

MEETING THE CHALLENGES OF GLOBAL BRAIN HEALTH: DIAGNOSIS AND TREATMENT FOR THE 21ST CENTURY

HEARING

BEFORE THE

SUBCOMMITTEE ON GLOBAL HEALTH, GLOBAL
HUMAN RIGHTS AND INTERNATIONAL ORGANIZA-
TIONS

OF THE

COMMITTEE ON FOREIGN AFFAIRS
U.S. HOUSE OF REPRESENTATIVES

ONE HUNDRED EIGHTEENTH CONGRESS

SECOND SESSION

November 20, 2024

Serial No. 118–136

Printed for the use of the Committee on Foreign Affairs



Available: <http://www.foreignaffairs.house.gov/>, <http://docs.house.gov>,
or <http://www.govinfo.gov>

U.S. GOVERNMENT PUBLISHING OFFICE

63–407 PDF

WASHINGTON : 2026

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MEETING THE CHALLENGES OF GLOBAL BRAIN HEALTH: DIAGNOSIS AND TREAT- MENT FOR THE 21ST CENTURY

Wednesday, November 20, 2024

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

The subcommittee met, pursuant to notice, at 2:30 p.m., in room 2172, Rayburn House Office Building, Hon. Christopher H. Smith (chairman of the subcommittee) presiding.

OPENING STATEMENT OF CHAIRMAN CHRISTOPHER H. SMITH

Mr. SMITH. Good afternoon. The subcommittee hearing of the Global Health, Global Human Rights, and International Organizations will come to order. And first let me apologize for the lateness. I was on the floor along with Kathy Manning with a couple of bills that she sponsored and one that I sponsored, so I do apologize and it just finished, so please accept my apologies. And thank you so very, very much for being here.

Without objection, the chair is authorized to declare a recess at any point and all members will have 5 days to submit statements, extraneous material, and questions for the record, subject to the length limitations of the rules. I note the presence of a quorum and I now recognize myself for an opening statement.

Today, we turn our attention to the vitally important issue of global brain health with the specific focus of Alzheimer's disease, autism spectrum disorders, and hydrocephalus. Global brain health is critically neglected. The United States is the leader in health assistance globally with foreign assistance that has saved millions of lives through programs that target malaria, HIV/AIDS, tuberculosis, and many, many other diseases and infectious diseases as well. But comparatively, brain health is overlooked and misunderstood.

A major new study shows that more than three billion people worldwide live with a neurological condition. Neurological conditions are the leading cause of poor health and disability globally. I would note parenthetically that my wife deals with a very rare disease that is known as Marfan's disease. It has to do with brain encephalitis. She is doing very well overcoming it, but it is every-

where and it is not being, I don't think, adequately addressed on a global scale at least by our Government.

As life expectancy grows and healthcare costs rise, policymakers must consider the looming health crisis of brain diseases and disorders, especially in low-and middle-income countries. I have introduced my bill, the Global Brain Health Bill in Congress after Congress after Congress and have not been able to get it passed, but I am absolutely determined that in the next Congress we will see it come to fruition.

Take Alzheimer's disease. Alzheimer's is the most common form of dementia, usually affecting persons aged 60 and older. As we all know, it is degenerative, irreversible, and a terrible disease that progressively corrodes the brain's memory, thinking, and reasoning skills. Currently over 55 million people worldwide live with a form of dementia and 60 percent of those are in developing countries. With life expectancy on the rise, a tsunami of Alzheimer's cases is on the global horizon. In 2011, when I chaired the very first congressional hearing on the topic of the global crisis of Alzheimer's disease, projections estimated at 80 million people would get Alzheimer's or another form of dementia by 2050. In 2015, the projection was revised to a whopping to 115 million.

Today, Alzheimer's Disease International estimates 139 million cases of dementia by 2050 and again, things are getting worse, not better. This increase will be felt more drastically in the low-and middle-income countries as populations grow rapidly and life expectancy, good news story, lengthen.

One recent study found that dementia cases in Sub-Saharan African will grow by over 300 percent. Low-and middle-income countries will struggle to manage this health challenge due to a small and untrained health workforce and inadequate and inaccessible care.

Little public awareness and health professional training on the signs and symptoms of Alzheimer's pose a challenge. A global study by Alzheimer's Disease International found that over two-thirds of people incorrectly think that Alzheimer's and other forms of dementia are just normal parts of aging. As the co-founder and co-chair of the congressional Alzheimer's Task Force, Ed Markey and I formed it back in the year 2000. We have maintained—I have maintained and we have maintained for over a decade that the administration of both parties must pay more careful attention to this mounting crisis. Yes, we have provided more money to NIH. There has been a quadrupling of funding for research and that is absolutely welcome, but more needs to be done, again, on the international level.

I also co-chair the congressional Autism Caucus which I founded in 1999 and I authored the Autism Statistics Surveillance Research and Epidemiology Act, a bill to authorize grants and contracts for the collection, analysis, and reporting of data on autism and pervasive developmental disabilities and establish regional centers of excellence in autism and epidemiology. Passed as part of the Child Health Act in 2000, it was offered as an amendment by yours truly, this provided the basis for future iterations of autism legislation including the Autism Cares Act.

Earlier this year, the House passed my bill, H.R. 7213, the Autism Cares Act of 2024 and I am happy to say after it was blocked in the Senate, that block seems to have been lifted and maybe as early as tonight they may unanimous consent the bill, both sides through the hotline procedure, have agreed to it, so it will become law. And it is a substantial, not only reiteration of current policy and reauthorization, but an expansion as well.

About 1 in 100 children all around the world it is estimated have autism, a spectrum disorder marked by degrees of difficulty with social interaction and communication. While research and care for autism has improved in wealthier countries, such as the U.S. and including chronically how many, it is seriously neglected in much of the developing world. For many living in low-income countries, care is often inaccessible. I will never forget I had a mother was from Cote d'Ivoire at one of my hearings on global autism and she testified and said I couldn't get any help for my son until she moved and migrated to Ohio and then received a plethora of very good intervention and her son was performing and doing very well. There was autism in their family. They were off often socially isolated and stigmatized. Some communities attribute autism to witchcraft which is horrible.

The United States can play a vital role in supporting developing countries and addressing autism spectrum disorders by raising awareness, developing culturally appropriate screening tools, and training parents, teachers, and healthcare professionals on interventions so as to improve the lives of individuals with autism.

Last Congress, I also introduced the Global Autism Act which would establish a program within USAID. I hope to update that and reintroduce that in the next Congress and hopefully we will have some success there.

Finally, our third very important topic of discussion will be on the issue of hydrocephalus. Hydrocephalus is a condition where fluid buildup in the brain leads to swelling of the head and serious brain damage that often ends in death. Hydrocephalus is a tragically common childhood condition. There are nearly half a million cases annually and perhaps many, many more. The most precious gifts in our society, our emphasis on children are the most vulnerable when it comes to hydrocephalus and yet this condition also affects our elderly.

Once again, hydrocephalus plagues infants in the developing countries and again we have a man here today who, Dr. Benjamin Warf, who has been before our committee before, who developed an amazing procedure that has been applied in Uganda and throughout Africa that doesn't require a stent. It has revolutionized the effort. And I will never forget, we had a few of the doctors that he worked with, including indigenous Ugandans, who testified via remote as well as in person and they said when the moms got their kids back and the pain, as well, is mitigated and ended through this, the flow of tears was just almost unimaginable.

So Dr. Warf, you have been a lifesaver. You all have been. But you have been a lifesaver when it comes to hydrocephalus and we thank you. I thank you. We all thank you for the great work you have done.

I will introduce our very, very fine group of individuals in a moment, but I would like to yield to Dr. Bera for any comments you may have.

OPENING STATEMENT OF REPRESENTATIVE AMI BERA

Mr. BERA. Thank you, Mr. Chairman. And I know the Ranking Member, Ms. Wild, is tied up as Ranking Member in the Ethics Committee and will join us as soon as she can. She has got an opening statement.

But again, thank you for holding this hearing on an incredibly important topic.

I am going to focus mostly on Alzheimer's disease with regards to brain health. As the chairman pointed out, the number of people living with Alzheimer's disease and dementia is projected to triple from over 55 million people today to more than 152 million by 2050. The cost of Alzheimer's disease and dementia to the global economy is \$1.3 trillion in 2019 and it will continue to grow exponentially in the coming years as demographic transitions lead to an aging global population.

And while the U.S. Government has increased the domestic R&D budget on Alzheimer's at the NIH by tenfold over the last decade from \$400 million to \$4 billion, there is currently no funding for global Alzheimer's and dementia programs at the global level. So as a doctor, I have seen acutely and as an internist, I am acutely aware of how Alzheimer's disease and dementia affect not only the patient, but also the impact it has on the caregivers and the family and disproportionately in cases affect the female population.

In our district, we have held nine annual brain health forums working with our local Alzheimer's association to provide our constituents with information and resources on the latest Alzheimer's research and what is available to them to assist caregivers and persons living with Alzheimer's or other dementias. That said, however, nearly all Alzheimer's research has been conducted on Caucasian populations of lesser European origin leaving out 90 percent of the world which has significantly limited progress.

That is why today I introduced the bipartisan Global Alzheimer's Initiative Now, or the GAIN Act, alongside my co-leads, Representative Brian Fitzpatrick and Young Kim. The GAIN Act will authorize U.S. participation in and contributions to the Davos Alzheimer's Collaborative. The Davos Alzheimer's Collaborative, or DAC, was launched in 2021 as the first global alliance of governments, non-profits, academia, and the private sector driving efforts to combat Alzheimer's disease. DAC aims to invest over \$700 million over 6 years to link, scale, and build on existing efforts across every sector, and foster an innovative ecosystem to coordinate and accelerate the pace of innovation and Alzheimer's disease research and care and to improve brain health globally to achieve equitable and accessible healthcare.

It is critical at this time that we leverage U.S. resources to most effectively combat the step saving disease for our constituents, their families and individuals impacted by Alzheimer's disease and dementia around the world. I look forward to hearing testimony and again, thank you for holding this hearing. I yield back.

Mr. SMITH. It is now my honor to introduce our very distinguished witnesses beginning with Dr. Gladys Maestre who is the Director of the Rio Grande Valley Alzheimer's Disease Resource Center for Minority Aging Research. She is a physician, scientist, who has devoted much of her professional life to Alzheimer's research in low-resource settings. Her research has explored cultural, educational, and genetic risks for Alzheimer's disease and cognitive decline, as well as cognitive function and health among minorities and ethnically diverse populations. Dr. Maestre was also the Co-Director of the South Texas Alzheimer's Disease Resource Center where she focuses on personalized medicine's approaches to improve prevention, treatment, and care for patients with Alzheimer's disease and related dementia.

Dr. Benjamin Warf is the founding Chairman of NeuroKids, a nonprofit organization established in the year 2020 that exists to help children with hydrocephalus and spina bifida in low-resource countries. Dr. Warf is also a Professor of Neurology at Harvard Medical School and Director of Neonatal and Congenital Anomalies Neurosurgery at Boston Children's Hospital. He served as Chief Pediatric Neurosurgery and Director of Surgical Education at the University of Kentucky Medical Center in 2000 when he and his wife and six children moved to Uganda as a medical missionary with Cure International to be the founding medical director of a pediatric neurosurgery specialty hospital. While there, Dr. Warf developed and validated a new endoscopic neurosurgical procedure to treat infant hydrocephalus known as ETV/CPC and I will leave it to you to say what that stands for. He is also the first to identify neonatal infection as the most common cause of infant hydrocephalus in East Africa. And again, has been before this committee several times and has been amazing with the leadership he has provided.

Dr. Andy Shih is the Chief Science Officer at Autism Speaks, an organization we work very closely with on the Autism Caucus and I want to thank him. Dr. Shih has led important advancements toward the organization's mission including the development of several large international research consortia that delivered high impact scientific outcomes for the community. He was essential to the 2008 passage of the World Autism Awareness Day Resolution at the U.N. and subsequently led to the development of the Global Autism Public Health Initiative that provides technical support to country governments to enhance autism awareness advocacy and services worldwide. His leadership at Autism Speaks supports ministries, governments, agencies, and leading non-government organizations in more than 70 countries to deliver better outcomes. And of course, we all remember when G20 adapted a very, very monumental and you played such a role in it, to have a change in direction to come up with something that will ameliorate autism by 2025. It was a very, very important pivot and it helped us, all of us in countries and governments around the world to focus additional resources saying we have a target date, let's try to achieve it.

And then we have Dr. Yashodhara Rana, who serves as the Associate Director for Research at the Eleanor Crook Foundation. In this role, Dr. Rana oversees ECF's multi-million dollar portfolio of

grants in maternal and child nutrition and provides thorough leadership both to the ECF team and its community of partners. She is currently a member of the Power of Nutrition Technical Advisory Group and serves as a member of the Editorial Board of Maternal and Child Nutrition Journal.

Prior to ECF, Dr. Rana was Associate Director at the Results for Development overseeing a nutrition team's data and learning practices. There, Dr. Rana led DataDENT, a 5-year initiative aimed at strengthening the nutrition data value chain and informing the African Development Bank's nutrition strategy in costing and financial analyses.

Thank you all for being here. The testimony you will provide will be incredibly useful going forward as well as starting today. Dr. Maestre.

STATEMENT OF GLADYS E. MAESTRE

Dr. MAESTRE. Chairman Smith, Ranking Member Wild, and I am pretty sure she is going to look at this, Dr. Bera, distinguished members of this committee, it is an honor to testify before you today. To harness the promise of science to mitigate the suffering of the millions experiencing Alzheimer's dementia across the globe, we need to advance scientific knowledge, but also design the infrastructure and resources required to make this promise a reality.

A comprehensive, cohesive global agenda will allow our Nation to leverage the momentum that the national plan to address Alzheimer's Disease Act, known as NAPA, and the Alzheimers Accountability and Investment Act have facilitated. This bill was recently reauthorized with unanimous support in Congress. We are grateful to you, Chairman Smith, and all Members of the Congress who have championed and continue to support this bill, and Dr. Bera, for that initiative.

As a result of these investments, seminal advances were made in diagnosing and treating Alzheimer's disease. For example, we now know that Alzheimer's begins 20 years or earlier before memory loss or other symptoms develop. And in an unprecedented move, the FDA approved two treatments that can modify some changes in the brain of Alzheimer's dementia patients.

We are moving toward incorporating biomarker detection for Alzheimer's disease into routine preventive health care. Even though many aspects still need to be clarified, we can now detect brain changes in vivo by measuring cerebrospinal fluid and plasma molecules. We refer to these molecules as biomarkers and they may function similarly to prostate specific antigens, PSAs, where elevated levels from further assessments to rule out disease.

Our global brain health agenda needs to be cohesive and should take advantage of the momentum and consider the following facts. First, Africa, the most genetically diverse continent, offers a vast, yet under utilized resource for studying how genetic and environmental factors contribute to chronic and infectious diseases. While the African diaspora in the U.S. is growing, it represents a fraction of the genetic diversity found on the continent.

Second, the risk factors affecting every brain disease vary across ethnic groups due to genetic and cultural differences. However, most studies focus on European populations, limiting their applica-

bility to other groups. For instance, ApoE, the most common genetic risk factor for Alzheimer's in Europeans, has minimal impact on African Americans or Hispanics.

Third, without the knowledge of disease etiology in the ancestral source populations, our ability to fully address the needs of African Americans who are also experiencing a rising life expectancy remains limited.

China and the U.S. compete for a strategic influence in Africa and Latin America, includes U.S. investment in health research and infrastructure offers a strategic, cost effective way to counter China's advance and rebuild trust in the global south. One example of this that we have done in Latin America is the Maracaibo Aging Study in Venezuela. Despite efforts to move from programs, projects, to a cohesive strategy, brain health, especially Alzheimer's, still lacks a clear, global agenda.

I urge you to consider a global strategy to advance Alzheimer's research that benefits all people in America and it strengthens the U.S. position in African and all lower-income regions. This approach may leverage NIH funded programs that combine research training with community engagement such as the Resource Centers for Minority Aging Research, the RCMAR, and the Alzheimer's Disease Research Centers, ADRCs, and the Diversity Centers for Genomic Research.

Partnership with Alzheimer's Associations and other patient advocacy groups, as well as professional societies like the Gerontological Society of America are instrumental in implementing a concerted agenda.

Finally, we must develop a pipeline of experts in both brain health and foreign affairs. With over 250 North American universities offering global health education, we have the means to do that.

Thank you very much for the opportunity to testify today. I look forward to answering any questions you may have.

[The prepared statement of Dr. Maestre follows:]

Gladys E. Maestre, MD, PhD

Professor of Neuroscience and Human Genetics

Director, Rio Grande Valley Alzheimer's Disease Resource Center for Minority Aging Research (AD-RCMAR)

Co-Director, South Texas Alzheimer's Disease Research Center (ADRC)

Leader of Community Engagement Core, UTRGV Diversity Center for Genome research

University of Texas Rio Grande Valley School of Medicine

Written Testimony

United States House Committee on Foreign Affairs

Global Health, Global Human Rights, and International Organizations Subcommittee Legislative Hearing on
"Meeting the Challenges of Global Brain Health: Diagnosis and Treatment for the 21st Century".

November 20, 2024

Chair Smith, Ranking Member Wild, and distinguished members of the Subcommittee: Thank you for the opportunity to testify before you today. It is my pleasure to appear before you today to discuss the challenges of global brain health and the importance of advancing the prevention, diagnosis, and treatment of Alzheimer's disease in the 21st century. To harness the great promise of science to mitigate the suffering of millions experiencing or at high risk of Alzheimer's disease across the globe, we need to consider rigorously not only advances in scientific knowledge but also to design the infrastructure and resources required to make this promise a reality.

I am Dr. Gladys E. Maestre, MD, PhD, Professor of Neuroscience and Professor of Human Genetics at the University of Texas Rio Grande Valley School of Medicine located on the Southern Border of Texas. I am the Director of the Rio Grande Valley Resource Center for Minority Aging Research and Co-Director of the South Texas Alzheimer's Disease Research Center. I am also UTRGV's Community Engagement Core Leader of the NIH Diversity Center for Genome Research. I am an active researcher focused on Alzheimer's dementia and related disorders in low-resource settings in the United States and in low and middle-income countries (LMICs). I have conducted capacity-building activities for brain health in the Americas, including Venezuela, Colombia, Bolivia, and Haiti, and in Africa, where I have been organizing a biannual conference for more than 15 years with my colleague Dr. Raj Kalaria, in Nairobi, Kenya, to discuss research and care priorities for LMICs and to support the development of research networks focused on dementia in Africa. I have authored several books and more than 100 peer-reviewed articles.

The National Plan to Address Alzheimer's Disease Act, known as NAPA, and the Alzheimer's Accountability and Investment Act changed the trajectory of national investments in Alzheimer's disease research, clinical and long-term care, and public awareness in our nation. These bills were recently reauthorized with the unanimous support of Congress. We are grateful to you, Chair Smith, and all the champions in Congress who have led and continue to support these bills.

What is Alzheimer's dementia, and what is the magnitude of the problem?

Alzheimer's dementia is a term for a particular group of symptoms: Difficulties with memory, language, problem-solving, and other thinking skills affecting a person's ability to perform everyday activities. Signs and symptoms progress at different rates and patterns in different people; some of them can be handled with medications or in conjunction with non-pharmacological strategies, but currently, dementia of Alzheimer's type is relentless and incurable. For the family and caregivers, Alzheimer's dementia is a source of unimaginable suffering and, even in the best of circumstances, a significant and unpredictable financial burden. By 2050, an estimated 13 million Americans will be living with Alzheimer's, and total payments for all individuals with Alzheimer's or other dementias are projected to increase to more than \$1.1 trillion.

What is the difference between Alzheimer's dementia and Alzheimer's disease?

The origin of the signs and symptoms accompanying Alzheimer's dementia, mentioned above, is based in the brain. The brain changes in a relatively predictable way:

- Accumulation of beta-amyloid, a fragment of a larger protein, that acquires a particular conformation called beta-pleated sheet. The accumulation is thought to occur when there is excess production and/or defects in removing the beta-amyloid, or clearance.
- Accumulation of an abnormal protein that normally has an important role in transporting nutrients to different parts of the brain cells called neurons. They are part of the cytoskeleton, an important part of the cellular transportation system. This protein, called tau, gets abnormally phosphorylated, and basically, the railroad of the neurons gets disassembled, leading to fatal failure of the cells.
- Neurons in specific brain areas die, and then the neuronal death extends to areas that affect essential functions like sleeping, walking, and swallowing.

In brief, Alzheimer's dementia is the clinical presentation of the signs and symptoms, and Alzheimer's disease refers to specific brain changes. Although it is more common after 65, the changes in the brain are detectable 20 years earlier.

Can we diagnose dementia before symptoms appear? No, it is like diagnosing fever and there is no high temperature.

Can we diagnose brain disease before symptoms appear? Yes, it is like diagnosing an infection before there is a fever.

Can we treat the brain disease before Alzheimer's dementia appears? That is the hope that we can treat brain changes before they cause sufficient damage to detonate the signs and symptoms that characterize Alzheimer's dementia.

What are the implications of disease-modifying therapeutics?

Suppose we can treat, reverse, or stop the brain changes responsible for the presentation of dementia. In that case, it is possible that we can treat, reverse, or stop dementia, and this is the direction in which clinical trials are going.

So far, the two FDA treatments that have been approved target only the deposition of beta-amyloid. The treatments consist of systemic delivery of antibodies that attach and clear the beta-amyloid deposited in the brain. It is the first generation of disease-modifying therapeutics, but more are on the way, and they are not only focused on removing or preventing the deposition of beta-amyloid but also on tau and neuron survival or the genesis of neurons in old age.

The approved treatments are not as efficacious as expected. If brain changes are complex and only one is targeted, it is reasonable to expect that the others will continue their course, and the disease might slow down but will not be cured. This is similar to when somebody with coronary artery disease is treated with therapeutics affecting one of the risk factors, such as hypertension or hypercholesterolemia; we know that the multifactorial nature requires different therapeutic approaches -pharmacological and non-pharmacological. But they constitute an important step and a source of hope for everyone in the field.

It is also expected that the earlier we treat, stop, or reverse brain changes, the better the individual's brain health will be. Diagnosing those brain changes as early as possible is more urgent than ever.

The game-changing importance of biomarkers of brain changes

Biomarkers are detectable changes that indicate the presence or absence of a disease or the risk of developing a disease. For example, high cholesterol is a biomarker of cardiovascular health. For decades, we needed to see the brain directly through a biopsy or autopsy to be able to detect the amyloid and tau; then, we were able to see brain changes using radioligands and positron emission tomography (PET), which is a neuroimaging technique that can be used non-invasively but is very expensive and only available in high-resource settings and big academic centers.

Diagnostic tests have been developed that allow the measurement of different molecules in the cerebral spinal fluid, but still, lumbar puncture is invasive and not very appealing. What is new and very exciting is the fact that the new tests can be done in blood plasma, and a combination of panels allows the detection of species of

beta-amyloid (a ratio of beta amyloid1-42 and 1-40), abnormal tau isoforms (like ptau217) and markers of neurodegeneration, inflammation, and vascular damage.

Implications of new diagnostic and treatment approaches for low and middle-income countries LMICs

The impact of Alzheimer's dementia is significant, affecting approximately 50 million people globally, and is expected to triple to 150 million by 2050. In the African continent, Alzheimer's dementia is particularly alarming, with an expected rise from 3.6 million cases in 2020 to an estimated 16.2 million by 2050 (Beling et al 2024).

The implementation of circulating biomarkers could potentiate the current diagnostic process, guide the selection of additional diagnostic tools, and significantly influence patient treatment strategies by contributing to the identification of suitable candidates for anti-amyloid drugs and informing the management of other neurodegenerative diseases. Utilizing circulating biomarkers can provide a more readily available approach to defining the biological aspects of Alzheimer's in Africa, and with that of African Americans and admixed populations of the United States like Black Hispanics.

We need to consider that currently, in LMICs and low-resource settings in the United States, there is inadequate healthcare coverage and imaging, neuropsychological testing are not available or are too expensive, and sometimes tools for diagnosis are not culturally sensitive or not in the language that best reflects the cognitive performance of the subject. There is also stigma and competing health and family priorities that preclude help-seeking behavior in the healthcare system.

The collective efforts of scientists across the continent under the auspices of the Africa Dementia Consortium (ADC), Alzheimer's Disease Sequencing Project (ADSP), Global Brain Health Institute (GBHI), and Africa Fingers are poised to generate comprehensive clinical and socioeconomic datasets that are crucial for improving the characterization of dementia phenotypes in Africans.

Circulating biomarkers could serve as preliminary screening tools for Alzheimer's diagnosis by identifying individuals more likely to benefit from further, more expensive, and less accessible diagnostic methods, such as CT scans or MRI, and could open regional clinical trials. However, several studies have reported that the relative importance of the Alzheimer's disease biomarkers is different for African Americans, in the sense that not only levels of amyloid have been reported to be higher in African Americans than in other segments of the population, but also that beta-amyloid levels in plasma are the best predictor of cognitive status in African Americans, while in non-Hispanic whites is tau levels. In summary, we need to learn more about factors that affect the levels of biomarkers of Alzheimer's in blood and the specific importance of these concerning severity, progression, and response to treatments. There are difficulties, a lack of health insurance coverage and the interpretation of results is derived mainly from non-Hispanic Whites.

The Maracaibo Aging Study as a source of lessons for international work on Alzheimer's disease

Together with my classmates, Drs. Joe Terwilliger and Dr. Joe H. Lee, and a team of local clinicians, we established a longitudinal study in the border city of Maracaibo, Venezuela. This is where a US-based team led by Dr. Nancy Wexler discovered the gene for Huntington's disease. We included everyone living in two catchment areas to understand aging, cardiovascular risk, cognition and developed specific phenotypes that are now incorporated in current studies everywhere like blood pressure variability in 24 h. When the Zika epidemic hit we were the first to publish the damage on the eyes of adults and not only in newborns. We developed strategies to work in humanitarian settings, instilling the values of democracy, solidarity and collaboration with the United States. It is a perfect example of why this kind of work is needed, and how it benefits the United States: community members and even public officials were touched by our American colleagues' kindness and respect towards them.

Why and how can studies in Africa accelerate discoveries in Alzheimer's relevant to US populations?

African populations are genetically and culturally variable and are woefully understudied compared with European populations. As the most genetically variable continent on earth, these populations provide an enormous yet underused resource for understanding how genetic and environmental factors interact in the etiology of all chronic (and infectious) diseases, not just brain disorders. While we have a growing African diaspora in the United States, they are still relatively few and represent but a fraction of the diversity found on the continent. To this end, it is precious to science that we engage more and more with these populations to learn more about the etiology of chronic disease in general.

I will address what I consider one of the most exciting opportunities. Genomes from Africans harbor unprecedented genetic diversity, and the potential for discovery is vast. For example, despite the steady increase in data in international repositories, high-depth whole-genome sequence data from just over 400 Africans yielded over 3 million novel, previously undocumented variants. Imagine a garden that contains many colors; if you pick some of the flowers and develop gardens in another place, the number of colors in the garden derived will be lesser than the number of colors in the parent garden. Africa is our parent garden....in the United States we only have a few colors, i.e. gene variants that are found in Africa. So, the potential health impact could benefit Africans and the global community. Consortiums like the Alzheimer Disease Sequencing Project (ADSP led by Dr. Pericak-Vance at the University of Miami and Dr. Rufus Akiyemi in Nigeria) funded by the National Institutes of Health are mining this strategy.

However, the knowledge gaps are huge, not only for the role of genetics and biomarkers but also for the role of social determinants of health, including food insecurity, forced migration, sex trafficking, infectious disorders, and economic and financial characteristics among many others, that could only be addressed with broad participation from the community, experts in social and behavioral sciences and longitudinal follow-up.

Why is important to have more inclusive studies?

The risk factors (both genetic and environmental) affecting virtually every complex chronic disease vary tremendously between ethnic groups (both due to cultural as well as genetic differences). However, most genetic epidemiology studies that have been conducted have focused on European populations for historical reasons. It is well-known in AD, that the most common genetic risk factor in European populations, ApoE, has minimal impact in African Americans and Hispanics.

Minority populations are the ones who suffer when their health risk is evaluated based on knowledge obtained solely from studies of white people. A straightforward example is milk consumption. Studies of white people showed the benefits of milk drinking in attenuating the risk of osteoporosis, for example. In the late 1990s, China started a "Drink more milk" campaign based on this science. However Chinese never drank milk historically, so there was no evidence it benefited them. It turns out that virtually all East Asian adults lack the genetic variant that allows them to digest lactose, the sugar in milk. A big problem caused by the assumption that what works for white people applies to every other population.

In studies of age-related traits like Alzheimer's Disease, this bias is even greater because of differences in life expectancy combined with a lack of trust in science in minority populations due to past abuses (like Tuskegee). Furthermore, in studying minority populations, there are difficulties in studying old folks because of immigration history (relatively recent immigration makes these populations generally younger on average and greater admixture because of the multicultural nature of the United States).

In the case of African Americans, the admixture with Europeans creates special scientific issues, which require better knowledge of the disease etiology of the ancestral source populations. But so little work has been done in Africa that we don't have this information well-characterized. This is a very important motivating factor for additional studies of African populations. Without this knowledge, we are handicapped in our ability to effectively understand the health of African American populations, which are also facing a steady increase in life expectancy.

While we expect Alzheimer's Disease to increase in frequency as African populations age (due to increasing life expectancy), this assumption is mainly based on studies of white people in the US. As those populations age, we have a unique laboratory to study this.

Well-developed and executed health studies in the developing world have the potential to win hearts and minds and change how people see the United States. We have been carrying out the Maracaibo Aging Study since 1998; we have been able to continue a research project in impoverished communities in Venezuela despite their political difficulties with the United States. Despite this project having been funded by the US government, the positive relationship we developed with the local population shows a positive view of America, as has the successful long-term collaboration with US scientists in the community (i.e. these investments benefit America because they allow engagement and make us seen as being somewhat benevolent).

What is the positioning of the United States regarding brain health in Africa?

While serious attempts have been made to transition from a fragmented strategy—a characterization of many global health programs—to a more coherent and cohesive one, still for brain health, the strategy is not cohesive, not particularly concerning Alzheimer's. In the case of AIDS, for example, the coherent involvement of the United States has been critical in public health advances since the creation of the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) in 2002, the rollout of The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) in 2003, and the development of the Global Health Security Agenda (GHSa) in 2014.

The United States has made significant investments in research in Africa; in particular, the Fogarty International Center and the National Institute on Aging have played a significant role as catalyst of collaborations. However, we need to look at the role of the overall investment of the United States in the context of other large economies. For example, China has emerged as sub-Saharan Africa's largest individual country trading partner in the last 20 years. Today, one-fifth of the region's total good exports go to China. Metals, mineral products, and fuel represent about three-fifths of the region's exports to China.

China has increased its development programs around the world and, particularly in Africa. Besides investing in transportation infrastructure, higher education, and health infrastructure, China has sent more than 15,000 doctors to Africa and has treated nearly 180 million African patients, which has helped to ensure its long-term foreign policy interests in energy and food security (McGiffert, 2009).

In Africa and Latin America, China and the United States compete for economic and political influence. Investment in health research and infrastructure in Africa is a way to compete with China for influence by giving them something of value if it is done with no strings attached. As with the Maracaibo Aging Study, this has the potential to earn goodwill for the United States at a relatively low cost, in addition to the scientific benefits described above. The battle for influence in the global South is something the United States has not invested in the same degree as China over the past three decades, and while African countries fully realize China will exploit them, the infrastructure China has built is something they did not have another way to obtain quickly, so they went for it, knowing they were not given altruistically. Investment in research and health is an effective way to compete for hearts and minds, as we know from our work in Venezuela.

What models have high potential to support the leadership role of the United States in global brain health and accelerate translation to the US population?

There are several models and many ways to strengthen the leadership role in Alzheimer's research that I believe could be deployed to support more broadly global health progress. The overall notion is that efforts will benefit from a centralized and comprehensive strategy for global brain health, strengthening cooperative efforts with LMICs and targeted actions. To be sustainable, joint expertise in diplomacy and global brain health skills would be needed to draw support from appropriate health knowledge networks. A lack of this type of joint expertise has led to the deployment of technical assistance that does not leverage current infrastructure but also that is not targeted to specific geopolitical scenarios or does not account for what is needed to create new

tools and improve program delivery, advance scientific knowledge and mitigate suffering related to brain disorders.

Thinking about the education and skills needed to create a sustainable U.S. workforce with brain health and foreign diplomacy skills is essential. I believe several successful initiatives in place can be leveraged:

1.- Universities are already creating environments that support interdisciplinary education and research and blending majors to ensure cross-sector thinking and interaction. More than 250 North American universities now offer global health education. These programs are poised to enable global brain health and to cross-pollinate to harvest innovative solutions by incorporating global brain health tracks and integrating leadership and diplomacy skills in their curriculum. Programs like USAID's Higher Education Solutions Network might offer lessons on how to leverage built expertise.

2.- Expanding successful research training programs to develop new international frontiers. While there are a plethora of examples of successful research and service projects in Africa and other low-resource settings, there is a scarcity of programs that rely on building sustainable infrastructure, that includes mentoring, career advancement both locally (at the international site) and in the United States with a global health perspective.

For example, the network of **Resource Centers for Minority Aging Research** (RCMAR), supported by the Division of Behavioral and Social Research at the National Institute on Aging is a useful referent. The RCMARs have different cores to support career advancement in specific topic, like ours at the University of Texas Rio Grande Valley which is focused on Alzheimer's in Hispanic populations. The different cores supporting the research education component of the Center include the Administrative, Analysis and Community Liaison and Recruitment Cores.

3.- Supporting the research and care continuum. One successful example is the network of **Alzheimer's Disease Research Centers** (ADRCs), sponsored by the Division of Neuroscience at the National Institute on Aging, in which the research education component of individuals with high potential is supported by several cores devoted to each aspect necessary to advance knowledge, like Clinical, Imaging, Biomarker, Neuropathology, Data Management, Outreach, and Recruitment, Genomics/Genetics Cores as an example. Each of the ADRCs can incorporate and create the support cores as needed. One of the most vital characteristics is that the assessment and characterization processes of participants, their social determinants of health, and their context are standardized across the network facilitating obtaining a strong sample size.

An extension of RCMARs and ADRCs that are better positioned to carry out activities in LMICs will be a strategic step. It will create a sustainable infrastructure, empower our scientists, collaborations, and translate results to both local and abroad locations.

4.- Another example is the **Diversity Centers for Genome Research**, sponsored by the National Human Genome Research Institute of NIH. The network across the United States is focused on minority-serving institutions, each focused on specific populations and creating resources to study the admixed and original populations, such as the African or Asian Pacific populations.

All these "Center Programs" include capabilities to support career advancement, data sharing, and community engagement. Adding an international component linked will be an efficient solution.

5. The U.S.-based Alzheimer's Association, the largest voluntary health organization dedicated to Alzheimer's research, care, and support, hosts the Alzheimer's Association International Conference® (AAIC®) Satellite Symposium and recently convened the dementia science community in Africa. Leaders across Africa met to discuss how advances in public health, diagnosis, and treatment can be applied within the region. This meeting is part of the year-round learning opportunities offered by AAIC and is hosted in collaboration with the Global Brain Health Institute (GBHI) and the Atlantic Fellows for Equity in Brain Health.

We are poised to think outside the box and envision a better future for all. Diagnosis, treatment, and prevention for all is a tremendous challenge in low-resource settings in the United States and in LMICs. While today we have better treatments and prevention strategies, until we better understand a) how Alzheimer's biomarkers are reflective of brain disease when other conditions -both medical and social- are present, and b) which characteristics of the environment are preventable risk, we need to develop as many avenues as possible. Not only do we know that we can prevent 40% of dementia by focusing on 12 modifiable risk factors, but also that enriching the environment is conducive to a higher cognitive reserve and resiliency through better architecture, multisensorial stimulation, and creativity.

Thank you very much for the opportunity to testify before the Subcommittee today and I look forward to answering any questions you may have.

Mr. SMITH. Thank you very much, Doctor, and your very, very lengthy and scholarly testimony will be made a part of the record and any other extraneous material you want to include in the record. Dr. Warf.

STATEMENT OF BENJAMIN C. WARF

Dr. WARF. Thank you, Mr. Chairman and Dr. Bera and other members that will be listening. Thank you for this invitation. It is an honor as always. And thank you, Mr. Chairman, in particular, for your commitment and support over the last many years now. It is very valuable and very much appreciated.

Hydrocephalus is a common childhood condition that can be devastating or even fatal. The good news is that it is treatable. The bad news is that children in much of the world either get sub-optimal treatment or no treatment at all. The normal brain contains fluid-filled spaces called ventricles that communicate with the fluid space outside the brain. Anything that disrupts this circulation can cause a fluid called CSF, or cerebral spinal fluid, to accumulate within the ventricles which then enlarge under pressure. That is hydrocephalus. There are many causes of hydrocephalus. Some cases are congenital. And others are secondary to another condition.

In resource-poor countries, the two most common causes are neonatal infection and neural tube defects, commonly referred to as spina bifida. Together, these account for about two thirds of all causes of hydrocephalus in the developing world. Thus, a great deal of hydrocephalus could be prevented by reducing the incidents of newborn infections and spina bifida. Hydrocephalus is the most common condition treated by pediatric neurosurgeons, with close to one half million new cases per year. But it is tragically most common among those children who have the least access to treatment. The incidence of congenital hydrocephalus is highest in Africa and Latin America and it is lowest in the United States and Canada.

When you include cases related to neonatal infection and neural tube defects, the annual case volume in resource-poor countries is more than 20 times that for high-income countries. Three quarters of the world's case volume of childhood hydrocephalus can be found in Latin America, Africa, and Southeast Asia.

Infant hydrocephalus, whatever its cause, results in expansion of the brain's ventricles which stretch and compress the surrounding brain tissue causing mechanical injury and decreased blood flow. The head enlarges dramatically and the child suffers from progressive symptoms and about half will die without treatment within 2 years. Survivors typically have severe neurocognitive disabilities and spasticity and blindness. Untreated hydrocephalus is also costly. The estimated annual economic burden of untreated infant hydrocephalus in Sub-Saharan Africa is between 1.4 and 56 billion U.S. dollars per year using the value of a statistical life method. The estimated benefit-to-cost ratio for treatment is more than seven to one which is more than some of the other interventions that are more commonly performed.

The standard and most widely practiced treatment for infant hydrocephalus is to implant a tube called a shunt, that allows CSF to escape from the brain's ventricles to the abdominal cavity, but

60 percent of shunts will have failed at least once within in the first 4 years and the risk of failure which can be life threatening never ends. A minimally invasive endoscopic brain operation caused ETV/CPC which stands for endoscopic third ventriculostomy and choroid plexus cauterization, which is why we call it ETV/CPC, can permanently treat infant hydrocephalus without the need for a shunt in around two out of three infants and has been shown at least as effective and safe as shunts and with a far lower risk of infection. But unlike shunts that can fail repeatedly over a lifetime, virtually no ETV/CPC treatment failures will occur after the first 6 months.

It is notable that this procedure was originally developed and validated in Uganda with the support of funding from both USAID and NIH. Its subsequent adoption by major pediatric centers here in the U.S. demonstrates how Federal funding of projects abroad can benefit U.S. citizens.

Countries with the highest volume of hydrocephalus have the fewest neurosurgeons with around 330 pediatric neurosurgeons caring for a population of 1.2 billion children in low-resource countries where shunt dependence is more dangerous. Children with shunt failure and no access to emergency surgery often die. Therefore, training and equipping these neurosurgeons to perform this procedure will substantially reduce the number of shunts placed and save lives while also reducing the number of repeated shunt operations on an overburdened neurosurgical workforce.

NeuroKids is a nonprofit organization that uniquely focuses on training and equipping these neurosurgeons to perform ETV/CPC using a combination of onsite training in their home institution and subsequent remote mentoring that employs virtual presence technology during surgery. We prioritize partnerships with neurosurgeons in high volume referral centers and subsequently leverage their training by adding them to our growing international team of neurosurgical mentors.

NeuroKids currently works with partner sites in 13 countries of Latin America, Africa, the Middle East, and Southeast Asia.

In conclusion, more funding is needed to accelerate the elimination of untreated pediatric hydrocephalus and to minimize life threatening shunt dependence in low-resource countries, thus saving the lives of countless children. As well, public health strategies that reduce neonatal infection and neural tube defects would substantially reduce the number of children throughout the world who are affected by this condition.

Thank you again for the opportunity of being here.

[The prepared statement of Dr. Warf follows:]

WRITTEN STATEMENT

Witness: Benjamin C. Warf MD

Title and Organizational Affiliation: Founder and Chairman, NeuroKids

Committee: House Committee on Foreign Affairs
(Subcommittee on Global Health, Global Human Rights
and International Organizations)

Date: 20 November 2024

Title: Meeting the Challenges of Global Brain Health: Diagnosis and Treatment
for the 21st Century

Introduction

Chairman Smith, Congressman Wild, and honored members of the committee, it is a privilege to be here.

Hydrocephalus is a common childhood condition that can be devastating or even fatal. The good news is that it can be treated. The bad news is that children in much of the world get suboptimal or no treatment.

Definition of hydrocephalus

The normal brain contains fluid-filled spaces called ventricles that communicate with the fluid space outside the brain. Anything that disrupts this circulation pattern can cause the fluid (called CSF) to accumulate within the ventricles, which then enlarge under pressure. That is hydrocephalus.

Causes of hydrocephalus

There are many causes of infant hydrocephalus, some being congenital, and others resulting from another condition. In resource-poor countries, the two most common causes are neonatal infection and neural tube defects (commonly referred to as spina bifida), which together account for about two-thirds of all cases. Thus, a great deal of hydrocephalus could be prevented by reducing the incidence of neonatal infections and neural tube defects.

Prevalence of hydrocephalus

Hydrocephalus is the most common condition treated by pediatric neurosurgeons, with close to one-half million new cases per year; but it is tragically most common among those children who have the least access to treatment. The incidence of congenital hydrocephalus is highest in Africa and Latin America (145 and 316 per 100,000 births, respectively) and lowest in the United States and Canada (68 per 100,000 births). Including cases related to neonatal infection and neural tube defects, the annual case volume in resource-poor countries is more than 20 times that for high-income countries.

Consequences of hydrocephalus

Infant hydrocephalus, whatever its cause, results in expansion of the brain's ventricles, which stretch and compress the surrounding brain tissue, causing mechanical injury and decreased blood flow. The head enlarges dramatically, and the child suffers from progressive symptoms. About half will die within two years and survivors have severe neurocognitive disabilities, spasticity, and blindness.

Economic impact of hydrocephalus and its treatment

Untreated hydrocephalus is also costly. The estimated annual economic burden of untreated infant hydrocephalus in sub-Saharan Africa is between \$1.4 and \$56 billion USD using the value of a statistical life approach, and the estimated benefit-to-cost ratio for treatment is more than 7 to 1.

Treatment of hydrocephalus

The standard and most widely practiced treatment for infant hydrocephalus is to implant a tube, called a shunt, that allows CSF to escape from the brain's ventricles into the abdominal cavity. But 60% of shunts fail at least once within the first 4 years and the risk of failure, which can be life-threatening, never ends.

A minimally invasive endoscopic brain operation called ETV/CPC, can permanently treat infant hydrocephalus without the need for a shunt in 2 out of 3 infants, and has been shown to be at least as safe and effective as shunts, and with a far lower risk of infection. But unlike shunts, that can fail repeatedly over a lifetime, virtually no ETV/CPC treatment failures will occur after the first 6 months.

This procedure was originally developed and validated in Uganda with the support of funding from USAID and NIH. Its subsequent adoption by major pediatric centers in the US demonstrates how Federal funding of projects abroad can benefit US citizens.

The situation in low resource countries

Countries with the highest volume of hydrocephalus have the fewest neurosurgeons, with around 330 pediatric neurosurgeons caring for a population of 1.2 billion children in low-resource countries, where shunt-dependence is more dangerous. Children with shunt failure and no access to emergency surgery often die. Therefore, training and equipping these neurosurgeons to perform ETV/CPC will substantially reduce the number of shunts placed and save lives, while also reducing the number of repeated shunt revision operations on an over-burdened neurosurgical workforce.

NeuroKids

NeuroKids is a non-profit organization that uniquely focuses on training and equipping these neurosurgeons to perform ETV/CPC using a combination of on-site training in their home institution and subsequent remote mentoring that employs virtual presence technology during surgery. We prioritize partnerships with neurosurgeons in high-volume referral centers and subsequently leverage their training by adding them to our growing international team of neurosurgical mentors. NeuroKids currently works with partner sites in 13 countries of Latin America, Africa, the Middle East, and Southeast Asia.

Conclusion

More funding is needed to accelerate the elimination of untreated pediatric hydrocephalus and to minimize life-threatening shunt-dependence in low-resource countries, thus saving the lives of countless children. As well, public health strategies that reduce neonatal infection and neural tube defects would substantially reduce the number of children throughout the world who are affected by this condition.

Thank you.

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Mr. SMITH. Thank you, Dr. Warf. Thank you so very much for your leadership and being here. Dr. Shih.

STATEMENT OF ANDY SHIH

Mr. SHIH. Thank you, Chairman Smith, Ranking Member Wild, and distinguished—all distinguished member of the subcommittee for inviting me to testify and for holding this important hearing.

I am Dr. Andy Shih, Chief Science Officer at Autism Speaks, a national and not-for-profit organization dedicated to creating an inclusive world for people with autism through their life-span. We do this through advocacy, services, supports, research and innovation, and advances in care.

In addition to the work we engage in domestically, Autism Speaks has been committed for many years to developing and implementing strategies and programs that positively impact the lives of people with autism, other developmental disability around the world. The primary vehicle for this has been our Global Autism Public Health Initiative, also known as GAPH. GAPH is a community participatory research and advocacy programs where, in addition to facilitating high-impact science to inform program and policy development, we serve as technical advisors to governments and NGO's committed to enhancing support for our community. We help source expertise, support community-based knowledge co-production, and facilitate dissemination and implementation of sustainable solutions.

What we've learned from our many years of work in this space and throughout our Autism Leadership Network, a distinguished group of leading international autism advocates that Autism Speaks has supported for over a decade, is that there are some absolutely incredible individuals and organizations working in countries across the globe to raise awareness of autism and increase service—access to services. These are truly some of the most remarkable caring people you will ever meet, who often work with extremely limited resources in difficult political climates. What we've also learned is that while these advocates have made a significant impact, have only scratched the surface in terms of building the awareness and acceptance of autism and infrastructure for services that needed around the globe to meet the needs of autistic people.

Much of the work has engaged internationally involve—involving working directly with community organizations. Last year we had the opportunity to collaborate with the World Health Organization and UNICEF on a first-of-its-kind report, the Global Report on Children with Developmental Disability. This report provides a comprehensive perspective on the prevalence and characteristic of children with developmental disability globally and serve as a call to action for all nations.

Like to focus on a few of the findings and recommendation from this report. I think they are helpful for informing our conversation today. First, the report note that there are an estimated 317 million children and adolescents worldwide that have health condition that contribute to developmental disabilities and 95 percent have no access to appropriate care at all. Children and adolescents with developmental disability are at increased risk of mental health con-

ditions and premature death due to illnesses such as obesity, diabetes, heart and respiratory diseases. Their needs are largely neglected and they continue to experience stigmatization, prejudice, institutionalization and barriers to participation, as well as social, economic, educational, and other forms exclusion and barriers in access health care along with poorer quality of care when compare with their peers. This result in widespread inequities in terms of health outcomes, and tragically, premature mortality for many people with developmental disabilities.

Despite the depth of these challenges, this report provide hopes and a path forward. The overarching objective of this report is to take action for change. Children with developmental disability and their families have long been neglected to the margins, and that has to change. That has to change now. This report maps out 10 action area to accelerate change in policies and care system for children and young people with developmental disabilities. I encourage all member of the subcommittee to read through them.

One key takeaway from the report is that improving health outcome for those children must involve a holistic approach. To truly make progress institutional barriers to care must be addressed and the same time more personalized approaches must be utilized to address each child's individual needs.

To accomplish this one approach known as the stepped-care model is being increasingly recognized as an efficient and effective way to build tier system of care for children with developmental disabilities. This approach involve making available care options of varying levels of intensity linked through defined care systems.

Recently Autism Speak implemented the stepped-care approach by supporting UNICEF pilot that focus on early identification and intervention for children with developmental delays in three countries: Bulgaria, Peru, and Uganda, as part of Care for Child Development Initiative. The work being done in these countries is already having a substantial impact, and the Global Report on Children with Developmental Disabilities will continue to serve as a rallying point as well as a road map to make progress around the world.

Last, while millions of people with developmental disability around the world still struggle to access appropriate care—health care, like to acknowledge the progress that has been made in the development of tools to improve autism diagnosis. Autism Speaks support the development of two freely available tools: the Open Source Screening and Diagnostic tool, which is called OSSDx, for autism spectrum disorder, and the Nigerian Autism Screening Questionnaire. The ability to reliably screen and diagnose autism is critical in determining the most appropriate level of care for autistic children. High-quality screening tools like these are necessary to address the challenge and improving diagnosis and intervention.

Chairman Smith, throughout your career you have been an incredible champion for autistic people, not just here in the United States, but around the world. If passed, the Global Autism Act that you have previously proposed would be a tremendous step in the right direction in helping to address the—some of the challenges I've mentioned today. I am grateful to you for inviting me to testify at this particular hearing where we're focused on neglected aspect

of public health. People with autism and other developmental disability around the world have tragically been neglected for many years across the very system—across every system of care. As I said earlier, the time for change is now. I look forward to working with you and all members of subcommittee to making that change. Thank you again. I look forward to your questions.

[The prepared statement of Mr. Shih follows:]

House Foreign Affairs Committee

Subcommittee on Global Health, Global Human Rights and International Organizations

Subcommittee Hearing – November 20, 2024 at 2 PM

Hearing title: “Meeting the Challenges of Global Brain Health: Diagnosis and Treatment for the 21st Century”

Testimony of Dr. Andy Shih – Chief Science Officer, Autism Speaks

Thank you, Chairman Smith, Ranking Member Wild and all distinguished members of the Subcommittee for inviting me to testify and for holding this important hearing.

I am Dr. Andy Shih, Chief Science Officer for Autism Speaks, a national, non-profit organization dedicated to creating an inclusive world for people with autism throughout their lifespan. We do this through advocacy, services, supports, research and innovation, and advances in care.

In addition to the work we are engaged in domestically, Autism Speaks has been committed for many years to developing and implementing strategies and programs that positively impact the lives of people with autism and other developmental disabilities around the world. The primary vehicle for this has been our Global Autism Public Health initiative (also known as GAPH). GAPH is a community participatory research and advocacy program where, in addition to facilitating high impact science to inform program and policy development, we serve as technical advisors to governments and NGOs committed to enhancing support for our community. We help source expertise, support community-based knowledge co-production, and facilitate dissemination and implementation of sustainable solutions.

What we’ve learned from our many years of work in this space and through our Autism Leadership Network, a distinguished group of leading international autism advocates that Autism Speaks has supported for over a decade, is that there are some absolutely incredible individuals and organizations working in countries across the globe to raise awareness of autism and increase access to services. These are truly some of the most remarkable, caring people you will ever meet, who often work with extremely limited resources and in difficult political climates. What we’ve also learned is that while these advocates have made a significant impact, we have only scratched the surface in terms of building the awareness and acceptance of autism, and infrastructure for services that is needed around the globe to meet the needs of autistic people.

While much of the work that we engage in internationally involves working directly with community organizations, last year, we had the opportunity to collaborate with the World Health Organization and UNICEF on a first-of-its-kind report, *The Global Report on Children with Developmental Disabilities*. This report provides a comprehensive perspective on the prevalence and characteristics of children with developmental disabilities globally and serves as a call to action for all nations.

I’d like to focus on a few of the findings and recommendations from this report, as I think they are helpful in informing our conversation today. First, the report notes that there are an estimated 317

million children and adolescents worldwide that have health conditions that contribute to developmental disabilities and 95% have no access to appropriate care. Children and adolescents with developmental disabilities are at increased risk of mental health conditions and premature death due to illnesses such as obesity, diabetes, heart and respiratory diseases. Their needs are largely neglected and they “continue to experience stigmatization, prejudice, institutionalization and barriers to participation, as well as social, economic, educational and other forms of exclusion,” and “barriers in accessing health care [along with] poorer quality of care when compared with their peers.”¹¹ This results in widespread inequity in terms of health outcomes, and tragically, premature mortality for many people with developmental disabilities.

Despite the depth of these challenges, this report provides hope and a path forward. The overarching objective of this report is to **take action for change**. Children with developmental delays and their families have long been neglected to the margins, and that has to change. That has to change now. The report maps out 10 action areas to accelerate changes in policies and care systems for children and young people with developmental disabilities. I encourage all of the members of the subcommittee to read through them.

One key takeaway from the report is that improving health outcomes for these children must involve a holistic approach. To truly make progress, institutional barriers to care must be addressed and, at the same time, more personalized approaches must be utilized to address each child’s individual needs.

To accomplish this, one approach known as the “stepped-care” model is being increasingly recognized as an efficient and effective way to build tiered systems of care for children with developmental disabilities. This approach involves making available care options of varying levels of intensity, linked through defined care systems.

Recently, Autism Speaks implemented the stepped-care approach by supporting a UNICEF pilot that focuses on early identification and intervention for children with developmental delays in three countries (Bulgaria, Peru and Uganda) as part of the Care for Child Development Initiative. The work being done in these countries is already having a substantial impact, and *The Global Report on Children with Developmental Disabilities* will continue to serve as a rallying point, as well as a roadmap, to make progress around the world.

Lastly, while millions of people with developmental disabilities around the world still struggle to access appropriate health care, I would like to acknowledge the progress that has been made in the development of tools to improve autism diagnosis. Autism Speaks supported the development of two freely available tools, the Open Source Screening and Diagnostic (OSSDx) tool for autism spectrum disorder and the Nigerian Autism Screening Questionnaire. The ability to reliably screen and diagnose autism is critical in determining the most appropriate level of care for autistic children. High-quality screening tools like these are necessary to address the challenges of improving diagnosis and intervention.

Chairman Smith, throughout your career, you have been an incredible champion for autistic people not just here in the United States, but around the world. If passed, the Global Autism Act that you have previously proposed would be a tremendous step in the right direction in helping to address some of the challenges I’ve mentioned today. I’m grateful to you for inviting me to testify at this

particular hearing where we are focused on neglected aspects of public health. People with autism and other developmental disabilities around the world have tragically been neglected for many years and across every system of care. As I said earlier, the time for change is now and I look forward to working with you and all members of the subcommittee in making that change. Thank you again and I look forward to your questions.

¹ World Health Organization, & United Nations Children's Fund. (2023). Global report on children with developmental disabilities: from the margins to the mainstream. World Health Organization. <https://www.who.int/publications/i/item/9789240080232>

Mr. SMITH. Mr. Shih, thank you so very much and thank you for the great work Autism—I mean, geez, I just—for the great work that you have done at Autism Speaks. It is just incredible. Matter of fact, in 2005, when the Autism bill was going to die because of House inaction, it was Autism Speaks that saved it. And so I will never forget that. So deeply appreciate it.

Mr. SHIH. Thank you, Chairman Smith.

Mr. SMITH. Let me now turn to Dr. Rana for your comments.

STATEMENT OF YASHODHARA RANA

Ms. RANA. Chairman Smith, Ranking Member Wild, Representative Manning, thank you for the opportunity to discuss the critical role of combating malnutrition and promoting global brain health. Thank you to Chairman Smith and Ranking Member Wild for your leadership in the fight against child malnutrition.

I serve as the Associate Director of Research at the Eleanor Crook Foundation, or ECF, a U.S.-based philanthropy solely focused on ending malnutrition. I manage a multi-million dollar portfolio of grants that is focused on child and maternal nutrition.

Today I will summarize my written statement in three key points: First, malnutrition is harming the brain health of children worldwide. Second, the crisis of malnutrition is detrimental not only to children and their families, but entire nations and economies. And third, malnutrition is a solvable crisis. We have cost-effective solutions ready to be scaled today.

To my first point, malnutrition is a leading cause of child death and children who survive face stunted growth and cognitive impairment. As we all know, brain development begins during pregnancy. By the 4th week a fetus has 10,000 brain cells and by the 24th week this number expands to 10 billion. In fact, by age three a brain—a child's brain is about 80 percent the size of an adult's brain.

The importance of proper nutrition during these early years cannot be overstated. Malnourished mothers are more likely to give birth to children who are too small or born too soon and these vulnerable babies are likely to have worse neurodevelopment and cognitive outcomes and also are at a serious risk of illness, and even death.

This brings me to my second point, the harmful effects of malnutrition on brain health extend beyond individuals to entire nations and economies. As President Adesina of the African Development Bank frequently says, the greatest contributor to economic growth is not physical infrastructure; it's brain power, what he calls as gray matter infrastructure. Individuals who face childhood hunger earn 10 percent less over their life times and are 33 percent less likely to escape poverty. The economic cost is huge. Malnutrition is estimated to result in an annual productivity loss of up to \$3 trillion.

But for all these dire statistics there is hope, which brings me to my third point. Proven cost-effective solutions to malnutrition exist and are ready to be scaled up. Take the solution of prenatal multivitamins for pregnant women that you can see here, which we call as MMS. This complete prenatal vitamin is considered as one of the best buys in global health. It not only protects the health of

the mother, but it also prevents kids from being born too early or born too small. And we have studies showing that babies born too small have lower IQs than their counterparts.

On a personal note, when I had my two pregnancies here in the United States I took a prenatal multiple-vitamin just like MMS because I knew I wanted my children to have the best start in life and I could access these supplements. But in low and middle-income countries where the prevalence of malnutrition is much higher, pregnant women only get two nutrients: iron and folic acid.

Another cost-effective solution is breastfeeding. Breast milk is nature's superfood that protects—and that protects children's brain health. And it also protects the health of mothers and babies, yet only 41 percent of kids worldwide are exclusively breastfed. When breastfeeding moms are supported they're twice as likely to continue to breastfeeding their children.

Finally, despite global efforts to improve children's diet, there are still families that are still not able to meet the nutritional needs of infants. A food-based supplement here that I'm showing designed—is designed specifically for vulnerable children and it's called SQ-LNS. It's proven to save lives. It's proven to prevent malnutrition. And it contains the recommended intake of micronutrients as well as protein.

I want to end my remarks by talking about the impact of U.S. leadership. The U.S. has historically been the largest donor in the fight against malnutrition. My birth country of Nepal offers a notable example of the benefits of this leadership.

In 1995 Nepal had the highest stunting rate in the world. Seven out of ten children had delayed growth. But over the past 20 years, with strong government leadership, policies, and donor support, specifically USAID's Nutrition Program, Suaahara, Nepal has reduced stunting by half. And thanks to U.S. Government leadership we've seen a historic surge in treatment for children with severe acute malnutrition. In 2023, an estimated 1.2 million children's lives were saved because of this treatment.

This success highlights the critical role of bipartisan congressional support, but UNICEF recently reported that one in four children today is living in severe food poverty. That means 181 million children do not have the equal opportunity to grow, develop, and learn. That means 181 million minds are at risk of being wasted. It is not easy to comprehend a number so huge, but I urge you to remember that every one of that callosal figure stands for a child, a child who deserves to have ambitions and who, with the right nutrition and care, can grow and prosper. We know that progress is possible, and now we must stand—we must stay the course.

Thank you and I look forward to your questions.

[The prepared statement of Ms. Rana follows:]



**Statement of Dr. Yashodhara Rana, Associate Director for Research,
Eleanor Crook Foundation**

**Before the U.S. House Committee on Foreign Affairs –Subcommittee on Global Health,
Global Human Rights and International Organizations**

**“Meeting the Challenges of Global Brain Health: Diagnosis and Treatment for the 21st
Century”**

November 20, 2024

Chairman Smith, Ranking Member Wild, and distinguished members of this subcommittee, thank you for the opportunity to discuss the critical role of combating malnutrition in global brain health. I want to express my gratitude to Chairman Smith and Ranking Member Wild for their leadership in the fight against child malnutrition. Their commitment has raised awareness and mobilized resources for this urgent issue. I also want to specifically acknowledge Chairman Smith for his efforts in advancing the Global Food Security Act, which has shaped policies to enhance food security and ensured that vulnerable populations, especially pregnant women and children, receive the nutrition they need.

Furthermore, I extend my sincere appreciation to Ranking Member Wild for her strong advocacy and support of legislative action focused on tackling severe acute malnutrition, also known as child wasting. Her dedication to this cause has helped to shine a light on the devastating impacts of malnutrition and has driven forward initiatives aimed at providing effective solutions. I would also like to thank the members of the Foreign Affairs Committee for their bipartisan stewardship of the Global Malnutrition Prevention and Treatment Act, which was enacted into law two years ago.¹ Their collaborative efforts have laid a solid foundation for ongoing initiatives to prevent and treat malnutrition, demonstrating a united front in addressing this critical challenge.

Thanks to the leadership of the U.S. Government, we have witnessed a historic surge in treatment for wasted children. A recent UNICEF report, which was cited in *The New York Times* in October 2024, shared that in 2023, an estimated 1.2 million children’s lives were saved because of treatment for wasting.^{2,3} This remarkable achievement underscores the impact of our collective commitment to addressing child malnutrition, and it would not have been possible without critical bipartisan Congressional support. It is imperative that we continue to build on this momentum and ensure that every child has access to the nutrition necessary for their growth and development.

¹ <https://www.usaid.gov/nutrition/resources/usaid-resources/global-malnutrition-implementation-plan>

² [Nearly two million severely malnourished children at risk of death due to funding shortages for therapeutic food](#)

³ <https://www.nytimes.com/2024/10/14/health/children-malnutrition-africa-unicef.html>

I serve as the Associate Director for Research at the Eleanor Crook Foundation, where I manage a multi-million-dollar portfolio of grants focused on maternal and child nutrition. I provide leadership both within the Foundation and across our network of partners. I have worked in the global health space for more than a decade, including supporting research in countries in South Asia and Africa. Additionally, I am a member of the Technical Advisory Group for the Power of Nutrition and serve on the Editorial Board of Maternal & Child Nutrition journal.

The Eleanor Crook Foundation (ECF) is a U.S.-based philanthropy dedicated solely to ending child deaths due to malnutrition. Founded in 1997 by Eleanor Butt Crook and her late husband, Ambassador William H. Crook, the Foundation is rooted in Eleanor's family legacy in the food industry. Her grandmother, Florence Butt, opened a small grocery store in 1905 that eventually grew into H-E-B, Texas' largest private retailer and one of the biggest private companies in the U.S. Eleanor Crook is driven by a singular vision: a world where every mother can nourish her children. The Eleanor Crook Foundation embodies that mission.

At ECF, we fund and support research that identifies effective prevention and treatment methods for malnutrition, conduct policy analysis to promote systemic reform, and engage in advocacy and policy leadership through dozens of partner organizations across academia, NGOs, and faith-based organizations. ECF is committed to scaling the most proven and cost-effective solutions to child malnutrition and has already invested over \$100 million to catalyze their scale-up with far-reaching results.

There are three takeaways from my remarks that I hope to leave you with today: 1) Malnutrition is harming the brain health of millions of children worldwide. 2) The crisis of malnutrition and its negative impacts on brain health are detrimental not only to individual children and their families – but also nations and economies. 3) Malnutrition is a solvable crisis. We have cost-effective solutions for malnutrition and brain development that are ready to be scaled. These include but are not limited to prenatal multivitamins for pregnant women, breastfeeding support for mothers, and a food supplement known as SQ-LNS, or small quantity lipid-based nutrient supplements. Currently, these malnutrition solutions are not being delivered at scale – but by investing in them, millions of children's lives – and livelihoods – will be saved.

Global Malnutrition is Harming the Brain Health of Millions of Children

Malnutrition is the leading cause of death for children worldwide. And for those who survive, malnutrition is a threat to brain development. Today, nearly 148 million children around the world are malnourished. An additional 45 million children are wasted – a disturbingly precise term for the deadliest form of malnutrition.⁴

⁴ <https://www.gatesfoundation.org/goalkkeepers/report/2024-report/>

At ECF we focus on combating malnutrition because proper nutrition is crucial for children's physical growth, cognitive development, and future potential. Malnutrition leads to grave and long-lasting consequences. When a child suffers from malnutrition, they are deprived of essential resources. The condition weakens their immune system, leaving them up to 15 times more likely to die from common infectious diseases.⁵ And if a child experiences malnutrition in the first five years of life, they can suffer from stunted growth and cognitive impairment – in other words, their brain health can be directly impacted.⁶

A child's brain grows rapidly from the time of conception until three years of age.⁷ During this period, the developing brain is influenced by a range of environmental factors, including exposure to toxins and infections, the stimulation the child gets from interactions with people around them, and crucially, the nutrition the child receives.⁸

Brain development begins in the womb. At the fourth week of pregnancy, a fetus has 10,000 brain cells. This number expands to about 10 billion by the 24th week of pregnancy. Maternal nutrition, including essential nutrients like folic acid, iron, zinc, and protein, is the fuel that drives this development. A lack of these nutrients during pregnancy can lead to developmental delays and cognitive issues for children.⁹

After birth, exclusive breastfeeding for the first six months of a child's life, followed by continued breastfeeding for at least two years, provides strong protection against disease and malnutrition, supporting the health and well-being of both mothers and children. Breastfeeding directly contributes to a child's brain health.¹⁰

As toddlers, children's brains continue to develop quickly, reaching 80% of adult size by age three. At this stage, children are especially vulnerable to insufficient nutrient intake as they move from exclusive breastfeeding to eating family meals. Proper nutrition, particularly iron-rich foods, is necessary to support this growth and prevent deficiencies that can affect learning and behavior.¹¹

The importance of nutrition to early brain development cannot be overstated. Proper nutrition supports a child's cognitive skills and future success – and malnourishment not only hampers

⁵ <https://www.endmalnutrition.org/>

⁶ <https://www.who.int/data/nutrition/nlis/info/malnutrition-in-children>

⁷ <https://pmc.ncbi.nlm.nih.gov/articles/PMC4981537/#R1>

⁸ https://archive.cdc.gov/www_cdc.gov/ncbddd/childdevelopment/early-brain-development.html

⁹ <https://thousanddays.org/why-1000-days/building-brains/>

¹⁰ <https://now.tufts.edu/2023/07/27/how-breast-milk-boosts-brain>

¹¹ <https://thousanddays.org/why-1000-days/building-brains/>

<https://pmc.ncbi.nlm.nih.gov/articles/PMC4981537/#R1>

children's physical growth but also inhibits the development of their brains. And ensuring every child has access to proper nutrition is crucial for breaking cycles of poverty and fostering resilience. When a child is well-nourished, they are better equipped to learn and succeed academically, laying the groundwork for productive futures. When we commit to solving the crisis of malnutrition, we are committing to healthier communities and a brighter future.

Stunted Brains Today, Stunted Economies Tomorrow¹²

The harmful effects of malnutrition on brain health undermine the prosperity of entire nations and economies – because children who survive malnutrition carry lifelong consequences. Research has shown that individuals who faced childhood hunger go on to earn 10% less over their lifetimes and are 33% less likely to escape poverty.¹³ Studies have also found that a malnourished mother is more likely to give birth to a small and malnourished baby, which advances an intergenerational cycle of poverty and inequality.¹⁴ In short, the toll of malnutrition can be felt for generations.

The economic costs of malnutrition for nations around the world are therefore significant. Malnutrition is estimated to result in an annual productivity loss of up to US\$3 trillion, representing 3% to 16% (or more) of GDP in low-income countries – equivalent to a permanent global recession at 2008 levels.¹⁵ The World Bank estimates that for every \$1 spent on combating undernutrition, there is a return of \$23, resulting in an estimated \$2.4 trillion in economic benefits. The advantages of these investments significantly surpass the costs of inaction, which are projected to be around \$41 trillion over the next decade.¹⁶

Ending malnutrition is often presented as a moral obligation – and for good reason. But ending malnutrition is also an economic imperative. As President Akinwumi A. Adesina of the African Development Bank noted: “Stunted children today will lead to stunted economies tomorrow.”¹⁷ Each day without action to improve nutrition for children worldwide undermines the growth and prosperity of countries around the world and hinders our ability to create a more equitable, productive, and thriving world.

Malnutrition is a Solvable Crisis with Sustained U.S. Leadership

¹² <https://www.afdb.org/en/news-and-events/speeches/agenda-setting-remarks-dr-akinwumi-adesina-president-african-development-bank-group-african-leaders-nutrition-addressing-malnutrition-catalyzing-africas-transformation-through-enhanced-multisector-investments-68756>

¹³ <https://www.gatesfoundation.org/goalkeepers/report/2024-report/#Introduction>

¹⁴ <https://www.unicef.org/reports/undernourished-overlooked-nutrition-crisis>

¹⁵ https://www.gatesfoundation.org/-/media/goalkeepers/reports/2024-goalkkeepers-report_en.pdf?rev=e00724a8a95e476dbbce54cf4fccd70

¹⁶ <https://openknowledge.worldbank.org/entities/publication/2e0b8b5e-0f67-47fe-9eae-d4707d9ed195>

¹⁷ Remarks by Dr. Akinwumi A. Adesina, President of the African Development Bank Group at TICAD7: Ending Malnutrition in Africa: Towards Nutrition

For all the dire statistics and challenging realities that I've thus far presented, there is also hope. Because proven, cost-effective solutions to malnutrition exist and are ready to be scaled. These solutions are targeted for each phase of the critical 1,000-day window – from pregnancy, to infancy, to early childhood. ECF currently funds a number of these preventative solutions, and also supports wasting treatment, which saves lives now.

Pregnancy & the impact of prenatal vitamins: Today, more than one billion women and girls are malnourished, and two out of every three women of reproductive age worldwide have micronutrient deficiencies. When a woman is malnourished during pregnancy, she is more likely to have serious complications, including a higher risk of giving birth to infants who are born too soon and too small.

In 2020, one in every four newborns was born small and vulnerable.¹⁸ In addition to being at a greater risk for death or serious illness, babies born too small or too soon have been shown to suffer from worse neurodevelopment outcomes, and are likely to have worse cognitive and development outcomes throughout childhood and into adulthood.^{19,20}

Fortunately, there is a cost-effective solution that can reduce the risk of a baby being born too soon or too small. Prenatal multivitamins – known as Multiple Micronutrient Supplements (MMS) – have a cost of around \$4 per pregnancy, making them one of the best buys in global development. These multivitamins have been proven to prevent anemia, support a healthy pregnancy, and reduce the risk of babies being born small and vulnerable.²¹ MMS was also highlighted as a highly cost-effective intervention by the Copenhagen Consensus.²²

In high-income countries, pregnant women have long been advised by medical professionals to take multivitamins to guard against a range of nutrient deficiencies that can occur during pregnancy. Paradoxically, in low- and middle-income countries, where the prevalence of malnutrition is much higher, pregnant women typically receive a supplement containing only two nutrients: iron and folic acid.²³ An American philanthropist and friend of ECF, Spencer Kirk – of the family philanthropy Kirk Humanitarian – has been the leading champion of this intervention over the last two decades, and has worked closely with American manufacturer

¹⁸ https://impekacdn.s3.us-east-2.amazonaws.com/hmhbcconsortium.org/content/user_files/2024/05/09103452/MMS-Investment-Roadmap-Digital-B-9-July.pdf

¹⁹ <https://obgyn.onlinelibrary.wiley.com/doi/10.1002/uog.11112>

²⁰ <https://pmc.ncbi.nlm.nih.gov/articles/PMC5740123/>

²¹ https://impekacdn.s3.us-east-2.amazonaws.com/hmhbcconsortium.org/content/user_files/2024/05/09103452/MMS-Investment-Roadmap-Digital-B-9-July.pdf

²² <https://copenhagenconsensus.com/sites/default/files/2023-03/Nutrition%20Best%20Investment%20Manuscript%20230211.pdf>

²³ https://impekacdn.s3.us-east-2.amazonaws.com/hmhbcconsortium.org/content/user_files/2024/05/09103452/MMS-Investment-Roadmap-Digital-B-9-July.pdf

Contract Pharmacal Corp (CPC) based in New Jersey, which is currently the world's leading provider of high-quality, low-cost MMS.

For a total cost of \$1.1 billion, we could reach 260 million women with MMS by 2030. This investment would save 600,000 lives, improve birth outcomes for more than five million babies, and prevent anemia in over 15 million pregnant women.²⁴ Global momentum for MMS introduction and scale-up is now at an inflection point, and in several countries, delivering MMS to pregnant women has been identified as an urgent priority. ECF and other philanthropies are committed to unlocking private funding to meet this need.

Infancy & the impact of breastfeeding through two years of age: Breastmilk is nature's superfood. It protects mothers' health and newborns from malnutrition, infections, disease, and death. Mothers who breastfeed experience lower risks of cancer, diabetes, and high blood pressure, while their children benefit from improved health, cognitive development, and long-term economic outcomes likely due to the rich nutrients in breast milk and the enhanced caregiving it fosters.²⁵ Research shows that breastfeeding is linked to higher performance in intelligence tests during childhood and adolescence.²⁶

Yet only 41 percent of babies around the world are exclusively breastfed. Breastfeeding-friendly policies – such as paid maternity leave, restrictions on the marketing of breast-milk substitutes, and skilled breastfeeding counseling, among others – can help close this gap.²⁷ When breastfeeding is well-supported and safeguarded, women are more than twice as likely to breastfeed their babies.²⁸

Early childhood & the impact of SQ-LNS: In early childhood, children require a diverse, nutritious diet to support their bodies and brains to grow. Many global efforts, including USAID's Feed the Future initiative,²⁹ are working diligently to improve the quality of children's diets available through food systems around the world. Education programs on infant and young child feeding practices, long supported by USAID's Global Health programs,³⁰ help families to make good choices when nutritious foods are available to them.

However, many vulnerable families in low- and middle-income countries are still not able to access or afford foods to meet the nutritional needs of their young children. To help address this

²⁴ *ibid*

²⁵ <https://openknowledge.worldbank.org/entities/publication/2c0b8b5e-0f67-47fe-9eae-d4707d9ed195>

²⁶ https://iris.who.int/bitstream/handle/10665/79198/9789241505307_eng.pdf;jsessionid=1

²⁷ https://www.endmalnutrition.org/img/nourishthefuture_paper_v13.pdf

²⁸ <https://www.unicef.org/press-releases/world-breastfeeding-week-unicef-and-who-call-equal-access-breastfeeding-support>

²⁹ https://cg-281711fb-71ea-422c-b02c-ef79f539e9d2.s3.us-gov-west-1.amazonaws.com/uploads/2021/10/Global-Food-Security-Strategy-FY22-26_508C.pdf

³⁰ See, e.g., <https://www.iycn.org/>.

need, small quantity lipid-based nutrient supplements, or SQ-LNS, are food-based supplements designed for vulnerable infants and young children. SQ-LNS contains the daily recommended intake of necessary micronutrients and can be mixed with foods or consumed as is. Evaluations indicate that these supplements decrease anemia for children, as well as cases of severe wasting and severe stunting,³¹ and are proven to reduce developmental delays.³² SQ-LNS was also highlighted as a highly cost-effective intervention by the Copenhagen Consensus.³³ Within a growing global supply base, American manufacturers such as Edesia and Mana Nutrition produce SQ-LNS using peanuts, milk, and other ingredients sourced from farmers across the United States.

Despite the effectiveness of these low-cost, high-impact interventions, many families in LMICs do not have the access they need to these solutions. Addressing this gap is crucial to improving health outcomes for pregnant women – and the health outcomes and brain health of infants and young children. Support and investment for these interventions is essential.

Together We Can Be Bold and Achieve a Healthier Future for the World's Children

The U.S. has historically been the largest donor in the fight against malnutrition. This commitment reflects a broader recognition of the critical role that nutrition plays in fostering economic development and global stability. By investing in sustainable agricultural practices, enhancing maternal and child health, and promoting nutrition education, the U.S. aims to create lasting impacts in vulnerable communities. Continued bipartisan support ensures that these efforts continue, addressing both immediate needs and long-term solutions to malnutrition and food insecurity globally.

My birth country of Nepal offers a notable example of the benefits from U.S. government investments in nutrition. In 1995, Nepal had the highest stunting rate in the world. Nearly two million children in the country were stunted – which meant that seven out of 10 children had significantly delayed growth, and were too short for their age. But over the past 20 years, with strong government policies and donor support, Nepal has reduced stunting prevalence by nearly half.³⁴ One important contributor was the USAID-funded Suaahara program, a 2011 to 2023 initiative that ultimately targeted maternal and child nutrition in nearly half of the country.³⁵ The program promoted better dietary practices, increased access to health services, and encouraged community engagement. Impact evaluations showed significant improvements in maternal nutrition and feeding practices. Despite challenges like the 2015 earthquake and the COVID-19 pandemic, the program has led to healthier mothers and children, contributing to long-term

³¹ <https://openknowledge.worldbank.org/entities/publication/2c0b8b5e-0f67-47fe-9eae-d4707d9ed195>

³² <https://pubmed.ncbi.nlm.nih.gov/34590116/>

³³ <https://copenhagenconsensus.com/sites/default/files/2023-03/Nutrition%20Best%20Investment%20Manuscript%20230211.pdf>

³⁴ <https://www.exemplars.health/topics/stunting/nepal>

³⁵ <https://www.usaid.gov/sites/default/files/2023-01/Nepal%20Snapshot%20HO%2003%20Suaahara%20II.pdf>

public health improvements in Nepal.³⁶ These advancements have been vital for children's development in Nepal, and have helped to ensure a stronger future generation.

This example is but one of many that illustrates the direct impact of U.S. government funding for nutrition, and how transformative it has been on one population.

The importance of continuing to champion programming for malnutrition is underscored by a recent report from UNICEF, which highlighted that one in four children today is living in severe food poverty. Put simply, that means 181 million children do not have the equal opportunity to grow, develop, and learn.³⁷ Without intervention, these children won't have the chance to reach their full potential. 181 million children – that is about half the population of the United States.

It is not easy to comprehend a number like 181 million. But I urge you today to remember that every one of that colossal figure stands for a child – a child who deserves to have ambitions, and dreams, and who, with the right nutrition and care, can grow and prosper, and make their country, and our world, a better place. Because malnutrition not only threatens children's lives – it harms their brain health, and it has devastating impacts for countries and their economies.

We know that progress is possible. We've seen it over the past decades, and we've seen it in just the last two years, when – as noted earlier – historic funding for malnutrition from the U.S. government and other public and private donors led to the rapid scale-up of treatment for children worldwide. Simple, cost-effective solutions for malnutrition and brain development exist, and need only be scaled. And now we must stay the course. Each of these children depend on our commitment to them. Thank you again for inviting me to testify, and I look forward to your questions.

³⁶ https://pdf.usaid.gov/pdf_docs/PA0213DW.pdf

³⁷ <https://news.un.org/en/story/2024/06/1150706>

Mr. SMITH. Thank you so very much, Dr. Rana, for your testimony and leadership.

Just a few opening questions: First of all, your testimonies are—just answer many of the questions that all of us might have had, so that is deeply appreciated.

With regards to the 2013 G8 Summit that was held of course for—trying to find a disease-modifying or a cure for Alzheimer's, I wonder if you could speak to how well or poorly we are doing on that time line. NAPA did help us, and that was a total bipartisan effort, to have a strategy to quadruple the amount of money that is going toward—most of it to NIH in the area of Alzheimer's research, but if you could speak to—as 2025 rolls around—and of course the SDGs also speaks to health in a variety of ways, including in the dementia realm. If you could speak to that.

Second, I would say and ask Dr. Warf, when you testified in the past, not only have you pioneered and helped save countless lives with your intervention, the non-stunt intervention, you had spoken of the effort to train Ugandans and Africans at Cure International and other initiatives to be the neurologists, to be the surgeons, to be the brain health experts. And I am wondering if you could update us on how well that might be doing, whether or not it needs a major push.

And any estimate on how many—I mean, I remember you showed us pictures of kids in Uganda who—before and after, after their—unfortunately the fact that their brains had so swelled up and the after pictures with their parents with smiles from ear to ear because they had been cured. If you could speak to that.

And again, further elaborate briefly if you would on the issue of the infection-based, because we had a lot of people—I chair the Spina Bifida Caucus as well here in the House and it is completely different. We know interventions in utero can help mitigate the impact of spina bifida, but you pointed out; and you had experts to verify, this was infections-based. Because I went and spoke, as I do every time—Samantha Power, Mark Green, all the USAID administrators are all wonderful people. They always say, well, we are dealing with infectious diseases. They do not want to cross that line into global brain health.

That is why my bill has failed at the launching pad every year. It is not going to fail this coming year, and your testimonies and your help will help make that happen. I mean, why aren't we doing this? And so many people are so mal-affected by it. Yes, HHS does some good work, but it is mostly in the realm of diplomacy, health diplomacy, not funding projects, NGO's and the like to take all of the global brain health initiatives on.

With Regards to autism, just a brief little story: I was in Abuja and then went over to Lagos in the year 2000. It was on a combating human trafficking trip. And I spoke to about 500 people and a man came up and he says what are you doing about autism here? Nothing. So I went and had lunch with him, breakfast as you would say, and we had a great meeting. And I know you guys do a great work internationally and I thank you for that. But again, we need to make sure that our government is doing more, which is why this initiative I think just has to be—and I do think we can succeed.

And, Dr. Rana, if I could with you, I am a great believe in the first 1,000 days from conception to the second birthday. Food nutrition for the mom so that both mother and baby are as healthy as humanly possible. And we do know that folic acid—and this has come out of the research pursuant to the Autism Cares work and the—that folic acid can, if taken very early in the pregnancy or by a woman of reproductive age as she becomes pregnant—it greatly reduces autism. Greatly reduces it. And so the more of that initiative: ours and the U.N.'s and others, can be shared with everybody, the better.

But first 1,000 days. I remember I was in Guatemala the day they announced their cooperation with a first 1,000 days initiative, because they have a stunting problem, as does Nigeria and so many other places. And it works. Mother's healthier. Baby's healthier. I mean, it is the most crucial time health-wise in any of our lives and it seems to me that we need to be doing more.

We have the Global Food Security Act. I was the House sponsor. Got it passed twice. Went over to the Senate. It came back as a Senate bill. Who cares. It is a good bill. But are we doing enough when it comes to global food security? If you could speak to that.

And you did mention folic acid, but—and thank you for bringing some of the other things that are so important. But if you could also—your presence here, your testimonies, it will be the gist of a brand new, all-out effort to get the Global Brain Health Initiative enacted into law and to get as much by executive branch policy as possible, but also by statute. So I do ask you, if you could, speak to those issues as—and anything else you think we need to touch on.

Gladys?

Dr. MAESTRE. Thank you, Chairman Smith, for your question and your insights. So you asked me about the treatment and advances and how close are we to cure. And I have to elaborate a little bit on this. We didn't know the situation was so complex for the brain as the brain ages. So we thought we were going to have a patient with memory loss and dementia and that we were going to be able to treat it just like that.

But we learned that it takes 20 years or more to get to the point of memory loss and other cognitive changes. So it takes 20 years. So we are now looking forward to therapeutics that will begin early enough to really stop the progression to the disease. That's our hope.

With the current medications which have been approved by FDA, they are—they do work taking out of the brain one of the proteins that deposit—that is deposited in the brain, that accumulates in the brain of people with dementia, which is the beta-amyloid. So they do work. They are monoclonal antibodies. They get to the amyloid and they clean it. So if—but if there is too much amyloid already, then there are going to be already other changes in the brain like neuron death, deposition of other things. So it's not enough to cause a clinical improvement. Not too much. It delays few months, but not—it's not a cure. Are we closer? Yes. Are we there? No.

So we are hoping that we are going to develop similar techniques and that we are going to develop strategies for different elements

in the brain of people already with dementia enough to at least stop the progression and maybe reverse. But what we are really hoping is to—once that we have the capability now to detect earlier before the symptoms appear that we are going to be able to develop therapeutics to stop right there, preventing the onset of the disease.

Dr. WARF. My turn. So I'll try to address each of the—each of your categories of questions.

So first of all, you asked about, Mr. Chairman, the progress in training surgeons. And so the last time that I was here in this place was in 2011. And at the time we had a training program on-site in the hospital that we started in Uganda where we brought neurosurgeons from other countries, developing countries to train them there in this technique for a period of time and then sent them back home. All right?

And using—through that program we actually trained neurosurgeons in about 30 different countries.

There were challenges though with that and one of those was that we were taking sometimes the only neurosurgeon in the—in that region and taking them away from their practice for two or 3 months for training. They were being trained in an environment that was unlike the one they were going back to and treating a different population of children, and sometimes there were obstacles to implementing their training when they got home.

The pandemic sort of made us appreciate the role of remote presence teaching and technology. And around that time we founded NeuroKids, which has a different paradigm of training. In this way we identified partner neurosurgeons in needy places, high-volume centers that are seeing a lot of hydrocephalus. And we have a Zoom-based pre-site visit protocol. We do then a site visit and do hands-on interoperative training.

And then after the trainer goes back, what we're able to do is continue to mentor that surgeon through remote presence technology. For instance, I can sit at my desk in Boston and in real time with the screen, the video endoscope screen on my computer I can talk to the surgeon, take them through what they're doing. I can telestrate on the screen. They can see that. And so we can virtually be there in the operating room with them. And that continues their training over a few months thereafter.

In the last couple of years we've been able to train in a number of sites in different countries, not just in Sub-Saharan Africa, but also South America, Southeast Asia. And by the end of this year we will have close to 20 different sites.

And the strengths—one of the strengths of this program is that we aim to train trainers. And so the person that we train, once they're competent, we support their mentoring and training of other surgeons in the region. So that's—that helps us to scale this kind of work.

In regard to the folate question, I won't speak a lot on that, but simply to say that because spina bifida/neural tube defects is a major cause of hydrocephalus, preventing that is very important. And if—when there is adequate folate supplementation or fortification of the grain supply, that has the potential to reduce the inci-

dence of spina bifida in a country by about two—down to two-thirds of what it is. So it can make a significant impact on that condition.

And then finally in regard to the infectious origins of hydrocephalus, the pathogen causing that is largely unknown in most places in the world. Over the course of about the past 10 years and quite a bit of NIH funding we finally were able to identify, with the appropriate experts—not me—but we were able to, with leadership of Steve Schiff in particular, identify a new human pathogen that was actually causing the post-infectious hydrocephalus in Eastern Uganda to a bacteria called *Paenibacillus*. And that hadn't been known to be a pathogen in humans.

And so the next stage will be learning how to better treat and prevent that particular infection, but we have no illusions that that's what's causing these infections elsewhere. And so what's needed is similar research programs to identify what's causing the infections in the neonates in other parts of the world.

And then finally, one of the important interventions is a simple public health intervention around perinatal care. In Uganda, for instance, most of the children were born at home in the village without professional help. They're in an environment where they're constantly exposed to mud and animal dung. One of the practices was to place animal dung on the cut umbilical stump to staunch the bleeding after the baby was born.

And so there are a lot of sort of simple things that could be done, but on a big scale in terms of advancing basic public health measures to prevent neonatal infection, which in low-income countries neonatal infections are very, very common. We don't have that kind of burden here in the U.S. That's really a condition of poverty.

Here in the U.S. one of the most common causes of hydrocephalus, if not the most common, is hemorrhage in the brain in prematurely born babies that are preserved and supported in our NICUs. That's a condition, post-hemorrhagic hydrocephalus of prematurity, which is really a condition of prosperity you might say. We don't see that in the developing world because those children, those prematurely born babies don't survive.

Yes, so I think hopefully that covers some of your questions. Thank you.

Mr. SMITH. Mr. Shih?

Mr. SHIH. Thank you, Chairman Smith. I just wanted sum up some reflection here. I think one the last previous time that I testify in front of the committee may be almost 10 years ago now. I remember that time we focus on conversation around awareness and inclusion of our community.

Part of the reason we did that is because there were no tools, right, and programs and policy that could really facilitate the inclusion of our community in society and system of care.

But now that we have. I mention in my testimony about this diagnostic screening tool that we develop, like Nigerian autism screening tool and the OS—open-source diagnostic tool that we develop Sub-Saharan Africa, as well as the Care giver Skill Training Program, Early Intervention Program develop at WHO. They're now available globally. So is no longer a question of what to do, but how quickly can we do it, right? We have the tools now. We have the resources to make things—to make a change happen. So it's be-

come a implementation problem. And that's why with U.S. leadership I think we can greatly accelerate the implementation process and bring a better tomorrow to all of our community around the world. Thank you, Chairman Smith.

Ms. RANA. Thank you for the question, Chairman Smith. I just wanted to start by appreciating both the chair and ranking member for passing the Global Malnutrition Prevention and Treatment Act and for really codifying the approach of focusing on evidence-based cost-effective interventions.

in my testimony I mentioned U.S. leadership in scaling treatment for severe malnutrition, which you all might now more commonly as Plumpy'nut, or RUTF. Because of bipartisan support from Congress and USAID, RUTF was accessed by nearly 9.3 million children, saving 1.2 million lives in 2023.

And I'm sharing this success story as a proof that when we focus on high-impact cost-effective solutions and become razor-focused impact is possible.

And this is what we're to do with these improved prenatal supplements. They also contain folic acid. But the case is we have a solution but we still need to figure out how deliver it. And the challenges can be multiple. Women not taking—women not coming to antenatal care on time; so the folic acid is not taken in the early stages of pregnancy, it's not going to work the magic that we need to. Women could be coming to antenatal care, but not be able to afford or access these prenatal supplements. They might not be getting counseled on the importance of these supplements and there could also be misconception or other adherence-related issues.

So we have a solution, but there is still a lot of work to be done in order to deliver it to get to impact. For this reason our foundation along with three other philanthropies has developed a road map for how we can reach women in the 45 high-burden countries with these improved prenatal supplements.

So over the next 6 years with an investment of 1.1 million we aim to reach nearly 260 million women with these improved prenatal supplements which has the potential to save nearly 600,000 lives and prevent 5 million vulnerable births. And these births are at risk for also having impaired brain health. Thank you.

Mr. SMITH. Thank you.

Ms. Manning?

Ms. MANNING. Thank you.

Thank you to my good friend, Chairman Chris Smith and also to my friend—my good friend Susan Wild, who is in another meeting right now. It has been a real honor to work with you on this subcommittee. Let me just say how much I will miss this work in the future.

To our witnesses, thank you so much for your testimony today. You have given us wonderful examples of what can be done to help prevent or treat devastating brain and health issues with the right tools, training, and resources from the U.S.

So, Dr. Warf, I want to ask you a question first. The President-elect plans to establish a Department of Government Efficiency to cut government spending. Do you believe that cuts to medical research should be on the table and would reducing funding to entities like NIH, CDC, CMS, HHS hurt efforts to find the kinds of tools you have described or cures for diseases—cures or treatments I should say for diseases like Alzheimer's?

Dr. WARF. Well, thank you for that question. I of course think that reducing support for the entities that you describe would be harmful to the health of children in most of the world. I also think; and this is partly in reference to what my colleague to the right of me here pointed out, in my opinion, for what's worth, when the U.S. invests in helping other people in other countries, we show our best side. And I think few things could be more valuable to diplomacy, not that I know anything about that. But that's my humble opinion as I think—I think we need to show our best, which is caring about the rest of the world and being willing to invest and help them, because it—in a sense, if we want to look at it from a selfish way, that does come back to help us as well.

Ms. MANNING. Thank you for that.

Dr. Maestre, would you like to comment on that as well?

Dr. MAESTRE. Sure. Thank you very much, Representative Manning, for coming here today and for these thoughtful questions.

I like efficiency. I like to do things better. So I can only be hopeful that the advantages of research and aid will come up. So I don't think that it's—I hope, right, that the funding will only keep increasing and being redirected to the needs and where we have a chance to be more impactful. Alzheimer's disease without doubt we are at a moment where we need to take advantage of where we are and what we can do at the global level.

Ms. MANNING. So in 2023, the NIH announced \$3 million in funding for Alzheimer's research, a collaboration between the U.S. and countries in Africa. Can you share just a little bit about what the impact of funding for programs like that can do?

Dr. MAESTRE. The main success is that we have access to resources that we don't have in our Nation, and that's at least—to mention one of them is DNA, the diversity, the genetic and genomic diversity that we don't have. So and this implies that we have access to cures, to targets that we don't have now. And that—it's the leadership that we need in the world. We need to have access to resources in ways that we can use them right away. Because we have the technology, we have the infrastructure, and we have the desire.

I also want to mention that we have, I think, a secret weapon which is not a secret, which is the African American scientists. I think they are very eager to work even more with African scientists and the African communities. So I think that we have a lot of pieces to really accelerate the discoveries that we need to bring back home, but also to make stronger partnerships in Africa and in other low and middle-income countries. Thank you.

Mr. MANNING. Dr. Shih, the President-elect's nominee to be the Secretary of Health and Human Services, Robert F. Kennedy, Jr., said in a 2023 Fox News interview the following: He said, I do believe that autism does come from vaccines. As a doctor do you agree with him?

Mr. SHIH. Thank you for that question, Representative Manning. So there have been numerous studies that have been done, both in the U.S. and around the world to look at the causal link between autism and vaccine, and today there has been no established evidence that link the two, vaccination with autism. So it is a settled scientific question.

Ms. MANNING. I am sorry. Can you say that Again, please?

Mr. SHIH. It's a settled scientific question for the research community.

Ms. MANNING. That vaccines do not cause autism?

Mr. SHIH. That's correct.

Ms. MANNING. Are you at all concerned about the potential head of HHS who might hold these views?

Mr. SHIH. We have worked successfully with both parties over the years to advance the interests of our community, the well-being of our community, and we strongly believe that we'll be able to continue to.

Ms. MANNING. I have heard some discussion about the fact that people believe that autism is on the rise. You described I think in your testimony some of the tools' better ability to diagnose autism. So do you believe autism on the rise or is there—are we better able to diagnose autism which gives higher numbers?

Mr. SHIH. So certainly we're diagnosing autism more than ever before in history. And certainly part of the reason that we're able to do that has been the improvement in knowledge, right, and awareness, efficacy of clinicians, and so on, the tools that we have to assist in these processes. But I think there's still uncertainties. We know that autism is the result of genetic environmental factors interaction. We have some understanding of the genetic factors that are at play. We're beginning to understand what environmental factors are at play. So I think over time we'll have a better understanding on what are all the factor that are really contributing to this condition.

Ms. MANNING. And when you say over time, will it just occur or would investment in more research be helpful?

Mr. SHIH. Absolutely investment in more research.

Ms. MANNING. Thank you. Individuals with autism are far more likely than their peers to suffer from social isolation, exclusion, mental health conditions such as depression and anxiety. How can we help first of all reduce the stigmas around autism, but second try to address some of those issues?

Mr. SHIH. Yes, that's a excellent question. So I think first of all awareness, right? And not only about awareness of autism, but really advocating for acceptance and understanding of autism I think is crucial to make progress in the particular area.

And I think the second thing is to really try to create accommodations for autistic people and their loved ones on our community so they can be actively intentionally included in family life and in social life and so on and so forth.

Ms. MANNING. And gainfully employed?

Mr. SHIH. Absolutely. That is so crucial, right? Because with—by addressing all these social determinants that can lead to better health we can actually improve the well-being and outcome of our community overall.

Ms. MANNING. Wonderful. I have a question from my colleague who won't be able to make it here. Dr. Shih, in your written testimony you highlighted your collaboration with the World Health Organization and UNICEF to help publish the first Global Report on Children with Developmental Disabilities. How important are mul-

tilateral institutions including the WHO and UNICEF in supporting global autism and health research initiatives?

Mr. SHIH. I think it's very important because obviously as an organization we're limited in our reach and ability to influence programs and policy, but by collaborating with multinational organization like WHO UNICEF it allows us to expand our reach and further disseminate sustainable solution to community in need.

Ms. MANNING. Thank you.

Dr. Rana, Thank you for holding up some of those very small packages of items that can have just a huge impact on the health of children and the nutrition for families. Can you tell us what aspects of U.S. global nutrition assistance programs have proven the most effective, and also which have proven the least effective?

Ms. RANA. Thank you, Representative Manning, for your question. The ones that have proven most effective in my perspective had been the ones that have focused on cost-effective solutions, having a razor-focus on really upping the coverage of these interventions that we know works. It's a tragedy that we have these solutions but we haven't still figured out how to scale them at high coverage so that every woman everywhere and babies are able to access them.

On what has not worked is a question I'd like to followup with a written response because I haven't seen the entire portfolio of programs and it wouldn't be right for me right now make a comment beyond that.

Ms. MANNING. Thank you. I think that would be helpful because we do talk about wanting to make sure that we are putting our efforts in the right place. And I agree we want to be efficient and effective. So sometimes it is important not to just know what does work, but what is not working, what we should stop doing so that we can devote our resources to the things that are working.

And I had another question here. Dr. Rana, how can global health partnerships help feed children with neurodevelopmental needs in malnutrition-prone regions? How can we be partnering? We had a bill on the floor that we were discussing earlier today about the war in Sudan and how 14 million people have been impacted by that war, either relocated or put in devastating circumstances where they are at risk of malnutrition. How can we be partnering to address some of the nutritional needs that are going to be—that are affecting people in such difficult circumstances?

Ms. RANA. Thank you again for that thoughtful question, Representative Manning, especially as there are multiple crises worldwide that are happening simultaneously. And the people who bear the biggest brunt are pregnant women and young children, what you, Chairman Smith, called precious to our society.

We have again these cost-effective solutions. If you look at the packet of ready-to-use therapeutic food, it is specifically for kids who are severely malnourished. Given their condition, taking a normal meal is not going to be easy for them and so this provides them with the required nutrition for their treatment.

SQ-LNS, that I talked about, is also from a prevention angle of how do we get kids early on before they get too wasted? And similarly for pregnant women we are talking about solutions like prenatal vitamins that are more holistic. But also in some cases when

women are very undernourished we are looking at supplements for lactating and pregnant women also. So there are solutions that are feasible, that are possible.

But then the challenge again is financing. How do we finance given the scale at which these crises are happening and how do we reach these populations, which some of the U.N. agencies like UNICEF and WFP—they have baskets of food and services for both pregnant and vulnerable populations.

Ms. MANNING. Thank you. Well, let me just thank you all for the really important work you do. Thank you for being here today. My sister specializes in treating Alzheimer's patients at the UVA Medical School, so I am well aware of how devastating Alzheimer's can be for patients and families, how desperate they are for treatments that work either to arrest or prevent the disease from developing.

So I hope we continue to invest in the research and the great organizations and great researchers who can provide solutions and treatments for all of the diseases that we have been talking about today and that we continue to share our knowledges and our resources with the areas of the world that are most prone to having these problems where our small amount of help can provide an enormous benefit.

And not only do we help them, but, Dr. Warf, as you suggested, it also helps us in our standing in a world where there is great power competition right now and it is a good effective way for us to build friends and alliances. So thank you.

With that, I yield back.

Mr. SMITH. Thank you very much.

If I could just recognized Scott Badesch, who is now on my staff. Ten years as president of Autism Society and has been very helpful and as we write this new bill with all of the groups.

And, Stewart, great to see you again as always. We miss you already.

He just retired in September. Did a wonderful job in the Autism CARES legislation.

And I want to thank you especially for that.

But as we go forward, this is going to be an all-out push and I think we can succeed. I mean, your testimoneys, but your work, your life work is so important. You have saved so many lives and can enhance the lives of so many others. They have improved the quality of life. It is just extraordinary. So thank you for that.

I do have just one brief question to Dr. Shih about the—I remember when thimerosal was all the rage. Of course that has been out of our immunizations for quite some time. And some people still cling to that, but it is not there anymore, so how can you be suffering from that and contributing to autism?

And one of my first amendments I offered here as a new second-term Member of Congress was to provide \$50 million for the Child Survival Fund. It passed; it became law. And it was for one of the pillars of the Child Survival Fund was immunizations. And I actually traveled to El Salvador, and many Central American countries and African countries later, but for Days of Tranquility, when the FMLN were fighting against Duarte's government and they would stop all fighting to immunize the children against diphtheria, polio,

pertussis, the leading killers of children. So I do believe there is an absolute important role to be played.

But there is an argument made; and I would appreciate your thoughts on this, that if too many vaccinations are given at once that that could have a negative impact, maybe contributing to autism, but could have a negative impact on that child because of the absorption capacity of a very young child. If you get five immunizations at once, what does that do? So spreading them out might be a wise and prudent course of action for mothers. Just wondering what your thoughts are on that. Get the vaccination, but spread it out?

Mr. SHIH. Right. Whether or not it's vaccination, just spread it out. So this has been an issue in the community, as you know, for a couple of decades now. Certainly there's no evidence that suggests that having receiving multiple doses of vaccines a day is leads to autism or associative autism.

My understanding is that the developing child are able to tolerate this kind of vaccine schedule, right? And we have seen through history this is not a new program that's introduced. It's been around for decades and we certainly have not seen the evidence that this kind of vaccine schedule actually lead to significant harm for children's health.

Mr. SMITH. I appreciate that.

Let me just conclude. My hope is that your testimonies, the work you have done builds on a renewed call to action to the incoming administration to really take on global brain health. And we will do it by way of legislation. I do think we can get it passed this time. I have already spoken to some of the leadership including the Speaker about this. This is an idea whose time has come to quote, or paraphrase Victor Hugo. And you have been doing it. You all have been doing it. And we just need to do even more to make sure that USAID and not just HHS through diplomacy is embracing this achievable goal. So I want to thank you so much.

Anything else you wanted to add now or by way of written submissions? Please, yes, Gladys?

Dr. MAESTRE. Thank you very much, Chair Smith. I wanted to reaffirm some of the comments you made. I have been devoted all my life to international work, not only because I come from Venezuela and that my work has been in Africa and Latin America, but because now I work at the University of Texas, Rio Grande Valley, which is located in Brownsville, Texas. This is 10 minutes from the Rio Grande, from the river and 40 minutes from SpaceX.

Many of my patients and participants, when I talk to them, they mention the adversity of human trafficking in their lives. At least I would say that 20 to 25 percent of the women that I see as Alzheimer patients have been subjected to this type of abuse. And I wanted to lay that out because I think that the social determinants of health that we are experiencing in the border are many—in many ways related to what's happening in low and middle-income countries, the lack of access and the new opportunities that we have now to bring together issues which you have led for many, many years. And now we can envision a global health strategy with these diseases and these strategies, but also too that will benefit

not only low and middle-income countries, but low-resource settings like the Rio Grande Valley in South Texas.

Mr. SMITH. Thank you for that. Are you suggesting trauma-induced Alzheimer's?

Dr. MAESTRE. We——

Mr. SMITH. Is it because of beatings or because of sexual assault?

Dr. MAESTRE. We believe that adversity of that level

Mr. SMITH. Right.

Dr. MAESTRE [continuing]. Is increased vulnerability of the brain to confront aging and to develop a healthy life.

Mr. SMITH. Thank you for that. That bears us really focusing on that.

Just for the record, I am the author of the Frederick Douglass Trafficking Victims Prevention Act. Passed the House in February; still pending in the Senate. It is probably going to die in the dustbin called the U.S. Senate. It just kills me that it is just sitting there. And I have been calling. I have been asking. And it looks like it is going to die in the next 3 weeks. We are going to reintroduce it, start it all over again. And the original TVPA, which I wrote in the year 2000, took 3 years to get enacted. And we didn't know until the very end whether or not it would be pocket vetoed or approved by the Clinton administration. Clinton did sign it. Thank God for that.

But I mean it is like why isn't this a no-brainer and just do it? But that is an area that we need to look into. I have never heard that before, so I thank you.

So thank you so much. And we look forward to all of your input on what the bill should further look like. And maybe you might consider a collaborative letter from your organizations to Trump. We could highlight it as well. I will do one from Members of Congress. And I am sure I could get bipartisan signatures for it because we want to make sure there is no diminution of what we are focusing on. We don't want to see money stop going to Alzheimer's research, or autism, or all these other important initiatives. But I think we need to go big. And I thank you so very, very much.

Hearing is adjourned.

[Whereupon, at 3:53 p.m., the subcommittee was adjourned.]

APPENDIX

MATERIAL SUBMITTED FOR THE HEARING RECORD



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

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

November 15, 2024

Revised

TO: MEMBERS OF THE COMMITTEE ON FOREIGN AFFAIRS

You are respectfully requested to attend an OPEN hearing of the Committee on Foreign Affairs to be held by the Subcommittee on Global Health, Global Human Rights, and International Organizations at 2:00 pm in room 2172 of the Rayburn House Office Building. The hearing is available by live webcast on the Committee website at <https://foreignaffairs.house.gov/>.

DATE: Wednesday, November 20, 2024

TIME: 2:00 pm

LOCATION: 2172 RHOB

SUBJECT: Meeting the Challenges of Global Brain Health: Diagnosis and Treatment for the 21st Century

WITNESSES: Gladys E. Maestre, M.D., Ph.D.
Director
Alzheimer's Disease Resource Center for Minority Aging Research
University of Texas

Benjamin C. Warf, M.D.
Chairman
NeuroKids

Andy Shih, Ph.D.
Chief Science Officer
Autism Speaks

* Yashodhara Rana, Ph.D.
Associate Director of Research
Eleanor Crook Foundation

****NOTE:** Witnesses added or changed

*NOTE: Witnesses may be added.

By Direction of the Chair

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 202-226-8467 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 FULL COMMITTEE HEARING

Day Wednesday Date November 20, 2024 Room Rayburn 2172

Starting Time 2:26PM Ending Time 3:51PM

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

Presiding Member(s)

Rep. Christopher Smith

Check all of the following that apply:

Open Session ☒

Executive (closed) Session ☐

Televised ☒

Electronically Recorded (taped) ☒

Stenographic Record ☒

TITLE OF HEARING:

Meeting the Challenges of Global Brain Health: Diagnosis and Treatment for the 21st Century

COMMITTEE MEMBERS PRESENT:

Attached

NON-COMMITTEE MEMBERS PRESENT:

NA

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.)*

Rep. Smith - Alzheimer's Association and Alzheimer's Impact Movement SFR USHFA, Global Health Statement

Rep. Wild - Congresswoman Susan Wild - GH-HR-IO Subcommittee Hearing Remarks

TIME SCHEDULED TO RECONVENE _____

or

TIME ADJOURNED 3:51PM

Meg Wagner
Full Committee Hearing Coordinator

Committee on Foreign Affairs**Subcommittee on Global Health, Human Rights, and International Organizations**118th Congress

ATTENDANCE

Meeting on: Meeting the Challenges of Global Brain Health: Diagnosis and Treatment for the 21st Century

Date: 11/20/2024

Convened: 2:26 PM

Adjourned: 3:51 PM

Representative	Present	Absent	Representative	Present	Absent
Mr. Smith	X		Ms. Wild		
Ms. Salazar			Mr. Bera	X	
Ms. Radewagen			Ms. Jacobs		
Mr. Hill			Ms. Manning	X	
Mr. McCormick			Mr. Keating		
Mr. James					



Alzheimer's Association and Alzheimer's Impact Movement Statement for the Record

**United States House Committee on Foreign Affairs, Subcommittee on Global Health,
Global Human Rights, and International Organizations
Hearing on “Meeting the Challenges of Global Brain Health: Diagnosis and Treatment
for the 21st Century”**

November 20, 2024

The Alzheimer's Association and Alzheimer's Impact Movement (AIM) appreciate the opportunity to submit this statement for the record for the House Committee on Foreign Affairs, Global Health, Global Human Rights, and International Organizations Subcommittee hearing on “Meeting the Challenges of Global Brain Health: Diagnosis and Treatment for the 21st Century”. The Association and AIM thank the Subcommittee for its continued leadership on issues important to the millions of people living with Alzheimer's and other dementia and their caregivers. This statement provides an overview of the state of Alzheimer's disease worldwide, and the need for action to continue to increase prevention, diagnosis, and treatment methods for those living with Alzheimer's and other dementias worldwide.

The Alzheimer's Association is the world's leading voluntary health organization in Alzheimer's care, support, and research. It is the nonprofit with the highest impact in Alzheimer's research worldwide and is committed to accelerating research toward methods of treatment, prevention, and, ultimately, a cure. AIM is the advocacy affiliate of the Alzheimer's Association, working in strategic partnership to make Alzheimer's a national priority. Together, the Alzheimer's Association and AIM advocate for policies to fight Alzheimer's disease, including increased investment in research, improved care and support, and development of approaches to reduce the risk of developing dementia.

Alzheimer's Impact on Families and the Economy Worldwide

Alzheimer's is a progressive and fatal brain disorder that damages and eventually destroys brain cells, leading to a loss of memory, thinking, and other brain functions. There are no survivors.

In 2020, more than 55 million people were estimated to be living with Alzheimer's and other dementias worldwide. Because of the devastating effect of dementia on individuals, families, communities and health care systems, finding ways to prevent, slow, and better manage Alzheimer's and other dementias is a top priority for research centers around the globe. Without advances, the number of people living with dementia will continue to grow, and is projected to reach 78 million in 2030 and 139 million in 2050. Most of this increase – 76% – is projected to occur among low- and moderate-income countries, which have far less capacity to address the escalating epidemic than higher-income countries. The costs for caring for those with Alzheimer's worldwide are also expected to increase. While the estimated cost of care is currently more than \$1.3 trillion, costs will skyrocket as more people develop dementia, with the cost of care estimated to reach \$2.8 trillion by 2030. Unfortunately, our work is only becoming more urgent.

The Case for Increased Treatment and Research

Despite recent developments in Alzheimer's treatment, there is more work to be done to prevent the increase of Alzheimer's and other dementias worldwide. Some studies have shown that the rates of incidence and prevalence of Alzheimer's – the percentage of the population who develop and have Alzheimer's – have declined in the United States and other high income countries over the past 30 years. However, it is unclear that these declines have occurred across all racial and ethnic groups – and there is scant evidence that they are occurring in low- and moderate-income countries. Even with declining rates, because the number of older adults is dramatically increasing, the number of Alzheimer's cases – that is, the number of people living with the disease – will continue to rise.

The decline in incidence and prevalence rates has been attributed to increased levels of education and improved management of cardiovascular risk factors. The Lancet Commission recently estimated that as many as 45% of all dementia cases in the world could be attributed to modifiable risk factors. This offers hope that identifying and reducing risk factors for dementia may be effective at reducing the number of cases. On the other hand, the increase of obesity and diabetes among middle-aged people may have the opposite effect: increasing the number of older adults who are at risk of developing dementia in the coming decades.

Despite the promising opportunities for reducing risk – and thus, possibly reducing the number of cases – it will require an aggressive public health effort at addressing the modifiable risk factors for dementia. We must make that investment. But, even if successful, there will still be millions of people around the world who will be living with and who will develop the disease. So we must also redouble our efforts to ensure diagnosis and treatment to those living with Alzheimer's and other dementias have better health care outcomes.

Global Research Efforts

The Alzheimer's Association and AIM are committed to accelerating the global effort to eliminate Alzheimer's disease. No single organization can surmount a challenge as great as Alzheimer's. To help achieve our vision of a world without Alzheimer's, the Association partners with key government, industry, and academic stakeholders in the global race to end Alzheimer's. The Association formula for progress rests on four pillars: funding, increasing collaborations with investigators, sharing data, and overcoming barriers to progress.

The first pillar is funding and the Alzheimer's Association International Grant Program which funds independent researchers worldwide fits right in. The Association currently has more than \$430 million invested in over 1,110 active projects in 56 countries that span six continents. Our grants have funded some of the most instrumental research in Alzheimer's and dementia science, and focus on multiple areas of research, including our understanding of Alzheimer's disease and dementia, identifying new treatment strategies, improving support and care for people with dementia and their families, and furthering our knowledge of brain health and disease prevention. We have funded many of the most exciting advances in Alzheimer's and dementia research, including the development of Pittsburgh Compound B (PiB), the first radiotracer

capable of showing beta-amyloid in the living brain during a positron emission tomography (PET) scan. Identifying beta-amyloid in the living brain lets researchers determine if an experimental drug successfully decreases this hallmark Alzheimer's protein and provides invaluable information about disease progression.

The Association funds across the total spectrum of Alzheimer's and dementia 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. 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. The Alzheimer's Association International Conference (AAIC), will be held in Toronto, Canada in 2025. This conference is held to reveal progress, and develop new working collaborations to advance treatments for the disease. AAIC provides a platform for presentation and discussion of all aspects of Alzheimer's research from genetics to animal models, pathology, biomarkers, interventions, and social and behavioral issues. Our most recent conference, AAIC24, saw more than 14,000 attendees joining in Philadelphia and online at the world's largest dementia research conference. By encouraging the attendance of researchers from around the world, the Alzheimer's Association is able to bring new innovations in Alzheimer's and dementia research to a single thought forum designed to accelerate the understanding of Alzheimer's and related dementia. The Association is also the home of the International Society for the Advancement of Alzheimer's Research and Treatment (ISTAART), a collegial professional society that encourages focus groups for increased cooperation.

The third pillar of our program is sharing of information. We publish *Alzheimer's & Dementia*, the official journal of the Alzheimer's Association. This journal allows important progress to be collected in one place to increase the efficiency of Alzheimer's research. In 2011, 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 to diagnose Alzheimer's disease in 27 years. The new criteria were the result of a two-year effort by three expert workgroups. Additionally, the criteria were updated in 2018 by the NIA and the Alzheimer's Association to define Alzheimer's disease in the context of biomarkers to help accelerate research, and most recently in July 2024 by the Alzheimer's Association to include an updated biomarker classification system that includes blood-based biomarkers and a revised disease staging system.

The fourth and final pillar of our program is investing in projects to overcome common barriers in the field of Alzheimer's. Projects include TrialMatch™, Global Alzheimer's Association Interactive Network (GAAIN) and the Global Biomarkers Standardization Consortium (GBSC) work to overcome common barriers.

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

The Global Alzheimer's Association Interactive Network (GAAIN) is a gateway to providing access to a vast collection of Alzheimer's disease research data, sophisticated analytics tools and computational resources. GAAIN promotes data sharing among a federated, global network of data partners who are studying Alzheimer's disease and other dementia. The mission of GAAIN is to advance a global cooperation of sharing, investigation and discovery. As the sponsor of GAAIN, the Alzheimer's Association changes the way researchers work together to answer questions related to the causes, diagnosis, treatment and prevention of Alzheimer's and other neurodegenerative diseases.

The Alzheimer's Association® established the Global Biomarker Standardization Consortium (GBSC) over a decade ago to gather key researchers, clinicians, industry, regulatory and government leaders in Alzheimer's disease and dementias to achieve consensus on the best ways to standardize and validate biomarker tests for use in global clinical practices. In the past few years, the Alzheimer's and dementia field has developed improved techniques and technologies aimed at early diagnosis and detection of Alzheimer's disease and related dementias. The field has seen remarkable growth in research using clinical assessments, psychometric testing, cerebrospinal fluid (CSF) and blood-based biomarkers, magnetic resonance imaging (MRI) and positron emission tomography (PET) imaging of the brain to detect hallmarks of neurodegenerative diseases at its earliest stages. Before these and other diagnostic measures can be incorporated into clinical practice worldwide, they must be standardized and validated on a global scale. The GBSC convenes these experts to address the challenges inherent in this goal and to develop global standards required for worldwide implementation.

Dementia has been declared a public health priority by the World Health Organization (WHO), which has also prioritized research into dementia prevention. Risk reduction and prevention are pivotal in managing the dementia epidemic globally, and the sharing of data is vital to informing this process. In 2017, the Alzheimer's Association launched the World Wide Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (WW-FINGERS) based on the FINGERS study in Finland that was the first randomized controlled trial showing that it is possible to prevent cognitive decline using a multidomain lifestyle intervention among older at-risk individuals. WW-FINGERS will facilitate the use of data from several countries, creating a unique opportunity for rapid knowledge dissemination and implementation. The WW-FINGERS network is the first global network of multidomain lifestyle intervention trials for dementia risk reduction and ultimately prevention. Studies that participate in the WW-FINGERS network aim to apply, test and optimize the FINGER-like model to reduce risk across the spectrum of cognitive decline in different geographical, cultural and economic settings in individuals at greater risk as they age.

To support the expansion and opportunity for advancing this research, the Alzheimer's Association is launching a pilot funding program for WW-FINGERS Network projects. The ALZ WW-FNFP will provide initial/startup funding and/or opportunities for ongoing studies to initiate WW-FINGERS like studies, to expand these studies or to add/leverage unique opportunities that enhance the study. This will be a competitive funding program and all submissions will be reviewed.

Other Global Efforts

Beyond our scientific and research efforts, the Alzheimer's Association works globally in other

ways to enhance diagnosis and care. Both directly and through our membership in Alzheimer's Disease International, the Alzheimer's Association works closely with the World Health Organization to advance global action to address dementia prevention, treatment, care, and caregiver support. As one example, we provided funding for the development and evaluation of the WHO's iSupport program – a tablet-based training program for family caregivers of those living with dementia. This program has the potential to educate caregivers in low- and moderate-income countries in a cost-effective manner.

The iSupport initiative is just one example of the critical role the WHO plays in addressing dementia in countries around the world, particularly low- and moderate-income countries. However, the future of that work is in jeopardy. In 2017, the Member States of the WHO endorsed the *Global Action Plan on the Public Health Response to Dementia, 2017-2025*. We believe this plan and its associated seven action areas are the best and most robust way to manage the multifaceted challenges of dementia to health and long-term care systems, governments, society, and individuals directly affected by the condition. Unfortunately, a 2023 global status report by the WHO Secretariat concluded that no target in the Global Action Plan was on track to be met by 2025, and the plan is set to expire next year. Therefore, the Alzheimer's Association calls on the United States – and all Member States of the WHO – to approve an extension of the Plan for another 10 years.

The Alzheimer's Association also provides advice and communications support to the World Dementia Council (WDC), and our President and CEO, Joanne Pike, currently serves as the organization's Vice-Chair. The WDC was established after the 2013 G8 Summit in London to bring together individuals from a variety of fields – including research, the financial sector, and care providers – to collaborate in support of developing treatments, understanding risk reduction, and improving the lives of people living with dementia today and in the years ahead. The Council works to draw attention to the urgency of the issue and the need for action from national decision-makers by hosting international forums, engaging national policymakers, and providing evidence and examples of how policy challenges are being addressed globally.

A collaborative international effort led by the Alzheimer's Association is LINC-AD, a project funded by the National Institutes of Health. LINC-AD convenes psychosocial researchers from around the world in an effort to achieve better outcomes for those facing dementia. We are currently working to expand our international membership and collaboration. And we recently conducted a survey about person-centered dementia care with Alzheimer's associations and societies around the world. This survey is the first step in what we hope will be the development of a consensus global definition and key tenets of person-centered dementia care to help ensure that individuals and caregivers have consistent quality care and support around the world.

One final global initiative worth mentioning today is our Project ECHO work. As you probably know, Project ECHO is a proven, scalable virtual learning model that equips health care providers with the knowledge, training, and resources necessary to deliver high-quality care to their patients. Earlier this year, in recognition of the success of the Association's Alzheimer's and Dementia Care ECHO program in the United States, we were named the world's first Project ECHO Superhub for Alzheimer's and dementia care. As a Superhub, we support organizations across the globe in launching their own ECHO dementia programs by providing training, mentorship, and technical assistance. In addition, the Association facilitates connections and peer mentorship through the Alzheimer's and Dementia Care ECHO Global Collaborative, which

includes organizations around the world that are currently using ECHO for dementia training of providers as well as those who are interested in launching their own program. With the leadership and support of the Association, this effort provides a significant opportunity to expand the capacity of providers across the globe in improving diagnosis and care for those living with dementia and their caregivers.

Changing the Trajectory of Alzheimer's

In 2011, Congress passed the bipartisan National Alzheimer's Project Act (NAPA) (P.L. 111-375), resulting in the landmark National Plan to Address Alzheimer's Disease (The National Plan). The National Plan, which is updated by the Department of Health and Human Services (HHS) annually, continues to drive meaningful action, creating and implementing strategies to address Alzheimer's and other dementia on both national and state levels. NAPA also led to the creation of the Advisory Council on Alzheimer's Research, Care, and Services, which is a panel of federal and non-federal experts that convene regularly to provide recommendations and annually update the coordinated strategic National Plan. While the National Plan has driven enormous progress in research, clinical and long-term care, and public awareness, we still have much work to do.

The NAPA Reauthorization Act, which passed Congress and was signed into law by President Biden this year, will continue the great progress of the National Plan to Address Alzheimer's Disease through 2035 and add several federal seats to the Advisory Council on Alzheimer's Research, Care and Services, including the Department of Justice, Federal Emergency Management Agency, and Social Security Administration. The bill also adds language to help address healthy aging and risk reduction for Alzheimer's disease to reflect the new sixth goal of the National Plan. We are thankful for the swift passage of the NAPA Reauthorization Act through the House and the Senate, because it will provide HHS the certainty and stability to continue both immediate and long-term planning for a strategic nationwide approach to Alzheimer's and other dementia.

Conclusion

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

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

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

Congresswoman Susan Wild (D-PA-7)

November 20, 2024

Remarks for U.S. House of Representatives Committee on Foreign Affairs

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

**Meeting the Challenges of Global Brain Health: Diagnosis and Treatment for
the 21st Century**

Thank you, Mr. Chairman, and thank you to our witnesses for their work and for
appearing here today.

I would like to begin a personal note: In a few weeks, I will no longer serve as a
member of this body. It has been the greatest honor of my life to represent the
people of Pennsylvania's Greater Lehigh Valley in Congress over the past six
years, and it's been a particular privilege to serve as a member of the House
Foreign Affairs Committee and as Ranking Member of this Subcommittee.

During my time in Congress, I sought to advance a vision of a foreign policy that
reflects the best of who we are as a country and as a people: A vision centered on
combating hunger, inequity, and disease both here at home and around the world.
A vision that defends universal rights and dignity. A vision that stands with

workers and the labor movement wherever they come under attack. A vision that says that we can and must be a voice for prisoners of conscience who languish in prison cells the world over. A vision that says to all those whose rights and dignity are trampled on: You are not forgotten. You are not alone. We stand in solidarity with you.

Just two days ago, on November 18, the Egyptian political prisoner Alaa Abd Al Fattah turned forty-three years old. For most of the past decade, he has been arrested, put on show trials on draconian charges, and imprisoned for expressing views that are critical of the Egyptian government. A few years ago, I had the opportunity to meet with Alaa's sister and, ever since then, I've kept a copy of his book in my office. The title is "You Have Not Yet Been Defeated." Those words are a powerful message for every political prisoner, every dissident, every activist standing up to powerful forces. Their lesson to us is that democracy is sacred, and that no leader should ever be placed above the law or above their fellow citizens. As we prepare to see our democratic institutions here in the United States tested over the coming years, I hope that is a lesson that all of us take to heart.

This subcommittee has a unique opportunity when it comes to shaping the future of our nation's foreign policy and, in particular, making sure that human rights and

global health are not relegated to the margins but, rather, part of the unshakeable foundation of the United States' leadership and engagement around the world.

That brings me to today's hearing, which focuses on some of the international community's greatest global health threats: sustaining robust global brain health and nutritional care. As we will explore in this hearing, malnutrition is an entirely preventable factor that is acutely linked to global brain health challenges.

As a country, it is imperative that we continue supporting adequate funding for the integration of brain health care and treatments across our global health assistance programming. U.S. global health assistance enables developing countries to develop effective treatments for neurological and cognitive disorders and diseases, which often place heavy financial burdens on the most vulnerable members of the population.

Our global assistance, particularly for child and maternal health, has made a world of difference in supporting sustainable development and bolstering the capacity of health care systems in under-resourced regions. This isn't just an investment in these individual countries. Over time, it's also an investment in our own health security. Our own economic security. Our own national security. These investments must be sustained.

Global brain health challenges and their related social and economic impacts cannot be overcome without strong multilateral partnerships. A go-it-alone approach by the United States simply won't work. We must sustain bipartisan efforts in Congress, with civil society, and across multilateral organizations, to continue to save lives and improve the quality of life for women and children in developing countries.

I look forward to this hearing. In the time that I have left in this office, I look forward to continuing to speak out in support of—and work toward—a foreign policy that is worthy of the aspirations and ideals that have guided our country forward at its finest. And, whether in or out of Congress, I'll remain an unwavering ally for the fight against hunger, against poverty, against inequity, and in defense of universal rights and dignity.

Questions for the Record Submitted to
Dr. Andy Shih by
Chairman Christopher Smith
House Foreign Affairs Subcommittee on Global Health, Global Human Rights, and International
Organizations

November 20, 2024

1. Every year the United States spends billions of dollars on efforts to improve global health, primarily through combatting infectious diseases. By contrast, little is done to address issues of global brain health.
 - a. Which U.S. global health assistance and / or research programs abroad, if any, address brain health challenges such as autism?

The USAID's Inclusive Development Hub is one example of a program that has helped to advance disability-inclusive programming worldwide, including programming that has benefited autistic people. Other projects funded by USAID like the I-Thrive project in Vietnam have specifically been tailored to help meet the needs of children with intellectual and developmental disabilities, including autism. Importantly, the I-Thrive project adopted the World Health Organization (WHO) Caregiver Skills Training (CST) model (developed in partnership with Autism Speaks) – a culturally responsive program that empowers the caregivers of children with autism and other developmental disabilities with skills to improve social inclusion and communication. Autism Speaks was also proud to provide technical assistance to a USAID-funded education initiative in Nepal, where CST was incorporated as a part of the programming. All of that said, as noted in my testimony, the recent data showing that 95% of children and adolescents with developmental disabilities worldwide have no access to appropriate care, illustrates how far we have to go. The amount of funding that has been dedicated to addressing the health care challenges of people with autism and other disabilities worldwide is just a drop in the bucket compared to the need, and we greatly appreciate the emphasis of the Subcommittee on this, and hope to see increased investment at USAID as well as other relevant agencies in the future.

- b. How can the U.S. best help address the needs of populations living with autism in low-to-middle-income countries?

The U.S. is poised to help by expanding efforts to bring the tools that have already been developed to populations that have not been able to access them. As mentioned during the hearing, whereas we were in a different place about a decade ago, now we have diagnostic screening tools and early intervention programs like Caregiver Skills Training that are now readily available to be deployed. The issue is that we have an implementation problem – we have not been able to make these tools available to communities at a fast enough pace. Whether it's through Congress, the Executive Branch, or work with multilateral organizations focused on addressing the needs of people with

autism and other developmental disabilities, U.S. leadership could help bring about significant change.

- c. What legislative recommendations would you make to the Congress to pursue to address autism internationally?

Generally speaking, we would recommend that Congress invest additional funding into programs that can help deliver some of the existing tools and programs that have been developed to more places around the world. In addition, we would encourage Congress to examine the stepped-care approach mentioned in my testimony, and explore ways to continue to build upon the robust impact of existing early childhood development programs, similar to the early success we've seen with that model in some of the UNICEF pilot sites.

In terms of a specific piece of legislation, we were strong supporters of the Global Autism Act of 2021 (H.R. 4160), which was introduced in the 117th Congress, and believe that if reintroduced and passed, it would go a long way to assist many autistic people and their families around the globe. By establishing a Global Autism Assistance Program within USAID to support developing countries in providing services for autistic individuals, this legislation would create an increased and much-needed focus on addressing disparities in access to services that too many autistic people globally experience. As you know, that bill would have required USAID to designate at least two regions in developing countries that need assistance in addressing challenges faced by people with autism and would award grant funding to a nongovernmental organization with demonstrated experience serving the autism community to implement the program. One important component included in the bill is a requirement that a "Train the Trainers" program is established by each NGO that is awarded funding to provide specialized training to professionals working with individuals with autism. In our experience working on implementing the CST program in many different countries, this is an absolutely critical aspect to ensure community engagement and improved outcomes over the long-term.

We've seen in other countries, when investments like this have been made, they have been leveraged to increase overall investments in inclusive health systems. Passage of legislation like the Global Autism Act could have the potential to do the same thing, going far beyond the initial investment and leading countries to make systemic, positive changes. It would also align with the newly released USAID disability inclusion policy, "Nothing Without Us", which calls for the inclusion of persons with disabilities in the development process as a critical part of strengthening health systems for persons with disabilities.



Questions for the Record Submitted to
 Dr. Benjamin Warf by
 Chairman Christopher Smith
 House Foreign Affairs Subcommittee on Global Health, Global Human Rights, and International
 Organizations
 November 20, 2024

1. **Every year the United States spends billions of dollars on efforts to improve global health, primarily through combatting infectious diseases. By contrast, little is done to address issues of global brain health.**

a. Which U.S. global health assistance and / or research programs abroad, if any, address brain health challenges such as hydrocephalus?

The only relevant federal funding of which I am aware comes from the NIH, especially through the Fogarty Institute. Our randomized controlled trial of ETV/CPC vs. shunt placement being carried out in Uganda is funded by the National Institutes of Health; [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01936272) number, [NCT01936272](https://clinicaltrials.gov/ct2/show/study/NCT01936272). There has also been NIH funding to discover the pathogen most responsible for post-infectious hydrocephalus in Eastern Uganda: National Institutes of Health Director's Pioneer Award 5DP1HD086071 and National Institutes of Health Director's Transformative Award 1R01AI145057. To my knowledge there are no other studies funded by NIH directly related to hydrocephalus in low-middle income countries. In addition, I am aware of no funding related to the study or treatment of this problem (hydrocephalus in low-resource countries) from any other US government agency such as CDC or USAID.

b. How can the U.S. best help address the needs of populations living with hydrocephalus in low-to-middle-income countries?

To best answer this question, I need to provide some context.

The burden of hydrocephalus is highest in LMIC where the availability of neurosurgical care is lowest. In Africa, Latin America, and Southeast Asia there are close to 300,000 new cases of infant hydrocephalus every year. For sub-Saharan Africa, the latest information estimates there are 102 neurosurgeons (1 neurosurgeon per 2.62 million population)¹. It is estimated that more than 180,000 new infants are born with or develop hydrocephalus every year in sub-Saharan Africa.² Thus, for all infants with hydrocephalus in sub-Saharan Africa to receive an initial operation would require an average of about 1,800 operations per neurosurgeon per year, which is not feasible. Key strategies to address this problem include: 1) decreasing the incidence of hydrocephalus in LMIC; and 2) increasing access to treatment strategies for children affected by hydrocephalus that maximize long term success and minimize the operative burden on existing neurosurgical capacity.

1. Decreasing the incidence of hydrocephalus in low-middle income countries

In LMIC the three most common causes of infant hydrocephalus are neonatal infection, neural tube defects, and congenital hydrocephalus. The incidence of congenital hydrocephalus is greatest in Latin America (316 per 100,000 births) and in Africa (145 per 100,000 births)

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compared to North America, which has the lowest incidence (68 per 100,000 births). But at this point, there are no known ways to prevent congenital hydrocephalus. However, the incidence of post-infectious hydrocephalus, or PIH (caused by neonatal infection) and hydrocephalus associated with neural tube defects (often referred to as spina bifida) can be reduced. Improved perinatal care and *early diagnosis and treatment of neonatal infections* would decrease the incidence of PIH (which is rare in high-income countries). And the incidence of neural tube defects can be decreased in a population by either universal use of *prenatal folate supplementation among women of childbearing age or folate fortification of the grain supply*. Programs to support either of these could significantly impact the volume of infant hydrocephalus cases in low-resource countries.

2. Increasing access to treatment strategies for children affected by hydrocephalus that maximize long term success and minimize the operative burden on existing neurosurgical capacity.

Even if the case volume of infant hydrocephalus were cut by half through prevention, the burden of untreated hydrocephalus in LMIC would still be enormous. Increasing access to care for these children will require national healthcare system improvements that facilitate early detection of the condition and referral for treatment. But identification and referral are futile if treatment is unavailable or suboptimal. In many low- and middle-income countries the neurosurgical workforce is simply incapable of handling all cases of infant hydrocephalus at the present time. Increasing the long-term success rate of the initial treatment would not only save children's lives but also decrease the number of necessary operations per patient, thus easing the surgical case load of an overwhelmed neurosurgical workforce and consequently allowing more children to be treated.

The standard treatment for hydrocephalus since the 1960's has been placement of a ventriculoperitoneal shunt – an implanted device that drains cerebrospinal fluid from the brain's ventricles into the abdominal cavity. Shunts have saved countless lives but are very prone to failure (more than half requiring additional operations for failure in the first 5 years alone) and infection (about 5-10% incidence with every shunt operation). Shunt malfunction is an ongoing and lifelong risk, occurring at least once in nearly all patients, and can be fatal if not addressed quickly enough. It is common for a child to require several urgent shunt operations over time, and in the US the average child with a shunt requires 2 to 3 additional shunt operations after the original placement. Children who are shunt-dependent thus require regular follow up and access to emergency neurosurgical care when the shunt fails.

The same barriers that inhibit access to the initial operation for these infants (few neurosurgeons in addition to travel, logistical, and economic barriers) pose an even greater obstacle to emergency neurosurgical care. Shunt-dependence is much riskier for children in low- and middle-income countries, especially for those in rural areas for whom quick transport to a neurosurgical center is an impossibility. In other words, *shunt-dependence under these circumstances is life-threatening*. In addition, children who do make it to a neurosurgical center for their initial treatment may be unable to obtain a shunt in the first place. Shunts are sometimes simply not available at the time, or the family may be required to pay a price for the shunt that is beyond their means.

Fortunately, an alternative minimally invasive neurosurgical procedure that combines endoscopic third ventriculostomy with endoscopic choroid plexus cauterization (known as



ETV/CPC) has been demonstrated to permanently treat infant hydrocephalus in around 2/3 of eligible infants without the need for a shunt, and we have shown that more than half of all children presenting for treatment of hydrocephalus can avoid life-long shunt-dependence and its consequences. In a two-country prospective trial, we demonstrated that the same outcomes could be achieved at separate centers in Uganda and Nigeria by neurosurgeons who had been trained to perform ETV/CPC and followed a standard treatment protocol.³ For patients suitable for ETV/CPC, 75% were treated successfully without a shunt. When including those infants presenting for treatment who were not suitable for ETV/CPC and required a shunt as the initial procedure, more than half of all infants presenting for treatment were treated successfully without shunt-dependence at both centers. Importantly, outcomes for survival, neurocognitive outcome, and brain growth have been shown to be at least as good for ETV/CPC as for treatment by shunt placement.⁴

Similar outcomes in other low-resource countries, treating half of all children without a shunt, can be achieved. This will eliminate the need for very long-term follow up of these children, reduce the mortality from shunt-dependence, and reduce the overall number of hydrocephalus operations required in the population. This would, in turn, reduce the operative burden on a very limited and strained neurosurgical workforce, resulting in improved access to patients for their initial hydrocephalus treatment, as well as access for treatment of other neurosurgical conditions. *But this will require investment in the training and equipping of neurosurgeons.*

Neurosurgical aid to LMICs has long been dominated by short-term visits from high-income country volunteers. This has included bringing a supply of donated shunts and placing them in hydrocephalic children, leaving the follow up and inevitable shunt infections and failures to the local neurosurgeons. In the long run, this is not a helpful strategy. We must find ways to refocus our efforts on surgical education and prioritize the development of local neurosurgeons in the context of their local practice settings and patient populations. In regard to hydrocephalus, which is the greatest unmet neurosurgical need in children, the optimum strategy is to train and equip neurosurgeons in LMIC to perform ETV/CPC, as NeuroKids (www.NeuroKids.org) has been doing since 2021. But to achieve this at sufficient scale will require significant funding.

At this time, we are unaware of any federal funding opportunities for implementation of training and treatment. We suggest that Government funding priorities should include the following:

1. Facilitate the identification and referral of infants with hydrocephalus through education and healthcare system development. This can be most effectively done in partnership with ministries of health to educate both the public and community-level healthcare providers.
2. Train and equip neurosurgeons to perform ETV/CPC and to optimize their patient management skills regarding diagnosis and proper treatment selection. In addition, train their operating room support staff in the care, sterilization, and set up of the video-endoscopy equipment.
3. Enable neurosurgeons who have been trained to train their peers as well as their neurosurgery trainees in order to scale this capacity building over time.
4. Provide and train a clinical coordinator at each site to facilitate appropriate postoperative follow up for the patients and also to keep a record of treatment outcomes to monitor and

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support quality assurance and safety. For children treated by ETV/CPC, virtually all treatment failures will have occurred within the first 6 months, so this is the critical interval for assessing outcome.

5. Improve access to inexpensive shunts for those patients that need them.

With proper training and provision of the necessary endoscopic equipment, we would expect to achieve permanent, shunt-free treatment in more than half of all children presenting for treatment at that center. The ultimate goal is for every child with hydrocephalus to have the opportunity for shunt-free treatment. This will not be possible until there are more neurosurgeons, which will hopefully continue to increase as has been the case over the past decade. But training and equipping the existing neurosurgical workforce is a necessary beginning.

The US government has the opportunity to lead the world in saving the lives of these children by funding programs that train and equip neurosurgeons in LMIC and also facilitate the timely identification and referral for care of these children.

c. What legislative recommendations would you make to the Congress to address hydrocephalus internationally?

To the best of our knowledge, support by the US Government for surgical interventions to improve the health of children in low-resource settings is minimal. The NIH has funded some research looking into the effectiveness of surgical interventions including for hydrocephalus, but this does not support efforts to train, support, or provide surgical interventions. USAID has referenced its work partnering with the private sector to address neglected surgical conditions as outlined in its [July 2024 report to congress](#), but their focus is on surgeries to address conditions including cleft lip and cleft palate, club foot, cataracts, hernias, fistulas, and untreated traumatic injuries, many of which are non-life-threatening. Therefore, we are unaware of any US government funding for surgical interventions to treat hydrocephalus in newborns.

In order to fill this gap and save the lives of countless children globally, Congress should direct USAID to appropriate resources and report on progress to support the interventions outlined above including:

- Strengthen the identification and referral of infants with hydrocephalus
- Train and equip neurosurgeons to treat hydrocephalus, including through ETV/CPC
- Support trained neurosurgeons to train their peers to expand the capacity and reach of surgical interventions for hydrocephalus
- Provide and train clinical coordinators to ensure appropriate post-operative follow-up care
- Promote access to the tools needed for surgical intervention, including shunts and other endoscopic equipment

Funding from NIH has helped support research that has advanced the treatment of infant hydrocephalus in LMIC and has also identified one of the pathogens responsible for post-



infectious hydrocephalus in East Africa. But, to date, there has been no available funding to support large scale implementation of strategies that have developed from this research.

We recommend the introduction of legislation to create a funding opportunity for large scale implementation of the training and treatment strategies outlined above. One possibility among others would be to expand the mission of USAID to include this kind of life-saving capacity building in LMIC.

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2. J Neurosurg. 2018 Apr 27:1-15.
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4. NEJM, 2017, 377:2456-64.

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Questions for the Record Submitted to
Dr. Gladys Maestre by
Chairman Christopher Smith
House Foreign Affairs Subcommittee on Global Health, Global Human Rights, and International
Organizations
November 20, 2024

1. Every year the United States spends billions of dollars on efforts to improve global health, primarily through combatting infectious diseases. By contrast, little is done to address issues of global brain health.
 - a. Which U.S. global health assistance and / or research programs abroad, if any, address brain health challenges such as Alzheimer's disease?
 - b. How can the U.S. best help address the needs of populations living with Alzheimer's disease in low-to-middle-income countries?
 - c. What legislative recommendations would you make to Congress to pursue to address Alzheimer's disease internationally?

Response by Dr. Gladys Maestre:

Chairman Smith, thanks very much for the opportunity to expand my testimony in a way that might be more useful.

- 1. Every year the United States spends billions of dollars on efforts to improve global health, primarily through combatting infectious diseases. By contrast, little is done to address issues of global brain health.**

Indeed, although most of the health dollars spent in our nation go to the care and treatment of non-communicable chronic disorders, most of the research funded at global level by US goes to infectious disorders. In addition, there are no articulated strategy to address global brain health in a way that could successfully bring results home. Based on the diversity of US populations, results from research done abroad might accelerate the discoveries relevant and implementation of programs that benefit all.

- a. **Which U.S. global health assistance and / or research programs abroad, if any, address brain health challenges such as Alzheimer's disease?**

Examples of relevant ongoing research funded by HHS

- i. **HRS International Family of Studies and the Harmonized Cognitive Assessment Protocol** (<https://www.nia.nih.gov/research/dbsr/global-aging/hrs-international-family-studies-and-harmonized-cognitive-assessment-protocol>) and examples of funded projects:
 - Brazilian Longitudinal Study of Aging (ELSI-Brazil)
 - The China Health and Retirement Longitudinal Study (CHARLS)

- Costa Rican Longevity and Healthy Aging Study (CRELES)
- The Caribbean-American Dementia and Aging Study (CADAS) (Dominican Republic and Puerto Rico)
- English Longitudinal Study of Ageing (ELSA)
- Survey of Health, Aging, and Retirement in Europe (SHARE)
- Longitudinal Aging Study in India (LASI)
- Indonesia Family Life Survey (IFLS)
- The Irish Longitudinal Study on Ageing (TILDA)
- Japanese Study of Aging and Retirement (JSTAR)
- Longitudinal Study of Health and Ageing in Kenya (LOSHAK)
- Lebanon Study on Aging and Health (LSAHA)
- Malaysia Ageing and Retirement Survey (MARS)
- Malawi Longitudinal Study of Families and Health (MLSFH)
- Mexican Health and Aging Study (MHAS)
- Chitwan Valley Family Study (Nepal)
- The Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA)
- Healthy AGEing in Scotland (HAGIS)
- Health and Aging in Africa: A Longitudinal Study in South Africa (HAALSI)
- Korean Longitudinal Study of Aging (KLoSA)
- Health, Aging, and Retirement in Thailand (HART)
- Health and Retirement Study (U.S.) (HRS)

ii. **Global Environmental and Occupational Health (GEOHealth) Program**

1. Alzheimer's related GEOHealth Peru Hub
(<http://www.geohealthperu.org>)

iii. **Alzheimer's Disease Sequencing Project (ADSP)**

(<https://www.nia.nih.gov/research/dn/alzheimers-disease-sequencing-project-consortia>) and example international studies:

1. Asia (Korea, India):
 - a. Genetic Studies of Alzheimer's Disease in Koreans
(https://reporter.nih.gov/search/_dwAiWBomEeH1qy-vwWo3Q/project-details/10691356)
 - b. Harmonized Diagnostic Assessment of Dementia (DAD) for Longitudinal Aging Study of India (LASI)-Genomic study
(https://reporter.nih.gov/search/hKul3Vq__EmlFmtnXZfjfw/project-details/10836795)
 - c. KBASE2: Korean Brain Aging Study, Longitudinal Endophenotypes and Systems Biology
(https://reporter.nih.gov/search/8m7DVtnLQUOjE053_8pLXw/project-details/10199190)
2. Canada:

- a. Asian Cohort for Alzheimer's Disease (ACAD)
(https://reporter.nih.gov/search/8m7DVtnLQUOjE053_8pLXw/project-details/10555689)
 - 3. Africa:
 - a. Recruitment and Retention for Alzheimer's Disease Diversity Genetic Cohorts in the ADSP (READD-ADSP)
(<https://reporter.nih.gov/search/BYsWpk8P5UqNQ4x3RW8-Aw/project-details/10654529>)
 - 4. Latin America and the Caribbean:
 - a. GLASS-AD: Global Latino Sequencing Study for Alzheimer's Disease
(<https://reporter.nih.gov/search/BYsWpk8P5UqNQ4x3RW8-Aw/project-details/10650278>)
 - 5. Middle East:
 - a. Genetic Studies of Alzheimer's Disease in Jewish and Arab Populations
(https://reporter.nih.gov/search/p_WowsCEPEaaMSL7OfYVXA/project-details/10639024)
- iv. **Cohort Studies of Memory in an International Consortium (COSMIC)**
(<https://cheba.unsw.edu.au/consortia/cosmic>) | (RePORTER link: <https://reporter.nih.gov/search/CZmpSuPgkG91DbiACbMLA/projects>)
- v. **Multi-Partner Consortium to Expand Dementia Research in Latin America (ReDLat)** (<https://www.gbhi.org/projects/multi-partner-consortium-expand-dementia-research-latin-america-redlat#:~:text=This%20project%20fosters%20a%20consortium%20of%20multiple%20partners,data%20to%20improve%20dementia%20characterization%20in%20diverse%20populations.>) | (RePORTER link: <https://reporter.nih.gov/search/TphKUX3tiU2D-82Zy1GUrQ/projects>)
- vi. **ADRD Research in Native South American Populations: Tsimane and Mosen** (<https://reporter.nih.gov/search/d-QVX3p-10mzkcGTzkhXag/project-details/1087719>)
- vii. **Examples of global research projects -- behavioral and social research**
- 1. Late Life Learning Dementia and Overall Health: An Investigation of The University for Seniors in Beirut.
 - 2. Womens Social Ties and Psychosocial Well-Being in a Resource-Limited Patriarchal Setting: A Longitudinal Perspective

3. Advancing Alzheimers family caregiving interventions and research capacity in Vietnam
 4. Unstable Income Rising Stress? The Effects of Income Instability on Psychological and Physiological Health
 5. The economic and social impact of COVID-19 mitigation policies: A cross-country analysis of macro events
 6. Long-term Effects of a Natural Disaster on Cognitive Aging Dementia Health and Well-being of Older Adults
 7. Monitoring Social Change: Dynamics Of Aging And Cognitive Function
 8. Role of mid- and late-life risk factors in social inequalities in Alzheimer's Disease and Related Dementias
- viii. Besides the NIH programs, USAid has some programs across lifespan that could be tailored but are not explicit for Alzheimer's disease or dementia.
- ix. Alzheimer's Association and the Global Brain Health Institute fund international programs that in most cases, involve funds for capacity building.

In summary, US is funding international programs or that have an international component. What is missing is to decant lessons and to define strategic and targeted areas both thematically and geopolitically, to warrant that benefits of the knowledge acquired are translatable to US, whether research-wise or in the implementation of services or strategies. This is only possible if a cohesive and goal-oriented strategy exists.

b. How can the U.S. best help address the needs of populations living with Alzheimer's disease in low-to-middle-income countries?

I think that the US could support research into more affordable, pragmatic, and effective solutions to improve the quality of life and reduce expenses of hospitalization, long-term care loss of income, and indirect costs resulting from dementia. Equipping higher education institutions in HICs and LMICs to promote and motivate fellows and early career researchers to ensure the future of research responsive to the local needs of the respective populations.

c. What legislative recommendations would you make to Congress to pursue to address Alzheimer's disease internationally?

- i. To strengthen our nation's commitment to science and technology to address brain health and Alzheimer's disease. What I mean is that this field is dynamic and that leaders in Congress need to be equipped with the latest evidence and expertise necessary to inform science-based decision-making

on policies and initiatives to help move our nation forward and advance our competitive edge.

- ii. To support networks where US has a leadership role and relationships to support research and services that involve local, state, and regional leaders. It is also vital that the issue of capacity building for research and cooperation is clearly defined in these networks.
- iii. Expanding engagement of neuroscientists on foreign policy and improving the brain health skills and capabilities of the foreign affairs workforce. The nation has enough expertise, but the intersection of neuroscience and foreign affairs is weak in its relationship to dementia and Alzheimer's disease.
- iv. To build capacity in the U.S. STEM workforce to drive scientific excellence and economic development with a global perspective addressing brain health and Alzheimer's disease. It is not only important to add 200 million new STEM workers to the U.S. economy by 2050, but they are interested, specialized and devoted to areas of brain health, in particular dementia.
- v. Support dedicated funding for an international comprehensive plan for global brain health that includes AD among the disease to be supported.
- vi. Support NIH funding, including supporting extension of programs that could benefit of international initiatives and partners, such as the AD-Resource Center for Minority Aging Research (RCMARs), the Alzheimer's Disease Research Centers (ADRCs), Genome Diversity Centers, that already include capacity building, harmonized strategies and that include several if not all minorities.
- vii. Shifting the balance of investment further towards LMICs, which bear high burden, to tackle the challenges and seize opportunities, to mitigate the burden of dementias including AD. Health and social care systems should be better equipped to meet the needs of aging populations in the LMICs and in low-resource settings in the US. Thus, increasing funding directly for LMICs for worthy longitudinal projects rather than through WHO, or UN.

Questions for the Record Submitted to
Dr. Gladys Maestre by
Rep. Rich McCormick
House Foreign Affairs Subcommittee on Global Health, Global Human Rights, and International
Organizations
November 20, 2024

1. Patients experiencing traumatic brain injury (TBI), including our service members and veterans, face increased risk for Alzheimer's and other neurodegenerative conditions. What opportunities does the US have to collaborate internationally on researching and treating brain health issues affecting TBI patients?
2. Do you see potential for treatments focusing on mitochondrial dysfunction and therapies utilizing newly developed peptides have potential for effectively treating Alzheimer's symptoms or perhaps preventing the disease?
3. How effective has the work of groups such as the World Dementia Council or the Davos Alzheimer's Collaborative been in advancing brain health globally? What can Congress do to support already existing efforts to raise awareness and combat Alzheimer's disease around the world, without duplication, in a way that leads to tangible results?

Response by Dr. Gladys Maestre:

Representative McCormick, thanks very much for the opportunity to expand my testimony in a way that might be more useful.

1. Patients experiencing traumatic brain injury (TBI), including our service members and veterans, face increased risk for Alzheimer's and other neurodegenerative conditions.

Certainly, TBI is a major risk factor for Alzheimer's disease and other neurodegenerative conditions. Men are at higher risk of experiencing, being hospitalized and dying than women in the US.

a. What opportunities does the US have to collaborate internationally on researching and treating brain health issues affecting TBI patients?

There are several national and international collaborations, in particular, InTBIR: International Initiative for Traumatic Brain Injury Research, with projects currently ongoing in Europe, the US, and Canada. This collaborative effort has been quite productive and efficient. There are other cooperative efforts, some derived from the working groups of InTBIR. One of them is CENTER-TBI, a large European project that aims to improve the care of patients with TBI and has several US scientists affiliated. CREATIVE is another European initiative that seeks to improve the care of traumatic brain injury patients in the critical setting as part of the wider InTBIR network. The NIH already funds large program grants on the pathophysiology of TBI (like Boston- Anne McKee and Glasgow. GBIRG UK -Willie Stewart).

The opportunities for US global leadership in TBI research and care rely on the fact that there are very few initiatives focusing on TBI in low and middle-income countries (LMICs). These countries have a tremendous burden essentially created by traffic accidents rather than sports or warfare. Non-compliance with or adherence to wearing protective headgear is rife in Africa and India. Laws exist in many countries but are not always enforced, despite recognizing that the problem is taking a significant toll on society and that policies must be renewed/enforced. On the other hand, several high-income countries (HICs) have charities that offer help in various areas, including rehabilitation, but there are very few such organizations in LMICs. One recent study on TBI was initiated in Botswana – Lingani M (lingani.mbakile-mahlanza@gbhi.org) supported by Global Brain Health Institute and Alzheimer's Association.

There are several opportunities to improve the care of TBI patients in US. For example, developing integrated healthcare strategies where neurology, psychiatry, physical and occupational therapies, psychology, and social work synergize in their actions. Germany could be a good example. However, understanding the social and behavioral determinants of care is extremely important to understand the disparities of care in the US, including the availability of telehealth programs and support for care partners, and preferences for complementary medicine and traditional practices.

2. Do you see potential for treatments focusing on mitochondrial dysfunction and therapies utilizing newly developed peptides have potential for effectively treating Alzheimer's symptoms or perhaps preventing the disease?

Mitochondria are organelles that enable cells to meet their energy demands; consequently, they have a dynamic function as energy requirements fluctuate constantly. Several pathophysiological processes depend on the mitochondria, and research has suggested that cellular inflammation, synapse failure and loss, axon and dendrite degeneration, increased oxidative stress, excitotoxicity, and other cellular failures depend on mitochondrial dysfunction. Since there are so many pathways by which these processes can occur, there might be profiles of cellular defects associated with mitochondrial dysfunction among individuals with AD.

I definitely see potential for treatments focusing on mitochondrial dysfunction for treating AD symptoms and eventually preventing the progress and or onset of the disease. It is harder to answer the question when balancing direct effects on brain pathology or addressing the vascular system, for example. To exemplify this issue, let's consider the glucagon-like peptide-1 (GLP-1) receptor agonists, which have cardioprotective effects but also neuroprotective effects. Distinguishing between the two effects might be important for management and prevention. GLP-1 receptor agonists like Semaglutide preserve mitochondrial structure and function under chronic stress. Further research is warranted to understand how to maximize the effects of newly developed peptides, specifically in AD.

3. How effective has the work of groups such as the World Dementia Council or the Davos Alzheimer's Collaborative been in advancing brain health globally?

I would say limited overall.

The WDC was established in the UK in 2016, led by Dr. Peter Scheltzen, a prominent Dutch scientist. Among its trustees, some individuals play important roles in US advocacy groups, such as Alzheimer's Association and USAgainstAlzheimers, and an expert from Finland in dementia prevention (Dr. Mia Kimipelto). It has been registered as an entity in the UK with only one registered employee. The main impact of WDC has been in gathering stakeholders. WDC has projects, but these are just the beginning. WDC has a broad remit, particularly in Latin America (not in Africa or Asia), but many are still in the early stages.

The Davos Alzheimer's Collaborative (DAC) was established in 2021 in US, and in Switzerland and is led by George Vraderburg, a philanthropist in the US. Among its board members are prominent public health leaders such as Dr. Julio Frenk and Victor Dzau, but I could not identify AD experts among them. The main impact has been to bring together global stakeholders, including industry. DAC has programs in some LMICs and is building cohorts by collaboration between investigators in LMICs and HICs. DAC also has a program for clinical trial cohorts, mostly in HICs, western Europe and UK. The Healthcare Preparedness Program appears to be in its early stages. Among scientists, DAC still is not well known as its programs are not yet widely offered or implemented. So, it is trying but has not made a significant impact yet. But the truth is that it is a young collaborative.

4. What can Congress do to support already existing efforts to raise awareness and combat Alzheimer's disease around the world, without duplication, in a way that leads to tangible results?

I believe that Congress can take steps to support:

1.- Leadership of US in advancing dementia research and mitigating the burden of dementia.

2.- Bring back home results/programs/strategies that are successful abroad, both in HIC and LMICs that could be useful in different settings in the US.

3.-Include capacity building as part of the research efforts supported in LMICs, not only because we need strong collaborators to have a higher impact -collaborators that share our values for science and human rights- but also because the sustainability of programs depends on the ability to broaden and diversifying research funding and to implement high - quality programs. One example of this type of initiative is the Global Brain Health Institute, which has a program to develop scientists, implementers, and social leaders, and they are reaching a sufficient number of trained scientists to create projects articulated across

countries or continents. This program is between two institutions, UCSF directed by Bruce Miller, a world-renowned scientist, and Trinity College in Dublin. Board members include world-renowned scientists and the scientific officer of the Alzheimer's Association, Dr. Maria Carillo.

4.-Support dedicated funding for an international comprehensive plan for Alzheimer's disease of brain health that includes AD among the disease to be supported.

5.-Empower the Foreign Affairs workforce in different aspects of AD and related neurodegenerative disorders so national security, US interests, and critical thinking are complemented with AD or brain science diplomacy.

6.- Support NIH funding, including supporting extension of programs that could benefit of international initiatives and partners, such as the AD-Resource Center for Minority Aging Research (RCMARs), the Alzheimer's Disease Research Centers (ADRCs), Genome Diversity Centers, that already include capacity building, harmonized strategies and that include several if not all minorities.

7. Make policymakers, and lawmakers in LMICs more aware of the dementia burden. In many LMICs influenced by the US there are no national programs on dementia awareness, burden, or care. Thus, engage and influence policymakers and advocacy organizations to encourage implementing and evaluating population-level dementia risk reduction interventions. This would include promoting education, controlling cardiovascular risk and preventing stroke, and seriously considering nutritional factors. There are several risk factors identified for AD, but if only one, such as hypertension (low-hanging fruit), is seriously addressed in terms of prevention, it would reduce the burden of AD.