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RESEARCH ARTICLE

Epidemiology of Alzheimer's disease and other dementias: rising global burden and forecasted trends [version 1; peer review: awaiting peer review]

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Abstract

Background: The burden associated with Alzheimer's disease is recognized as one of the most pressing issues in healthcare. This study aimed to examine the global and regional burden of Alzheimer's disease and related dementias.

Methods: Epidemiological data from the latest Global Burden of Disease (GBD) dataset were analysed to determine the prevalence, incidence and mortality rates from 1990 to 2019 for 204 countries and world regions. This dataset derives estimates for health metrics by collating primary data from research studies, disease registries and government reports. Temporal forecasting was conducted using the GBD Foresight tool.

Results: An estimated 0.7% of the global population has dementia, translating to 51.6 million people worldwide. The total number of persons affected has more than doubled from 1990 to 2019. Dementia metrics showed a continuous increase in prevalence, incidence, mortality, and disability adjusted life years (DALYs) rates worldwide during the last three decades. Japan has the highest prevalence (3,079 cases per 100,000), followed by Italy, Slovenia, Monaco, Greece and Germany. The prevalence is higher in high-income regions such as Western Europe compared to Asia and Africa. However, total number of affected individuals is substantial in South and East Asian regions, in particular China, Japan and India. Dementia related deaths are projected to increase from the current 2.4 million per year to 5.8 million by 2040. Women are more likely to be affected by dementia than men. Age-standardized rates have not changed indicating possible stability of risk factors.

Conclusions: Alzheimer's disease and other dementias are rising rapidly and will more than double in mortality burden over the next 20 years. The tremendous burden in high- and middle-income countries

can potentially overwhelm communities and health systems. Urgent measures are needed to allocate funding and provide residential care for affected persons.

Keywords
Alzheimer's disease, dementia, epidemiology, prevalence, mortality, vascular dementia, Lewy body disease, frontotemporal lobar degeneration, neurocognitive disorders, mild cognitive impairment

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Introduction

Dementia remains one of the leading causes of morbidity and mortality worldwide[1]. The condition exerts a profound negative impact on families, communities and health care systems alike[2]. The World Health Organization (WHO) estimates that there are 10 million new cases of dementia each year[3]. Hence, the financial implication of the condition—arising from both the direct medical and social care costs as well as the cost of informal care—is equivalent to 1.1% of the global gross domestic product (GDP)[4]. Those affected by dementia and their informal caregivers also face difficulties and suffer poor health outcomes that are persistent[5,6]. People living with dementia and their informal caregivers are more likely to be diagnosed with comorbidities and subsequently experience poorer access to health and social care services when compared to their unaffected counterparts[7,8]. Research also demonstrates that people living with dementia are disproportionately more likely to report a poor quality of life[9]. This reduced quality of life and other inequalities in outcomes are recognized to be driven by factors such as economic hardship and social isolation that are ultimately caused by the stigma associated with this condition[10]. Thus, those affected represent a vulnerable population group that could be better served by changes within healthcare and social services systems.

The burden associated with Alzheimer's disease is now recognized as one of the most pressing issues in the field of public health. There is an urgent need for health care systems to identify novel and innovative solutions to meet the needs. The World Health Assembly (WHA) recently endorsed the "Global action plan on the public health response to dementia 2017–2025," calling for renewed efforts to increase awareness, research and innovation to tackle this urgent public health issue[3]. However, an effective response to the challenges arising from dementia first requires an accurate understanding of the patterns of prevalence and burden of dementia[11,12].

The aim of this study was to analyse the global and regional burden as well as trends and forecasts for Alzheimer's disease and related dementias. As a unique contribution, this study assessed yearly trends using age-standardized rates to control for the effect of population aging.

Methods
Data source

Based on the aim of study, the inclusion criteria for data included prevalence, incidence, mortality rates of dementia for global, regional and national levels. Exclusion criteria included subnational data such as hospital-based records and neurological diseases other than dementia such as Parkinson's disease and stroke. We extracted health metrics on dementia from the Global Burden of Disease (GBD) dataset. GBD is the largest and most up-to-date repository of epidemiological data for any given condition including dementia[13]. GBD 2019 release has data on 204 countries for 286 causes of death. The robustness of this dataset stems from its reliance on a wide range of primary sources, independent research studies, government reports, vital registration, verbal autopsies, disease registries, healthcare projects and census data. GBD 2019 utilized 990 primary data sources related dementia to develop its estimates. Based on statistical modelling from these data sources, GBD produces reliable estimates of health metrics. Furthermore, GBD incorporates modelling adjustment to address data sampling issues, missing data and variations in case definition. The methods used are compliant with Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER statement).

Data variables

Health metrics analysed in the present study included prevalence, incidence, mortality and disability-adjusted life years (DALY). DALY is a better measure of human suffering from a disease than prevalence or mortality, as it combines years lived with disability and the years of life lost due to premature death. Data for dementia were obtained from GBD using the Results tool. Dementia is listed under Neurological Disorders in GBD and coded as B.5.1 Alzheimer's disease and other dementias. Data visualization was conducted in Microsoft Excel 2016 as well as the GBD Compare tool. Sub-classification of dementias such as vascular, frontotemporal and dementia with Lewy bodies was not available in this dataset. Epidemiological data on mild cognitive impairments was not included in the GBD.

Data analysis

Data were analysed using GBD analytical tools including visualizations and forecasting. These tools were utilized in order to achieve the highest fidelity. We analysed both raw and age-adjusted rates of dementia prevalence and incidence. Age-standardized rates remove the effect of population age across countries as well as over time, thus enabling inferences about intrinsic changes in dementia burden. Age of onset of dementia was inferred from age-specific incidence rates. We sought to assess whether the age of onset was decreasing over time by comparing figures from 1990 with those from 2019. Forecasting for projections for the next 20 years was achieved using the GBD Foresight tool, with the following settings: scenario: reference; uncertainty: off; rank: off; and age: all ages (unstandardized). Statistical data analysis was conducted using SPSS version 26 (IBM Inc., Armonk, NY, 2019). Paired samples t-tests were used to compare differences in prevalence rates across gender and to evaluate changes in incidence rates over from 1990 to 2019. An alpha level of 0.05 was considered statistically significant.

Results
Prevalence

The global prevalence of dementia was 0.69% [uncertainty interval (UI); 0.59, 0.79] of the world population in 2019 (Table 1). The total number of persons affected has more than doubled from 1990 to 2019: increasing from 20.5 million to 51.6 million [UI; 44.2, 59.0 million] globally. The worldwide prevalence rate for all forms of dementia was 667.2 cases per 100,000 persons [UI; 572.2, 762.8]. In comparison to other major neurological diseases, the prevalence of dementia was considerably higher. For example, the prevalence of Parkinson's disease was 110 cases, and multiple sclerosis 22.7 cases per 100,000 persons. Women

Table 1. Burden of Alzheimer's disease and other dementias.

Region	Prevalence (cases per 100,000 population)	The burden of human suffering (DALY per 100,000)	Total number of cases
Global average	667	327	51,624,000
Europe	1,443	689	12,251,000
Russia	1,150	515	1,686,000
Germany	1,864	836	1,582,000
Italy	2,270	1,110	1,369,000
France	1,698	881	1,124,000
United Kingdom	1,241	651	834,000
Asia	598	297	27,230,000
China	924	420	15,299,000
Japan	3,079	1,613	4,579,000
India	266	153	4,249,000
South Korea	1,119	537	685,000
Iran	559	271	542,000
Americas	938	439	9,474,000
United States	1,495	618	4,902,000
Canada	1,459	666	532,000
Mexico	430	272	537,000
Brazil	786	395	1,702,000
Argentina	839	393	378,000
Africa	197	108	2,591,000
South Africa	381	192	211,000
Nigeria	124	84	266,000
Egypt	299	137	295,000
Algeria	461	228	193,000
Morocco	485	240	174,000

Notes: selected countries shown in this table (all countries were included in the analysis). Data from Global Burden of Disease, 2019. DALY, disability-adjusted life years.

were more likely to be affected by dementia than men. For instance, among persons over the age of 80, the prevalence rate among women was 20,244 per 100,000 [UI; 16,661, 34,236] compared to 14,378 per 100,000 [UI; 11,667, 17,478] in men.

Across regions, high-income Asia Pacific had the highest prevalence followed by Europe, Austrasia and North America (Figure 1). South Asia and Africa ranked the lowest in terms of prevalence of dementia. The highest prevalence rates in descending order were: Japan (3,079 cases per 100,000 population), Italy (2,269 cases per 100,000), Slovenia (1,963 cases), Monaco (1,962 cases), Greece (1,874 cases), and Germany (1,863 cases

per 100,000). In terms total number persons living with dementia, China (13.1 million cases), United States (4.9 million), Japan (3.9 million), India (3.6 million) and Brazil (1.7 million) have the highest burden in the world.

Trends
Dementia metrics showed a continuous increase in prevalence, incidence, mortality, and disability adjusted life years (DALYs) rates worldwide during the 29 years of estimates from 1990 to 2019. Certain regions, such as Western Europe, showed a faster rate of rise than the global average. Japan, in particular, experienced a marked increase in prevalence rates, from
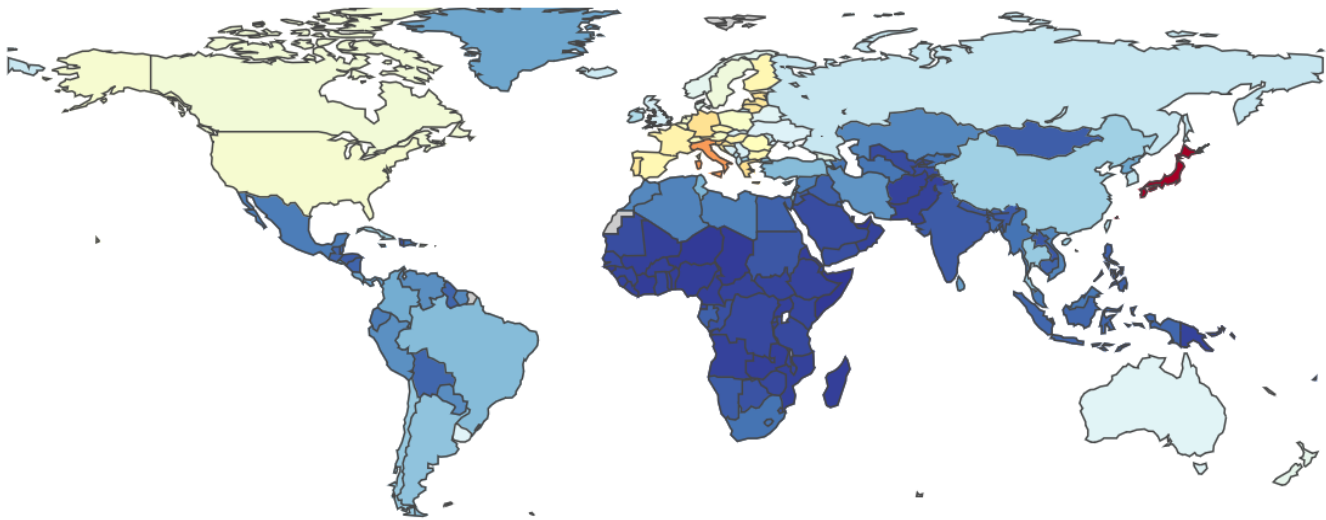
Figure 1. Global burden of Alzheimer's disease and other dementias. Notes: prevalence rates per 100,000 population by country. Red, orange and yellow shades indicate higher prevalence. Source: Global Burden of Disease, 2019.

772 cases per 100,000 population in 1990 to 3,079 per 100,000 in 2019. Thus, the total number of cases continued to rise with population growth and aging.

As prevalence rates are affected by the proportion of elderly in a population, we used age-standardized rates to aid in comparisons between countries. Age standardization adjusts for any differences in underlying population age distributions. After age-standardization (to control for the effect of population aging), incidence and prevalence rates appeared to remain stable during the same period (Figure 2). Hence, there appeared to be no intrinsic increase in rates of dementia after controlling for population aging.

Age of onset
The age distribution of new cases showed incidence starting from the latter half of the fifth decade of life. The age distribution of new cases of dementia has not changed since 1990 (Figure 3A). As expected, the incidence was highest at older ages (Figure 3B).

Mortality
Mortality rates have been rising rapidly and continuously since 1990. The global death rate due to dementia increased from 10.49 deaths per 100,000 in 1990 to 20.98 deaths per 100,000 in 2019 [UI; 5.27, 54.36]. Statistical forecasting showed a rising rate reaching 66.4 deaths per 100,000 [UI; 51.6, 85.2] by 2040. Most regions are forecasted to continue to follow this rising trend over the next 20 years. The highest death rates due to dementia are expected in Japan at 265 deaths per 100,000 population by 2040. Total deaths due to dementia are projected to increase from the current 2.4 million per year to 5.8 million by 2040 [UI; 4.5, 7.5 million].

Discussion
This study adds important insights on the global burden of dementia and its predicted trajectory. Based on the latest data from GBD, three key findings have emerged from our analysis. The incidence of dementias is rising especially in Western Europe and Japan. A large burden of dementia (total number of cases) was present in developing countries. When standardized for population aging, the rates are stable. These findings have considerable implications for the health and social care sectors, which need to adapt and prepare in advance to meet the rising demand.

The burden arising from Alzheimer's disease and other dementias is acknowledged to be markedly high when compared to other non-communicable conditions affecting older age groups[14]. The associated burden of care correlates with the severity of dementia as the subsequent cognitive and functional decline negatively impacts the affected individual's ability to be independent and engage in activities of daily living[15,16]. These factors combined with rising prevalence rates due to population growth and aging as well as the absence of curative therapies forecast a bleak picture of the future. It is not surprising that dementia has now become the focus of public health policy and research[16–18].

Japan depicts a grim case study of the social burden of dementia. Our analysis revealed a rapid increase in prevalence and mortality rates from 1990 to 2019, and a forecasted meteoric rise over the next two decades. The proportion of Japanese people over the age of 65 is now 26.7%[19]. Consequently, meeting the healthcare demands of the aging population has become a public health priority. However, the rising demand can easily overwhelm healthcare and social services capacity[20].
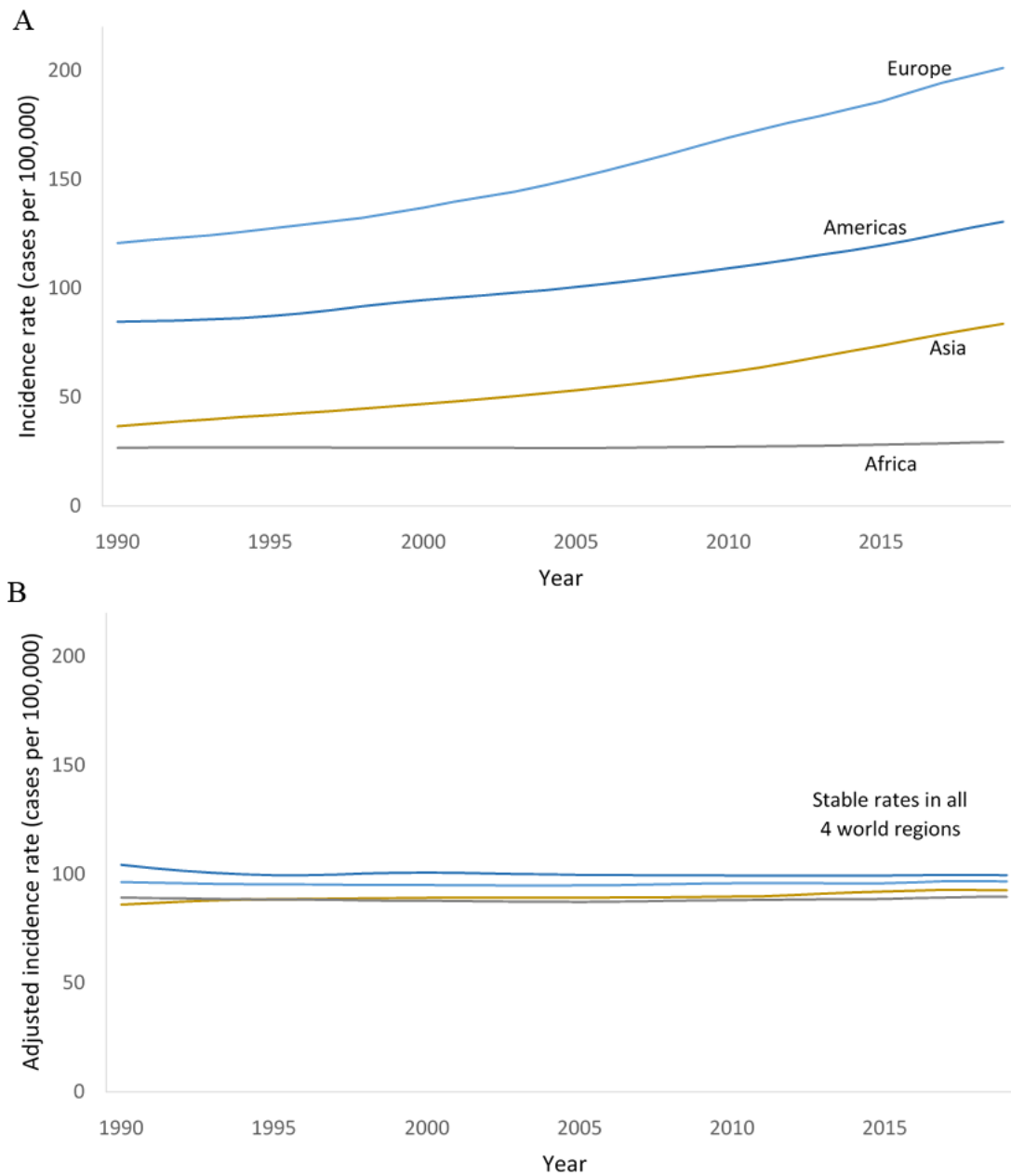
Figure 2. Trends in the burden of dementia. (**a**) Incidence (unadjusted rates). (**b**) Age-standardized incidence.

The number of residential care homes in Japan for people living with dementia remains suboptimal and the accessible care available is provided in hospital settings[16–18]. Hospital environments have long been considered inappropriate for long-term care of those affected. These issues raise serious concerns about how countries such as Japan and those in Western Europe will meet this ever-increasing burden of dementia, perhaps representing the greatest challenge for their current and future health care systems. On the other hand, it is important to recognize that the lower prevalence rates of dementia found in certain regions

such as South Asia may arise from lack of accessible healthcare services. All forms of dementia are underdiagnosed[21]. Amongst other factors, the lack of accessible health care may impede timely recognition[18,19].

A novel finding emerging from our analysis is the stability of age-standardized rates. This implies that (apart from age) risk factors for dementia have remained constant over the last three decades. The stability of age-standardized prevalence rates over time may be a reflection of age continuing to represent
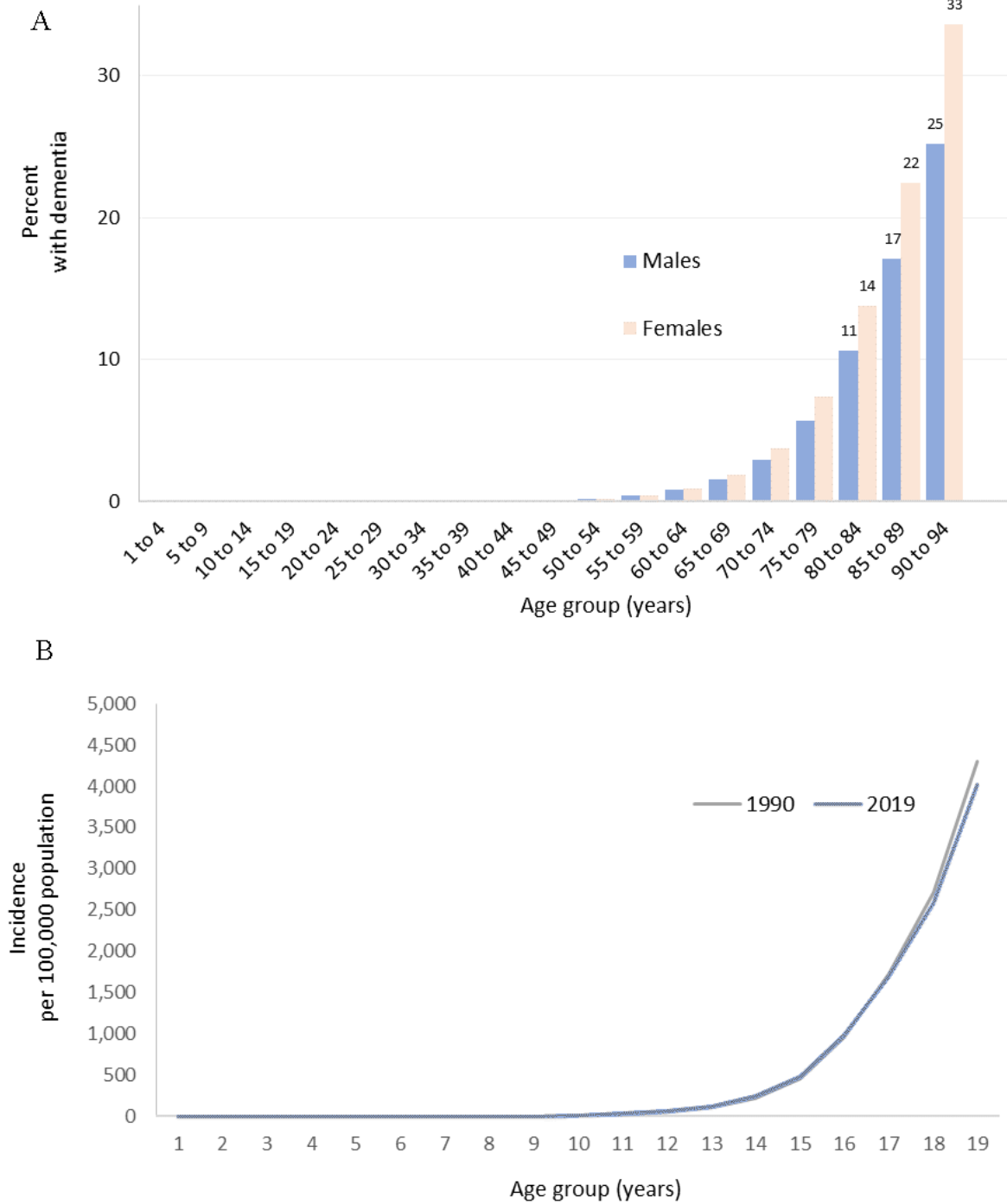
A

B

Figure 3. Age distribution of dementia. (**a**) Prevalence (per 100 persons) by gender. p = .059, paired samples t-test, comparing prevalence in each age group for males and females. (**b**) Incidence (age of onset of new cases) change over three decades. p = .33, paired samples t-test, comparing incidence in each age group for 1990 and 2019.

the strongest predictor of dementia[22]. Epidemiological studies exploring the relationship between age and dementias have found that the rate of cognitive decline is 10 times greater during the last three years of life, irrespective of the country of residence[22]. Potential risk factors such as diabetes, hypertension, smoking, sedentary lifestyle and obesity are rising globally, and yet are not reflected in age-standardized rates of dementia. The reasons for this remain unresolved. Insights from certain studies indicate that obesity affects dementia selectively[23]. A national registry-based study from Denmark indicated a steady decline incidence since 2003[24]. These results have not been consistently reported in other regions. It is possible that improvements in dietary intake, physical activity level and reductions in tobacco consumption may contribute to these remarkable trends[25].

This study is subject to a few limitations. Country-level comparisons are generalizations that are susceptible to ecological bias. The GBD dataset relies on multiple sources that adopt heterogeneous methodologies including varying case definitions, which can make comparisons less robust. However, statistical modelling techniques employed by GBD adjust for these potential sources of error. At present, GBD provides the most comprehensive and current data available on the burden of dementia.

Conclusions

Dementia now represents one of the most pressing issues facing global public health resulting in a burden of care that profoundly impacts families, communities, and healthcare systems alike. Our findings can be used to inform policies and global health agendas that direct the allocation of resources with a need to address and support specific subgroups and regions. Research is needed to identify mild cognitive impairment and early markers of disease progression[26]. Future research needs to explore differences in prevalence rates of the various forms of dementia and the associated care burden. There remains an urgent need for public health initiatives that aim to promote

healthier living among older populations in recognition of the many risk factors now associated with the development of dementia. Otherwise, several countries provide a stark example of the potential for healthcare systems to become overwhelmed.

Data availability

Source data

The data used in this study was obtained from the Institute of Health Metrics and Evaluation, University of Washington. http://ghdx.healthdata.org/ihme_data. The search term used was: B.5.1 Alzheimer's disease and related dementias.

Data are available under the terms of the Open Data Commons Attribution License.

Underlying data

Open Science Foundation: Dementia. https://doi.org/10.17605/OSF.IO/DYBTM[27].

This project contains the following underlying data:

- Supplementary Appendix – Dementia 2019 data (numeric estimates for prevalence, incidence, mortality and DALYs)

Reporting guidelines

Open Science Foundation: GATHER checklist for 'Epidemiology of Alzheimer's disease and other dementias: rising global burden and forecasted trends'. https://doi.org/10.17605/OSF.IO/DYBTM[27].

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