

Global burden of dementia in younger people: an analysis of data from the 2021 Global Burden of Disease Study



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Summary

Background Dementia among younger people is rapidly emerging as a global health concern; however, comprehensive research on its shifting burden trends remains insufficient.

Methods Data on the prevalence, incidence, mortality, and disability-adjusted life years (DALYs) associated with dementia occurring in individuals <70 years were extracted from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021. Average annual percentage changes (AAPCs) were calculated to assess trends in age-specific rates (ASRs), including age-specific prevalence rates (ASPRs), age-specific incidence rates (ASIRs), age-specific mortality rates (ASMRs), and age-specific DALY rates (ASDRs) while young-onset dementia (YOD) burden trends were analyzed. The correlation between ASR/AAPC and the sociodemographic index (SDI) was evaluated.

Findings In 2021, the global prevalence of dementia in individuals <70 years increased by 122.33%, with a 128% increase in new cases since 1990. Concurrently, deaths and DALYs of individuals <70 years with dementia rose by 119.28% and 119.77%, respectively. The AAPCs of YOD ASRs during 1990–2021 initially increased and then decreased with increasing SDI levels, with the highest AAPCs of ASPR (2.20 [95%CI: 2.08–2.32] per 100,000), ASIR (2.25 [95%CI: 2.06–2.45] per 100,000), ASMR (2.04 [95%CI: 1.93–2.15] per 100,000), and ASDR (2.06 [95%CI: 1.99–2.13] per 100,000) observed in middle-SDI levels. Additionally, females <70 years bore a higher burden of dementia globally, and gender differences are still widening.

Interpretation The growth rate of YOD is accelerating, particularly in the middle to high SDI region with females bearing a disproportionately higher burden of YOD.

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Introduction

The incidence of dementia increases with age and thus is commonly perceived as a disease among the elderly.¹ However, recent studies have highlighted the prevalence of young-onset dementia (YOD),^{2–4} indicative of symptom onset at a younger than usual age.^{5–7} Two meta-analyses conducted in 2021 determined the global age-standardized prevalence and incidence rates of YOD as 119 and 11 per 100,000, respectively, and nearly 3.9

million people aged 30–64 years live with dementia worldwide.^{8,9} Undoubtedly, YOD is rapidly emerging as a major global health challenge. Owing to its earlier onset, dementia among young patients places a greater burden on patients, their families, and society.^{10,11} However, reports on deaths and the DALY burden caused by dementia in younger patients are currently limited. Furthermore, the prior meta-analysis data used for global dementia among the younger group predominantly

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Research in context

Evidence before this study

Dementia is a global challenge. Although commonly associated with the older, the impact of dementia on the younger should not be overlooked. In order to gather existing evidence, we searched PubMed, and Web of Science database, from database inception to May 31, 2024, for papers published in English, using the terms (“dementia”OR“young-onset dementia”OR“early-onset dementia”), AND (“GBD” OR “global disease burden”). Our search yielded 1338 results. Past epidemiological estimates of global young-onset dementia (YOD) were analysis primarily sourced from published research reviews from 1980 to 2018. Moreover, previous data lacks reporting on the burden of young-onset dementia in different regions. These studies highlighted the highest prevalence of dementia among 30–64 is increasing.

Added value of this study

This is the first study to systematic estimate the burden of global dementia death on people under 70/65 by SDI level, region, sex and age during 1990–2021. Our research indicates

that, across the last thirty years, the prevalence, incidence, mortality, and DALYs cases of dementia in individuals under 70 have doubled, particularly in middle to high SDI region. The study unveils the uneven global distribution of YOD and significant gender disparities. Of particular significance is the employment of Joinpoint regression analysis in the study to examine temporal patterns in the burden of dementia under 70/65, identifying crucial instances where significant shifts in disease indicators occurred.

Implications of all the available evidence

These results offer the newest and most reliable understanding of YOD's disease burden, serving an international community of healthcare practitioners such as doctors, health policymakers, epidemiologists, and YOD-focused researchers. By emphasizing the vital necessity for ongoing enhancements in diagnosing, treating, and managing YOD, the study promotes the refinement of strategic interventions and the pursuit of novel therapeutic methodologies.

originated from Europe and North America over a substantial timeframe, potentially introducing bias into the results. More importantly, analysis is also lacking on the trend of the dementia burden in younger groups.

As the number of dementia cases among younger individuals increases,¹² quantifying the dementia burden in these individuals is essential to inform effective policy decisions and health system planning. Herein, we aimed to estimate the trends in dementia-related prevalence, incidence, deaths, and disability-adjusted life-years (DALYs) in people <70 and 65 years old from 1990 to 2021 by region, age, gender, and sociodemographic index (SDI). These findings pave the way for strategic and coordinated actions to enhance health and social security.

Methods

Data sources

This study assessed the prevalence, incidence, mortality, and DALY burden of dementia using data from the 2021 Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) (<https://vizhub.healthdata.org/gbd-results/>), adhering to the GBD protocol and the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).¹³ The GBD is the most extensive ongoing project to estimate the global disease burden and is updated every 2–3 years. For the 2021 version, the GBD used a vast array of data sources, including surveys, censuses, vital statistics, and other health data, to estimate the incidence, prevalence, and DALYs. Specifically, 36,916 and 22,236 data sources were used for incidence and prevalence, respectively,

while 100,983 data sources (19,189 new sources in 2021) provided DALY estimates. The GBD 2021 estimated the burden of disease from 288 causes of death, 371 diseases and injuries, and 88 risk factors across 204 countries and territories, 18 subregions, and five SDI regions.^{14,15} The SDI, an indicator representing fertility rates among females <25 years, average years of education for individuals >15 years, and lag-distributed income per capita, is estimated to represent a comprehensive development status that exhibits a robust correlation with health outcomes.^{15,16} Detailed descriptions of the methodology for estimating the burden of diseases in GBD 2021 can be found in the Appendix.

In this study, the categories of dementia are referred to as “Alzheimer’s disease (AD) and other dementias” in the 2021 GBD. A total of 254 data points were collected to determine the prevalence of Alzheimer’s disease and other types of dementia.¹⁷ Definitions for estimating the burden of AD and other types of dementia were based on the criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III, DSM-III-R, DSM-IV, DSM-5, and the International Classification of Diseases (ICD)-8, ICD-9, or ICD-10.^{18,19} The term YOD indicates dementia with symptom onset at a younger than usual age, with onset occurring at 60, 65, or 70 years old according to different studies.^{5–7,20,21} Herein, the dementia-related burden occurring <70 years was considered as the YOD burden initially caused by AD. We also analyzed dementia in patients aged <65.

Risk factors for dementia

The GBD study estimated the burden of dementia in individuals <70 years attributable to three risk factors:

high body mass index (BMI), high fasting plasma glucose (HFPG), and smoking.²² Each risk factor has a theoretical minimum risk exposure level (TMREL), representing the level at which the risk of health outcomes is the lowest. The TMREs for each risk factor were 4.8–5.4 mmol/L for HFPG, 20–25 kg/m² for BMI, and zero for smoking.^{22,23}

Data analysis

The prevalence, incidence, mortality, and DALY of patients with dementia <70 and 65 years were evaluated according to location, age, and gender. The average annual percentage changes (AAPC), calculated using a generalized linear model to describe the age-specific prevalence rate (ASPR), age-specific incidence rate (ASIR), age-specific mortality rate (ASMR), and age-specific DALY rate (ASDR) trend over time, were used to quantify the trends in YOD burden.²⁴ AAPC values indicate the annual percentage change (increase, decrease, or no change). Joint point analysis of the entire range (1990–2021) was used to reflect the full trend of the YOD burden.²⁵ The relationship between ASR/AAPC and SDI was evaluated using Spearman's rank-order correlation. Gender differences were calculated by subtracting the ASR of prevalence, incidence, mortality, and DALYs in women from those in men.²⁶ In addition, the population-attributable fraction (PAF) was used to quantify the proportion of deaths and DALY attributable to specific risk factors.

The 95% confidence interval, based on 1000 draws from the posterior distribution of each step in the estimation process, was calculated using the 2.5th and 97.5th percentiles of the ordered 1000 values. All statistical analyses were performed using the R software (version 4.2.1). Significance was set at $P < 0.05$.

Ethics

Due to the use of publicly available data that does not contain confidential or personally identifiable information, the institutional review board has granted an exemption for this study.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Global dementia burden in individuals <70 years during 1990–2021

The global prevalence of dementia in individuals <70 years increased by 122.33%, rising from 5.91 million in 1990 to 13.14 million in 2021. This corresponded to an age-specific prevalence rate increase of 54.25%, growing from 115.17 per 100,000 to 177.66 per 100,000. During the same period, the proportion of prevalence attributed to

individuals <70 years decreased from 27.11% to 23.11%. Substantial changes in the prevalence of dementia in individuals under <70 years occurred in 2003, 2010, and 2015. The most significant period of increase in age-specific prevalence rate occurred between 2010 and 2015, with an AAPC of 2.66 (95%CI: 2.35–2.98). Globally, the incidence of dementia in individuals <70 years rose by 128%, increasing from 1.00 million to 2.28 million during the past three decades. This corresponds to an age-specific incidence rate increase of 56.75%, from 19.63 per 100,000 to 30.77 per 100,000. The period from 2010 to 2015 exhibited the highest growth rate (AAPC: 2.55 [95%CI: 2.09–3.02]) (Figs. 1 and 2 and Supplementary Table S1).

The adverse consequences, deaths, and DALY cases of dementia in individuals <70 increased by 119.28% and 119.77% during 1990–2021, respectively. Meanwhile, the age-specific mortality rate increased by 51.77%, rising from 1.41 per 100,000 to 2.14 per 100,000, and the age-specific DALY rate increased by 52.67%, rising from 61.11 per 100,000 to 93.30 per 100,000. Similar to prevalence trends, highest growth rate of age-specific mortality rate (AAPC: 2.86 [95%CI: 2.63–3.10]) and age-specific DALY rate (AAPC: 2.69 [95%CI: 2.50–2.87]) occurred during 2010–2016 (Figs. 1 and 2 and Table 1).

Dementia burden in individuals <70 years stratified by SDI between 1990 and 2021

The proportion of individuals with a dementia burden <70% of the total dementia burden was inversely correlated with the SDI. In 2021, the dementia burden in individuals <70 years accounted for 35.20%, 35.77%, 16.24%, and 31.02% of the total prevalence, incidence, death, and DALYs in low-SDI areas, respectively (Fig. 1a).

Consistent with global trends, the ASRs of YOD prevalence, incidence, deaths, and DALYs increased in most sub-SDI regions (Fig. 1). The ASRs for YOD initially increased and then decreased with increasing SDI levels ($P < 0.05$) (Supplementary Fig. S1). The highest age-specific prevalence rate (287.85 [95%CI: 239.17–343.96] per 100,000), age-specific mortality rate (3.25 [95%CI: 0.72–8.29] per 100,000), and age-specific DALY rate (143.97 [95%CI: 68.89–318.76] per 100,000) in 2021 were observed in high-SDI regions, whereas the highest age-specific incidence rate (48.78 [95%CI: 38.97–60.20] per 100,000) was observed in high-middle-SDI regions. The highest AAPCs of the age-specific prevalence rate (2.20 [95%CI: 2.08–2.32] per 100,000), age-specific incidence rate (2.25 [95%CI: 2.06–2.45] per 100,000), age-specific mortality rate (2.04 [95%CI: 1.93–2.15] per 100,000), and age-specific DALY rate (2.06 [95%CI: 1.99–2.13] per 100,000) in the middle-SDI region (Table 1, Fig. 1, Supplementary Fig. S1).

Notably, the trend of dementia burden in individuals <70 years in low-SDI regions deviated from that in other sub-SDI regions. Despite an increase in the prevalence, incidence, death, and DALYs cases of dementia in individuals <70 years, the ASRs in low-SDI regions

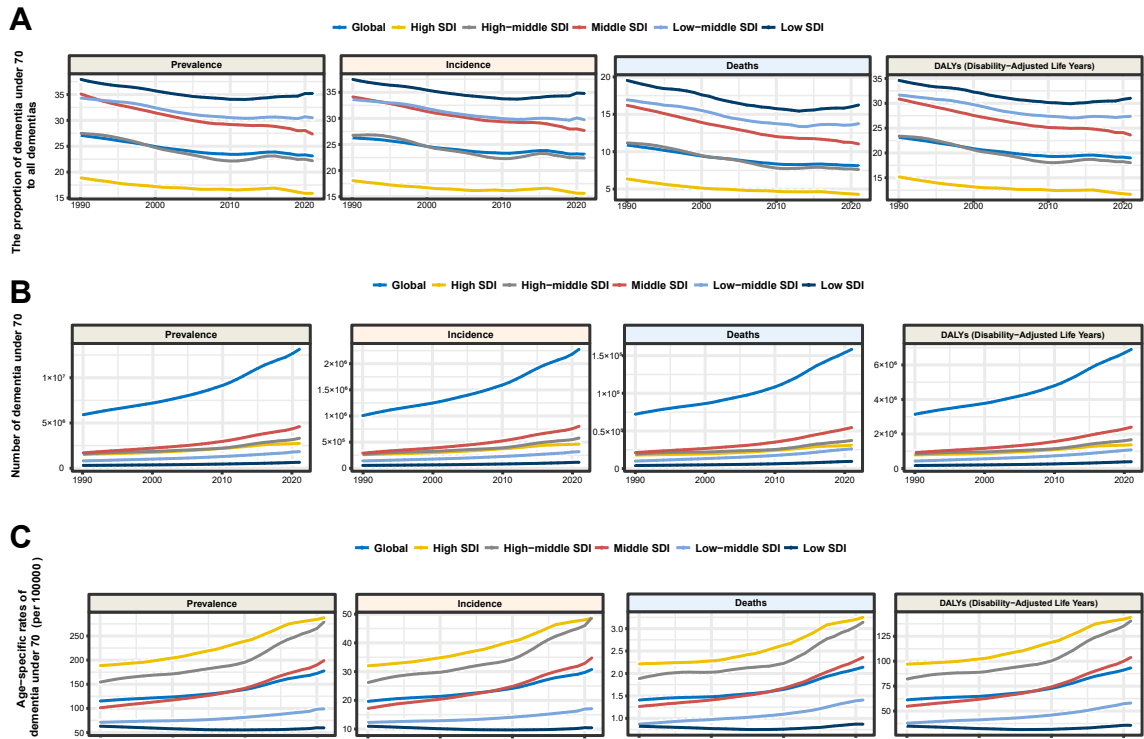


Fig. 1: Dementia burden under 70 during 1990–2021 (A) The proportion of dementia in people under 70 to total AD from 1990 to 2021; (B) Number of prevalence, incidence, death, and DALYs for dementia under 70 from 1990 to 2021; (C) Age specific rate of prevalence, incidence, death, and DALYs for dementia under 70 from 1990 to 2021. DALY: Disability Adjusted Life Years; SDI: sociodemographic index.

remained stable from 1990 to 2021. Joint point regression analysis revealed that the prevalence, incidence, death, and DALYs among individuals <70 years in low-SDI regions underwent an initial decrease followed by an increase (Figs. 1 and 2, Table 1, and Supplementary Fig. S1).

Dementia burden in individuals <70 years stratified by countries and territories during 1990–2021

At the regional level, the most pronounced increase in the prevalence of dementia in individuals <70 years during 1990–2021 was in East Asia (from 129.15 [95% CI: 106.09–155.37] per 100,000 population to 328.72 [95% CI: 268.20–396.00] per 100,000 population; the AAPC 3.02 [95% CI: 2.90–3.14]) and the most pronounced increases in the incidence (AAPC: 3.14 [95% CI: 2.89–3.40]), death (AAPC: 2.38 [95% CI: 2.34–0.42]), and DALY (AAPC: 2.56 [95% CI: 2.46–2.67]) were in East Asia, Central Latin America, and East Asia, respectively. By 2021, the highest rate of prevalence (339.82 [95% CI: 281.06–406.06] per 100,000), death (3.79 [95% CI: 0.82–11.52] per 100,000), and DALY (167.08 [95% CI: 97.55–372.04] per 100,000) was observed in high-income North America. Meanwhile, the highest rate of incidence of dementia in individuals <70 years (58.46 [95% CI:

46.97–72.13] per 100,000) was observed in East Asia (Table 1). Data for countries and territories are shown in Fig. 3 and Supplementary Table S1.

Dementia burden in individuals <70 years by gender

Females aged <70 years consistently exhibited a higher incidence, mortality, and DALY rates for dementia than males both globally and regionally. As of 2021, the worldwide prevalence and incidence of dementia in women <70 years will have surpassed those in men by 7.41 million and 1.30 million, respectively. Moreover, gender disparities in the number of deaths and DALYs reached 0.01 million and 0.51 million, respectively. Notably, higher SDI regions showed greater gender disparities, with the most significant gender difference observed in the high–middle-SDI region (Fig. 4a and b).

Consistent with the overall trend, the dementia burden in those <70 years increased in both men and women (AAPC > 0). Specifically, the gender gap in dementia-induced age-specific prevalence rate and age-specific incidence rate swelled by 42.91% (from 34.49 per 100,000 in 1990 to 49.29 per 100,000 in 2021) and 52.61% (from 6.14 per 100,000 in 1990 to 9.37 per

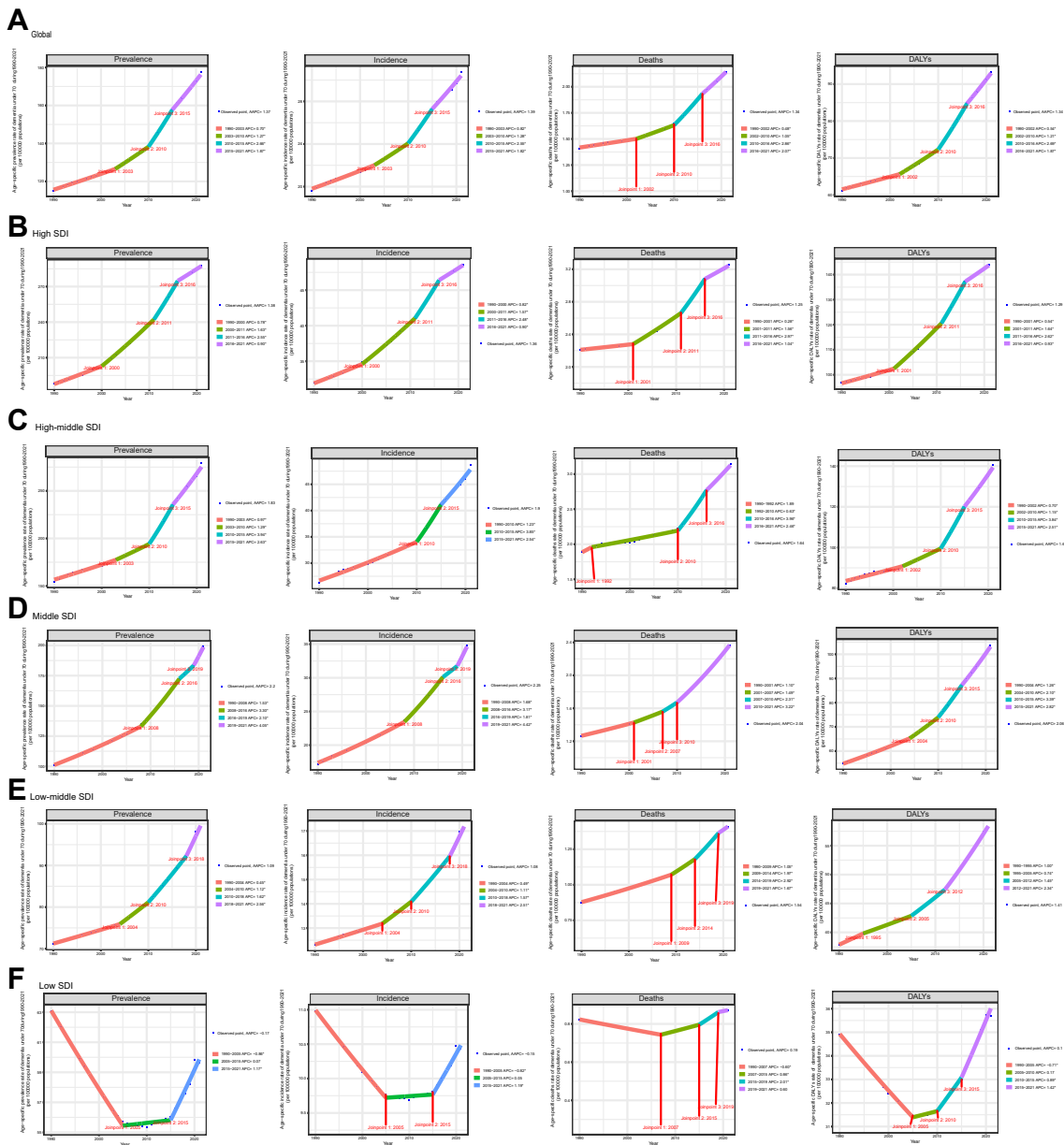


Fig. 2: Jointpoint regression analysis of dementia prevalence, incidence, mortality, and DALYs in people under 70 from 1990 to 2021 (A) Jointpoint regression analysis of global dementia prevalence, incidence, mortality, and DALYs in people under 70 from 1990 to 2021. (B) Jointpoint regression analysis of dementia prevalence, incidence, mortality, and DALYs in people under 70 in high SDI region from 1990 to 2021 (C) Jointpoint regression analysis of dementia prevalence, incidence, mortality, and DALYs in people under 70 in high-middle SDI region from 1990 to 2021. (D) Jointpoint regression analysis of dementia prevalence, incidence, mortality, and DALYs in people under 70 in middle SDI region from 1990 to 2021 (E) Jointpoint regression analysis of dementia prevalence, incidence, mortality, and DALYs in people under 70 in low-middle SDI region from 1990 to 2021. (F) Jointpoint regression analysis of dementia prevalence, incidence, mortality, and DALYs in people under 70 in low SDI region from 1990 to 2021. APC: annual percentage change; AAPC: average annual percentage changes. DALYs: disability-adjusted life-years; SDI: sociodemographic index. *P < 0.05.

100,000 in 2021), respectively. Concurrently, the gender disparity in the mortality rate increased from 1.24 per 100,000 to 1.68 per 100,000 and the corresponding DALY gender gap widened from 20.91 per 100,000 to 30.04 per 100,000 (Fig. 4a and b).

Dementia burden in individuals <70 by age group
Globally, the prevalence and incidence rates increased across all age groups from 1990–2021, and the growth rate was positively correlated with age (AAPC > 0). The highest increase in age-specific prevalence rate (AAPC

Location	Prevalence					Incidence					Deaths					DALYs				
	Number in 1990	Number in 2021	ASR in 1990	ASR in 2021	AAPC	Number in 1990	Number in 2021	ASR in 1990	ASR in 2021	AAPC	Number in 1990	Number in 2021	ASR in 1990	ASR in 2021	AAPC	Number in 1990	Number in 2021	ASR in 1990	ASR in 2021	AAPC
Global	5910266.18 (4891831.94 -7077139.03)	13141474.85 (10836303.36 -15745478.71)	115.17 (95.33 -137.91)	177.66 (146.5 -212.86)	1.37 (1.3 -1.44)	1007401.96 (820058.94 -1229999.59)	2276118.65 (1831520.71 -2784264.32)	19.63 (15.98 -23.97)	30.77 (24.76 -37.64)	1.39 (1.29 -1.5)	72219.28 (15367.89 -219701.14)	158362.29 (34952.26 -490087.98)	1.41 (0.3 -4.28)	2.14 (0.47 -6.63)	1.34 (1.27 -1.41)	3140146.52 (1444537.39 -7193271.06)	6901208.85 (3198798.07 -15731191.17)	61.19 (28.15 -140.18)	93.3 (43.24 -212.67)	1.34 (1.29 -1.4)
SDI region																				
High SDI	1528255.83 (1270735.87 -1827774.54)	2736220.96 (2273433.92 -3269522.44)	188.56 (156.79 -225.52)	287.85 (239.17 -343.96)	1.38 (1.32 -1.44)	259525.93 (209519.07 -320473.15)	461830.63 (369932.53 -575288.58)	32.02 (25.85 -39.54)	48.58 (38.92 -60.52)	1.36 (1.31 -1.42)	17923.81 (3863.34 -93964.72)	30903.82 (6800.06 -1787860.63)	2.21 (0.48 -6.81)	3.25 (0.72 -9.89)	1.25 (1.18 -1.31)	786036.91 (372330.77 -1787860.63)	1368528.1 (654824.9 -3030006.42)	96.98 (45.94 -220.59)	143.97 (68.89 -318.76)	1.29 (1.23 -1.35)
High-middle SDI	1562346.09 (1288345.36 -1877071.2)	3311939.48 (2715879.34 -3987831.44)	154.37 (127.3 -185.47)	279.1 (228.87 -336.06)	1.83 (1.69 -1.98)	265106.13 (214078.05 -325631.97)	578801.74 (462433.69 -714353.37)	26.19 (21.15 -32.17)	48.78 (38.97 -60.2)	1.9 (1.74 -2.07)	19080.76 (4140.49 -57292.93)	37296.13 (8401.86 -115678.69)	1.89 (0.41 -5.66)	3.14 (0.71 -9.75)	1.64 (1.46 -1.83)	830595.45 (381615.47 -1867342.17)	1666147.32 (778776.57 -3758284.72)	82.07 (37.71 -184.51)	140.41 (65.63 -316.72)	1.67 (1.52 -1.81)
Middle SDI	1696186.47 (1402620.02 -2036074.93)	4597198.03 (3774246.23 -5520334.65)	101.13 (83.63 -121.4)	199.22 (163.56 -239.23)	2.2 (2.08 -2.32)	288039.71 (234860.75 -350180.03)	803201.18 (649888.27 -985135.39)	17.17 (14 -20.88)	34.81 (28.16 -42.69)	2.25 (2.06 -2.45)	21193.38 (4496.2 -63721.01)	54442.22 (12015.24 -167872.33)	1.26 (0.27 -3.8)	2.36 (0.52 -7.27)	2.04 (1.93 -2.15)	918605.01 (416642.17 -2100771.15)	2395398.73 (1114136.47 -5409175.64)	54.77 (24.84 -125.25)	103.81 (48.28 -234.41)	2.06 (1.99 -2.13)
Low-middle SDI	806778.12 (672560.17 -964932.77)	1832878.08 (1523965.86 -2203125.84)	71.07 (59.25 -85)	99.02 (82.33 -119.02)	-0.17 (-0.21 to -0.13)	139603.27 (114949.34 -168926.53)	316223.41 (258446.87 -384597.56)	12.3 (10.13 -14.88)	17.08 (13.96 -20.78)	-0.15 (-0.2 -0.11)	9896.44 (2088.24 -30934.44)	26072.7 (5524.88 -80190.75)	0.87 (0.18 -2.73)	1.41 (0.12 -4.33)	0.19 (0.12 -0.25)	429995.14 (196023.21 -1006149.84)	1074846.25 (475043.13 -2574884.18)	37.88 (17.27 -88.63)	58.07 (25.66 -139.11)	1.41 (1.36 -1.45)
Low SDI	310251.97 (259197.88 -369945.31)	653128.87 (541718.22 -779452.68)	63.06 (52.69 -75.2)	59.62 (49.45 -71.15)	1.09 (1.01 -1.16)	54014.35 (44322.47 -65559.39)	114314.7 (94018.9 -137646.58)	10.98 (9.01 -13.33)	10.44 (8.58 -12.57)	1.08 (1.01 -1.15)	4050.14 (861.72 -12627.38)	9526.68 (1994.35 -29383.19)	0.82 (0.18 -2.57)	0.87 (0.18 -2.68)	1.54 (1.44 -1.65)	171610.91 (77.092 -407653.13)	391017.68 (173375.82 -954037.81)	34.88 (15.67 -82.86)	35.69 (15.83 -87.09)	0.1 (0.04 -0.16)
Sub-region																				
Andean	21745.18 (17989.08 -26243.11)	60497.63 (50274.42 -72952.13)	58.81 (48.65 -70.98)	96.25 (79.99 -116.07)	1.61 (1.56 -1.65)	3610.26 (2929.61 -4406.39)	9909.04 (8061.08 -12060.14)	9.76 (7.92 -11.92)	15.77 (12.83 -19.19)	1.57 (1.52 -1.61)	267.28 (57.63 -791.41)	754.43 (162.58 -2320.04)	0.72 (0.16 -2.14)	1.2 (0.26 -3.69)	1.64 (1.54 -1.75)	11701.05 (5418.57 -26280.51)	32791.65 (15202.97 -76933.62)	31.65 (14.66 -71.08)	52.17 (24.19 -122.4)	1.63 (1.57 -1.7)
Latin America	31635.85 (26042.03 -38008.29)	60514.86 (49708.94 -72371.34)	168.11 (138.38 -201.97)	221.52 (181.96 -264.92)	0.91 (0.86 -0.95)	5399.95 (4283.21 -6714.56)	10330.02 (8348.92 -12798.85)	28.69 (22.76 -35.68)	37.81 (30.56 -46.85)	0.9 (0.86 -0.95)	371.36 (79.08 -1119.42)	744.16 (165.32 -2233.74)	1.97 (0.42 -5.95)	2.72 (0.61 -8.18)	1.06 (0.97 -1.14)	16195.53 (7787.04 -36085.16)	31953.04 (15020.78 -72300.28)	86.06 (41.38 -191.75)	116.97 (54.98 -264.66)	0.99 (0.93 -1.05)
Caribbean	30684.27 (25536.78 -36916.83)	61698.4 (51349.92 -74178.7)	90.74 (75.52 -109.17)	139.4 (116.02 -167.6)	1.39 (1.36 -1.42)	5350.08 (4342.03 -6567.6)	10777.01 (8689.77 -13228.92)	15.82 (12.84 -19.42)	24.35 (19.63 -29.89)	1.4 (1.35 -1.44)	355.4 (74.57 -1098.46)	727.47 (157.96 -2285.08)	1.05 (0.22 -3.25)	1.64 (0.36 -5.16)	1.46 (1.42 -1.49)	15788.7 (7495.48 -36282.92)	32145.51 (14965.24 -74357.65)	46.69 (22.17 -107.29)	72.63 (33.81 -168)	1.43 (1.4 -1.47)
Central Asia	65621.01 (54044.29 -78722.37)	126279.8 (104681.95 -152432.09)	97.86 (80.59 -117.39)	136.65 (113.28 -164.95)	1.14 (0.95 -1.33)	11191.66 (9106.48 -13722.63)	21642.21 (17525.44 -26642.1)	16.69 (13.58 -20.46)	23.42 (18.96 -28.83)	1.15 (0.95 -1.34)	716.04 (150.6 -2219.03)	1404.72 (302.81 -4352.42)	1.07 (0.22 -3.31)	1.52 (0.33 -4.71)	1.18 (0.89 -1.47)	32866.06 (15506.9 -73545.25)	63702.03 (30093.57 -148524.84)	49.01 (23.12 -109.67)	68.93 (32.57 -160.72)	1.14 (0.97 -1.32)
Central Europe	224707.39 (185480.68 -269564.5)	280798.23 (231749.21 -338700.72)	191.74 (158.27 -230.02)	279.63 (230.78 -337.29)	1.23 (1.19 -1.27)	38374.05 (37897.42 -47673.05)	47614.35 (37897.42 -59254.53)	32.74 (26.18 -40.68)	47.42 (37.74 -59.01)	1.18 (1.13 -1.23)	2605.46 (549.61 -8021.77)	3364.66 (735.14 -10161.88)	2.22 (0.47 -6.84)	3.35 (0.73 -10.12)	1.29 (1.15 -1.43)	114598.08 (53752.09 -262302)	144819.78 (68820.69 -322807.66)	97.79 (45.87 -223.82)	144.22 (68.53 -321.46)	1.24 (1.17 -1.31)
Central Latin America	114723.13 (95137.51 -138159.84)	333558.93 (277324.76 -402161.13)	71.54 (59.32 -86.15)	139.37 (115.87 -168.03)	2.18 (2.15 -2.22)	20064.05 (16390.95 -24546.49)	56914.77 (45848.85 -70120.52)	12.51 (10.22 -15.31)	23.78 (19.16 -29.3)	2.1 (2.07 -2.13)	1208.42 (253.96 -3719.01)	3716.62 (795.53 -11361.87)	0.75 (0.16 -2.32)	1.55 (0.33 -4.75)	2.38 (2.34 -2.42)	55897.35 (26814.52 -126933.38)	167858.06 (79243.78 -383509.92)	34.86 (16.72 -79.15)	70.13 (33.11 -160.24)	2.29 (2.25 -2.32)
Central Sub-Saharan Africa	42793.74 (35740.95 -51183.27)	101200.52 (84476.5 -121158.36)	79.03 (66 -94.52)	74.94 (62.56 -89.72)	-0.17 (-0.24 to -0.1)	7799.58 (6388.79 -9553.72)	18495.94 (15164.21 -22241.24)	14.4 (11.8 -17.64)	13.7 (11.23 -16.47)	-0.17 (-0.23 -0.1)	588.72 (124.96 -1774.03)	1546.51 (320.42 -4743.85)	1.09 (0.23 -3.28)	1.15 (0.24 -0.27)	0.16 (0.05 -0.27)	24489.63 (10860.46 -57769.27)	62773.59 (26979.66 -157511.23)	45.22 (20.06 -106.68)	46.48 (19.98 -116.64)	0.09 (0 -0.17)
East Asia	1522071.44 (1250280.91 -1831107.45)	4435103.36 (3618591.14 -5342755.76)	129.15 (106.09 -155.37)	328.72 (268.2 -396)	3.02 (2.9 -3.14)	254278.26 (205375.32 -310.934)	788795.86 (633698.93 -973194.01)	21.58 (17.43 -26.38)	58.46 (46.97 -72.13)	3.14 (2.89 -3.4)	20596.67 (4336.82 -59098.05)	48991.13 (11311.62 -147342.56)	1.75 (0.37 -5.01)	3.63 (0.84 -10.92)	2.27 (2.28 -2.45)	868740.17 (389671.07 -1947282.96)	2210708.92 (1031482.29 -4891157.28)	73.71 (33.06 -165.23)	163.85 (76.45 -362.52)	2.56 (2.46 -2.67)
Eastern Europe	409010.93 (331792.51 -496006.05)	498400.75 (407530.06 -602888.56)	193.53 (156.99 -234.69)	268.83 (219.81 -325.19)	1.08 (0.61 -1.54)	68363.19 (54802.52 -84914.09)	83102.18 (65623.68 -103174.29)	32.35 (25.93 -40.18)	44.82 (35.4 -55.65)	0.93 (0.49 -1.37)	4499.1 (949.02 -13873.92)	5925.45 (1294.04 -18173.23)	2.13 (0.45 -6.56)	3.2 (0.61 -9.8)	1.29 (0.61 -1.96)	203481.67 (96173.3 -465230.9)	256991.97 (119546.23 -580712.99)	96.28 (45.51 -220.13)	138.62 (64.48 -313.22)	1.2 (0.55 -1.86)
Eastern Sub-Saharan Africa	116718.86 (97482.57 -139959.15)	254390.42 (211944.58 -304554.46)	62.18 (51.93 -74.56)	60.68 (50.56 -72.65)	-0.06 (-0.1 to -0.01)	20359.97 (16744.5 -24588.73)	44775.08 (37103.04 -53534.18)	10.85 (8.92 -13.1)	10.68 (8.85 -12.77)	-0.03 (-0.07 -0.01)	1498.18 (326.2 -4636.88)	3587.53 (759.87 -10741.62)	0.8 (0.17 -2.47)	0.86 (0.18 -2.56)	0.27 (0.2 -0.35)	63836.35 (29319.84 -150412.52)	149122.96 (66310.08 -364133.27)	34.01 (15.62 -80.13)	35.57 (15.82 -86.86)	0.18 (0.13 -0.24)
High-income Asia Pacific	285932.75 (237693.93 -343498.52)	481161.69 (399161.27 -577661.66)	176.37 (146.61 -211.87)	319.69 (265.21 -383.81)	1.92 (1.74 -2.1)	47596.77 (39351.2 -57946.81)	82506.23 (66403.9 -101419.78)	29.36 (24.27 -35.74)	54.82 (44.12 -67.39)	2.05 (1.92 -2.19)	3469.05 (748.57 -10669.39)	5625.24 (1255.67 -16550.64)	2.14 (0.46 -6.58)	3.74 (0.83 -11)	1.78 (1.56 -1.99)	152387.69 (70722.84 -349305)	247051.92 (118058.01 -540347.32)	93.99 (43.62 -215.46)	164.15 (78.44 -359.02)	1.78 (1.59 -1.98)

(Table 1 continues on next page)

Location	Prevalence					Incidence					Deaths					DALYs				
	Number in 1990	Number in 2021	ASR in 1990	ASR in 2021	AAPC	Number in 1990	Number in 2021	ASR in 1990	ASR in 2021	AAPC	Number in 1990	Number in 2021	ASR in 1990	ASR in 2021	AAPC	Number in 1990	Number in 2021	ASR in 1990	ASR in 2021	AAPC
(Continued from previous page)																				
High-income America	565337.25 (469492.45)	1110750.84 (918700.62)	218.96 (181.84)	339.82 (281.06)	1.43 (1.39)	93925.14 (75297.34)	177569.89 (141606.07)	36.38 (29.16)	54.32 (43.32)	1.31 (1.27)	6485.8 (1418.58)	12322.04 (2683.32)	2.51 (0.55)	3.77 (0.82)	1.32 (1.26)	284272.11 (136263.06)	546124.12 (263283.64)	110.1 (52.78)	167.08 (80.55)	1.36 (1.3)
North America	-674645.59	-1327272.53	-261.3	-406.06	-1.48	-114751.18	-219125.72	-44.44	-67.04	-1.35	-19889.15	-37648.39	-7.7	-11.52	-1.37	-640003.27	-1216067.02	-247.88	-372.04	-1.42
North Africa and Middle East	310274.58 (259828.1)	799473.28 (665877.4)	93.46 (78.27)	132.66 (110.49)	1.14 (1.11)	57,021 (46960.62)	147371.33 (120502.08)	17.18 (14.15)	24.45 (19.99)	1.15 (1.12)	3699.72 (798.05)	8989.29 (1985.12)	1.11 (0.24)	1.49 (0.33)	0.95 (0.91)	162316.05 (75205.32)	402532.96 (190409.82)	48.89 (22.65)	66.79 (31.59)	1.01 (0.98)
Oceania	4958.64 (4127.72)	11854.64 (9773.43)	76.93 (64.04)	86.84 (71.59)	0.39 (0.29)	878.38 (719.65)	2108.17 (1728.36)	13.63 (11.16)	15.44 (12.66)	0.4 (0.31)	62.72 (13)	143.78 (29.83)	0.97 (0.2)	1.05 (0.22)	0.24 (0.12)	2721.32 (1237.55)	6371.84 (2892.72)	42.22 (19.2)	46.67 (21.19)	0.32 (0.23)
South Asia	646136.42 (535861.85)	1578733.69 (1297992.79)	60.39 (50.08)	89.03 (73.19)	1.28 (1.16)	110262.06 (90470.02)	265648.98 (214920.44)	10.31 (8.46)	14.98 (12.12)	1.24 (1.13)	8198.02 (1718.73)	24220.52 (5086.84)	0.77 (0.16)	1.37 (0.29)	1.93 (1.81)	351148.76 (157614.05)	969750.65 (421607.96)	32.82 (14.73)	54.68 (23.77)	1.69 (1.63)
Southeast Asia	458992.04 (379479.64)	1173361.59 (969400.93)	100.97 (83.48)	175.59 (145.07)	1.81 (1.77)	78151.79 (64726.07)	198597.4 (162482.95)	17.19 (14.24)	29.72 (24.32)	1.79 (1.77)	4932.33 (1031.62)	14177.76 (3071.85)	1.09 (0.23)	2.12 (0.46)	2.21 (2.14)	227638.52 (108104.92)	624898.59 (286542.54)	50.08 (23.78)	93.52 (42.88)	2.07 (2.01)
Southern Latin America	59712.75 (49715.89)	100444.36 (83576.27)	127.31 (106)	161.49 (134.37)	0.76 (0.71)	10126.65 (8195.21)	16978.87 (13692.2)	21.59 (17.47)	27.3 (22.01)	0.74 (0.69)	611.43 (129.94)	1101.37 (235.26)	1.3 (0.28)	1.77 (0.38)	0.97 (0.88)	28513.67 (14016.64)	49844.66 (23912.89)	60.79 (29.88)	80.14 (38.45)	0.89 (0.85)
Southern Sub-Saharan Africa	41138.91 (34164.19)	88755.71 (73381.3)	80.48 (66.83)	114.32 (94.52)	1.15 (1.1)	7106.29 (5800.08)	15161.83 (12398.17)	13.9 (11.35)	19.53 (15.97)	1.12 (1.07)	473.02 (99.78)	1111.84 (238.28)	0.93 (0.2)	1.43 (0.31)	1.48 (1.33)	21043.44 (9900.02)	47765.52 (21,892)	41.16 (19.37)	61.52 (28.2)	1.32 (1.25)
Tropical Latin America	175260.56 (144395.2)	490326.62 (405009.58)	118.27 (97.44)	230.03 (190)	2.17 (2)	29712.39 (24572.84)	85608.85 (69229.06)	20.05 (16.58)	40.16 (32.48)	2.27 (2.14)	2301.48 (502.06)	6520.56 (1426.47)	1.55 (0.34)	3.06 (0.67)	2.24 (2.15)	97035.14 (43846.58)	273149.12 (124399.28)	65.48 (29.59)	128.14 (58.36)	2.14 (2.06)
Western Europe	684665.43 (564406.13)	877849.25 (716301.97)	197.27 (162.62)	236.24 (192.77)	0.57 (0.51)	121334.91 (97555.95)	155613.95 (122712.23)	34.96 (28.11)	41.88 (33.02)	0.58 (0.54)	8014.02 (1724.71)	10365.18 (2285.02)	2.31 (0.5)	2.79 (0.61)	0.59 (0.53)	351459.69 (167495.5)	453485.49 (216638.44)	101.27 (48.26)	122.04 (58.3)	0.59 (0.53)
Western Sub-Saharan Africa	98145.06 (81442.94)	216320.26 (178218.15)	51.89 (43.06)	44.91 (37)	-0.46 (-0.48)	16495.52 (13462.28)	36596.69 (30175.99)	8.72 (7.12)	7.6 (6.26)	-0.44 (-0.47)	1265.07 (270.42)	3022.03 (631.32)	0.67 (0.14)	0.63 (0.13)	-0.2 (-0.3)	54015.53 (24087.79)	127366.48 (55076.65)	28.56 (12.74)	26.44 (11.43)	-0.26 (-0.33)
	-118141.72	-262317.1	-62.46	-54.46	to -0.44	-19939.59	-43883.05	-10.54	-9.11	-0.42	-3857.2	-9280.99	-2.04	-1.93	to -0.11	-129400.23	-305875.05	-68.42	-63.5	to -0.19

DALY: Disability-Adjusted Life Years; SDI: sociodemographic index; AAPC: average annual percentage changes.

Table 1: Global and sub-regional dementia burden under 70 during 1990–2021.

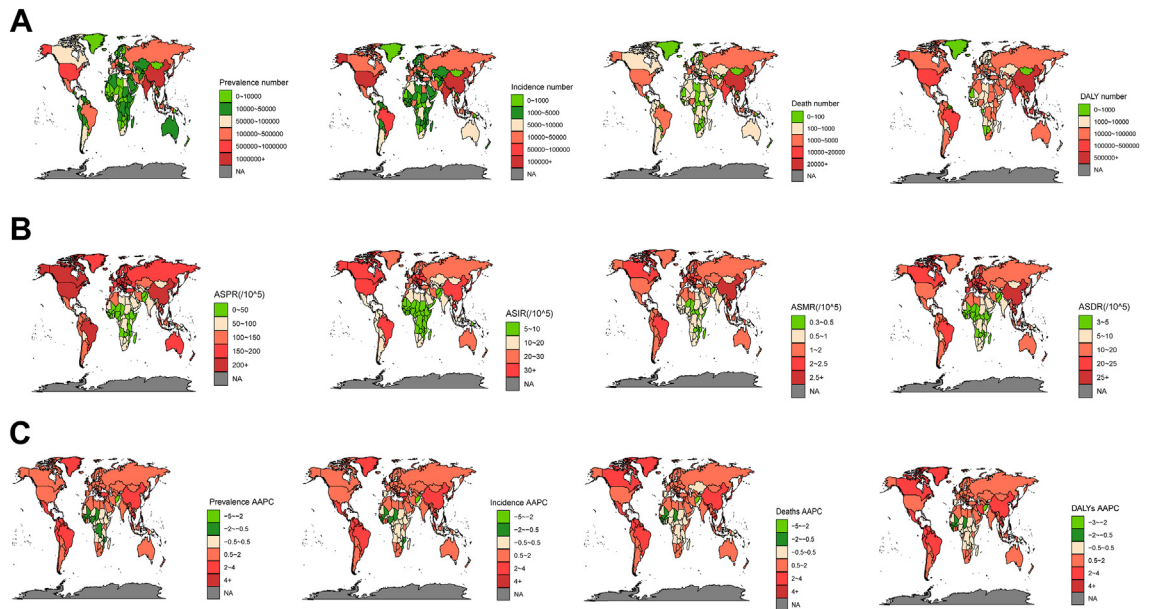


Fig. 3: Dementia burden under 70 by countries and territories (A) The number of prevalence, incidence, death and DALY of dementia under 70 in countries and territories by the year 2021; (B) The rate of prevalence, incidence, death and DALY of dementia under 70 in countries and territories by the year 2021; (C) The AAPC of prevalence, incidence, death and DALY of dementia burden under 70 in countries and territories by the year 2021. DALY: Disability-Adjusted Life Years; AAPC: average annual percentage changes. ASPR: age-specific prevalence rate; ASIR: age-specific incidence rate; ASMR: age-specific mortality rate; ASDR: age-specific DALY rate.

of 0.23 [95%CI: 0.17–0.29]) and ASIR (AAPC of 0.26 [95%CI: 0.21–0.31]) was observed in the 65–69 age group. Meanwhile, the highest increase in mortality rates was observed in the 40–44 age group (AAPC: 0.08 [95%CI: 0.04–0.11]) while the DALY rate increased only after 50 years during 1990–2021. For different SDI regions, the increase in mortality and DALY rates among different age groups in the low- and low-middle-SDI regions was significantly higher than that in the other SDI regions ($P < 0.05$) (Supplementary Tables S2 and S3).

The proportion of the dementia burden escalates with age; notably, the 65–69 age group represents >40% of the dementia burden in individuals <70. Compared with that in 1990, the proportion of dementia burden in all age groups <70 years had decreased by 2021. Changes in the age distribution of the dementia burden <70 years during 1990–2021 in most SDI subregions were similar to global trends (Fig. 4; Supplementary Tables S2 and S3).

Dementia induced deaths and DALYs in individuals <70 years attributable to risk factors

The GBD 2021 study specifically assessed the impact of high BMI, HFPG, and smoking on the mortality and DALYs associated with dementia in patients <70 years (Supplementary Fig. S2). Globally, smoking is responsible for over 7% of both dementia-related deaths and DALYs in individuals <70. Nearly 8% of dementia-

related deaths and DALY in individuals <70 was related to high BMI while 25% of dementia-induced deaths and DALY in individuals <70 was related to HFPG. The PAF of high BMI and HFPG increased by nearly 40% and 100% during 1990–2021, respectively. Conversely, the PAF related to smoking declined by 25%. Across different SDI regions, a higher SDI correlated with increased PAFs for these risk factors. Smoking and HFPG had a greater impact on men while a high BMI had a greater impact on women.

Dementia burden in individuals <65 years

Similar to the burden of dementia under 70 years old, the burden of dementia under 65 years old is also rapidly increasing. The global prevalence of dementia in individuals <65 years increased from 3.68 million in 1990 to 7.76 million in 2021, corresponding to an increase in the age-specific prevalence rate from 341.24 to 363.45 per 100,000. Meanwhile, the global incidence rate of dementia among people <65 years rose from 59.42 to 64.74 per 100,000 people. The adverse consequences, deaths, and DALY cases, of dementia in individuals <65 years increased by >100% during 1990–2021, respectively. The age-specific mortality rate increased from 3.26 to 3.44 per 100,000 people while the age-specific DALY rate increased from 166.78 to 176.82 per 100,000. The most significant increase in age-specific prevalence, mortality and DALY rates occurred between 2006 and 2015 (Supplementary Figs. S3 and S4

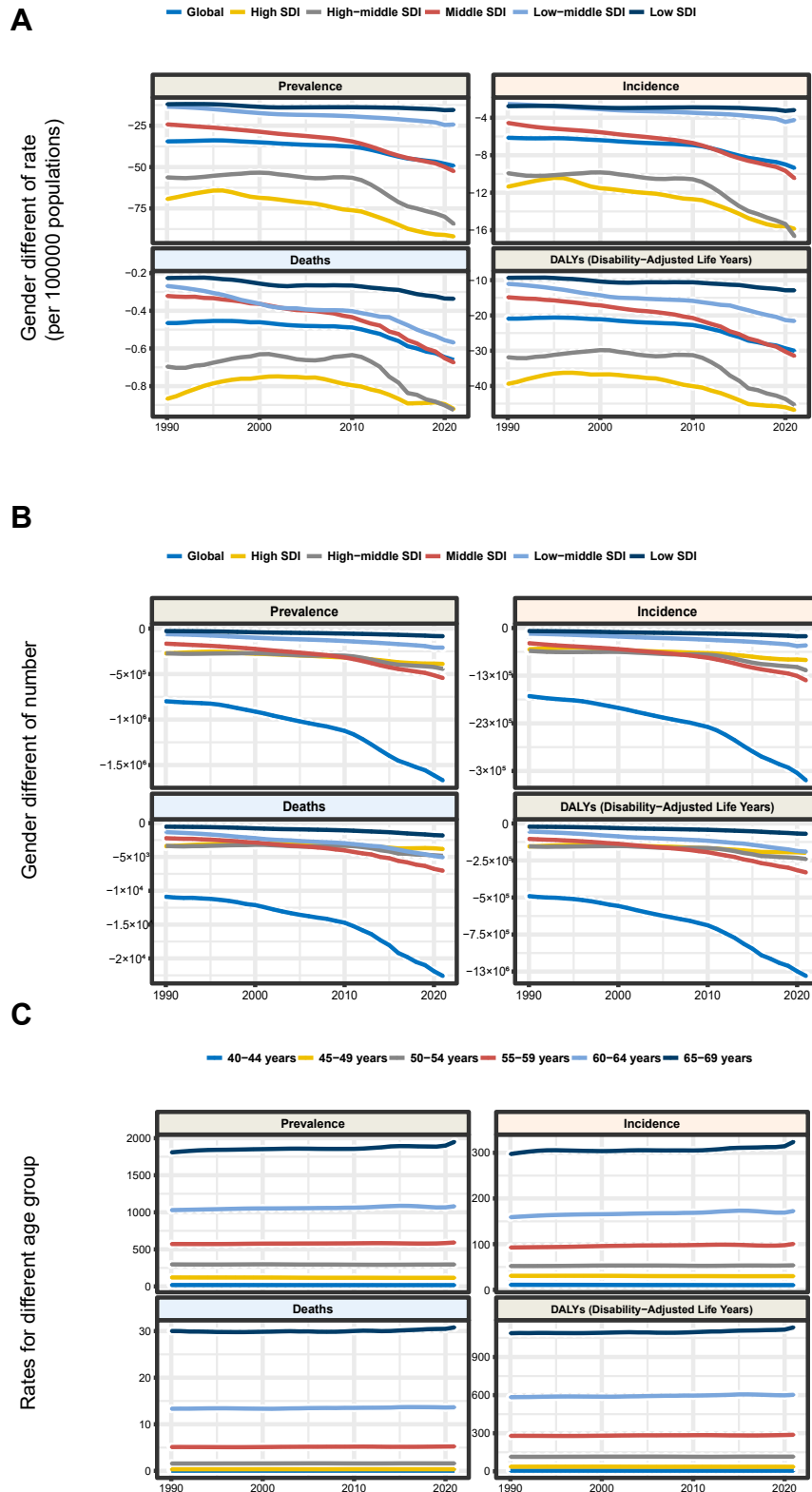


Fig. 4: Gender difference of dementia burden under 70 and dementia burden by age group during 1990–2021; (A) Gender difference of ASPR, ASIR, ASMR and ASDR of dementia burden under 70 during 1990–2021; (B) Gender difference of the number of prevalence, incidence, death

and Table S4). Similar to that of dementia in individuals <70 years, the proportion of dementia burden in individuals <65 years within the total dementia burden was inversely correlated with SDI. Age-specific rates of dementia prevalence, incidence, deaths, and DALYs in individuals <65 years increased in most sub-SDI regions except for the low-SDI regions. The highest age-specific incidence rate (75.90 [95%CI: 49.32–107.83] per 100,000) and the age-specific prevalence rate in 2021 (3.73 [95%CI: 0.72–11.78] per 100,000) were observed in the high–middle-SDI region. The highest age-specific mortality rate (423.50 [95%CI: 321.26–546.1] per 100,000) and age-specific DALYs rate (183.18 [95%CI: 82.36–431.73] per 100,000) was observed in high- and middle-SDI region, respectively. At the regional level, the most pronounced increase in the prevalence, death, and DALYs of dementia in individuals <65 years during 1990–2021 was in high-income North America (prevalence: AAPC 0.66 [95% CI: 0.61–0.71], deaths: AAPC 0.66 [95% CI: 0.54–0.79]; DALY: AAPC 0.65 [95% CI: 0.56–0.73]) and the most pronounced increase in the incidence (AAPC 0.89 [95% CI: 0.64–1.13]) of dementia in individuals <65 years was in East Asia (Supplementary Figs. S3 and S4 and Table S4).

Similar to that of dementia in individuals <70 years, females <65 years consistently exhibited higher incidence, mortality, and DALY rates for dementia than males both globally and sub-SDI regionally, and gender differences were still widening (Supplementary Figs. S5 and S6).

Discussion

Dementia remains a global challenge. However, the focus on late-onset dementia (LOD) may marginalize the burden of dementia in younger individuals.²⁷ To the best of our knowledge, this is the first study to systematically estimate the burden of global dementia in younger individuals by SDI level, region, gender, and age. Our research indicates that over the last 30 years, the global prevalence, incidence, mortality, and DALY cases of dementia in individuals <70 years have doubled, alongside a notable acceleration in the growth rate of the YOD burden over the past decade. Notably, the AAPCs of YOD ASRs initially increased and then decreased with increasing SDI levels, with the highest increase in YOD burden in the middle-SDI level. Women bear a disproportionately heavier burden of YOD, and gender differences expanded during 1990–2021. Additionally, the growth rate of YOD burden varied across different age groups, with a noteworthy observation that in regions with lower SDI levels,

and the YOD death and DALY burden escalated more rapidly among younger age groups.

Although dementia is commonly associated with older adults, its effects on younger individuals should not be overlooked. Recent meta-analyses encompassing data from 1980 to 2018 indicate that the prevalence and incidence of dementia between the ages of 30–64 have reached 3.9 and 0.37 million, respectively.^{8,9} Our current study, however, reveals that in 2021, the prevalence and incidence of dementia in individuals <65 years escalated to 13.14 million and 2.28 million, respectively. Notably, the prevalence and incidence figures for those <65 years, standing at 7.76 million and 1.38 million respectively in 2021, starkly exceed prior estimates. This discrepancy could be partly attributed to the fact that the meta-analysis used findings from various studies conducted between 1980 and 2018, whereas our study identified a more than two-fold increase in the prevalence and incidence rates over the past three decades. Relying on historical data to estimate the current burden of YOD may cause underestimation. Although the incidence of YOD is substantially lower than that of LOD, the extended survival underscores its significance as a public health concern. In addition to prevalence and incidence analyses, we also estimated the deaths and DALY burden of YOD for the first time. Between 1990 and 2021, the number of dementia-related deaths and DALY cases in individuals <70 years surged by nearly 120%. Notably, we found that the growth rate of the YOD burden has significantly accelerated in the past decade, both globally and regionally. To date, the timing of interventions and prevention efforts for dementia remain unclear. As YOD has become a public health issue, middle-aged people should take measures to prevent dementia development.

Concerns about dementia burden have historically focused on regions with a higher SDI.^{28,29} Our study also demonstrated that high- and high–middle-SDI regions experienced a heavier burden during 1990–2021. The historically high prevalence of dementia burden in regions with higher SDI is likely a consequence of economic development related to longer lifespans and the accumulation of risk factors.³⁰ However, economic development also implies having strong forces to intervene in risk factors and improve medical conditions. Economic development has gradually westernized the lifestyles of middle-SDI countries. Prevention programs for risk factors in middle-SDI countries commenced later than those in high-SDI countries.³¹ As more than one-third of YOD dementia cases originate from the middle-SDI region, the increase in YOD burden in these regions will drive the global YOD burden. To reduce the

and DALY of dementia under 70 during 1990–2021; (C) ASPR, ASIR, ASMR and ASDR of dementia under 70 during 1990–2021 by age group. ASPR: age-specific prevalence rate; ASIR: age-specific incidence rate; ASMR: age-specific mortality rate; ASDR: age-specific DALY rate; DALYs: disability-adjusted life-years; SDI: sociodemographic index.

global YOD burden, dementia care must be added to the basic medical system in middle-SDI regions.

Previous studies have indicated no substantial gender disparities in the incidence or prevalence of YOD.^{8,9} However, our results show that women bear a more substantial burden than men regarding the incidence, prevalence, and adverse outcomes after the disease. This discrepancy may stem from variations in data sources analyzed. Although some studies from North and South America have not observed a gender difference in the incidence of AD,^{32–34} several studies conducted in Europe and Asia have suggested a higher incidence in women.^{35,36} The greater burden of dementia on women is the result of the dual influence of physiological and social environment.^{37,38} The level of S-nitrosamine C3 in the brain of women is higher than that of men, making them more prone to dementia.³⁹ Furthermore, the inequality in education level and medical resources makes women more susceptible to the adverse effects of dementia.^{40,41}

As a disease related to aging, the burden of dementia will undoubtedly increase with age.¹⁶ More importantly, this is the first study to examine the YOD burden in low-SDI regions by age group. Notably, the present study found that dementia burden under 70 increased in all age groups in low-SDI regions during 1990–2021, and the older the age, the faster the increase. Although this may be related to the increased impact of dementia-related risk factors on older people, this could also be related to limited medical and health resources, as well as a lack of recording of some older dementia.^{18,42,43}

To the best of our knowledge, this study is the first to analyze the global burden of YOD based on the 2021 GBD study, which not only describes the YOD burden by region, gender, and SDI but also shows the effect of related risk factors. However, this study has some limitations. First, although most epidemiological data in the 2021 GBD classified dementia burden using DSM or ICD definitions, criteria differences between the DSM versions could have affected the estimates. Moreover, owing to the challenges of early diagnosis, the burden of dementia may have been underestimated, especially in underdeveloped areas. Third, owing to the limited risk factors included in the GDB database, some important risk factors, such as hyperlipidemia, blood pressure, and the environment, could not be evaluated. Fourth, our study focused on the changes in the burden of YOD in different SDI regions and may have overlooked the impact of other factors on the distribution differences of YOD in different regions. Fifth, due to the lack of further segmentation of dementia types in the GBD data, we could not analyze the impact of different dementia subtypes on the disease burden.

In conclusion, the growth rate of the YOD burden is accelerating, particularly in the middle to high SDI regions. Females bore a disproportionately higher burden of YOD, and gender differences were still widening.

Contributors

All authors have made substantial contributions to this study. Huabing Zhang, Ziyi Li, Wei Li and Yuxiu Li had accessed and verified the data. Huabing Zhang, Ziyi Li, Wei Li and Yuxiu Li planned the concept of this study. Huabing Zhang, Ziyi Li, Yucheng Yang, Xuechen Wang, and Yiwen Liu conducted data extraction and analysis. Ziyi Li, Fan Ping, Lingling Xu and Wei Li carried out data cleaning and material support. All authors critically reviewed, revised, and contributed to the final manuscript.

Data sharing statement

The data were obtained from GBD 2021 study (<http://ghdx.healthdata.org/gbd-results-tool>).

Editor note

The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Declaration of interests

No potential conflicts of interest relevant to this article were reported.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.eclinm.2024.102868>.

References

- Arvanitakis Z, Shah RC, Bennett DA. Diagnosis and management of dementia: review. *JAMA*. 2019;322(16):1589–1599.
- Harvey RJ, Skelton-Robinson M, Rossor MN. The prevalence and causes of dementia in people under the age of 65 years. *J Neurol Neurosurg Psychiatry*. 2003;74(9):1206–1209.
- Ikejima C, Yasuno F, Mizukami K, Sasaki M, Tanimukai S, Asada T. Prevalence and causes of early-onset dementia in Japan: a population-based study. *Stroke*. 2009;40(8):2709–2714.
- Lambert MA, Bickel H, Prince M, et al. Estimating the burden of early onset dementia; systematic review of disease prevalence. *Eur J Neurol*. 2014;21(4):563–569.
- Lai M, Jeon YH, McKenzie H, Withall A. Journey to diagnosis of young-onset dementia: a qualitative study of people with young-onset dementia and their family caregivers in Australia. *Dementia*. 2023;22(5):1097–1114.
- van Gils AM, Rhodius-Meester HFM, Leeuwis AE, et al. Young-onset dementia in memory clinics in The Netherlands: study design and description of PRECODE-GP. *Alzheimers Dement (Amst)*. 2023;15(3):e12471.
- van de Veen D, Bakker C, Peetoom K, et al. An integrative literature review on the nomenclature and definition of dementia at a young age. *J Alzheimers Dis*. 2021;83(4):1891–1916.
- Hendriks S, Peetoom K, Bakker C, et al. Global prevalence of young-onset dementia: a systematic review and meta-analysis. *JAMA Neurol*. 2021;78(9):1080–1090.
- Hendriks S, Peetoom K, Bakker C, et al. Global incidence of young-onset dementia: a systematic review and meta-analysis. *Alzheimers Dement*. 2022;19(3):831–843.
- van Vliet D, de Vugt ME, Bakker C, Koopmans RTCM, Verhey FRJ. Impact of early onset dementia on caregivers: a review. *Int J Geriatr Psychiatry*. 2010;25(11):1091–1100.
- Gronning H, Kristiansen S, Dyre D, Rahmani A, Gyllenberg J, Høgh P. Caregiver burden and psychosocial services in patients with early and late onset Alzheimer's disease. *Dan Med J*. 2013;60(7):A4649.
- Kruger J, Aaltonen M, Aho K, et al. Incidence and prevalence of early-onset dementia in Finland. *Neurology*. 2024;103(4):e209654.
- GBD 2021 Gout Collaborators. Global, regional, and national burden of gout, 1990–2020, and projections to 2050: a systematic

- analysis of the Global Burden of Disease Study 2021. *Lancet Rheumatol.* 2024;6(8):e507–e517.
- 14 GBD 2021 Carbon Monoxide Poisoning Collaborators. Global, regional, and national mortality due to unintentional carbon monoxide poisoning, 2000–2021: results from the Global Burden of Disease Study 2021. *Lancet Public Health.* 2023;8(11):e839–e849.
 - 15 GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet.* 2024;403(10440):2133–2161.
 - 16 GBD 2016 Dementia Collaborators. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18(1):88–106.
 - 17 GBD 2021 Nervous System Disorders Collaborators. Global, regional, and national burden of disorders affecting the nervous system, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet Neurol.* 2024;23(4):344–381.
 - 18 GBD 2019 Collaborators. Global mortality from dementia: application of a new method and results from the global burden of disease study 2019. *Alzheimers Dement (N Y).* 2021;7(1):e12200.
 - 19 GBD 2019 Dementia Forecasting Collaborators. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health.* 2022;7(2):e105–e125.
 - 20 Li R, Li R, Xie J, et al. Associations of socioeconomic status and healthy lifestyle with incident early-onset and late-onset dementia: a prospective cohort study. *Lancet Healthy Longev.* 2023;4(12):e693–e702.
 - 21 Hendriks S, Ranson JM, Peetoom K, et al. Risk factors for young-onset dementia in the UK biobank. *JAMA Neurol.* 2024;81(2):134–142.
 - 22 Avan A, Hachinski V. Global, regional, and national trends of dementia incidence and risk factors, 1990–2019: a Global Burden of Disease study. *Alzheimers Dement.* 2022;19(4):1281–1291.
 - 23 Li H, Liang H, Wei L, et al. Health inequality in the global burden of chronic obstructive pulmonary disease: findings from the global burden of disease study 2019. *Int J Chron Obstruct Pulmon Dis.* 2022;17:1695–1702.
 - 24 Huang J, Wu Y, Wang M, et al. The global disease burden of varicella-zoster virus infection from 1990 to 2019. *J Med Virol.* 2022;94(6):2736–2746.
 - 25 Collaborators GI. Global, regional, and national incidence of six major immune-mediated inflammatory diseases: findings from the global burden of disease study 2019. *EClinicalMedicine.* 2023;64:102193.
 - 26 Xie J, Wang M, Long Z, et al. Global burden of type 2 diabetes in adolescents and young adults, 1990–2019: systematic analysis of the Global Burden of Disease Study 2019. *BMJ.* 2022;379:e072385.
 - 27 Loi SM, Eratne D, Goh AMY, et al. A 10 year retrospective cohort study of inpatients with younger-onset dementia. *Int J Geriatr Psychiatry.* 2021;36(2):294–301.
 - 28 Morovatdar N, Avan A, Azarpazhooh MR, et al. Secular trends of ischaemic heart disease, stroke, and dementia in high-income countries from 1990 to 2017: the Global Burden of Disease Study 2017. *Neurol Sci.* 2022;43(1):255–264.
 - 29 Dodge HH, Buracchio TJ, Fisher GG, et al. Trends in the prevalence of dementia in Japan. *Int J Alzheimer's Dis.* 2012;2012:956354.
 - 30 Larson EB, Yaffe K, Langa KM. New insights into the dementia epidemic. *N Engl J Med.* 2013;369(24):2275–2277.
 - 31 International ASD. *WHO Global action plan: The time to act is now.* 2022.
 - 32 Tyas SL, Tate RB, Wooldrage K, Manfreda J, Strain LA. Estimating the incidence of dementia: the impact of adjusting for subject attrition using health care utilization data. *Ann Epidemiol.* 2006;16(6):477–484.
 - 33 Hebert LE, Scherr PA, McCann JJ, Beckett LA, Evans DA. Is the risk of developing Alzheimer's disease greater for women than for men? *Am J Epidemiol.* 2001;153(2):132–136.
 - 34 Ganguli M, Dodge HH, Chen P, Belle S, DeKosky ST. Ten-year incidence of dementia in a rural elderly US community population: the MoVIES Project. *Neurology.* 2000;54(5):1109–1116.
 - 35 Ruitenberg A, Ott A, van Swieten JC, Hofman A, Breteler MM. Incidence of dementia: does gender make a difference? *Neurobiol Aging.* 2001;22(4):575–580.
 - 36 Yoshitake T, Kiyohara Y, Kato I, et al. Incidence and risk factors of vascular dementia and Alzheimer's disease in a defined elderly Japanese population: the Hisayama Study. *Neurology.* 1995;45(6):1161–1168.
 - 37 Mielke MM, Aggarwal NT, Vila-Castelar C, et al. Consideration of sex and gender in Alzheimer's disease and related disorders from a global perspective. *Alzheimers Dement.* 2022;18(12):2707–2724.
 - 38 Sindi S, Kåreholt I, Ngandu T, et al. Sex differences in dementia and response to a lifestyle intervention: evidence from Nordic population-based studies and a prevention trial. *Alzheimers Dement.* 2021;17(7):1166–1178.
 - 39 Yang H, Oh CK, Amal H, et al. Mechanistic insight into female predominance in Alzheimer's disease based on aberrant protein S-nitrosylation of C3. *Sci Adv.* 2022;8(50):eade0764.
 - 40 Hasselgren C, Ekbrand H, Halleröd B, et al. Sex differences in dementia: on the potentially mediating effects of educational attainment and experiences of psychological distress. *BMC Psychiatry.* 2020;20(1):434.
 - 41 Yelverton V, Qiao S, Menon JA, et al. Criminalization of sexual and gender minorities and its consequences for the HIV epidemic in Zambia: a critical review and recommendations. *J Assoc Nurses AIDS Care.* 2021;32(4):423–441.
 - 42 Draper B, Cations M, White F, et al. Time to diagnosis in young-onset dementia and its determinants: the INSPIRED study. *Int J Geriatr Psychiatry.* 2016;31(11):1217–1224.
 - 43 van Vliet D, de Vugt ME, Bakker C, et al. Time to diagnosis in young-onset dementia as compared with late-onset dementia. *Psychol Med.* 2013;43(2):423–432.