Current trends and challenges on dementia management and research in Latin America

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This manuscript presents an overview of the current scenario and challenges on dementia practice and research in Latin America (LA). We review the main demographic and socioeconomic indicators from LA, epidemiology and diagnosis of dementia, knowledge of dementia by the general public, by general practitioners (GPs) and by other health care professionals, costs of dementia, and the research on dementia in the continent. The main aim of this article is to integrate information regarding some of the action areas aligned by the World Health Organization (WHO, 2017) global action plan on the public health response to dementia [1], which will need to be addressed by the countries in the region, as they prepare their local dementia action plans.

MAIN DEMOGRAPHIC AND SOCIOECONOMIC CHARACTERISTICS

LA is constituted by territories where mainly the Spanish or Portuguese languages are spoken today, from Mexico in the north, to Argentina and Chile in the south, including Central and South America, as well as many Caribbean countries.

A recent publication of the Pan American Health Organization [2] compares area and demographic indicators from LA to Canada and the USA. Although the geographic area is quite similar, the population of the region is 1.8 times greater than that of Canada and the USA combined. The population growth per year is reducing in both regions, but the number of older adults (65+ years) is increasing at a faster pace in LA, representing 9.0% of the total population nowadays, due to a rapid advance of life expectancy (**Table 1**).

In relation to socioeconomic indicators, the same report states that the mean educational level is 8.3 years in LA, compared to 13.5 years in Canada and the USA. The gross national income per capita is three times higher in the USA and around four times higher in Canada than in LA. The gross domestic product (GDP) growth was 1.7% in the region in 2017, compared to 2.3% and 3.0% in USA and Canada, respectively. Health expenses, expressed as percentage of annual GDP, are 60% lower in LA, according to 2015 data, both in public and private sectors (**Table 2**).

> The high prevalence of dementia in Latin America represents a considerable challenge to local health and economic systems and this scenario may be worse as the numbers of people living with dementia tend to increase fourfold from 2015 to 2050.

Table 1. Area and demographic indicators of Latin America and Canada/USA (2018)*

	LATIN AMERICA	CANADA + USA
Area	19 197 000 km²	19 509 737 km2
Population	644 481 000	363 721 000
Population growth/y	1.0%	0.7%
Population aged 65+ years	9.0%	16.0%
Life expectancy at birth	76 y	80 y

*Source: Pan American Health Organization [2].

Table 2. Socioeconomic indicators in Latin America and Canada/USA*

	LATIN AMERICA	CANADA + USA
Mean years of schooling (2015)	8.3	13.5
Gross National Income ppp US$ per capita (2017)	15 288	Canada: 45 750
		USA: 60 200
Annual GDP growth (2017)	1.7%	Canada: 3.0%
		USA: 2.3%
National health expenditure as % of GDP (2015)	Public: 3.6	Public: 8.5
	Private: 3.4	Private: 7.8

ppp – purchasing power parity, GDP – gross domestic product
*Source: Pan American Health Organization [2].

The distribution of income in LA is strikingly unequal. GINI is an index that measures the extent to which the distribution of income, among individuals within an economy, deviates from a perfectly equal distribution. A GINI index of zero represents perfect equality, while an index of 100 implies complete inequality. Fifteen LA countries are among the 40 nations with the worst GINI in the world [3].

Prevalence of cardiovascular risk factors is higher in LA when compared to Canada and USA. Age-adjusted prevalence rates of high blood pressure are 23.7% among men and 18.1% among women in LA, dropping to 15.3% and 10.5% among men and women, respectively, in Canada and the USA. In these latter countries, the prevalence of diabetes or raised fasting blood glucose is 8.0% in men and 6.2% in women, while in LA these figures are higher, in both men (8.9%) and women (9.6%). On the other hand, tobacco smoking and alcohol consumption are lower in LA than in Canada/USA, namely, 15.3% vs 21.2% and 6.9% vs 9.7%, respectively [2].

EPIDEMIOLOGY OF DEMENTIA IN LA

Several population-based studies, as well as some systematic reviews, meta-analyses and opinion papers on dementia in LA have been published in the last 25 to 30 years [4-14]. These studies have shown that dementia is an emergent giant problem for LA.

A review of eight population-based investigations from six different countries found a crude prevalence of 7.1% (95% confidence interval (CI) = 6.8-7.4) of dementia in individuals aged 65+ years [8]. This rate was comparable with the prevalence observed in developed countries, although among the higher rates previously reported. Subsequently, a systematic review and meta-analysis [9] estimated that dementia prevalence in the region was 8.5% among individuals aged 60+ years, representing the highest rate in the world. In a more recent systematic review, Zurique-Sánchez et al. reported a prevalence of dementia in LA of 11.5% in the population aged 65+ years, with dementia being more common in women and in urban areas [10].

Epidemiological studies on the prevalence of dementia in Latin America have been performed in several countries and have shown large variations in prevalence rates, such as prevalence rate of 2.0% in a Brazilian population study[11] and of 13.1% in a Venezuelan population study [12], both including individuals aged 65+ years. These differences are probably more related to methodological variability, from the diagnostic criteria of dementia to definitions of cognitive and functional impairment, than to

> National Dementia Plans should be implemented in every Latin American country and local governments need to increase research funding and create support programs to enable better care, including insurance, for people living with dementia and their caregivers.

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cultural, social, environmental or genetic conditions of each country [15]. Even when methods are harmonized, differences in prevalence rates may be observed across countries in the region. In one population-based cross-sectional survey, which included five LA countries and used the 10/66 Dementia Research Group diagnostic algorithm, the prevalence of dementia ranged from 6.2% in Venezuela to 12.6% in Cuba for individuals aged 65 + years, and the response proportion was at least 80% [5]. However, heterogeneity in prevalence rate data are also common in studies from other regions of the world, as described by a meta-analysis of the global prevalence of dementia, where heterogeneity of prevalence was higher in South Asia, Western Europe and Asia Pacific than in LA [9].

The high prevalence of dementia represents a considerable challenge to the local health and economic systems and this scenario may be worse as the numbers of people living with dementia will have increased 4-fold in LA from 2015 to 2050 [16].

Dementia has been associated with low education and poor cardiovascular health in prevalence studies, but there are only a few incidence studies in LA to evaluate risk factors [17-20]. In these studies, incidence was similar [17,19] or higher in LA countries than in Western countries [18]. Besides age, other risk factors included markers of low cognitive reserve [18], poor cardiovascular health [20], and being a carrier of at least one APOE-ε 4 allele [19].

There is an urgent need to ensure some level of methodological harmonization among researchers when performing epidemiological studies on dementia in LA, to include more geographical areas in each country and to have more studies on incidence and mortality rates [15]. Joint efforts of clinicians and epidemiologists would be essential to improve the quality of epidemiological data on dementia in LA.

Besides the high overall prevalence of dementia reported in most studies, prevalence among younger elderly (ie, 65-69 years) was found to be 2.4%, exactly twice the rate reported by a systematic review of 21 studies conducted in Europe [8]. In addition, two studies that were more recently conducted in Argentina [13] and in Brazil [14], including individuals with 60+ years, also found higher rates within this age range in comparison to North America and Western European countries.

These numbers suggest that dementia may start earlier in the region. However, plausible explanations for this finding are challenging. These figures could represent a bias, due to difficulties in diagnosis of dementia. Alternatively, environmental factors could account for these features.

Environmental factors

Low educational level is a well-known risk factor for dementia. It is usually associated with low socio-economic status and with reduced access to health care, from the prenatal period to advanced ages. Hence, low education might increase dementia risk by limiting adequate diagnosis and treatment of comorbidities, particularly cardiovascular diseases and diabetes mellitus, as well as being commonly associated with impaired nutritional status. Moreover, low educational attainment is also associated with low cognitive reserve [21], thus possibly leading to the earlier manifestation of dementia symptoms. In the collaborative study on prevalence of dementia in six LA countries, mentioned above, the prevalence among illiterate elderly was twice the rate among literate individuals, namely 15.7% *vs.* 7.2% [8].

Illiteracy in the adult population is not particularly high in LA. In fact, the average literacy rate is 94% in the continent [22]. However, the illiteracy rate among the elderly population is high, currently at 21%. Moreover, at least in Brazil, there is an unequal distribution of literacy rates, with lower figures in specific regions (North and Northeast) and rural areas of the country. Hence, low education and illiteracy are key issues affecting the lives of older people in LA.

Besides formal illiteracy, another problem is functional illiteracy. Functional illiterates are able to read and to write short sentences, but they are unable to use written language – including numbers – to deal with the daily-life requirements. In a Brazilian study, 312 healthy individuals with mean age of 47.3 years and mean educational level of 9.7 years (ranging from 1-17 years) were evaluated with a test of

functional health literacy. Functional illiteracy was found in 32.4% of the sample. Of note, only a small proportion of individuals with one to seven years of schooling performed in the adequate range [23].

Another relevant issue is the high presence of indigenous people in LA. In 2010, there were 42 million indigenous people living in the continent, corresponding to 8% of the total population. About 34 million (80.1%) live in Bolivia, Guatemala, Mexico and Peru. Most of these individuals live in urban areas and are bilingual, but their educational level is lower than other groups [24].

So far, we do not have a large number of studies on cognitive impairment and dementia in the indigenous populations of LA. In a Colombian study, Moreno et al [25] found that Native American ancestry was associated with lower risk of late-onset Alzheimer disease (AD), while African ancestry individuals displayed a higher risk. In a systematic review that included Australia, Brazil, Canada, Guam and the USA, [26], the prevalence of dementia among indigenous populations appears to be higher than in non-indigenous populations, but there is a paucity of high quality epidemiological research regarding this issue. In another systematic review, it was suggested that indigenous people may be more vulnerable to cognitive disorders, due to low cognitive reserve and exposure to poor health status throughout the life span [27]. Indeed, a survey of 217 indigenous individuals living in in the Brazilian Amazon found high rates of cognitive impairment and dementia, namely 43.0% in individuals aged 50+ years and 51.1% in those aged 65+ years [28]. Of note, in this study, cognitive impairment was assessed with a culturally adapted instrument.

In summary, the demographic and clinical factors that may be responsible for the increased prevalence of dementia in LA are low education (leading to low cognitive reserve), low socioeconomic level (contributing to low brain reserve), low health expenditures as percentage of GDP in LA countries, high rates of high blood pressure and raised blood glucose levels/diabetes. In relation to the latter issue, two neuropathological studies from a Brazilian brain bank have shown high rates of vascular changes among elderly subjects. Indeed, the prevalences of vascular dementia in these two studies were higher than those that have been reported in developed countries [29,30].

It is important to note that the factors listed above are all modifiable and thus, cognitive impairment and dementia related to these aspects may be preventable. In 2017, Livingston et al. [31] suggested that nine potentially modifiable risk factors (less childhood education, midlife hearing loss, hypertension and obesity, later-life smoking, depression, physical inactivity, social isolation, and diabetes) account for 35% of worldwide dementia cases. In 2019, using similar analytical strategies, Mukadam et al [32] indicated that five dementia risk factors were more prevalent in low- and middle-income countries (LMIC) than worldwide estimates, such as less childhood education, smoking, hypertension, obesity, and diabetes. Estimates presented in the study suggested that 56% of dementia cases in LA (using data from Cuba, Dominican Republic, Mexico, Peru, Puerto Rico, and Venezuela) are accounted by such modifiable factors [24]. Therefore, the dementia prevention potential in the region is larger than in high-income countries.

Difficulties in the diagnosis of dementia

Higher prevalence of dementia may also be explained by difficulties in the diagnosis. The use of paper and pencil tests, developed in high-income countries, to detect cognitive impairment in low educated individuals may lead to an elevated number of false positive cases, even with education-adjusted cut-off scores. To attenuate this bias, several screening tests, such as the Mini-Mental State Examination (MMSE) [33], Montreal Cognitive Assessment test [34], Clock Drawing Test [35], and verbal fluency measures [35] have been culturally adapted and validated and are widely used in the region with adjusted cut-off scores in research and in clinical settings. Similarly, global cognitive batteries, such as the Mattis Dementia Rating Scale [36] and the Addenbrooke's Cognitive Examination-Revised [37], are also used.

On the other hand, there are cognitive tests proposed for multicultural populations which are expected to be less influenced by education, for instance, the Consortium to Establish a Registry for Alzheimer Disease [38], Rivermead Behavioural Memory Test [39], Fuld Object Memory Evaluation [40], Short-term Memory Binding Test [41], Rowland Universal Dementia Assessment Scale [42], Neuropsi battery [43], Brief Cognitive Screening Battery [44,45] and the Stick Design Test [46] which have been used in LA studies. For recent reviews of cognitive screening studies conducted in low literacy settings, see Ortega et al [47] and Paddick et al. [48].

Another important strategy that may contribute to dementia detection in LA is the association of brief cognitive tests with questionnaires of functional activities applied to informants. Instruments, such as the Pfeffer Functional Activities Questionnaire (PFAQ) [49], have been used in combination with cognitive

tests, such as the MMSE, in population-based studies on dementia in Brazil, Chile and Peru [50-52]. Other previously used instruments are the Informant Questionnaire on Cognitive Decline in the Elderly [53], the AD8 [54] and the Cognitive Change Questionnaire-8 [55].

We shall consider that diagnostic bias is not a probable explanation for the dementia prevalence figures in LA. Several studies conducted in various LA countries with different methods and tests have shown a high prevalence of dementia. Moreover, studies performed in different LA countries and abroad, using similar methods, confirmed the high prevalence of dementia in LA [5,9].

If a conservative prevalence of 10% among individuals aged 65+ years is taken into account, and that 9% of the entire population of the region is within this age range, the estimated total number of elderly individuals with dementia in LA would be 5.8 million. With the estimation that the number of people living with dementia will nearly double every 20 years [16], LA countries should be prepared for this huge burden [3,16].

PUBLIC AWARENESS AND KNOWLEDGE ABOUT DEMENTIA AND AD

Few studies so far have investigated knowledge and public awareness of dementia in LA countries. In a recent study conducted in Brazil, 1414 individuals were interviewed and the researchers observed a very low level of information about AD, even among relatives and caregivers of demented patients [56]. In an editorial comment on this work, Lawlor [57] stated that it is imperative to raise public awareness of dementia in the region.

In this sense, in LA it is vital to make efforts to increase awareness about dementia and its most common early simptoms in order to increase diagnosis and timely treatment, to reduce stigma, to treat modifiable risk factors and increase the potential for dementia prevention in adult life. These features may increase bottom-up effects on policy makers, as society may demand change in current practice and settings to accommodate dementia care [58]. We definitely need more studies regarding dementia awareness in LA, with follow-up data collection after campaigns, to assess efficacy [56].

Another important issue is knowledge of dementia by GPs. In LA, the diagnosis is usually made by specialists and sporadically by a GP [4], in contrast to usual procedures in many European countries, where most patients with dementia are diagnosed by a GP [59]. We shall acknowledge that medical conditions with very high prevalence must be primarily diagnosed and treated by GPs, such as high blood pressure, diabetes mellitus, headache, depression and also dementia.

In a study conducted in Brazil, 248 randomly selected elderly patients seen in a GP outpatient clinic from a university hospital were submitted to cognitive and functional evaluations. Among subjects with confirmed cognitive impairment, only 16.3% had information on cognitive complaints or decline in their medical files [60]. These numbers represent a very low rate of identification of cognitive impairment by GPs, in comparison to what is found in Europe and North America (20% to 65%) [61,62].

Within this scenario, strategies to increase knowledge on dementia among GPs and health care providers are needed. Information on dementia should be included even in elementary, middle and high school. It should also be explored in more detail in medical schools and in graduate courses of other health disciplines in our continent. GPs need to actively investigate whether her/his patient has cognitive decline, to prescribe treatment and to orient healthier behavior [59]. It is also essential to combat nihilism and to advocate that changes in adult life and in relatively younger elderly may contribute to prevent dementia [63,64].

Finally, it is necessary to show that it is possible to easily screen for dementia. Indeed, brief and accessible instruments for cognitive and functional evaluation are available for use by GPs in most LA countries. For example, the combination of PFAQ (>2) and verbal fluency test (<10 animals/min.) displayed 88.3% of sensitivity and 76.5% of specificity for the detection of cognitive impairment [65]. Category fluency (animals) is a one-minute task, which has been proven to be sensitive and specific for AD dementia diagnosis in populations with variable degrees of schooling, from illiterates to university-level. Indeed, in a recent study conducted in the USA, category fluency (animals in one minute) did not differ from either the MMSE or Memory Impairment Screen in relation to diagnostic accuracy [66]. Therefore, there should be a call for action among health professionals, especially in primary care.

COSTS OF DEMENTIA

Research on dementia costs have been performed in Argentina [67], Brazil [68,69], Chile [70-72] and Peru [73]. Also, studies of the 10/66 Dementia Research Group in LMIC included data from Cuba, Dominican Republic, Mexico, Peru and Venezuela [74,75]. The available data suggest that costs increase

with the severity of the dementia, as reported in two studies (67,73] and indirect (informal) costs predominate in LA [69,70].

In high-income countries, direct costs (professional care in the community, and the costs of residential and nursing home care) account for most of the expenses (16, 76,77]. In many LA countries, a few direct costs (doctors, medicines) are paid by the public health system. However, formal caregivers, home-based meal programs, institutionalization in residential and nursing home care or support to family caregivers are not generally available [6,16,69].

The costs of dementia in LMIC are much lower when compared to high-income countries [76,77]. Costs of dementia for upper-middle income countries is approximately US$ 5284.00 per person per month [76]. In Chile, the monthly cost was higher for low SES (US$ 1,588) than for high SES (US$ 1,083), but most (74%) of it is spent in informal care [70]. In Brazil, the cost of dementia was estimated at US $ 1405.72 per person per month, with 56.6% attributable to informal care costs (costs associated with caregiver productivity loss and time spent by caregiver on patient support) [69]. Informal care costs are afforded by the families due to lack of social / public support. Although the estimated cost does not seem high, informal care represents a significant financial burden, as the average family income tends to be very low. For instance, the costs of informal care reported by Ferretti et al. [69] represent more than 3 times the national minimum wage.

Among the family caregivers, women perform most of the tasks [78,79]. When they cannot leave their job, families tend to hire untrained and inexperienced women to undertake poorly paid and unsupervised care-work with no social support [74]. Informal care is not an exclusive problem of LMIC as it is a significant challenge for high-income countries too (16). However, in LMIC, many people with dementia face several other overlapping disadvantages, such as low education, low or no income, lack of pension or health insurance [75].

With both the expected increase in the number of dementia cases due to aging of the population [80] and reduction in the number of members of the urban families in LA [81], informal care will be even more difficult in the near future and it is already one of the main challenges that need to be faced by the society and policy makers in the region.

As it was proposed for prevalence and incidence studies, strategies for the evaluation of costs in dementia need to be harmonized for regions within each country and across countries in LA. Hamonization efforts should reveal the real burden of dementia in the region and it should aid policy makers to plan the ideal funds to meet the health needs of the population [15].

RESEARCH ON DEMENTIA IN LA

Undoubtedly, conducting research in LA is quite challenging. There is a clear lack or limited availability of public and private grants. In spite of this, the total number of publications related to dementia carried out in LA and indexed in PubMed increased five times in the last 10 years, representing 3.35% of the papers indexed in that period. In the Web of Science platform, the total number of publications increased 2.5 times in 10 years, representing 3.71% of the indexed papers on this topic in that period.

Although there is a significant amount of research activity in dementia carried out in LA, much more public funding is needed to attend to the key priority issues, as established by the WHO global action plan [1]. In addition, regional collaborative research is needed, based on harmonized protocols and with data sharing.

CONCLUSIONS

Dementia is an alarming emergent problem for LA. The prevalence of dementia in LA is one of the highest in the world and, with the expected aging of the population, the number of cases of dementia tends to increase 4-fold from 2015 to 2050.

More epidemiological studies on dementia prevalence are needed in several regions in each country and in all LA countries, using harmonized methods to assess the actual prevalence and the evolution of the prevalence rates in the near future. Incidence studies are also needed to identify risk factors and the evolution of incidence after the control of such factors. Harmonized methods for epidemiological studies should unite clinicians and epidemiologists.

Dementia manifests earlier in LA. Prevalence of dementia is higher among illiterate and low educated individuals. The higher prevalence and its earlier emergence are probably related to low cognitive reserve (including low brain reserve), vascular diseases and other potentially modifiable factors.

Diagnosis of dementia among low educated individuals is challenging but may be feasible with questionnaires and cognitive tests less biased by education. Research and sharing of experiences among LA experts on dementia will be important to reach a consensus regarding common or similar methods based on questionnaires and short cognitive tests for diagnosis of dementia by the general practitioner, who cares for most of the elderly population in LA.

Knowledge about dementia should be increased among lay people using public health awareness campaigns to promote early diagnosis and better support after diagnosis. Information on strategies to reduce dementia risk by changing life-style risk factors should be a significant part of these campaigns. Participation of people living with dementia should be stimulated.

Reducing stigma is also a very important issue. The creation of friendly communities for people with dementia should be encouraged.

The costs of dementia care should not be paid solely by families. Local governments need to increase the funding and create support programs to enable better care, including policies related to employment, health and insurance for people living with dementia and their caregivers. Costs of dementia need to be evaluated in every country using harmonized methods to plan funds to meet the health needs of the people living with dementia and their caregivers.

National Dementia Plans have been implemented in a few LA countries. Exchanges of experiences among the countries who have such plans and also with other LA countries are needed to understand the successes and failures of each plan.

It will be necessary to increase research funding from local governments or international agencies to foster local and collaborative studies among LA countries.

A higher synergy among LA countries is needed for information integration and coordinated actions, as countries in the region stride to address the challenges associated to the expected increase in dementia prevalence rates.

The potential for dementia risk reduction in LA seems larger than in high-income countries, therefore, regional collaborative efforts should also focus on prevention. Interventions conducted locally should test strategies aiming to change lifestyle-related risk factors, such as physical inactivity, obesity, unbalanced diets, harmful use of tobacco and alcohol, and the control of diabetes mellitus and midlife hypertension. In addition, interventions based on LA culture and experiences should be devised aiming to reduce social isolation, cognitive inactivity and mid-life depression. Finally, dementia prevention starts in early childhood, as low education is perhaps the most important modifiable dementia risk factor. Therefore, in LA, significant investments in high quality education throughout the life cycle should be a first order priority.
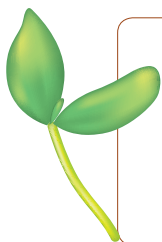
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