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

GBD 2016 Dementia Collaborators*

Summary

Background The number of individuals living with dementia is increasing, negatively affecting families, communities, and health-care systems around the world. A successful response to these challenges requires an accurate understanding of the dementia disease burden. We aimed to present the first detailed analysis of the global prevalence, mortality, and overall burden of dementia as captured by the Global Burden of Diseases, Injuries, and Risk Factors (GBD) Study 2016, and highlight the most important messages for clinicians and neurologists.

Methods GBD 2016 obtained data on dementia from vital registration systems, published scientific literature and surveys, and data from health-service encounters on deaths, excess mortality, prevalence, and incidence from 195 countries and territories from 1990 to 2016, through systematic review and additional data-seeking efforts. To correct for differences in cause of death coding across time and locations, we modelled mortality due to dementia using prevalence data and estimates of excess mortality derived from countries that were most likely to code deaths to dementia relative to prevalence. Data were analysed by standardised methods to estimate deaths, prevalence, years of life lost (YLLs), years of life lived with disability (YLDs), and disability-adjusted life-years (DALYs; computed as the sum of YLLs and YLDs), and the fractions of these metrics that were attributable to four risk factors that met GBD criteria for assessment (high body-mass index [BMI], high fasting plasma glucose, smoking, and a diet high in sugar-sweetened beverages).

Findings In 2016, the global number of individuals who lived with dementia was 43·8 million (95% uncertainty interval [UI] 37·8–51·0), increased from 20.2 million (17.4–23.5) in 1990. This increase of 117% (95% UI 114–121) contrasted with a minor increase in age-standardised prevalence of 1.7% (1.0–2.4), from 701 cases (95% UI 602–815) per 100 000 population in 1990 to 712 cases (614–828) per 100 000 population in 2016. More women than men had dementia in 2016 (27.0 million, 95% UI 23.3–31.4, vs 16.8 million, 14.4–19.6), and dementia was the fifth leading cause of death globally, accounting for 2.4 million (95% UI 2.1–2.8) deaths. Overall, 28.8 million (95% UI 24.3–34.0) DALYs were attributed to dementia; 6.4 million (95% UI 3.4–10.5) of these could be attributed to the modifiable GBD risk factors of high BMI, high fasting plasma glucose, smoking, and a high intake of sugar-sweetened beverages.

Interpretation The global number of people living with dementia more than doubled from 1990 to 2016, mainly due to increases in population ageing and growth. Although differences in coding for causes of death and the heterogeneity in case-ascertainment methods constitute major challenges to the estimation of the burden of dementia, future analyses should improve on the methods for the correction of these biases. Until breakthroughs are made in prevention or curative treatment, dementia will constitute an increasing challenge to health-care systems worldwide.

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Research in context

Evidence before this study
Over the past decade, there have been substantial research efforts to describe the global epidemiology of Alzheimer’s disease and other dementias. Other efforts to summarise the evidence, including the World Dementia Report, have compiled evidence through systematic reviews and meta-analyses, but they report only on dementia prevalence by world region. The Global Burden of Diseases, Injuries, and Risk Factors (GBD) Study has published regular updates of estimates for dementia in 195 countries and territories and subnational locations, such as the provinces of China and states in countries such as Brazil, the USA, and Mexico. However, there has been no dedicated and detailed publication of GBD methods and estimates for dementia. GBD 2016 estimates for dementia incorporated 43 new data sources on the prevalence and incidence of dementia, updating a previous review that covered 1980 to 2015; new sources were identified through a systematic review of English-language articles published in PubMed from 23 Jan, 2015, to Oct 7, 2016, with the search terms “dementia” [Title/Abstract] AND (“prevalence” OR “incidence”) [Title/Abstract].

Added value of this study
GBD 2016 added 5-year age groups from ages 80 to 95 years to replace the oldest category (≥80 years) used in GBD 2015, providing more detailed estimates where the burden from dementia was highest. Our report examined more closely the methods, results, and limitations specific to Alzheimer’s disease and other dementias with the aim of making this information more accessible to clinicians and researchers. The data informing estimates were heterogeneous, with 230 different diagnostic procedures across 237 studies. Over time, the global age-standardised prevalence was fairly stable: 701 cases (95% uncertainty interval [UI] 602–815) per 100 000 population in 1990 and 712 cases (614–828) per 100 000 population in 2016, constituting an increase of 1·7% (95% UI 1·0–2·4). However, because of population ageing and growth, the number of people affected by dementia more than doubled since 1990 and almost 44 million prevalent cases were estimated globally in 2016. Age-standardised prevalence was 1·17 (1·17–1·18) times higher in females than in males. We also estimated that 22·3% (11·8–35·1) of the total global DALYs due to dementia in 2016 could be attributed to the four modifiable risk factors that met GBD criteria for assessment (high body-mass index, high fasting plasma glucose, a diet high in sugar-sweetened beverages, and smoking).

Implications of all the available evidence
This analysis identified substantial heterogeneity in case-ascertainment methods throughout the dementia literature, highlighting the need for more consistency in future research. Nevertheless, there is no doubt about the striking increase in the numbers of individuals living with dementia since 1990 due to ageing and population growth. Despite some evidence indicating small decreases in age-specific incidence, without a major scientific breakthrough the continuation of sweeping demographic trends in population ageing and growth will lead to further increases in the number of people living with dementia. With limited scope for prevention and the absence of an effective disease-modifying treatment, the burden on caregivers and the parts of health-care systems devoted to care of the elderly will continue to increase rapidly.

Methods

Overview and data sources
General methods of GBD, including methods for calculating the Socio-demographic Index (SDI), a composite indicator combining income per person, education, and fertility, can be found in the general methods overview (appendix) and in the GBD 2016 overview papers. In this Article, we have highlighted the methods pertaining to processes specific to the estimation of Alzheimer’s disease and other dementias (hereafter referred to as dementia).

For the GBD analyses, the reference case definitions were either those from the Diagnostic and Statistical Manual of Mental Disorders (DSM; DSM-III, DSM-IV, or DSM-5), which are used in surveys and cohort studies, or those from the International Classification of Diseases (ICD; ICD-8, ICD-9, and ICD-10), which are used in vital registration and claims data sources. For GBD analyses of dementia, the relevant ICD-9 codes were 290, 291.2, 291.8, 294, and 331, and the relevant ICD-10 codes were F00, F01, F02, F03, G30, and G31. In GBD, for each disease a reference case definition was chosen that represents the most recent consensus or the most commonly used
definition. Data based on alternative case definitions were adjusted if systematic bias was detected. We included 237 sources of data from the scientific literature, and 3 years of medical claims data from the USA. We identified 176 sources reporting on prevalence, covering 17 of 21 world regions, and 64 sources on incidence, covering ten of 21 world regions (appendix). No input data were available for Oceania, central Asia, eastern Europe, or southern sub-Saharan Africa.

We could not adjust the data for different study designs or case definitions because of the extreme heterogeneity in case-ascertainment methods. We identified 230 different methods of screening and diagnosis in the 237 scientific literature sources. Data points that had an age range of greater than 20 years were split into new data points for the 5-year age groups within the age range, using the age pattern from the USA as the country for which we had the most detailed information.

Natural-history model

We did not use the typical GBD cause of death ensemble modelling (CODEm) approach for dementia because we noted large inconsistencies between cause of death data and prevalence data over time and between countries. Data from the US Vital Registration system showed that the age-standardised rates of deaths from dementia between 1990 and 2016 increased by a factor of five, whereas there has been no corresponding increase in the prevalence of dementia over the same period.11–21 Additionally, the highest age-standardised death rates were more than 50 times higher than the lowest age-standardised death rates across different locations for 2016, possibly indicating that the practice of coding a death to dementia as an underlying cause of death has not been consistent over time or between countries. To adjust for this bias, we jointly modelled cause of death and non-fatal outcomes for dementia. We first ran an initial cause of death model using CODEm, and an initial non-fatal model using DisMod-MR 2.1, the Bayesian meta-regression tool used in most non-fatal models for GBD.22,23 DisMod-MR 2.1 enforces consistency between the different parameters, because incidence determines the inflow into the pool of prevalent cases and excess mortality determines outflow via death. The rates of inflow and outflow then determine the average duration of disease. Both DisMod MR 2.1 and CODEm use covariates and borrow strength from locations in the same region that have data to make estimates for locations where there are no input data.

The initial CODEm model included 16,226 site-years of data (ie, data for a unique combination of location and calendar year). The covariates used in the initial CODEm model included diabetes prevalence, mean cholesterol, and mean body-mass index (BMI; full list in the appendix). The initial DisMod-MR 2.1 model included settings of no remission (ie, no cure), and no incidence before age 40 years. We also excluded incidence data from the model, because data for incidence and prevalence were inconsistent. In many locations, the incidence data combined with mortality data suggested a prevalence higher than the available prevalence data, and the model fitted above the prevalence data and below the incidence data. Because measurement of prevalent cases of dementia probably has less error than measurement of incident cases, we decided to exclude incidence data and rely on prevalence data.

We let DisMod-MR 2.1 adjust medical claims data to correct for under-reporting compared with survey data. We used average years of education in the population aged 15 years and older and smoking prevalence as predictive covariates, because these risk factors for dementia have a large evidence base.24,25 From the initial model results we identified the locations with high-quality vital registration systems that most often coded to dementia as a cause of death per prevalent case in the most recent year of estimates. For GBD 2016, these locations were the USA, Finland, Sweden, and Puerto Rico. We then used the log-transformed ratio between cause-specific mortality and prevalence for these locations to run a fixed-effects linear regression with dummy variables on 5-year age bins and sex. Because the ratio of cause-specific mortality and prevalence is an estimate of excess mortality rate, we used the results of this regression to predict data inputs for every GBD location and all years in a second DisMod-MR 2.1 model. As an exception, we retained the 2016 ratios of cause-specific mortality and prevalence for the four locations used in the regression analysis but assumed the 2016 ratios applied to the whole 1990–2016 period. Otherwise, the model included the same assumptions and covariates as the initial DisMod-MR 2.1 model. We used the prevalence outputs from this model to estimate years lived with disability (YLDs). We also used the cause-specific mortality estimated from this model for our final cause-specific mortality results.

YLDs and risk estimation

To derive YLDs for dementia, we first divided dementia prevalence into three severity categories. We used data from a systematic review of studies reporting on the Clinical Dementia Rating Scale (CDR)26 and pooled proportions of mild (CDR 1), moderate (CDR 2), and severe dementia (CDR 3) in random-effect meta-analyses. We did this separately for ages 40–69, 70–79, and 80 years or more. For GBD 2016, we included seven studies identified through systematic review published from 1980 to 2015, covering two world regions. To calculate YLDs, we multiplied the prevalence at each severity level by the corresponding disability weight27 and further corrected for comorbidity using a simulation assigning all non-fatal outcomes to hypothetical individuals for each age group, sex, location, and year.28 We made estimates for high BMI, high fasting plasma glucose, smoking (including all smoked tobacco products),
## Deaths

|                      | 2016 counts     | Percentage change in age-standardised rates, 1990–2016 | 2016 counts     | Percentage change in age-standardised rates, 1990–2016 | 2016 counts     | Percentage change in age-standardised rates, 1990–2016 |
|----------------------|------------------|--------------------------------------------------------|------------------|--------------------------------------------------------|------------------|--------------------------------------------------------|
|                      |                  | (2060 410 to 2 777 610)                                 |                  | (37 556 336 to 51 028 051)                             |                  | (24 530 789 to 33 952 387)                             |
| Global               | 2 382 129        | 3.6 (1.1 to 5.6)                                        | 43 835 665       | 1.7 (1.0 to 2.4)                                        | 28 764 110       | 2.1 (0.1 to 3.8)                                        |
| High SDI             | 969 191          | 2.5 (0.2 to 5.2)                                        | 1 516 411        | -0.3 (-1.2 to 1.7)                                      | 9 886 396        | -0.3 (-2.3 to 2.0)                                      |
| High-middle SDI      | 448 457          | 4.1 (-0.6 to 9.1)                                       | 8 858 166        | 8.1 (6.7 to 10.4)                                      | 5 561 354        | 4.4 (0.4 to 8.6)                                       |
| Middle SDI           | 658 727          | 0.9 (-4.5 to 5.0)                                       | 13 200 041       | 1.5 (0.7 to 2.3)                                       | 8 905 818        | 0.8 (-3.4 to 3.7)                                      |
| Low-middle SDI       | 246 768          | 9.6 (1.7 to 16.5)                                       | 5 248 335        | -2.7 (-3.4 to -2.1)                                    | 3 530 640        | 5.6 (0.3 to 10.6)                                      |
| Low SDI              | 57 730           | 8.8 (2.8 to 15.8)                                       | 1 110 454        | -3.0 (-3.9 to -1.9)                                    | 8 442 222        | 6.0 (1.5 to 11.0)                                      |
| High-income North America | 260 080       | 9.9 (3.3 to 16.6)                                       | 4 347 849        | -1.6 (-7.3 to 4.9)                                     | 2 688 057        | 2.5 (-3.4 to 8.9)                                     |
| Canada               | 211 800          | -1.4 (-2.0 to 9.9)                                      | 317 027          | -5.9 (-10.1 to 0.0)                                    | 214 389          | -4.6 (-15.1 to 3.5)                                    |
| Greenland            | 5                | -2.0 (-16.3 to 13.4)                                    | 151              | -4.0 (-7.1 to -1.0)                                    | 99               | -4.1 (-16.1 to 9.1)                                    |
| USA                  | 238 895          | 11.6 (4.4 to 19.1)                                      | 4 029 450        | -0.5 (-6.4 to 6.4)                                     | 2 473 390        | 3.8 (-2.5 to 10.8)                                     |
| Australasia          | 17 668           | -6.3 (-13.0 to 1.7)                                     | 251 413          | -9.1 (-15.4 to -4.0)                                   | 176 255          | -8.3 (-14.5 to -1.2)                                   |
| Australia            | 14 977           | -6.0 (-14.2 to 3.7)                                     | 211 208          | -9.2 (-16.5 to -3.1)                                   | 148 229          | -8.3 (-15.6 to 0.2)                                    |
| New Zealand          | 2691             | -7.0 (-15.6 to 1.9)                                     | 40 206           | -8.4 (-15.1 to -3.5)                                   | 28 026           | -7.6 (-14.9 to 0.1)                                    |
| High-income Asia-Pacific | 262 278        | 9.2 (4.6 to 14.3)                                       | 4 216 158        | 15.6 (13.7 to 17.4)                                    | 2 678 775        | 9.3 (5.0 to 14.2)                                      |
| Brunei               | 61               | -2.7 (-7.4 to 13.3)                                     | 1 311            | -4.1 (-7.1 to -0.8)                                    | 876              | 0.8 (-7.8 to 10.0)                                     |
| Japan                | 224 138          | 10.2 (6.8 to 13.6)                                      | 3 520 611        | 17.8 (17.5 to 19.8)                                    | 2 226 531        | 10.5 (7.5 to 13.2)                                     |
| Singapore            | 2265             | 3.2 (-17.6 to 28.4)                                     | 37 905           | 11.5 (0.5 to 26.8)                                     | 24 746           | 6.3 (-12.2 to 28.8)                                    |
| South Korea          | 35 814           | -2.6 (-25.2 to 24.9)                                    | 646 331          | -4.2 (-9.4 to 0.5)                                     | 426 622          | -4.5 (-23.7 to 18.3)                                   |
| Western Europe       | 452 515          | -7.4 (-10.8 to -3.7)                                    | 6 586 827        | -8.1 (-10.9 to -5.3)                                   | 4 499 078        | -8.6 (-12.0 to -5.3)                                   |
| Andorra              | 99               | -3.2 (-21.4 to 23.7)                                    | 1 253            | -4.9 (-8.4 to -1.6)                                    | 901              | -4.4 (-20.4 to 17.7)                                   |
| Austria              | 8270             | -5.7 (-21.4 to 23.7)                                    | 1 060 410        | -3.9 (-7.3 to -0.1)                                    | 84 853           | -5.8 (-11.1 to 0.3)                                    |
| Belgium              | 12 590           | -7.3 (-17.1 to 1.9)                                     | 181 350          | -9.2 (-15.4 to -3.8)                                   | 125 538          | -8.8 (-17.2 to 0.8)                                    |
| Cyprus               | 670              | -8.1 (-14.9 to 0.6)                                     | 9644             | -1.7 (-4.6 to 1.5)                                     | 6844             | -9.0 (-14.6 to -2.3)                                   |
| Denmark              | 3984             | -12.3 (-24.3 to -0.7)                                   | 55 336           | -2.0 (-29.4 to -13.7)                                  | 39 831           | -17.1 (-28.1 to -6.6)                                  |

(Table continues on next page)
### Deaths (95% UI)

| Country | 2016 counts | Percentage change in age-standardised rates, 1990–2016 |
|---------|-------------|------------------------------------------------------|
| Finland | 6686        | -2.3 (-11 to 6.7)                                    |
| France  | 65775       | -6.5 (-8.5 to 8.0)                                   |
| Germany | 77624       | -20.8 (-35.2 to -8.9)                                |
| Greece  | 12568       | -5.4 (-12.3 to 2.1)                                  |
| Iceland | 241         | -0.1 (-8.9 to 9.0)                                   |
| Ireland | 2791        | -5.0 (-15.1 to 6.9)                                  |
| Israel  | 4730        | -5.2 (-19.2 to 10.8)                                 |
| Italy   | 9098        | -2.9 (-12.1 to 9.1)                                  |
| Luxembourg | 353    | -6.6 (-16.8 to 3.6)                                  |
| Malta   | 312         | -4.0 (-18.5 to 10.2)                                 |
| Netherlands | 1371 | -14.2 (-22.3 to -5.3)                                |
| Norway  | 4777        | -7.2 (-16.2 to 3.8)                                  |
| Portugal| 10824       | -4.2 (-11.1 to 2.8)                                  |
| Spain   | 5798        | -9.6 (-17.3 to -1.8)                                 |
| Sweden  | 9668        | -0.4 (-10.5 to 11.4)                                 |
| Switzerland | 8234 | -1.7 (-19.8 to 19.9)                                 |
| UK     | 60525       | -6.8 (-8.8 to -4.3)                                  |
| Southern Latin America | 23831 | -3.5 (-10.7 to 5.0)                                  |
| Argentina | 15412   | -2.7 (-10.5 to 5.7)                                  |
| Chile   | 6508        | -5.3 (-23.4 to 15.6)                                 |
| Uruguay | 1911        | -5.2 (-12.4 to 2.5)                                  |
| Eastern Europe | 84368 | -0.3 (-16.0 to 17.6)                                 |
| Belarus | 4060        | 1.3 (-12.4 to 16.8)                                  |
| Estonia | 805         | 0.2 (-11.9 to 8.9)                                   |
| Latvia  | 1202        | 0.0 (-10.0 to 11.7)                                  |
| Lithuania | 1769     | 0.6 (-6.0 to 8.5)                                    |
| Moldova | 1100        | -3.5 (-13.7 to 7.5)                                  |

### Prevalence (95% UI)

| Country | 2016 counts | Percentage change in age-standardised rates, 1990–2016 |
|---------|-------------|------------------------------------------------------|
| Finland | 83950       | -7.4 (-13.6 to -2.7)                                  |
| France  | 877760      | 1.1 (-5.4 to 10.2)                                   |
| Germany | 1201668     | -17.7 (-28.4 to -10.3)                                |
| Greece  | 192563      | -3.7 (-7.1 to -0.3)                                  |
| Iceland | 337         | -3.7 (-7.2 to -0.8)                                  |
| Ireland | 42325       | -9.6 (-19.2 to -1.0)                                 |
| Israel  | 69596       | -3.7 (-7.2 to -0.8)                                  |
| Italy   | 1370308     | -2.9 (-10.9 to 7.2)                                  |
| Luxembourg | 5022    | -10.9 (-17.7 to -5.4)                                |
| Malta   | 5145        | -4.8 (-10.9 to 5.6)                                  |
| Netherlands | 19242 | -16.8 (-24.8 to -8.7)                                |
| Norway  | 67207       | -9.7 (-16.4 to -0.7)                                 |
| Portugal| 166660      | -4.3 (-24.0 to -1.6)                                 |
| Spain   | 830955      | -12.7 (-17.0 to -8.7)                                |
| Sweden  | 142753      | -4.0 (-9.5 to 0.4)                                   |
| Switzerland | 115476 | -6.1 (-10.6 to -2.2)                                 |
| UK     | 838693      | -10.3 (-11.7 to -9.1)                                |
| Southern Latin America | 375684 | -4.4 (-7.0 to -2.0)                                  |
| Argentina | 243618   | -4.0 (-7.0 to -1.0)                                  |
| Chile   | 104522      | -5.9 (-12.4 to 0.0)                                  |
| Uruguay | 27837       | -4.6 (-7.4 to -0.7)                                  |
| Eastern Europe | 1554081 | -1.2 (-3.7 to 1.3)                                  |
| Belarus | 72664       | -1.2 (-5.2 to -2.9)                                  |
| Estonia | 13540       | -1.6 (-6.5 to -2.5)                                  |
| Latvia  | 20677       | -0.5 (-3.9 to 1.1)                                   |
| Lithuania | 30147     | -0.8 (-4.3 to 3.2)                                   |
| Moldova | 20777       | -1.6 (-4.5 to 1.9)                                   |

### DALYs (95% UI)

| Country | 2016 counts | Percentage change in age-standardised rates, 1990–2016 |
|---------|-------------|------------------------------------------------------|
| Finland | 66130       | -5.0 (-13.0 to 2.6)                                   |
| France  | 611185      | -1.7 (-5.4 to 10.2)                                  |
| Germany | 82373       | -18.4 (-29.4 to -8.5)                                 |
| Greece  | 106552      | -5.4 (-10.1 to 1.1)                                  |
| Iceland | 248         | -2.9 (-10.4 to 4.7)                                  |
| Ireland | 29432       | -6.0 (-14.3 to 4.2)                                  |
| Israel  | 46920       | -6.1 (-18.5 to 7.2)                                  |
| Italy   | 89839       | -4.4 (-13.4 to 6.6)                                  |
| Luxembourg | 3566       | -9.7 (-18.6 to 6.6)                                  |
| Malta   | 3465        | -5.0 (-16.8 to 7.1)                                  |
| Netherlands | 136421 | -15.9 (-23.7 to -7.2)                                |
| Norway  | 46464       | -9.3 (-17.6 to 0.4)                                  |
| Portugal| 113147      | -4.9 (-24.6 to 8.7)                                  |
| Spain   | 551548      | -12.4 (-19.1 to -6.0)                                |
| Sweden  | 93782       | -2.7 (-23.6 to 13.3)                                 |
| Switzerland | 80676   | -5.0 (-12.0 to 18.1)                                 |
| UK     | 593711      | -8.4 (-10.2 to 6.3)                                  |
| Southern Latin America | 257496 | -4.6 (-10.7 to 2.5)                                  |
| Argentina | 167002   | -1.6 (-12.0 to 2.9)                                  |
| Chile   | 70944       | -1.7 (-12.4 to 10.9)                                 |
| Uruguay | 16515       | -6.1 (-11.7 to 0.4)                                  |
| Eastern Europe | 1037741 | -0.5 (-13.7 to 15.0)                                 |
| Belarus | 48734       | 0.4 (-11.3 to 13.3)                                  |
| Estonia | 9159        | -1.1 (-10.9 to 7.3)                                  |
| Latvia  | 12994       | -0.4 (-9.4 to 9.4)                                   |
| Lithuania | 20304     | 0.1 (-6.0 to 6.9)                                    |
| Moldova | 13823       | -2.1 (-10.7 to 7.2)                                  |

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| Country                  | Deaths (95% UI)          | Prevalence (95% UI)         | DALVs (95% UI)          |
|-------------------------|--------------------------|-----------------------------|-------------------------|
|                         | 2016 counts              | Percentage change in age-standardised rates, 1990-2016 | 2016 counts              | Percentage change in age-standardised rates, 1990-2016 |
| Russia                  | 55,562                   | 0.0                         | 102,660                  | -1.0                      |
| (39,767 to 75,905)      | (-23 to 27)              | (849,865 to 1,229,568)      | (48 to 3)                | (20 to 27)                |
| Ukraine                 | 19,870                   | -1.3                        | 370,615                  | -1.6                      |
| (15,171 to 26,624)      | (-18 to 18)              | (306,917 to 442,613)        | (-4 to 2)                | (-10 to 16)               |
| Central Europe          | 59,119                   | -2.9                        | 1,033,615                | -3.5                      |
| (49,158 to 71,242)      | (-6.8 to -1.1)           | (861,756 to 1,235,186)      | (-6.8 to -1.4)           | (-7.9 to -0.2)            |
| Albania                 | 998                      | -3.4                        | 18,048                   | -1.6                      |
| (772 to 1,165)          | (-15 to 8.5)             | (15,048 to 21,732)          | (-5.3 to 2.9)            | (9.6 to 14.10)            |
| Bosnia and Herzegovina  | 757                      | -2.2                        | 31,804                   | -0.5                      |
| (1,288 to 2,195)        | (-6.5 to 12.8)           | (26,614 to 77,994)          | (-4.0 to 3.5)            | (17.002 to 26.502)        |
| Bulgaria                | 1,410                    | -1.4                        | 76,246                   | -0.6                      |
| (3,320 to 5,247)        | (-12 to 10.5)            | (63,003 to 93,266)          | (-4.8 to 2.8)            | (51,289)                  |
| Croatia                 | 2,960                    | -0.3                        | 45,148                   | -1.3                      |
| (2,727 to 3,355)        | (-12 to 12.2)            | (37,772 to 53,815)          | (-4.9 to 2.3)            | (3,076)                   |
| Czech Republic          | 5,474                    | -2.6                        | 96,200                   | -1.6                      |
| (4,532 to 6,592)        | (-8.8 to 4.1)            | (80,221 to 115,100)         | (-4.9 to 2.6)            | (6,428)                   |
| Hungary                 | 5,523                    | -1.0                        | 96,033                   | -1.6                      |
| (4,050 to 6,773)        | (-10.4 to 8.8)           | (78,970 to 113,490)         | (-5.7 to 2.0)            | (6,428)                   |
| Macedonia               | 654                      | 1.2                         | 12,787                   | 0.3                       |
| (543 to 798)            | (-5.8 to 8.6)            | (10,606 to 15,262)          | (-3.4 to 4.0)            | (8600)                    |
| Montenegro              | 248                      | 1.4                         | 45,533                   | 0.4                       |
| (200 to 302)            | (-10.4 to 12.7)          | (277,547 to 572)            | (-0.6 to 3.8)            | (3,040)                   |
| Poland                  | 19,488                   | -6.6                        | 223,656                  | -8.8                      |
| (15,936 to 23,766)      | (-15.8 to 3.2)           | (277,898 to 399,034)        | (-18.1 to -3.0)          | (224,088)                 |
| Romania                 | 10,260                   | -1.3                        | 182,066                  | -0.9                      |
| (8,497 to 12,553)       | (-10.7 to 7.4)           | (151,548 to 217,820)        | (-4.6 to 3.0)            | (122,264)                 |
| Serbia                  | 4,305                    | 1.8                         | 76,985                   | -0.4                      |
| (3,582 to 5,283)        | (-6.1 to 11.1)           | (64,273 to 91,993)          | (-3.8 to 3.5)            | (52,068)                  |
| Slovakia                | 2,259                    | -0.6                        | 39,642                   | -1.3                      |
| (1,826 to 2,804)        | (-10.1 to 11.1)          | (33,110 to 47,216)          | (-4.9 to 2.8)            | (27,138)                  |
| Slovenia                | 1,359                    | -4.6                        | 21,745                   | -2.4                      |
| (1,095 to 1,665)        | (-16.0 to 7.7)           | (18,129 to 26,165)          | (-5.5 to 1.3)            | (14,785)                  |
| Central Asia            | 12,669                   | -1.0                        | 247,867                  | -0.9                      |
| (10,564 to 15,413)      | (-5.5 to 3.9)            | (207,340 to 294,247)        | (-6.2 to 0.9)            | (162,755)                 |
| Armenia                 | 1,069                    | 3.6                         | 18,476                   | 0.5                       |
| (876 to 1,307)          | (-6.8 to 14.7)           | (15,412 to 22,206)          | (-3.9 to 3.0)            | (12,426)                  |
| Azerbaijan              | 1,506                    | 1.9                         | 30,747                   | 0.4                       |
| (1,197 to 1,883)        | (-10.2 to 17.7)          | (25,808 to 36,380)          | (-3.7 to 3.9)            | (20,191)                  |
| Georgia                 | 1,806                    | 2.2                         | 30,310                   | 0.2                       |
| (1,461 to 2,234)        | (-13.3 to 16.3)          | (25,251 to 36,053)          | (-3.7 to 3.3)            | (20,039)                  |
| Kazakhstan              | 2,603                    | -4.2                        | 56,927                   | -0.8                      |
| (2,091 to 3,358)        | (-17.6 to 10.7)          | (47,459 to 68,027)          | (-4.7 to 2.7)            | (35,883)                  |
| Kyrgyzstan              | 677                      | -0.2                        | 13,141                   | -0.2                      |
| (557 to 816)            | (-7.9 to 8.1)            | (11,032 to 15,644)          | (-4.3 to 2.6)            | (8,02)                    |
| Mongolia                | 465                      | -1.8                        | 56,355                   | -0.2                      |
| (213 to 327)            | (-13.6 to 10.9)          | (47,012 to 66,48)           | (-6.3 to 3.2)            | (3,735)                   |
| Tajikistan              | 655                      | -2.2                        | 12,872                   | -4.2                      |
| (535 to 806)            | (-12.2 to 11.0)          | (10,814 to 15,311)          | (-7.3 to 0.7)            | (85,96)                   |
| Turkmenistan            | 506                      | -4.6                        | 10,455                   | -2.3                      |
| (424 to 608)            | (-10.8 to 2.3)           | (8,785 to 12,366)           | (-5.6 to 1.1)            | (6,766)                   |
| Uzbekistan              | 3591                     | -1.3                        | 69,303                   | -0.9                      |
| (2942 to 4390)          | (-9.7 to 7.9)            | (57,761 to 81,697)          | (-4.5 to 2.5)            | (45,817)                  |

(Table continues on next page)
| Central Latin America | Deaths | Percentage change in age-standardised rates, 1990–2016 | Prevalence | Percentage change in age-standardised rates, 1990–2016 | DALYs | Percentage change in age-standardised rates, 1990–2016 |
|----------------------|--------|------------------------------------------------------|------------|------------------------------------------------------|--------|------------------------------------------------------|
| Colombia             | 12384  | -7.3 (-14.6 to 0.9)                                   | 24858      | -4.9 (-7.8 to -1.8)                                   | 158120 | -6.8 (-13.1 to 0.3)                                   |
| (10 275 to 14 879)   |        |                                                      | (210 857 to 295 501) |                                                    | (130 273 to 189 645) |                                                    |
| Costa Rica           | 1687   | -6.0 (-13.7 to 1.5)                                   | 31865      | -4.2                                                 | 20526  | -5.8                                                 |
| (1417 to 2021)       |        |                                                      | (26 781 to 37 969) |                                                    | (17 088 to 24 631) |                                                    |
| El Salvador          | 2124   | -6.3 (-15.6 to 3.3)                                   | 37416      | -3.7                                                 | 25185  | -7.0                                                 |
| (1761 to 2553)       |        |                                                      | (31 301 to 44 669) |                                                    | (20 658 to 30 567) |                                                    |
| Guatemala            | 2552   | -2.6 (-20.9 to 18.0)                                  | 57453      | -2.6                                                 | 28267  | -3.8                                                 |
| (2304 to 3292)       |        |                                                      | (48 552 to 67 876) |                                                    | (29 854 to 48 962) |                                                    |
| Honduras             | 1847   | -2.0 (-19.8 to 17.0)                                  | 30055      | -4.3                                                 | 22506  | -3.6                                                 |
| (1418 to 2291)       |        |                                                      | (25 259 to 35 678) |                                                    | (17 410 to 28 506) |                                                    |
| Mexico               | 37128  | -6.2                                                 | 679581     | -3.9                                                 | 47563  | -5.5                                                 |
| (31 423 to 44 041)   |        |                                                      | (57 934 to 80 887) |                                                    | (36 299 to 52 498) |                                                    |
| Nicaragua            | 1390   | -5.0 (-17.2 to 8.3)                                   | 25410      | -3.9                                                 | 16428  | -4.8                                                 |
| (1136 to 1696)       |        |                                                      | (21 451 to 30 239) |                                                    | (13 333 to 20 057) |                                                    |
| Panama               | 1227   | -8.2                                                 | 22346      | -6.6                                                 | 14478  | -8.3                                                 |
| (1014 to 1507)       |        |                                                      | (18 860 to 26 700) |                                                    | (11 898 to 17 779) |                                                    |
| Venezuela            | 6605   | -5.1                                                 | 135574     | -13.4                                                | 86441  | -15.4                                                |
| (5342 to 8050)       |        |                                                      | (115 292 to 158 925) |                                                   | (69 422 to 106 289) |                                                   |
| Andean Latin America | 15153  | -2.2 (-12.3 to 6.9)                                   | 201807     | -6.0                                                 | 172206 | -4.5                                                 |
| (9504 to 14 155)     |        |                                                      | (171 079 to 237 657) |                                                   | (113 336 to 168 798) |                                                   |
| Bolivia              | 2285   | 2.9                                                  | 38118      | -3.5                                                 | 27439  | 0.5                                                  |
| (17 579 to 28 899)   |        |                                                      | (31 800 to 45 400) |                                                    | (21 628 to 34 385) |                                                    |
| Ecuador              | 3023   | -6.3                                                 | 55856      | -5.1                                                 | 36711  | -7.0                                                 |
| (25 005 to 36 068)   |        |                                                      | (47 213 to 65 937) |                                                    | (30 333 to 44 513) |                                                    |
| Peru                 | 6205   | -4.0                                                 | 107824     | -7.5                                                 | 73056  | -5.1                                                 |
| (4847 to 7733)       |        |                                                      | (91 186 to 126 721) |                                                   | (58 539 to 90 994) |                                                   |
| Caribbean            | 13624  | -3.5 (-8.4 to 1.6)                                   | 244819     | -4.9                                                 | 161853 | -4.4                                                 |
| (11 487 to 16 276)   |        |                                                      | (206 229 to 289 536) |                                                   | (135 793 to 197 434) |                                                   |
| Antigua and Barbuda  | 21     | 0.6                                                  | 372        | -1.6                                                 | 252    | -0.5                                                 |
| (17 to 25)           |        |                                                      | (31 243 to 493) |                                                    | (206 307) |                                                   |
| The Bahamas          | 88     | 4.1                                                  | 1688       | 0.5                                                  | 1162   | 2.1                                                  |
| (71 to 108)          |        |                                                      | (14 133 to 20 212) |                                                    | (9 444 to 14 240) |                                                    |
| Barbados             | 136    | 5.7                                                  | 2224       | -2.0                                                 | 1557   | 2.7                                                  |
| (111 to 164)         |        |                                                      | (18 669 to 26 641) |                                                    | (12 848 to 18 909) |                                                    |
| Belize               | 37     | 4.6                                                  | 707        | -3.9                                                 | 505    | 2.7                                                  |
| (30 to 49)           |        |                                                      | (59 938 to 836) |                                                    | (4 190 to 6 09) |                                                    |
| Bermuda              | 21     | -1.0                                                 | 356        | -4.0                                                 | 249    | -3.2                                                 |
| (17 to 26)           |        |                                                      | (301 to 423) |                                                    | (201 to 309) |                                                   |
| Cuba                 | 6148   | -3.2                                                 | 103227     | -4.8                                                 | 70115  | -4.3                                                 |
| (5123 to 7370)       |        |                                                      | (86 496 to 122 320) |                                                   | (58 080 to 84 845) |                                                   |
| Dominican Republic   | 2233   | -7.6                                                 | 39760      | -6.2                                                 | 26694  | -8.0                                                 |
| (17 956 to 27 473)   |        |                                                      | (33 575 to 45 321) |                                                    | (21 505 to 32 836) |                                                    |
| Grenada              | 28     | 5.1                                                  | 449        | -2.7                                                 | 319    | 2.8                                                  |
| (23 to 34)           |        |                                                      | (37 534 to 53 471) |                                                    | (26 150 to 39 390) |                                                    |
| Guyana               | 80     | 2.5                                                  | 1830       | -1.6                                                 | 1221   | 0.1                                                  |
| (66 to 96)           |        |                                                      | (15 707 to 21 868) |                                                    | (1 002 to 14 80) |                                                    |
| Haiti                | 1192   | -1.7                                                 | 24561      | -6.3                                                 | 17213  | -0.7                                                 |
| (931 to 1499)        |        |                                                      | (20 588 to 29 210) |                                                    | (13 710 to 21 591) |                                                    |

(Table continues on next page)
### Articles

| Country                                      | Deaths (95% UI) | Prevalence (95% UI) | DALYs (95% UI) |
|----------------------------------------------|-----------------|---------------------|---------------|
|                                              | 2016 counts     | Percentage change in age-standardised rates, 1990–2016 | 2016 counts | Percentage change in age-standardised rates, 1990–2016 |
| Jamaica                                      | 951 (773 to 1166) | 1.5 (-12.2 to 16.2) | 15,075 (12,743 to 17,797) | -4.3 (-7.6 to -1.3) |
| Puerto Rico                                  | 2081 (1688 to 2525) | 1.3 (-7.3 to 10.8) | 31,203 (26,216 to 37,065) | -2.9 (-6.1 to 0.3) |
| Saint Lucia                                  | 57 (47 to 69) | 1.2 (-6.3 to 9.0) | 975 (811 to 1,158) | -2.1 (-5.5 to 1.2) |
| Saint Vincent and the Grenadines             | 24 (20 to 29) | -5.8 (-14.2 to 3.1) | 454 (383 to 539) | -4.6 (-7.5 to -1.6) |
| Suriname                                     | 118 (98 to 143) | 7.3 (-2.3 to 16.8) | 2,097 (1,764 to 2,484) | -1.6 (-4.3 to 1.5) |
| Trinidad and Tobago                          | 340 (283 to 410) | -3 (-10.7 to 4.9) | 6,239 (5,667 to 7,967) | -2.9 (-5.1 to 0.4) |
| Virgin Islands                               | 48 (39 to 58) | -5.6 (-13.7 to 5.0) | 881 (737 to 1,051) | -4.0 (-7.2 to -0.5) |
| Tropical Latin America                       | 82,383 (70,588 to 97,167) | 0.1 (-3.7 to 4.0) | 1,275,736 (1,470,749 to 2,025,314) | 5.0 (2.4 to 7.9) |
|                                              | 11,049 (9,316 to 13,247) | 0.1 (-3.0 to 6.7) | 8,666,579 (8,123,253 to 9,086,374) | 0.2 (-6.6 to 4.0) |
| Brazil                                       | 70,600 (69,174 to 94,940) | 0.1 (-3.7 to 4.0) | 1,691,024 (1,440,967 to 1,983,529) | 5.2 (2.5 to 8.2) |
| Paraguay                                     | 2,783 (1,463 to 2,186) | -0.1 (-12.6 to 8.8) | 34,712 (29,050 to 41,134) | -6.5 (-8.9 to -3.0) |
| East Asia                                    | 1,157,428 (423,608 to 582,677) | -0.5 (-9.5 to 4.3) | 10,767,581 (9,212,998 to 12,591,276) | 5.4 (4.2 to 6.7) |
|                                              | 6,866,579 (5,812,325 to 8,086,374) | 0.2 (-6.6 to 4.0) |
| China                                        | 47,698 (40,769 to 56,628) | -0.1 (-9.5 to 4.9) | 10,427,487 (8,937,543 to 12,156,329) | 5.6 (4.4 to 6.9) |
| North Korea                                  | 90,787 (50,625 to 75,151) | 3.4 (-9.5 to 19.6) | 136,430 (114,541 to 161,576) | -8 (-8.9 to -3.0) |
| Taiwan (province of China)                   | 1,222 (987 to 1,478) | -1.6 (-26.6 to 0.6) | 202,264 (176,950 to 238,879) | 11.1 (3.6 to 23.8) |
| Southeast Asia                               | 168,498 (143,918 to 200,845) | -5.5 (0.3 to 14.6) | 3,337,721 (2,835,683 to 3,942,605) | -1.5 (-2.6 to -0.4) |
|                                              | 2,295,779 (1,935,096 to 2,717,204) | 3.8 (-2.2 to 10.5) |
| Cambodia                                     | 2,439 (2,073 to 2,955) | 17.8 (4.0 to 44.7) | 59,393 (42,605 to 95,560) | -3.9 (-7.3 to -0.6) |
| Indonesia                                    | 45,591 (38,307 to 54,896) | 3.6 (17.1 to 54.6) | 1,111,081 (942,834 to 1,320,195) | -0.1 (-1.3 to 1.1) |
| Laos                                         | 919 (760 to 1,126) | 5.5 (2.7 to 33.4) | 206,787 (174,931 to 244,443) | -1.5 (-5.1 to 2.1) |
| Malaysia                                     | 657 (551 to 789) | -7.6 (-14.0 to 0.7) | 159,491 (135,859 to 189,529) | -0.9 (-4.8 to 3.3) |
| Maldives                                     | 70 (55 to 87) | -1.2 (-20.4 to 11.6) | 146,641 (123,676 to 173,711) | -2.5 (-20.4 to 0.0) |
| Mauritius                                    | 462 (382 to 559) | -5.0 (-15.5 to 5.6) | 99,441 (84,000 to 116,689) | -3.1 (-6.7 to 0.2) |
| Myanmar                                      | 17,857 (15,099 to 21,127) | 8.8 (-23.2 to 22.6) | 2,312,112 (1,986,027 to 2,729,903) | -3.1 (-6.4 to 0.2) |
| Philippines                                  | 14,942 (12,113 to 19,759) | 1.3 (-20.3 to 13.4) | 339,689 (290,842 to 426,756) | -0.8 (-3.8 to 2.3) |
| Sri Lanka                                     | 968 (777 to 1,268) | -2.8 (-10.2 to 6.1) | 2,427,331 (1,076,861 to 1,498,887) | -1.1 (-3.1 to 3.9) |
| Seychelles                                   | 36 (30 to 43) | -2.4 (-10.7 to 6.4) | 653 (551 to 769) | -1.1 (-3.9 to 2.0) |
| Thailand                                     | 30,293 (24,884 to 37,126) | -5.2 (-15.9 to 7.6) | 537,598 (505,189 to 703,496) | -1.5 (-5.0 to 2.2) |

(Table continues on next page)
| Articles |

| Country                  | Deaths (95% UI) | Prevalence (95% UI) | DALYs (95% UI) |
|--------------------------|-----------------|---------------------|---------------|
|                          | 2016 counts     | Percentage change in age-standardised rates, 1990-2016 | 2016 counts | Percentage change in age-standardised rates, 1990-2016 | 2016 counts | Percentage change in age-standardised rates, 1990-2016 |
| Vietnam                  | 172 (134 to 219) | 16.0               | 39.76 (3338.2 to 4745) | -1.2 | 2761 (2165.2 to 3458) | 11.5 | (-6.4 to 38.4) |
| Guinea                   | 54 (35.59 to 50.802) | -10.9 to 17.8     | 655,099 (558,892 to 775,483) | -6.0 to 0.7 | 475,067 (398,602 to 568,773) | -0.4 | (-11.3 to 13.1) |
| American Samoa           | 8 (6 to 9)      | -17.5 to 8.9       | 173 (147 to 204) | -2.7 to 4.7 | 114 (92 to 138) | -4.5 | (-15.4 to 8.2) |
| Federated States of Micronesia | 18 (14 to 22) | -15.4 to 13.3     | 31 (262 to 331) | -7.4 to 2.8 | 251 (197,943 to 304,101) | -3.3 | (-11.1 to 12.8) |
| Fiji                     | 127 (99 to 163) | -24.3 to 13.5      | 3382 | -4 to 31 | 2049 | -6.3 | (-9.2 to 10.6) |
| Guam                     | 54 (44 to 66)   | -15.3 to 4.4       | 1061 | -5.1 to 1.8 | 721 | -5.5 | (-12.3 to 1.8) |
| Kiribati                 | 18 (15 to 23)   | -5 to 31.0         | 298 (253 to 352) | -4.4 to 1.7 | 269 | 9.1 | (2.7 to 24.1) |
| Marshall Islands         | 5 (4 to 7)      | -25.5 to 5.2       | 159 (134 to 189) | -5.0 to 1.8 | 92 (74 to 115) | -13.8 | (-22.4 to -4.0) |
| Northern Mariana Islands | 6 (5 to 7)      | -19.5 to 15.7      | 129 | -5.2 to 1.9 | 85 | -5.1 | (-18.3 to 12.0) |
| Papua New Guinea         | 555 (439 to 701) | -11.1 to 16.3      | 15,398 (12,008 to 18,206) | -5.7 to 1.0 | 9665 | -0.7 | (-16.7 to 10.7) |
| Samoa                    | 50 (41 to 62)   | -15.9 to 9.5       | 784 (662 to 930) | -5.0 to 1.3 | 628 (518 to 770) | -4.4 | (-15.3 to 8.6) |
| Solomon Islands          | 63 (52 to 78)   | -7.9 to 17.2       | 1280 | -8.5 to 2.5 | 974 (791 to 1195) | 1.2 | (-8.7 to 14.6) |
| Tonga                    | 31 (26 to 38)   | -12.9 to 16.9      | 499 | -9.0 to 3.6 | 374 (308 to 460) | -0.1 | (-8.7 to 14.5) |
| Vanuatu                  | 33 (27 to 42)   | -8 to 15.2         | 708 | -4.3 to 2.5 | 530 (429 to 669) | 1.2 | (-9.6 to 13.4) |
| North Africa and Middle East | 120,035 (102,120 to 141,552) | -1.8 | (7-4 to 8-4) | 2,613,225 (1,220,174 to 3,975,480) | -0.1 | (2-7 to 1.5) | 1,669,040 (1,404,465 to 1,982,410) | -1.3 | (-6.2 to 4.0) |
| Afghanistan              | 2903 (2350 to 3584) | -2.9 to 22.4      | 65,639 (54,920 to 77,796) | -8.2 to 2.5 | 48,654 (39,657 to 59,945) | 51 | (-4.1 to 17.0) |
| Algeria                  | 11,868 (9,916 to 14,314) | -10.9 to 8.0      | 223,164 (188,279 to 265,420) | -7.4 to -1.0 | 156,627 (130,028 to 189,001) | -2.4 | (-10.1 to 6.7) |
| Bahrain                  | 128 (102 to 160) | -16.2 to 15.6      | 3091 (263,836 to 3618) | -5.1 to 1.0 | 1983 (157,665 to 2469) | -3.4 | (-15.6 to 11.2) |
| Egypt                    | 14,929 (12,172 to 18,150) | -12.1 to 10.7     | 355,367 (306,353 to 409,862) | -3.0 to 5.4 | 218,670 (181,299 to 263,812) | -0.8 | (-10.3 to 9.7) |
| Iran                     | 793 (694 to 894) | -10.5 to 21.9      | 368,528 | -1.2 | 235,690 | 2.4 | (-10.5 to 18.8) |
| Iraq                     | 439 (343 to 534) | -16.4 to 13.4      | 99,831 (84,081 to 119,541) | -8.2 to 2.2 | 86,480 (51,940 to 80,425) | -1.8 | (-15.9 to 12.4) |
| Jordan                   | 1106 (888 to 1416) | -20.5 to 16.4     | 25,413 (21,281 to 30,183) | -6.7 to 2.7 | 16,197 (12,628 to 20,464) | -3.5 | (-19.2 to 15.0) |
| Kuwait                   | 265 (197 to 344) | -20.8 to 25.1      | 7097 | -5.6 to 0.3 | 4411 | 0.6 | (-18.5 to 21.5) |
| Lebanon                  | 2071 (1704 to 2531) | -25.6 to 3.4      | 45,656 (37,962 to 54,771) | -6.5 to 0.4 | 27,451 (22,314 to 33,347) | -12.6 | (-24.2 to 2.0) |
| Libya                    | 1313 (1096 to 1585) | -10.9 to 10.5     | 25,567 (21,548 to 30,392) | -8.2 to 2.6 | 17,978 (14,741 to 21,844) | -1.2 | (-10.8 to 8.9) |
| Morocco                  | 9169 (7460 to 11,204) | -6.5 to 38.1      | 19,480 | -7.6 to 0.8 | 126,157 (103,001 to 153,822) | 45 | (-6.9 to 24.9) |

(Continued from previous page)
| Deaths (95% UI) | Prevalence (95% UI) | DALYs (95% UI) |
|----------------|---------------------|----------------|
| 2016 counts   | Percentage change in age-standardised rates, 1990–2016 | 2016 counts | Percentage change in age-standardised rates, 1990–2016 | 2016 counts | Percentage change in age-standardised rates, 1990–2016 |
| Oman          | 439                 | (374 to 526)  | -7.5 | (882 to 12 263) | -3.9 | (5393 to 783) | -8.7 |
| Palestine     | 497                 | (414 to 605)  | -2.7 | (11635) | -1.6 | (769) | 2.3 |
| Qatar         | 93                  | (68 to 124)   | -4.2 | (2706) | -2.7 | (1682) | 4.8 |
| Saudi Arabia  | 4148                | (3515 to 4980)| -3.8 | (9123) | -0.2 | (58 495) | 2.5 |
| Sudan         | 4164                | (3425 to 5077)| -0.6 | (99 360) | -2.8 | (63 559) | 5.0 |
| Syria         | 3132                | (2608 to 3727)| -7.9 | (68 793) | -2.5 | (44 016) | -1.2 |
| Tunisia       | 4558                | (3881 to 5399)| -1.9 | (85 220) | -2.3 | (58 122) | -2.3 |
| Turkey        | 35 355              | (28 754 to 43 999)| -7.2 | (75 169) | -2.5 | (46 429) | 4.1 |
| United Arab Emirates | 318 | (261 to 389) | -1.9 | (10 301) | -4.3 | (63 03) | 0.2 |
| Yemen         | 2547                | (2088 to 3117)| -6.0 | (61 063) | -4.5 | (40 803) | 2.9 |
| South Asia    | 17 664              | (14 748 to 22 198) | 16.6 | (374 443) | -4.6 | (2 494 935) | 9.1 |
| Bangladesh    | 16 463              | (12 589 to 20 470)| -2.9 | (401 28) | -0.6 | (2 293 128) | 2.6 |
| Bhutan        | 150                 | (100 to 123)  | -10.6 | (1212) | -2.8 | (1 249) | 1.5 |
| India         | 142 927             | (117 019 to 177 846) | 23.4 | (2 933 814) | -5.5 | (1 996 152) | 13.5 |
| Nepal         | 3294                | (2678 to 4084)| -7.0 | (64 140) | -5.4 | (46 390) | 14.8 |
| Pakistan      | 15 880              | (12 814 to 19 871)| -6.2 | (346 449) | -4.3 | (2 22 007) | 5.8 |
| Southern sub-Saharan Africa | 10 893 | (9 030 to 12 374) | 9.9 | (295 047) | -3.9 | (141 999) | 16.6 |
| Botswana      | 189                 | (94 to 267)   | -2.2 | (398 6) | -3.2 | (2 759) | -0.5 |
| eSwatini      | 86                  | (55 to 123)   | -7.5 | (198 7) | -4.8 | (1 336) | -8.6 |
| Lesotho       | 214                 | (157 to 278)  | -7.4 | (436 312) | -5.2 | (2 290 385) | -22.6 |
| Namibia       | 226                 | (140 to 305)  | -2.2 | (417 4) | -3.4 | (3 186) | -0.7 |
| South Africa  | 8545                | (7 118 to 10 394)| -6.4 | (164 274) | -3.4 | (1 106 78) | 3.4 |
| Zimbabwe      | 1634                | (1262 to 2091) | 17.4 | (23 393) | -2.5 | (2 162 05) | 12.1 |
| Western sub-Saharan Africa | 19 288 | (15 849 to 23 579) | 3.7 | (353 434) | -2.7 | (2 861 143) | 1.8 |
| Benin         | 622                 | (506 to 789)  | -4.5 | (11 021) | -7.1 | (9 361) | -5.0 |
| Burkina Faso  | 884                 | (722 to 1104) | -1.6 | (15 600) | -3.9 | (1 312 4) | -2.2 |
| Cameroon      | 1811                | (1405 to 2332) | -0.2 | (26 814) | -4.2 | (18 665 3070) | -1.4 |

(Table continues on next page)
| Country          | Deaths (95% UI) | Prevalence (95% UI) | DALYs (95% UI) |
|------------------|-----------------|--------------------|---------------|
|                 | 2016 counts     | Percentage change in age-standardised rates, 1990–2016 | 2016 counts | Percentage change in age-standardised rates, 1990–2016 | 2016 counts | Percentage change in age-standardised rates, 1990–2016 |
| Cape Verde      | 74              | -4.4 (-6.6 to 15.4) | 1185         | -3.8 (-7.2 to 0.0) | 866          | 1.7 (-7.8 to 11.3) |
| Chad            | 723             | -4.2 (-13.4 to 5.8) | 2174         | -4.0 (-6.8 to -1.1) | 10,307       | 4.8 (-13.2 to 4.9) |
| Côte d’Ivoire   | 1287            | 3.1 (-6.0 to 13.3)  | 2289         | -3.1 (-6.6 to 0.3)  | 19,796       | 2.2 (-6.4 to 11.7) |
| The Gambia      | 94              | 4.4 (-8.5 to 18.9)  | 1696         | -3.7 (-6.9 to 0.1)  | 1428         | 2.5 (-9.9 to 15.4) |
| Ghana           | 1990            | 12.0              | 32390        | -3.0              | 27,517       | 8.7 (-3.4 to 23.4) |
| Guinea          | 1593            | 23.9              | 32473        | -6.4              | 22,421       | 8.4 (-3.4 to 23.4) |
| Guinea-Bissau   | 109             | -2.2              | 1993         | -4.4              | 1681         | -3.4 (-12.9 to 8.6) |
| Liberia         | 247             | -6.0              | 4642         | -3.5              | 3766         | 1.3 (-6.0 to 12.5) |
| Mali            | 924             | 4.6               | 15724        | -3.7              | 12,949       | 1.3 (-10.5 to 15.6) |
| Mauritania      | 291             | 3.9               | 4793         | -3.0              | 4113         | 0.4 (-14.1 to 15.0) |
| Niger           | 868             | -9.1              | 17365        | -2.8              | 13,730       | 0.9 (-9.7 to 19.5) |
| Nigeria         | 6911            | -6.0              | 15273        | -0.9              | 107,197      | 3.8 (-11.7 to 18.3) |
| São Tomé and Príncipe | 16     | 3.2               | 259          | -3.5              | 199          | 1.4 (-10.0 to 12.2) |
| Senegal         | 1043            | -9.8              | 2593         | -6.4              | 159,035      | 1.6 (-9.3 to 11.6) |
| Sierra Leone    | 246             | -2.4              | 1595         | -6.0              | 11,952       | 3.4 (-9.3 to 11.6) |
| Togo            | 376             | 4.4               | 5612         | -3.6              | 4222         | -0.3 (-10.5 to 10.4) |
| Eastern sub-Saharan Africa | 29577 | 6.5               | 508756       | -4.1              | 406,808      | 3.3 (-1.6 to 9.7) |

| Country          | Deaths (95% UI) | Prevalence (95% UI) | DALYs (95% UI) |
|------------------|-----------------|--------------------|---------------|
| Burundi          | 639             | 4.2                | 12,408        | -4.4              | 9278         | 0.9 (-9.7 to 12.0) |
| Comoros          | 58              | 4.0                | 933           | -4.1              | 807          | 1.3 (-10.0 to 13.2) |
| Djibouti         | 98              | 6.4                | 1595         | -6.0              | 11,952       | 2.5 (-9.3 to 11.6) |
| Eritrea          | 296             | -12.2              | 1569         | -6.1              | 1235         | 3.3 (-13.8 to 19.9) |
| Ethiopia         | 8664            | 9.3                | 145,109      | -4.1              | 120,681      | 6.0 (-9.5 to 15.7) |
| Kenya            | 3205            | 15.3               | 145,109      | -4.1              | 120,681      | 6.0 (-9.5 to 15.7) |
| Madagascar       | 1486            | -1.4               | 13188        | -3.1              | 21,798       | 1.2 (-7.0 to 16.0) |
| Malawi           | 1509            | 4.3                | 24,419       | -3.4              | 20,730       | 1.9 (-7.0 to 16.0) |
| Mozambique       | 254             | -2.6               | 41,436       | -4.0              | 34,956       | 4.1 (-16.8 to 11.5) |
| Rwanda           | 1004            | 16.2               | 15,536       | -4.1              | 12,682       | 1.1 (-7.2 to 16.0) |
| Somaliland       | 680             | -0.4               | 12,957       | -5.2              | 10,031       | -1.7 (-11.2 to 10.3) |

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and diet high in sugar-sweetened beverages as risk factors for dementia. For each of these risk factors we set a theoretical minimum exposure level (TMREL) at which the risk of health outcomes is lowest. The TMREL was set to greater than 20 and less than 25 kg/m² for BMI; greater than 4 and less than 5 mmol/L for high fasting plasma glucose; zero for smoking; and less than 5g/day for sugar-sweetened beverages.

Criteria for inclusion as a risk factor in GBD included sufficient evidence of a causal relationship, availability of exposure data, and potential for modification. Although physical inactivity and absence of education were not assessed for inclusion as risk factors for dementia in GBD 2016, these will be considered in upcoming rounds. We calculated population-attributable fractions based on relative risk data, exposure data, and a theoretical minimum level of exposure. When aggregating risks, we assumed a multiplicative function and accounted for instances where one risk was mediated through another. Additional details on risk factor calculations are in the GBD 2016 risk factor overview paper.

Compilation of results

Years of life lost (YLLs) were calculated by multiplying the reference life expectancy at each age, taken from the GBD reference life table, by the number of deaths in each age group. Disability-adjusted life years (DALYs) were then calculated as the sum of YLLs and YLDs. Age-standardised rates were calculated using the GBD world population standard. Uncertainty was propagated through all calculations by sampling 1000 draws at each step of the calculations, which enabled us to carry through uncertainty from multiple sources, including input data, corrections of measurement error, and estimates of residual non-sampling error. 95% uncertainty intervals (95% UI) were defined as the 25th and 975th values of the ordered draws. Any report on significant differences was based on the 95% UI of the difference not including zero.

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. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between 1990 and 2016, the number of prevalent dementia cases increased by 117% (95% UI 114–121), from 20.2 million (17.4–23.5) in 1990 to 43.8 million (37.8–51.0) in 2016, whereas there was an increase of only 1.7% (95% UI 1.0–2.4) in age-standardised prevalence, from 701 (602–815) per 100,000 population in 1990 to 712 (614–828) per 100,000 population in 2016.

| Country                  | Deaths (95% UI) | Prevalence (95% UI) | DALYs (95% UI) |
|--------------------------|----------------|---------------------|---------------|
|                          | 2016 counts    | Percentage change in age-standardised rates, 1990–2016 | 2016 counts | Percentage change in age-standardised rates, 1990–2016 | 2016 counts | Percentage change in age-standardised rates, 1990–2016 |
| South Sudan              | 881 (677 to 1138) | 10.2 (-6.9 to 28.6) | 18,205 (15,254 to 21,613) | -4.9 (-8.5 to -1.6) | 13,002 (10,053 to 16,543) | 7.0 (-8.2 to 24.7) |
| Tanzania                 | 472 (380 to 599) | -0.2 (-12.9 to 12.4) | 74,748 (63,715 to 87,463) | -5.9 (-10.0 to -2.2) | 83,516 (50,730 to 78,321) | -1.6 (-13.1 to 9.9) |
| Uganda                   | 253 (2015 to 3154) | 2.4 (-9.4 to 15.3) | 42,050 (35,224 to 50,418) | -4.2 (-7.4 to -0.6) | 33,609 (27,179 to 41,603) | -0.2 (-10.6 to 11.0) |
| Zambia                   | 1222 (907 to 1609) | 6.2 (-15.1 to 30.3) | 20,223 (16,876 to 24,320) | -2.5 (-6.1 to 1.2) | 17,098 (12,886 to 22,139) | 4.7 (-15.4 to 27.2) |
| Central sub-Saharan Africa | 10,351 (8,428 to 12,697) | 8.1 (0.2 to 17.5) | 210,389 (176,712 to 249,382) | -2.5 (-4.9 to 0.0) | 154,400 (126,681 to 187,843) | 5.0 (-13.1 to 13.1) |
| Angola                   | 2795 (1354 to 2336) | 23.7 (1.2 to 57.1) | 36,872 (30,732 to 43,858) | -3.1 (-6.6 to 0.3) | 27,363 (20,993 to 35,154) | 15.4 (-3.8 to 40.7) |
| Central African Republic | 597 (418 to 722) | 2.9 (-13.0 to 17.9) | 12,817 (10,652 to 15,123) | 3.4 (-2.2 to 12.0) | 8,538 (6,626 to 10,751) | 42 (-10.7 to 19.6) |
| Congo (Brazzaville)      | 594 (477 to 725) | 10.7 (-5.4 to 27.6) | 11,393 (9,953 to 12,938) | 2.3 (-4.4 to 9.3) | 8,511 (6,924 to 10,410) | 7.9 (-7.4 to 23.7) |
| Democratic Republic of the Congo | 6905 (5626 to 8637) | 4.8 (-3.7 to 15.4) | 141,576 (118,678 to 168,058) | -3.4 (-6.8 to 0.5) | 103,557 (83,950 to 127,231) | 3.3 (-4.1 to 11.8) |
| Equatorial Guinea        | 93 (60 to 131) | 11.8 (-20.0 to 46.6) | 1,716 (1452 to 2015) | -4.4 (-8.4 to -0.8) | 1,267 (847 to 1769) | 4.0 (-22.7 to 33.2) |
| Gabon                    | 407 (326 to 504) | 10.0 (-5.0 to 26.1) | 6170 (5123 to 7355) | -2.0 (-5.3 to 1.8) | 5132 (4121 to 6324) | 6.6 (-6.7 to 21.4) |

Data are n (95% UI) or percentage change in age-standardised rates (95% UI). DALYs= disability-adjusted life years. SDI=Socio-demographic Index. UI=uncertainty interval.

Table: Deaths, prevalence, and DALYs for Alzheimer’s disease and other dementias in 2016, and percentage change of age-standardised rates by location, 1990–2016
For all-age prevalence over the same period, there was an increase of 54.7% (95% UI 52.1–57.5), from 383 (330–447) per 100 000 population in 1990 to 593 (511–690) per 100 000 population in 2016. The percentage change from 1990 to 2016 in age-standardised prevalence was highest for the high-middle SDI quintile (table). Age-standardised prevalence varied by a factor of three across countries in 2016. Turkey had the highest age-standardised prevalence (1192 [95% UI 1007–1405] cases per 100 000 population), followed by Brazil (1037, 882–1220). Nigeria (397, 335–462) and Ghana (406, 342–483) had the lowest age-standardised prevalence estimates (figure 1).

The number of deaths due to dementia increased by 148% (140–157) between 1990 and 2016. Globally in 2016, dementia was the fifth-largest cause of death (2.4 million [95% UI 2.1–2.8] deaths) after ischaemic heart disease, chronic obstructive pulmonary disease, intracerebral haemorrhage, and ischaemic stroke. In 2016, deaths due to dementia accounted for 4.4% (95% UI 3.8–5.1) of total deaths but 8.6% (7.4–10.1) of deaths in individuals aged more than 70 years (2.2 million [1.9–2.6] deaths), making dementia the second largest cause of death in this age group after ischaemic heart disease. Globally, dementia caused 28.8 million (24.5–34.0) DALYs, making it the 23rd largest cause of DALYs globally in 2016, up from 41st in 1990. Dementia accounted for 1.2% (95% UI 1.0–1.4) of DALYs across all ages. Over the age of 70 years, this increased to 6.3% (5.4–7.5) of DALYs (23.9 million DALYs, 20.1–28.6).

More women than men died from dementia in 2016 (1.5 million, 95% UI 1.3–1.8 vs 0.8 million, 0.7–1.0). The age-standardised death rates in women were also higher than in men, in line with a higher prevalence in women than in men, indicating the female predominance was not simply due to the longer lifespan of women. Age-standardised global prevalence in females was 1.17 times (1.17–1.18) the age-standardised prevalence in males in 2016, with more women globally affected by dementia (27.0 million, 95% UI 23.3–31.4) than men (16.8 million, 14.4–19.6).

Both YLLs and YLDs increased sharply with age (figure 2). However, YLL rates increased faster with age and were much higher than YLD rates at the oldest ages. Prevalence also increased substantially with age in both men and women, approximately doubling every 5 years between the ages of 50 and 80 years, after which the increase slowed owing to the high prevalence in the oldest ages (figure 3).

There was no clear pattern between age-standardised DALY rates for the 21 GBD world regions and SDI over the 1990–2016 estimation period (figure 4). At each SDI level, there was a large amount of heterogeneity between DALY rates due to dementia. There was no uniformity between regions in the changes over time in DALY rates,
with some regions increasing and others decreasing over the 1990–2016 period.

Overall, 6·4 million (95% UI 3·4–10·5) DALYs (22·3% [95% UI 11·8–35·1] of DALYs due to dementia) in 2016 could be attributed to risk factors analysed as part of GBD: 3·5 million (1·4–6·7) DALYs (12·2% [4·7–23·1]) were attributed to high BMI; 2·1 million (0·4–4·9) DALYs (7·4% [1·6–16·1]) to high fasting plasma glucose; 1·3 million (0·6–2·0) DALYS (4·4% [2·0–6·7]) to smoking; and 18·9 thousand (7·8–34·1) DALYs (0·07% [0·03–0·12]) to a diet high in sugar-sweetened beverages. There was no significant difference in the proportion of all dementia DALYs in 2016 explained by risk factors in men (24·7%, 12·7–37·6) compared with women (20·8%, 8·6–35·7). More detailed estimates, including values for all years from 1990–2016, and all locations, all age groups, and both sexes, can be found in our online results tool.

**Discussion**

We estimated that in 2016, 27·0 million (95% UI 23·3–31·4) women and 16·8 million (14·4–19·6) men lived with dementia in the 195 countries and territories that were included in the 2016 round of GBD. The number of prevalent cases of dementia more than doubled from 1990 to 2016, contrasting with relatively minor changes in age-standardised prevalence and pointing to population ageing and growth as the main drivers of the increase. The numbers of DALYs and age-standardised DALY rates showed similar patterns to the prevalence figures. Dementia was the fifth leading cause of cause of death in 2016.

Our overall global estimate of 43·8 million people living with dementia in 2016 is close to the estimate in the World Alzheimer Report 2015 of 46·8 million for 2015. Additionally, the GBD estimate of a doubling in number of prevalent cases and a 148% (140–157) increase in dementia deaths over the 26-year period from 1990 to 2016 is of the same order as the doubling time of 20 years previously reported. However, the previous studies reported results only at the region level and did not use data across regions to generate estimates for all countries.

The increase in the number of cases of dementia is of even more importance given that there is currently no effective disease-modifying cure or treatment for the disease. Additionally, even when clinical trials are initiated, many more end in failure than success in bringing a new disease-modifying drug to market, with ratios of more than 100:1 compared with the 14–6:1 pharmaceutical industry average. Without potential treatments, increasing numbers of cases will pose undue burden on individuals who have dementia, their caregivers, and health-care systems more generally.

In GBD 2016, only four risk factors were judged to have sufficient evidence for a causal link to Alzheimer’s disease and other dementias: high BMI, high fasting plasma glucose, smoking, and high intake of sugar-sweetened beverages. In GBD, the effect of high intake of sugar-sweetened beverages was posited to be mediated through BMI on the basis of scientific literature linking BMI with dementia, but sugar-sweetened beverages as such explained only a negligible fraction of dementia burden attributed to risks. GBD is continuously reviewing new evidence for risk-outcome pairs and will update estimates of dementia burden attributable to risks in upcoming cycles for risk factors that meet GBD criteria for causality.
A Lancet Commission Report suggested that modifiable risk factors including hearing loss, education, smoking, depression, physical inactivity, social isolation, diabetes, and obesity could account for as much as 35% of dementia burden. In the context of our finding of a doubling of the prevalence of this terminal disease every 5 years over age 50 years, and the absence of a cure, the impetus to examine risk factors is clear.

Furthermore, the timing of interventions and prevention efforts focused on modifiable risk factors for dementia warrants further investigation. The prodrome of disease is thought to be long, with evidence pointing to a length of 20–30 years, but potentially longer. The inability to identify individuals accurately in the prodromal stage complicates the study of risk factors. Efforts to explore the timing of risk factors during this period are further limited by the span of observational studies and the short length of randomised controlled trials, as well as uncertainty over whether exposures are causative, are bystanders of highly correlated factors, or are even early symptoms of disease. Because of these issues, there are so far no official international lifestyle guidelines for preventing dementia. However, attention on the effects of dementia risks is increasing, and WHO has created a group tasked with the development of risk-reduction guidelines.

By 2050, the number of people living with dementia could be around 100 million. Tackling this will require training of health professionals, as well as planning and building facilities to cater to increasing numbers of individuals with dementia. The cost of care for those living with dementia is also very high, especially in high-income countries. According to recent estimates, in the USA the cost was US$818 million in 2015, an increase of 35% since 2010. Since ageing is expected to continue, the only way to reduce burden and associated costs is to identify effective preventive or treatment measures. Despite the low return on research investment in dementia in the past, the size of the burden and its increasing trend warrant a continued effort to find effective means of intervening. Until such breakthroughs are made, dementia will constitute an increasing challenge to health-care systems across the globe.

There were several limitations, separate from the broader limitations of GBD, relevant to the modelling process for dementia. First, to correct for changes in coding practices in cause of death data, we selected the countries that were most willing to code to dementia as a cause of death per prevalent case, and we assumed that certification and coding practices in these countries are correct. Although coding practices are probably not perfect in these countries, we selected them as the best available benchmark. Second, in this correction we then assumed that the excess mortality derived from these countries applied to all countries across the entire timeseries. Although this assumption was clearly approximate, it was necessary to address the changes in coding practices that led to large changes over the study period in cause of death data from countries with high-quality vital registration. Third, in correcting for the bias in cause of death data, we relied on prevalence data to determine patterns in geographical distribution of both prevalence and mortality. Although this assumption was clearly approximate, it was necessary to address the changes in coding practices that led to large changes over the study period in cause of death data from countries with high-quality vital registration. Third, in correcting for the bias in cause of death data, we relied on prevalence data to determine patterns in geographical distribution of both prevalence and mortality. Although we had a large number of data sources from western Europe, east Asia, high-income Asia-Pacific, and high-income North America, for 13 of the 21 regions we had fewer than five prevalence sources. Fourth, there was a large amount of heterogeneity in the ways in which dementia was diagnosed within the available data. Of the 237 available data sources, 230 different diagnostic procedures were used.
Although most of the data ultimately classified dementia cases using the DSM or ICD definitions, differences between different versions of the DSM criteria could have led to differences in prevalence estimates, as suggested in a meta-regression analysis of prevalence studies in China.\(^6\) Even if the same screening test was used, different studies often used different cutoff scores. For example, although 42% of studies used the Mini-Mental State Examination in the screening phase, the absolute cutoff scores that were used ranged from 18 to 28, and other studies used different cutoff scores by educational attainment level. In this round of GBD we did not find a way to correct for such bias because of the extreme variability in methods, so it is likely that part of the observed variation in prevalence was due to measurement bias rather than reflecting true geographical variation.

A potential next step in the GBD is to consider dividing dementia into subtypes, as these might have different epidemiological features and potentially different prevention and treatment strategies. A first subdivision could be Alzheimer’s disease dementia, vascular dementia, and remaining types. The challenges of subdividing include sparse data and the complication of how to handle mixed types of dementia.\(^19\) However, increased use of biomarkers in the classification of dementia and Alzheimer’s disease might help facilitate subdivision.\(^39\,40\) Additionally, the data on severity distributions over age rely on few data sources and can be strengthened. We also aim to expand our data coverage through increased use of claims data and other data types, including general practitioner data, which have been used to estimate dementia prevalence.\(^6\,41\,42\)

Monitoring trends in dementia is difficult because of the extreme variation in cause of death coding practices and the large heterogeneity in case-ascertainment methods. Although previous guidelines have been developed to systematise the reporting of neurological disorders generally, because of the diagnostic challenges noted with dementia, disease-specific guidelines are warranted and resources should be directed towards creating and implementing more systematic methods.\(^6\) The GBD study will continue to update its estimates for dementia annually, and estimates might become more robust if data collection methods improve. Additionally, as new data become available on risk factors for dementia that meet GBD criteria for causal links, they can be incorporated into future iterations of GBD.

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EN prepared the first draft of the manuscript and analysed the data. CEIS, SEV, VLF, and TV edited the first draft and final versions of the manuscript. EN finalised all drafts and approved the final version of the manuscript. All other authors provided data, developed models, reviewed results, provided guidance on methodology, or reviewed the manuscript, and approved the final version of the manuscript.

Declaration of interests
YB reports grants and personal fees from AstraZeneca and Boehringer-Ingelheim, and personal fees from Daichi-Sankyo, BMS, Pfizer, Medtronic, Bayer, Novex pharma, and Merck-Sharpie-Dohme (MSD); SL reports personal fees from AMGEN, Berlin-Chemie, MSD, Novo Nordisk, Sanofi-Aventis, Synlab, and Unilever, and non-financial support from Preventicus; WM reports grants and personal fees from Siemens Diagnostics, Aegerion Pharmaceuticals, AMGEN, Astrazeneca, BASF, Danone Research, Hoffmann LaRoche, Numares AG, Berlin-Chemie, and Pfizer, personal fees from MSD, Sanofi, and Synagevac, grants from Abbott Diagnostics, and is employed by Synlab Holding Deutschland GmbH; CDP reports personal fees from Nutricia advisory board, acted as an unpaid consultant to the Wickmg Dementia Research and Education Centre in Tasmania for development of general practitioner (GP) education on dementia (airfares and accommodation paid), and was paid as a dementia clinical lead and dementia pathways advisor for the Sydney North Primary Health Network and as a GP educator for Presbyterian Aged Care; CEIS reports grants from the National Health and Medical Research Council, Lundbeck, Alzheimer’s Association, and the Royal Australasian College of Practitioners, and has a patent PCT/AU2008/001556 issued. MS is an employee of Bayer (Istanbul, Turkey). All other authors declare no competing interests.

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