

Aging and Dementia: Implications for Cuba's Research Community, Public Health and Society

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ABSTRACT

Dementia is a syndrome that has great repercussions for quality of life of patients and their families, as well as a high social cost. A [2009] systematic review of research evidence and consensus of expert opinions showed that 36 million people live with dementia worldwide, with 4.6 million new cases every year (similar to the global incidence of nonfatal stroke). The prevalence of dementia in older Cubans is high, with rates ranging from 6.4% to 10.2%, or about 130,000 persons (1.1% of the total population). This number is expected to rise to 260,000 by 2030. The age-standardized annual incidence of dementia is also high: 21 per 1000 population, with 28,750 new cases annually. Dementia is the leading cause of disability among older adults and is the main cause of dependency, financial burden and caregiver stress.

In this review, we highlight the importance of epidemiological research to obtain greater knowledge of the disease, improve health services, promote actions for prevention and early diagnosis, and implement a national strategy to address dementia in the Cuban population, itself now immersed in two processes: accelerated demographic aging and epidemiologic transition.

KEYWORDS Dementia, Alzheimer disease, epidemiology, risk factors, prevention, diagnosis, treatment

INTRODUCTION

In 1906, during a lecture at the 37th Conference of Southwest German Psychiatrists, an outstanding German neuropsychiatrist, Alois Alzheimer, presented his report *Concerning a peculiar disease of the cerebral cortex*,^[1] thus identifying the disease that bears his name today. However, he probably never imagined the future impact this disease would have with the progressive aging of the global population.

The most frequent cause of dementia is Alzheimer disease (AD), a progressive degenerative condition characterized by cognitive impairment and dementia, and at the neuropathological level, by the presence of neurofibrillary tangles and neuritic plaques. In over 90% of cases it develops in those aged >65 years, doubling in prevalence with each successive decade of life, from 10% in those aged 60–70 years to 40% in those aged ≥80 years.

Globally, an estimated 35.6 million people were living with dementia in 2009. By 2030, that number is expected to reach 65 million, and by 2050, a total of 113 million, two thirds of whom will live in developing countries.^[2]

In a country like Cuba, immersed in two interrelated processes—population aging and epidemiologic transition—AD should become a national priority.

POPULATION AGING AND EPIDEMIOLOGICAL TRANSITION

In recent decades, we have witnessed impressive progress in human development, population aging being one of the most important and occurring in all regions of the world, particularly in low- and middle-income countries. The global population is expected to increase by an estimated 2.7 billion between 2005 and 2050, from 6.5 billion to 9.2 billion. This will be coupled with a dramatic increase in the number and proportion of older adults, the number of people aged ≥60 years tripling between 2000 and 2050, from 606 million to 1.9 billion.^[3,4]

This demographic transition—seen particularly in Latin America, China and India—is the result of declining fertility and replacement rates, reduced mortality and higher life expectancy. In the last half of the twentieth century, life expectancy at birth in Latin America and the Caribbean increased by approximately 20 years (from 50 to 70 years), and the fertility rate decreased by half, from approximately 6 children to <3.^[4]

As a result of demographic, social and economic changes worldwide, population aging is accompanied by a process known as the epidemiologic or health transition, in which infectious diseases are gradually replaced by chronic non-communicable diseases as the main cause of death.^[4]

Chronic non-communicable diseases are now the leading cause of death in all regions of the world except Sub-Saharan Africa. Of the 35 million deaths in 2005 from such diseases, 80% occurred in low- and middle-income countries.^[2,4] This is due in part to the fact that the vast majority of older adults live in these regions—60%, increasing to 80% by 2050.

Shifting risk factor patterns also contribute to this picture. Latin America is an example of the third stage of epidemiologic transition. With increased life expectancy, high-fat diets, smoking, and sedentary lifestyles, cardiovascular diseases become the number one public health problem—greater than in regions in the second stage of epidemiologic transition (China and India), where such risk factors are less prominent, and regions in stage four (Europe), where public health policies have reduced exposure levels.^[4] Nevertheless, 80% of premature deaths from cardiovascular diseases, stroke and diabetes mellitus could be avoided by healthy lifestyles, coupled with early diagnosis and pharmacological interventions.^[3,4]

Despite growing interest in giving high priority to chronic diseases in national and global health agendas and strategies, mental illnesses in general and dementias in particular are not a priority in most developing countries.^[2] Dementias, however, are the major contributor to disability, dependence and mortality among older adults.

Cuba is a developing country with health indicators similar to those in developed countries, and with a rapidly aging population: 17.9% aged >60 years, a life expectancy at birth of 77.97 years (76 years for men and 80.02 for women), life expectancy at age 60 of 22.09 years and 8.8 at 80. By 2020 Cuba is predicted to have the highest proportion of older adults of any Latin American country (with 25% of total population aged ≥60 years).[5]

DEMENTIA IS A GLOBAL HEALTH PROBLEM

Recent estimates (based on systematic reviews of prevalence data and expert consensus) suggest that the number of people living with dementia worldwide is 36 million, with 4.6 million new cases annually (similar to the annual incidence of nonfatal stroke). [2,6] This number will double every 20 years, reaching 80 million people with dementia worldwide by 2040, an increase more marked in developing than in developed regions.

In Latin America, the numbers of people with dementia are rising faster than in any other region in the world; they will increase by 120% between 2000 and 2020. The current figure of 2 million people with dementia in Latin America will increase to 4.1 million by 2020 and to 9.1 million by 2040; that is, numbers will be similar to those in the USA and Canada.[7]

Dementia prevalence in Cuba varies from 6.4% to 10.2% among people aged ≥65 years, with female sex predominating. AD is the most common cause, followed by vascular dementias.[7,8] Considering the rapid aging of the Cuban population, it is estimated that the number of people suffering from AD or other dementias (130,000) is expected to double by the year 2020.[9] Without effective intervention—that is, if a cure is not found in the next few years—the number of Cubans with dementia will increase 2.3 times by 2040, reaching 300,000 people, or 2.7% of the population. During the next 30 years, there will be a tenfold increase in demand for long-term care for people with dementia.

A prospective longitudinal study on aging and AD undertaken over 4.1 years with people aged ≥65 years in the cities of Havana and Matanzas found an annual dementia incidence by DSM-IV criteria of 9.3 per 1000 population, and 21.2 per 1000 population by 10/66 criteria. Dementia was associated with several risk factors, particularly advanced age, stroke, carriage of one or two alleles of apolipoprotein E4 (a susceptibility marker), signs of Parkinsonism, lower educational level and mild cognitive impairment. [10] We found dementia incidence similar to that reported by the Canadian Study of Health and Aging, the largest longitudinal study in the world conducted on adults aged ≥65 years, which reported an annual incidence of 21.8 per 1000 population for women and 19.1 per 1000 population for men;[11] and slightly higher than that reported by the United Kingdom's *Cognitive Function and Ageing Study*. [12]

Based on these results, we estimate 28,750 new cases of dementia per year in Cuba. If these projections hold true, the number of new cases of dementia among people aged ≥65 years will increase 2.5 fold by 2040, from 28,670 new cases annually, or one new case every five minutes, to 71,675 new cases annually or one new case every three minutes.

THE IMPACT OF DEMENTIA

Dementia's effects are apparent at three interrelated levels:

1. The person suffering from dementia, a devastating disease causing disability, deterioration in quality of life and reduced life expectancy.
2. The family and caregivers of the person suffering from dementia. As the cornerstone of care and support systems throughout the world, family members and caregivers will be subject to adverse psychological, physical, social and financial effects. These include high levels of anxiety and depression, effects on their physical health, and a negative impact on their finances, directly (e.g., bearing drug costs), and indirectly (e.g., payment for services, including those of other caregivers). Caregivers are crucial to avoid institutionalization and to keep people with dementia in their communities. When there is no caregiver or the caregiver is prevented by stress or physical illness from taking care of the person with dementia, the probability of institutionalization increases exponentially.
3. Society as a whole, which bears the high economic cost of the disease, including health care and institutional costs, social costs, and lost productivity of the person with dementia as well as their family members and caregivers.

Among people aged ≥60 years, dementia is the major contributor to the indicator, *disability-adjusted life years lost*: 11.2%, compared to 9.5% for cerebrovascular disease, 8.9% for musculoskeletal diseases, 5.0% for cardiovascular illness and 2.4% for cancer.[13]

The worldwide financial cost of dementias was estimated at US\$604 billion annually in 2010, with the highest expenditures in North America (US and Canada) and Europe.[14] The costs were primarily related to informal care, as well as social care (provided by formal caregivers and professionals in communities, day centers and nursing homes), and medical treatment (at the various levels of the health system) for care of dementias and for associated comorbidity. In Cuba, the current annual US\$500 million spent on dementias will triple in the next 30 years.[9]

These heavy costs resulting from dementias, along with the challenge posed by increasing numbers of older adults, will produce a dramatic shift in care systems worldwide. As the number of people with dementia doubles every 20 years, a proportional increase in costs is to be expected. However, the human cost represents the highest cost of dementias, its magnitude incalculable.

DEMENTIA RISK AND PROTECTIVE FACTORS

The term *risk factor* is used in epidemiology to describe the future likelihood of a disease based on a particular exposure in the population.

It is widely accepted that dementia and AD are associated with genetic and environmental factors. There is growing interest in the scientific community in further research into modifiable factors. A high-risk environment contributes to clinical expression or early disease onset; thus, prevention should aim to reduce environmental factors, delaying symptom onset.

Although aging is the most widely accepted risk factor for AD (dementia prevalence doubling every five years after age 65), several epidemiological studies suggest involvement of other risk factors. Some of the most discussed are factors associated with decreased cognitive reserve, including reduced brain volume, low

levels of education and cognitive training, poor intellectual activity in early life, and reduced physical and mental activity in later life. [15,16]

Brain reserve capacity is directly related to the number of neurons and synapses as well as dendritic arborization, together with lifestyle and development of cognitive strategies. Research has posited two types of brain reserve: passive and active.[15] In the passive cognitive reserve model, the brain's structure (neurons, synapses, brain volume) provides the basis for this reserve and is determined primarily by genetics, although it is also influenced by environment (for instance, environmental factors in life's early years, nutrition, etc.). The active reserve model, most commonly known as *cognitive reserve*, is more related to neural processing and synaptic organization, rather than to neuroanatomical differences. Synaptic processing and organization are more influenced by environment, such as education and intellectual stimulation—and so these are potential factors for increasing cognitive reserve. [15,16] Low cognitive reserve capacity has been associated with earlier manifestation of the neuropathological changes characteristic of dementia.[10,15] Therefore, environmental factors enhancing cognitive reserve can delay symptom onset, so that, of two individuals with the same degree of neuropathological lesions, the one with greater cognitive reserve may be able to compensate more effectively and thus delay onset of symptoms and disability.

Epidemiological, biological and social evidence supports the hypothesis that risk factors operate throughout the lifespan (gestation, childhood, adolescence, and early and late adulthood), acting in an independent, cumulative and interactive manner to cause the disease.[17] This theory, based on the life-course epidemiological model, stresses the importance of temporal exposure order [to risk factors] and emphasizes gene–environment and environment–environment interactions.

Early-life risk factors Risk of dementia and AD begins in the womb. Fetal malnutrition, low birth weight, and absence of breastfeeding may have long-term negative impacts. There is evidence that these and other conditions in early life increase susceptibility to several chronic diseases, particularly cardiovascular disease and its risk factors (e.g., hyperinsulinemia, diabetes, atherosclerosis, hypertension, lipid disorders).[18,19] Poor socioeconomic conditions are associated with other disadvantages (nutrition, environmental stimulation, access to education, neurodevelopment, physical growth) and subsequent cognitive performance. Several studies in which anthropometric indices such as height, leg length, arm length and head circumference were used as markers of neurodevelopment in the first years of life have found an inverse association with dementia and AD in late life.[8,10,19]

The factor that has received most attention is educational level. Findings consistently show an association between low educational level and increased risk of cognitive impairment and dementia.[18–20] Several explanations have been posited concerning the association between low intellectual level and dementia: (1) education produces a selection bias, since people with a higher educational level may perform better on cognitive tests; (2) education is associated with other early-age factors such as socioeconomic status, nutrition and IQ, and with adulthood factors such as occupation, health and better lifestyles; and (3) education increases cognitive reserve, offering long-term potentiation and inducing neuroprotection.[15]

Mid- and late-life risk Various studies suggest that risk factors for vascular diseases—including smoking, diabetes mellitus, hypertension in midlife, hypercholesterolemia, ischemic heart disease, and metabolic syndrome—predispose to both AD and vascular dementias.[16–20]

Epidemiological investigations suggest, moreover, that up to 50% of dementias could be prevented.[15,18] Since age is the non-modifiable factor most associated with dementias, any measure delaying onset would be an effective intervention.

Obesity, high blood pressure in midlife, and diabetes account for a substantial proportion of cases of dementia and AD, either through vascular damage or production of substances important for metabolism (adipokines) and inflammation (cytokines) in fatty tissue, and/or insulin resistance and hyperinsulinemia.

Of patients suffering their first stroke, 7.4% develop post-stroke dementia.[19] As stroke is associated with cardiovascular risk factors and lifestyle, its link with dementia may be explained by a number of mechanisms. First, stroke directly injures brain regions associated with cognitive function, such as the thalamus and thalamic cortical projections. Moreover, stroke increases myeloid beta (A β) protein deposits, leading to cognitive impairment. Finally, acute stroke induces an inflammatory response.

Other evidence, although not conclusive, suggests that AD risk may be reduced with intake of vitamins associated with homocysteine metabolism (vitamin B12 and folate), antioxidants such as vitamins C and E, unsaturated fatty acids, moderate amounts of alcohol (especially red wine), as well as vegetables and fish.

Epidemiological evidence from several sources has identified head trauma as a risk factor.[18] Whether head injury initiates the pathogenic cascade leading to plaque and neurofibrillary tangle formation or simply reduces brain reserve capacity, the pathogenic mechanism has not yet been fully demonstrated.

Genetic factors AD is usually classified according to age at onset. Most patients (>95%) who develop it are aged >65 years (late onset), while 5% are in the early-onset bracket, usually aged 40–60 years. From a clinical standpoint, there is no difference between early-onset and late-onset AD, although disease progression is faster with early onset.

Point mutations have been found in early-onset AD in amyloid precursor protein (APP) on chromosome 21, presenilin 1 (PS1) on chromosome 14, and presenilin 2 (PS2) on chromosome 1, all genes that cause autosomal dominant transmission.[18] In nonfamilial or sporadic AD, which accounts for 95% of cases, the apolipoprotein E ϵ 4 (APOE) gene on chromosome 19 is the genetic risk factor most widely replicated in various studies since 1993.[18,21]

CLINICAL SIGNS OF ALZHEIMER DISEASE

AD is a progressive disease that develops slowly and insidiously, affecting episodic memory and other cortical functions. Symptoms may include aphasia; apraxia; agnosia; disordered reasoning, planning and decision making; and disorientation; as well as behavioral symptoms that disrupt patients' functional ability to perform daily life activities.

Neurodegeneration in AD begins 20–30 years before clinical symptoms appear.[16] During this preclinical phase, deposit of amyloid plaques and neurofibrillary tangles increases, and the first symptoms appear. This [early] clinical phase is often recognized as mild cognitive impairment (MCI), detected on the basis of subjective memory complaints confirmed by a reliable informant and by standardized neuropsychological tests, using cutoff points specific to age and educational level.[22]

Amnesic MCI is the subtype most strongly associated with AD development. In longitudinal studies, 70% of people with MCI evolve to AD or another form of dementia over the ensuing five years, equivalent to a conversion rate of 12% annually.[20,22]

Language difficulties may appear during the course of AD, including difficulties retrieving the names of relatives or friends, finding the right word in conversation, progressing in more severe stages to decreased verbal fluency that may lead to total loss of speech.

Visuospatial difficulties are common, causing individuals to get lost in familiar environments—in their own homes or on the street—or they may forget their parking spot or driving destination. Trouble with calculations is common. Patients experience difficulties in executive functioning, in planning and implementing various activities, or in managing their own finances. Dyspraxia can manifest itself in their ability to get dressed and/or cook or perform other domestic activities.

Two thirds of AD patients exhibit one or more noncognitive or behavioral symptoms at initial assessment and incidence increases as the disease progresses.[23] Apathy, loss of initiative or interest, occurs at early stages in the disease. About 30% of patients in this stage experience symptoms of depression, including loss of appetite and insomnia, bouts of weeping, anxiety and phobias, reflected in continual questions about the future and fear of being left alone when they interact with groups of people or travel outside their home environment.

As the disease progresses to moderate and severe stages, 15%–50% of patients show other behavioral symptoms, such as paranoid ideation and delusions: that objects are being stolen from them, that the place where they live is not their home, that their caregiver is an impostor, that they are victims of abandonment or infidelity. Errors in identification or perception may show up in the conviction that there are strangers in their home (the phantom boarder syndrome), failure to recognize their own body in a mirror, inability to recognize family and friends, and misidentifying events on television (thinking they are happening in their own three-dimensional physical space).

In more advanced stages there can be agitation (in the form of physical and verbal aggression toward family members or caregivers), hallucinations, wandering, flights, repetitive purposeless activity, and inappropriate activity (hiding objects or throwing them away). These develop in up to 75% of patients, either as isolated symptoms or in combination.

Physical and neurological examination Clinical examination of patients with dementia has two important objectives: (1) identify, through a general physical and neurological examination, signs that may point to other causes of dementia, and to document those that may be directly related to AD, and (2) explore patients'

mental state, identifying cognitive deficits compatible with a diagnosis of dementia, to stage disease severity, and if warranted, run a more extensive battery of neuropsychological tests to more precisely define disease extent or to provide initial diagnosis for patients in early disease stages.[24]

The most important purpose of the clinical evaluation is to rule out reversible or potentially curable causes of dementia.

Two sets of criteria are the most widely used by researchers and attending physicians for AD diagnosis: those proposed in the Diagnostic and Statistical Manual of Mental Disorders by the American Psychiatric Association, 4 ed.; 1994 [26] and the consensus criteria established by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer Disease and Related Disorders Association, now known as the NINCDS-ADRDA criteria.[27]

In its April 21, 2011 issue, the *Journal of the Alzheimer's Association, Alzheimer's & Dementia* published the final version of the revised criteria for AD clinical diagnosis, replacing those established by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) working group in 1984 (NINCDS-ADRDA, currently the Alzheimer Association).[28]

These new criteria may be applied to specific conditions of clinical practice such as AD in young adults or difficult-to-diagnose cases, as well as in research projects, well-defined cohorts and clinical trials requiring early-stage diagnoses based on specific tests of memory impairment and the more recent contribution of biomarkers.

Biomarkers As yet there are no pathognomonic markers for AD. The ideal AD biomarker should be: able to detect a characteristic feature of the disease; validated in confirmed cases in neuropathological studies; at least as sensitive and specific as clinical diagnosis (>85% and >80%, respectively); reproducible; easy to measure; inexpensive; and minimally invasive (identified in blood, urine, saliva, cytology smear, cerebrospinal fluid or through structural or functional imaging techniques).

A field of continuing research is the definitive diagnosis of AD in vivo, in specialized centers, with 90% certainty, using highly specific neuropsychological tests and biomarkers. Cerebrospinal fluid studies (combining decreased beta amyloid levels and increased tau and phosphorylated tau protein levels), medial temporal lobe atrophy on magnetic resonance imaging, and studies with positron emission tomography (PET) using Pittsburgh compound B (PiB) to quantify amyloid- β burden, increase AD diagnosis accuracy and allow better identification of persons with MCI that would evolve to AD, identifying individuals at presymptomatic stages. [22,28]

RECOMMENDATIONS FOR A NATIONAL STRATEGY

The scientific community plays a vital role in drawing attention to population aging, and to the growing numbers of people living with dementia, the impact of the disease and related needs for care—and in securing commitment from state institutions, health managers and the general public [to address the problem]. Quality research, if promoted effectively, will allow us to further our

knowledge, develop policies based on the best evidence appropriate to our context, and develop services needed as the population ages.

The Cuban Alzheimer Disease Section, working together with investigators from several research centers; with providers of primary, secondary and tertiary health care services; and with families and caregivers of Alzheimer patients, has indicated the following recommendations for a national strategy:

Increase promotion, information, education, and support for families, recognizing the role they play WHO and Alzheimer's Disease International (ADI) have been calling on governments, policymakers and the scientific community to make dementia a global public health priority.[29]

A national society-wide participatory campaign and implementation of a prevention strategy aimed at reducing risk factors and enhancing protective factors has potential for substantial impact in reducing the number of people with dementia over the coming years. It would promote early diagnosis by getting more people to consult their family physicians at early stages. It would improve the health care system's diagnostic capacity by identifying people at risk. And it would have a potential beneficial impact on patients' and families' quality of life.

It is likely that dementia risk associated with smoking and high blood pressure will decrease over the coming years, but at the same time we are seeing an epidemic increase in the rates of obesity and diabetes mellitus type 2, which can lead to increased dementia incidence.

It will be vital to work with families to alleviate the caregiver burden, depression and stress produced by the disease, and at the same time promote cognitive stimulation in the early stages and development of centers specialized in the various stages of dementias.

Focus efforts on prevention and early diagnosis both in the health sector and in society at large Current research suggests a potential for dementia prevention through healthy lifestyles, early public health interventions, early diagnosis and appropriate treatment of chronic diseases; however, the evidence is still scattered.

A more realistic goal is to postpone dementia's clinical onset to increasingly advanced ages. One year's delay in clinical onset of dementia would mean 12 million fewer cases worldwide by 2050 and a considerable reduction in costs.[18]

Prevention is a lifelong endeavor, with requirements specific to life stages: better access to education, healthy eating, healthy growth and neurodevelopment patterns in early life; prevention and appropriate treatment of cardiovascular disease and risk factors (smoking, obesity, diabetes, hypertension, high cholesterol, etc.), physical and mental activity, and adequate treatment of depression in midlife; and in later life, avoiding malnutrition (micronutrient deficiency and anemia), maintaining physical activity and learning, social networks, reduced stress, a healthy diet and control of vascular risk factors. A 10%–25% reduction in seven risk factors could prevent 1.1–3.0 million cases of AD world wide.[30]

Early AD diagnosis has many potential benefits: starting treatment as soon as possible; helping the patient's family members

understand and accept the condition, and to plan financial and legal matters, if needed; better compliance and management of other medical conditions; preventing unintentional injuries (driving, handling of weapons); securing early access to health care and community support; and even the option of involvement in clinical trials, with disease-modifying treatments.

Increase research in all areas: biomedical, risk factors, quality of life, service development Improvement of diagnostic tools such as neuropsychological testing, genetics, neuroimaging and biomarkers would facilitate early diagnosis and intervention, as well as more effective long-term followup of people with the disease.

Implement Good Clinical Practice Guidelines for prevention and management of chronic diseases, with a community outreach component The number of people with chronic non-communicable diseases will increase over the coming years, given the demographic and epidemiologic transitions.

A population-based house-to-house survey on aging and AD revealed a high prevalence of cardiovascular risk factors, up to 85.8% of adults aged ≥ 65 years, about 50% of respondents when hypertension as a risk factor was excluded. Chronic non-communicable disease prevalence was found to be high; in decreasing order of frequency: hypertension 73.0% (95% CI 71.4–74.7), diabetes mellitus 24.8% (95% CI 22.9–26.5), ischemic heart disease 14.1% (95% CI 12.9–15.4), dementia 10.8% (95% CI 9.7–12.0) and stroke 7.8% (95% CI 6.9–8.8).[31]

Criteria must be standardized for prevention, timely diagnosis, and appropriate treatment of chronic diseases, as well as their risk factors. Although practice guidelines do not replace health professionals' clinical judgment, they do provide guidance based on the best scientific evidence for decisionmaking in daily clinical practice on appropriate health care for specific clinical problems.

Increase availability of specialists in primary health care Cuba's Ministry of Public Health has implemented a strategy in response to population aging. Measures include increasing the number of specialists: geriatricians, neurologists, psychiatrists, nurses, psychologists and social workers (among other professionals) in primary health care settings (multidisciplinary geriatric care teams, mental health centers, day centers, etc.); development of health services more responsive to the needs of older adults, training of health professionals; and development of community and home-care programs, among others.

Extend availability of prescription-only medications with proven efficacy for symptom treatment, and enhance cognitive stimulation strategies for patients Current AD treatments are insufficient for the following reasons: effects are modest, limited in the long term, and do not alter underlying progression. Cholinesterase inhibitors such as donepezil, rivastigmine and galantamine have limited gastrointestinal tolerability (side effects may include nausea, vomiting, diarrhea, weight loss),[32] and N-methyl-D-aspartate receptor antagonists, such as memantine, which have a better tolerability profile, may cause hallucinations, delusions and agitation.[33]

There remains, therefore, an unmet need for drugs that are better tolerated and provide greater and broader clinical benefits over

multiple domains; i.e., medications with better tolerability that provide an expanded and markedly improved clinical benefit in such areas as cognition, general functioning and behavior.


Promising Phase III studies are under way on anti-amyloid monoclonal antibodies such as crenezumab, bapineuzumab, solanezumab, and EV gamma globulins.[34]

Findings show that cognitive stimulation and physical exercise slow cognitive decline. A pilot controlled clinical trial using structured group discussions, games and other cognitively stimulating activities and group interventions led by professionals, and/or individual cognitive stimulation, applied to patients in the community for 26 weeks, three 30-minute sessions per week, revealed effectiveness similar to that achieved by acetylcholinesterase inhibitors, the medication now most widely used.[35] This is a viable option in our country.

Ongoing physician–caregiver partnership is essential in treatment of AD patients. Caregivers monitor patients in their daily routines;

they are responsible for administering medications, for implementing nonpharmacological treatments (including cognitive training), and for general health and quality of life. Since caregivers must make decisions on legal issues, financial management and home safety, among other matters, it is vitally important to provide families with education and guidance.

CONCLUSIONS

- The world is facing a new epidemic of unprecedented proportions.
- The epidemic's impact will be greatest in low- and middle-income countries, the least prepared to face the challenge posed by dementias.
- The unrelenting rise in costs for society-at-large will lead to an increase in long-term care needs.
- Effective prevention using a multifactorial, life-course approach (particularly of cardiovascular diseases and their risk factors), development of services for better care and treatment to delay disease onset, further research and active involvement by society as a whole constitute a national priority. 

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