

# **Testimony for the United States House of Representatives Foreign Affairs Committee, Sub-Committee on Africa, Global Health and Global Human Rights**

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## **Brain Health: A Global Perspective**

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Chairwoman Bass, Ranking Member Smith, and Distinguished Members of the Sub-Committee, thank you for the opportunity to share information on challenges and opportunities for global brain health, particularly in relationship to Alzheimer's disease and aging.

My name is Gladys Maestre. I am a Professor of Neuroscience and Human Genetics at the University of Texas Rio Grande Valley (**UTRGV**) School of Medicine. There, I am also the Director of the federally-funded Rio Grande Valley Alzheimer's Disease Resource Center for Minority Aging Research (**RGV AD-RCMAR**). I am a physician scientist that have devoted more than 30 years to the care of seniors and research of Alzheimer's disease and other dementias and have been responsible for the care of about 12,000 individuals either concerned about their memory, with cognitive impairment or with any form of dementia.

After obtaining my medical degree in Venezuela and financed by University of Zulia and the Venezuelan government, I did a fellowship at the Department of Psychiatry at the Massachusetts General Hospital in Boston, and then continue to obtain a master's degree at Columbia University in Neurobiology and Behavior and a PhD in Pathobiology, focused on Alzheimer's disease. I worked in a large longitudinal study that include adults from diverse racial, ethnic, linguistic, and socioeconomic backgrounds known as Washington Heights-Inwood Columbia Aging Project (WHICAP) directed by Dr. Richard Mayeux.

In 1996, I went back to Venezuela to establish a similar cohort with the technical support of Dr. Richard Mayeux and his team financed by the Venezuelan government. This was the first longitudinal cohort of older adults in Venezuela and in Latin America. In 1998, Hugo Chavez won the presidency and the Maracaibo Aging Study continued to receive support from the Venezuelan equivalent to NIH for many years until health sciences were eliminated from funding priorities.

As the country moved towards collaboration with Russia, Libya and China, I applied with the director of the Genome Center at Columbia University, Dr. Conrad Gilliam, for a research training grant from Fogarty International Center (FIC) to be established in Maracaibo Venezuela at University of Zulia. We were funded then and many other times to sustain the cohort in Venezuela to this day.

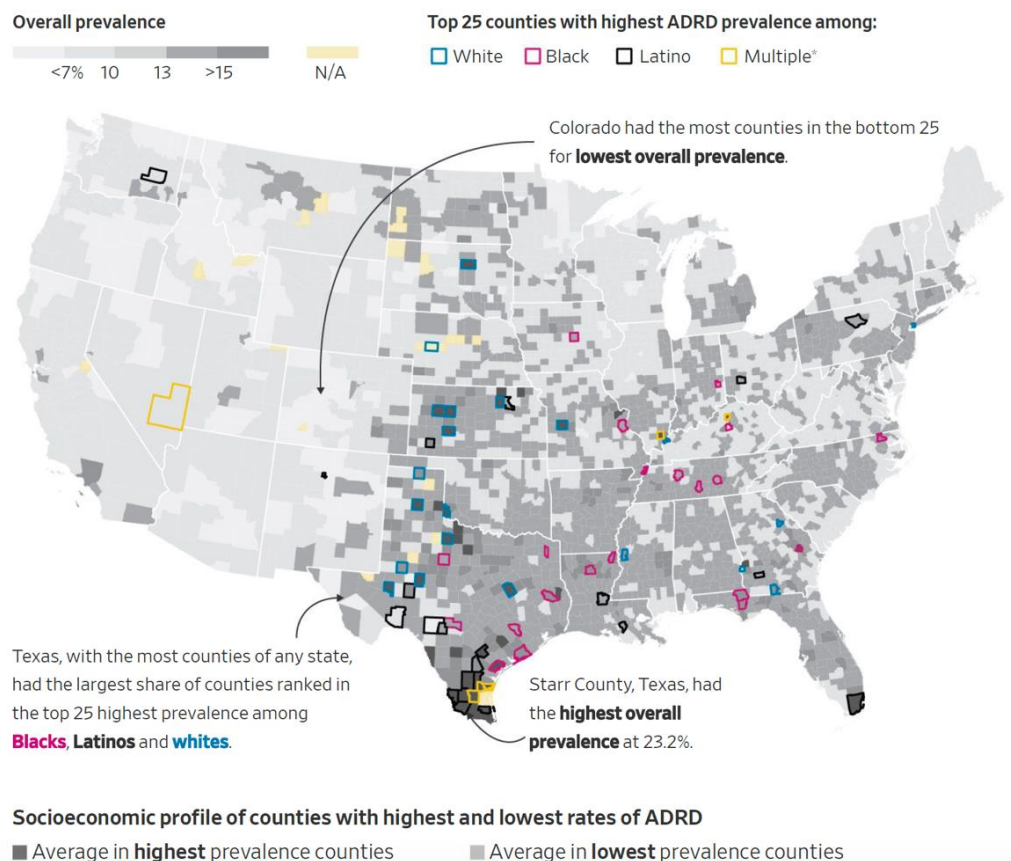
When the situation in Venezuela became very unsafe, I was hired by Columbia University and after 13 years of service, became US citizen and I moved to the University of Texas Rio Grande Valley. UTRGV was funded in 2015 and is located in the Texas-Mexico border with clinics along the Rio Grande from South Padre Island to Starr County.

In the Rio Grande Valley, about 95% of older adults are Hispanics and the culture, food, and values are aligned very much with my own values. I was able to establish a robust Alzheimer's research program funded by the National Institute of Aging and the Texas Alzheimer's Research and Care Consortium. I established the first Alzheimer's Resource Center for Minority Aging Research in Texas

that, since 2018, has trained 9 assistant professors, mostly from underrepresented groups. Between trainees and faculty, we have published 82 publications related to brain health and to minoritized groups. <https://www.utrgv.edu/som/alzheimers-disease-resource-center/publications/index.htm>

I continue to have funded projects in Venezuela that are very committed to capacity building in low- and middle-income countries. With funding from FIC, the International Brain Organization, Dana Foundation, and the Society for Neuroscience, I have led courses and conferences in Venezuela, Colombia, Dominican Republic, Haiti, Mexico, Bolivia, Cuba and organized 5 events related to brain health and aging in Kenya where we bring world experts and invite young biologists, neurologists, psychiatrists, and pathologists for training. We expect to have this conference again in December in Nairobi and obtained funding for that from the Alzheimer’s Association and the National Institute of Aging. Early this month, funded by NIA and in collaboration with Alzheimer’s Association. I organized the Health Disparities Alzheimer’s Disease and Other Dementias Conference that had more than 1200 registrants from 40 countries.

My experience working in developing countries and the support I received from mentors and colleagues has allowed me to implement training programs at UTRGV, engage and recruit older Hispanics and establish partnerships with scientists from around the globe to support the research in Rio Grande Valley, that contains the four poorest counties in Texas and the county with the higher prevalence of Alzheimer’s disease in the nation: Starr County (**Figure 1**).



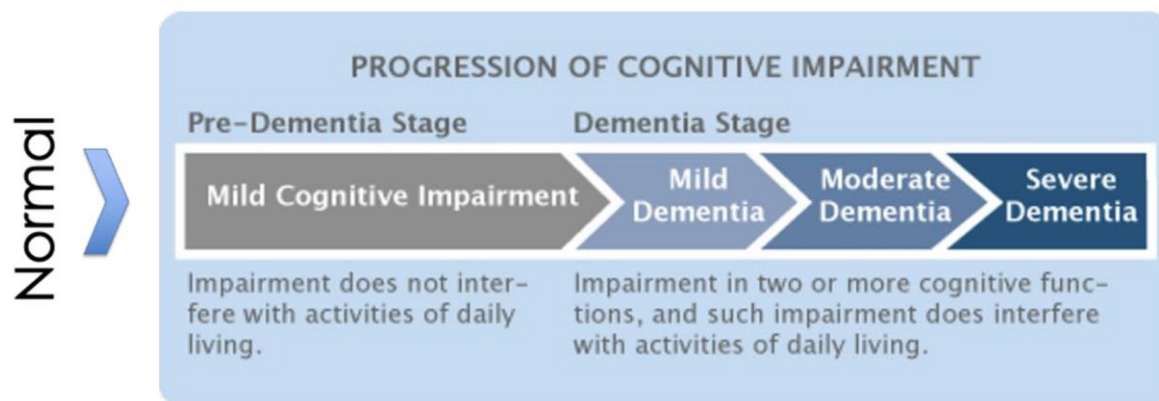
**Figure 1. Prevalence of Alzheimer’s Disease and Related Dementias in the U.S.**  
<https://aspenbraininstitute.org/blog-posts/alzheimers-research-looks-at-hot-spots-across-the-us>

## Overview:

Over the last decade we have seen a tremendous increase in the federal investment for research on Alzheimer's disease. While this investment has accelerated our understanding of the disease, still there is no cure. People residing in low resource settings in the U.S. and in low- and middle-income countries (LMICs) have a higher burden of the disease, with a high cost in human suffering and economic cost but also a high toll for development and national security. Today, my goal is to shed some light on why and how we can narrow global health care gaps in terms of Alzheimer's diagnosis and treatment disparities in Alzheimer's disease risk, diagnosis, and access to care and long-term services.

## What is Alzheimer's disease and dementia and what are the causes?

How we think, perceive, and interpret the world changes from birth until we die in older age. From the moment we acquire self-awareness as children, we know who we are and accumulate memories, skills, wisdom through our life. However, about 10% of older adults suffer from thinking problems, memory and wayfinding impairments, forgetting their own values and preferences, do not recognize their loved ones or even themselves in a mirror. In summary, cognitive impairment is not normal aging. Rather, limitations in daily life due to deterioration of cognitive abilities, develop as part of a disease process. This is what we know as dementia, an umbrella term for cognitive difficulties that have their onset in adulthood that affect a person's ability to independently perform everyday activities. The continuum of cognitive decline from mild cognitive impairment (MCI) to progressively more severe levels of dementia is shown in **Figure 2**.



**Figure 2. The cognitive impairment continuum**

There are several different types of dementia, and each type is associated with a unique set of clinical characteristics and cognitive profile. Alzheimer's disease is the most common cause of dementia; it accounts for approximately 60%-80% of all dementia cases<sup>1</sup>. Alzheimer's disease is a clinical syndrome that is caused by loss of brain function. It has a gradual onset and is a progressive disease that becomes worse with time. The neuropathology (abnormal changes in the brain) associated with Alzheimer's disease appears in the fifth and sixth decade of life, many years before the onset of symptoms.

The first symptoms of Alzheimer's disease usually occur in older adulthood and are typically subtle problems with memory that may be noticeable to the individual and their family and friends, but do not interfere with everyday activities. Over time memory problems worsen and other areas of cognitive

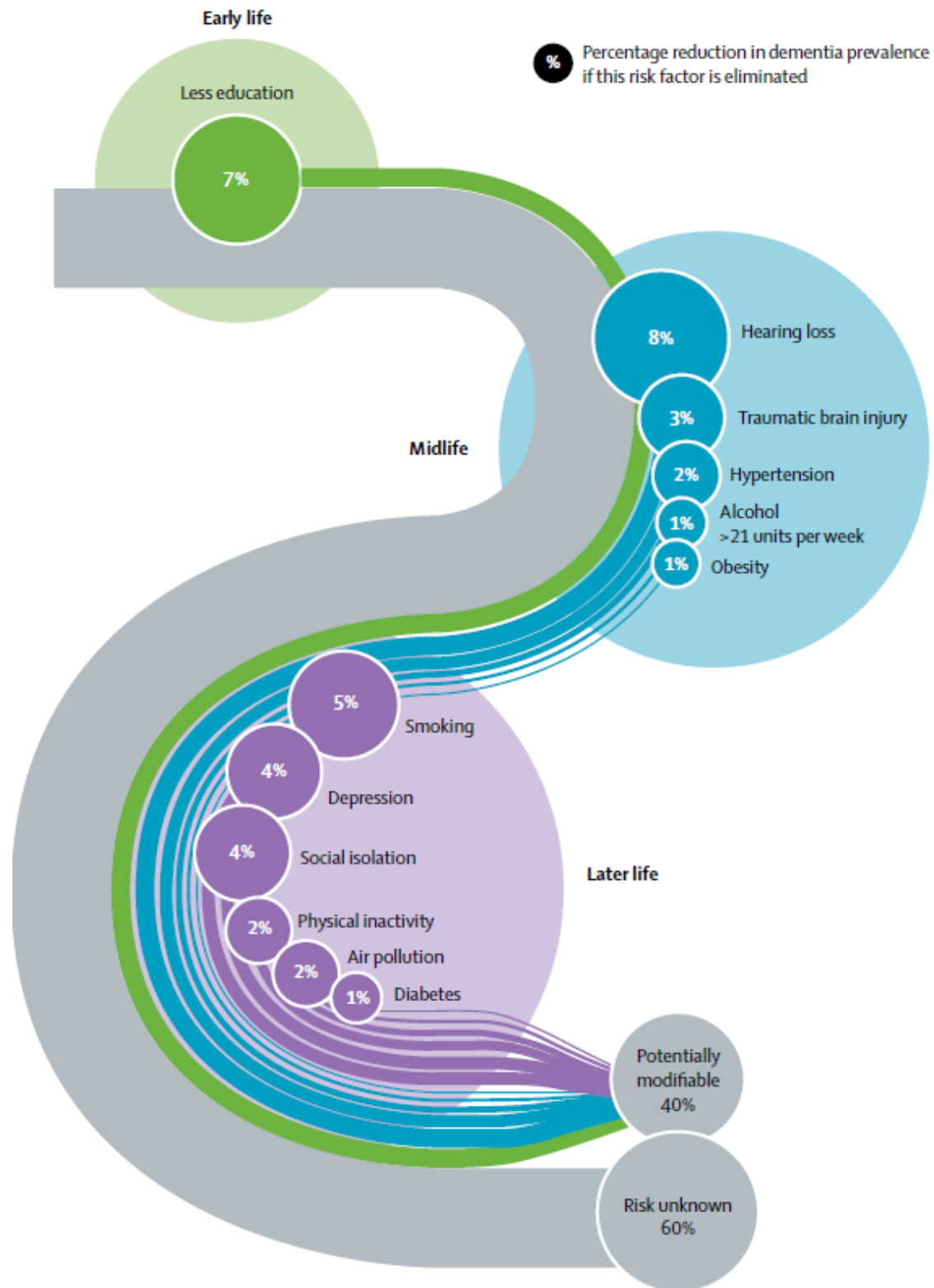
function also decline. Gradually, the ability to independently complete complex daily activities, such as driving, learning new routines, remembering appointments, finances, following a recipe, doing laundry, and housecleaning, begins to decline. Eventually, cognitive impairment gets to the point where an individual is no longer able to remember names and faces of family members, and complete very basic tasks such as toileting, dressing, and/or feeding. At the severe stage of the disease, individuals are no longer able to swallow.

Alzheimer’s dementia is a complex disease, and quite heterogeneous. Not two cases are identical. Not even two brains of identical twins with the disease are identical. There are two main types: One that has early onset and is mostly caused by dominant genetic variants, and the most common the “sporadic” type that accounts for about 90% of all Alzheimer cases that appear later in life and where there is not dominant gene to explain it. In my book “Alzheimers the lost identity” I say that Alzheimers disease can be seen in the brain but affects profoundly the family.

The 2020 dementia prevention, intervention, and care report from the Lancet Commission concluded, “Together the 12 modifiable risk factors account for around 40% of worldwide dementias, which consequently could theoretically be prevented or delayed”<sup>2</sup>. Those factors are (less education, hearing loss, traumatic brain injury, hypertension, excessive alcohol, obesity, smoking, depression, social isolation, physical inactivity, diabetes and air pollution (**Figure 3**) that are responsible for 39.9% of dementia cases (**Table 1**).

**Table 1. Relative Risk and Population Attributable Factor of Risk Factors for Dementia<sup>2</sup>**

	Relative risk for dementia (95% CI)	Risk factor prevalence	Communality	Unweighted PAF	Weighted PAF*
<b>Early life (&lt;45 years)</b>					
Less education	1.6 (1.3-2.0)	40.0%	61.2%	19.4%	7.1%
<b>Midlife (age 45-65 years)</b>					
Hearing loss	1.9 (1.4-2.7)	31.7%	45.6%	22.2%	8.2%
TBI	1.8 (1.5-2.2)	12.1%	55.2%	9.2%	3.4%
Hypertension	1.6 (1.2-2.2)	8.9%	68.3%	5.1%	1.9%
Alcohol (>21 units/week)	1.2 (1.1-1.3)	11.8%	73.3%	2.1%	0.8%
Obesity (body-mass index ≥30)	1.6 (1.3-1.9)	3.4%	58.5%	2.0%	0.7%
<b>Later life (age &gt;65 years)</b>					
Smoking	1.6 (1.2-2.2)	27.4%	62.3%	14.1%	5.2%
Depression	1.9 (1.6-2.3)	13.2%	69.8%	10.6%	3.9%
Social isolation	1.6 (1.3-1.9)	11.0%	28.1%	4.2%	3.5%
Physical inactivity	1.4 (1.2-1.7)	17.7%	55.2%	9.6%	1.6%
Diabetes	1.5 (1.3-1.8)	6.4%	71.4%	3.1%	1.1%
Air pollution	1.1 (1.1-1.1)	75.0%	13.3%	6.3%	2.3%



**Figure 3. Population attributable fraction of potentially modifiable risk factors for dementia. <sup>2</sup>**

There are many more factors that were not included in the analysis such as maternal separation, early adverse exposures (domestic violence, bullying), etc. But if you look at these factors, all of them are more frequent in poor neighborhoods and people of color.

Over the last decade we have seen a tremendous increase in the federal investment for research on Alzheimer's disease. While this investment has accelerated our understanding of the heterogeneity of the disease and has allowed us to engage a more diverse group of Americans in Alzheimer's research, still we do not know what the cause is or causes of sporadic Alzheimer's disease. We find in the brain deposits of different molecules, such as beta amyloid and hyper-phosphorylated tau, there is also death of neurons, loss of synapsis which are responsible for communications between the cells, excess of inflammatory cells and vascular damage is detected in at least 50% of the cases. We do not know what elicits these changes in the brain, but when memory problems arise, there is already substantial damage.

### **What is its impact in diverse population particularly those in developing countries/low resource environments?**

Globally, Alzheimer's disease and other dementias constitute a major public health priority with substantial negative individual, social, and economic impacts.<sup>3,4</sup> The current estimates from the World Health Organization (**WHO**) indicate that by 2050, 150 million persons, representing a 204% increase from 2017, will be living with dementia.<sup>5,6</sup> Indications are that the majority of these increases will be found in low- and middle-income countries (**LMIC**) including within Africa.<sup>5-7</sup> Worldwide, dementia is the 5<sup>th</sup> leading cause of death and the second leading contributor to death from neurological diseases.<sup>8</sup> Recent estimates suggest that over 818 billion USD is spent annually on dementia related care worldwide and by 2028 the worldwide cost of dementia care is estimated to be >2 trillion USD.<sup>9</sup> These include direct medical and other formal and informal health and social care costs.

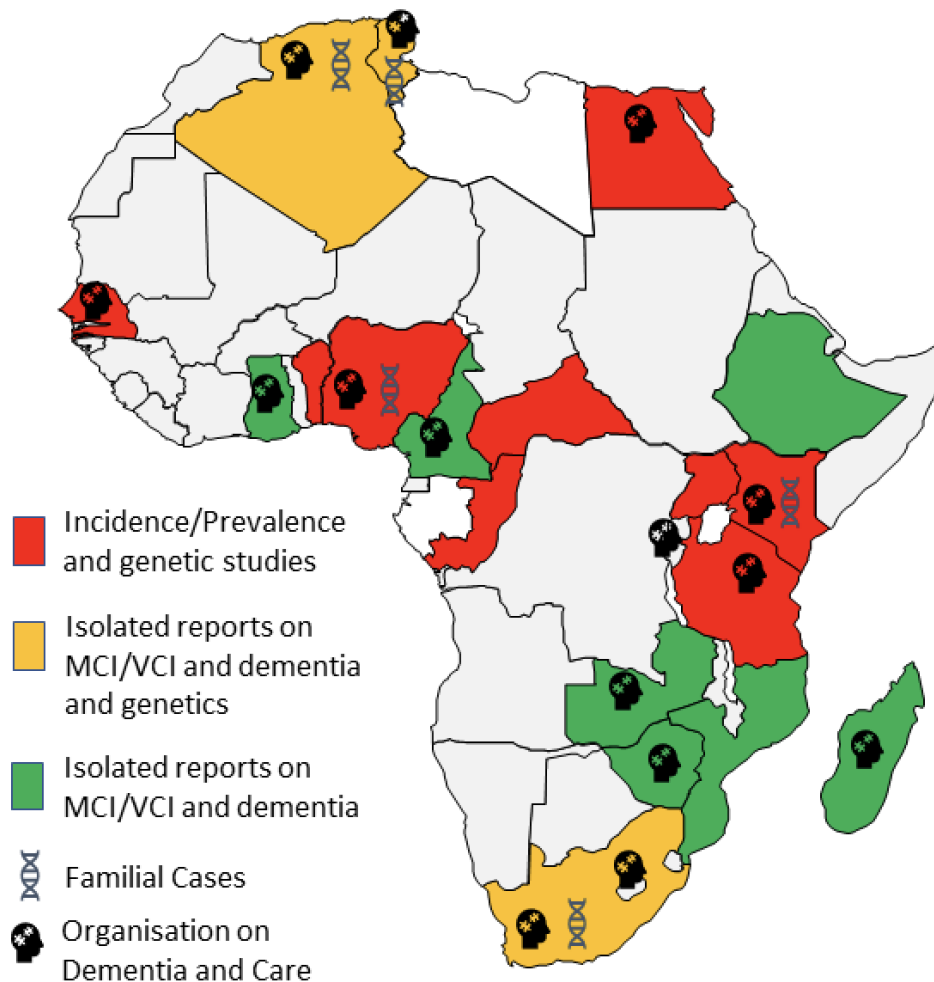
The projection that over 68% of persons with dementia will reside in LMICs by 2050<sup>7</sup> is largely due to the demographic transition and population growth in the LIMCs including certain African countries, which are amongst the world's most populous. The burden of dementia is shared by the person, their immediate family, caregivers, and the health, social, legal, and financial systems of the community at large. In Africa, as in many other underserved populations, additional strains on dementia care exist, attributable to globalization, rapid socio-economic transitions, and the gradual erosion of key informal care systems such as multigenerational family structures which are the bedrock of dementia care.<sup>10</sup> As such, the continent needs to devise robust alternate plans for the care of persons with dementia within the formal healthcare sector, taking advantage of global advancements in preventive, therapeutic and rehabilitative care of the condition.

In the U.S., rates of Alzheimer's disease are higher among Black or African Americans and Latinx or Hispanics than non-Hispanic White older adults<sup>11-13</sup>. In other words, at the same age, a higher proportion of Black and Hispanic older adults live with Alzheimer's disease than White older adults. More women are affected by Alzheimer's disease than men<sup>1</sup> because women live longer. Of the approximately 6.2 million Americans of age 65 and older currently living with Alzheimer's disease, about 3.8 million are women<sup>14,15</sup>. Women also represent approximately two-thirds of the dementia caregivers in the United States<sup>16</sup>. It is now well established that people who had fewer opportunities to receive education when they were children, are at higher risk for Alzheimer's disease later in life<sup>17 18</sup>.

I mentioned that South Texas and particularly border counties have the highest proportion of cases of dementia (**Figure 1**). Other areas such as the "Stroke Belt" including Georgia and the Carolinas, also have a concentration of cases. There is an overlapping between the risk factors mentioned above and the clustering of cases. I do not believe that the differences in rates of dementia in diverse populations is based on genetic differences, as individuals of the same genetic background living in different conditions have a different risk of Alzheimer's disease.

## Africa

More than two-thirds of the world's population of older people ( $\geq 65$  years old) reside in less developed countries, many of whom are in Africa.<sup>19</sup> The prevalence and incidence of dementia increase with age.<sup>20</sup> However, despite the projected large increases in the number of persons living with dementia, current estimates of prevalence and incidence of dementia from multiple studies in Africa are among the lowest in the world. While this may be due to numerous factors including low life expectancy in many African nations, it is however to be noted that dementia data derived from observational studies using similar methodological approaches and designed to reflect the diversity of Africa are still relatively few even though growing. The paucity of data is a reflection of the challenges of conducting quality research in many resource-poor African countries. (Figure 4)



**Figure 4. Dementia in Africa and Dementia Care and Support Organisations**

Map of Africa showing limited number of countries where incidence and prevalence studies have been conducted over the past 30 years. Some countries have reported isolated reports on dementia cases in particular Alzheimer's disease or vascular dementia. Limited number of countries in which candidate gene investigations have been carried out. In several African countries dementia care and support organizations exist. Most of these are member organizations of ADI (<https://www.alzint.org>). Further reports of cases and deaths due to dementia in African countries are known ([www.afro.who.int](http://www.afro.who.int)) but are not published in peer-reviewed sources.

There are four recent reports on dementia incidence from Western Africa, and one each from Central Africa and Northern Africa respectively. Notably, most of the data on incidence are from one country, Nigeria. Current incidence estimates from Sub-Saharan Africa (SSA) are similar to that for other low-

and middle- income countries at 13.26/1,000 person years implying 367,698 new cases each year.<sup>21</sup> The Alzheimer's Disease International (ADI) meta-analysis shows that incidence doubles for every 7.7 year increase in age in sub- Saharan Africa (SSA) .<sup>21</sup> For Northern Africa, a recent review on the epidemiology of dementia in the Middle East and North Africa (MENA) estimated a crude incidence of 27/1,000 over a 20-year period for Egypt.<sup>22</sup> Similar to prevalence, the reported annual incidence rates of dementia in Africa are generally lower than rates reported among populations of older persons living in Europe and North America.<sup>23</sup> Differences in diet and burden of cardiovascular risk factors, medical co-morbidities, access to quality health care and mortality have been suggested as possible reasons for the lower incidence of dementia in Africa compared to higher income regions of the world.<sup>24</sup> In one study comparing the incidence of dementia and Alzheimer's disease in two comparative cohorts of African Americans and Yoruba Nigerians aged 70 years or over and evaluated a decade apart in 1992 and 2001 respectively, the standardised annual incidence rates of dementia and AD were relatively stable in the Yoruba African cohort (dementia: 1.7% vs 1.4%; AD: 1.5% vs 1.0%) whereas there was a significant decline among the African Americans (dementia: 3.6% vs 1.4%; AD: 2.5% vs 1.3%).<sup>25</sup>

Prevalence studies in Africa have generally reported varied but generally lower prevalence of dementia compared with findings in Europe and America.<sup>26</sup> Limitations with many African studies include low quality of methods used, types of study settings (i.e. in-patients, outpatients, nursing homes, autopsy), and limited coverage of the different African regions.<sup>27</sup>(Table 1). The pattern of the findings is such that hospital-based studies report the lowest prevalence estimates of dementia in Africa.<sup>27</sup> However, 48% of a sample of nursing home residents in Nigeria met the clinical diagnostic criteria for dementia.<sup>28</sup>

As highlighted in a systematic review by Mavrodaris et al, variation in dementia prevalence depends on the criteria used and methodology employed.<sup>29</sup> Overall, higher prevalence estimates of up to 20.0% have been reported in community-based studies using different approaches and multiple rating scales for defining dementia.<sup>30,31,30</sup> There are also important geographical variations in the prevalence estimates of dementia. The lowest prevalence rate of 2.3% has been reported from Ibadan, Nigeria<sup>32</sup> and Al Kharga in Egypt.<sup>33</sup> The reported prevalence of dementia appears low in Western Africa with most studies reporting prevalence around 3%<sup>34-36</sup> and much lower than figures above 6% in Central, Eastern, and Southern Africa.<sup>31,37-40</sup> Figures from Northern Africa tend to be intermediate and range from 2.3% to 5.1%.<sup>33,41-44</sup>

The recent report on dementia in SSA published by ADI included results from four African studies that have estimated dementia mortality risk. The result showed an increased mortality risk with a hazard ratio ranging from HR=1.5 (95%CI: 1.2-1.8)<sup>45</sup> to HR=6.3 (95%CI: 3.2-12.6)<sup>46</sup> and an estimate from meta-analysis of HR=2.3 (95%CI: 1.0-3.5)<sup>21</sup>. Contrary to expectations of a higher risk of dying from dementia in the developing compared to developed countries, some studies in Africa reported a lower risk of mortality from dementia than has been reported in several middle- and high-income countries.<sup>45</sup> Urban dwelling and anthropometric evidence of under-nutrition were independent predictors of dementia mortality in the Ibadan Study on Aging cohort.<sup>45</sup>

Data on the direct costs of dementia in Africa are largely non-existent. However, it has been estimated that the cost of dementia in 2015 represented 6.2 billion US dollars for SSA, of which 70% is attributable to the cost of informal care most often provided by relatives and families of people living with dementia (Guerchet et al., 2017).<sup>21</sup> A limit of this estimate is that it is based on imputations using the countries' Gross Domestic Product and the medical/social/informal cost distribution from a multicentric study in LMICs from the 10/66 Dementia Research Group. There is a lack of original data



regarding health service utilization and cost of services in African countries, which could inform a better and more precise estimation of the cost of dementia in the region.<sup>47</sup>

### **What are the programs that have been established to raise awareness, diagnose and treatment of Alzheimer's in developing countries/low resource environments?**

Capacity building programs are critical. There is still widespread belief in Latin America and the Caribbean as well as other low resource settings, that detrimental changes in personality and behavior are a natural result of aging<sup>48</sup>. Therefore, many dementia sufferers and caregivers do not seek medical attention and support unless the symptoms are severe, and their specific problems and needs are often invisible to healthcare providers and policymakers<sup>49</sup>. Training programs for healthcare personnel and educational programs for individuals at risk or in early stages of dementia, and their caregivers, are powerful strategies for increasing awareness and early diagnosis skills. One result is that the services and resources available in the community become more closely matched to the local burden of dementia.

In Latin America and the Caribbean (**LAC**) I have been involved in the following activities:

- 1.- Establishment and support of partnerships between advocacy groups, clinicians, and academic centers, which deliver training programs for healthcare professionals. For example, the Nueva Esparta Chapter of the Venezuelan Alzheimer's Foundation (Fundación Alzheimer de Venezuela), the University of Zulia, the Experimental University of Liberator, and the Ministry of Higher Education, collaborate in offering the Certificate for Comprehensive Care for Persons with Cognitive Impairment through a national scholarship program, FUNDAYACUCHO. The certificate requires 23 credits, including 98 hours of classroom instruction, and 90 hours of hands-on team projects and case studies.
- 2.- Education of dementia patients, high risk individuals, family members, and caregivers can facilitate the timely seeking of health care and support but can also clarify the rights of patients and caregivers to various services, including access to medication and caregiver support. For example, the School of Caregivers of Older Adults in Maracaibo, Venezuela, provides education to non-professional caregivers of older adults, with or without dementia, residing at home. During 32 academic hours, a team of healthcare professionals acts as facilitators of peer-driven discussions and other interactions for groups of 30 participants, covering basic needs, such as hygiene, comfort, mobility, sleep, safety, nutrition, social intervention, cognitive and physical stimulation, and handling of difficult situations. Several activities are devoted to the wellbeing of the caregivers.
- 3.- Workshops offering physical, social, and/or cognitive stimulation. The workshops, often led by expert caregivers supported by health professionals, allow dementia patients to participate in activities such as dancing, singing, storytelling, painting, physical exercise, and formal cognitive exercises. In Maracaibo, such workshops have been held for more than 19 years and have generated a manual of cognitive exercises that allows implementation by community members. This Manual is being used also in Bolivia, Colombia and Mexico, and now in South Texas.
- 4.- Partnerships that bring together individuals and/or organizations with a common interest: improving the lives of people with dementia and their caregivers, promoting early diagnosis, facilitating access to services and medication, promoting educational programs, or carrying out awareness events. In optimal situations, the partnership involves representatives of many levels: patients and

caregivers, advocacy groups, academic centers, private industry, and policymakers. In LAC, the partnerships focused on dementia are often loosely organized. For example, an advocacy group might obtain financial support from the local Chamber of Commerce and retail stores as sponsors for a public event, such as a walk or a lecture series, but do not articulate a long-term vision for the partnership. Other types of partnerships important for developing healthcare infrastructure are those that include researchers, such as the 10/66 Dementia Research Group<sup>50</sup>.

5.- Public engagement usually involves educating patients, their families, caregivers, and the broader community about cognitive impairment and its effects at personal, organizational, and societal levels. This is challenging in many parts of LAC, due to generally low levels of health literacy, poverty that increases the urgency of competing needs, and lack of open discussion about dementia among peers, healthcare providers, and advocacy groups. Furthermore, there are often no financial or human resources for implementing and sustaining community engagement, particularly in rural areas.

One example is the Interdisciplinary Symposium on Alzheimer's disease and related disorders, which has been held annually for eighteen consecutive years in Maracaibo, Venezuela. We have involved healthcare providers and researchers, who developed a plan to educate the public about the origins of dementia, signs and symptoms, risk factors, diagnostic strategies, treatment options, and caregiver issues. Advocacy groups, the media, local educators, and other interested parties come together with the focus is on improving the quality of life for patients and caregivers, and effective actions to allow a life with dignity. People with dementia are also encouraged to participate in group activities, such as dances, plays, concerts, and exercise routines, that demonstrate their potential for action, creativity, and emotional development. An important lesson from these experiences is that creativity and emotional rapport among presenters and participants are crucial for the success of such activities; strict presentation of scientific facts is much less effective.

### Africa

1.-Capacity building through scientific conferences focused on Brain health and aging in low and middle-income countries: Five scientific conference has been centered directly in (Kenya) since 2001, engaging and mentoring young and LMIC-based dementia and healthcare systems researchers, and leveraging the knowledge, experience and networks developed over the years.

2.- IBRO schools and Society for Neurosciences workshops as well as other professional societies.

3.- SONA or the Society for Neuroscience in Africa has developed several initiatives for capacity building in brain health.

4.-Local non-profit organizations such as Africa Mental Health Research and Training Foundation a non-governmental organization based in Kenya, dedicated to research in mental and neurological health as well as substance use research to generate evidence for policy and best practice in the provision of affordable, appropriate, available and accessible mental health services. AMHRTF brings together the widest possible spectrum of professionals from both mental health and non-mental health fields to work together under one roof working in research and interventions in mental health.

### **What have you learned from your experiences working with populations in the U.S. and abroad?**

I have learned that international collaborations to better understand Alzheimer's disease and other dementias, are not only good from the economical, humanitarian, and scientific perspective, but is also a matter of national security.

**First**, I want to emphasize the value of building track through diplomacy with countries where we have difficult relationships. Venezuela being a prime example. Although we have bad relations between governments, the presence of a US-funded research study on the ground on a sensitive topic, works to improve the image of the US in the eyes of the people.

The frequent interaction that American scientists have had with people, through community assemblies, celebrating health fairs, gave a positive impression of Americans. I remember once my classmate and now colleague at Columbia University, Dr. Joe Terwilliger, spoke at the town hall and said "you probably get nothing out of participating", and they respected the honesty and all the rest – it is a way to use American soft power to affect hearts and minds. Interaction with people in countries that have bad formal relations with the US provides an opportunity to show the humanitarian side of America and build grassroots people-to-people relationships. The use of the power of nonpolitical actors like scientists and musicians and athletes to build relationships that do not involve the government is one of the processes suggested by diplomacy. It is about science diplomacy, and how that has benefits that are independent of political diplomacy and can be used when political diplomacy fails, as science is not political.

That said, government funding to such programs that is not conditional on political factors in those countries is an important way to demonstrate that the rhetoric America uses about its eagerness to help people around the world is not just blind talk but supported by funding and real actions.

**How working with people in Venezuela helps America.** Besides the value of discovery and accelerating development, the value is in trying to get people from those countries to think independently and critically, and in the process also learn to think independently and creatively in other areas. In our courses in Venezuela, Haiti, Dominican Republic, Colombia, Bolivia our emphasis is on "question everything" and that science is always looking for better ideas, and always knows its current models are suboptimal. This has great potential to influence people if they start thinking critically about science and then apply the same techniques to other areas. Indeed, it is not so important or useful to teach someone in another country to apply instruments so they can serve as "errand boys" for us, collecting data for us. It is much more important and useful to get them thinking critically about what they can do that we cannot do, and how they can do things differently. Spreading democracy, rule of law, meritocracy, discoveries cannot be done in "difficult" countries by teaching politics, but it can be done teaching critical thinking in science, and the skills will transfer.

As a **second** issue I will touch is the issue of leadership and border security.

America is limited by two oceans at East and at West. At North, the American-Canadian border is a long thin frontier with middle class where everything is under control, including the middle-class population on the American border. However, it is in the Southwest where America is vulnerable. The borderland between USA and Mexico is broad, indistinct, and porous. Mexico and Central America constitute a growing demographic powerhouse with which the US has an inextricable relationship.

When I was considering selecting a place to reside, and visited the Rio Grande Valley region, I thought it looks very much like Maracaibo in the good times, maybe because Maracaibo was modeled by the oil companies, including of course Texaco. The Rio Grande basin in South Texas contains the four poorest counties of Texas and also contains the county with the largest proportion of dementia patients.

The income gap between the USA and Mexico is the largest between any two contiguous countries in the world, with the American GDP 17 times that of Mexico <https://data.worldbank.org/indicator/NY.GDP.MKTP.CD?locations=US>. As everyone knows, northern Mexico is plagued with cartels, human and drug trafficking and exerts a big push in illegal immigration. While the young people in northern Mexico are recruited by the cartels, every family hope that the violence ends and that their kids could live in a different world, which means the United States. Creating conditions in the border for improved quality of life, is not only a matter of military enforcement. The role of higher education institutions is crucial. As an example, the University of Rio Grande Valley was created right on the border, specifically the School of Medicine. The Alzheimer's Disease Resource Center for Minority Aging Research has allowed me to provide training not only to early investigators that are faculty at UTRGV and UT Health Sciences San Antonio, but also undergraduates, graduates high schoolers, and communities at the two sides of the border.

One could argue that with Herculean border controls, a functional and nationalistic America can coexist alongside a dysfunctional northern Mexico. Probably in the short run. But in the long term, as Toynbee suggested a border between a highly developed society and a less developed society will not attain an equilibrium<sup>51</sup>, meaning that as energy, the society will move from the higher level of entropy (disorganization) to a lower level of entropy. Kaplan arguments that "if the U.S. and Mexico does not eventually come together to the degree that Canada and U.S. already have it will adversely affect America's other relationships, especially as Mexico and Central America's population grows at a much higher rate than ours".<sup>52</sup>

### **How do gaps in treatment and awareness in other countries impact the U.S.?**

- 1.- Increase burden of disease in low resource settings, means less availability of resources to promote development, perpetuating poverty while hindering economic development.
- 2.- The growing burden of dementias also exacts an economic cost, as people are less productive, work for fewer years, and die prematurely.
- 3.- The burden of dementia in low resource settings will compete with the need to address the infectious diseases (e.g., ending the HIV epidemic) that may impact the U.S. population.
- 4.-Contributing to address issues in LMICs may allow the development of innovative technologies and solutions that when similar problems arise in the U.S. solutions are already at hand.
- 5.- Lack of attention to the burden of disease in LMICs, which receive 42 percent of U.S. exports, may depress demand for those goods and services and thus threaten the jobs of Americans.
- 6.- Deteriorating health conditions also create political risks in countries of strategic importance, for example, Mexico. Poor public health increases the likelihood of political instability, disenfranchises persons with inadequate social capital, limits economic growth, and exacerbates the human damage caused by social and economic dislocation.
- 7.- Without strong leadership by the United States in a sensitive issue, other donors in the public and private sectors, as well as developing countries themselves, will not assume a significant portion of the costs.
- 8.- Improving the health of people in other countries makes both strategic and moral sense. Beyond enhancing security, prosperity, and democracy-and addressing the criticism that the benefits of globalization leave out the poor-a vigorous international health policy provides an opportunity for leadership that is grounded in the United States' strength in biomedical science and its applications.

9.- Dementia is an area where the US has leading research and services. Actions in world health improvements strengthen the global system, and this, in turn, benefits the United States as the dominant power and main supporter of that system.

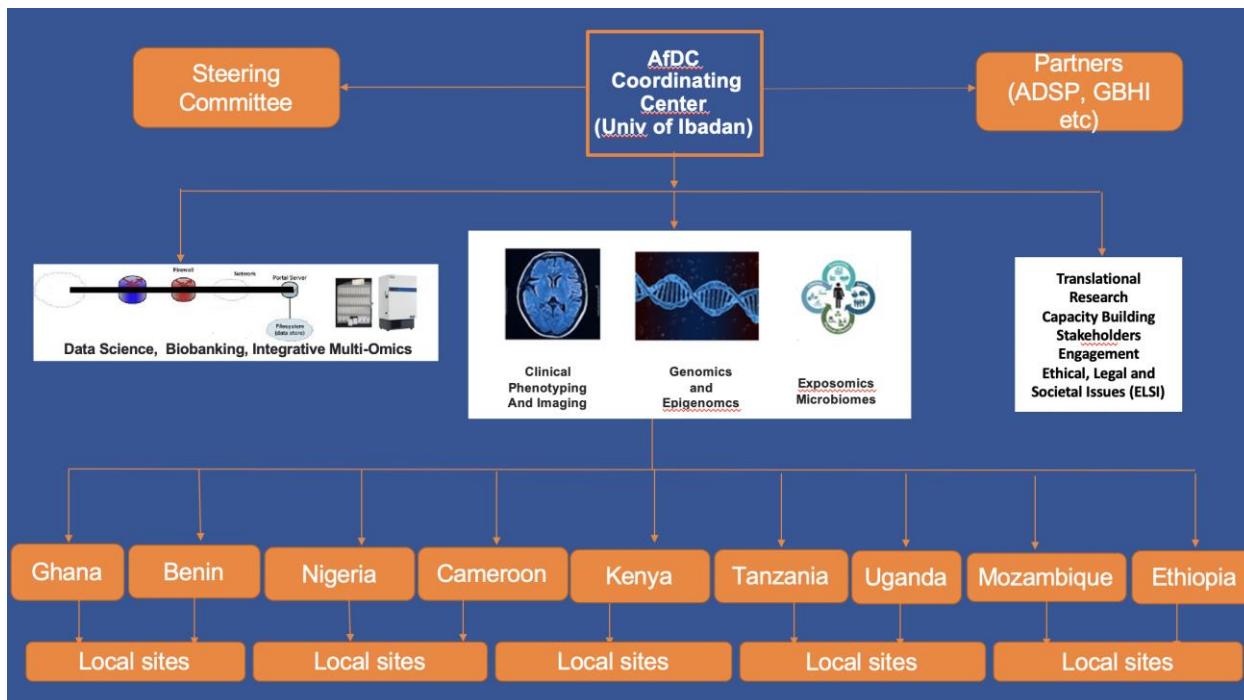
10.- Discoveries are needed, access to resources that may not be available in the US. Loss of skilled government officials, highly trained military leaders, and members of the entrepreneurial class undermines political leaders' capacity to govern. The same patterns could easily be repeated in LMICs where the impact is even higher.

**What are your recommendations to congress for addressing the global health care gaps in terms of Alzheimer's diagnosis and treatment?**

*1.- Creation of the African Dementia Consortium (AfDC)*

The broad aim of the AfDC is to bring together African dementia researchers in a multidisciplinary framework and generate clinical, cognitive, socioeconomic, neuroimaging, genomic and biomarker data to improve the phenotypic characterization of dementia in Africans. The network will also identify novel biomarkers and interventions for prevention and treatment. The AfDC will further foster the translation of evidence to policy and practice and contribute to efforts to reduce the burden of dementia among Africans, African ancestry populations in Diaspora and ultimately contribute to the reduction of the global burden of dementia.

In order of priority, AfDC will focus on research areas including: (1) epidemiological studies to define trends in prevalence, incidence, and risk factors for dementia in Africa; (2) genetic studies to unmask novel variants that predispose to Alzheimer's disease and related dementias (ADRD) in African populations and also increase African participation in global genomic studies including trans - ancestry meta analyses in dementia; (3) detection of unique biomarkers for dementia; (4) conduct of dementia clinical trials involving African populations; (5) capacity building and networking among dementia researchers living or working in Africa particularly early career investigators; (6) facilitation of translational dementia research (7) promotion of implementation science for translation of research evidence to practice and policy in Africa and (8) training and education of the next generation of research leaders. The consortium will build effective synergies through collaborative research networks with researchers within Africa and with partners from North America, Latin America, Europe, Asia and other regions of the world. See **Figure 5** for the schematics of organization.



**Figure 5. Organizational Structure of the Proposed Africa Dementia Consortium**

### 2.-Continue to Support Research

- Sustain support for key investigators who have track records and delivering. Particularly for longitudinal multi-disciplinary including epidemiology projects which can generate much knowledge and applications.
- Propose excellence centers in key North and SSA regions that will cost a fraction of what such cost in North America but deliver with high gains.
- In Latin America in the Caribbean, I suggest implementing programs like the RCMARs/ADRCs at a Hispanic Serving Institution, like UTRGV, with wit research training embedded in a research education core, and capacity building at societal level through an outreach, recruitment and dissemination core. Bioinformatic core, Clinical Core, Biomarkers and Imaging cores as well.
- Consider and effort similar to STRIDE, which is a four-year research capacity building program funded by the UK's Global Challenges Research Fund. STRIDE intent to synthesize and generate policy-relevant evidence to support development of policies to respond to dementia in LMICs and to implement formative research to inform dementia policies (<https://stride-dementia.org>)

### 3.-Global Leadership

- Leverage action from the World Dementia Council established in 2014. In 2013, G8 set out an international response to dementia with the aim of identifying a cure or a disease modifying therapy by 2025. Members are from a wide range of experts from research, academia, industry, the NGO sector, people living with dementia & governments. In 2015, a Global Observatory of Dementia was established with participation of Alzheimer's Association. Even though this is a global initiative, the role of UK is predominant.
- Create a space of bilateral exchanges between actions in response to the challenge of dementia in USA and LMICs, and also a global space for collaboration addressing specific questions, including migration, COVID-19, women issues, redesign of urban spaces.
- **Dementia Discovery Fund (UK)** – a ground-breaking public/private venture capital fund which aims to finance pre-clinical research to find new drugs to treat dementia.

- *Global Council on Brain Health (GCBH)* is an independent collaborative of scientists, health professionals, scholars and policy experts from around the globe working in areas of brain health related to human cognition. CBCH is convened by AARP with support from Age UK.
- *The Davos Alzheimer Collaborative (DAC)*, with participation with UsAgainstAlzheimers leading some initiative, including 1) the development of a global cohort in partnership with the International HundredK+ Consortium Cohort, the Broad Institute, ADI and others, aims to build a global cohort with innovative high-quality, detailed data on a well-characterized, diverse population. 2) Global clinical trials support platform. DAC aims to build a global clinical trial network that engages Europe, Asia, Central and South America. 3) Healthcare system preparedness for Alzheimer.
- Alzheimer's Association international initiative including the International Grants Program and also the Satellites Conference Meetings and particular the Alzheimer Association International Conference which is the main conference for scientists to share and establish collaborations.

#### *4.-Lifecourse and social determinants of health*

- Investment in schools that serve Black and Hispanic children in the US as well as in LMICs and safe neighborhoods, housing, and primary health care attacking the 12 factors associated with 40% of risk for dementia will impact the burden of disease.

#### *5.-Public engagement*

- Initiatives such as the one from The Milken Institute Center for the Future of Aging has launched the Alliance to Improve Dementia Care in July 2020 to engage public, private, and nonprofit sector decision makers, advance dementia-care and payment models, and build a dementia-capable system and workforce.
- Community-based organizations, including museums, art centers, senior coalitions and institutions supporting heritage and legacy are valuable allies. For Example the River Pierce Foundation based in Zapata county in South Texas is supporting efforts to restore not only buildings but to support the memory of older adults.

#### *6.-Dementia-competent and diverse workforce*

- Health professionals able to competently evaluate and manage patients with changes in cognition,
- Direct care workers including nursing and home assistants.

#### *7.-Support for family caregivers*

- Both in terms of development of skills, emotional support and economic compensation.
- Disease management programs

#### *8.-Use evidence-based guidelines from Neuroarchitecture to:*

- Support healthy cognitive aging
- Facilitate aging in place
- Improve public spaces that mitigate social isolation and promote creativity and cognitive stimulation through arts, cultural and social activities.

**Thank you for giving me the opportunity to share my perspective with you today. I look forward to addressing your questions and comments.**

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