

The health and economic burden of brain disorders: Consequences for investment in diagnosis, treatment, prevention and R&D

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ARTICLE INFO

Keywords:

Economic burden
Brain disorders
Dementia
Quality of life

ABSTRACT

Brain disorders are prevalent across all age groups but particularly in the elderly, highlighting the importance of preserving brain health in ageing populations. There have been few previous studies to address the complete scope of burden of brain disorders, including direct and indirect costs as well as intangible costs from morbidity and mortality. We seek to illustrate the full health and economic impact of brain disorders by leveraging data from previous large-scale epidemiological and health economic studies to estimate the total direct, indirect and intangible cost of brain disorders in 2019. Two alternative methods were used to estimate indirect costs: the human capital (HC) method (data from the CBDE2010 study), and the willingness-to-pay (WTP) per DALY method (data from GBD2019). Less than 10% of the costs of Alzheimer's disease (AD) and other dementias are incurred by the health care system, while Alzheimer's disease and other dementias is the costliest condition using the HC approach and stroke is the costliest condition due to the large number of life-years lost, followed by AD using the WTP approach. Using per-capita GDP as a proxy for WTP, the indirect costs were nearly four times higher compared to the conventional HC approach. We found that Indirect costs of brain disorders outweigh the direct costs for diagnosis, treatment and care even in high-income countries with advanced, universally accessible systems in Europe. There is likely underinvestment in R&D for brain disorders, and health care systems may lack sufficient incentives to invest in their treatment and prevention.

Introduction

Brain disorders are heterogenous group of conditions, that include both common as well as severe disorders, that together constitute a major component of overall morbidity and mortality [1]. They are prevalent across all age groups, but old age is the most important risk factor for some of the conditions with highest socioeconomic burden, including Alzheimer's disease and other dementia disorders, and stroke. These conditions are associated with a decline in cognitive and physical abilities, often requiring long-term care, emotional support, and financial resources [2,3]. The impact extends beyond the individual, straining healthcare systems and causing emotional distress for caregivers [4]. As the global population ages, the societal and familial burden of these disorders is expected to grow even further, highlighting the urgent need for research, treatment advancements, and public health strategies. Preserving brain health in the ageing population is therefore a priority, and is increasingly being made possible by recent advances in diagnosis, treatment and prevention [5].

Cost-of-illness (COI) studies attempt to quantify the economic impact

of disease in terms of direct costs (the value of resources used for diagnosis, treatment and care) and indirect costs (the value of resources lost due to morbidity and mortality). Information from COI studies can be helpful to inform decisions on health and research policy, as they indicate the absolute and relative magnitude of the burden of brain disorders in relation to other disease areas and overall burden of illness.

Probably the most comprehensive assessment of the economic burden of brain disorders to date was the Cost of Brain Disorders in Europe project (CBDE2010), under the auspice of the European Brain Council. They estimated the 2010 cost of brain disorders (mental and neurological disorders) in Europe to 798 billion EUR, based on a systematic review of the health economic and epidemiological literature [6]. The estimate was an update of an earlier estimate from 2005 and covered 19 categories of disorders and 30 countries. The CBDE2010 project included estimates of direct medical costs, direct non-medical costs and indirect costs through the human capital method. This entails quantifying the impact on work productivity, and valuing this loss of productivity by the mean wage. This estimate of indirect costs disregards any other value of morbidity and mortality beyond effects on

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<https://doi.org/10.1016/j.cccb.2025.100377>

Received 30 August 2024; Received in revised form 17 December 2024; Accepted 5 January 2025

Available online 9 January 2025

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work productivity.

There have to our knowledge been no similar attempts to estimate the cost of brain disorders globally, perhaps due to the paucity of data from cost-of-illness studies in many world regions. Global costs have however been estimated for individual brain disorders such as Alzheimer's disease (AD). Wimo and colleagues [7] estimated the global costs of AD and other dementia disorders to 1.3 trillion USD in 2019.

Several previous studies have estimated the burden of neurological and mental disorders respectively based on data from the Global Burden of Disease (GBD) study. The GBD study provides information on the prevalence and burden of a large number of conditions for all countries and demographics globally. Deuschl and colleagues used data from the 2017 GBD study to estimate the burden of neurological disorders in Europe reporting that neurological disorders ranked third after cardiovascular diseases and cancers representing 13.3% of total DALYs and 19.5% of total deaths [8]. Bloom et al. estimated the global cost of mental health conditions in 2010 to be US\$ 2.5 trillion, with the cost projected to surge to US\$ 6.0 trillion by 2030 [9]. GBD 2019 Mental Disorders Collaborators estimate that the global number of DALYs due to mental disorders increased from 80.8 million to 125.3 million, and the proportion of global DALYs attributed to mental disorders increased from 3.1% to 4.9% between 1990 and 2019 [10]. These studies based on GBD data do not include the direct medical or non-medical costs of care, but rather provide an estimate only of the indirect costs through approximating an economic value of disability-adjusted life-years (DALYs) through willingness-to-pay. DALYs is a concept that combines burden of illness due to disability and mortality into a single metric. It is composed of two components: years of life lost (YLL), and years of life with disability (YLD). The value of a DALY is often estimated by GDP per capita.

In this study we seek to combine data from these previous studies to obtain a comprehensive estimate of the economic burden of brain disorders. We explore alternative estimates of the indirect costs of brain disorders, the largest and most uncertain component of economic costs. Finally, we discuss the implications of the size and structure of the burden of illness for investment decisions in health care, research and development for new diagnostics and treatments for brain disorders.

Materials and methods

From GBD 2019 we obtained the prevalence rate (per 100,000), the number of disability-adjusted life-years (DALYs) in all age groups, per country, globally. Data was accessed on February 1, 2024.

Our study focused on the estimates in Europe because the data availability of worldwide financial costings was limited, and we derived the annual cost per patient with different brain disorders from the 2010 Cost of Brain Disorders study [11]. For cost calculations we included data for the same 30 European countries as the Cost of Brain Disorders study: Austria, Belgium, Bulgaria, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and United Kingdom.

We defined brain disorders based on a comprehensive list of mental and neurological disorders included in both the GBD2019 and CBDE2010 studies. Data availability and granularity for different disorders varied somewhat between the two studies. When prevalence estimates were available from both studies, we chose the most recent estimates from GBD2019. GBD2019 does not provide specific estimates of prevalence and burden for sleep disorders (insomnia, hypersomnia, narcolepsy, sleep apnea), chronic pain or somatoform disorder. These conditions are highly co-prevalent with other mental and neurological conditions, so we did not include specific DALY estimates for these conditions, however they were included in the assessment of direct costs based on the CBDE2010. We decided to base our study on the GBD2019 data rather than the more recent GBD2021 data set, as the latter was

Table 1

Prevalence of brain disorders in Europe.

	GBD2019	CBDE2010	OUR
Alzheimer's disease and other dementias	8.79	6.34	8.79
Anxiety disorders	29.31	69.06	29.31
Brain and central nervous system cancer	0.20	0.24	0.20
Child/Adolescent disorders			
Attention-deficit/hyperactivity disorder	4.80	3.26	4.80
Autism spectrum disorders	2.64	0.55	2.64
Conduct disorder	1.97	2.12	1.97
Eating disorders			
Anorexia nervosa	0.53	0.82	0.53
Bulimia nervosa	1.28	0.66	1.28
Headache			
Medicine overuse headache		8.31	8.31
Migraine	94.03	49.90	94.03
Other headaches		10.21	10.21
Tension-type headache	183.79	84.89	183.79
Idiopathic developmental intellectual disability	2.14	4.19	2.14
Idiopathic epilepsy	2.39	2.64	2.39
Mood disorders			
Bipolar disorder	4.97	2.99	4.97
Depressive disorders	22.91	30.29	22.91
Motor neuron disease	0.06	0.05	0.06
Multiple sclerosis	0.57	0.54	0.57
Other mental disorders	10.44	8.64	10.44
Other neurological disorders	0.00	0.20	0.20
Parkinson's disease	1.41	1.25	1.41
Schizophrenia	1.77	5.00	1.77
Self-harm	1.70		1.70
Sleep disorders			
Hypersomnia		3.12	3.12
Insomnia		29.18	29.18
Narcolepsy		0.09	0.09
Sleep apnea		12.50	12.50
Somatoform disorder		20.41	20.41
Stroke	7.46	8.24	7.46
Substance use disorder			
Alcohol use disorders	12.54	14.57	12.54
Drug use disorders	5.10	0.97	5.10
Traumatic brain injury		3.75	3.75

greatly affected by COVID-19 pandemic [12].

CBDE2010 included specific cost estimates for rare neuromuscular disorders (CIDP, GBS, MMN, muscular dystrophies, myasthenia gravis, PDN). These were assumed to be included under 'other neurological disorders' in the GBD2019. Similarly, 'other mental disorders' in GBD were assumed to include personality disorders. Further, the GBD2019 did not include estimates for other headaches than migraine and tension-type headache, so other headaches were excluded from DALY estimates.

Self-harm was included in the GBD2019 but not in the CBDE2010. We included the consequences of self-harm in terms of DALYs, but not in terms of direct costs. Traumatic brain injury was not reported separately from other accidents and injuries in GBD2019, and was therefore excluded from the DALY estimates (but included in direct cost estimates).

In the CBDE2010, costs were reported separately for direct health-care costs, direct non-medical costs and indirect costs. We inflated costs reported in CBDE2010 from 2010 to 2019 using the Harmonized Index of Consumer Prices (HICP) for the European Union. The index was 92.49 in 2010 and 105.42 in 2019, so costs were inflated by 14.0%. The total cost per patient for each brain disorder was calculated by adding direct medical costs, direct non-medical costs, and indirect costs. Finally, the total costs of brain disorders in 2019 were calculated by multiplying these costs with the updated prevalence estimates for each brain disorder, as described above.

The CBDE2010 estimate of indirect costs is based on the human capital method, including the value of lost productivity due to morbidity and mortality. As an alternative estimate of indirect costs, we used the

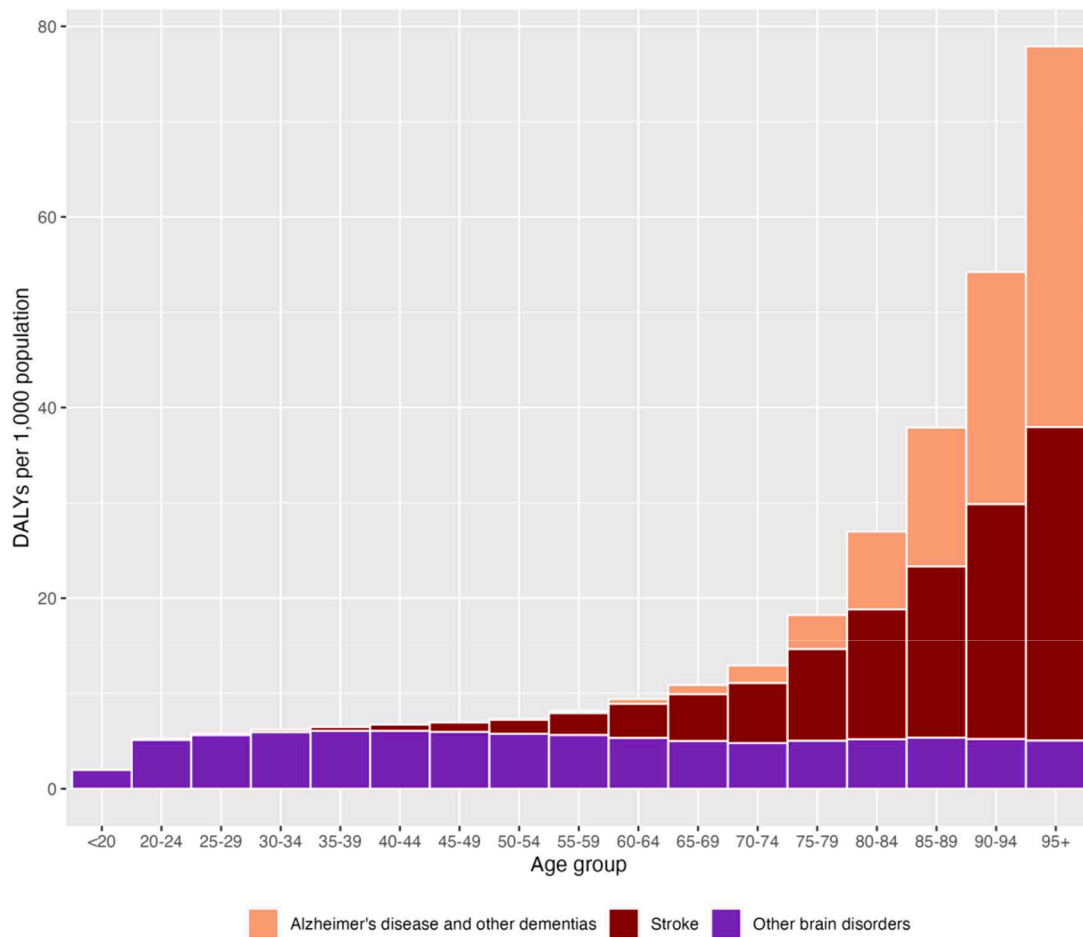


Fig. 1. Age-specific DALYs per 1000 population of different brain disorders.

estimated DALYs from the GBD2019, and assumed the willingness-to-pay for a DALY equal to the annual gross domestic product (GDP) per capita. The purchasing-power adjusted GDP per capita in the European Union in 2019 was 31,300 EUR [13]. Total costs of brain disorders in Europe in 2019 are reported using each of these two valuation principles. We did not consider adding the human capital-based indirect cost estimate and the DALY-based estimate, as this would risk double-counting morbidity and mortality.

Results

Table 1 presents and compares prevalence estimates for the included brain disorders from the GBD2019 and CDBE2010 studies. For many conditions the prevalence estimates were similar, though there were some notable exceptions. The prevalence of tension-type headache and

migraine was considerably high in the GBD study, while anxiety disorders were lower. For drug use disorders the prevalence were more than 5 times higher in the GBD study.

Fig. 1 shows the age-specific burden of different neurological disorders, measured in Disability-Adjusted Life Years (DALYs) per 1000 population. The disorders were categorized into Alzheimer’s disease and other dementias, stroke, and other brain disorders. The burden of Alzheimer’s disease and other dementias and stroke significantly increases with age. For Alzheimer’s disease and other dementias, a notable rise begins in the 65–69 age group, where DALYs reach approximately 5 per 1000 population, peaking in the 95+ age group at around 75 per 1000 population. Similar trends are also observed in stroke with the peak of its burden in the 85–89 age group at approximately 30 DALYs per 1000 population. In contrast, other brain disorders show a relatively stable pattern across the age groups, suggesting they are less influenced by age

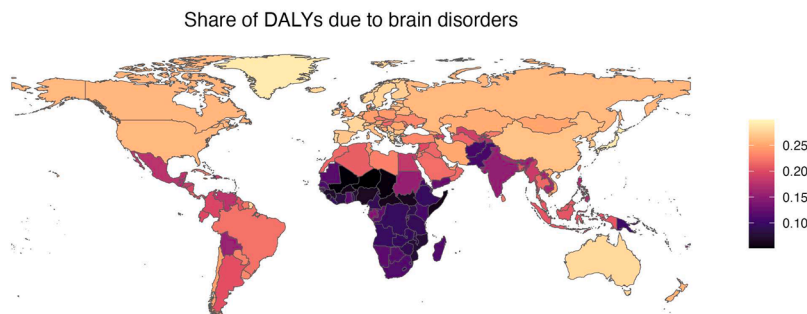


Fig. 2. Share of DALYs due to brain disorders.

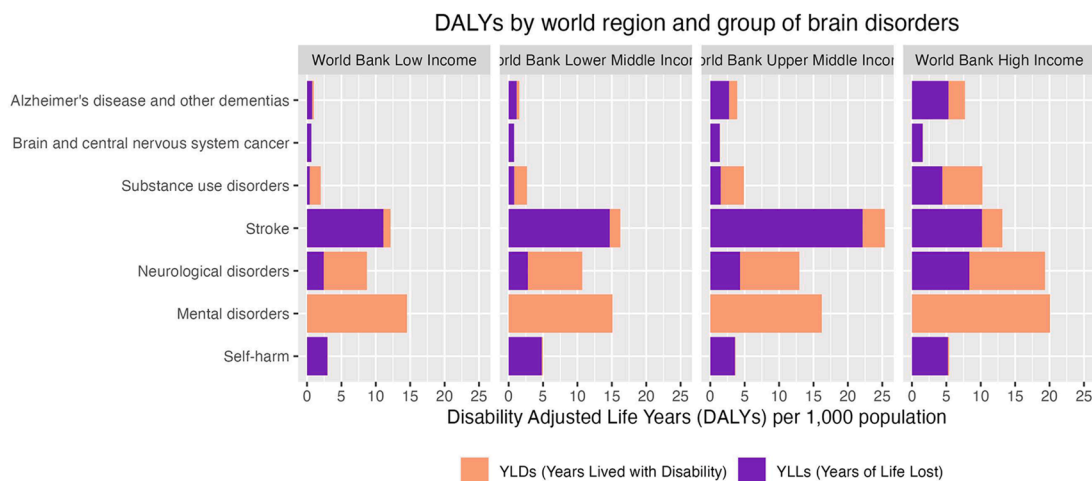


Fig. 3. DALYs by world region and group of brain disorders.

Table 2
Annual cost per patient with brain disorders (EUR).

	Direct cost		Indirect cost			Total cost		
	Health care	Non-medical	Total	HC method	WTP method		HC method	WTP method
					YLL	YLD		
Alzheimer's disease and other dementias	3047	15,856	0	11,090	4945	16,036	18,902	34,938
Anxiety disorders	764	2	462		3108	3108	1228	3874
Brain and central nervous system cancer	15,258	0	9350	170,177	3793	173,970	24,608	189,229
Child/Adolescent disorders								
Attention-deficit/hyperactivity disorder	544	346	0		402	402	890	1292
Autism spectrum disorders	1430	29,642	0		4974	4974	31,072	36,046
Conduct disorder	189	1788	0		4027	4027	1978	6004
Eating disorders								
Anorexia nervosa	809	91	214	254	6996	7250	1115	8151
Bulimia nervosa	17	9	17	20	6940	6959	43	6986
Headache								
Medicine overuse headache	348	0	2264				2611	
Migraine	96	0	326		1245	1245	422	1341
Other headaches	38	0	27				65	
Tension-type headache	27	0	47		80	80	73	107
Idiopathic developmental intellectual disability	7944	3834	0		1548	1548	11,779	13,327
Idiopathic epilepsy	2805	712	2435	4079	7476	11,556	5951	15,073
Mood disorders								
Bipolar disorder	709	638	6841		7011	7011	8187	8358
Depressive disorders	908	517	2031		5658	5658	3458	7084
Motor neuron disease	12,811	13,175	5317	157,193	7026	164,218	31,302	190,205
Multiple sclerosis	11,183	9618	9945	9908	8292	18,200	30,745	39,000
Other mental disorders	881	712	5618		2416	2416	7212	4010
Other neurological disorders	6915	4676	23,429	46,258	22,881	69,140	35,020	80,730
Parkinson's disease	6413	5034	1264	18,414	4649	23,063	12,712	34,510
Schizophrenia	6617	0	14,807		20,878	20,878	21,424	27,495
Self-harm				45,591	1565	47,156		
Sleep disorders								
Hypersomnia	935	0	522				1457	
Insomnia	174	0	0				174	
Narcolepsy	2110	0	4313				6423	
Sleep apnea	1149	0	1264				2413	
Somatoform disorder	533	0	650				1182	
Stroke	5860	2319	683	30,690	5502	36,191	8862	44,371
Substance use disorder								
Alcohol use disorders	1925	1051	1905	2067	3275	5342	4879	8318
Drug use disorders	3620	163	112	3006	5893	8899	3894	12,682
Traumatic brain injury	3074	1018	5949				10,040	

compared to Alzheimer's disease and stroke.

Globally, the number of DALYs due to brain disorders in 2019 was 469.5 million, including 229.4 million years of life lost and 240.1 years lived with disability. This constitutes 18.5% of the total DALYs from all causes globally. Fig. 2 presents how the share of DALYs due to brain disorders is distributed globally. The share of DALYs due to brain

disorders is lower in sub-Saharan Africa, India and some parts of southeast Asia as well as south America.

As shown in Fig. 3, the burden of brain disorders is related to the degree of economic development. The number of DALYs is higher in high-income countries for most categories of brain disorders including substance use disorder, neurological disorders and mental disorders. The

Table 3
Cost of brain disorders in Europe in 2019 (million EUR).

	Direct cost		Indirect cost				Total cost	
	Health care	Non-medical	Total	HC method			HC method	WTP method
				YLL	YLD	Total		
Alzheimer's disease and other dementias	26,786	139,401	0	97,505	43,477	140,982	166,187	307,169
Anxiety disorders	22,384	67	13,531		91,089	91,089	35,981	113,540
Brain and central nervous system cancer	3052	0	1870	34,038	759	34,797	4922	37,849
Child/Adolescent disorders								
Attention-deficit/hyperactivity disorder	2609	1663	0		1929	1929	4271	6200
Autism spectrum disorders	3782	78,374	0		13,151	13,151	82,156	95,307
Conduct disorder	373	3530	0		7947	7947	3903	11,850
Eating disorders								
Anorexia nervosa	425	48	113	134	3675	3808	586	4281
Bulimia nervosa	22	12	22	25	8865	8889	55	8923
Headache								
Medicine overuse headache	2889	0	18,810				21,698	
Migraine	9003	0	30,653		117,097	117,097	39,656	126,100
Other headaches	384	0	279				663	
Tension-type headache	5028	0	8589		14,655	14,655	13,616	19,682
Idiopathic developmental intellectual disability	17,034	8221	0		3320	3320	25,255	28,575
Idiopathic epilepsy	6692	1699	5808	9731	17,836	27,567	14,199	35,958
Mood disorders								
Bipolar disorder	3526	3175	34,028		34,872	34,872	40,730	41,573
Depressive disorders	20,808	11,853	46,525		129,606	129,606	79,187	162,268
Motor neuron disease	778	801	323	9551	427	9978	1902	11,557
Multiple sclerosis	6368	5476	5663	5642	4722	10,363	17,507	22,207
Other mental disorders	9200	7436	58,639		25,212	25,212	75,274	41,848
Other neurological disorders	1411	954	4781	9440	4669	14,109	7147	16,475
Parkinson's disease	9069	7120	1788	26,040	6575	32,615	17,976	48,803
Schizophrenia	11,720	0	26,228		36,982	36,982	37,948	48,702
Self-harm				77,483	2660	80,143		
Sleep disorders								
Hypersomnia	2919	0	1631				4550	
Insomnia	5089	0	0				5089	
Narcolepsy	193	0	395				588	
Sleep apnea	14,356	0	15,794				30,150	
Somatiform disorder	10,889	0	13,262				24,152	
Stroke	43,719	17,306	5094	228,977	41,048	270,025	66,119	331,050
Substance use disorder								
Alcohol use disorders	24,142	13,179	23,885	25,922	41,072	66,994	61,205	104,315
Drug use disorders	18,470	832	570	15,338	30,069	45,407	19,872	64,709
Traumatic brain injury	11,520	3815	22,293				37,628	
Total	294,640	304,962	340,574	539,826	681,714	1221,537	940,172	1688,941

number of life years lost due to stroke increases from lower income countries to upper middle-income economies.

Table 2 shows the estimated annual direct and indirect cost per patient for different brain disorders in Europe. Costs are subdivided by direct costs for health care and non-medical care, respectively, and indirect costs. Two alternative methods were used to estimate indirect costs: the human capital (HC) method, based on data from the CBDE2010 study, and the willingness-to-pay per DALY (WTP) method, based on data from GBD2019. As expected the WTP method yielded higher or much higher cost estimates for most conditions. The exception was mental disorders, which could be explained by the GBD2019 study not including lost life years for these conditions. If self-harm is included under mental health, the WTP method would yield far higher results. The most costly condition per patient were CNS cancers, motor neuron disease and 'other neurological disorders' which includes e.g. rare neuromuscular disorders.

Table 3 presents the aggregated costs of brain disorders in Europe in 2019, by combining the prevalence estimates in Table 1 with the estimates of cost per patient from Table 2. Alzheimer's disease and other dementias is the costliest condition using the HC method by a wide margin. Using the WTP method, stroke is the costliest condition due to the large number of life-years lost, followed by Alzheimer's disease. The estimated total cost of brain disorders in Europe varied from 940 billion EUR with the HC method to 1.7 trillion EUR with the WTP method.

Discussion

In this study we attempt to estimate the cost of brain disorders by applying two different approaches to valuing indirect costs. For brain disorders, the economic impact of the disability and loss of life caused by these conditions outweighs the direct costs for diagnosis, treatment and care, therefore the principals used to value the indirect costs have important consequences for the results. Using per-capita GDP as a proxy for willingness to pay per DALY results in almost four times as high indirect costs as the (conventional) human capital approach, which only values lost work productivity due to morbidity and mortality. In economic evaluations of new treatments or other medical technologies, health gains are typically evaluated separately from costs, therefore the value from lost life-years or disability is not included in the cost estimate to avoid double-counting these effects. However, in COI studies where the purpose is to illustrate the full societal impact of disease, it can be argued that these 'intangible costs' should be included.

An important conclusion of these results is that only a small fraction of the costs of brain disorders are affecting the health care systems. The vast majority of costs are outside of health care – even in high-income countries with advanced, universally accessible health care systems such as in Europe. For example, less than 10% of the costs of AD and other dementias are incurred by the health care system, using the WTP method. This means that health care systems may not be fully incentivized to invest in treatment and prevention of brain disorders, as most of the gains from treatment and prevention lie elsewhere. Further, there

is also likely underinvestment in R&D for brain disorders. As an example, the total spending on clinical trials in AD over the past several decades has been estimated to around 40 billion USD [14]. This can be contrasted with the estimated cost of AD and other dementias in a single year of over 300 billion EUR, in Europe alone.

We found the increasing burden of neurological disorders with age, with Alzheimer's disease and other dementias and stroke, which aligns with the findings of previous research [15,16]. The sharp increase in economic burden in older age highlights the increasing importance of public health interventions targeting these conditions. Notably, stroke is also recognized as a potential risk factor for dementia [17], suggesting that interventions aimed at improving cardiovascular health could provide a dual benefit by reducing the burden of both stroke and dementia among older population. This is also supported by the FINGER project, emphasizing that healthy lifestyle prevention can lower the risk of both cardiovascular disease and dementia [18,19]. This prevention initiative, rooted in primary care, integrates cardiovascular health management into dementia prevention strategies. Additionally, further studies on health economic evaluations are also needed to assess the cost-effectiveness of such lifestyle prevention initiatives for dementia by incorporating the effect of cardiovascular diseases [20]. In sum, the findings in this study emphasize the important role of cardiovascular health in lifestyle prevention of dementia in the context of the aging population. By addressing the shared risk factors among older adults, we can potentially reduce the burden of both stroke and dementia, improving the quality of life for older adults and alleviating the strain on healthcare systems.

Limitations

We were not able to produce a global estimate of the cost of brain disorders, as estimates for direct costs are lacking for large regions. The GBD2019 study did not include mortality due to mental disorders. Arias, Saxena and Verguet (2022) proposed a method to include years of life lost due to mental disorders through a population attributable fraction approach [21]. Therefore, we decide not to replicate this approach here. Additionally, the cost of brain disorders were summarized only for the European region because the aim of this study is to update the evidence of the existing European literature [11]. A global systematic review is anticipated and could provide more information for the burden of brain disorders.

CRedit authorship contribution statement

Yunfei Li: Writing – review & editing, Writing – original draft, Conceptualization. **Linus Jönsson:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

We declare we have no potential competing interests.

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