

The Epidemiology of Dementia and Alzheimer Disease in Portugal: Estimations of Prevalence and Treatment-Costs



Epidemiologia da Demência e da Doença de Alzheimer em Portugal: Estimativas da Prevalência e dos Encargos Financeiros com a Medicação

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RESUMO

Introdução: A incidência e prevalência de demência e de Doença de Alzheimer aumentam com a idade, duplicando a cada cinco anos após a sexta década de vida. Portugal é um país envelhecido, previsivelmente com um número crescente de casos de demência. No entanto, os dados epidemiológicos são escassos e os estudos sobre os custos da doença praticamente inexistentes. Propomo-nos apresentar uma estimativa actualizada da prevalência de demência/ Doença de Alzheimer em Portugal e inferir, a partir da prescrição específica para demência, o número de diagnósticos efectivos e os encargos financeiros com esses medicamentos.

Material e Métodos: À população residente em Portugal (2013), aplicámos os valores de prevalência de demência para a Europa Ocidental (estudo da Alzheimer's Disease International). A estimativa dos diagnósticos efectivos de Doença de Alzheimer e dos encargos financeiros com medicação específica baseou-se nas informações do Intercontinental Marketing Services Health (IMSH) – 2013.

Resultados: O número estimado de Portugueses com mais de 60 anos e com demência foi 160287, o que corresponde a 5,91% deste universo populacional. Sabendo que a Doença de Alzheimer representa 50-70% dos casos, inferimos que existirão entre 80144 e 112201 doentes. Por outro lado, os dados da IMSH indicam que estarão diagnosticados e a receber anti-demenciais 76250 doentes, representando um encargo financeiro de 37 M€/ano.

Conclusão: O envelhecimento da população incrementa o número de casos de demência. Aparentemente, nem todos os doentes com Doença de Alzheimer recebem a medicação aconselhada, sugerindo que esta condição ainda está sub-diagnosticada. A evolução tem sido positiva, com incremento do número de doentes tratados e redução dos custos com fármacos específicos.

Palavras-chave: Custos do Tratamento; Demência; Doença de Alzheimer; Portugal; Prevalência.

ABSTRACT

Introduction: The incidence and prevalence of global dementia and Alzheimer's disease (AD) increase with age, almost doubling every five years after the sixth decade of life. Demographic aging is a reality in Portugal, being expectable that the number of dementia cases also increases. Even so, dementia-epidemiological data in Portugal is scarce and cost-of-illness studies are almost inexistent. Our aims were to obtain up-to-date information about the prevalence of dementia/ Alzheimer's disease in Portugal, to estimate the number of cases effectively diagnosed as Alzheimer's disease and to determine illness-costs with specific dementia treatment.

Material and Methods: The numbers of age-adjusted prevalence of dementia obtained for Occidental Europe (Alzheimer's Disease International study), where applied to the resident population in Portugal (2013). Estimations related to diagnosis and treatment-costs were based in data provided by the Intercontinental Marketing Services Health (IMSH) – 2013.

Results: The estimated number of Portuguese people with dementia among those aged ≥ 60 years, is 160287, representing 5.91% of this population-stratum. Knowing Alzheimer's disease is responsible for 50-70% of all cases, we might conclude there are between 80144 and 112201 patients. According to IMSH-data, 76250 receive anti-dementia drugs and the costs of this kind of medication is 37 M€/year.

Conclusions: As a consequence of the demographic aging, also the number of dementia cases increases. Apparently, not all Alzheimer's disease patients receive the recommended medication, suggesting this condition is still under-diagnosed. However, figures indicate a positive progression with an increment of treated cases and a reduction of medication-costs.

Keywords: Alzheimer Disease; Cost of Illness; Dementia; Portugal; Prevalence.

INTRODUCTION

Dementia is a clinical manifestation of several disease processes. Alzheimer's disease (AD) is the most prevalent illness and corresponds to 50-70% of the patients. There is an increasing incidence and prevalence of dementia with ageing, almost doubling every five years.¹⁻⁹

The global incidence of dementia has severely increased over the last few decades. While in 2005 about 7.5/1,000 people were estimated to be affected per year, i.e. about one new patient every 7 seconds,¹⁰ in 2012 it was estimated to reach approximately 7.7/1,000 people per year, around

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1 new patient every 4 seconds.¹¹ As regards prevalence and according to a recent meta-analysis, the prevalence of dementia above 60 years of age varies between 5-7%, higher in Latin America (8.5%) and lower in Sub-Saharan Africa (2-4%).¹² As such, it is expected that, at present, there are 35.6 million people with dementia worldwide and projections suggest that this figure may double every 20 years, to 65.7 million by 2030 and 115.4 million by 2050.^{11,12} However, recent studies suggest a stabilization or even reduction in the incidence of dementia in developed countries, associated to lifestyle improvement and reduction in cardiovascular diseases; in addition, control of risk factors will lead to a reduction in mortality and therefore it seems difficult to predict their real impact on dementia's prevalence.¹³⁻¹⁶

According to the World Health Organization (WHO), in 2004 dementia was the sixth major cause of death in developed countries and AD was considered as the fifth more frequent cause of death in 2006.^{17,18} Nevertheless, dementia-associated morbidity is perhaps more relevant than mortality. In this regard, when considering disability measured in years of life in people aged above 60, it is estimated that dementia may contribute with more than 11.9%, a higher figure than the one calculated for stroke (9.5%), cardiovascular diseases (5.0%) or cancer (2.4%).^{11,19} This high morbidity, associated to dementia's chronicity, involves very high direct and indirect costs, reflected in a huge overload to national health systems in addition to a significant impact on family economy.²⁰⁻²³

As ageing is the major risk factor to dementia, any epidemiological approach made in Portugal in this regard implies knowledge of national demographic characteristics. The recent demographic tendencies in Portugal are defined by a sustained increase in the average life expectancy at birth, a reduction in child mortality, an increase in emigration, a steep decline in fertility and ensuing population ageing.²⁴ The increase in the average life expectancy at birth is one of the most relevant factors contributing to population ageing. Regarding 2011-2013, the average life expectancy at birth was 80.0 years in the population living in Portugal (82.79 years in women and 76.91 in men), having increased about three years over the last decade (3.36 years more for men and 2.58 for women) according to the 2001-2003 estimates (73.55 and 80.21 years for men and women, respectively).²⁴ The projections of the National Institute of Statistics (*Instituto Nacional de Estatística* [INE]) establish that the average life expectancy at birth in Portugal will reach 84.21 years in men and 89.88 years in women, by 2060.²⁴

The percentage of people aged 65 or above has doubled over the last few decades from 8% of the total Portuguese population by 1960 to 17% in 2005 and 19% in the 2011 census. This reflects the deep changes in the age structure of the population living in Portugal, with a reduction in younger population and narrowing the base of the age pyramid, with an increase in the elderly population widening the top of the age pyramid. Therefore, there is an increase in population ageing, a current reality with a

chronic tendency. The last estimates for the population living in Portugal confirm the double demographic ageing with an increase in the number of elderly and a reduction in the number of young and working age people. The ageing index of 102 that was found in 2001 means that for each 100 young people there were 102 elderly people. Ten years later the index rose to 128 by 2011 and to 136 by 2013. It is therefore estimated that the elderly population will continue to rise in Portugal over the next decades, reaching 36 to 43% of the population by 2060, corresponding to an ageing index of 287 to 464 elderly per each 100 young people.²⁴

There are few studies published in Portugal regarding dementia's epidemiology and there are no direct data on prevalence of the different forms of dementia.

A projection of dementia and AD prevalence for the Portuguese population was published in 1994²⁵ based on data obtained from the studies of the EURODEM group²⁶ and from the 1991 population census. In 1991, for age above 30, Garcia *et al.* have extrapolated a total of 92,470 patients with dementia and 48,706 with AD in Portugal.²⁵

The first population-based study was carried out in Portugal between 2003 and 2008, to assess the prevalence of dementia and mild cognitive impairment (MCI).²⁷ This two-stage study involved a group of patients aged between 55 and 79 from two communities from the North of Portugal: a first stage (Stage I) for case detection through an interview, using classification scales and neuropsychological tests and a second stage of clinical validity, through interview and clinical examination carried out by a neurologist (Stage II). In Stage I, 88 patients meeting dementia criteria were found. Stage II, with a compliance rate of just 56.2%, showed a 2.7% global prevalence of dementia. Overall, a 12.3% MCI prevalence was found.^{27,28}

There are several indirect indicators of the prevalence of a specific disease or nosological group, beyond epidemiological data obtained by population-based studies or by extrapolating from European meta-analysis. These are data obtained from family doctor, hospital or Emergency clinical records, as well as diagnosis obtained from residential institutions, death certificates and also from the consumption of specific medications for a certain disease.²⁹ As regards dementia, most data sources are unreliable, firstly due to the complexity of dementia's diagnosis, involving resources poorly accessible to some populations and secondly due to misdiagnosis by healthcare providers; for these reasons, it is surely underdiagnosed in primary healthcare; in addition, as it is a chronic situation with high morbidity, although rarely directly attributed as cause of death, it is probably under-identified in death certificates. In fact, the INE's 2000 data found 616 deaths related to AD, in total, corresponding to about 41% of deaths caused by central nervous system diseases in that same year.³⁰ More recent data from 2012³¹ found an official record of 1,740 deaths related to AD, mainly in female (65%) and in elderly population (83.1 was the average age at the time of death by this cause, with no record below the age of 45). Deaths related to AD represent 1.6% of global Portuguese mortality,

with a 16.6 deaths per 100,000 people gross mortality rate and 66.7 per 100,000 standardized mortality rate in people aged 65 or above.

Data regarding the use of specific medications is more interesting and presumably more reliable, as medication for cognitive symptoms is only used in individuals with dementia and mainly in AD treatment. It may therefore provide a rough estimate of diagnosis and the direct costs involved in such prescriptions.²⁹

With the progressive demographic ageing it is likely that the number of patients with dementia has risen over the last few years. Our study aims to obtain a more updated estimate of the prevalence of dementia in Portugal, using a projection for the Portuguese population from prevalence rates for dementia found in Western Europe in the study by Ferri *et al.*¹⁰ and the most recent data from the INE according to the 16th June 2014 Resident Population Estimates.³²

These results were compared to the estimate of patients identified in Portugal (actual diagnosis), calculated from the consumption of specific medications for dementia. This assessment allows for an estimate of expenditure for the SNS as well as for patients/family, which will correspond to a share of the direct costs assigned to dementia.

MATERIAL AND METHODS

The values of age-adjusted prevalence of dementia were calculated from the study by Ferri *et al.*,¹⁰ carried out by "Alzheimer's Disease International" (the methodology of this study is shown in Appendix 1). In our study we used the estimates of dementia prevalence for the EURO A region, where Portugal is included, and applied these to the resident population living in Portugal, according to the most recent (16th June 2014) Resident Population Estimates.³² Estimated prevalences were calculated within 95% confidence intervals.³³

The estimate of the AD diagnosis and financial costs related to the specific medication was based on data provided by the Intercontinental Marketing Services Health for 2009-2013. The following formula was used to calculate the number of treated patients, itself an indicator of current diagnosis:

$[\text{Number of Tablets} \times (\text{Tablet dosage} / \text{Recommended Daily Dosage} / 365)].$

RESULTS

According to the most recent (16th June 2014) Resident Population Estimates³² pointing to a total population of 10,427,301 people, from which 2,713,715 are aged above 60, the estimated prevalence of dementia for the EURO A region applied to the Portuguese population revealed that, in 2013 there are 160,287 people with dementia, corresponding to 5.91% of the population aged above 60. The estimates by age group are shown in Table 1. In the 60-64 age group there are 5,795 patients, the figure rising to approximately 62,826 above the age of 85.

The same calculation procedure was applied to the values derived from the Resident Population Estimates for 2003 and 2008 in order to obtain a longitudinal estimate measure. In 2003, there were an estimated 120,506 people with dementia in Portugal and that value had increased to 138,390 people in 2008, a 17,884 increment between both years, i.e. a 3,577 annual average increase. When we compared the estimated number of people with dementia in 2008 with the estimated value in 2013, we found a new increment by 21,879 patients, i.e. a 4,377 annual average increase. The longitudinal results by age group are shown in Figure 1.

Based on the value of 160,287 patients with dementia in Portugal and knowing that 50 to 70% of these are associated to AD, we may estimate that in 2013 there would exist between 80,144 and 112,201 patients with AD in Portugal.

In addition, in 2013, data from the IMSH show that 76,250 patients would have been diagnosed and would be receiving specific medication, corresponding to a financial cost of 37 M€ per year (Table 2). According with the same IMSH estimates, there has been a positive evolution, as the number of patients receiving medication for dementia has increased from 47,940 patients in 2009 to 76,250 patients in 2013. In addition, a total of 60M€ per year in costs was recorded in 2010, from which 22M were assigned to the SNS and 38M to the patients (Table 2). Despite the increasing number of medications taken, suggesting a rise in the number of patients under treatment, there was a reduction in the total cost associated to medication consumption, from approximately 60M€ per year in 2010 to 37 M recorded in 2013.

Table 1 - Estimate of the prevalence of dementia in Portugal. in 2013

Age	Prevalence (%)	CI min – CI max	Population	Nº of patients
60-64	0.90	0.88-0.92	643,872	5,795
65-69	1.53	1.47-1.53	575,925	8,639
70-74	3.60	3.55-3.65	480,062	17,282
75-79	6.00	5.93-6.07	436,117	26,167
80-84	12.20	12.09-12.31	324,407	39,578
85+	24.80	24.63-24.94	253,332	62,826
Total	5.91	5.88-5.93	2,713,715	160,287

CI = Confidence Interval

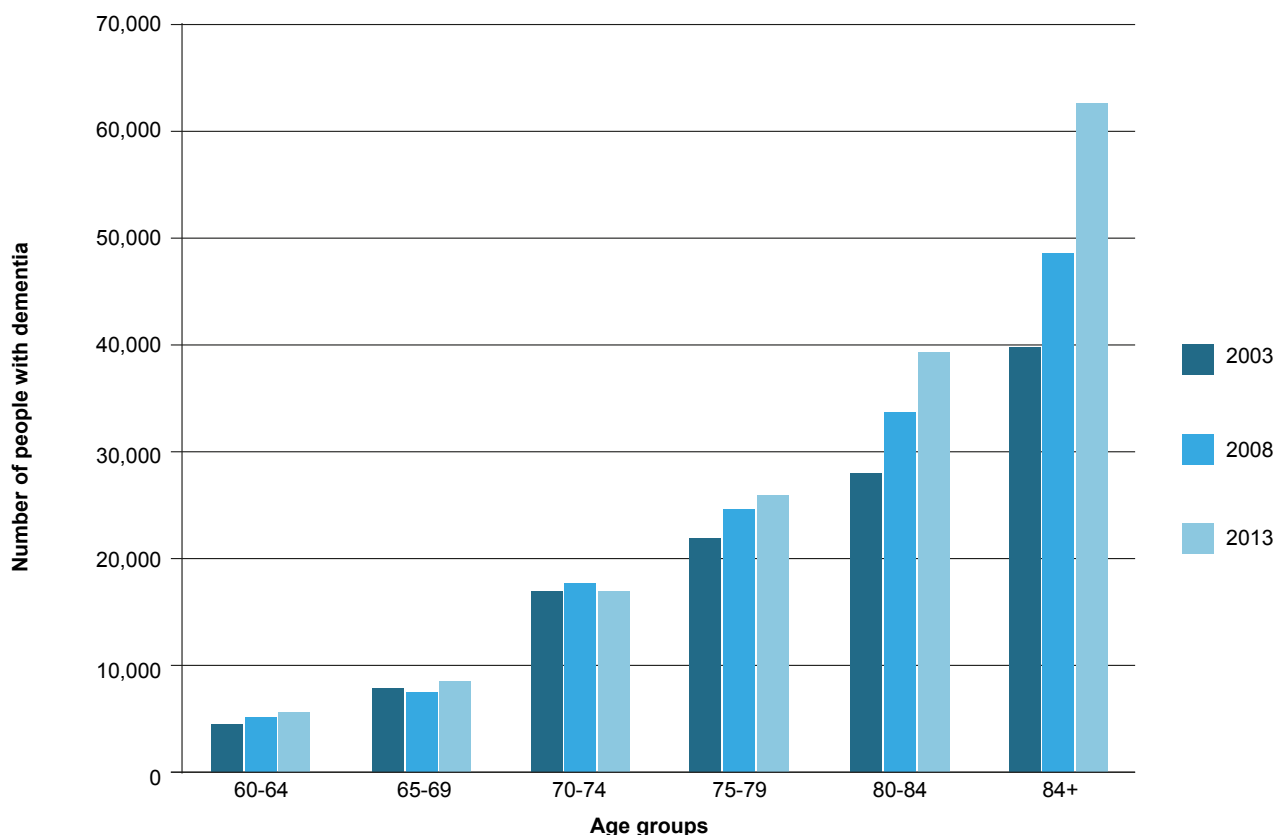


Figure 1 - Longitudinal perspective of the estimate of the number of people with dementia in Portugal

DISCUSSION

Due to the lack of a sufficiently comprehensive Portuguese population-based study, European estimates are probably the most reliable and objective grounds to know the Portuguese situation. The study by Ferri *et al.*,¹⁰ in which our projection was based, used the Delphi method and an agreement was reached regarding the age-adjusted prevalence of dementia for every region of the world (defined by the WHO). The Delphi method aims to obtain quantitative estimates through a qualitative analysis of data, allowing for the analysis of methodologically very different studies. When the published information is scarce, it allows for inferences by experts in consensus boards, using comparable context data. Estimates by all experts are grouped and delivered anonymously to each participant, allowing the latter to review initial responses vs. responses by the group. As the group does not need to meet, this method ensures anonymity, allowing for a free expression of opinions.¹⁰ The application of estimates of consensus to the Portuguese population assume that the results of this study are valid and that the prevalence of dementia in Portugal is in line with the other Western European countries. The study by Ferri has some limitations as, for some regions, epidemiological data are scarce and therefore the estimates may not be valid. However, for the EURO A region, in which Portugal is included, there are several studies with good methodological quality. The two studies carried out in Spain should be specifically mentioned,^{34,35} a culturally similar country to Portugal. In addition, the degree of agreement

between the experts within the Delphi board was excellent at the very first stage¹⁰ and therefore the estimate is expected to be valid.

We found that in 2013 approximately 160,287 people would be expected to suffer from dementia in Portugal, corresponding to 5.91% of the people included in these age groups. We should recall that in 1991 an equivalent estimate calculated from studies by the group EURODEM, proposed a 4.6% rate,²⁵ suggesting an increase in prevalence over the last decade. We assume that this increase in dementia prevalence above the age of 60 between 1991 and 2013 may be explained by the increased percentage of very elderly people in Portugal, according to the INE's data. These are in line with most of the population-based studies in which dementia's prevalence increases almost exponentially with age.¹³⁻¹⁶ In fact, this corresponds to 5,795 patients in the age group 60-64 increasing to 62,826 over the age of 85, where most patients are found. Of note, the 5.91% prevalence is much above the previous 2.7% rate suggested by the only population-based study carried out in Portugal until now.^{27,28} We should nevertheless mention that Nunes *et al.* have restricted their study to a population aged between 55 to 79, excluding many elderly people and, according to our estimate, more than 64% of the patients with dementia are aged above 80.

In addition, the more recent data from the IMSH (2013) show that 76,250 people would follow a treatment in Portugal with medication specifically targeted to cognitive impairment in dementia (cholinesterase inhibitors and memantine). The

Table 2 - Estimate of the number of patients and financial charges with specific medication

Reference year	2009	2010	2011	2012	2013
N° Patients⁽¹⁾	46,940	59,499	64,592	68,087	76,250
Total value of medication	54,515,763 €	59,872,287 €	57,183,996 €	42,976,801 €	37,252,264 €
State⁽²⁾	20,170,832 €	22,152,746 €	21,158,079 €	15,901,416 €	13,783,338 €
Patient	34,344,931 €	37,719,541 €	36,025,917 €	27,075,385 €	23,468,927 €

⁽¹⁾ Calculation of the Number of Patients: [N° of Tablets x (Dosage of tablets / Recommended Daily Dosage)] / 365.

⁽²⁾ A value of 37% of total state budget was considered as State value; it was not possible to obtain reliable values for the Special Social Security Scheme.

Note: Data from Intercontinental Marketing Services Health (IMSH) – 2013.

extrapolation of these figures to AD diagnosis is acceptable, due to several reasons: 1) According to literature, this is a methodology applicable to neurodegenerative disorders and to AD, although the study suggests a tendency to underestimate the number of diagnosis when compared to assessments made through health administrative databases,²⁹ 2) this class of drugs is somewhat restricted to AD, when we exclude the recommendation to be used in epidemiologically less relevant situations like Lewy body dementia and dementia associated to Parkinson's disease; 3) the prescription of these two classes of drugs covers the entire severity rank of dementia as cholinesterase inhibitors are indicated for mild and moderate forms and memantine is mainly used in severe cases. However, we should mention that our estimate may over-estimate the patients with AD actually identified/treated, not only because the patients with other forms of dementia were excluded from our assessment but also because the two classes of drugs are sometimes used in association. The comparison between this result of 76,250 patients and the absolute number of patients with AD suggested by the estimate based in the European study (80,144 and 112,201) shows that the disease is still underdiagnosed and undertreated. This is a very relevant conclusion in order to assess the quality of the healthcare provided in Portugal to the patients with this form of dementia. The efficacy of these drugs in controlling symptoms and their association with an improvement in the quality of life of patients and their carers has been repeatedly demonstrated in robust randomized and double-blind clinical trials. In addition, these drugs are formally recommended for the treatment of AD in Portugal, as established by the Norm 053/2011 from 27/12/2011 issued by the Health Directorate General "Abordagem Diagnóstica e Terapêutica das Alterações Cognitivas (Demências; Doença de Alzheimer)" (<http://www.dgs.pt/?cr=21530>).³⁶ Reliable institutions such as the American Academy of Neurology³⁷ or the European Federation of Neurological Societies^{38,39} have issued clear indications on the use of these drugs regarding the proven benefits in the different symptoms of the disease. According to the described estimates there is a positive evolution, as the number of patients receiving pharmacological therapy for dementia has almost doubled in 5 years. In addition, there has been a reduction in total costs associated to the

consumption of specific drugs for dementia, from about 60M€ shown in 2010 to about 37M€ shown in 2013. This cost reduction is probably due to the progressive introduction of generic medicines in the national prescriptions. Also, based on informations from the *INFARMED - Autoridade Nacional do Medicamento e Produtos de Saúde, I. P. (INFARMED)*, we found that in 2011, 22.19% of the charges of the *Serviço Nacional de Saúde (SNS)* were accounted for by Central Nervous System medication and that this group of drugs was the second with higher charges, only overcome by Cardiovascular medications (29.85% of the charges). Three from the drugs used to treat AD (rivastigmine, donepezil and memantine) were amongst the 100 active substances with higher charges to the SNS, each one of them with more than 100 thousand packets sold in 2011.⁴⁰

When assessing the financial charges regarding diseases, the costs with medication are included amongst the direct costs (associated to treatment, professional fees, clinical tests, hospital stays, external service expenses required to support daily healthcare to the patient, among others). In dementia, so called indirect costs (exemplified by patient's early dropout from work, informal carer's absenteeism/professional dropout, increase in carer's morbidity, amongst others) have an even higher impact on the family economy and the health system.²⁰⁻²² The world's estimates of expenses with dementia reached 604 billion dollars in 2010. In developed countries, 45% of these expenses were assigned to informal care, 40% to formal care and only 15% to direct medical costs.¹¹ In addition, the data obtained by several studies show a wide variation of financial charges with dementia, which obviously relate to the quality of healthcare but also to early institutionalization and presence of family support vs. formal care networks.⁴¹ It is also consensual and confirmatory from these studies that there is a direct relationship between expenses and related variables with the severity of the disease, namely with severity of cognitive impairment, degree of functional disability, prevalence of psychopathological changes and carer's burnout.²³

Objective assessment studies to characterize the support global network and dementia-related direct and indirect costs are needed in Portugal. These are some of the strategic objectives of the joint evaluation with Prof

Joël Ménard, Professor Emeritus in Public Health at the Faculty of Medicine Paris-Descartes, ex-Health General Director in France, President of the drafting committee of the “Plane Alzheimer France 2008-2012” and President of the International Advising Board of the *Fondation pour la Maladie d’Alzheimer et les Maladies Apparentées*, as group leader. The 2nd seminar took place at the end of 2014, in which the initiatives that were promoted in the meantime were analysed. These included research projects with financial support by the PNSM, aimed to increase the production of Portuguese scientific evidence in which the planned national intervention program in dementia will be based on; the future National Program for Healthcare of the Elderly (*Programa Nacional para a Saúde das Pessoas Idosas [PNSPI]*), ratified by ministerial decree and planned to be reactivated linked to the National Program for Mental Health (*Programa Nacional para a Saúde Mental*).

CONCLUSION

The growth of the Portuguese elderly population seems to be followed by an increase in the number of patients with dementia. It is expectable this number will increase as, according to our estimate, more than 64% of patients with dementia are aged above 80. In addition, the extrapolation of the number of actual diagnosis of AD obtained from its

specific medication suggests that dementia is still an under-diagnosed situation. Even so, there has been a positive evolution, as the number of treated patients almost doubled in 5 years and the costs with medication have almost halved. The recognition of the importance of dementia in the current epidemiological scenario is a mandatory starting point for the definition of institutional strategies of support and treatment of patients with dementia in Portugal and cannot be overemphasised.

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CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

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