

RESEARCH ARTICLE

Global mortality from dementia: Application of a new method and results from the Global Burden of Disease Study 2019

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Abstract

Introduction: Dementia is currently one of the leading causes of mortality globally, and mortality due to dementia will likely increase in the future along with corresponding increases in population growth and population aging. However, large inconsistencies in coding practices in vital registration systems over time and between countries complicate the estimation of global dementia mortality.

Methods: We meta-analyzed the excess risk of death in those with dementia and multiplied these estimates by the proportion of dementia deaths occurring in those with severe, end-stage disease to calculate the total number of deaths that could be attributed to dementia.

Results: We estimated that there were 1.62 million (95% uncertainty interval [UI]: 0.41–4.21) deaths globally due to dementia in 2019. More dementia deaths occurred in women (1.06 million [0.27–2.71]) than men (0.56 million [0.14–1.51]), largely but not entirely due to the higher life expectancy in women (age-standardized female-to-male ratio 1.19 [1.10–1.26]). Due to population aging, there was a large increase in all-age mortality rates from dementia between 1990 and 2019 (100.1% [89.1–117.5]). In 2019, deaths due to dementia ranked seventh globally in all ages and fourth among individuals 70 and older compared to deaths from other diseases estimated in the Global Burden of Disease (GBD) study.

Discussion: Mortality due to dementia represents a substantial global burden, and is expected to continue to grow into the future as an older, aging population expands globally.

KEYWORDS

burden of disease, dementia, global health, mortality

1 | INTRODUCTION

While there is a wealth of evidence indicating that individuals with dementia have a higher risk for mortality, the mechanisms by which dementia leads to death are less clear.¹ The International Classifica-

tion of Disease (ICD) guidelines on the certification of causes of death define the underlying cause of death as the condition which gave rise to all other conditions leading to the death of the individual.² Prior evidence indicates that conditions such as bronchopneumonia and pulmonary embolisms are often the immediate causes of death among

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those with dementia and that these conditions are more frequent in those with dementia than in those without dementia, suggesting that dementia may actually be the underlying cause of death in many of these cases.³⁻⁵ However, oftentimes, these immediate causes of death are listed on the death certificate without mention of dementia.⁶

Due to these challenges in the certification of deaths due to dementia, the use of vital registration data for the estimation of mortality due to dementia is highly susceptible to changes over time in coding practices that exist within and between vital registration systems and the societies in which they operate. Previous studies have shown increases over time in the certification of dementia as a cause of death on death certificates, while the estimated prevalence of the disease has remained stable or even decreased.⁷⁻⁹ Comparisons of the certification of dementia deaths on death certificates with information on dementia patients from population-based epidemiological studies have indicated that dementia has been previously underreported on death certificates.^{6,10-13}

Published estimates of dementia mortality are largely from the United States and Western Europe and have either focused on the estimation of mortality in those with dementia rather than mortality that can be ascribed to dementia as the underlying cause, or have relied on the generalization of prevalence and mortality risk estimates from one population-based cohort to the entire country.¹⁴⁻¹⁶ The only available global estimates of dementia mortality are from previous iterations of the Global Burden of Disease (GBD) study. However, these estimates are subject to a number of known limitations. For GBD 2010, estimates were based on vital registration data.¹⁷ The recognition of the biases that exist in reporting dementia as a cause of death in vital registration data led to a new methodology for the estimation of dementia mortality, introduced in GBD 2015. For GBD 2015, 2016, and 2017, we used estimates of excess mortality derived from countries most likely to code to dementia as a cause of death per prevalent dementia case, and prevalence estimates to calculate mortality due to dementia.^{18,19} While this method allowed for the global estimation of dementia deaths and accounted for the under-reporting present in vital registration data, it was sensitive to the choice of how many countries to include in the estimation of excess mortality, and it assumed that the coding practices in these countries do not under- or over-assign dementia as a cause of death.

This study aims to improve on prior methods of estimation for dementia mortality and describe the results over time and across geographies. By removing all reliance on vital registration data and instead calculating mortality due to dementia as the product of total excess deaths and the proportion of these deaths in individuals with severe, end-stage disease, this study addresses some of the primary weaknesses in previous estimation methods.

2 | METHODS

The category of dementia as used in this article is equivalent to the GBD disease designation of “Alzheimer’s disease and other dementias.”

RESEARCH IN CONTEXT

1. Systematic review: The authors reviewed the literature using traditional sources (PubMed). Prior estimates of dementia mortality are from previous iterations of the Global Burden of Disease study or are limited in geographic scope.
2. Interpretation: Our study improves on prior methods for the estimation of mortality by removing any reliance on inconsistent vital registration data from the modeling process. We estimated there were 1.62 million (0.41–4.21) deaths due to dementia globally in 2019.
3. Future directions: Future work should seek to strengthen the analyses by incorporating additional data sources on dementia prevalence, the excess risk of death, and the proportion of individuals with end-stage disease, both to limit the effect of data sparsity on the precision of estimates and to increase the geographic coverage of available data. More precise and accurate estimates will increase the utility of the results for the purposes of public health planning and resource allocation.

Information on general GBD methods can be found in the GBD 2019 summary papers.^{20,21} This GBD study used de-identified data, and the waiver of informed consent was reviewed and approved by the University of Washington Institutional Review Board (Study 9060).

2.1 | Overview of analytic strategy

The goal of this study was to estimate the number of individuals globally who died of dementia as an underlying cause of death, in line with ICD-10 principles. To conduct this analysis, we first estimated the attributable risk of all-cause mortality via systematic review and meta-analysis, and multiplied this estimate by the number of individuals with dementia to calculate excess deaths due to dementia. However, not all excess deaths among individuals with dementia are likely attributable to dementia as an underlying cause of death due to the presence of common comorbid conditions such as cardiovascular diseases. Therefore, to calculate deaths attributable to dementia as an underlying cause of death, we multiplied excess dementia deaths by the proportion of individuals who died with end-stage dementia out of the total number of excess dementia deaths, using Formula 1:

$$\text{Dementia Deaths} = \text{Excess Dementia Deaths} * \frac{\text{Dementia Deaths with End – Stage Conditions}}{\text{Excess Dementia Deaths}} \quad (1)$$

The overall analytic framework can be visualized in Figure 1. This strategy assumes that individuals who die with conditions signaling

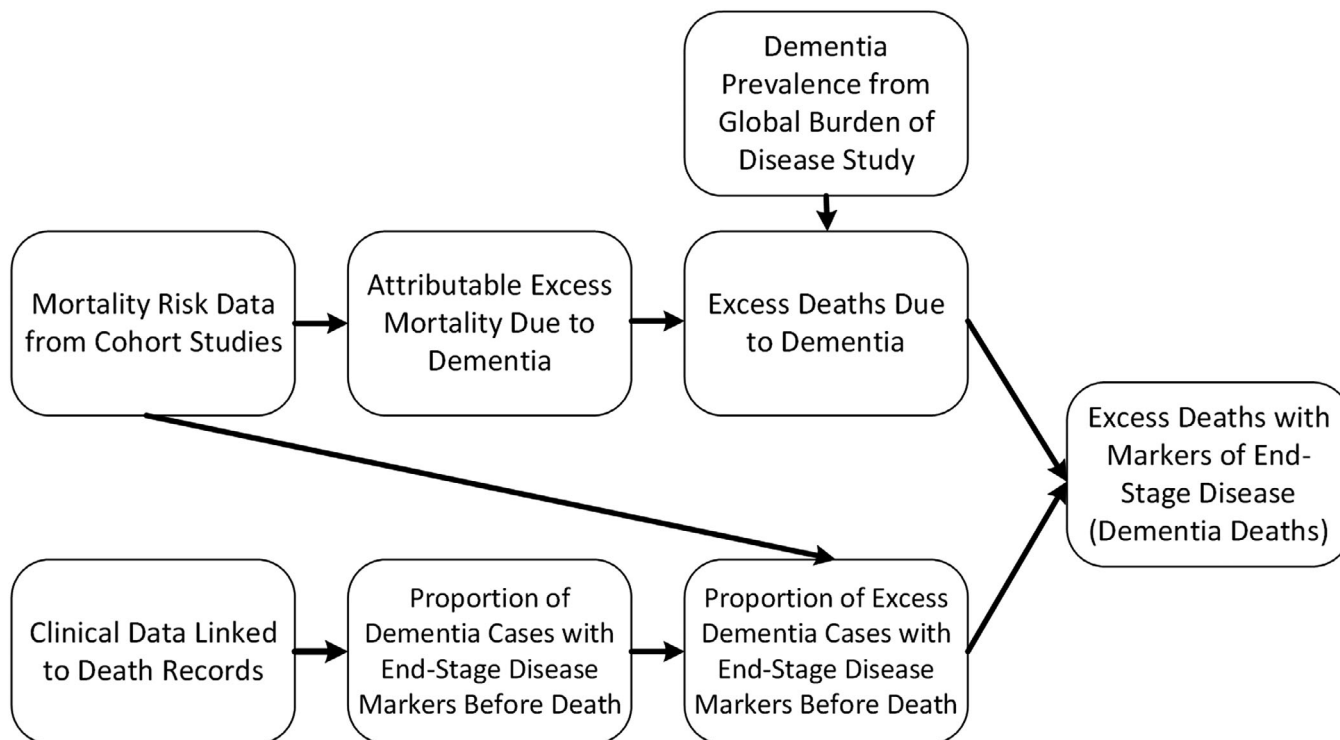


FIGURE 1 Analytical overview for the calculation of deaths attributable to dementia as an underlying cause of death. We multiplied prevalence estimates and attributable excess risk due to dementia from systematic review and meta-analysis to calculate excess deaths due to dementia. Then, we estimated the proportion of excess dementia cases with end-stage markers of disease markers by combining information from clinical data linked to death records and our meta-analysis of mortality risk. We assumed deaths attributable to dementia as the underlying cause of death was the product of excess deaths due to dementia and the proportion of these deaths with markers of end-stage disease

end-stage dementia die from dementia as an underlying cause of death. This assumption is supported by prior research indicating that end-stage conditions such as pneumonia, febrile illness, and eating problems are associated with extremely high short-term mortality rates among those with advanced disease.²²

2.2 | Systematic review of the literature on excess mortality

Through a PubMed literature review focused on dementia excess mortality and relative risk spanning 1980 to 2018, we identified 4470 total hits, of which 34 studies were marked for extraction (additional details in supporting information).^{23–56} The data sources included clinical or community-based cohorts and excluded studies conducted solely in nursing homes. Studies reporting odds ratios, hazard ratios, or relative risks of death given dementia or similar exposure were extracted. Although our case definition was either the Diagnostic and Statistical Manual of Mental Disorders (DSM) or ICD definitions of dementia based on clinical ascertainment by a physician in a population-representative study, we accepted a wider range of exposures including Alzheimer's disease (AD) and cognitive impairment and adjusted for differences in our modeling strategy to increase data volume (Table 1).

2.3 | Calculation and meta-analysis of attributable risk

Using the data on relative risks extracted from each study and the GBD estimate of all-cause mortality rate for the given study location and time period,²¹ we calculated attributable risk of all-cause mortality. By multiplying the excess risk in the exposed (relative risk – 1) by the event rate in the unexposed (approximated using all-cause mortality rates) we estimated the all-cause mortality rate difference, or attributable risk, using Formula 2:

$$\text{Attributable Risk} = (\text{Relative Risk} - 1) * \text{All-Cause Mortality Rate} \quad (2)$$

We then conducted a Bayesian meta-regression on the attributable risk data. The model includes covariates to predict between-study heterogeneity and adds uncertainty from unexplained heterogeneity to coefficient estimates and predictions. Additionally, the model incorporates automatic outlier identification as part of the likelihood function, which identifies data with implausible combinations of means and variances, such that even if a data point is far from the mean, it may not be identified as an outlier if it has a high variance (additional details in supporting information).

TABLE 1 Results of systematic review of 32 studies on all-cause excess mortality with dementia

Characteristics of Data		N (%)
		60
Region name	East Asia	4 (6.7)
	Eastern sub-Saharan Africa	2 (3.3)
	High-income Asia Pacific	4 (6.7)
	High-income North America	22 (36.7)
	North Africa and Middle East	1 (1.7)
	Tropical Latin America	1 (1.7)
	Western Europe	26 (43.3)
Exposure	Alzheimer's disease	11 (18.3)
	Cognitive impairment	10 (16.7)
	Dementia (total)	35 (58.3)
	Vascular dementia	4 (6.7)
Conducted in clinical setting	Clinical setting	10 (16.7)
	Community setting	50 (83.3)
Adjusted for education		32 (53.3)
Adjusted for cardiovascular disease [†]		33 (55.0)
Extensive cardiovascular disease adjustment [†]		15 (25.0)
Adjusted for smoking and alcohol		11 (18.3)
Adjusted for factors in causal pathway		13 (21.7)

[†]Base cardiovascular disease covariates included broad categories such as history of cardiovascular disease or stroke; extensive cardiovascular disease adjustment included more detailed information on specific conditions such as high blood pressure or hyperlipidemia.

Notes: All values represent the number of data points (% in parentheses).

The meta-regression included covariates for the exposure used in each study (all dementia, AD, cognitive impairment), whether the study was conducted in a clinical sample, and five indicators for categories of variables commonly adjusted for in the component studies. These indicator variables described whether each component study of the meta-regression adjusted for educational attainment, basic cardiovascular disease comorbidities (e.g., stroke and heart disease), more extensive cardiovascular disease factors (e.g., blood pressure and cholesterol), and smoking and alcohol consumption. Additionally, some studies adjusted for factors including activities of daily living, or residence in nursing homes, which may be on the causal pathway between dementia exposure and death, and these were grouped together into a dummy variable for the category of "over-controlling." Attributable risk was estimated from this model by generating predictions by age

group for the mean population-based study on dementia, which did not control for education, cardiovascular disease, or other factors.

2.4 | Prevalence estimation and the calculation of excess deaths

We used all available data on the prevalence of dementia from cross-sectional studies, cohort studies, and administrative claims databases for the estimation of dementia prevalence (additional details in supporting information; data sources are available at the Global Data Health Exchange [<http://ghdx.healthdata.org/>]). Using DisMod-MR 2.1, the Bayesian meta-regression tool primarily used in nonfatal modeling for GBD with settings of no remission and no incidence before age 40, we generated estimates for the prevalence of dementia by age, sex, year, and location (additional details in supporting information).⁵⁷ We then calculated the total number of excess deaths due to dementia as the product of prevalence and attributable risk.

2.5 | Calculation of the proportion of excess deaths attributable to dementia

Our estimate of the total number of excess deaths in those with dementia likely includes deaths that should be attributed to other conditions, such as cardiovascular diseases, that are more common in those with dementia due to shared risk factors such as high blood pressure or lower educational attainment.⁵⁸ To calculate the number of deaths caused by dementia from the number of excess dementia deaths, we used mortality records linked to inpatient records, covering deaths from 2003 to 2017 in the Emilia Romagna region of Italy, and looked for markers of severe, end-stage disease up to 1 year before death. A similar strategy of identifying cases of end-stage disease using ICD codes has been implemented using Medicare data in the United States.⁵⁹ To select these markers, for each ICD code in the data we calculated the difference in the proportion of individuals who died with dementia and had a record of such a code in the year before death and the proportion of individuals who died without dementia and had a record of the same code in the year before death. We defined dementia as any ICD-9 code for dementia (290–290.4, 294.1–294.2, 294.8–294.9, 331.0–331.2), in either inpatient records or death records. We reviewed the 150 codes with the highest difference and selected codes that could indicate end-stage disease, excluding codes for conditions such as cardiovascular disease or cancers that cannot plausibly be caused by dementia. Codes for decubitus ulcer, malnutrition, sepsis, pneumonia, urinary tract infections, falling from bed, senility, dehydration, sodium imbalance, muscular wasting, bronchitis, dysphagia, hip fracture, and bedridden status were used as indicators of severe disease (ICD code lists in supporting information).

To determine the proportion of excess deaths that could be ascribed to dementia as the underlying cause of death, we calculated the proportion of dementia deaths with markers of end-stage disease in the year prior to death, above and beyond the occurrence of end-stage disease

markers in those who died without dementia. The subtraction of the proportions with end-stage disease markers in those without dementia from the proportions in those with dementia we deemed to represent individuals who died with severe, end-stage dementia.

To apply the estimates of the proportion who died with severe, end-stage dementia out of those who died with dementia (died with severe disease/total deaths with dementia) to the total excess deaths we adjusted these proportions using the adjustment factor (relative risk/[relative risk - 1]) to calculate the proportion of individuals who died with end-stage dementia out of excess dementia deaths with Formula 3:

$$\frac{\frac{\text{Died with Severe Disease}}{\text{Excess Dementia Deaths}}}{\frac{\text{Relative Risk}}{\text{Relative Risk} - 1}} = \frac{\text{Died with Severe Disease}}{\text{Total Deaths with Dementia}} * \quad (3)$$

Relative risks of mortality with dementia were estimated using a second meta-regression model and the same studies identified through the literature review described in section 2.2.

2.6 | Calculation of final results

We calculated the number of deaths due to dementia as the product of total excess dementia deaths and the proportion of those who died with severe disease out of excess dementia deaths. These results were combined with mortality estimates from all other causes of death and scaled to sum to the total estimated all-cause mortality in a particular age, sex, year, and location combination. Age-standardized rates were calculated using the world population standard for GBD.⁶⁰ Regional and global estimates were calculated by aggregating the estimates from the most-detailed locations. The Socio-demographic Index (SDI), a composite measure of income, education, and fertility, was calculated as the geometric mean of normalized estimates of per capita income, the fertility rate in women under 25, and the average years of education in individuals 15 and older.²¹ Countries were divided into quintiles of SDI for analyses. Throughout all steps included in the analytic process, uncertainty in the estimates was propagated by sampling 1000 draws at each step. For example, the calculation of the product of two estimates involved conducting a draw-wise multiplication of 1000 draws from the distribution of each estimate. We defined uncertainty intervals as the 25th and 975th values of the ordered draws.

3 | RESULTS

We identified 34 studies containing 60 unique estimates (on a given, age, sex, and/or exposure category) on the excess mortality associated with dementia. These data covered 7 of the 21 world regions, most from high-income North America and Western Europe (Table 1).

Attributable risk increased with age, and this relationship became more pronounced after 70 years of age. In 40- to 44-year-olds, the attributable risk was 0.019 (0.003–0.087), and in the 95+ age group

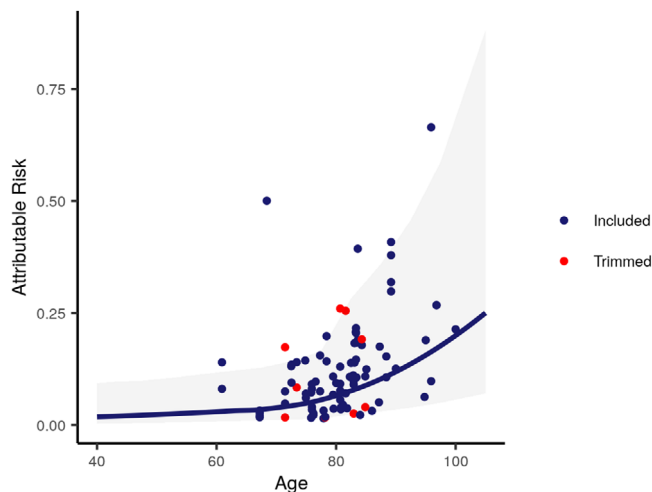


FIGURE 2 Attributable risk for all-cause mortality due to dementia by age. Dots represent individual studies, and the line shows the results of the meta-regression. Trimmed data points are those identified as outliers during the model-fitting process; all other data points are included in the model. These estimates are applied across all years and geographies estimated in this study

these estimates reached 0.169 (0.0472–0.574; Figure 2). This indicates that individuals over 95 with dementia experience a mortality rate that is 16,900 per 100,000 person-years higher than those over 95 who do not have dementia.

Of the 14 markers of severe, end-stage disease considered, the fraction of people who had pneumonia in the last year before death out of those who died with dementia was the highest (0.31). This proportion remained the highest (0.13) after subtracting the fraction of people without dementia who had the same end-stage condition in the last year before death to calculate the excess proportion with pneumonia in those who died with dementia. The next end-stage conditions with the largest absolute and excess proportions were dehydration (absolute: 0.15; excess: 0.11), urinary tract infections (0.12; 0.06), and decubitus ulcer (0.06; 0.05). The proportion of individuals who died with dementia and had any end-stage disease marker in the year before death was 0.59, and the proportion of individuals with an end-stage disease marker in the year before death who died without dementia was 0.35. Therefore, we calculated the proportion of people with dementia who died with severe, end-stage dementia (the excess proportion) as 0.24 (Figure 3).

Overall, we estimated there were 1.62 million (0.41–4.21) deaths due to dementia globally in 2019. Far more deaths occurred in women (1.06 million [0.27–2.71]) than men (0.56 million [0.14–1.51]), giving a female-to-male ratio of 1.94 (1.76–2.11; Table 2). The female-to-male ratio for age-standardized rates was 1.19 (1.10–1.26), suggesting that a portion of the sex difference was independent of the higher life expectancy in women. Between 1990 and 2019, there was a significant increase globally in age-standardized mortality rates among males (5.1% [0.4–12.0]), but a non-significant increase in age-standardized mortality rates among females (3.0% [-2.6–11.0]). Among males, the largest increase was observed for low SDI countries (9.6% [0.3–26.3]).

TABLE 2 Deaths in 2019 and percentage change of all-age and age-standardized mortality rates by location for dementia

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Global	559,228.5 (135,257.1 to 1505721.2)	114.4 (102.1 to 132.5)	5.1 (0.4 to 12.0)	1,064,047.4 (274,500.8 to 2,705,358.7)	92.9 (80.4 to 112.3)	3.0 (−2.6 to 11.0)
Low SDI	25,788.3 (6018.1 to 73,781.0)	33.9 (21.5 to 53.8)	9.6 (0.3 to 26.3)	36,307.3 (9062.9 to 97,442.0)	47.3 (29.1 to 71.9)	10.6 (−3.0 to 28.8)
Low-middle SDI	75,886.8 (17,739.8 to 212,133.3)	109.8 (90.1 to 140.2)	9.1 (0.3 to 24.0)	109,380.8 (27,179.5 to 289,174.0)	128.4 (102.0 to 163.9)	5.8 (−6.0 to 22.0)
Middle SDI	145,060.8 (34,246.2 to 397,115.0)	140.7 (117.6 to 173.1)	3.4 (−4.5 to 15.9)	242,455.4 (58,645.8 to 626,326.7)	127.4 (103.4 to 169.8)	−0.3 (−9.7 to 18.1)
High-middle SDI	135,182.4 (31,908.3 to 368,661.4)	136.0 (117.9 to 159.0)	1.7 (−4.1 to 8.9)	289,148.3 (73,256.3 to 753,758.8)	120.4 (102.3 to 147.4)	1.7 (−4.8 to 11.8)
High SDI	176,987.3 (44,259.2 to 469,442.4)	140.8 (126.4 to 161.1)	5.8 (1.4 to 11.7)	386,228.6 (103,824.8 to 924,598.2)	102.9 (86.1 to 124.7)	3.6 (−2.3 to 11.8)
Central Asia	2879.9 (675.3 to 8160.8)	−7.4 (−15.7 to 4.8)	9.5 (2.1 to 25.6)	6067.6 (1472.1 to 16,430.4)	−11.6 (−18.2 to −4.6)	8.3 (0.9 to 16.7)
Armenia	315.3 (74.0 to 858.6)	188.0 (151.7 to 233.2)	16.8 (3.0 to 35.0)	557.7 (134.0 to 1497.2)	166.2 (132.6 to 207.5)	13.7 (−0.1 to 30.2)
Azerbaijan	352.0 (79.9 to 1,037.9)	−5.7 (−24.9 to 32.6)	12.4 (−6.8 to 82.5)	588.7 (126.7 to 1698.2)	−32.9 (−49.2 to 3.2)	18.1 (−5.3 to 91.7)
Georgia	483.6 (113.9 to 1325.8)	209.1 (164.8 to 265.2)	5.7 (−6.4 to 20.7)	1236.9 (307.6 to 3240.4)	204.6 (157.8 to 271.8)	1.5 (−10.9 to 18.5)
Kazakhstan	655.8 (151.2 to 1902.7)	25.1 (8.2 to 48.0)	12.3 (−0.7 to 37.0)	1663.6 (387.9 to 4673.7)	8.7 (−3.0 to 21.9)	9.4 (−1.9 to 21.3)
Kyrgyzstan	242.8 (58.3 to 667.0)	11.4 (−0.1 to 24.1)	10.1 (−0.6 to 21.3)	480.0 (113.7 to 1362.3)	−20.8 (−30.8 to −11.5)	11.5 (−1.8 to 24.1)
Mongolia	77.9 (17.9 to 225.7)	8.7 (−11.1 to 31.4)	−1.5 (−15.2 to 15.2)	146.7 (34.1 to 420.4)	−2.0 (−20.3 to 19.3)	−1.6 (−18.5 to 17.6)
Tajikistan	167.9 (38.8 to 481.3)	−58.7 (−67.3 to −50.8)	12.8 (−5.6 to 31.1)	277.7 (66.5 to 754.4)	−56.3 (−64.3 to −48.3)	14.3 (−5.9 to 33.7)
Turkmenistan	179.7 (42.9 to 499.0)	46.3 (23.6 to 77.3)	0.2 (−14.2 to 20.3)	402.5 (100.2 to 1058.6)	68.1 (43.4 to 102.7)	−1.7 (−15.7 to 16.6)
Uzbekistan	405.0 (94.6 to 1151.2)	−63.5 (−71.3 to −55.7)	5.2 (−6.6 to 17.2)	713.8 (168.5 to 2057.7)	−63.7 (−71.0 to −57.1)	11.9 (−2.0 to 22.3)
Central Europe	15,986.2 (3813.1 to 42,672.8)	122.6 (100.3 to 149.0)	−1.2 (−9.1 to 7.9)	35,119.8 (8472.2 to 91,059.3)	132.1 (110.2 to 161.7)	−1.9 (−9.8 to 7.9)
Albania	344.3 (78.1 to 913.5)	303.2 (222.9 to 404.0)	−2.0 (−19.7 to 21.6)	572.5 (138.4 to 1477.1)	167.1 (114.4 to 232.1)	−3.1 (−21.6 to 20.2)
Bosnia and Herzegovina	390.2 (90.1 to 1064.5)	200.4 (150.9 to 256.7)	−3.1 (−18.5 to 13.7)	689.5 (160.4 to 1871.6)	184.1 (136.3 to 236.6)	−4.7 (−20.7 to 12.2)
Bulgaria	1057.3 (239.8 to 3004.6)	135.0 (95.1 to 178.8)	1.6 (−12.0 to 17.8)	2088.7 (485.9 to 5832.3)	188.9 (142.0 to 252.1)	−1.6 (−15.4 to 15.3)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Croatia	660.9 (151.8 to 1832.8)	151.7 (112.5 to 206.0)	−0.2 (−14.7 to 18.2)	1504.6 (360.7 to 3891.0)	144.3 (105.2 to 194.5)	1.7 (−13.9 to 21.1)
Czech Republic	1609.2 (375.9 to 4202.4)	123.4 (91.2 to 165.5)	1.5 (−11.3 to 18.5)	3,511.6 (865.5 to 9000.4)	97.6 (69.7 to 139.3)	4.2 (−9.6 to 24.4)
Hungary	1 335.7 (306.5 to 3611.5)	98.9 (73.2 to 132.9)	−0.8 (−12.0 to 13.7)	3 514.0 (840.8 to 8909.8)	125.2 (94.6 to 167.9)	3.3 (−9.5 to 21.3)
Montenegro	67.2 (15.3 to 182.9)	63.3 (40.6 to 90.5)	−0.4 (−13.1 to 18.4)	117.4 (27.4 to 309.8)	60.3 (38.0 to 112.7)	3.9 (−9.7 to 41.7)
North Macedonia	169.4 (38.3 to 474.1)	56.9 (30.7 to 89.3)	6.8 (−9.3 to 33.0)	267.2 (59.6 to 741.7)	66.2 (36.3 to 105.9)	9.6 (−8.4 to 41.4)
Poland	5430.2 (1260.0 to 14,735.3)	117.5 (84.0 to 161.0)	−5.5 (−18.1 to 11.0)	13,038.4 (3096.3 to 35,654.9)	116.3 (83.8 to 157.8)	−6.5 (−20.0 to 10.7)
Romania	2 973.2 (718.3 to 7868.4)	158.9 (121.8 to 202.9)	−1.0 (−12.4 to 13.0)	5901.3 (1457.2 to 15,674.1)	208.9 (162.3 to 270.1)	−0.6 (−14.0 to 15.7)
Serbia	1 010.4 (224.3 to 2771.2)	65.4 (37.1 to 108.1)	3.7 (−10.9 to 28.7)	1,557.0 (349.5 to 4456.0)	57.6 (28.5 to 101.5)	−1.6 (−17.2 to 23.5)
Slovakia	562.8 (129.2 to 1490.3)	57.4 (31.6 to 87.8)	−2.4 (−17.4 to 14.5)	1396.7 (329.5 to 3535.6)	83.1 (53.9 to 122.5)	−2.1 (−17.7 to 17.2)
Slovenia	375.5 (90.3 to 991.7)	140.3 (87.9 to 205.9)	4.1 (−16.8 to 30.7)	961.1 (249.1 to 2423.8)	179.3 (112.8 to 274.5)	0.8 (−22.0 to 31.0)
Eastern Europe	18,376.8 (4327.3 to 49,475.5)	142.5 (118.0 to 177.5)	6.1 (−2.9 to 18.6)	54,705.3 (13,131.1 to 149,095.2)	94.8 (75.7 to 118.7)	6.5 (−2.6 to 17.8)
Belarus	844.2 (198.4 to 2243.7)	59.0 (34.5 to 90.8)	4.6 (−10.6 to 24.4)	2841.3 (695.2 to 7511.8)	81.3 (52.9 to 119.6)	4.4 (−11.6 to 26.1)
Estonia	182.9 (44.1 to 489.5)	194.1 (145.4 to 256.5)	14.7 (−2.3 to 36.7)	573.8 (145.1 to 1510.1)	169.3 (122.3 to 224.8)	13.5 (−5.0 to 35.2)
Latvia	243.5 (58.4 to 670.6)	124.8 (90.1 to 168.0)	8.6 (−5.9 to 27.5)	787.5 (185.6 to 2045.9)	136.6 (95.9 to 189.3)	7.3 (−11.1 to 29.9)
Lithuania	382.4 (92.1 to 1029.4)	94.1 (67.4 to 121.8)	5.4 (−7.7 to 19.1)	1159.7 (286.4 to 3061.9)	153.2 (119.0 to 195.0)	4.4 (−9.5 to 20.1)
Moldova	377.9 (89.8 to 1046.9)	167.3 (137.7 to 204.3)	−1.8 (−11.0 to 9.1)	881.3 (217.8 to 2361.8)	184.7 (151.7 to 232.3)	−0.4 (−9.9 to 13.3)
Russia	12,039.2 (2888.0 to 32,033.2)	178.4 (140.4 to 234.6)	4.7 (−7.3 to 20.0)	36,398.0 (8759.0 to 97,034.3)	93.9 (68.9 to 123.6)	4.1 (−7.8 to 18.3)
Ukraine	4306.7 (994.6 to 12,348.2)	107.6 (80.4 to 140.8)	10.4 (−1.5 to 25.1)	12,063.6 (2805.3 to 32,884.6)	91.0 (61.8 to 126.2)	14.3 (−2.3 to 33.6)
Australasia	4561.0 (1113.8 to 12,133.4)	155.7 (133.8 to 189.7)	0.3 (−5.8 to 9.6)	8745.6 (2319.4 to 21,727.2)	90.0 (75.7 to 112.2)	−0.5 (−6.2 to 8.5)
Australia	3841.2 (935.1 to 10,162.1)	157.6 (133.3 to 194.3)	0.6 (−6.2 to 11.8)	7399.1 (1971.3 to 18,237.9)	91.1 (75.6 to 115.3)	−0.6 (−7.1 to 9.8)
New Zealand	719.9 (176.3 to 1965.0)	147.7 (126.9 to 176.5)	−0.8 (−7.7 to 8.5)	1346.6 (351.7 to 3385.6)	84.7 (70.9 to 105.6)	−0.2 (−6.3 to 8.7)
High-income Asia Pacific	56,677.3 (14,611.8 to 148,035.7)	425.2 (375.0 to 506.3)	28.5 (19.4 to 41.0)	128,148.5 (37,175.4 to 293,499.2)	436.5 (357.5 to 548.1)	21.8 (8.1 to 38.8)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Brunei	7.3 (1.7 to 19.5)	100.5 (69.0 to 137.7)	9.2 (−3.4 to 24.4)	16.3 (3.8 to 45.4)	83.5 (63.7 to 108.8)	9.5 (−2.3 to 23.2)
Japan	50,832.5 (13,165.2 to 132,325.7)	456.7 (401.3 to 545.3)	32.2 (22.6 to 45.6)	114,041.4 (33,669.4 to 259,294.0)	475.1 (387.0 to 602.7)	25.8 (10.5 to 43.8)
South Korea	5329.9 (1302.9 to 14,658.1)	412.4 (344.2 to 503.2)	−5.2 (−17.0 to 9.5)	13,121.0 (3431.0 to 32,727.1)	337.5 (280.1 to 427.8)	−5.9 (−16.5 to 10.4)
Singapore	507.7 (124.3 to 1 325.9)	197.3 (169.7 to 240.2)	−0.5 (−7.7 to 10.9)	969.8 (261.3 to 2 345.0)	175.6 (147.6 to 213.6)	−1.6 (−10.3 to 10.9)
High-income	51,662.1 (12,640.0 to 134,630.7)	78.5 (64.1 to 98.8)	−2.1 (−10.2 to 8.0)	109,320.0 (28,623.1 to 263,132.9)	47.7 (35.5 to 64.8)	−0.9 (−8.5 to 9.1)
North America						
Canada	5579.0 (1372.3 to 14,551.0)	121.5 (101.1 to 147.8)	−5.4 (−14.1 to 5.3)	11,472.9 (3009.7 to 28,285.5)	86.8 (71.0 to 108.1)	−6.1 (−13.4 to 3.4)
Greenland	3.5 (0.8 to 9.5)	214.3 (167.7 to 265.7)	0.5 (−12.5 to 16.5)	5.5 (1.4 to 14.5)	150.3 (111.0 to 208.6)	0.2 (−14.8 to 21.3)
USA	46,078.8 (11,288.7 to 120,166.5)	74.5 (59.8 to 94.8)	−1.8 (−10.2 to 8.5)	97,839.9 (25,611.1 to 235,757.6)	44.3 (32.2 to 61.7)	−0.4 (−8.3 to 9.9)
Southern Latin America	5893.1 (1420.9 to 16,373.0)	86.3 (74.6 to 102.6)	1.7 (−3.7 to 8.6)	12,453.3 (3063.9 to 32,452.5)	96.4 (83.1 to 112.5)	0.5 (−4.8 to 6.4)
Argentina	3694.7 (875.9 to 10,300.6)	69.4 (56.0 to 86.1)	2.0 (−5.6 to 11.5)	8349.9 (2038.8 to 21,613.4)	80.9 (66.4 to 97.1)	1.4 (−5.5 to 8.7)
Chile	1761.1 (429.1 to 4751.0)	149.2 (128.7 to 178.3)	2.7 (−4.4 to 13.4)	3042.8 (786.9 to 7969.3)	173.4 (150.7 to 211.1)	0.2 (−7.1 to 10.3)
Uruguay	437.0 (106.3 to 1210.8)	74.1 (59.4 to 92.2)	−3.0 (−9.8 to 5.4)	1 059.8 (268.5 to 2712.3)	90.2 (76.5 to 108.1)	−1.1 (−7.6 to 6.3)
Western Europe	82,115.7 (19,923.2 to 224,410.0)	126.6 (114.1 to 144.8)	−1.4 (−4.9 to 3.7)	182,650.0 (47,390.6 to 451,716.7)	82.1 (71.4 to 97.8)	−3.8 (−7.5 to 2.0)
Andorra	12.8 (3.2 to 33.6)	273.6 (180.5 to 404.8)	−5.0 (−23.6 to 15.1)	23.6 (6.4 to 60.4)	355.3 (218.5 to 541.6)	−3.8 (−28.9 to 24.8)
Austria	1391.5 (332.7 to 3783.9)	113.0 (96.3 to 137.0)	−1.4 (−8.1 to 7.4)	3410.3 (867.8 to 8730.4)	71.8 (56.5 to 93.9)	−2.0 (−8.2 to 6.8)
Belgium	1950.6 (469.2 to 5385.4)	109.6 (90.7 to 132.6)	−4.0 (−11.5 to 4.7)	4664.0 (1196.1 to 11,653.6)	70.4 (54.1 to 91.4)	−6.5 (−13.7 to 2.6)
Cyprus	114.2 (27.0 to 330.4)	69.5 (46.9 to 96.1)	−12.6 (−22.5 to 0.4)	209.9 (51.1 to 570.8)	120.0 (84.8 to 164.6)	−9.6 (−19.8 to 3.2)
Denmark	850.3 (203.5 to 2331.7)	54.9 (38.1 to 72.9)	−0.5 (−11.2 to 11.0)	1852.5 (476.1 to 4761.0)	37.6 (20.2 to 57.1)	0.6 (−11.3 to 13.2)
Finland	947.1 (227.0 to 2553.2)	167.3 (145.3 to 196.9)	−5.8 (−12.4 to 3.1)	2333.1 (604.5 to 5811.3)	101.7 (80.8 to 130.3)	−6.0 (−15.0 to 3.8)
France	13,214.6 (3219.8 to 34,550.9)	145.1 (119.8 to 179.4)	2.9 (−5.3 to 15.0)	32,793.3 (8754.9 to 77,733.2)	102.0 (82.4 to 133.9)	3.5 (−5.7 to 18.3)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Germany	14,694.6 (3500.3 to 40,974.5)	97.5 (77.0 to 122.4)	-14.8 (-23.6 to -4.9)	34,861.9 (8873.8 to 88,539.8)	45.6 (26.6 to 65.5)	-17.5 (-28.1 to -7.4)
Greece	2694.1 (642.9 to 7496.8)	198.4 (167.4 to 248.5)	1.1 (-6.0 to 13.3)	4302.2 (1073.8 to 11,309.6)	166.8 (142.9 to 196.8)	-0.9 (-7.1 to 7.1)
Iceland	49.8 (12.2 to 130.5)	73.3 (58.2 to 91.0)	0.9 (-7.9 to 11.0)	100.8 (26.9 to 240.5)	70.2 (51.9 to 96.3)	-3.8 (-13.4 to 9.7)
Ireland	546.3 (127.8 to 1499.1)	98.2 (81.3 to 122.8)	0.1 (-7.3 to 10.9)	1110.7 (282.0 to 2781.9)	74.5 (58.6 to 97.6)	-0.3 (-7.3 to 10.2)
Israel	969.7 (236.1 to 2587.2)	74.2 (57.8 to 98.2)	-0.7 (-7.2 to 7.5)	1807.1 (474.3 to 4561.1)	123.6 (100.4 to 159.8)	-1.6 (-7.9 to 7.8)
Italy	15,854.3 (3907.5 to 43,081.1)	246.8 (223.5 to 279.0)	19.5 (10.2 to 32.1)	32,908.4 (8694.0 to 83,572.0)	206.1 (184.8 to 236.1)	16.4 (7.7 to 29.3)
Luxembourg	70.4 (17.1 to 191.1)	73.2 (51.1 to 103.0)	-3.6 (-14.2 to 11.6)	171.1 (45.1 to 426.7)	55.5 (35.1 to 86.6)	-5.7 (-16.4 to 9.9)
Malta	67.9 (16.1 to 185.3)	174.9 (150.1 to 211.7)	0.7 (-7.5 to 13.3)	151.8 (38.8 to 374.0)	191.7 (162.3 to 236.9)	-0.7 (-10.3 to 12.2)
Monaco	9.2 (2.2 to 24.4)	60.1 (36.7 to 91.9)	6.5 (-8.6 to 23.6)	19.1 (4.9 to 48.1)	29.9 (5.8 to 60.1)	5.8 (-15.4 to 28.8)
Netherlands	2826.1 (689.6 to 7493.6)	98.4 (85.4 to 116.1)	-4.1 (-10.3 to 4.4)	5888.5 (1523.4 to 14,301.4)	52.7 (42.4 to 68.8)	-7.3 (-13.0 to 0.6)
Norway	800.4 (193.2 to 2149.6)	29.4 (21.5 to 40.0)	-7.0 (-11.3 to -1.2)	1832.9 (474.6 to 4476.3)	21.2 (12.8 to 32.9)	-6.3 (-10.6 to 1.7)
Portugal	2003.9 (467.5 to 5470.8)	229.3 (196.0 to 275.1)	3.9 (-3.8 to 14.5)	4597.9 (1161.5 to 11,636.9)	200.8 (172.4 to 250.2)	1.9 (-5.6 to 14.2)
San Marino	6.4 (1.5 to 17.1)	138.2 (74.1 to 209.4)	-2.5 (-27.5 to 24.0)	13.2 (3.3 to 33.7)	114.1 (57.0 to 187.5)	-2.5 (-29.2 to 31.9)
Spain	8297.1 (2005.4 to 22,012.2)	100.6 (75.7 to 128.4)	-16.8 (-25.1 to -7.7)	20,910.6 (5456.7 to 50,985.5)	110.0 (88.9 to 140.6)	-14.6 (-20.6 to -5.4)
Sweden	1882.2 (451.4 to 5170.4)	48.3 (34.7 to 65.3)	-8.3 (-15.3 to 0.5)	3755.2 (953.2 to 9502.8)	19.6 (8.7 to 32.4)	-13.2 (-20.1 to -5.2)
Switzerland	1560.4 (386.5 to 4188.2)	98.4 (81.7 to 123.3)	3.2 (-3.7 to 13.2)	3577.9 (945.9 to 8761.0)	68.3 (53.6 to 89.2)	4.5 (-2.7 to 14.2)
UK	11,230.0 (2706.1 to 30,400.6)	103.2 (90.9 to 120.9)	3.6 (-0.3 to 9.7)	21,194.9 (5393.2 to 53,699.3)	33.9 (26.2 to 46.8)	-1.5 (-5.4 to 6.0)
Andean Latin America	4943.7 (1190.8 to 12,671.0)	98.4 (64.6 to 136.8)	2.9 (-14.1 to 22.6)	6231.1 (1516.5 to 15,850.1)	117.7 (84.7 to 164.0)	-0.4 (-14.8 to 20.5)
Bolivia	611.2 (137.5 to 1635.8)	96.3 (57.8 to 147.1)	5.3 (-14.9 to 31.7)	781.4 (180.3 to 2072.7)	75.9 (47.6 to 112.3)	7.5 (-9.9 to 30.2)
Ecuador	1169.1 (282.2 to 3327.5)	71.9 (41.8 to 105.9)	6.4 (-12.2 to 26.5)	1469.2 (350.9 to 4015.4)	104.5 (70.5 to 145.8)	-1.0 (-16.2 to 17.8)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts (95% UI)	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts (95% UI)	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Peru	3163.4 (754.4 to 8193.0)	114.8 (69.5 to 174.5)	1.3 (−20.2 to 31.2)	3980.6 (994.2 to 10,023.5)	137.5 (89.6 to 208.6)	−2.0 (−21.5 to 27.4)
Caribbean	4597.5 (1153.7 to 11,746.2)	87.0 (66.1 to 111.8)	1.1 (−9.7 to 13.2)	6396.5 (1655.1 to 15,821.9)	112.1 (89.1 to 143.4)	0.5 (−9.5 to 12.5)
Antigua and Barbuda	6.4 (1.5 to 17.3)	21.3 (6.0 to 38.2)	−0.5 (−12.1 to 12.6)	10.0 (2.4 to 27.2)	−20.4 (−29.5 to −11.9)	4.7 (−6.4 to 15.6)
The Bahamas	23.0 (5.4 to 63.5)	119.1 (85.7 to 160.3)	−0.3 (−13.1 to 15.9)	37.9 (9.6 to 101.5)	73.8 (50.3 to 104.2)	−0.9 (−14.3 to 15.2)
Barbados	39.6 (9.6 to 106.8)	65.9 (45.2 to 91.1)	3.0 (−8.8 to 16.6)	60.9 (14.6 to 159.9)	37.5 (20.9 to 57.0)	7.2 (−5.3 to 21.4)
Belize	22.5 (5.4 to 59.1)	34.2 (18.2 to 54.5)	6.5 (−6.0 to 22.2)	25.1 (6.3 to 64.1)	11.4 (−1.1 to 27.0)	0.3 (−10.8 to 14.3)
Bermuda	10.8 (2.6 to 28.9)	193.4 (160.1 to 237.9)	−2.6 (−12.8 to 12.0)	21.0 (5.4 to 53.0)	185.0 (146.5 to 246.3)	−0.8 (−13.6 to 20.5)
Cuba	1940.9 (478.3 to 5167.7)	123.3 (88.9 to 163.6)	1.5 (−13.1 to 18.5)	2562.3 (659.1 to 6742.3)	166.0 (125.6 to 216.7)	−0.9 (−15.8 to 16.0)
Dominica	7.2 (1.7 to 19.6)	50.9 (27.8 to 79.4)	−1.4 (−16.1 to 16.9)	12.1 (2.9 to 32.2)	35.4 (16.6 to 58.7)	0.5 (−12.5 to 17.2)
Dominican Republic	692.0 (161.6 to 1874.1)	85.7 (49.4 to 128.2)	−2.9 (−20.5 to 17.3)	937.1 (225.1 to 2476.2)	134.1 (94.9 to 185.2)	−1.3 (−17.4 to 19.8)
Grenada	4.7 (1.1 to 13.1)	−36.9 (−45.4 to −26.6)	5.2 (−4.0 to 16.8)	11.5 (2.8 to 30.4)	−15.9 (−23.7 to −6.9)	5.7 (−3.7 to 16.9)
Guyana	32.6 (7.6 to 88.7)	70.7 (40.1 to 108.7)	4.6 (−12.5 to 25.0)	46.6 (11.2 to 125.6)	81.4 (51.4 to 117.9)	1.1 (−14.9 to 19.7)
Haiti	370.5 (82.2 to 1 017.0)	52.6 (22.5 to 89.8)	3.9 (−14.4 to 25.8)	396.1 (87.6 to 1 151.9)	30.3 (−1.0 to 77.1)	17.0 (−11.6 to 58.1)
Jamaica	308.2 (76.1 to 781.0)	74.1 (47.6 to 107.3)	1.6 (−13.9 to 20.0)	471.9 (119.4 to 1 181.8)	83.1 (55.6 to 117.5)	−0.3 (−14.9 to 18.4)
Puerto Rico	768.9 (190.9 to 1968.7)	189.6 (140.4 to 257.5)	−2.4 (−18.2 to 19.6)	1257.2 (322.9 to 3170.4)	235.9 (180.6 to 313.0)	−2.1 (−17.6 to 19.4)
Saint Kitts and Nevis	2.7 (0.6 to 7.5)	−12.3 (−21.7 to 0.0)	−3.5 (−13.1 to 9.5)	5.5 (1.3 to 14.8)	10.7 (−4.0 to 33.1)	−3.7 (−14.3 to 12.7)
Saint Lucia	15.6 (3.8 to 42.2)	161.4 (128.2 to 202.6)	1.2 (−9.6 to 15.6)	25.3 (6.2 to 66.4)	139.3 (110.9 to 179.4)	4.0 (−7.3 to 19.7)
Saint Vincent and the Grenadines	9.8 (2.3 to 26.6)	122.1 (97.4 to 152.7)	−5.6 (−14.8 to 5.3)	12.1 (2.9 to 32.1)	53.9 (39.5 to 71.2)	−6.3 (−15.1 to 3.7)
Suriname	41.8 (9.9 to 109.9)	58.7 (36.8 to 84.3)	2.1 (−11.9 to 18.6)	67.3 (16.8 to 171.4)	49.2 (30.1 to 72.5)	3.3 (−10.2 to 19.5)
Trinidad and Tobago	133.9 (31.3 to 364.5)	163.0 (111.4 to 233.4)	−2.5 (−19.1 to 18.9)	201.2 (49.5 to 517.9)	163.7 (117.2 to 234.1)	−0.3 (−17.2 to 23.5)
Virgin Islands	10.7 (2.5 to 28.8)	171.7 (131.8 to 219.9)	−5.4 (−17.3 to 7.9)	18.7 (4.6 to 49.2)	176.1 (137.5 to 222.3)	−4.9 (−17.4 to 9.9)
Central Latin America	22,046.6 (5370.3 to 55 473.9)	142.1 (115.2 to 175.0)	3.2 (−7.6 to 16.1)	29,344.4 (7535.4 to 75 028.8)	169.9 (140.5 to 211.1)	0.2 (−9.6 to 14.6)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Colombia	5678.3 (1422.9 to 14,469.7)	227.2 (167.3 to 302.3)	0.8 (−17.0 to 24.2)	7994.1 (2047.8 to 19,681.9)	263.4 (204.2 to 350.4)	−1.0 (−17.0 to 21.7)
Costa Rica	541.3 (134.3 to 1361.9)	125.9 (87.1 to 177.8)	3.5 (−14.1 to 25.9)	753.9 (198.2 to 1821.8)	155.6 (113.6 to 211.7)	1.8 (−14.1 to 24.0)
El Salvador	666.4 (161.4 to 1716.1)	133.8 (91.5 to 180.5)	6.2 (−13.2 to 27.2)	1028.7 (261.4 to 2522.0)	144.8 (99.2 to 199.6)	4.9 (−15.1 to 29.0)
Guatemala	801.8 (188.5 to 2236.1)	68.0 (34.9 to 109.0)	1.6 (−15.0 to 20.8)	1139.2 (272.9 to 3013.9)	149.7 (105.7 to 207.1)	−2.9 (−17.4 to 16.2)
Honduras	512.8 (120.9 to 1411.4)	52.9 (25.9 to 112.0)	14.4 (−5.4 to 59.2)	545.2 (126.9 to 1509.6)	50.3 (20.4 to 102.6)	16.2 (−6.1 to 55.2)
Mexico	10,665.9 (2510.6 to 29,581.7)	133.6 (100.6 to 173.2)	5.5 (−8.0 to 22.2)	12,991.0 (3178.0 to 35,284.5)	157.3 (123.2 to 203.1)	−1.2 (−13.4 to 14.4)
Nicaragua	283.4 (69.6 to 802.6)	85.6 (55.8 to 111.3)	−0.3 (−15.1 to 12.6)	422.8 (104.4 to 1103.7)	65.4 (40.9 to 86.6)	13.9 (−2.3 to 28.2)
Panama	449.8 (111.1 to 1145.0)	92.8 (57.6 to 133.2)	3.3 (−16.0 to 25.0)	604.0 (158.8 to 1467.4)	120.6 (84.6 to 168.4)	2.4 (−14.2 to 25.4)
Venezuela	2 447.1 (585.7 to 6349.0)	143.3 (100.4 to 194.7)	0.3 (−17.4 to 20.8)	3 865.7 (977.6 to 9437.2)	170.7 (124.2 to 238.8)	−1.9 (−18.2 to 20.9)
Tropical Latin America	21,334.4 (5340.7 to 55,586.3)	170.3 (153.0 to 199.4)	−1.0 (−5.8 to 5.9)	34,520.5 (8799.4 to 88,150.5)	181.8 (162.6 to 210.1)	−6.0 (−10.3 to 0.8)
Brazil	20 831.7 (5224.0 to 54,506.7)	174.1 (156.0 to 203.4)	−1.4 (−6.4 to 5.8)	33,762.4 (8603.2 to 86,309.3)	185.5 (165.7 to 214.7)	−6.4 (−10.8 to 0.3)
Paraguay	502.8 (121.9 to 1253.3)	65.8 (35.2 to 103.6)	4.9 (−14.8 to 28.3)	758.1 (189.9 to 1902.3)	75.7 (42.7 to 117.5)	4.0 (−15.6 to 28.0)
North Africa and Middle East	33,001.5 (8027.2 to 86,655.5)	73.4 (59.5 to 103.6)	−3.5 (−10.1 to 11.6)	37,481.3 (9380.5 to 98,165.8)	59.3 (45.8 to 101.1)	−0.6 (−9.0 to 24.5)
Afghanistan	875.2 (206.7 to 2374.4)	−56.8 (−64.7 to −48.9)	−3.4 (−19.2 to 11.9)	899.7 (214.1 to 2458.6)	−47.7 (−57.3 to −36.9)	−2.8 (−18.5 to 14.5)
Algeria	2658.5 (643.0 to 7417.4)	141.2 (91.4 to 205.3)	−7.3 (−23.3 to 12.9)	2550.8 (602.0 to 7338.0)	129.7 (82.6 to 218.0)	−4.6 (−19.2 to 20.8)
Bahrain	36.0 (8.7 to 100.1)	68.2 (35.6 to 114.0)	−6.7 (−20.9 to 12.3)	37.7 (9.1 to 102.0)	73.7 (43.8 to 110.4)	−1.3 (−16.4 to 17.0)
Egypt	4204.1 (944.3 to 11,324.0)	51.7 (23.9 to 89.4)	−2.4 (−18.8 to 20.6)	2713.9 (609.7 to 7663.6)	−11.3 (−29.4 to 28.4)	3.2 (−15.7 to 46.7)
Iran	6894.6 (1 707.3 to 18 560.6)	265.1 (220.5 to 357.9)	−4.4 (−11.7 to 20.0)	7015.5 (1755.2 to 18,668.1)	209.0 (175.5 to 355.0)	3.5 (−6.1 to 53.2)
Iraq	1372.4 (319.3 to 3659.0)	−3.1 (−19.6 to 15.1)	−1.6 (−16.4 to 15.5)	1886.2 (455.0 to 4862.0)	−0.2 (−17.1 to 28.1)	0.1 (−16.1 to 28.1)
Jordan	388.2 (95.3 to 1057.6)	56.0 (24.1 to 96.0)	−7.8 (−25.1 to 14.2)	378.8 (89.7 to 1023.6)	41.3 (14.5 to 93.9)	−6.3 (−23.3 to 29.8)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Kuwait	244.3 (60.8 to 635.1)	195.6 (147.0 to 250.7)	2.0 (−13.2 to 18.7)	180.8 (47.8 to 441.7)	51.6 (31.3 to 80.9)	−3.7 (−16.4 to 13.9)
Lebanon	487.8 (115.9 to 1331.5)	118.2 (76.4 to 228.6)	−1.6 (−19.5 to 48.7)	767.5 (184.9 to 2079.4)	117.4 (78.6 to 237.5)	−3.6 (−20.7 to 48.4)
Libya	500.0 (126.9 to 1328.2)	60.5 (28.3 to 105.1)	−4.8 (−23.7 to 22.3)	593.9 (149.9 to 1501.2)	68.6 (36.2 to 116.9)	−3.0 (−21.6 to 24.5)
Morocco	2388.6 (549.1 to 6468.5)	100.5 (60.0 to 142.7)	0.5 (−17.0 to 21.2)	2556.2 (585.6 to 6989.0)	71.6 (46.6 to 99.5)	0.6 (−13.7 to 15.3)
Oman	72.2 (16.6 to 200.0)	−0.3 (−20.1 to 31.4)	−4.6 (−20.9 to 30.8)	90.6 (20.9 to 255.9)	−4.4 (−24.1 to 50.9)	−2.0 (−20.7 to 57.6)
Palestine	118.2 (27.1 to 336.8)	−24.3 (−37.3 to −4.8)	−5.0 (−20.5 to 26.0)	207.7 (48.7 to 585.0)	−12.3 (−28.0 to 9.0)	−6.2 (−22.3 to 17.0)
Qatar	29.7 (6.9 to 84.7)	17.5 (−16.0 to 62.3)	4.5 (−17.6 to 31.9)	11.4 (2.7 to 33.5)	−49.0 (−62.7 to −30.1)	13.3 (−7.4 to 40.0)
Saudi Arabia	899.5 (215.6 to 2384.9)	−2.3 (−19.3 to 34.6)	−3.2 (−18.8 to 29.7)	808.0 (195.3 to 2181.4)	−11.1 (−31.5 to 37.8)	−0.4 (−22.7 to 55.3)
Sudan	1417.2 (322.1 to 3962.5)	22.0 (3.3 to 47.3)	−5.3 (−19.4 to 13.2)	1397.6 (330.7 to 3987.7)	8.9 (−4.3 to 29.5)	−4.5 (−16.1 to 13.0)
Syria	858.4 (201.3 to 2341.0)	74.5 (33.0 to 133.6)	2.6 (−18.8 to 39.1)	733.2 (165.1 to 2160.7)	38.1 (4.3 to 108.0)	6.9 (−15.3 to 65.1)
Tunisia	1066.1 (246.5 to 2895.3)	146.1 (88.0 to 240.6)	−4.0 (−24.0 to 27.8)	1480.7 (346.3 to 3912.1)	189.3 (122.7 to 340.2)	−2.8 (−24.2 to 45.2)
Turkey	7586.2 (1892.8 to 21,707.6)	114.5 (79.1 to 165.9)	−3.9 (−19.6 to 16.9)	12 135.1 (3 113.1 to 32,987.7)	112.5 (72.2 to 164.5)	−3.4 (−21.5 to 20.0)
United Arab Emirates	97.7 (22.0 to 276.9)	35.1 (0.2 to 92.9)	−4.4 (−20.5 to 32.8)	40.5 (9.5 to 116.9)	4.6 (−19.7 to 48.5)	−6.5 (−23.2 to 27.4)
Yemen	773.2 (178.3 to 2221.7)	96.1 (57.5 to 146.7)	1.0 (−14.8 to 24.3)	957.4 (223.5 to 2623.4)	16.7 (−1.8 to 44.6)	1.3 (−14.8 to 24.5)
South Asia	70,103.1 (16,090.3 to 205,489.8)	136.0 (101.8 to 182.8)	12.4 (−2.0 to 35.5)	88,010.7 (21,633.3 to 238,065.3)	192.8 (135.4 to 269.7)	14.9 (−7.0 to 45.3)
Bangladesh	8204.9 (1963.9 to 23,345.3)	134.8 (92.5 to 191.2)	7.3 (−11.2 to 31.0)	7409.4 (1752.7 to 19,527.4)	137.0 (86.7 to 215.1)	6.9 (−16.2 to 44.5)
Bhutan	37.5 (8.8 to 103.8)	380.5 (277.3 to 535.1)	23.4 (−0.7 to 66.4)	43.1 (10.4 to 111.5)	192.7 (132.9 to 301.7)	28.2 (1.3 to 78.9)
India	55,824.9 (12,615.8 to 163,454.2)	191.9 (140.8 to 260.9)	18.2 (0.3 to 45.4)	73,186.4 (17,794.0 to 199,775.5)	261.7 (185.6 to 368.7)	22.8 (−2.2 to 56.5)
Nepal	965.8 (220.9 to 2837.9)	145.0 (87.7 to 226.0)	21.3 (−6.9 to 62.8)	1 482.3 (345.6 to 4119.6)	148.5 (90.2 to 236.3)	35.0 (1.9 to 88.0)
Pakistan	5070.0 (1134.4 to 14,658.6)	−29.1 (−43.4 to −10.3)	9.2 (−11.3 to 39.4)	5889.6 (1380.9 to 16,629.7)	−10.7 (−28.6 to 17.0)	13.6 (−9.3 to 49.0)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
East Asia	110,468.6 (25,700.8 to 320,046.5)	194.9 (140.4 to 270.3)	5.2 (−9.3 to 25.6)	224,209.2 (53,560.4 to 585,210.4)	182.3 (127.6 to 259.5)	−1.8 (−18.6 to 22.7)
China	106,005.4 (24,780.9 to 304,484.6)	192.9 (136.8 to 269.7)	6.2 (−9.4 to 27.7)	214,709.5 (51,099.6 to 559,556.0)	180.9 (125.0 to 259.7)	−2.0 (−19.5 to 23.4)
North Korea	1093.2 (247.1 to 3139.7)	106.2 (77.4 to 140.6)	−2.5 (−15.6 to 12.6)	4114.6 (1001.2 to 11,542.2)	129.5 (92.9 to 181.7)	−3.6 (−18.6 to 18.6)
Taiwan (province of China)	3369.9 (793.9 to 9005.2)	373.0 (271.1 to 505.4)	8.5 (−11.2 to 32.7)	5385.0 (1361.0 to 13,572.1)	352.1 (268.9 to 462.2)	6.3 (−11.9 to 30.5)
Oceania	280.8 (64.8 to 769.1)	22.1 (5.8 to 42.2)	−5.5 (−16.2 to 7.8)	391.9 (91.6 to 1051.6)	26.6 (7.9 to 51.1)	−1.9 (−16.9 to 16.0)
American Samoa	2.6 (0.6 to 7.2)	131.3 (106.8 to 158.3)	−6.9 (−17.1 to 4.0)	4.7 (1.1 to 11.9)	154.7 (113.2 to 214.7)	−4.8 (−20.2 to 15.8)
Cook Islands	1.8 (0.4 to 4.7)	156.1 (125.3 to 197.6)	−14.5 (−24.8 to −1.8)	2.7 (0.7 to 7.0)	129.1 (85.3 to 184.1)	−14.9 (−31.4 to 5.0)
Fiji	24.0 (5.4 to 65.7)	48.2 (20.3 to 84.3)	−4.7 (−18.1 to 11.2)	49.3 (11.8 to 133.6)	82.6 (44.5 to 134.7)	−9.7 (−27.8 to 14.6)
Guam	13.3 (3.2 to 35.0)	288.1 (215.5 to 384.1)	−14.0 (−27.2 to 1.0)	25.0 (6.3 to 62.4)	331.5 (254.4 to 455.8)	−19.1 (−33.2 to −1.5)
Kiribati	2.2 (0.5 to 6.2)	11.1 (−7.2 to 32.9)	8.6 (−5.2 to 30.9)	5.6 (1.3 to 15.3)	29.6 (4.1 to 63.4)	17.1 (−3.9 to 47.1)
Marshall Islands	1.4 (0.3 to 4.1)	60.2 (30.7 to 96.2)	−2.9 (−18.4 to 16.2)	1.6 (0.4 to 4.3)	0.7 (−20.3 to 24.8)	−0.7 (−18.2 to 20.7)
Federated States of Micronesia	2.6 (0.6 to 7.5)	36.6 (8.0 to 68.3)	−2.0 (−18.6 to 16.5)	5.0 (1.2 to 14.0)	57.7 (20.9 to 110.6)	3.2 (−18.9 to 37.1)
Nauru	0.1 (0.0 to 0.3)	−29.1 (−42.3 to −12.5)	−6.2 (−19.9 to 10.8)	0.1 (0.0 to 0.4)	−30.4 (−44.4 to −12.2)	−8.9 (−24.3 to 8.3)
Niue	0.2 (0.0 to 0.4)	18.5 (1.3 to 36.4)	−12.6 (−25.1 to 0.9)	0.3 (0.1 to 0.9)	−12.7 (−29.8 to 10.2)	−11.7 (−28.3 to 11.0)
Northern Mariana Islands	2.2 (0.5 to 6.1)	290.1 (245.8 to 340.3)	−4.9 (−15.0 to 6.5)	3.1 (0.8 to 8.6)	379.6 (277.0 to 513.3)	−3.0 (−22.9 to 24.0)
Palau	0.7 (0.2 to 2.0)	50.4 (21.6 to 82.3)	−7.8 (−24.8 to 9.3)	1.2 (0.3 to 3.2)	62.4 (20.3 to 110.7)	−6.5 (−30.0 to 22.1)
Papua New Guinea	179.8 (41.2 to 487.9)	12.5 (−7.0 to 36.8)	−5.2 (−19.1 to 12.6)	222.0 (50.3 to 608.5)	14.9 (−6.6 to 43.2)	4.0 (−15.4 to 29.9)
Samoa	10.5 (2.5 to 29.3)	65.6 (43.8 to 93.1)	−6.5 (−17.7 to 7.5)	17.7 (4.3 to 47.5)	30.2 (4.7 to 66.0)	−3.8 (−22.5 to 21.7)
Solomon Islands	10.6 (2.5 to 30.6)	25.4 (3.0 to 56.2)	8.1 (−5.9 to 36.9)	11.5 (2.7 to 32.2)	64.1 (27.0 to 117.1)	18.9 (−6.6 to 55.7)
Tokelau	0.1 (0.0 to 0.3)	9.6 (−5.9 to 29.3)	−10.4 (−22.6 to 4.2)	0.2 (0.0 to 0.4)	5.3 (−16.6 to 34.9)	−10.9 (−28.7 to 12.1)
Tonga	5.5 (1.3 to 15.3)	69.0 (44.0 to 97.6)	−6.3 (−18.2 to 7.5)	12.6 (3.1 to 32.2)	112.8 (74.6 to 167.0)	−1.6 (−18.7 to 22.1)
Tuvalu	0.6 (0.1 to 1.8)	73.2 (39.0 to 124.0)	−7.4 (−24.1 to 14.0)	1.0 (0.2 to 2.8)	38.1 (3.4 to 85.0)	−3.9 (−27.7 to 28.5)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Vanuatu	9.3 (2.1 to 26.4)	40.8 (16.0 to 69.4)	−0.3 (−16.2 to 18.4)	9.9 (2.3 to 29.5)	59.8 (23.2 to 109.0)	2.6 (−20.1 to 35.2)
Southeast Asia	31,415.4 (7352.9 to 86,315.6)	96.4 (74.5 to 125.1)	5.7 (−5.0 to 20.5)	61,980.9 (14,844.5 to 157,635.4)	102.5 (80.2 to 147.4)	2.2 (−8.9 to 26.0)
Cambodia	585.9 (139.5 to 1600.8)	101.6 (64.6 to 137.7)	17.6 (−3.0 to 42.1)	1208.6 (292.1 to 3263.0)	148.6 (105.5 to 218.8)	20.9 (−0.1 to 59.8)
Indonesia	8724.0 (1937.5 to 24,089.4)	73.6 (42.3 to 111.9)	18.0 (−1.0 to 43.1)	15,657.2 (3663.3 to 44,009.1)	92.6 (55.2 to 139.4)	15.5 (−6.9 to 45.5)
Laos	194.9 (47.3 to 558.3)	68.1 (35.3 to 112.3)	9.1 (−9.4 to 42.1)	334.0 (82.2 to 933.4)	64.3 (30.9 to 119.4)	14.0 (−9.8 to 56.3)
Malaysia	1639.2 (386.7 to 4309.3)	64.1 (35.2 to 99.8)	1.6 (−16.0 to 23.9)	2028.2 (477.9 to 5 620.7)	63.7 (33.2 to 97.0)	0.7 (−16.9 to 20.3)
Maldives	23.4 (5.6 to 61.0)	108.5 (71.7 to 154.4)	7.2 (−9.4 to 30.0)	24.3 (6.0 to 62.0)	347.2 (252.8 to 488.0)	2.3 (−16.9 to 28.8)
Mauritius	102.2 (24.4 to 273.0)	207.2 (161.7 to 264.4)	−0.2 (−13.1 to 16.1)	220.7 (55.3 to 560.1)	174.9 (135.5 to 227.8)	−0.7 (−13.9 to 17.8)
Myanmar	2092.8 (490.9 to 5866.7)	111.3 (79.3 to 154.4)	15.3 (−0.2 to 39.3)	4691.3 (1134.6 to 12,593.6)	110.8 (78.1 to 157.1)	6.4 (−9.4 to 31.7)
Philippines	3871.2 (888.9 to 11, 236.2)	34.3 (8.2 to 66.8)	−12.8 (−27.6 to 5.2)	6601.9 (1499.8 to 18,757.1)	54.0 (23.0 to 92.4)	−18.5 (−32.5 to −0.4)
Seychelles	5.3 (1.3 to 15.1)	7.3 (−6.0 to 23.5)	−6.0 (−17.2 to 7.1)	13.0 (3.2 to 33.6)	11.7 (−0.8 to 25.1)	0.3 (−10.9 to 12.0)
Sri Lanka	1379.4 (320.3 to 3740.9)	82.3 (43.6 to 131.7)	−3.3 (−21.8 to 20.7)	2761.5 (654.3 to 7244.7)	160.9 (105.0 to 236.6)	−3.8 (−23.5 to 24.3)
Thailand	7452.5 (1768.8 to 19,825.0)	265.5 (183.0 to 370.5)	−6.2 (−25.3 to 19.9)	14,100.2 (3615.3 to 35,484.5)	223.8 (153.7 to 317.9)	−8.0 (−27.4 to 18.9)
Timor-Leste	43.1 (9.8 to 120.3)	144.1 (90.3 to 200.9)	14.2 (−10.3 to 41.7)	58.8 (14.4 to 163.3)	96.9 (55.2 to 153.4)	12.6 (−10.9 to 45.0)
Vietnam	5260.5 (1216.7 to 14,837.6)	88.3 (57.3 to 161.9)	15.5 (−2.4 to 60.6)	14,199.9 (3465.7 to 36,017.6)	75.1 (46.5 to 157.6)	9.2 (−8.7 to 61.0)
Central sub-Saharan Africa	2027.3 (478.0 to 5748.1)	11.9 (−4.0 to 32.0)	9.8 (−3.6 to 26.9)	4200.4 (1045.0 to 10,907.3)	72.1 (43.7 to 111.3)	12.1 (−5.7 to 35.5)
Angola	408.7 (96.9 to 1137.6)	17.0 (−3.5 to 58.9)	19.6 (0.1 to 70.2)	734.3 (184.3 to 1954.0)	43.5 (9.2 to 108.7)	29.5 (−2.6 to 92.4)
Central African Republic	46.6 (10.7 to 135.2)	−17.2 (−30.8 to −2.7)	−7.2 (−21.3 to 10.9)	113.5 (25.2 to 325.0)	−1.3 (−23.6 to 27.6)	5.1 (−17.2 to 33.6)
Congo (Brazzaville)	120.6 (28.1 to 334.6)	61.2 (38.2 to 93.8)	10.4 (−4.2 to 29.2)	187.9 (45.3 to 503.8)	53.8 (21.6 to 104.1)	15.0 (−7.9 to 50.4)
DR Congo	1379.5 (326.7 to 3964.5)	9.6 (−8.3 to 32.3)	7.7 (−7.3 to 26.0)	3004.8 (748.8 to 7823.7)	98.2 (58.5 to 148.9)	7.9 (−11.5 to 31.5)
Equatorial Guinea	21.9 (5.0 to 60.2)	−0.8 (−22.8 to 47.2)	23.4 (−3.1 to 92.3)	43.1 (10.1 to 118.9)	37.4 (−4.9 to 113.3)	40.1 (−5.0 to 121.1)
Gabon	50.0 (11.7 to 136.7)	29.9 (11.2 to 49.1)	4.6 (−8.4 to 18.0)	116.7 (28.0 to 310.4)	7.9 (−11.5 to 36.5)	4.1 (−14.5 to 32.8)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Eastern sub-Saharan Africa	7893.1 (1855.5 to 22,255.7)	24.4 (10.8 to 43.9)	13.9 (3.3 to 32.2)	13,536.8 (3309.1 to 36,125.5)	46.2 (28.6 to 72.0)	13.9 (0.6 to 35.2)
Burundi	191.1 (44.5 to 545.7)	−3.0 (−20.6 to 23.2)	18.0 (−0.7 to 49.7)	288.0 (68.2 to 824.3)	−5.6 (−25.5 to 23.9)	20.1 (−4.3 to 56.4)
Comoros	30.9 (7.6 to 87.6)	85.9 (53.8 to 136.5)	14.4 (−2.9 to 42.1)	54.3 (13.4 to 147.2)	122.5 (83.1 to 185.4)	17.7 (−2.3 to 52.0)
Djibouti	23.7 (5.6 to 65.2)	161.9 (114.2 to 225.0)	17.1 (−1.0 to 43.5)	34.6 (8.5 to 95.3)	110.8 (71.8 to 163.3)	14.9 (−5.6 to 43.2)
Eritrea	62.6 (13.8 to 183.8)	109.5 (66.1 to 229.1)	39.9 (10.5 to 122.0)	185.4 (41.9 to 522.8)	126.2 (53.5 to 266.7)	57.3 (7.8 to 153.8)
Ethiopia	2964.0 (694.2 to 8560.0)	111.4 (62.3 to 191.5)	18.7 (−3.7 to 64.3)	3469.0 (844.7 to 9488.3)	101.3 (52.9 to 192.8)	24.8 (−6.9 to 87.6)
Kenya	881.6 (202.4 to 2491.7)	−4.0 (−17.8 to 12.3)	10.3 (−3.2 to 25.4)	1823.7 (444.7 to 4951.5)	43.1 (22.0 to 67.6)	6.7 (−8.9 to 25.2)
Madagascar	342.7 (77.3 to 942.4)	−34.6 (−46.0 to −20.5)	1.7 (−15.6 to 20.9)	515.9 (120.4 to 1427.4)	−12.5 (−31.3 to 11.1)	7.3 (−15.0 to 35.2)
Malawi	277.6 (65.8 to 762.9)	5.2 (−8.8 to 22.2)	12.4 (−1.4 to 31.2)	741.6 (187.3 to 1994.1)	66.6 (41.3 to 100.6)	7.2 (−9.7 to 28.9)
Mozambique	448.9 (106.1 to 1313.9)	−17.3 (−29.8 to 1.2)	18.4 (0.7 to 47.4)	1080.5 (256.1 to 2929.0)	22.2 (−2.6 to 60.6)	13.0 (−9.5 to 48.6)
Rwanda	229.7 (54.2 to 660.6)	36.6 (14.8 to 75.0)	20.5 (2.6 to 59.6)	542.5 (130.7 to 1480.7)	84.3 (51.0 to 144.0)	27.5 (3.4 to 73.7)
Somalia	155.1 (35.4 to 427.7)	−28.3 (−41.6 to −10.1)	9.6 (−8.0 to 37.0)	351.1 (77.8 to 1021.0)	5.6 (−18.1 to 42.9)	15.9 (−9.8 to 58.4)
South Sudan	208.2 (47.1 to 584.5)	22.3 (−1.0 to 50.9)	4.2 (−14.7 to 27.2)	248.0 (60.5 to 662.2)	−10.0 (−27.4 to 9.7)	3.6 (−15.5 to 25.2)
Uganda	545.2 (128.8 to 1 481.6)	−10.1 (−22.5 to 6.2)	16.7 (1.5 to 40.1)	1309.2 (322.6 to 3497.3)	29.7 (8.9 to 62.5)	12.6 (−5.6 to 40.0)
Tanzania	1235.7 (291.3 to 3569.3)	28.8 (5.8 to 53.7)	1.0 (−16.4 to 19.8)	2408.8 (580.0 to 6366.5)	48.3 (29.2 to 75.4)	3.4 (−10.0 to 20.8)
Zambia	289.9 (69.2 to 818.2)	−3.9 (−18.7 to 15.1)	9.9 (−5.9 to 33.3)	473.2 (113.9 to 1309.5)	35.0 (8.3 to 70.3)	6.9 (−14.0 to 36.2)
Southern sub-Saharan Africa	2313.5 (543.9 to 6677.3)	24.6 (15.9 to 36.2)	4.3 (−2.8 to 12.9)	5665.6 (1350.0 to 15,688.1)	42.4 (29.8 to 65.2)	3.4 (−5.6 to 19.5)
Botswana	42.3 (9.8 to 121.9)	33.6 (8.9 to 61.8)	13.4 (−6.1 to 39.4)	110.5 (26.8 to 305.4)	58.5 (16.8 to 126.8)	7.5 (−20.3 to 55.2)
eSwatini	13.3 (3.1 to 38.4)	11.3 (−3.0 to 32.6)	−1.7 (−15.4 to 15.4)	41.3 (9.2 to 119.8)	28.6 (−12.8 to 72.0)	2.8 (−30.3 to 35.8)
Lesotho	31.3 (7.4 to 90.1)	−0.6 (−14.9 to 15.8)	0.6 (−12.8 to 15.0)	97.7 (22.9 to 277.8)	−7.1 (−33.6 to 19.5)	5.4 (−23.2 to 32.2)
Namibia	67.5 (15.9 to 196.5)	51.1 (28.7 to 77.5)	13.9 (0.4 to 31.8)	160.6 (38.9 to 453.7)	85.5 (50.3 to 140.3)	14.3 (−7.1 to 48.0)
South Africa	1906.8 (451.5 to 5444.1)	23.5 (13.0 to 36.3)	4.4 (−3.5 to 14.4)	4696.3 (1111.1 to 13,008.1)	46.0 (33.0 to 70.7)	3.5 (−5.7 to 20.8)

(Continues)

TABLE 2 (Continued)

Location	Male			Female		
	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)	2019 counts	Percentage change in all-age rates between 1990 and 2019 (95% UI)	Percentage change in age-standardized rates between 1990 and 2019 (95% UI)
Zimbabwe	252.3 (59.1 to 739.9)	22.9 (6.4 to 40.2)	2.2 (−10.3 to 16.7)	559.3 (135.0 to 1560.9)	21.0 (−4.4 to 50.9)	1.2 (−19.9 to 26.5)
Western sub-Saharan Africa	10,650.8 (2584.4 to 30,235.5)	16.8 (0.5 to 38.2)	13.8 (−1.0 to 33.6)	14,867.9 (3536.1 to 39,148.4)	−1.2 (−14.0 to 18.3)	12.2 (−2.2 to 35.9)
Benin	247.8 (58.4 to 701.8)	−29.8 (−41.0 to −17.6)	5.0 (−10.1 to 22.7)	447.6 (111.1 to 1198.1)	−10.5 (−22.8 to 4.6)	3.1 (−11.5 to 21.4)
Burkina Faso	449.3 (107.4 to 1263.7)	−12.0 (−24.1 to 3.6)	−0.7 (−13.9 to 17.3)	795.4 (194.5 to 2094.2)	10.4 (−6.5 to 33.0)	−4.5 (−18.9 to 15.3)
Cape Verde	32.4 (7.8 to 89.5)	22.9 (1.7 to 44.9)	24.9 (4.2 to 46.3)	67.0 (16.4 to 176.6)	49.5 (26.1 to 91.3)	16.3 (−1.1 to 47.0)
Cameroon	569.3 (130.3 to 1636.7)	−11.1 (−26.5 to 6.6)	5.9 (−10.2 to 25.3)	935.2 (226.4 to 2606.7)	1.4 (−16.6 to 26.2)	−0.4 (−17.4 to 21.8)
Chad	330.5 (76.9 to 953.0)	−22.2 (−35.7 to −5.3)	10.3 (−8.2 to 34.4)	384.6 (92.3 to 1043.5)	−38.2 (−47.0 to −25.7)	6.5 (−9.5 to 28.4)
Côte d'Ivoire	491.0 (117.3 to 1387.5)	50.6 (28.0 to 77.5)	5.2 (−9.2 to 22.5)	693.1 (167.5 to 908.3)	68.6 (45.5 to 97.5)	−0.9 (−14.1 to 15.2)
The Gambia	57.3 (13.9 to 157.8)	87.3 (52.3 to 131.0)	11.6 (−7.1 to 33.6)	96.9 (23.5 to 273.9)	74.7 (41.7 to 112.6)	6.6 (−13.4 to 28.8)
Ghana	737.5 (172.4 to 2040.3)	42.8 (20.2 to 73.3)	14.8 (−1.3 to 38.1)	1204.2 (293.0 to 3283.3)	54.0 (29.6 to 85.4)	0.1 (−15.4 to 19.2)
Guinea	371.9 (90.0 to 1048.8)	−7.8 (−24.1 to 11.2)	10.6 (−7.6 to 34.4)	558.7 (136.2 to 1474.4)	1.9 (−17.3 to 26.8)	5.3 (−14.3 to 32.2)
Guinea-Bissau	27.6 (6.4 to 77.4)	−12.9 (−28.3 to 8.4)	8.1 (−8.2 to 35.0)	51.1 (12.2 to 141.1)	15.0 (−11.7 to 53.9)	6.9 (−17.5 to 45.5)
Liberia	130.4 (31.3 to 375.0)	−21.5 (−36.4 to −1.3)	3.8 (−12.5 to 28.4)	153.9 (37.3 to 409.0)	−10.6 (−25.4 to 10.2)	2.2 (−14.2 to 25.7)
Mali	562.3 (131.0 to 1607.5)	20.9 (1.1 to 45.9)	7.8 (−8.2 to 29.3)	663.9 (157.8 to 1793.0)	−5.8 (−20.2 to 14.0)	4.8 (−12.1 to 28.1)
Mauritania	162.3 (38.3 to 449.8)	65.5 (40.4 to 99.8)	4.1 (−8.8 to 23.2)	184.9 (45.0 to 493.4)	10.4 (−6.6 to 35.4)	4.7 (−11.2 to 29.6)
Niger	370.1 (86.9 to 1028.3)	28.3 (5.4 to 68.7)	12.5 (−5.8 to 46.7)	483.4 (113.4 to 1355.0)	12.7 (−7.0 to 47.2)	12.3 (−7.3 to 48.8)
Nigeria	5260.8 (1262.9 to 14,752.3)	29.5 (−1.9 to 77.8)	20.1 (−6.6 to 61.7)	6852.6 (1552.8 to 17,791.8)	−13.8 (−32.6 to 17.5)	21.6 (−4.1 to 65.1)
São Tomé and Príncipe	5.5 (1.3 to 15.1)	22.9 (3.3 to 49.3)	6.3 (−7.7 to 25.3)	8.7 (2.0 to 24.1)	2.3 (−14.8 to 38.6)	9.3 (−8.9 to 48.6)
Senegal	526.7 (127.1 to 1483.8)	32.9 (13.9 to 60.8)	9.7 (−4.9 to 31.0)	719.3 (176.6 to 1880.9)	53.3 (32.5 to 84.0)	8.5 (−6.3 to 30.1)
Sierra Leone	197.1 (47.3 to 567.3)	−23.9 (−36.9 to −8.3)	9.3 (−6.6 to 30.3)	287.9 (69.7 to 769.5)	−12.7 (−27.3 to 7.8)	7.4 (−10.1 to 32.5)
Togo	120.9 (28.2 to 348.5)	5.3 (−11.3 to 26.0)	8.1 (−7.4 to 27.5)	279.1 (68.2 to 738.9)	42.4 (22.8 to 69.1)	−2.2 (−15.1 to 16.0)

Abbreviations: SDI, Socio-demographic Index; UI, uncertainty interval.

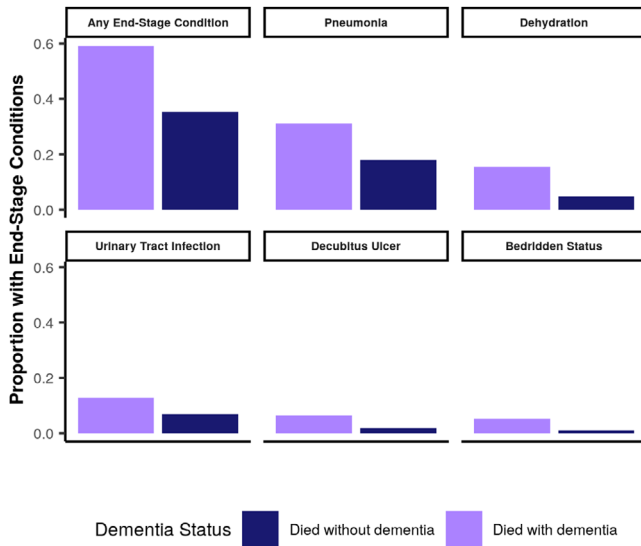


FIGURE 3 Proportion of individuals who died with end-stage conditions in the last year before death for all conditions combined and the conditions with the top five excess proportions, shown separately for individuals who died with and without dementia. These estimates are derived from linked clinical and death records from 2003 to 2017 in the Emilia Romagna region of Italy. They are assumed to apply globally and over the time period considered in this study

Between 1990 and 2019, there were no significant changes globally in age-standardized mortality rates for both sexes combined (3.0% [-1.2–9.8]), but a large increase in all-age mortality rates (100.1% [89.1–117.5]) due to population aging.

The total number of deaths from dementia increased with SDI quintile, from 62.1 thousand (15.1–171.3) deaths in the low SDI quintile to 563.2 thousand (148.2–1394.4) deaths in the high SDI quintile. However, the age-standardized rates were not significantly different between SDI quintiles, indicating that differences in the numbers stem from differences in population size and population age structure. The age-standardized rates by SDI quintile ranged from a high of 23.2 per 100,000 (5.69–60.43) in the middle SDI quintile to a low of 21.61 per 100,000 (5.22–56.36) in the low-middle SDI quintile.

There was a 1.7-fold variation in age-standardized mortality rates between countries. The countries (with population over 1 million) with the highest age-standardized mortality rates due to dementia were Afghanistan (30.79 deaths per 100,000 [7.46–82.34]), Mozambique (29.74 [7.29–80.08]), and Vietnam (29.21 [7.24–74.60]). The countries with the lowest age-standardized mortality rates due to dementia were Bangladesh (18.23 deaths per 100,000 person-years [4.50–49.29]), India (19.12 [4.57–52.01]), and Nepal (19.51 [4.53–53.31]; Figure 4).

In data from vital registration systems, huge variations in the patterns of deaths due to dementia were observed both over time and between countries. In Brazil, for example, the number of deaths due to dementia reported in vital registration data increased more than 300-fold between 1980 and 2017. Across countries with vital registration data in 2015, the proportion of deaths attributed to dementia ranged from 0% (Qatar) to 17% (Finland). In contrast, our esti-

mates were more stable both over time, and between countries, similar to trends observed in prevalence estimates. In the majority of locations and years, our estimated mortality due to dementia exceeded the mortality reported on death certificates in vital registration systems. Returning to the example of Brazil, our estimates were 2.12 (0.54–5.52) times the reported 21,653 deaths in vital registration data. However, in some high-income countries in recent years our estimates were lower than those reported via vital registration systems. In the United States in 2015, our estimates were 0.54 (0.14–1.32) times the 250,863 deaths recorded in the vital registration system.

Comparing dementia to all other diseases estimated in the GBD study (at Level 3 of the GBD cause hierarchy), in 1990 dementia was the 20th leading cause of death globally comparing all-age mortality rates and the sixth leading cause of death among individuals 70 and older. However, by 2019, deaths due to dementia were estimated to rank seventh globally across all ages and fourth among individuals 70 and older.

4 | DISCUSSION

Globally, 1.62 million (0.41–4.21) people were estimated to have died of end-stage dementia in 2019. Age-standardized rates were stable over time but there were large increases in all-age rates as a result of population aging. With this trend expected to increase in the future, an increase in dementia deaths can also be anticipated.

We found that conditions such as decubitus ulcer, bronchitis, dysphagia, hip fracture, pneumonia, and bedridden status appear in those who die with dementia substantially more than those who die without dementia. This finding is consistent with previous evidence from both autopsies and vital registration data that identifies conditions such as bronchopneumonia, aspiration pneumonia, and sepsis as common among those who die with dementia.^{5,61} This convergent evidence also supports our assumption that these end-stage conditions are indicative of individuals who died of dementia as an underlying cause of death, in line with ICD-10 principles.⁶²

Our new method of estimating dementia mortality updated the methods used in previous iterations of the GBD study. In prior iterations, we used an excess mortality regression strategy that was sensitive to the choice of which countries to include and assumed that the level of coding deaths to dementia was correct in countries that had the highest rates of coding per prevalent dementia case (i.e., there was no over-coding).^{18,19} Through the use of estimates of attributable risk from cohort studies and data on the proportion of deaths with end-stage disease, we avoided any reliance on vital registration data and cause of death coding practices. As we have found extreme changes in mortality rates from vital registration data both over time and between countries, use of these data risks incorporating a large source of measurement error. While removing this reliance could be seen as an improvement, as we do not have a gold-standard measure to which we can compare our estimates of dementia mortality, we do not have the ability to assess their accuracy.

As a result of this change in strategy we no longer assume that the highest rates of coding dementia as a cause of death per prevalent case

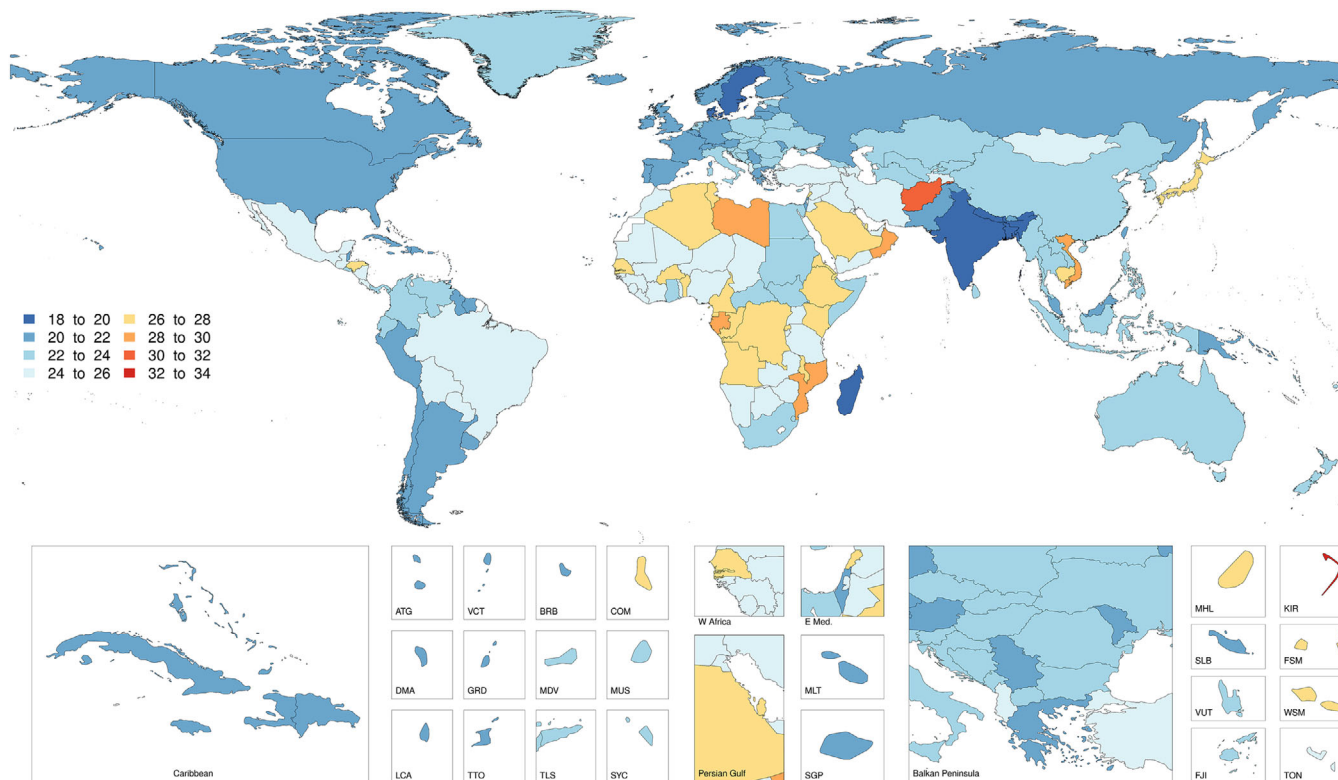


FIGURE 4 Both-sex age-standardized mortality rate per 100,000 due to dementia in 2019 by location. Values are expressed in rates per 100,000 population

is correct and we have estimated fewer deaths due to dementia. Where in previous iterations of the GBD study our estimates were always the same or higher than dementia mortality reported in vital registration data, now our estimates are in some cases lower than what is seen in vital registration data, particularly in recent years for high-income countries, including the United States, Finland, Sweden, and the United Kingdom. This suggests that in these countries in the most recent years there may be over-coding to dementia as an underlying cause of death. However, our estimates suggest much higher levels of dementia mortality than reported in vital registration systems in many countries, including Brazil and Germany. Improvements in the awareness of the mortality associated with dementia and clearer guidelines for death certification may help improve the quality of data from vital registration systems.

Our estimates are lower compared to prior studies that have estimated dementia-related mortality in the United States without using vital registration data (114,838 95% uncertainty interval [UI]; 30,031–281,180) deaths in adults 75 and older in 2010 vs. 503,400 deaths in James et al.;⁴⁷ 119,916 [31,261–296,271] deaths in adults 65 and older in 2010 vs. 600,000 deaths in Weuve et al.¹⁴). However, both of these studies used Cox proportional hazard models to estimate the risk of mortality among individuals with dementia, and did not control for common comorbidities such as vascular diseases. While James et al. did report that adjustment for vascular comorbidities did not change results, this could be due to measurement error in the vascular risk index or the specific characteristics of the sample used.⁴⁷ Without

adjusting for common risk factor profiles, comorbid conditions, or subsetting to deaths with end-stage conditions, these estimates are representative of the total number of excess deaths due to dementia and not just those attributable to dementia as an underlying cause of death.

A number of limitations still remain. First, the data on the risk of all-cause mortality due to dementia are heterogeneous, resulting in uncertain estimates of absolute and relative mortality risk. This large source of uncertainty contributes greatly to the large uncertainty intervals for our final estimates. Second, we remain reliant on our estimates of prevalence to calculate excess deaths from data on attributable risk, and these data are also heterogeneous and sparse, particularly in low-income settings. Third, we are assuming that the risk of dying from end-stage dementia across locations is the same. While there are no available therapies that can slow or prevent death, differences in the composition of comorbidities and the quality of care could influence mortality.^{63–65} Fourth, we assume that administrative data can be used to accurately identify markers of end-stage disease. Administrative data was used to classify dementia in the analysis of end-stage disease, and prior studies have shown administrative records can have poor sensitivity, particularly when considering mild disease.⁶⁶ However, it is more likely that individuals with severe, end-stage dementia would be correctly classified, particularly when considering the long time span of our linked data (2003 to 2017). Fifth, due to a lack of available data sources with death record linkages, we are using data from Italy for the measurement of end-stage conditions, and are generalizing these findings to the rest of the world. With no disease-modifying treatments

currently available, the biological drivers of disease progression are likely to be similar across locations, leading to similarities in the profiles of end-stage conditions.^{63,64} However, this assumption may be violated to the extent that health-care practices and other cultural factors influence the proportion of individuals with dementia who have end-stage disease. The integration of data sources from other locations should these become available would strengthen the analysis. Finally, the process of scaling all cause-specific mortality to add up to the total estimated all-cause mortality can be sensitive to estimates of all-cause mortality, which are challenging at the oldest ages when dementia mortality is highest, and can affect geographic variation.⁶⁰

In the context of population aging and growth, the importance of dementia as a public health concern will rise.⁶⁷ Our estimates can be used by health- and social-care authorities involved in end-of-life and palliative care to improve planning for services addressing the needs of people who die from dementia. By helping funders and policymakers better understand the global distribution of dementia burden and mortality across locations and time, and make fair comparisons between dementia and other diseases, these estimates will help guide evidence-driven resource allocation and health system planning.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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