level of deaths from injury, violence and external deaths, one would presume that Russia was a sub-Saharan conflict or post-conflict state, is a – it is a complete outlier from the rest of the developed world's experience.

To make matters even worse, Russia's health disaster is concentrated in its working-age population. For men between their late 20s and late 50s, death rates are typically 100 percent – and I said 100 percent – higher than they were 40 years ago. And for women, death rates are typically 50 percent higher than they were 40 years ago.

One sense one can get of the fragility of the Russian working – workforce's health status is by comparing death rates for Russian men at age 30 with death rates for, let's say, Dutch men at different ages. As of more or less today, a Dutch man who is age 58 has a lower risk of mortality in the coming year than a guy from Russia who is 30 years old. It is an enormously health-challenged population.

And this is true for older people in Russia as well. Their health levels are much more tenuous than those of their Western European comparators.

Russia has a very badly underfunded social security system, makes our Social Security discussions look like a bagatelle, raising the whole question about what is to become of a sick, frail and poor senior population in Russia in the decades immediately ahead.

In doing my research, I thought that Russia's education would be the redeeming virtue that one would find in this otherwise grim human resource system. Unfortunately, not so. If one takes a look at the numbers of patents awarded for inventions generated in different countries, one finds that Russia is orders of magnitudes lower than the G-7, orders of magnitude lower than most of the BRICS, and even lower than some of the tiny East Asian tigers.

The place that most closely tracks Russia, year for year, in total patent awards, is the state of West Virginia. And there many redeeming things about the state of West Virginia, but it is not known as the knowledge center in the United States. It has a tiny population in relation to Russia's huge population.

If one tries to do more detailed comparisons, one can see that Russia is punching below its weight in knowledge generation in any sort of – any sort of way one tends to make the comparison. And this is not true of all postcommunist societies. China, for example, is punching well above its weight. And we see the same thing from other metrics.

So what does this all mean for the long run?

All of the prognoses from different demographic authorities – from our Census Bureau, from the United Nations Population Division, even from Russia’s Goskomstat – sees excess death over birth and population decline more or less as far as a demographer’s eye can go. And pressures for fewer births are going to continue to come as the cohort of women moving into childbearing ages collapses, in echo of previous births in the recent past.

Russia’s working-age labor force is on the way down. It is on track to shrink by about 20 percent over the next 20 years, and no less dramatically, Russia’s urban population is shrinking. Russia is the most prominent place in the world where the total number of people living in cities is on a downward spiral. Cities are the growth engines of a modern global economy. And in Russia’s urban centers health levels are lower than in urban centers in China, in Brazil, in Egypt, in Indonesia, even in India. Thus we have a tremendous challenge for eliciting economic growth.

Russia also has immense and unavoidable demographic constraints in mustering military manpower. Russia’s military – Russia’s manpower of military ages is set to shrink by about 50 percent over the period of 2005 to 2020.

And Russia has vast open spaces. Think of the Russian Far East. The Russian Far East has over 6 million square kilometers and fewer than 6 million people inhabiting. It is more densely populated than Antarctica. It is more densely populated than the Sahara Desert. It is not more densely populated than the Amazonia or Mongolia.

And to make matters even more interesting, people are moving out of Siberia. Russian citizens are moving out of Siberia, not in.

How is Russia going to maintain the sovereignty and integrity of the – of this area in the future? Many Russian demographers wonder whether this is possible.

I’ll stop right there. Thank you, Mr. Chairman.

**Testimony before the**  
**Commission on Security and Cooperation in Europe**  
  
**at the hearing entitled**  
**2050: Implications of Demographic Trends in the OSCE Region**  
  
**by**  
**Richard Jackson**  
**Senior Fellow**  
**Center for Strategic and International Studies**  
  
**June 20, 2011**

Mr. Chairman and Commission Members, I am grateful for the opportunity to testify before the Commission on this important topic.

Many have observed that the recent global economic crisis is helping to accelerate the relative decline of today's developed countries and to drive the rise of today's emerging markets. It is less well understood that demography is pushing in the same direction, though over a much longer time horizon. Demographic change shapes economic and geopolitical power like water shapes rock. Up close the force may appear trivial, but given enough time it can move mountains. The long-term prosperity and security of the United States may depend in crucial ways on how effectively it prepares for the demographic transformation now sweeping the world.

**The Demographic Transformation**

Most of the developed world finds itself on the cusp of an unprecedented new era of rapid population aging and population decline. The developed countries have of course been aging for decades, due to falling birthrates and rising life expectancy. But during the 2010s and 2020s, this aging will get an extra kick as large postwar baby boom generations move fully into retirement. According to the United Nations Population Division (whose projections are cited throughout this testimony), the median ages of Western Europe and Japan, which were 34 and 33 respectively as recently as 1980, will soar to 47 and 52 by 2030, assuming no increase in fertility. In Italy, Spain and Japan, more than half of all adults will be older than the official retirement age—and there will be more people in their seventies than in their twenties.

Meanwhile, the working-age population has already begun to contract in several large developed countries, including Germany and Japan. By 2030, it will be contracting in nearly all developed countries, the only major exception being the United States. In a growing number of countries, total population will also begin a gathering decline. Unless birthrates or immigration surge, Japan and some European nations are on track to lose nearly one-half of their total current populations by the end of the century.

These trends threaten to undermine the ability of today's developed countries to maintain global security. There is, to begin with, the direct impact on population size and GDP size, and hence the manpower and economic resources that nations can deploy—what RAND scholar Brian Nichiporuk calls “the bucket of capabilities” perspective. But population aging and population decline can also indirectly affect capabilities—or even alter national goals themselves. Rising pension and health-care costs will place intense pressure on government budgets, potentially crowding out spending on other priorities, including national defense and foreign assistance. Economic performance may suffer as workforces gray and rates of savings and investment decline. As societies and electorates age, growing risk aversion and shorter time horizons may weaken not just the ability of the developed countries to play a major geopolitical role, but also their will.

The weakening of the developed countries might not be a cause for concern if the world as a whole were becoming increasingly pacific. But this is unlikely to be the case. Over the next few decades, the emerging markets will be buffeted by its own potentially destabilizing demographic storms. China will face a massive age wave that could slow economic growth and precipitate political crisis just as it is overtaking the United States as the world's leading economic power. Russia will be in the midst of the steepest and most protracted population implosion of any major power since the plague-ridden Middle Ages. Meanwhile, many other developing countries, especially in the Muslim world, will experience a sudden new resurgence of youth whose aspirations they may not be able to meet. The risk of social and political upheaval could grow throughout the developing world—even as the developed world's ability to deal with the threats declines.

Yet if the developed world seems destined to see its geopolitical stature diminish, there is one partial but important exception to the trend: the United States. While it is fashionable to observe that U.S. power has peaked, demography suggests that America will play as important a role in shaping the world order in this century as it did in the last.

### **The Impact on Economies**

Although population size alone does not confer geopolitical stature, no one disputes that population size and economic size together constitute a powerful double engine of national power. A larger population allows greater numbers of young adults to serve in war and occupy and pacify territory. A larger economy allows more spending on the hard power of national defense and the semi-hard power of foreign assistance. It can also enhance what political scientist Joseph Nye Jr. calls “soft power” by promoting business dominance, leverage with NGOs and philanthropies, social envy and emulation, and cultural clout in the global media and popular culture.

The expectation that the aging of its populations will diminish the geopolitical stature of the developed world is thus based in part on simple arithmetic. By the 2020s and 2030s, the working-age population of Japan and many European countries will be contracting by between roughly 0.5 and 1.5 percent per year. Even at full employment, the growth in real GDP could stagnate or decline, because the number of workers may be falling faster than productivity is rising. Unless economic performance improves, some

countries could face a future of secular economic stagnation—in other words, of zero real GDP growth from peak to peak of the business cycle.

Economic performance, in fact, is more likely to deteriorate than improve. Workforces in most developed countries will not only be stagnating or contracting, but also graying. A vast literature in the social and behavioral sciences establishes that worker productivity typically declines at older ages, especially in eras of rapid technological and market change. Economies with graying workforces are also likely to be less entrepreneurial. According to the 2007 Global Entrepreneurship Monitor, which surveys fifty-three countries, new business start-ups in high-income countries are heavily tilted to the young. Of all “new entrepreneurs” (defined as an owner of a new business founded within the last three and one-half years), 40 percent are under age thirty-five and 69 percent are under age forty-five. Only 9 percent are aged fifty-five or older.

At the same time, savings rates will decline as a larger share of the population moves into the retirement years. If savings falls more than investment demand, as much macroeconomic modeling suggests is likely, either businesses will go starved for investment funds or the dependence of the developed economies on capital from higher-saving emerging markets will grow. In the first case, the penalty will be borne in the form of lower output. In the second, it will be borne in higher debt service costs and loss of political leverage, which history teaches is always ceded to creditor nations.

Even as economic growth slows, the developed countries will have to transfer a rising share of society’s economic resources from working-age adults to nonworking elders. Graying means paying—more for pensions, more for health care, more for nursing homes and social services for the frail elderly. According to CSIS projections, the cost of maintaining the current generosity of today’s public old-age benefit systems would, on average across the developed countries, add an extra 7 percent of GDP to government budgets by 2030. The extra cost in most continental European countries, with their expansive welfare states, would be even greater.

Yet the old-age benefit systems of most developed countries are already pushing the limits of fiscal and economic affordability. By the 2020s, political warfare over deep benefit cuts seems unavoidable. On one side will be young adults who face stagnant or declining after-tax earnings. On the other side will be retirees, who are often wholly dependent on pay-as-you-go public plans. In France, Germany, Italy, and Spain, over 70 percent of the income of the typical elderly person comes in the form of a government check, compared with roughly 40 percent in the United States. In the 2020s, young people will have the future on their side. Elders will have the votes on theirs.

Faced with the choice between economically ruinous tax hikes and politically impossible benefit cuts, many governments will choose a third option: cannibalize other spending on everything from education and the environment to foreign assistance and national defense. As time goes by, the fiscal squeeze will make it progressively more difficult to pursue the obvious response to emerging military manpower shortages—investing massively in military technology, and thereby substituting capital for labor.

Secretary Gates recently warned that the hollowing out of the defense budgets of our European allies already renders the long-term outlook for NATO “dim, if no dismal.” Demographic trends threaten to make a bad situation even worse.

To be sure, there is significant variation in the demographic outlook across Europe. In France and northern Europe, including the low countries, Scandinavia, and the UK, the fertility rate now averages a relatively buoyant 1.9, not much less than the U.S. rate of 2.1. In Italy and the rest of Mediterranean Europe, the fertility rate averages 1.4—and in Germany and Central Europe, it averages 1.3, on par with Japan. If the demographic outlook for northern Europe is challenging, the outlook for the rest of Europe can only be described as bleak. While Europe’s northern high-fertility zone faces a future of zero workforce growth between now and 2050, the working-age population of Italy and Mediterranean Europe is projected to decline by 22 percent; that of Germany and Central Europe is projected to decline by 29 percent.

This variation poses a serious threat to the economic viability of the European Union, and, in particular, the EMU. The monetary union, of course, is already being buffeted by the sovereign debt crisis. Yet this near-term challenge pales before the longer-term challenge posed by the aging of Europe. The viability of the EMU depends crucially on the effective coordination of fiscal policy among member countries. Yet member countries not only have diverging demographics, but welfare states that vary greatly in their generosity. As the fiscal pressures of aging mount at different rates in different countries, coordination will become increasingly problematic. Some governments may rise to the fiscal challenge and rein in spending. But if others do not, they could end up unleashing inflation on the prudent and profligate alike.

### **The Impact on Social Mood**

The impact of population aging on the collective temperament of the developed countries is more difficult to quantify than its impact on their economies, but the consequences could be just as important—or even more important. With the size of domestic markets fixed or shrinking in many countries, businesses and unions may lobby for anticompetitive changes in the economy. We may see growing cartel behavior to protect market share and more restrictive rules on hiring and firing to protect jobs. We may also see increasing pressure on governments to block foreign competition. Historically, eras of stagnant population and market growth—think of the 1930s—have been characterized by rising tariff barriers, autarky, corporatism, and other anticompetitive policies that tend to shut the door on free trade and free markets.

The shift in business psychology could be mirrored by a broader shift in social mood. Psychologically, older societies are likely to become more “small c” conservative in outlook and possibly more risk-averse in electoral and leadership behavior. Elder dominated electorates may lock in current public spending commitments at the expense of new priorities and shun decisive confrontations in favor of ad hoc settlements. Smaller families may be less willing to risk scarce youth in war. We know that extremely youthful societies are in some ways dysfunctional—prone to violence, instability, and

state failure. Extremely aged societies may also prove to be dysfunctional in some ways, favoring consumption over investment, the past over the future, and the old over the young.

Meanwhile, the rapid growth in ethnic and religious minority populations, due to ongoing immigration and higher-than-average minority fertility, could strain civic cohesion and foster a new diaspora politics in some countries. With the demand for low-wage labor rising, immigration (assuming no rise over today's rate) is on track to double the percentage of Muslims in France and triple it in Germany by 2030. Some large European cities, including Amsterdam, Marseille, Birmingham and Cologne, may be majority Muslim. The problem is not growing diversity itself, but rather the failure of many European countries to assimilate migrants economically and socially. In the United States and the other traditional "immigration countries" like Australia and Canada, migrants constitute an important comparative advantage.

In Europe, the demographic ebb tide may deepen the crisis of confidence reflected in such best-selling books as "France is Falling," by Nicolas Baverez; "Can Germany Be Saved?" by Hans-Werner Sinn; or "The Last Days of Europe," by Walter Laqueur. The media in Europe are already rife with dolorous stories about the closing of schools and maternity wards, the abandonment of rural towns, and the lawlessness of immigrant youths in large cities. A recent cover of *Der Spiegel* shows a baby hoisting 16 old Germans on a barbell with the caption: "The Last German -- On the Way to an Old People's Republic." In Japan, the government half-seriously projects the date at which there will be only one Japanese citizen left alive.

### **U.S. Demographic Exceptionalism**

Over the next few decades, the outlook in the United States will increasingly diverge from that in the rest of the developed world. Yes, America is also graying, but to a lesser extent. The United States is the only developed nation with replacement-rate fertility of 2.1 children per couple. By 2030, its median age, now 37, will rise to only 39. Its working-age population, according to both United Nations and U.S. Census Bureau projections, will also continue to grow through the 2020s and beyond, both because of its higher fertility rate and because of substantial net immigration, which America assimilates better than most other developed countries.

None of this is meant to downplay the serious structural challenges facing the United States, which include a bloated health-care sector, a chronically low savings rate, growing dependence on foreign capital, and a political system that finds it difficult to make meaningful resource trade-offs between competing priorities. All of these threaten to become growing handicaps as our population ages—and, if not addressed, will ultimately undermine our national prosperity and national power.

Yet unlike Europe and Japan, the United States will still have the youth and the economic resources to play a major geopolitical role in the decades ahead. In the end, the biggest challenge facing America by the 2020s may not be so much its inability to lead



the developed world as the inability of the other developed nations to lend much assistance.

### **Tomorrow's Geopolitical Map**

The demographer Nicholas Eberstadt has warned that demographic change may be “even more menacing to the security prospects of the Western alliance than was the Cold War for the past generation.” Although it would be fair to point out that such change usually poses opportunities as well as dangers, his basic point is incontestable: Planning national strategy for the next several decades with no regard for population projections is like setting sail without a map or a compass. In this sense, demography is the geopolitical cartography of the twenty-first century.

Although tomorrow's geopolitical map will be shaped in important ways by political choices yet to be made, the basic contours are already emerging. During the era of the Industrial Revolution, the population of what we now call the developed world grew faster than the rest of the world's population, peaking at 25 percent in 1930. Since then, its share has declined. By 2010, it stood at just 13 percent and it is projected to decline still further in the future to 10 percent by 2050. The collective GDP of the developed countries will also decline as a share of the world total—and much more steeply. According to new projections by the Carnegie Endowment for International Peace, the G-7's share of total G-20 GDP will fall from 72 percent in 2009 to 40 percent in 2050. Driving this decline will be not just the slower growth of the developed world, as workforces in Japan and Europe age and stagnate or contract, but also the surging expansion of large, newly market-oriented economies, especially in East and South Asia.

There is only one large country in the developed world that does not face a future of stunning relative demographic and economic decline: the United States. Thanks to its relatively high fertility rate and substantial net immigration, its current global population share will remain virtually unchanged in the coming decades. According to the Carnegie projections, the U.S. share of total G-20 GDP will drop significantly, from 34 percent in 2009 to 24 percent in 2050. The combined share of Canada, France, Germany, Italy, Japan, and the UK, however, will plunge from 38 percent to 16 percent. By the middle of the twenty-first century, the dominant strength of the U.S. economy within the developed world may have only one historical parallel: the immediate aftermath of World War II, exactly 100 years earlier at the birth of the “Pax Americana.”

All told, population trends point inexorably toward a more dominant U.S. role in a world that will need us more, not less. For the past decade or so, the United Nations has published a table ranking the world's twelve most populous countries over time. In 1950, six of the top twelve were developed countries. In 2000, only three were. By 2050, only one developed country will remain—the United States, still in third place. By then, it will be the only country among the top twelve with a long historical commitment to democracy, free markets, and civil liberties.

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Steven W. Mosher  
 “2050: Implications of Demographic Trends in the OSCE Region”  
 Hearing before the Commission on Security and Cooperation in Europe  
 Monday, June 20, 2011

Uncorrected remarks

I'm an anthropologist and a China hand by training, so I'm going to concentrate on the cultural factors at work here. I will not pit anthropology's four spheres against Dr. Eberstadt and Jackson's demographic statistical juggernaut. But I would say that this is the first time I have ever been on a panel discussing the issue of population when the word “overpopulation” has not once arisen, because we're all concerned today about not what may have seemed to have been the case in 1960 and 1970 but what is actually the real situation on the ground today in this decade, in this century. The real population crises we face today is not a population explosion but a population implosion in country after country around the world.

The old demographic transition charts that I learned back in the 1960s, when I first went to college, showed birth rates leveling off precisely at the replacement rate. Everything was going to be fine. The mortality rate would decline first. Then the fertility rate would follow. Everyone would wind up with a perfect family of a boy for me and a girl for you, and heaven help us if we have three.

That is obviously not the case, since the family of even two children has been scorned by many moderns on their way to extinction, and the declining number of traditional families have been unable to fill the fertility gap thus created.

Recall Peter Drucker, who was a colleague of mine out at Claremont College, at the Light Management Group wrote way back in 1997 that, quote, “the dominant factor for business in the next two decades, absent war, pestilence or collision with a comet, is not going to be economics or technology. It will be demographics.”

Now he was concerned with the increasing underpopulation of developed countries, but decades later – a decade and a half later, this reproductive malaise has spread to many countries in the less developed world and is truly a global phenomenon, affecting all OSCE countries and all OSCE partners.

There is a sentiment out there which I think I saw reflected in the 2010 revision of the U.N. Population Division, where in their median variant they felt somehow that fertility rates were going to swing upward again, and their median variant is actually based on the very optimistic – in my view, rosy – projection that the people in countries with low fertility will suddenly raise their total fertility rate back up to replacement. A few years ago the median variant was based on this rise in fertility rates up to 1.85. Now it's based on a rise in fertility rates up to about 2.1. They give no reason for this optimism, and I can see none. It does, however, make the population projections that they put out somewhat more robust than they would otherwise be.

I believe the real numbers will be lower. They have been lower for the last few decades. The low variant seems to be the best predictor of future population.

I went to Japan for the first time in 1972 as an officer with the U.S. Navy at the tail end of the Vietnam War, and of course the Japanese economic boom was well under way by that time. Industry was flourishing under the guidance of long-range vision plans issued by elite bureaucrats in the Ministry of International Trade and Industry. The salaried men were grinding away at their usual 70-hour work week. Economic growth was consistently running at 4 to 5 percent a year, and Japan's trade surplus with the U.S. was surging towards a hundred billion dollar mark, which seemed a lot at the time.

Later, a decade later, my colleague Ezra Vogel from Harvard wrote a book called *Japan as Number One*, telling Americans that we were falling behind because of our lack of Japanese-style central direction and government and business cooperation. We should, he said, adopt policies more suited to the post-industrial age.

It wasn't long after *Japan as Number One* was published – and of course, it wasn't just Professor Vogel; everyone was looking to Japan to overtake the United States in those years – the Japanese economy ran into a demographic brick wall. Economic growth stalled, averaging an anemic 1 percent growth for most of the '90s. During the Asian economic downturn of 1998, Japan's GNP actually shrank by 2.8 percent. Never number one, Japan soon slipped to fourth behind the EU and China.

What's going on here, of course, is now, since 1964, the Japanese total fertility rate has been below replacement. The Japanese for over four decades now have been having too few children to replace the current population. During the 1990s, Japanese journalists invented a term "demographic shock." In 1993, the demographic shock was that the birthrate was only 1.53 children per woman. It has fallen since then, hovering around 1.3, 1.4 now. The voluntary childlessness of the Japanese exceeds even the forced-pace population reduction in China's one-child policy. Back in 1996, Yamada Masahiro of Gakugei University said that Japan was entering the world's first low-birthrate recession.

So here we have a depopulation crisis that has already forced Japan to slash pensions, to raise the retirement age from 60 to 65 to keep pension funds afloat. We've also – we've had earlier discussion of what's happening in demographic terms, so I won't dwell on the numbers. But Japan is suffering today from the four D's: It is suffering from debt, from deflation and from declining demographics. And the latter two, declining demographics, is ultimately responsible for the first two. It is difficult to see how Japan can pay off its national debt of 2,000 – 200,000 – not 2,000 – 200 percent of GDP with a declining and aging population.

In reaction to this, the government has been encouraging older people to rejoin the workforce and more women to take jobs. They have been focused on the development of industrial robots and, to some extent, encouraging immigration to keep the economy growing. Each of these proposed measures, however, is either a temporary stopgap measure or in some sense self-defeating. The newly rehabilitated elderly, of course, will soon be re-forced to retire again, this

time for good. And as for women joining the workforce in greater numbers, of course, everyone is in favor of giving women every opportunity, but this will surely drive the birthrate down even more and exacerbate the labor shortage over time even further. It would take an estimated 600,000 immigrants a year to offset the impending decline and labor force, and an influx of such magnitude would shake Japan's homogenous and insular monoculture to the core.

What can a country like Japan do to reverse the declining birthrate? The Japanese government has been studying this question now for five years and has – continues to repeatedly revisit the same – the same old solutions, which I do not believe will at all turn around this demographic collapse that we see.

The crises of the empty cradle has crept upon us quietly. We have not reached a stable equilibrium of a lowered mortality rates and low birth rates. Instead, once people are educated, urbanized and begin to enjoy a certain level of wealth, birth rates plummet. More and more couples live in urban conditions where children provide no economic benefits, but rather are, as the Chinese say, goods on which one loses.

I studied – my dissertation research back in the 1970s was a comparative analysis of a fishing and farming community in Taiwan and a close look at the economic value of children who, because they were not allowed on fishing boats, were of less economic value to the fisherman than to the farmers, who could put them to work in the fields at a relatively early age. And of course, the birth rate in the fishing village was lower.

Education delays marriage even further. For materially minded couples in countries where the state provides old age benefits, the way to get ahead is to remain perpetually childless. Why give up a second income to bring a child into the world who will never, at least in material terms, repay your investment? Why provide for your future in the most fundamental way by providing the next generation if the government has pledged to keep you out of the poor house in your old age anyway?

So the modern nanny state has created a strange new world in which the most successful individuals in material terms are the most unfit in biological terms. Wealth and children no longer go together. Wealth used to make it possible to marry earlier, to bring more children into the world, and ensure that more of these children survived. But no longer. Cradle-to-grave welfare systems found in developed countries along with a heavy tax burden leaves Japan – have made the care and feeding of children superfluous to wealth. In fact, they have made children wealth's enemy.

I have the example of Korea before me. In Korea, of course, back in 1961, Korea became one of the guinea pigs in the earliest population control campaigns carried out by our government. Along with Taiwan, South Korea was encouraged to embark upon a population stabilization program. The program quickly evolved into a de facto two-child-per-family policy, complete with strong punitive measures against those who dared violate this limit. Civil and military officials with more than two children were denied promotions and even demoted. Third and higher order children were declared ineligible for medical insurance coverage, educational

opportunities and other government benefits. Couple who agreed to sterilization were given priority access to scarce public housing.

There did matters stand for three long decades. By the time the government of South Korea began to rethink this policy in the mid '90s, the fertility rate had dropped to an anemic 1.7 children. The population was aging rapidly and a full-blown labor shortage had developed. You also had an epidemic of sex-selective abortions where Confucian-minded parents, anxious for sons, were ending the lives of girl fetuses because of their gender.

In 1996 the South Korean government finally got out of the population control business, announcing on June 4th that all restrictions on childbearing would be lifted. No new pre- or no new pro-natal measures were enacted, however, until many years later. The Japanese – the South Korean population is now – now has a TFR of 1.2 or thereabouts, and the South Korean population is beginning to shrink in absolute numbers.

Would that we had left well enough alone in South Korea and in Taiwan, which also has a labor shortage, and would that we would now leave the Philippines alone. We are continuing to press through our embassy there for the Philippines to adopt a two-child policy with some of the same measures that we saw earlier enacted in Taiwan and specifically in Korea. This because the Philippine people have the temerity to be averaging almost three children still, and a robust birthrate which provides immigrants to countries like Japan and South Korea and Taiwan to make up for the demographic shortfall there.

The hundreds of millions of dollars that foreign agencies like USAID have poured into Korea's two-child policy, of course, is but a tiny fraction of the 100 billion (dollars) or so that has been spent on fertility reduction programs in the world at large. Imagine putting billions of dollars into programs to undo the Industrial Revolution or the Information Revolution, and you will understand how our current approach makes no sense. We're making an old-age tsunami even worse, and causing a flood of human misery and global economic malaise at the same time.

So I believe, Mr. Chairman, the sooner that we end population stabilization programs, fertility reduction programs – whatever you want to call them – family planning programs, the better.

What should countries that are experiencing demographic decline do? Well, the European countries, which are in dire straits, all have child allowances in place. In the Germanic countries it's called Kindergeld. But this relatively small amount of money that's given to parents of one or two or three children every month does not begin to compensate for the exactions of the state. I believe that one of the principal anti-natal factors in the world today, and especially in countries that provide cradle-to-grave welfare systems, are tax rates of – that take over 50, even over 60 percent of a young couple's income.

Now, if you reduce a young couple's income by nearly 60 percent, you leave them with so little disposable income that they postpone marriage, they postpone childbearing, and you ultimately reduce completed family size. So one thing that these countries, I believe, should do is when

young couples have children, they should abandon the program of subsidies and instead move to a program where they protect young couples from all taxation.

With one child, perhaps, you would not pay – your taxes would be reduced by one third, with two children, reduced by two thirds, with three children you would pay no taxes to the state, because you would be in the business of paying the cost of raising future taxpayers, which are vital to the continued existence of retirement and pension programs, vital to the continued existence of the people itself.

Governments can do many things, some well, many poorly. But governments cannot reproduce; only people can do that. And young couples who are willing to provide for the future of countries in the most fundamental way by providing the future generation should be cherished and treasured. That is the message that I will be taking to Moscow next week when I go with Professor Eberstadt for the demographic summit there.

It is a drastic measure, to be sure. It is not revenue neutral. It will pit tax breaks for the young against the increasing demands of the increasingly numerous elderly, for the intergenerational compact to be – that the pledges they were given to be kept. But if these countries are to survive, I believe that such measures are certainly called for.

Thank you very much.



## Report: High-Level Seminar at the European Parliament - January 26, 2011

### Executive summary

#### Event objectives

The seminar aimed to:

- Discuss the advancements being made on the innovative idea of building a global virtual imaging laboratory based on grid/cloud computing.
- Call for more action at the political level, generate support from EU policy-makers and advocate for an allocated budget, which will be necessary to implement neuGRID globally.
- Address the possible barriers to harmonisation, namely financial support, interoperability and transparency.
- Facilitate pan-European research on degenerative brain diseases and help develop effective treatments for those diseases.
- Igniting the process to lead these three e-infrastructures to converge into one unique worldwide facility.
- Promote the exchange of technical information, direct the development of the infrastructures towards interoperability and promote specific international calls aiming to achieve full interoperability.
- Increase awareness among policy-makers and populations of the great impact that research infrastructures could have on drug development and medicine as a whole.



This event creates an opportunity for a debate which will pave the way for actions at the political level. Today, we can work to facilitate a better budget line for the promotion of ICT for Health

said MEP Mario Mauro



#### e-Science in action: about neuGRID/outGRID

neuGRID is a user-friendly online network that was created to dramatically accelerate the rate of research into Alzheimer's and other neurodegenerative diseases, facilitating the development of markers of disease progression (such as glycated hemoglobin for diabetes). These will foster the development of effective drugs in clinical trials.

The online platform provides neuroscientists across Europe with a vast database of 3D brain scans and powerful yet accessible computational tools to analyse them. It thus represents a platform of understanding and collaboration between ICT, technical experts and the clinical community.

The neuGRID project, which was implemented from 2004-2011, achieved a major success in September 2009 when it extracted an Alzheimer's disease marker through the use of neuGRID's online archive of thousands of brain scans. With the use of the neuGRID infrastructure, a process that used to take as much as five years was completed in only two weeks. Now that neuGRID has proven its usefulness, the next step will be to harmonise and unify the neuGRID infrastructure with similar networks around the world. outGRID, neuGRID's international umbrella organization, is currently working to coordinate projects across the United States, Canada and Europe.

neuGRID is currently funded by the European Commission. However, in order to maximise the effectiveness of the platform, the project needs to be implemented globally. Harmonizing neuGRID with the few but significant homologous initiatives worldwide will increase the data available, and in turn, render the analysis of brain images significantly more conclusive.

outGRID was created to foster harmonisation and collaboration between neuGRID and two major initiatives in the US and Canada. In Canada and the United States, CBRAIN and the Laboratory of Neuroimaging at UCLA (LONI) currently offer computational resources and algorithm pipelines, by shifting the brain scan analysis process to cloud-computing and relocating all data to a global online platform, outGRID will ultimately lead to the development of a user-friendly, easily accessible global virtual imaging laboratory.

## Event conclusions

### On EU initiatives for the development of new technologies for medical research:

- ICT sector is a key tool to finding new drugs.
- Funding for research in new innovative computing systems should be increased.
- Governments should start investing in the link between research and innovation, which will ultimately lead to healthier lives.

### Challenges ahead:

- The global online network should provide a provenance system in neuGRID allowing users to determine where the medical data comes from.
- In order to make sure that the quality and capacity of the infrastructure is fully used, it is necessary to ensure the complete transparency of the software.
- The question of interoperability remains the major technical obstacle. Establishing a system that is operable and downloadable from anywhere around the world, and useable by any medical expert, is the key priority.

### Next steps:

- Advocating for continued financial support which is necessary to develop a global infrastructure.
- Continuing expert discussions on improving worldwide interoperability.
- Increasing awareness among policy-makers and the public on the role that innovative technologies can play in helping the research for neuro-degenerative diseases, through the organisation of informative seminars.



If this infrastructure is made global, the long term scenario is that many more scientists will contribute to the successful development of disease markers for Alzheimer's disease, the markers will be used in clinical trials, and the drug development process will be greatly facilitated

explained Dr. Giovanni Frisoni.



## Event overview

The seminar event brought together a total of 60 guests, including technical scientists from Europe and North America, policy officers from DG Research and DG INFSO, and a number of third party organisation members and European medical professionals. The objective of the event was to **create momentum for debating how the link between computational power and medical research could be put to best use**. There was **unanimous agreement that funding for research in new innovative computing systems should be increased**, and that the **ICT sector was a key tool to finding new drugs**.

The structure of the event comprised of three parts: an introductory outline of the role which ICT and innovation play in research; a technical outline of the existing grid-computing infrastructures in Europe, the U.S and Canada; and a policy roundtable on the outreach and future of the project.

## Speakers and panellists

The event featured a range of high-profile speakers and participants. The policy part involved speeches by **Mr. Robert Madelin**, Director General INFSO and **Mr. Mario Campolargo**, Director of Emerging Technologies and Infrastructures at DG INFSO. The technical section comprised presentations by **Dr. Giovanni B. Frisoni**, Coordinator of neuGRID and outGRID and Deputy Scientific Director of the IRCCS Fatebenefratelli Institute in Brescia, Italy; **Prof. Richard McClatchey**, Technical Supervisor of neuGRID and Research Director of the Centre for Complex Cooperative Systems, University of the West of England in Bristol, UK; **Dr. Alan Evans**, Principal Investigator of CBRAIN in Montreal, Canada; and **Mr. David Manset**, Technical Coordinator of outGRID and CEO of maatG in Archamps, France.

The presentations were followed by a policy roundtable. The aim of the panel discussion was to **identify common grounds for partnership and address any obstacles to the development of a fully compatible system at the global level**. Composed of North American researchers and European policy-makers in the fields of research and information technologies, the panel was able to bring together perspectives that are relevant and necessary to the global implementation of the neuGRID/outGRID projects. **Mr. Rémi Quirion**, Executive Director of the Canadian Institute of Health Research in Montreal, discussed the current developments in the area of cloud-computing in Canada.



Two members of the European Commission's Directorate General for Information Technologies, **Mr. Kostas Glinos**, Head of Géant & e-Infrastructures Unit, and **Mr. Pāteris Zilgalvis**, Head of ICT for Health Unit, expanded on the Commission's current and planned involvement in e-Infrastructures. **Dr. Philippe Cupers**, scientific officer in the Major Diseases Unit and Joint Programming Representative at DG Research, **advocated a comprehensive approach on technology for the improvement of drug treatments in Europe**, an opportunity enabled by Joint Programming. **Ms. Karin Lohmann**, WP Chair Process Plan in Euro-Imaging, promoted the deployment of biomedical imaging infrastructure in Europe and fostered the liaison and cooperation of all relevant experts in Europe.

### Policy landscape

**All participants were focused on the options for working together to make this research platform a global tool for medical research.** **Mr. Mario Campolargo**, who introduced Mr. Madelin and chaired the first two parts of the event, emphasised that this project was addressing an issue which was not only European, but global.

**The current lack of awareness with regards to the need for a harmonised effort is mirrored in the still insufficient public resource allocation.** In view of this situation, the speakers all called for a revision of the current mindset, and referred to the neuGRID project as a great example of the promising prospects for drug development. **MEP Mario Mauro**, who hosted of the event, called for more action at the political level. He explained that **the challenges ahead laid in sensitising policy-makers and populations** of the great impact which research infrastructures could have on drug development, and medicine as a whole.

"Scientific research can help solve health problems which are present in every house and every street around us", stated Mr. Madelin. "We should see neuGRID and outGRID as the platforms that will begin to bring solutions. We should overcome the tendency of the neuroscientists to resist cross-disciplinary work. **neuGRID is the perfect example of the sort of scientific cooperation that the world requires today.**"



Such discussions are crucial in generating the broad support without which scientific endeavours could not bear fruit

emphasised the Director General INFOS  
Mr. Robert Madelin.



### Technical overview

Dr. Giovanni B. Frisoni explained that Alzheimer's disease develops because, over time, two toxic proteins accumulate in a patient's brain. For maybe 10 or 20 years, the disease remains asymptomatic. After a certain threshold, mild memory problems start to appear. Previously, we were diagnosing the disease on clinical ground, within the dementia window, but we now believe that we can diagnose the disease earlier, before the symptoms appear, through the extraction of a disease marker. **The long term scenario is that we will be able to pick patients with very early Alzheimer's and develop effective drugs on this population. The drugs will hopefully prevent the loss of self-sufficiency and keep the patient in the window of mild memory loss.** In this complex chain, neuGRID aims to foster the implementation of drug trials.

Prof. Richard McClatchey, the approach used to develop neuGRID was to consult the end user community, run requirements analyses and technical reviews, and test the prototypes with periodic data challenges. **Having reached the extraction of marker in 2009, we focused throughout 2010 on training scientists to use the infrastructure prototype, and used the feedback received to build a business plan for the future.** The development of a provenance server in neuGRID was developed specifically so that people can determine where the data come from.

Prof. Alan Evans: "Similar activities have been running in Canada and the US, notably with the creation of CBRAIN in Montreal (McGill University) and LONI in Los Angeles (UCLA), two platforms similar to neuGRID which allow to process data in flexible manner. Our ultimate objective is to expand this process at the global level, and create one single interoperable online platform for research. The scientific projects currently undertaken in various parts of the world are highly compatible, and we should now work on ways to make them converge."

David Monser: "outGRID aims at promoting interoperability between the three infrastructures, CBRAIN, neuGRID and LONI". Facing the task of reaching semantic interoperability, meaning, solving the question of how to make one system understand the other, the outGRID developed a preliminary prototype. "If the current tests succeed, we will be able to prove the reliability and viability of the concept, and start developing a grid-cloud based infrastructure for neuroscientists to expand biomarkers development especially for Alzheimer's, reduce costs of clinical trials, accelerate the rate of research for new drugs, and improve care and health of patients. You therefore need the strong commitment of decision-makers to initiate a larger effort of development worldwide."

### Roundtable and Q&A

During the roundtable, panellists discussed the **interoperability between CBRAIN in Canada, LONI in Los Angeles, and neuGRID in Europe**, and address the possible barriers to harmonisation. Mr. Rémi Quirion gave an overview of the initiatives currently under way at the Canadian Institute of Health Research (CIHR), which are seeking to implement an international collaborative research strategy combining clinical research, personalised research, genetics, Alzheimer's and dementia. Mr. Quirion concluded by stating that the priority was for partners to identify common priorities on research and establish funding and support necessities. "I hope that the outcome of today's conference is that Alan (Dr. Alan Evans) will knock on our door asking to partner with his team and with the Europeans."

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We are open for business; we want to partner with colleagues around the world. We can have an impact in terms of treatment

said Mr. Rémi Quirion.



The question of interoperability remains a challenge but should not be an obstacle. Such events are organised to ensure that all compatibility issues are overcome. Mr. Kostas Glinos explained that we are entering an era where e-infrastructures are important because they allow sharing. Knowledge sharing has great potential, but a number of obstacles, such as interoperability issues, need to be removed. "The challenge today is not how the science itself, but the way you use it. neuGRID and outGRID are a testament of an effort to remove such obstacles to allow scientific progress to advance enormously. This should be a convincing argument to increase funding in the area of e-infrastructures." For this reason, the Commission will publicise a number of documents outline its plans in terms of access and sharing and its views for the next framework programme.

Changes at the EU policy level are noticeable, notably with the funding for research currently having reached 100 million Euros a year. However, in order to make sure the quality and capacity of the infrastructure, complete transparency of the software is crucial, so that neuro-scientists know the scope of the software tools they are using. To achieve this, the tasks of the ICT for Health Unit will be to analyse the current barriers to innovation and map existing initiatives.

Mr. Philippe Cupers provided an overview and political horizon of the Joint Programming on Neuro-Degenerative Research (JPNDR). Behind the establishment of this initiative was the desire to develop a common strategy to address certain societal problems, in this case, neuro-degenerative diseases.

The JPNDR is a voluntary platform which allows Member States to join, share ideas, and maximize the efficiency of national funding schemes. The commission will hold an observer role. Throughout this year, the board will define its strategic agendas and priorities, and launch its pilot call, which might be: "Harmonisation of Cerebrospinal Fluid Biomarkers for Neurodegeneration" (tentative topic). The pilot project will be implemented in 2012.

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Seeing the crucial role which innovation plays in the Europe 2020 Strategy, it is now important to turn societal challenges into opportunities, and start investing in the link between research and innovation, and ultimately build prospects for healthier lives

explained Mr. Pēteris Zilgalvis.

