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Incidence of Dementia in Elderly Latin Americans: Results of the Maracaibo Aging Study

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Abstract

INTRODUCTION—There are few longitudinal studies of dementia in developing countries. We used longitudinal data from the Maracaibo Aging Study (MAS) to accurately determine the age- and sex-specific incidence of dementia in elderly Latin Americans.

METHODS—The DSM IV-R was used to diagnose dementia, which was classified as Alzheimer's disease (AD), vascular dementia (VaD), or other. Age- and sex-specific incidence was estimated as the number of new cases of dementia divided by person-years of follow-up (p-y).

RESULTS—The incidence of all dementia diagnoses was 9.10 per 1000 p-y (95% CI 7.13–11.44; 8026 total p-y), 5.18 for AD (95% CI 3.72–7.03; 7916 total p-y), and 3.35 for VaD (95% CI 2.19–4.91; 7757 total p-y).

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CONFLICTS OF INTEREST

Dr. Maestre and The University of Texas Rio Grande Valley have research-related interests in Fundaconciencia, Inc.

DISCUSSION—Among MAS participants under 65 years of age, the incidence of dementia was higher than that of US whites. Among individuals over 65 years of age, the incidence was comparable to the mean of previous incidence estimates for other populations worldwide.

Keywords

Alzheimer's disease; Epidemiology; Vascular dementia; Population-based; Hispanics

1. INTRODUCTION

The prevalence of dementia, a condition that disproportionately affects the elderly, is higher in most Latin American countries than in developed countries [1–3]. In 2015, approximately 70.9 million Latin Americans were over 60 years of age. By 2030, that number will exceed 121 million [4]. As such, the aging of the population puts an increasing number of individuals at risk. However, because prevalence reflects both the incidence and duration of disease, it is a limited measure of risk.

Incidence, the rate of occurrence of new cases, is a more useful measure of risk that is essential for evaluating temporal trends and for assessing the effects of preventative measures. The World Health Organization′s estimates of the incidence of dementia in developed countries ranged from 3.4 per 1000 person-years (p-y) at age 60–64 years to 99.4 per 1000 p-y at >95 years [3]. There are only nine reports on the incidence of dementia in developing countries [5–12], all among those older than 65 years, and ranging from 3.2 per 1000 p-y in India [11] to 21.85 per 1000 p-y in Nigeria [7]. None of these studies included complete neuropsychological and clinical assessments of all participants.

The goal of the present study is to provide an accurate estimate of dementia incidence in Venezuela, a developing country. Longitudinal data from the Maracaibo Aging Study (MAS) [13] were used to determine the age- and sex-specific incidence of dementia and its subtypes, Alzheimer's disease (AD) and vascular dementia (VaD).

2. METHODS

2.1 Sample

The MAS is a population-based study of community-dwelling individuals aged 55 years and older who resided in downtown Maracaibo, Santa Lucia County, Venezuela, between January and August 1998 [14]. The MAS investigated cognitive, cardiovascular, nutritional, and social changes associated with aging, with a special emphasis on memory-related disorders. The baseline assessment was conducted between September 1998 and December 2001. A total of 2453 out of 3765 residents ≥55 years of age underwent a standardized, multidimensional assessment of laboratory tests and their neuropsychological, neuropsychiatric, cardiovascular, and nutritional status. Of the 2453 assessed at the baseline evaluation, 198 participants were diagnosed as having dementia, and one participant was not assigned a Clinical Dementia Rating (CDR) [15]. Of the remaining 2254 assessed patients who composed the at-risk population, 411 (19.74%) died or relocated before the second evaluation, 28 (1.24%) were not available for any of the three reevaluation visits, and 122

(5.12%) declined to participate in the second evaluation. The 1693 participants who were reexamined at least once between 2001 and 2009 composed the sample for our study (Figure 1).

The MAS was approved by the Institutional Review Board of the Cardiovascular Center at the University of Zulia in Maracaibo. Informed consent was obtained from each participant, or from a surrogate when appropriate, after they were provided with a complete explanation of the study.

2.2 Dementia Assessments and Diagnoses

The assessment and diagnostic procedures of the MAS have been previously described in detail [13]. Briefly, a social worker visited the home of each participant and conducted a family interview. Two social workers were available during the study period, both of whom received the same training, which consisted of practice interviews, roleplaying, visits to Santa Lucía with various members of the team (psychologists, physicians, historian) to understand the geography and history of the area, and biweekly feedback meetings. An informant (usually a spouse or adult child residing in the same home as the participant) was identified as knowledgeable about the participant's daily activities and health issues. Information regarding changes in the abilities of the participant was collected using an adapted version of the Dementia Questionnaire [16], the third part of the Blessed Dementia Scale [17], and the Self-Maintaining and Instrumental Activities of Daily Living Scale [18], as well as information on the family history of dementia. All the participants were invited to undergo an in-depth neuropsychiatric evaluation (performed by a trained neurologist, psychiatrist, or internist), neuropsychological testing (by a psychologist), routine laboratory tests, and apolipoprotein E (*APOE*) genotyping [19, 20].

The neuropsychiatric assessment included a neurological examination, original and modified versions of the Mini-Mental State Examination (MMSE) [21, 22], the Blessed Orientation-Memory and Concentration Test [17], the Schwab and England Scale to assess activities of daily living [23], the Zung Depression Scale [24], and the Neuropsychiatric Inventory [25].

The neuropsychological assessment included 17 tests for memory, abstract reasoning, orientation, constructional ability, language, and attention [22]: the Selective Reminding Test [26]; the Benton Visual Retention Test [27]; similarities from Wechsler Adult Intelligence Scale-Revised [28]; identities and oddities from Mattis [29]; five items from the Rosen Drawing Test [30]; the Boston Naming Test [31]; the Benton Multilingual Aphasia Examination [32]; comprehension and repetition from the Boston Diagnostic Aphasia Examination [31]; and cancellation (TMX and shapes).

Results of the neuropsychological tests were used as complementary information; diagnoses were not based on cutoff scores. The assessments were conducted on two consecutive mornings, usually at the Cardiovascular Center of the University of Zulia. If the participant could not leave their home, the assessment took place at the their residence.

Diagnoses of dementia were made by consensus during a conference of physicians, psychologists, and social workers, who discussed all ancillary information and followed the

diagnostic strategy developed for the Washington Heights-Inwood Columbia Aging Project in New York [22]. Subjects were classified as having dementia if they obtained a rating of Category 1 or higher on the CDR scale [15], and they had cognitive impairment resulting in a functional decline in their social or occupational activities from their previous level of functioning not explained by other conditions. Baseline and incident dementia diagnoses were classified as AD, VaD, or other dementia, based on standardized criteria for each illness in the Diagnostic and Statistical Manual of Mental Disorders (4^{th} Edition) [33] and specific criteria for each dementia subtype [34–40]. Brain magnetic resonance scans (Phillips 1.5 T) were offered to all individuals with CDR 0.5 or higher, and to a randomly selected individuals for a total of 400 imaging studies. When available, neuroimages were included in the discussion, and they were mostly used for differential diagnosis. Dementia onset was estimated as the age at which the individual met the criteria for dementia, based on a systematic review of the chronological history of cognitive and functional changes. The consensus panel was blind to *APOE* genotype, previous CDR, and dementia type.

2.3 Data Analysis

The at-risk population consisted of MAS participants who were not diagnosed with dementia during the baseline assessment. For each participant, p-y was calculated as the number of years from baseline until (1) the time of dementia onset or (2) the time of completion of the last assessment at which the individual was found not to have dementia, whether they subsequently remained in the cohort, dropped out, or died. Incidence per 1000 p-y was estimated as the number of new cases of dementia, divided by the at-risk p-y, multiplied by 1000 [41]. Confidence intervals (CIs) were calculated assuming a Poisson distribution for the number of cases within each age interval. Incidences were standardized using the Venezuelan population based on the 2001 national census [42] and the WHO world population data [43].

We added competing risk analyses suggested by the reviewer. In the methods section we added: “Because factors leading to nonparticipation could be linked to the same factors that affect dementia incidence [44], we conducted two types of analyses to assess the influence of dropouts (due to death, relocation, refusal or other cause of non participation) having developed dementia if they have stayed in the study. First, a sensitivity analysis was conducted that assumed that dementia incidence in nonparticipants was the same, 50%, 100%, or 200% higher than the incidence in the assessed cohort. The second approach consisted of adjustment of incidence for competing risk due to death using a proportional subdistribution hazards model developed by Fine and Gray[45] and modified by Chang et al. [46]. Briefly, a propensity model was developed using a logistic regression model with covariates (age, sex, and education) assigning each individual a propensity score that reflected his/her estimated probability of developing dementia, have all they been assessed for dementia an additional time after baseline. Based on the median of the propensity score of those that actually developed dementia a cutpoint was established. If the propensity score of participants who died without developing dementia were above the cutpoint, they were reclassified as an event and incidence of dementia recalculated.

We fitted three types of regression models to estimate the effect of age, education, sex (female) and *APOE*-ε4 genotype on the incidence of dementia (all causes, AD and VaD). First, Cox proportional hazard regression models[47], in which participants who survived and remained dementia-free, as well as those who died without developing dementia, were treated as censored. Second, the modified Fine and Grey (FG) competing risks regression models that focus on cumulative incidence[45] were generated using the command stcrreg in STATA. Third, the FG models were generated after reclassification of individuals, i.e. participants who remained alive and dementia-free were again treated as censored, but those who died without developing dementia were treated either as competing risks (if their propensity scores were above the cutpoint) or as censored (if their propensity scores were below the cutpoint)."

Mean values of population parameters (± SD) were compared using the Mann-Whitney rank sum test, and p values ≤.05 were considered to be statistically significant. Statistical analyses were performed with Epi-Info 6.04b and SPSS version 23.0, 2016.

3. RESULTS

The mean age at baseline for study participants with longitudinal data was 66.3 years of age, and 69.5% of the study participants were women (Table 1). The study participants had, on average, 6 years of education and their mean MMSE was 23.7. The average number of follow-up visits by participants was 2.4 (range 2–5), and the time between the baseline and last assessments averaged 3.45 ± 3.05 years (Table 2). The mean age at first diagnosis of incident dementia was 75.1 ± 8.11 years. Table 1 provides statistics for individuals who did not participate in any follow-up evaluation due to death, relocation, refusal, or other cause. They were slightly older than those who did participate and included a smaller proportion of women. The nonparticipant group did not differ from participants with respect to years of education, *APOE-ε4* genotype, or mean MMSE score obtained during the baseline evaluation.

Incidence of all dementia diagnoses was 9 cases per 1000 p-y for participants ≥55 years, and 16 cases per 1000 p-y for participants ≥65 years. The incidence of dementia increased exponentially with age, reaching 91 cases per 1000 p-y for individuals 85 years or older (Table 3, Figure 2). The incidence of AD and VaD also increased with age (Table 3). AD accounted for 56% and VaD for 36% of all incident dementia cases with marginal cases of frontotemporal dementia, Lewy body disease, Parkinson's with dementia, and dementia related to alcoholism. The incidence of all dementias, AD, and VaD was similar for men and women. The incidence of all dementias and AD was higher among *APOE-ε4* carriers than noncarriers, but the presence of an *APOE*-e4 allele did not affect the incidence of VaD (Table 4).

In the sensitivity analyses, the age-specific incidence of dementia was recalculated to include nonparticipants, assuming that the nonparticipants had 1.5 to 5 times greater incidence of dementia than participants (Table A.1). As expected, the recalculated incidence was higher, particularly in the older groups, than when nonparticipants and participants were assumed to have the same incidence of dementia. When incidence was calculated using the

modified FG competing risks regression models, incidence was substantially higher than the unadjusted models (Table A.1), particularly in the older groups.

Results of the Cox models indicated that being older, female or a carrier of at least one *APOE*-ε 4 allele was associated with an increased incidence of dementia of all causes (Table A.2). However, only age and *APOE*-ε4 status were significant risk factors for AD, and only age was a risk factor for VaD. In undjusted models, low education level was not a significant risk factor for all dementias, AD, or VaD. After adjusting for death as competing risk, results were not radically changed, except for education, that became marginally significant for all-cause dementia and VaD, but not for AD, and sex which became significant for the three dementia groups.

4. DISCUSSION

The MAS previously reported a high prevalence of dementia in the elderly population of Santa Lucia compared with other population-based studies in Latin America.[2] However, it was uncertain whether the high prevalence reflected a high incidence of dementia. We conducted an extensive follow-up evaluation of each participant by experienced local clinicians, using standardized full neuropsychological testing, neurological examination, and a multimodal examination of decline in activities of daily living. The results of the present longitudinal study confirm that age at onset of dementia is somewhat earlier than in US Whites [48] as evident by the relatively high incidence of dementia among MAS participants who are younger than 65 years of age. However, the incidence of dementia in those older than 65 years of age was comparable to other population-based data from other studies.[5–10, 12] When adjusting for death as a competing risk for dementia, using a relative conservative approach, the resulting incidence per age group have not precedents. This finding suggests that dementia and death shared common risk factors, and once the development of public health sector and of medical science allows decreasing mortality rates, the magnitude of dementia rates could be much higher.

Consistent with the prevalence data, AD was the most frequent type of incident dementia. As expected, age, sex and *APOE*-ε4 were important risk factors for dementia. The average years of education was six years, which is consistent with the average years of schooling of adults in the Venezuela [49] for that age range, and was associated to dementia only when competing risks were considered. The mild significant association with education level could be due to the overall low level of education of the cohort.

The present study has several limitations. The primary limitation is that incidence rates were derived from a geographically restricted area and are not necessarily representative of all Venezuelans or Latin Americans. Moreover, our dementia diagnoses rely on extensive clinical evaluation but have not been autopsy confirmed by neuropathological evaluation. Thus, we may have underestimated subtypes of dementia, such as VaD and others. Unlike other community-based studies of dementia in developing countries, however, we were able to verify VaD using neuroimaging data because 67% of cases of dementia had neuroimaging. The high incidence of dementia might reflect anticipation of onset, more severe manifestation during early stages, or highly sensitive diagnoses. None of these

possibilities can be excluded in the present study. The Santa Lucia population lives in poor conditions relative to other populations in developed countries, including limited access to health care, which leads to high rates of uncontrolled co-morbidities such as systemic hypertension and diabetes. When compared with incidence rates among Caribbean Hispanics residing in northern Manhattan, the incidence of AD in the Santa Lucia cohort was higher (3.8% *vs.* 6.9% per 1000 p-y, respectively). Because both studies used similar diagnostic procedures and analytical methods, the possibility that there is a risk factor for AD specific to the MAS population cannot be ruled out.[50] However, most of the Caribbean Hispanics in the US study were from the Dominican Republic and Puerto Rico; few were from Venezuela. Finally, results of the sensitivity analysis indicate that the estimated incidence would have been higher if dementia-related incapacity, relocation, or death accounted for a significant proportion of nonparticipants, and modeling death as a competing risk of dementia revealed that the overall dementia rate could be twice as the unadjusted.

On the other hand, the present study has many strengths. This community-based study is as representative as possible of the population in the region, because all residents 55 years or older were invited to participate and the participation rate at baseline was higher than 75%.[13] The nonparticipation rate in follow-ups, excluding death and relocation, was approximately 5%; thus, the probability that self-selection influenced the estimates of incidence is low. We used validated questionnaires and detailed neuropsychological instruments that provided extensive, in-depth clinical phenotyping. The diagnostic strategy and most of the health professionals involved in assessments were the same for the baseline and follow-up studies, thus minimizing assessment bias. The health professionals involved in the MAS diagnostic process included a psychiatrist, a geriatrician, and usually also a neurologist, all with specific training, expertise, and experience in dementia. Although ‘diagnostic drift’ (the tendency to expand the parameters of a diagnosis leading to more diagnoses) cannot be excluded, cognitive performance cutoffs were established giving careful consideration to education level to minimize the possibility that the tests penalized individuals with lower education level and to ensure that the same diagnostic criteria were applied. The noted association between the *APOE*-ε4 genotype and the incidence of AD, but not VaD, further validates our results.

The present study provides the first estimates of the incidence of dementia, AD, and VaD for a population in the developing world that was not subject to a screening phase prior to assessment, and in which diagnoses were not paradigm-based, but the result of clinical consensus. The incidence of dementia, AD, and VaD in participants older than 65 years reported herein are comparable to the range of estimates previously reported for both developed [44, 51, 52] and developing [8–10, 12] countries (Figure 2). The incidence among those 55–64 years of age is quite high compared with studies in the developed world [48], and there is only one other reported study in the developing world for this age group, which took place in India and which also found lower rates than MAS.[5] However, direct comparisons to previous estimates of dementia incidence are difficult due to differences in the diagnostic methods, the age structure of the samples, and the use of different age strata in the analyses. We did not preselect individuals to be evaluated in depth by expert clinicians, to undergo extensive neuropsychological assessment, or for all participants to undergo

laboratory tests. Previous incidence studies of dementia in the developing world have carefully validated their methods, diagnostic strategies. We are building on their insight of the difficulties of carrying out this studies in low-resource settings, not only presenting data of Venezuela but also adding some methodological features. All previous incidence studies in the developing world [5–12] applied a screening phase to select those individuals who were more likely to be diagnosed as having dementia. Some used laboratory tests to evaluate physical health,[5, 9, 11] three obtained information on daily living activities from the participant and a proxy [7–10] and two included magnetic resonance imaging of the brain.[5, 11] Only other study reported using a consensus conference of multidisciplinary health professionals to reach a diagnosis for all participants.[9]

The incidence rates reported herein would have been even higher if participants with a CDR of 0.5 were counted as having dementia and if competing risk analyses account for those individuals that die before a diagnosis of dementia is actually recorded in the study.. Thus, methodology can have a significant effect on estimates of incidence, and the wide range of incidence estimates in previous studies might reflect differences in methodology as much as actual differences in the incidence of dementia.

In summary, an accurate estimated incidence of dementia in the population of Maracaibo, Venezuela, showed fairly high rates in those younger than 65 years, and rates comparable to previous estimates in those older than 65 years for other countries. The wide range among previous estimates might be at least partly attributable to variation in methodology. Although the incidence of dementia was highest among the most elderly MAS participants, the impact is more important for relatively young individuals (55–64 years) who contribute to the economic support of their families, which are typically multigenerational and poor. Although AD had the highest incidence of the subtypes of dementia, VaD also had a relatively high incidence. Unlike AD, VaD currently offers significant opportunities for prevention. Although extrapolation to other Latin American countries or to Hispanic populations living in developed countries is not straightforward, the relatively high incidence of dementia reported here is of concern, especially given life expectancy in these developing countries has been increasing significantly. The burden on the health care system is likely to be notable when health care resources are limited.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

MAS	Maracaibo aging study
AD	Alzheimer's disease
VaD	vascular dementia
p-y	person-years of follow-up
LA	Latin Americans

References

1. Llibre Rodriguez JJ, Ferri CP, Acosta D, Guerra M, Huang Y, Jacob KS, et al. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey. Lancet. 2008; 372:464–74. [PubMed: 18657855]
2. Nitrini R, Bottino CM, Albala C, Custodio Capunay NS, Ketzoian C, Llibre Rodriguez JJ, et al. Prevalence of dementia in Latin America: a collaborative study of population-based cohorts. International psychogeriatrics /IPA. 2009; 21:622–30.
3. WHO. Dementia:A public health priority. London: World Health Organization; 2012.
4. United Nations DoEaSA, Population Division. World Population Ageing 2015 (ST/ESA/SER.A390). 2015.
5. Chandra V, Pandav R, Dodge HH, Johnston JM, Belle SH, DeKosky ST, et al. Incidence of Alzheimer's disease in a rural community in India: the Indo-US study. Neurology. 2001; 57:985–9. [PubMed: 11571321]
6. Chen R, Hu Z, Wei L, Ma Y, Liu Z, Copeland JR. Incident dementia in a defined older Chinese population. PloS one. 2011; 6:e24817. [PubMed: 21966372]
7. Gureje O, Ogunniyi A, Kola L, Abiona T. Incidence of and risk factors for dementia in the Ibadan study of aging. Journal of the American Geriatrics Society. 2011; 59:869–74. [PubMed: 21568957]
8. Mejia-Arango S, Gutierrez LM. Prevalence and incidence rates of dementia and cognitive impairment no dementia in the Mexican population: data from the Mexican Health and Aging Study. J Aging Health. 2011; 23:1050–74. [PubMed: 21948770]
9. Nitrini R, Caramelli P, Herrera E Jr, Bahia VS, Caixeta LF, Radanovic M, et al. Incidence of dementia in a community-dwelling Brazilian population. Alzheimer disease and associated disorders. 2004; 18:241–6. [PubMed: 15592138]
10. Prince M, Acosta D, Ferri CP, Guerra M, Huang Y, Rodriguez JJ, et al. Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: a 10/66 Dementia Research Group population-based cohort study. Lancet. 2012; 380:50–8. [PubMed: 22626851]
11. Raina SK, Pandita KK, Razdan S. Incidence of dementia in a Kashmiri migrant population. Annals of Indian Academy of Neurology. 2009; 12:154–6. [PubMed: 20174494]

12. Wu XG, Tang Z, Fang XH, Guan SC, Liu HJ, Diao LJ, et al. Study on the incidence and risk factors of dementia in elderly residents from communities in Beijing. Zhonghua Liu Xing Bing Xue Za Zhi. 2010; 31:1245–9. [PubMed: 21176685]
13. Maestre GE, Pino-Ramirez G, Molero AE, Silva ER, Zambrano R, Falque L, et al. The Maracaibo Aging Study: population and methodological issues. Neuroepidemiology. 2002; 21:194–201. [PubMed: 12065882]
14. Molero AE, Pino-Ramirez G, Maestre GE. High prevalence of dementia in a Caribbean population. Neuroepidemiology. 2007; 29:107–12. [PubMed: 17940342]
15. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology. 1993; 43:2412–4.
16. Kawas C, Segal J, Stewart WF, Corrada M, Thal LJ. A validation study of the Dementia Questionnaire. Arch Neurol. 1994; 51:901–6. [PubMed: 8080390]
17. Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. Br J Psychiatry. 1968; 114:797–811. Maestre *et al*. [PubMed: 5662937]
18. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969; 9:179–86. [PubMed: 5349366]
19. Mayeux R, Stern Y, Ottman R, Tatemichi TK, Tang MX, Maestre G, et al. The apolipoprotein epsilon 4 allele in patients with Alzheimer's disease. Ann Neurol. 1993; 34:752–4. [PubMed: 8239575]
20. Hixson JE, Vernier DT. Restriction isotyping of human apolipoprotein E by gene amplification and cleavage with HhaI. J Lipid Res. 1990; 31:545–8. [PubMed: 2341813]
21. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12:189–98. [PubMed: 1202204]
22. Stern Y, Andrews H, Pittman J, Sano M, Tatemichi T, Lantigua R, et al. Diagnosis of dementia in a heterogeneous population. Development of a neuropsychological paradigm-based diagnosis of dementia and quantified correction for the effects of education. Arch Neurol. 1992; 49:453–60. [PubMed: 1580806]
23. Schwab, RS., England, AC. Projection technique for evaluating surgery in Parkinson's disease. Third Symposium on Parkinson's Disease; Edinburgh: E & S Livingstone; 1969. p. 152-7.
24. Zung WW. A Self-Rating Depression Scale. Arch Gen Psychiatry. 1965; 12:63–70. [PubMed: 14221692]
25. Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. Neurology. 1997; 48:S10–6.
26. Buschke H, Fuld PA. Evaluating storage, retention, and retrieval in disordered memory and learning. Neurology. 1974; 24:1019–25. [PubMed: 4473151]
27. Benton, A. The Visual Retention Test. New York: The Psychological Corporation; 1955.
28. Wechsler, D. Wechsler Adult Intelligence Scale Revised. New York: The Psychological Corporation; 1981.
29. Mattis, S. Mental Status Examination for organic mental syndrome in the elderly patient. In: Bellak, L., Karasu, TB., editors. Geriatric psychiatry: a handbook for psychiatrists and primary care physicians. New York: Grune & Stratton; 1976. p. 77-121.
30. Rosen, W. The Rosen Drawing Test. Bornx: Veterans Administration Medical Center; 1981.
31. Kaplan, EF., Goodglass, H., Weintraub, S. The Boston Naming Test. 2. Philadelphia: Lea & Febiger; 1983.
32. Benton, A., Hamsher, KS. The Multilingual Aphasia Examination. Iowa City: University of Iowa; 1978. Revised Manual
33. APA. Diagnostic and statistical manual of mental disorders. 4. Washington, DC: American Psychiatric Association; 1994.
34. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. Br J Psychiatry. 1982; 140:566–72. [PubMed: 7104545]

35. Chui HC, Victoroff JI, Margolin D, Jagust W, Shankle R, Katzman R. Criteria for the diagnosis of ischemic vascular dementia proposed by the State of California Alzheimer's Disease Diagnostic and Treatment Centers. Neurology. 1992; 42:473–80. [PubMed: 1549205]
36. McKeith IG, Galasko D, Kosaka K, Perry EK, Dickson DW, Hansen LA, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology. 1996; 47:1113–24. [PubMed: 8909416]
37. McKeith IG, Perry EK, Perry RH. Report of the second dementia with Lewy body international workshop: diagnosis and treatment. Consortium on Dementia with Lewy Bodies. Neurology. 1999; 53:902–5. Maestre *et al.* [PubMed: 10496243]
38. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984; 34:939–44. [PubMed: 6610841]
39. Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology. 1998; 51:1546–54. [PubMed: 9855500]
40. Roman GC, Tatemichi TK, Erkinjuntti T, Cummings JL, Masdeu JC, Garcia JH, et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology. 1993; 43:250–60. [PubMed: 8094895]
41. Breslow, NE., Day, NE. Statistical Methods in Cancer Research. Lyon: International Agency for Research on Cancer; 1987.
42. INE. Censo de Población y Vivienda Caracas. Venezuela: Instituto Nacional de Estadística; 2001.
43. Ahmad, OB., Boschi-Pinto, C., Lopez, AD., Murray, CJL., Lozano, R., Inoue, M. Age standardization of rates: A new WHO standard. Geneva: World Health Organization; 2001. GPE Discussion Paper Series
44. Kukull WA, Higdon R, Bowen JD, McCormick WC, Teri L, Schellenberg GD, et al. Dementia and Alzheimer disease incidence: a prospective cohort study. Arch Neurol. 2002; 59:1737–46. [PubMed: 12433261]
45. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. Journal of the American Statistical Association. 1999; 94:496–509.
46. Chang CC, Zhao Y, Lee CW, Ganguli M. Smoking, death, and Alzheimer disease: a case of competing risks. Alzheimer Dis Assoc Disord. 2012; 26:300–6. [PubMed: 22185783]
47. Cox, DR. Breakthroughs in Statistics. New York: Springer; 1992. Regression Models and Life-Tables; p. 527-41.
48. Rocca WA, Cha RH, Waring SC, Kokmen E. Incidence of dementia and Alzheimer's disease: a reanalysis of data from Rochester, Minnesota, 1975–1984. Am J Epidemiol. 1998; 148:51–62. [PubMed: 9663404]
49. Barro, RJ., Lee, JW. A new data set of educational attainment in the world, 1950–2010. 2010. Cambridge: National Bureau of Economic Research; Apr. 2010
50. Tang MX, Cross P, Andrews H, Jacobs DM, Small S, Bell K, et al. Incidence of AD in African-Americans, Caribbean Hispanics, and Caucasians in northern Manhattan. Neurology. 2001; 56:49–56. [PubMed: 11148235]
51. Rocca WA, Petersen RC, Knopman DS, Hebert LE, Evans DA, Hall KS, et al. Trends in the incidence and prevalence of Alzheimer's disease, dementia, and cognitive impairment in the United States. Alzheimers Dement. 2011; 7:80–93. [PubMed: 21255746]
52. Launer LJ, Andersen K, Dewey ME, Letenneur L, Ott A, Amaducci LA, et al. Rates and risk factors for dementia and Alzheimer's disease: results from EURODEM pooled analyses. EURODEM Incidence Research Group and Work Groups. European Studies of Dementia. Neurology. 1999; 52:78–84. [PubMed: 9921852]

RESEARCH IN CONTEXT

1. Systematic review

We reviewed the literature using PubMed and reference lists from relevant articles. Studies of incidence of dementia in developing countries and in particular, in Latin America are scarce. We identified several publications on subjects older than 65 y, but none among younger than 65 and residing in a Latin American country.

2. Interpretation

Studies have shown that overall prevalence of dementia in Latin Americas as high as in developed countries. We extend research of epidemiology of dementia by including a population-based incidence study and including individuals 55 y or older. We found that compared with Whites in the US, this Latin American population has high incidence in 55 – 64 age group, and intermediate incidence in older than 65y.

3. Future directions

As incidence of dementia is higher than expected in the relatively young segment of this Hispanic population, uncovering the risk factors and understanding the mechanisms for the higher risk of dementia is important. The possibility that the reported higher incidence is not only limited to this population of Venezuelans, but is also the case for Hispanics living in their country of origin or in other countries warrant extending epidemiological studies in Hispanics to a minimum of 55 years of age.

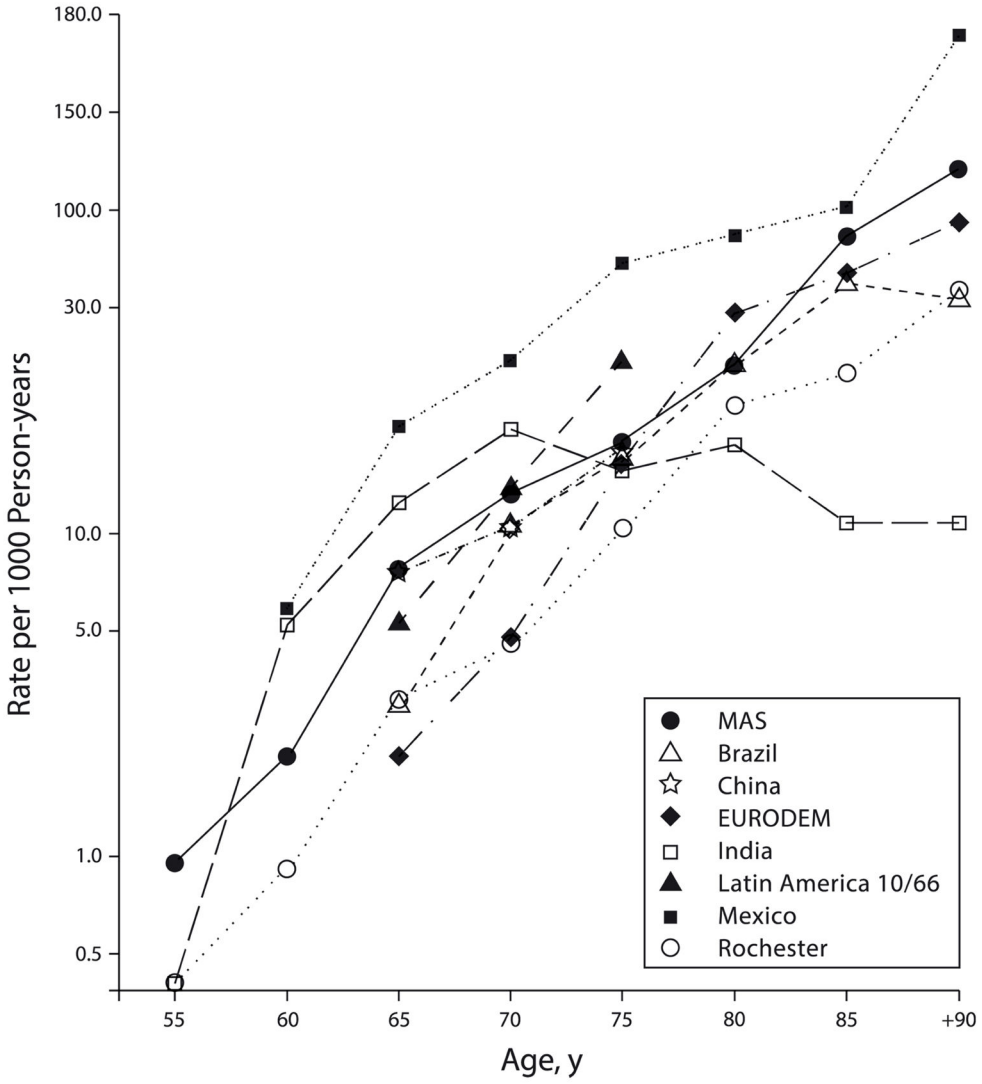

Figure 1.

Flow diagram showing numbers and percentages of Maracaibo Aging Study (MAS) participants included in the baseline and follow-up assessments and incidence estimates.

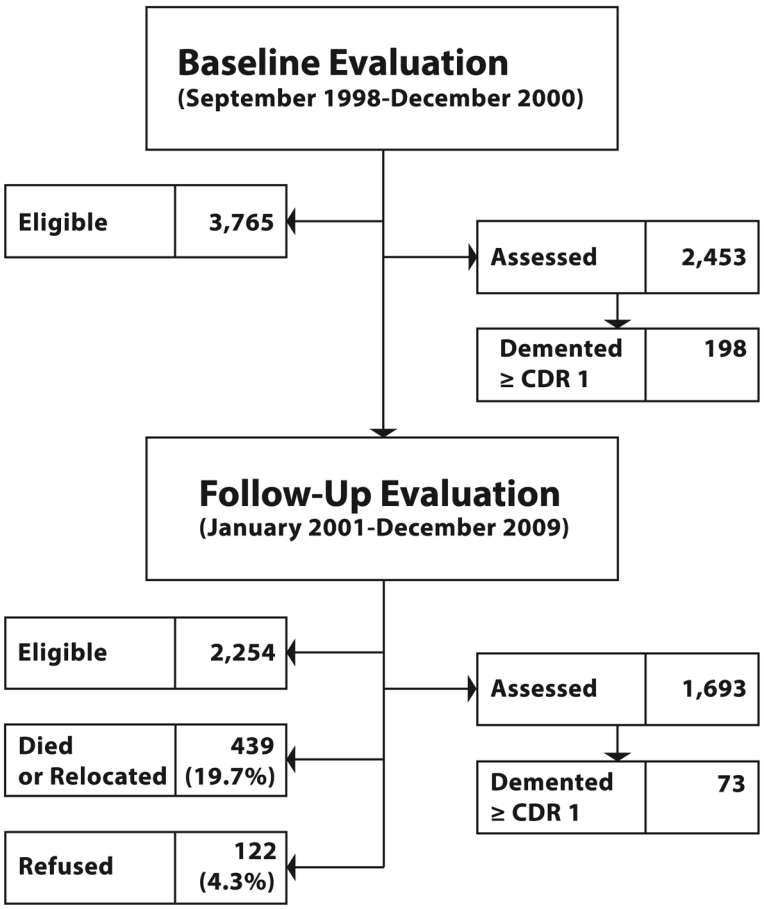

Figure 2.

Incidence of dementia vs. mean age reported herein for the Maracaibo Aging Study (MAS, Venezuela) and for comparison purposes, in six previous studies: Brazil = Catanduva, Brazil Study [9]; China = Anhui Cohort Study [6]; EURODEM = European Studies of Dementia (Denmark, France, Netherlands, United Kingdom) [52]; Latin America 10/66 (Dominican Republic, Peru, Venezuela) [10]; Mexico = Mexican Health and Aging Study [8]; and Rochester = Rochester, MN, Study (USA).[48]

Table 1

Demographic characteristics (mean±SD) of participants in the baseline and follow-up assessments of the Maracaibo Aging Study.

N= 2254	Subjects with only baseline assessment					Subjects with ≥1 follow-up assessment	*p* value
	Dead n=232	Relocated n=179	Refused n=122	Other n=28	All n=561	n=1693	
Age at baseline, y ± SD	70.6±9.70	65.9±8.21	65.0±7.45	65.5±8.20	67.6±9.05	66.3±8.25	.05
Women, n (%)	130(56.0)	113(63.1)	64(53.5)	19 (67.9)	326 (58.1)	1177.(69.5)	<.001
Years of formal education, y, mean ± SD	5.52±4.51	6.83±4.56	6.61±4.11	4.82±3.46	6.14±4.43	5.87±4.11	.75
Any *APOE*-ε4, n (%)	43(18.1)	22(12.3)	16(13.1)	7 (25.0)	88 (15.7)	311 (21.0)	.09
MMSE score, mean ± SD	21.5±11.2	24.2±4.09	24.2±3.69	23.0±6.62	23.0±7.94	23.7±4.19	.08

Abbreviations: *APOE*-ε4 = Allele ε4 of the Apolipoprotein E; MMSE = Mini Mental State Examination (18); SD = standard deviation.

p indicates the significance of the difference between subjects with only the baseline assessment and those with ≥1 follow-up assessment.

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Table 2

Characteristics of participants in the Maracaibo Aging Study.

	Non-Demented CDR<1 n=1620	Demented CDR≥1 n=73	All	*p* value
Mean baseline age, y ± SD	65.6±7.89	75.1±8.11	66.3±8.25	<.001
Mean last follow-up age, y ± SD	70.5±8.39	82.6±6.44	70.96±8.60	<.001
Women, n (%)	1127 (69.6)	50 (68.4)	1177 (69.5)	<.86
Years of formal Education ± SD	6.17±4.07	4.08 ± 3.69	5.87±4.11	<.001
Baseline MMSE score ± SD	23.9±4.00	19.4±4.71	23.65±4.19	<.001
Last MMSE score ± SD	23.4+4.24	14.0+5.59	23.08±4.62	<.001
APOE-ε4, % (3/4+4/4+2/4)	291(18.0)	20 (27.4)	311 (21.04)	0.02
Duration of follow-up, y ± SD	4.74±2.56	5.49±3.26	4.78±2.60	<.001

Abbreviations: *APOE*-ε4 = Allele ε4 of the Apolipoprotein E; MMSE = Mini Mental State Examination (18); CDR = Clinical Dementia Rating Scale (30); SD = standard deviation.

p indicates the difference between subjects by dementia status.

Table 3

Incidence of all dementia diagnoses, Alzheimer's disease, and vascular dementia for different age groups of the Maracaibo Aging Study population.

	Age group	Cases	Person-Years	Incidence/1000 p-y (95% CI)
Dementia				
	55–64	6	3796	1.58 (0.58–3.44)
	65–74	33	3014	10.95 (7.54–15.4)
	75–84	22	1084	20.30 (12.7–30.7)
	85+	12	132	90.90 (47.0–159)
	All ages	73	8026	9.10 (7.13–11.4)
	Women, all ages	50	5699	8.77 (6.51–11.6)
	Men, all ages	23	2328	9.88 (6.26–14.8)
	≥ 60	71	5885	12.06
	≥ 65	67	4230	15.84
	Standardized incidence			11.53[1] 10.72[2]
Alzheimer's disease				
	55–64	3	3784	0.79 (0.16–2.32)
	65–74	19	2962	6.42 (3.86–10.02)
	75–84	12	1055	11.37 (5.88–19.87)
	85+	7	115	60.87 (24.47–125.41)
	All ages	41	7916	5.18 (3.72–7.03)
	Women, all ages	29	5618	5.16 (3.46–7.41)
	Men, all ages	12	2298	5.22 (2.7–9.12)
	≥ 60	39	5775	6.75
	≥ 65	38	4132	9.20
	Standardized incidence			6.97[1] 6.42[2]
Vascular dementia				
	55–64	3	3772	0.8 (0.16–2.32)
	65–74	11	2875	3.83 (1.91–6.85)
	75–84	9	1012	8.89 (4.07–16.88)
	85+	3	98	30.61 (6.31–89.46)
	All ages	26	7757	3.35 (2.19–4.91)
	Women, all ages	17	5495	3.09 (1.8–4.95)
	Men, all ages	9	2262	3.98(1.82–7.55)
	≥ 60	26	5631	4.62
	≥ 65	23	3985	5.77
	Standardized incidence			4.36[1] 4.09[2]

Abbreviations: p-y = person-years; CI = confidence intervals.

[1] Age-standardized incidence based on the age structure of the Venezuelan population [42].

[2]Age-standardized incidence based on the age structure of the world population [43].

Table 4

Incidence of all dementia diagnoses, Alzheimer's disease, and vascular dementia for carriers and non-carriers of the *APOE*-ε4 allele.

	***APOE*-ε4 status**	**Cases**	**Person-Years**	**Incidence/1000 p-y (95% CI)**
Dementia				
	Carrier of *APOE*-ε4	20	1477	13.50 (8.27–20.9)
	Non-carrier of *APOE*-ε4	51	5658	9.01 (6.70–11.8)
Alzheimer's disease				
	Carrier of *APOE*-ε4	13	1448	8.98 (4.78–15.4)
	Non-carrier of *APOE*-ε4	27	5581	4.84 (3.19–7.04)
Vascular dementia				
	Carrier of *APOE*-ε4	5	1373	3.64 (1.18–8.50)
	Non-carrier of *APOE*-ε4	20	5494	3.64 (2.22–5.62)

Abbreviations: *APOE*-ε4 = Allele ε4 of the Apolipoprotein E; p-y = person-years; CI = confidence intervals.