

Burden of disease and cost of illness of Alzheimer's disease in Portugal

João Costa^{1,2,3*}, Margarida Borges^{1,2,4*}, Rosa Encarnação⁵, Horácio Firmino⁶, Manuel Gonçalves-Pereira⁷, Patrícia Lindeza⁸, Filipa Sampaio^{1*}, Isabel Santana⁹, Rita Sousa^{1*}, Ricardo Taipa¹⁰, Ana Verdelho¹¹, Luís Silva-Miguel^{1*}

¹Centro de Estudos de Medicina Baseada na Evidência, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal; ²Laboratório de Farmacologia Clínica e Terapêutica, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal; ³Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal; ⁴Unidade de Farmacologia Clínica, Centro Hospitalar Lisboa Central EPE, Lisboa, Portugal; ⁵Hospital de Magalhães Lemos, EPE, Porto, Portugal; ⁶Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; ⁷Comprehensive Health Research Centre, Chronic Diseases Research Center, Faculdade de Ciências Médicas / NOVA Medical School, Universidade Nova de Lisboa, Lisboa, Portugal; ⁸Instituto de Saúde Ambiental, Faculdade de Medicina da Universidade de Lisboa, Universidade de Lisboa, Lisboa, Portugal; ⁹Serviço de Neurologia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; ¹⁰Neuropathology Unit / Portuguese Brain Bank and Department of Neurology, Centro Hospitalar Universitário do Porto, Hospital Santo António, Porto, Portugal; ¹¹Serviço de Neurologia, Departamento de Neurociências e Saúde Mental, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal; *At the time of the study, J.C, M.B, F.S, R.S and L.S.M were working at Centro de Estudos de Medicina Baseada na Evidência, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal.

BACKGROUND AND OBJECTIVE:

- Alzheimer's disease (AD) is a progressive, multifactorial neurodegenerative brain disorder. (1,2).
- AD is the most common cause of dementia affecting mainly people over the age of 65. However, the pathophysiology of the disease initiates decades before the onset of the first symptoms. (3,4).
- The progressive cognitive decline compromises patients' behavior and daily living skills with substantial humanistic and economic burden. (5).
- This study aimed to estimate the social costs and health losses associated with AD in patients aged ≥ 65 years in mainland Portugal during 2018.

METHODS AND INPUTS:

Burden of disease

- Burden of disease was measured as disability-adjusted life years (DALY), estimated as the sum of the Years of Life Lost (YLL) due to premature mortality and Years Lived with Disability (YLD) (Figure 1). (6)
- YLL were calculated from the number of deaths multiplied by a global standard life expectancy at the age of death. (6)
- Given the under reporting of AD as a cause of death on official certificates it was necessary to estimate AD attributable deaths for which other cause was reported on official certificates. (7–11)
- To attain that, a population-attributable fraction (PAF) was estimated according to the hazard ratios (HR) reported by Stokes et al. (9) and the prevalence of dementia amongst those who died (using Portuguese Diagnosis Related Groups [DRG] microdata as a proxy for the general population). This was further adjusted considering the ratio between AD cases and any specified dementia cases amongst inpatient deaths.
- YLD were computed as the number of cases of AD multiplied by an estimated disability weight based on the AD and other dementias GBD Study (Table 1). (12)
- Prevalence of AD was estimated from the prevalence of dementia reported by Gonçalves-Pereira et al. that employed the 10/66 Dementia Research Group algorithm. It was considered that AD accounts for 69,4% of all dementia cases. (13)

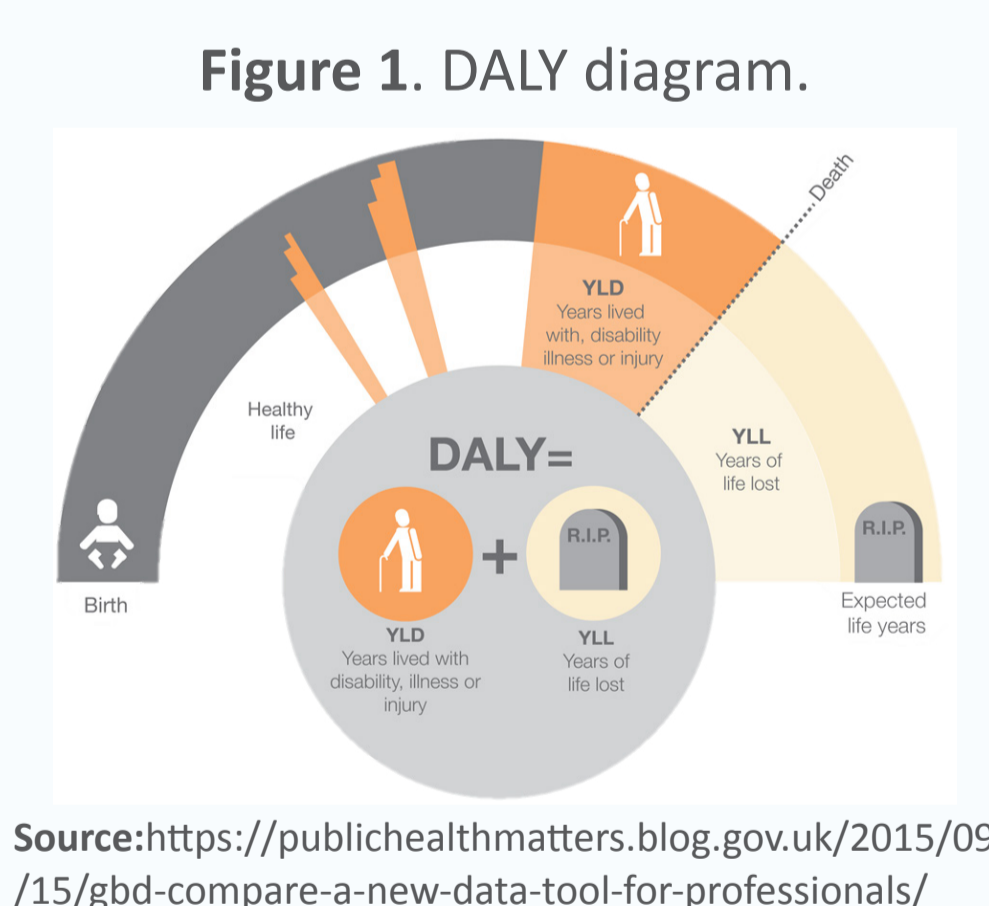


Table 1. Disability weights and distribution per dementia stage.

Dementia stages	Disability Weights (IC95%) *	Distribution**
Mild dementia	0.069 (0.046-0.099)	26%
Moderate dementia	0.377 (0.252-0.508)	41%
Severe dementia	0.449 (0.304-0.595)	33%
Total	NA	100%

Source: *adapted from Nichols et al., 2019 (7); ** Experts' panel (N=7).

Costs

- Cost of illness was estimated using a societal perspective and a prevalence-based approach.
- Total costs included direct medical costs (inpatient care and outpatient care and drugs) and direct non-medical costs (informal care, social care, mobility aids, personal care, home adaptations, and transportation).
- Indirect costs related with productivity loss were not included as it was assumed that the majority of the ≥ 65 Portuguese population does not have any professional activity.
- Inpatient costs were estimated using the DRG 2018 database covering National Health Service (NHS) hospitals.
- Outpatient resource use (including diagnostic and patient's follow-up, rehabilitation, psychotherapy, and cognitive intervention) were estimated according to experts' opinion. Unit costs were based on official NHS tariffs.
- Drug costs were estimated using national sales data for dementia and data from a convenience sample for co-medication related to Behavioral and Psychological Symptoms of Dementia (BPSD) provided by Centro de Estudos e Avaliação em Saúde (CEFAR).
- Mobility aids, personal care and home adaptations were estimated according to data from Freitas 2019. (14)
- Social care includes costs with residential structures and in-home care. Costs were estimated according to data from multiple Portuguese social sector reports and national legislation. (15–19)
- The proportion of patients relying on informal care was based on data from RNCCI 2019 report (15), being the time spent by caregivers valued according to the minimum wage. (20)
- Transportation for each visit, rehabilitation treatments, psychotherapy and cognitive intervention, and day center was also considered and valued according to Portuguese data. (21)

RESULTS:

- Prevalence of AD was estimated at 143,334 elderly patients in 2018 (7% of the population with ≥ 65 years) in Portugal mainland (Table2).

Table 2. Prevalence of AD per dementia stage.

Dementia stages	Prevalence of AD in each stage
Mild dementia	36,789
Moderate dementia	59,245
Severe dementia	47,300
Total	143,334

Source: Authors' estimation.

- Disease burden sums up 122,643 DALY: 76,709 YLL due to 7,538 premature deaths and 45,754 YLD arising from people living with the disease. Therefore, 63% of disease burden is caused by premature deaths (Figure 2).
- Direct medical costs amount to €219 million (including €166 million for outpatient care, €29 million for inpatient care and €24 million for drugs) (Table 3 and Figure 3).

- Non-medical direct costs totaled 1.8 billion (including €1.1 billion attributed to informal care, €551 million for social care, €122 million for mobility aids, personal care and home adaptations, and €40 million for transportation costs) (Table 3 and Figure 3).
- The total estimated cost amounted to €2 billion in 2018.

Figure 2. DALY attributable to AD in mainland Portugal in 2018.

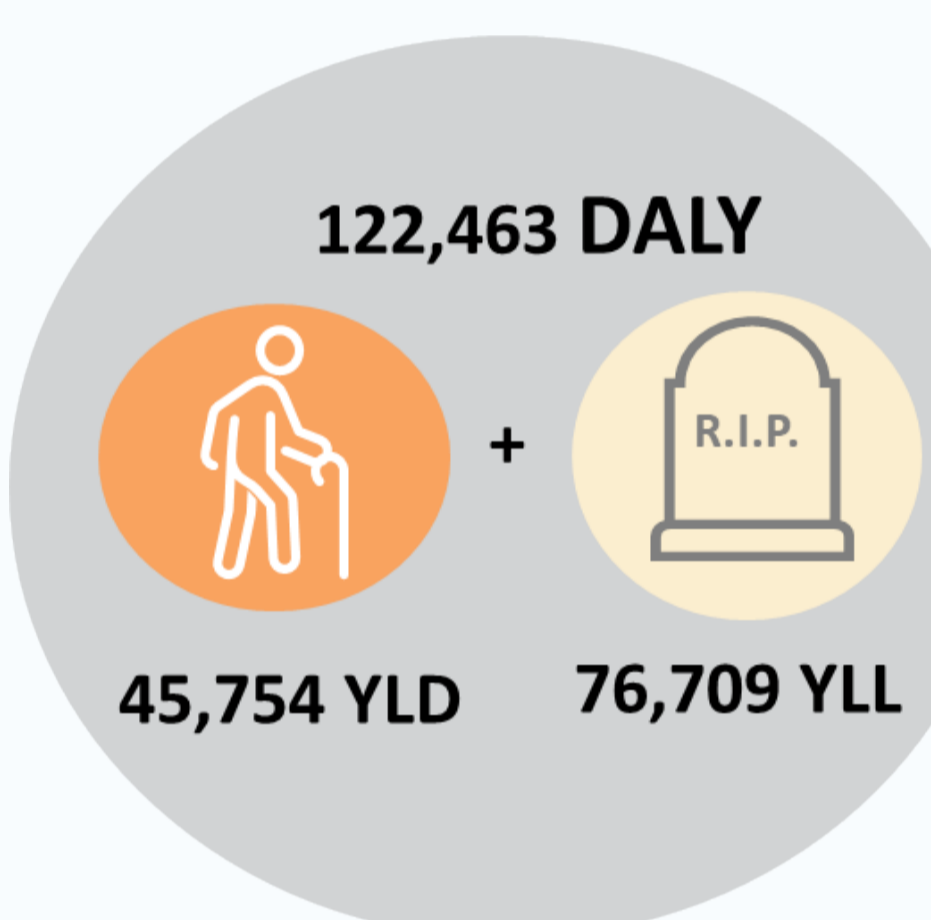
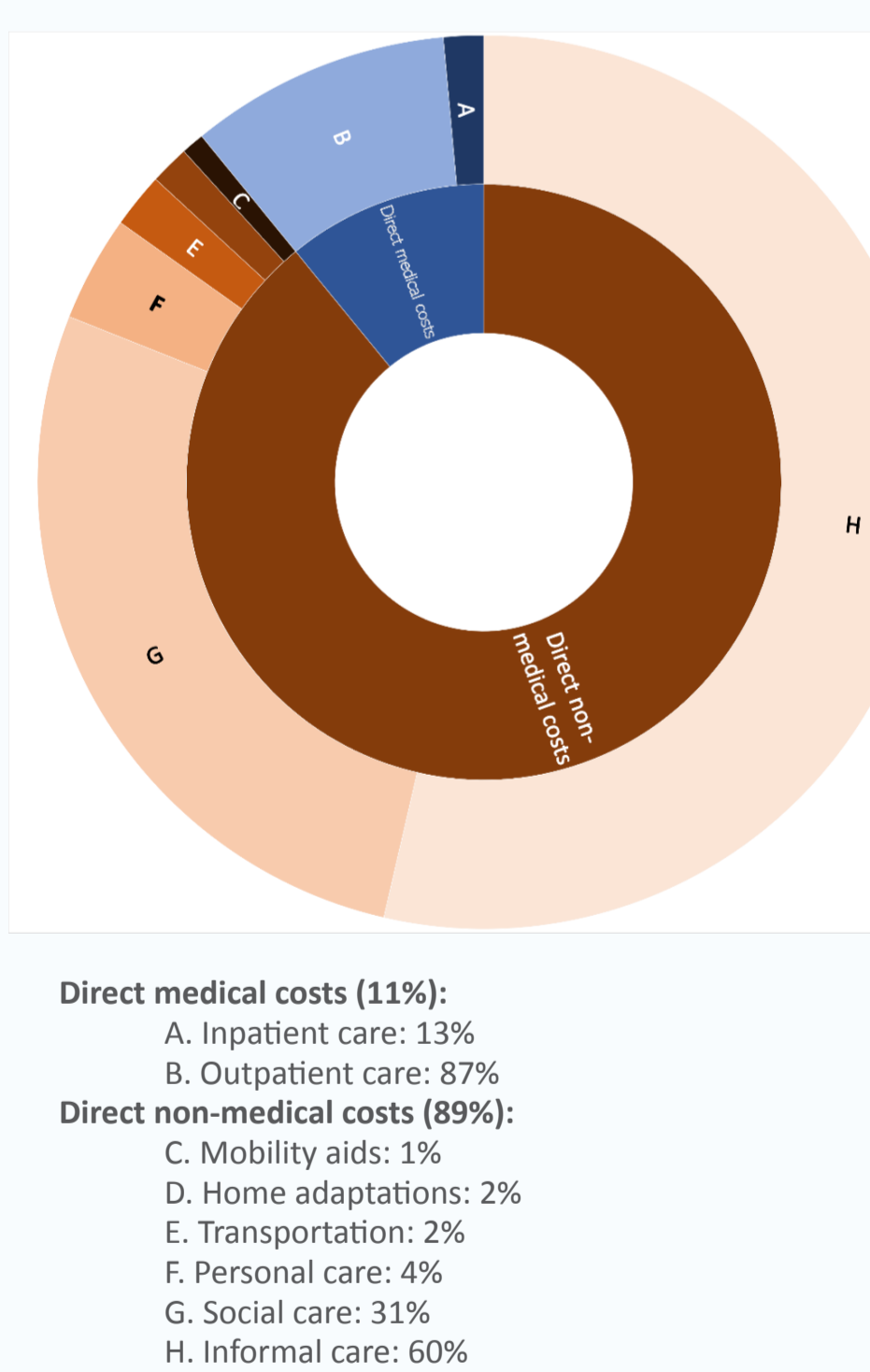


Figure 3. Distribution of direct medical and non-medical costs.



REFERENCES:

[1] DeTure MA, Dickson DW. The neuropathological diagnosis of Alzheimer's disease [Internet]. Vol. 14, Molecular Neurodegeneration. BioMed Central Ltd.; 2019 [cited 2023 Apr 1]; p. 1–18. Available from: <https://doi.org/10.1186/s13024-019-0333-5>; [2] Jack CR, Bennett DA, Blennow K, Carrillo MC, Dunn B, Haeberlein SB, et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease [Internet]. Vol. 34, Alzheimer's and Dementia. Elsevier Inc.; 2018 [cited 2023 Mar 30]; p. 510–526. Available from: <https://doi.org/10.1016/j.jalz.2018.02.018>; [3] Alzheimer's Association. 2023 Alzheimer's Disease Facts and Figures. Alzheimer's Dement. 2023;17(1):1–61. [4] Livingston G, Sommerich A, Orvaschel H, Sommerich A, Orvaschel H, Sommerich A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Vol. 396, The Lancet. Lancet Publishing Group; 2020; p. 413–446; [5] Jack CR, Bennett DA, Blennow K, Carrillo MC, Dunn B, Haeberlein SB, et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimer's Dement. 2018 Apr;14(4):510–526; [6] Murray CL, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet (London, England). 1997 May;349(9061):1269–76; [7] Nichols BL, Abdalla F, Abdalla F, Abdalla F, Abdalla F, Abdalla F, et al. Global, regional, and national burden of Alzheimer's disease and other dementias: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan;18(1):118–128; [8] Nichols BL, Abdalla F, Abdalla F, Abdalla F, Abdalla F, Abdalla F, et al. Global, regional, and national burden of Alzheimer's disease and other dementias: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan;18(1):118–128; [9] Nichols BL, Abdalla F, Abdalla F, Abdalla F, Abdalla F, Abdalla F, et al. Global, regional, and national burden of Alzheimer's disease and other dementias: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan;18(1):118–128; [10] Nichols BL, Abdalla F, Abdalla F, Abdalla F, Abdalla F, Abdalla F, et al. Global, regional, and national burden of Alzheimer's disease and other dementias: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan;18(1):118–128; [11] Nichols BL, Abdalla F, Abdalla F, Abdalla F, Abdalla F, Abdalla F, et al. Global, regional, and national burden of Alzheimer's disease and other dementias: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan;18(1):118–128; [12] Nichols BL, Abdalla F, Abdalla F, Abdalla F, Abdalla F, Abdalla F, et al. Global, regional, and national burden of Alzheimer's disease and other dementias: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan;18(1):118–128; [13] Nichols BL, Abdalla F, Abdalla F, Abdalla F, Abdalla F, Abdalla F, et al. Global, regional, and national burden of Alzheimer's disease and other dementias: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan;18(1):118–128; [14] Freitas M, Marques M, Balduino M, Balduino A, Machado AL, Verdelho A, et al. Needs for care and service use in dementia: a descriptive study of Portuguese participants in the active cohort study. Acta Med Port [Internet]. 2019 May; [cited 2023 Mar 23];31(5):355–67. Available from: <http://www.actamedportuguesa.com>; [15] RNCCI 2019 report. Direcção Geral de Saúde. Monitorização em Portugal - Estado da mortalidade dos residentes em Portugal. 2020; [16] Freitas M, Marques M, Balduino M, Balduino A, Machado AL, Verdelho A, et al. Needs for care and service use in dementia: a descriptive study of Portuguese participants in the active cohort study. Acta Med Port [Internet]. 2019 May; [cited 2023 Mar 23];31(5):355–67. Available from: <http://www.actamedportuguesa.com>; [17] Freitas M, Marques M, Balduino M, Balduino A, Machado AL, Verdelho A, et al. Needs for care and service use in dementia: a descriptive study of Portuguese participants in the active cohort study. Acta Med Port [Internet]. 2019 May; [cited 2023 Mar 23];31(5):355–67. Available from: <http://www.actamedportuguesa.com>; [18] Direcção Geral de Saúde. Monitorização em Portugal - Estado da mortalidade dos residentes em Portugal. 2020; [19] Direcção Geral de Saúde. Monitorização em Portugal - Estado da mortalidade dos residentes em Portugal. 2020; [20] Direcção Geral de Saúde. Monitorização em Portugal - Estado da mortalidade dos residentes em Portugal. 2020; [21] Barros PS, Loureiro A, Moreira A, Moura J, Silveiro F, Gomes JP, et al. Políticas Públicas em Saúde: 2011 - 2014 Avaliação do Impacto. 2015 Sep