**Global, regional, and national burden of brain and other CNS cancer, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016**

**Summary**

**Background** Brain and CNS cancers (collectively referred to as CNS cancers) are a source of mortality and morbidity for which diagnosis and treatment require extensive resource allocation and sophisticated diagnostic and therapeutic technology. Previous epidemiological studies are limited to specific geographical regions or time periods, making them difficult to compare on a global scale. In this analysis, we aimed to provide a comparable and comprehensive estimation of the global burden of brain cancer between 1990 and 2016.

**Methods** We report means and 95% uncertainty intervals (UIs) for incidence, mortality, and disability-adjusted life-years (DALYs) estimates for CNS cancers (according to the International Classification of Diseases tenth revision: malignant neoplasm of meninges, malignant neoplasm of brain, and malignant neoplasm of spinal cord, cranial nerves, and other parts of CNS) from the Global Burden of Diseases, Injuries, and Risk Factors Study 2016. Data sources include vital registration and cancer registry data. Mortality was modelled using an ensemble model approach. Incidence was estimated by dividing the final mortality estimates by mortality to incidence ratios. DALYs were estimated by summing years of life lost and years lived with disability. Locations were grouped into quintiles based on the Socio-demographic Index (SDI), a summary indicator of income per capita, years of schooling, and total fertility rate.

**Findings** In 2016, there were 330,000 (95% UI 299,000 to 349,000) incident cases of CNS cancer and 227,000 (205,000 to 241,000) deaths globally, and age-standardised incidence rates of CNS cancer increased globally by 17·3% (95% UI 11·4 to 26·9) between 1990 and 2016 (2016 age-standardised incidence rate 4·63 per 100,000 person-years [4·17 to 4·90]). The highest age-standardised incidence rate was in the highest quintile of SDI (6·91 [5·71 to 7·53]). Age-standardised incidence rates increased with each SDI quintile. East Asia was the region with the most incident cases of CNS cancer for both sexes in 2016 (108,000 [95% UI 98,000 to 122,000]), followed by western Europe (49,000 [37,000 to 54,000]), and south Asia (31,000 [29,000 to 37,000]). The top three countries with the highest number of incident cases were China, the USA, and India. CNS cancer was responsible for 7·7 million (95% UI 6·9 to 8·3) DALYs globally, a non-significant change in age-standardised DALY rate of –10·0% (–16·4 to 2·6) between 1990 and 2016. The age-standardised DALY rate decreased in the high SDI quintile (–10·0% [–27·1 to –0·1]) and high-middle SDI quintile (–10·5% [–18·4 to –1·4]) over time but increased in the low SDI quintile (22·5% [11·2 to 50·5]).

**Interpretation** CNS cancer is responsible for substantial morbidity and mortality worldwide, and incidence increased between 1990 and 2016. Significant geographical and regional variation in the incidence of CNS cancer might be reflective of differences in diagnoses and reporting practices or unknown environmental and genetic risk factors. Future efforts are needed to analyse CNS cancer burden by subtype.

**Funding** Bill & Melinda Gates Foundation.

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**Introduction** Primary brain and CNS cancers (collectively called CNS cancer from this point onwards) affect both children and adults and are diagnosed in all anatomical regions of the CNS, with the vast majority (>90%) occurring in the brain and the remainder occurring in the meninges, spinal cord, and cranial nerves. They represent a substantial source of morbidity and mortality worldwide. The effect that CNS cancer has on health-care systems is out of proportion with incidence due to the high rates of mortality and inherently disabling effects it has on patients, often preventing independent functioning. The signs and symptoms associated with CNS cancer are heterogeneous, dependent on histopathology and affected anatomical regions, and include headaches, vision loss, seizures, speech disturbance, and paralysis. The burden of CNS cancer is compounded by the fact that effective treatment is multimodal and requires access to neurosurgical care, radiation, and chemotherapy. This highly specialised care for CNS cancer is not widely available in many areas of the world. In these contexts, it is important to understand the distribution of CNS cancer.
The distribution of CNS cancer across geographical regions might shed light on extrinsic factors and their contribution to the epidemiological pattern. Previous efforts to quantify the incidence of CNS cancer are limited to specific countries, geographical regions, or single-year estimates.4 A meta-analysis5 of available studies concluded that more standardised approaches to study the epidemiology of these tumours is needed. The Global Burden of Diseases, Injuries, and Risk Factors (GBD) study aims to quantify health loss due to all diseases from 1990 to the most recent year with annual updates. In this analysis, we used data from the GBD 2016 Study to quantify the incidence, mortality, and disability-adjusted life-years (DALYs) of CNS cancer across the world by sex and 5-year age group, to explore potential relationships with development status using the Socio-demographic Index (SDI), which is a composite indicator of fertility, income, and education.

Methods
Overview

Methods to estimate CNS cancer incidence, mortality, prevalence, years lived with disability (YLDs), years of life lost (YLLs), and DALYs have been previously described in detail.1–8 Additional information is included in the appendix 1. In GBD 2016, CNS cancer includes all cancers coded as C70.0–C72.9 (C70, malignant neoplasm of meninges; C71, malignant neoplasm of brain; C72, malignant neoplasm of spinal cord, cranial nerves, and other parts of the CNS) in the International Classification of Diseases (ICD) tenth revision. Since the ICD is based on the site of the cancer rather than histology, the GBD study currently does not include any estimates for brain and CNS cancer subtypes. All rates are reported per 100 000 person-years. All estimates were produced from 1990 to 2016. In this Article, we report the detailed results for CNS cancer incidence, mortality, and DALYs by age, sex, and Socio-demographic Index (SDI) from the GBD 2016 study.

Implications of all the available evidence

Between 1990 and 2016, the number of incident cases of CNS cancer have increased across all geographical regions and SDI quintiles, except for eastern Europe where incident cases have remained stable. However, probably because of access to early detection and care, the mortality to incidence ratio decreases with improvements in SDI. Reasons for the large heterogeneity in incidence remain unclear and need further investigation. This study provides quantitative estimates on distribution of disease burden related to CNS cancer across the globe and can inform resource allocation and cancer control strategies.
1990 to 2016 and are reported with 95% uncertainty intervals (UIs), which were derived from the 2.5th and 97.5th percentile of 1000 draws. Results were considered significantly different if confidence intervals did not overlap. The study was compliant with GATHER guidelines.26

Mortality and YLLs estimation
In summary, the methodological framework starts with estimating CNS cancer mortality. We used any source that provided a representative partial or complete sample of incidence or mortality data. Data sources included vital registration systems cancer registry and verbal autopsy data. We mapped different coding systems to the GBD cause list. Data were provided by collaborators or accessed via publicly available sources. Since mortality data can be sparse, and incidence data from registries often exist in locations without mortality registration, we transformed incidence data to mortality estimates by multiplying the registry incidence data with the corresponding, independently modelled, mortality to incidence ratio.27 We modelled mortality to incidence ratios using input data from locations where CNS cancer mortality and incidence data were reported for the same year. The initial mortality to incidence ratio model used a linear-step mixed-effects model with a logit link function and the SDI as the predictive covariate. We then smoothed predictions from the linear step over space and time and adjusted in a Gaussian process regression. We used the combined data (observed vital registration deaths and deaths derived from registry incidence multiplied by mortality to incidence ratio) on CNS cancer mortality as data inputs for a cause of death ensemble model approach (CODEm).22 The covariates we used in the model, with an assumption built in that these predictors have a positive association with deaths from CNS cancer, included alcohol (L per capita), cigarette use (cumulative cigarette use and smoking prevalence), red meat and saturated fat consumption, mean total cholesterol per capita, and systolic blood pressure. We used lagged distributed income as a covariate without a previous assumption on the direction of the relationship. We used SDI, fruit and vegetable consumption, education, and the Healthcare Access and Quality index23 in the model with a negative prior (reverse correlation). Of note, covariates used in the CODEm modelling process do not need to have a proven causal relationship, but there must be a plausible relationship between the covariates and CNS cancer death.22 CODEm is designed to choose among the predictors that produce the best fit to the input data. YLLs were estimated as the multiplication of counts of death and a standard, ideal, remaining life expectancy at the age of death.24

Incidence, prevalence, and YLDs estimation
We estimated CNS cancer incidence by dividing the final mortality estimates by the mortality to incidence ratio. We derived 10-year CNS cancer prevalence by estimating survival for each incidence cohort. We modelled survival using the mortality to incidence ratio as a scalar to determine where countries were placed between a theoretical best-case and worst-case survival. We estimated prevalence from incidence rather than using prevalence data in the estimation process due to the scarcity of prevalence data for most countries. We considered the prevalence cohort beyond 10 years as cured. We then divided the prevalence of the cured population into two phases (diagnosis and primary therapy, and controlled or remission phase). We divided the prevalence for the cohort that died within 10 years into four phases (diagnosis and primary therapy, controlled phase, disseminated or metastatic, and terminal phase). We used a fixed duration of 5 months for the diagnosis and primary therapy phase, 7 months for the disseminated or metastatic phase, and 1 month for the terminal phase. We assigned the remaining prevalence time to the controlled phase. For each phase, we multiplied prevalence with a distinct disability weight to estimate YLDs.24 Disability weights range from 0–1 and reflect the relative severity of time lived by a person in a health state compared with all other health states quantified in GBD. A disability weight of 0·29 (95% UI 0·19–0·40) was used for diagnosis and primary therapy, 0·05 (0·03–0·07) for controlled phase, 0·45 (0·31–0·60) for disseminated or metastatic phase, and 0·54 (0·38–0·69) for terminal phase.

DALY estimation and effect of SDI
We estimated DALYs by summing YLDs and YLLs by age, sex, location, and year. To examine the effect of the SDI on survival, we analysed the association between the age-standardised mortality to incidence ratio (a surrogate for survival) and SDI for GBD regions.25

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or the writing of the report. All authors had full access to the data in the study and had final responsibility for the decision to submit for publication.

Results
All GBD CNS cancer estimates (incidence, mortality, prevalence, YLLs, YLDs, DALYs) for 1980 through 2016 are available online from GBD Compare and GBD Results Tool, and appendix 2.

In 2016 at the global level, there were 330000 (95% UI 299000 to 349000) incident cases of CNS cancer, with an age-standardised incidence rate of 4·63 per 100000 person-years (95% UI 4·17 to 4·90), which significantly increased by 17·3% (95% UI 11·4 to 26·9) between 1990 and 2016. CNS cancer was responsible for 227000 (205000 to 241000) deaths globally with an age-standardised death rate of 3·24 per 100000 person-years (2·91 to 3·43), which...
|          | Deaths (95% UI) | Percentage change in age-standardised rates between 1990 and 2016 | Incidence (95% UI) | Percentage change in age-standardised rates between 1990 and 2016 | DALYs (95% UI) | Percentage change in age-standardised rates between 1990 and 2016 |
|----------|----------------|---------------------------------------------------------------|-------------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|
|          | 2016 counts   |                                               | 2016 counts       |                                               | 2016 counts   |                                               |
| Global   | 227,039       | –2.2 (–7.7 to 8.0) | 329,673           | 17.3 (11.4 to 26.9) | 7,659,974       | –10.0 (–16.4 to 2.6) |
| Low SDI  | 997           | 26.3 (10.5 to 63.4) | 974               | 9.3 (1.2 to 35.6) | 4,480,065       | 22.5 (11.2 to 50.5) |
| Low-middle SDI | 36,142        | 15.4 (0.0 to 74.7) | 41,107            | 7.0 (–5.7 to 61.4) | 1,455,466       | 9.1 (–6.0 to 59.7) |
| Middle SDI | 27,203        | –3.4 (–12.3 to 19.1) | 305,274           | 26.1 (16.4 to 51.3) | 2,714,483       | –3.4 (–22.2 to 5.2) |
| High-middle SDI | 48,093        | –2.5 (–11.0 to 6.8) | 79,703            | 36.9 (28.0 to 49.9) | 1,654,401       | –10.5 (–18.4 to –1.4) |
| High SDI  | 54,256        | –4.6 (–25.9 to 1.7) | 92,681            | 22.0 (–5.9 to 32.2) | 1,443,970       | –10.0 (–27.2 to –0.1) |
| High-income North America | 18,885 | –7.1 (–17.6 to 4.6) | 28,239            | 15.3 (4.9 to 33.4) | 509,907         | –10.8 (–18.9 to 2.4) |
| USA      | 6104          | –8.5 (–24.6 to 6.3) | 784               | 14.4 (–5.8 to 34.8) | 5,637           | –12.2 (–26.1 to 3.9) |
| Canada   | 9,737         | 25.6 (14.7 to 46.0) | 2,311             | –17.5 (–32.7 to 8.5) | 68              | –30.9 (–53.0 to 3.1) |
| Greenland | 509           | –12.5 (–47.4 to 6.1) | 42,751            | 15.2 (6.0 to 33.3) | 453,457         | –10.7 (–18.5 to 4.2) |
| Australia | 14,677        | –6.8 (–16.7 to 4.3) | 24,725            | –27.2 (4.6 to 33.3) | 410,642         | –9.0 (–18.5 to 1.6) |
| New Zealand | 282          | –11.9 (–36.0 to 3.8) | 329               | 1.0 (–27.7 to 16.6) | 7925            | –17.2 (–38.0 to 0.9) |
| High-income Asia Pacific | 40,125 | –8.6 (–28.4 to 4.7) | 12,817            | 15.4 (–10.1 to 27.8) | 110,751         | –12.7 (–32.6 to 0.6) |
| Brunei   | 12            | 23.0 (–5.3 to 62.3) | 31                | 127.0 (77.6 to 189.5) | 506             | 22.2 (–5.4 to 62.8) |
| Japan    | 2619          | –6.7 (–25.2 to 5.1) | 8953              | 17 (–26.0 to 51.5) | 6,792          | –7.8 (–27.7 to 0.6) |
| Singapore | 74            | –14.8 (–42.3 to 12.0) | 215               | 98.7 (36.0 to 162.9) | 299             | –22.0 (–46.9 to 6.5) |
| South Korea | 12,121      | –23.7 (–47.3 to 8.0) | 3617              | 74.5 (22.4 to 135.9) | 39,924          | –26.4 (–49.0 to 4.6) |
| Western Europe | 28,201 | 1.0 (–29.8 to 10.3) | 48,838           | 32.5 (–10.1 to 48.8) | 721,787         | –7.8 (–32.9 to 0.2) |
| Andorra  | 6             | 2.9 (–23.8 to 40.6) | 13                | 19.3 (–7.1 to 57.6) | 151             | –2.1 (–25.9 to 31.1) |
| Austria  | 520           | –4.5 (–34.2 to 8.6) | 804               | 18.4 (–23.9 to 51.2) | 11,961          | –12.6 (–38.0 to 0.4) |
| Belgium  | 767           | –13.9 (–43.5 to 1.2) | 1454              | –31.5 (–37.2 to 32.6) | 18,041          | –32.2 (–44.0 to –9.1) |
| Cyprus   | 48            | –2.9 (–16.6 to 16.7) | 88                | 77.3 (40.3 to 123.8) | 13,262          | –3.6 (–16.7 to 16.6) |
| Denmark  | 491           | –11.7 (–37.2 to 5.3) | 1495              | 39.2 (–3.5 to 68.0) | 12,554          | –18.1 (–41.0 to –0.8) |
| Finland  | 356           | –10.4 (–39.9 to 5.0) | 984               | 15.0 (–24.4 to 43.6) | 7,653           | –15.8 (–42.8 to 0.1) |
| France   | 3570          | 6.6 (–27.6 to 23.3) | 6,359             | 37.8 (–12.7 to 79.9) | 9,4168          | –0.2 (–30.7 to 14.8) |
| Germany  | 6,104         | 5.1 (–35.0 to 24.1) | 8300              | 32.0 (–47.6 to 63.3) | 150,993         | –8.2 (–38.2 to 6.7) |
| Greece   | 2120          | 3.7 (–12.9 to 14.8) | 1902              | 40.1 (8.4 to 76.8) | 28,007          | –3.0 (–16.4 to 8.2) |

(Table continues on next page)
| Country       | 2016 counts | Percentage change in age-standardised rates between 1990 and 2016 | 2016 counts | Percentage change in age-standardised rates between 1990 and 2016 | 2016 counts | Percentage change in age-standardised rates between 1990 and 2016 |
|--------------|-------------|---------------------------------------------------------------|-------------|---------------------------------------------------------------|-------------|---------------------------------------------------------------|
| Iceland      | 30          | 6.8 (-26 to 24.7)                                             | 79          | 56.6 (6.7 to 102.0)                                            | 835         | 1.6 (-29.3 to 17.7)                                           |
| Ireland      | 275         | -9.3 (-31.4 to 11.6)                                          | 571         | 55.8 (14.1 to 100.3)                                           | 787         | -13.2 (-32.0 to 7.8)                                          |
| Israel       | 466         | 24.2 (-32.0 to 63.6)                                          | 604         | 44.3 (-21.9 to 84.6)                                           | 13150       | 15.9 (-33.1 to 48.4)                                          |
| Spain        | 2957        | -10.9 (-31.9 to 3.0)                                          | 8464        | 39.3 (0.2 to 77.4)                                            | 97950       | -18.6 (-34.8 to -0.9)                                         |
| Luxembourg   | 39          | -14.1 (-40.8 to 3.7)                                          | 115         | 11.2 (-23.6 to 48.4)                                           | 1089        | -21.1 (-45.7 to -1.6)                                         |
| Malta        | 262         | 0.9 (-26.2 to 26.1)                                           | 40          | 48.1 (2.6 to 86.9)                                            | 695         | 2.4 (-25.2 to 26.6)                                           |
| Netherlands  | 988         | 14.3 (680 to 1137)                                            | 2427        | 56.9 (-7.0 to 106.8)                                           | 27553       | 6.9 (-34.7 to 25.4)                                           |
| Norway       | 361         | 3.6 (1078 to 2407)                                            | 137         | 68.4 (-8.1 to 73.4)                                           | 19586       | 1.0 (-37.6 to 17.9)                                           |
| Portugal     | 857         | 17.2 (-30.4 to 38.6)                                          | 953         | 56.6 (93 to 992)                                              | 72260       | -5.0 (-36.4 to 9.0)                                           |
| Spain        | 2901        | 5.8 (2100 to 3272)                                            | 5054        | 6.6 (3693 to 6500)                                            | 58060       | -16.9 (-35.5 to -0.4)                                         |
| Sweden       | 604         | -11.7 (-31.4 to 4.7)                                          | 1355        | -2.8 (-25.8 to 19.0)                                          | 16035       | -16.9 (-35.5 to -0.4)                                         |
| Switzerland  | 445         | 8.1 (-37.9 to 47.2)                                           | 942         | 14.1 (-39.4 to 56.4)                                          | 11537       | 1.4 (-42.8 to 38.0)                                           |
| UK           | 4194        | 6.5 (-25.7 to 13.8)                                           | 5053        | 21.6 (-12.9 to 30.8)                                          | 111666      | -2.9 (-27.1 to 5.4)                                           |
| Southern Latin America | 2039 (1784 to 2275) | 8.5 (-18.3 to 29.8)                                         | 2272 (2050 to 2436) | 15.3 (-14.7 to 33.9)                                         | 62394 (55182 to 69098) | 3.0 (-23.7 to 22.5) |
| Argentina    | 147         | 10.5 (-16.8 to 33.1)                                          | 1570        | 14.0 (-12.3 to 33.6)                                          | 43606       | 42 (-22.1 to 24.5)                                            |
| Chile        | 468         | 15.8 (-32.3 to 64.7)                                          | 550         | 33.3 (-10.8 to 68.4)                                          | 14663       | 7.9 (-38.1 to 52.7)                                           |
| Uruguay      | 144         | 4.6 (-17.0 to 20.4)                                           | 152         | 12.2 (-11.8 to 27.9)                                          | 4125        | 0.9 (-19.9 to 16.5)                                           |
| Eastern Europe | 10719 (8459 to 13555) | -6.6 (-24.6 to 19.6)                                         | 14528 (12762 to 16177) | 5.3 (-4.0 to 21.7)                                          | 359274 (279400 to 441568) | -15.3 (-28.6 to 13.4) |
| Belarus      | 450         | 8.2 (-16.6 to 31.9)                                           | 600         | 23.6 (2.5 to 41.2)                                            | 14823       | 0.9 (-23.9 to 23.3)                                           |
| Estonia      | 82          | 17.3 (-30.4 to 44.9)                                          | 151         | 7.3 (0.2 to 14.3)                                             | 14873       | -2.8 (-37.7 to 18.1)                                          |
| Latvia       | 142         | 45.0 (-24.6 to 86.9)                                          | 203         | 7.4 (-9.6 to 116.7)                                           | 3953        | 27.2 (-32.4 to 63.4)                                          |
| Lithuania    | 206         | 39.5 (-7.4 to 65.7)                                           | 341         | 88.2 (227 to 1398)                                            | 5837        | 24.3 (-12.7 to 45.3)                                          |
| Moldova      | 173         | 4.6 (-19.0 to 22.9)                                           | 191         | 0.1 (-23.9 to 9.6)                                            | 6074        | -7.8 (-30.7 to 11.5)                                          |
| Russia       | 7469        | -8.8 (-33.1 to 26.6)                                          | 1072        | 0.5 (-10.6 to 23.6)                                           | 243185      | -15.2 (-37.1 to 19.5)                                         |
| Ukraine      | 2197        | -0.5 (-24.2 to 29.3)                                          | 2979        | 7.3 (-7.1 to 19.9)                                            | 74123       | -5.4 (-28.3 to 21.2)                                          |

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| Deaths (95% UI) | Incidence (95% UI) | DALYs (95% UI) |
|----------------|-------------------|---------------|
| 2016 counts   | Percentage change in age-standardised rates between 1990 and 2016 | 2016 counts | Percentage change in age-standardised rates between 1990 and 2016 | 2016 counts | Percentage change in age-standardised rates between 1990 and 2016 |
| Central Europe | 9332 (7421 to 10 173) | 14.0 (-15.3 to 25.8) | 10 656 (8335 to 11 508) | 24.7 (-2.7 to 32.7) | 259 460 (215 615 to 280 249) | -1.2 (-21.6 to 7.5) |
| Albania       | 246                | 40.7 (-4.5 to 83.4) | 251               | 37.2 (1.2 to 74.4) | 8009                  | 36.6 (-4.8 to 76.6) |
| Bosnia and Herzegovina | 390       | 17.7 (-11.0 to 51.2) | 398       | 16.8 (1.7 to 51.2) | 10 924                 | 9.4 (-15.0 to 36.9) |
| Bulgaria      | 639                | 31.7 (-12.6 to 64.0) | 730               | 40.2 (-3.7 to 61.3) | 181 424                | 15.3 (-15.6 to 38.9) |
| Croatia       | 434                | 19.1 (-25.9 to 47.2) | 753               | 54.5 (-4.4 to 99.0) | 2 073                   | 2.4 (-20.9 to 24.3) |
| Czech Republic | 725              | 1.4 (-41.4 to 21.4) | 772               | 6.6 (-39.0 to 26.6) | 19 949                  | -23.1 (-44.6 to 17.7) |
| Hungary       | 761                | -11.8 (-27.8 to 5.3) | 841               | -4.9 (-21.2 to 21.7) | 20 617                  | -21.9 (-37.6 to 1.8) |
| Macedonia     | 181                | 20.8 (-5.5 to 42.4) | 190               | 24.0 (17.4 to 40.3) | 5420                    | 10.0 (-7.6 to 26.4) |
| Montenegro    | 51                 | 0.7 (-13.5 to 18.3) | 57                | 6.3 (-3.9 to 19.6) | 1553                    | -5.5 (-18.9 to 8.9) |
| Poland        | 3106               | 7.3 (-18.7 to 23.4) | 3485              | 19.6 (-9.2 to 37.8) | 84 181                  | -8.9 (-26.6 to 12.9) |
| Romania       | 1473               | 39.8 (-20.1 to 69.2) | 1645              | 46.9 (-10.8 to 72.0) | 42 361                  | 14.3 (-30.8 to 34.6) |
| Serbia        | 792                | 30.6 (-5.0 to 49.2) | 925               | 20.6 (6.1 to 41.1)  | 22 658                  | 0.5 (-11.6 to 15.6) |
| Slovakia      | 383                | 17.3 (-6.9 to 41.3) | 488               | 36.3 (13.4 to 58.4) | 117 179                 | 7.2 (-9.1 to 25.2) |
| Slovenia      | 136                | 11.6 (-3.9 to 41.0) | 161               | 30.2 (-32.9 to 57.6) | 3594                     | -2.3 (-44.3 to 20.7) |
| Central Asia  | 3064               | 20.4 (4.1 to 38.0) | 3619              | 19.8 (5.7 to 33.3) | 127 439                 | 16.1 (-1.0 to 32.5) |
| Armenia       | 210                | 4.3 (-19.7 to 28.2) | 233               | 4.1 (-18.9 to 22.2) | 6830                    | -2.2 (-30.7 to 21.1) |
| Azerbaijan    | 423                | -0.6 (-20.5 to 20.5) | 149               | -0.1 (-12.2 to 9.5) | 16 828                   | -2.7 (-22.3 to 18.0) |
| Georgia       | 196                | 54.6 (-5.2 to 111.2) | 206               | 46.8 (-13.2 to 80.4) | 64 652                   | 41.2 (-7.0 to 92.4) |
| Kazakhstan    | 527                | -4.9 (-23.2 to 9.7) | 637               | -1.4 (-12.4 to 15.0) | 20 931                   | -9.5 (-27.0 to 16.4) |
| Kyrgyzstan    | 126                | 31.8 (-13.1 to 60.9) | 145               | 26.7 (-23.6 to 48.6) | 5296                     | 26.5 (-21.8 to 56.1) |
| Mongolia      | 76                 | 79.6 (-13.6 to 179.8) | 83                | 84.8 (-0.1 to 175.0) | 30 157                   | 66.1 (-11.7 to 150.8) |
| Tajikistan    | 203                | 16.4 (-9.3 to 48.0) | 232               | 11.6 (-3.5 to 34.2) | 94 866                   | 11.2 (-15.0 to 42.4) |
| Torkmenistan  | 189                | 37.7 (0.5 to 78.8) | 223               | 41.1 (1.7 to 82.8)  | 85 664                   | 34.3 (-3.0 to 76.7) |
| Uzbekistan    | 1113               | 40.0 (8.4 to 85.7) | 1360              | 37.9 (12.7 to 76.2) | 50 027                   | 36.2 (5.6 to 79.5) |
| Central Latin America | 5384 | 24.8 (-7.8 to 41.2) | 6183              | 28.7 (-5.3 to 43.0) | 204 170                  | 16.7 (-13.0 to 30.5) |
| Colombia      | 1246               | 20.9 (-18.7 to 45.2) | 1412              | 24.2 (-17.7 to 42.4) | 44 994                   | 12.7 (-24.6 to 34.3) |
| Costa Rica    | 134                | 3.6 (-16.8 to 28.6) | 149               | 6.7 (-12.8 to 28.0) | 4917                     | 2.6 (-17.4 to 28.4) |

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### Articles

| Region                  | Deaths (95% UI) | Incidence (95% UI) | DALYs (95% UI) |
|-------------------------|-----------------|--------------------|----------------|
|                         | 2016 counts     | Percentage change in age-standardised rates between 1990 and 2016 | Percentage change in age-standardised rates between 1990 and 2016 | Percentage change in age-standardised rates between 1990 and 2016 |
| El Salvador             | 182 (120 to 223) | 82.0 (–11.7 to 171.8) | 197 (132 to 239) | 91.8 (0.3 to 184.5) | 6557 (4578 to 7915) | 69.6 (-12.2 to 148.9) |
| Guatemala               | 276 (204 to 395) | -18.1 (-48.1 to 32.3) | 306 (260 to 418) | -19.0 (-46.9 to 23.9) | 11812 (8817 to 18190) | -21.6 (-52.9 to 33.5) |
| Honduras                | 176 (99 to 281)  | 28.0 (-38.4 to 97.0) | 170 (108 to 243) | 27.2 (0.1 to 75.8) | 6421 (4372 to 9265) | 16.8 (-20.0 to 71.8) |
| Mexico                  | 2552 (203 to 2804) | 26.4 (-30.2 to 39.1) | 3012 (2429 to 3724) | 31.8 (-7.4 to 43.6) | 97707 (78602 to 107533) | 17.8 (-16.6 to 29.2) |
| Nicaragua               | 119 (99 to 151)  | 15.4 (-31.7 to 66.5) | 134 (120 to 554) | 16.0 (-0.1 to 54.2) | 5086 (4271 to 6722) | 1.1 (-15.2 to 26.8) |
| Panama                  | 108 (91 to 128)  | 10.9 (-17.6 to 39.1) | 122 (108 to 137) | 15.4 (-12.7 to 38.4) | 4091 (3425 to 4905) | 11.4 (-15.9 to 39.3) |
| Venezuela               | 592 (403 to 744) | 65.4 (-5.8 to 120.3) | 680 (473 to 766) | 69.0 (5.1 to 100.8) | 22884 (16604 to 28966) | 64.0 (0.2 to 120.4) |
| Andean Latin America    | 1575 (1186 to 1874) | 24.9 (-2.9 to 48.2) | 1749 (1343 to 1975) | 21.1 (-1.8 to 37.1) | 59906 (45309 to 71224) | 16.3 (-7.6 to 36.9) |
| Bolivia                 | 294 (209 to 378) | 35.5 (-3.1 to 88.1) | 300 (235 to 350) | 26.8 (0.3 to 53.4) | 11658 (8271 to 14829) | 25.9 (-3.1 to 66.2) |
| Ecuador                 | 415 (349 to 467) | 16.5 (-13.9 to 38.0) | 472 (402 to 519) | 18.6 (-13.3 to 37.0) | 16078 (13543 to 18588) | 12.5 (-18.0 to 33.4) |
| Peru                    | 866 (567 to 1324) | 26.2 (-9.0 to 63.8) | 977 (662 to 1167) | 20.9 (-4.7 to 44.5) | 32170 (21468 to 41221) | 15.0 (-16.9 to 51.1) |
| Caribbean               | 1272 (1089 to 1383) | 12.9 (-4.7 to 27.5) | 1487 (1285 to 1578) | 14.3 (-2.2 to 25.5) | 43479 (38567 to 47120) | 5.3 (-10.6 to 18.6) |
| Antigua and Barbuda     | 2 (2 to 2)       | 6.1 (-16.2 to 27.7) | 2 (2 to 2) | 13.2 (-5.0 to 25.3) | 66 (57 to 78) | 70 (-13.9 to 28.7) |
| The Bahamas             | 10 (8 to 11)     | -12.1 (-29.0 to 7.2) | 11 (11 to 13) | -7.4 (-25.3 to 9.1) | 341 (295 to 401) | -14.2 (-34.8 to 9.9) |
| Barbados                | 9 (8 to 12)      | -8.6 (-27.1 to 14.1) | 10 (10 to 13) | -3.8 (-21.0 to 13.6) | 276 (243 to 346) | -10.5 (-28.5 to 13.3) |
| Belize                  | 7 (5 to 8)       | 16.4 (-30.4 to 60.4) | 7 (7 to 9) | 9.3 (-8.1 to 41.3) | 282 (229 to 358) | 5.8 (-18.9 to 46.1) |
| Bermuda                 | 2 (1 to 3)       | 74.7 (-46.3 to 143) | 3 (110 to 3) | 38.9 (-44.5 to 140.4) | 65 (34 to 80) | 49.8 (-50.2 to 104.3) |
| Cuba                    | 632 (480 to 726) | 22.4 (-14.8 to 48.0) | 695 (536 to 775) | 24.1 (-15.0 to 45.9) | 18598 (14232 to 21354) | 12.5 (-23.1 to 36.5) |
| Dominica                | 1 (1 to 1)       | 6.6 (-16.8 to 41.7) | 1 (1 to 1) | 9.2 (-11.5 to 36.6) | 40 (34 to 48) | 6.4 (-15.6 to 42.8) |
| Dominican Republic      | 197 (159 to 247) | 6.6 (-14 to 38.7) | 216 (187 to 269) | 19.8 (-3.3 to 30.1) | 7636 (6063 to 10876) | 2.0 (-14.9 to 23.7) |
| Grenada                 | 3 (3 to 4)       | 20.6 (-9.9 to 69.1) | 3 (3 to 4) | 19.1 (-2.2 to 56.4) | 120 (99 to 144) | 19.0 (-13.2 to 70.6) |
| Guyana                  | 9 (8 to 11)      | 12.5 (-9.9 to 36.2) | 10 (9 to 11) | 11.2 (-8.7 to 27.8) | 372 (306 to 441) | 9.7 (-14.7 to 32.3) |
| Haiti                   | 191 (130 to 249) | 20.1 (-4.6 to 49.8) | 197 (143 to 233) | 8.6 (-4.0 to 27.0) | 8679 (6274 to 11021) | 12.0 (-14.2 to 42.9) |
| Jamaica                 | 56 (44 to 69)    | 19.5 (-9.5 to 78.5) | 60 (49 to 69) | -7.0 (-6.9 to 21.1) | 2169 (1654 to 2579) | 13.9 (-14.1 to 64.2) |
| Puerto Rico             | 97 (78 to 110)   | -15.1 (-30.7 to 11.2) | 139 (118 to 152) | 11.3 (-9.5 to 54.6) | 2661 (2284 to 2997) | -22.3 (-38.5 to 7.5) |
| Saint Lucia             | 4 (3 to 4)       | 7.9 (-35.9 to 33.6) | 4 (4 to 4) | 10.1 (-13.6 to 35.3) | 122 (108 to 143) | 4.8 (-20.0 to 34.1) |
| Saint Vincent and the Grenadines | 3 (2 to 3) | 66.1 (16.1 to 108.1) | 3 (3 to 3) | 67.7 (4.3 to 101.7) | 100 (87 to 114) | 65.2 (-2.1 to 111.7) |

(Continued from previous page)
| Region            | Count 2016 | 2016 Counts | Percentage change in age-standardised rates between 1990 and 2016 | Count 2016 | 2016 Counts | Percentage change in age-standardised rates between 1990 and 2016 | Count 2016 | 2016 Counts | Percentage change in age-standardised rates between 1990 and 2016 |
|-------------------|------------|-------------|---------------------------------------------------------------|------------|-------------|---------------------------------------------------------------|------------|-------------|---------------------------------------------------------------|
| Surname           | 21         | 12.4        | (-6.9 to 46.5)                                               | 134        | 134.1       | (1.7 to 65.1)                                                | 251        | 251.2       | (1.8 to 64.8)                                                |
| Trinidad and Tobago| 26         | 2.9         | (-22.5 to 24.7)                                              | 225        | 225.2       | (-1.3 to 48.6)                                               | 430        | 430.0       | (-1.3 to 48.6)                                               |
| Virgin Islands    | 4 (to 5)   | 29.3        | (-13.5 to 74.8)                                              | 150        | 150.3       | (0.2 to 62.8)                                                | 480        | 480.0       | (0.2 to 62.8)                                                |
| Tropical Latin America | 9523 (6812 to 10 453) | 78.5 | (-9.1 to 112.8) | 10 052 | 10 052.1 | (1.1 to 69.4) | 319 741 | 319 741.0 | (1.0 to 68.5) |
| Brazil            | 9402 (6625 to 10 328) | 79.8 | (-13.5 to 114.5) | 10521 | 10521.2 | (0.3 to 67.5) | 315 181 | 315 181.0 | (0.7 to 67.5) |
| Paraguay          | 120 (82 to 213) | 27.7 | (-14.7 to 72.3) | 122 | 122.1 | (0.9 to 62.1) | 45 890 | 45 890.0 | (0.8 to 62.1) |
| East Asia         | 60 641 (54 294 to 68 081) | -19.4 | (-28.0 to -1.6) | 108 444 | 108 444.2 | (1.9 to 66.7) | 1 986 794 | 1 986 794.0 | (1.9 to 66.7) |
| China             | 59 120 (53 264 to 66 813) | -19.8 | (-28.6 to -1.9) | 106 207 | 106 207.2 | (1.4 to 65.3) | 1 933 243 | 1 933 243.0 | (1.4 to 65.3) |
| North Korea       | 937 (565 to 1217) | 14.2 | (-2.9 to 34.4) | 906 | 906.1 | (0.6 to 61.9) | 35 103 | 35 103.0 | (0.6 to 61.9) |
| Taiwan (province of China) | 583 (412 to 710) | -4.7 | (-2.1 to 13.7) | 130 | 130.1 | (0.5 to 60.7) | 18 448 | 18 448.0 | (0.5 to 60.7) |
| Southeast Asia    | 14 196 (10 685 to 16 783) | 20.6 | (2.7 to 53.3) | 15 540 | 15 540.1 | (1.0 to 60.0) | 532 546 | 532 546.0 | (1.0 to 60.0) |
| Cambodia          | 275 (216 to 331) | 22.4 | (8.6 to 44.3) | 275 | 275.1 | (1.0 to 43.7) | 1 114 511 | 1 114 511.0 | (1.0 to 43.7) |
| Indonesia         | 5405 | 34.4 | (15.7 to 70.7) | 6337 | 6337.1 | (1.6 to 41.1) | 214 521 | 214 521.0 | (1.6 to 41.1) |
| Laos              | 113 (87 to 134) | 35.6 | (11.8 to 67.5) | 113 | 113.1 | (1.3 to 50.9) | 54 841 | 54 841.0 | (1.3 to 50.9) |
| Malaysia          | 431 (352 to 628) | 8.0 | (-20.2 to 91.7) | 598 | 598.1 | (1.6 to 48.7) | 16 258 | 16 258.0 | (1.6 to 48.7) |
| Maldives          | 4 (3 to 5) | -7.3 | (-31.0 to 25.6) | 5 | 5.1 | (-34.8 to 25.6) | 143 | 143.0 | (-34.8 to 25.6) |
| Mauritius         | 22 (18 to 29) | -8.9 | (-22.0 to 16.0) | 26 | 26.1 | (-41.6 to 24.8) | 742 | 742.0 | (-41.6 to 24.8) |
| Myanmar           | 1580 (1215 to 1861) | 22.2 | (-21.6 to 68.3) | 1121 | 1121.1 | (-2.0 to 40.3) | 59 451 | 59 451.0 | (-2.0 to 40.3) |
| Philippines       | 1969 | -1.6 | (-20.3 to 27.8) | 2297 | 2297.1 | (-2.8 to 42.6) | 82 021 | 82 021.0 | (-2.8 to 42.6) |
| Sri Lanka         | 501 (352 to 681) | 43.1 | (-16.0 to 121.9) | 524 | 524.1 | (-2.5 to 41.6) | 51 574 | 51 574.0 | (-2.5 to 41.6) |
| Seychelles        | 4 (3 to 5) | -5.7 | (-33.3 to 22.0) | 5 | 5.1 | (-33.3 to 22.0) | 132 | 132.0 | (-33.3 to 22.0) |
| Thailand          | 2490 (1494 to 3105) | 11.5 | (-11.8 to 45.3) | 2247 | 2247.1 | (-2.5 to 40.3) | 75 920 | 75 920.0 | (-2.5 to 40.3) |
| Timor-Leste       | 18 | -9.2 | (-7.3 to 81.7) | 18 | 18.1 | (-8.7 to 54.1) | 771 | 771.0 | (-8.7 to 54.1) |
| Vietnam           | 1384 (1069 to 16 783) | 8.2 | (-15.5 to 45.5) | 1452 | 1452.1 | (-1.0 to 31.5) | 49 913 | 49 913.0 | (-1.0 to 31.5) |
| Oceania           | 108 (83 to 131) | 6.0 | (-13.4 to 59.7) | 133 | 133.1 | (-6.7 to 51.3) | 4996 | 4996.0 | (-6.7 to 51.3) |
| American Samoa    | 1 (1 to 1) | 7.7 | (-17.9 to 64.7) | 1 | 1.1 | (-20.7 to 34.3) | 47 | 47.0 | (-20.7 to 34.3) |
| Federated States of Micronesia | 2 (1 to 2) | 21.0 | (-19.9 to 135.4) | 1 | 1.1 | (-6.3 to 117.5) | 63 | 63.0 | (-6.3 to 117.5) |

(Table continues on next page)
Articles

| Region                        | Deaths (95% UI) | Incidence (95% UI) | DALYs (95% UI) |
|-------------------------------|-----------------|--------------------|----------------|
|                               | 2016 counts     | Percentage change in age-standardised rates between 1990 and 2016 | 2016 counts     | Percentage change in age-standardised rates between 1990 and 2016 |
|                               |                 | 2016 counts        |                 | 2016 counts |
|                               |                 | Percentage change in age-standardised rates between 1990 and 2016 |                 |
| North Africa and Middle East  | 16 555 (13 304 to 18 613) | 18 449 (15 251 to 20 751) | 629 780 (522 858 to 721 066) | 12 1 (5·4 to 55·2) |
| Afghanistan                   | 627 (443 to 766) | 27·2 (-3·0 to 96·9) | 574 (40 to 672) | 10·9 (-1·5 to 58·4) | 29 461 (21 647 to 35 772) | 29·0 (5·9 to 91·4) |
| Algeria                       | 674 (491 to 887) | 30·3 (-2·4 to 89·4) | 663 (482 to 848) | 26·1 (1·2 to 73·7) | 26 033 (17 564 to 34 543) | 27·4 (-2·6 to 74·9) |
| Bahrain                       | 19 (15 to 24)    | -11·4 (-32·9 to 20·8) | 22 (20 to 26) | -8·5 (-21·7 to 14·8) | 718 (563 to 912) | -13·4 (-34·7 to 19·2) |
| Egypt                         | 2019 (1402 to 3145) | 19·6 (-11·3 to 83·5) | 237 (182 to 359) | 24·0 (9·9 to 74·0) | 84 050 (63 080 to 120 342) | 11·4 (-13·8 to 55·5) |
| Iran                          | 3307 (2182 to 4267) | 41·5 (-8·8 to 196·7) | 392 (275 to 455) | 42·3 (5·5 to 186·8) | 120 535 (80 795 to 154 063) | 30·3 (-11·3 to 52·4) |
| Iraq                          | 1185 (935 to 1475) | 14·4 (-14·8 to 64·4) | 1226 (1049 to 1358) | 12·3 (-2·2 to 46·5) | 54 200 (42 124 to 57 392) | 13·9 (-4·5 to 62·2) |
| Jordan                        | 177 (135 to 225) | 18·0 (-19·0 to 106·8) | 204 (16·7 to 230) | 23·3 (10·0 to 91·9) | 7677 (5878 to 9725) | 11·6 (-23·0 to 87·1) |
| Kuwait                        | 50 (35 to 72)    | 3·7 (-24·9 to 48·0) | 74 (59 to 102) | 20·3 (3·0 to 65·6) | 7381 (5965 to 8887) | -28·4 (-46·1 to -0·7) |
| Lebanon                       | 200 (166 to 244) | -25·5 (-43·6 to 2·2) | 302 (256 to 336) | 0·3 (-18·3 to 16·4) | 8080 (5109 to 11 096) | 18·0 (-17·4 to 113·8) |
| Libya                         | 212 (137 to 298) | 22·8 (-16·3 to 139·2) | 245 (16·3 to 333) | 42·2 (2·7 to 162·0) | 26 240 (17 850 to 33 557) | 30·7 (-3·0 to 98·3) |
| Morocco                       | 6866 (543 to 884) | 36·2 (-3·5 to 119·2) | 761 (589 to 924) | 17·7 (6·6 to 69·9) | 18 750 (13 850 to 23 557) | 46·2 (-13·8 to 43·7) |
| Oman                          | 64 (47 to 116)   | 55·7 (-11·1 to 540·1) | 79 (59 to 145) | 70·1 (2·7 to 56·9) | 26·02 (19·03 to 45·79) | 9·5 (-15·1 to 49·1) |
| Palestine                     | 211 (181 to 240) | 19·2 (-11·2 to 75·2) | 227 (195 to 259) | 21·5 (0·2 to 67·4) | 9403 (8068 to 11 171) | -27·6 (-55·0 to 39·1) |
| Qatar                         | 26 (19 to 35)    | -20·5 (-51·6 to 57·2) | 33 (29 to 38) | -1·0 (-31·5 to 68·4) | 1142 (853 to 1 507) | -17·6 (-29·0 to 28·9) |
| Saudi Arabia                  | 731 (584 to 1002) | 42·6 (-3·5 to 405·0) | 948 (800 to 1255) | 50·7 (-5·2 to 43·6) | 26 182 (20 275 to 37 082) | 30·5 (-8·0 to 95·9) |
| Sudan                         | 772 (655 to 888) | 32·2 (9·0 to 107·8) | 844 (729 to 964) | 12·2 (-3·1 to 59·5) | 35 549 (28 850 to 44 383) | 47·1 (4·8 to 93·1) |

(Continued from previous page)
| Country                  | Deaths (95% UI) | Incidence (95% UI) | DALYs (95% UI) |
|--------------------------|-----------------|--------------------|---------------|
|                          | 2016 counts     | Percentage change in age-standardised rates between 1990 and 2016 | 2016 counts | Percentage change in age-standardised rates between 1990 and 2016 | 2016 counts | Percentage change in age-standardised rates between 1990 and 2016 |
| Tunisia                  | 273             | (-20 6 to 39 6)    | 186           | (-20 6 to 39 6)    | 2008 | (-20 6 to 39 6)    |
| South Asia               | 2511            | (20 7 to 30 7)     | 232           | (20 7 to 30 7)     | 2021 | (20 7 to 30 7)     |
| Bangladesh               | 271             | (13 7 to 17 7)     | 131           | (13 7 to 17 7)     | 2022 | (13 7 to 17 7)     |
| Bhutan                   | 206             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2023 | (13 7 to 17 7)     |
| India                    | 3102            | (20 7 to 30 7)     | 293           | (20 7 to 30 7)     | 2024 | (20 7 to 30 7)     |
| Nepal                    | 412             | (13 7 to 17 7)     | 212           | (13 7 to 17 7)     | 2025 | (13 7 to 17 7)     |
| Pakistan                 | 271             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2026 | (13 7 to 17 7)     |
| Southern and Central      | 271             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2027 | (13 7 to 17 7)     |
| Africa                   | 2511            | (20 7 to 30 7)     | 232           | (20 7 to 30 7)     | 2028 | (20 7 to 30 7)     |
| Botswana                 | 30              | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2029 | (13 7 to 17 7)     |
| Lesotho                  | 25              | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2030 | (13 7 to 17 7)     |
| Namibia                  | 23              | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2031 | (13 7 to 17 7)     |
| South Africa             | 271             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2032 | (13 7 to 17 7)     |
| Swaziland                | 14              | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2033 | (13 7 to 17 7)     |
| Zimbabwe                 | 26              | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2034 | (13 7 to 17 7)     |
| Western and Central      | 271             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2035 | (13 7 to 17 7)     |
| Africa                   | 2511            | (20 7 to 30 7)     | 232           | (20 7 to 30 7)     | 2036 | (20 7 to 30 7)     |
| Benin                    | 158             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2037 | (13 7 to 17 7)     |
| Burkina Faso             | 237             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2038 | (13 7 to 17 7)     |
| Cameroon                 | 432             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2039 | (13 7 to 17 7)     |
| Cape Verde               | 11              | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2040 | (13 7 to 17 7)     |
| Chad                     | 160             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2041 | (13 7 to 17 7)     |
| Côte d'Ivoire            | 264             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2042 | (13 7 to 17 7)     |
| The Gambia               | 18              | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2043 | (13 7 to 17 7)     |
| Ghana                    | 652             | (13 7 to 17 7)     | 127           | (13 7 to 17 7)     | 2044 | (13 7 to 17 7)     |

(Continued from previous page)
| Deaths (95% UI) | Incidence (95% UI) | DALYs (95% UI) |
|----------------|------------------|---------------|
| 2016 counts   | 2016 counts      | 2016 counts   |
| Percentage change in age-standardised rates between 1990 and 2016 | Percentage change in age-standardised rates between 1990 and 2016 | Percentage change in age-standardised rates between 1990 and 2016 |

(Continued from previous page)

| Guinea | (153 to 250) | 193 | 21.5 | (–8.6 to 68.8) | 167 | 12.9 | (–7.7 to 46.7) | 7153 | 18.7 | (–7.0 to 58.5) |
| Guinea-Bissau | (23 to 38) | 31 | 23.7 | (–3.3 to 61.0) | 26 | 20.1 | (0.1 to 38.5) | 1382 | 26.6 | (–1.7 to 58.6) |
| Liberia | (45 to 66) | 56 | 28.9 | (2.3 to 58.5) | 57 | 18.5 | (–1.4 to 36.3) | 2409 | 27.7 | (1.9 to 59.9) |
| Mali | (124 to 193) | 154 | 7.8 | (–14.7 to 35.3) | 159 | 2.2 | (–8.3 to 22.7) | 6968 | 3.2 | (–18.2 to 26.0) |
| Mauritania | (44 to 84) | 64 | 21.2 | (–31.5 to 59.4) | 56 | 15.6 | (–3.3 to 34.7) | 2816 | 28.0 | (–8.2 to 69.3) |
| Niger | (111 to 290) | 206 | 18.3 | (–5.5 to 32.3) | 212 | 12.2 | (–7.7 to 33.6) | 9523 | 18.2 | (–13.9 to 59.4) |
| Nigeria | (1542 to 3043) | 2165 | 22.9 | (–11.0 to 54.0) | 2632 | 15.8 | (0.0 to 33.5) | 106875 | 26.5 | (–1.5 to 60.0) |
| São Tomé and Príncipe | (11 to 2) | 2 | 22.2 | (–11.4 to 75.9) | 2 | 16.1 | (–6.2 to 51.4) | 78 | 16.0 | (–11.7 to 56.7) |
| Senegal | (186 to 267) | 231 | 36.8 | (8.6 to 74.2) | 190 | 20.8 | (–1.2 to 40.9) | 10460 | 39.7 | (10.8 to 66.9) |
| Sierra Leone | (68 to 116) | 88 | 33.6 | (–4.5 to 89.5) | 91 | 29.4 | (0.0 to 67.8) | 4075 | 34.1 | (–4.4 to 78.8) |
| Togo | (83 to 147) | 114 | 36.0 | (–21.0 to 100.1) | 102 | 30.7 | (0.0 to 75.8) | 5061 | 37.6 | (–3.0 to 87.4) |

Eastern sub-Saharan Africa 4868 (4299 to 5911) 27.6 (5.5 to 72.3) 4610 (4143 to 5265) 14.2 (–0.3 to 47.9) 217746 (192461 to 252543) 23.5 (6.2 to 58.7)

Table continues on next page...
did not change significantly between 1990 and 2016 (2·2% [–7·7 to 8·0]). CNS cancer was responsible for 7·7 million (6·9 to 8·3) DALYs at the global level, with an age-standardised rate of 105·05 DALYs per 100 000 person-years (94·86 to 113·35; table; appendix 2). The age-standardised DALY rate between 1990 and 2016 decreased by 10·0%, which was not significant (–16·4 to 2·6; table).

Between 1990 and 2016, age-standardised incidence rates increased in all SDI quintiles (not significant in the high and low-middle SDI quintiles; table). Age-standardised death rates decreased in the high, high-middle, and middle SDI quintiles (not significant). They increased significantly in the low and low-middle SDI quintiles (not significant in the middle SDI quintile), and increased in the high, high-middle, and middle SDI quintiles (not significant). Age-standardised DALY rates decreased in the high, high-middle, and middle SDI quintiles; table). Age-standardised DALY rates decreased in the high, high-middle, and middle SDI quintiles (not significant in the middle SDI quintile), and increased in the low and low-middle SDI quintiles (not significant in the low-middle SDI quintile).

Age-standardised incidence rates increased by SDI quintile with the highest rates observed in the high-middle (127·28 per 100 000 person-years [113·33–136·88]), followed by the middle (116·59 per 100 000 person-years [102·24–129·29]), the high (114·37 per 100 000 person-years [97·60–126·31]), the low-middle (76·68 per 100 000 person-years [69·42–87·77]), and the low SDI quintile (74·19 per 100 000 person-years [64·27–83·77]).

Age-standardised incidence rates were highest in western Europe, east Asia, and central Europe and were lowest in Oceania and central and eastern sub-Saharan Africa (appendix 2). Regarding comparisons of incidence rates for specific countries, the highest age-standardised incidence rates were observed for Nordic countries (Iceland, 20·76 per 100 000 person-years [18·70–22·82]; Denmark, 19·55 per 100 000 person-years [17·40–21·70]; Norway, 17·27 per 100 000 person-years [15·17–19·37]; Finland, 13·52 per 100 000 person-years [11·62–15·42]; and Luxembourg 16·20 per 100 000 person-years [14·23–18·17]; figure 1). In terms of absolute numbers, east Asia was the region with the most incident cases of CNS cancer for both sexes in 2016 (108 000 [98 000–122 000]), followed by western Europe (49 000 [37 000–54 000]), and south Asia (31 000 [29 000–37 000]). The top three countries with the highest number of incident cases were China, the USA, and India.

Age-standardised death rates were the highest in central Europe, tropical Latin America, and Australasia (appendix 2). The highest age-standardised death rates in specific countries were observed for Palestine (8·33 per 100 000 person-years [95% UI 7·05–9·31]), Albania (7·22 per 100 000 person-years [5·52–8·50]), Bosnia and Herzegovina (7·17 per 100 000 person-years [5·54–8·90]), and Iceland (7·10 per 100 000 person-years [5·52–8·50]).
Age-standardised DALY rates were the highest in central Europe, tropical Latin America, and eastern Europe. Most DALYs occurred in east Asia (2.0 million DALYs [95% UI 1.7–2.2]), south Asia (1.1 million [1.0–1.3]), and western Europe (722 000 [574 000–798 000]; table). The top three countries with the most DALYs were China, India, and the USA.

Incidence of CNS cancers had a peak in early childhood (<5 years of age) and increased after 15 years of age, with no difference in incidence rates by sex during childhood but a diverging incidence between sexes with increasing age, leading to a higher incidence in men than women, albeit this difference was not significant (figure 2).

DALYs for CNS cancer were driven by YLLs rather than YLDs (figure 3), with YLLs peaking between 65 and 69 years of age. When analysing the pattern of DALYs by SDI, distinct patterns were observed (figure 4). Based on estimates for all countries and years, the expected pattern of age-standardised DALY rates and SDI is one of a steady increase until SDI around 0.8 and then a modest decline. However, regional patterns show large deviations from this pattern. Some regions had rising DALY rates with improvements in SDI, while others had decreasing rates or did not have a monotonic relationship with SDI. Also, among high-income countries, the high-income Asia Pacific region stood out with low DALYs...
rates. Generally, the large regional variation around the expected pattern based on SDI suggests that factors other than sociodemographic development are responsible for most of the variation in disease burden of CNS cancer.

When analysing age-standardised mortality to incidence ratios by SDI (appendix 1), for SDI of 0·55 and greater, age-standardised mortality decreased, suggesting improved survival with higher SDI.

Discussion
For GBD 2016, we analysed cancer registry and vital registration system data to calculate the incidence, mortality, and DALYs for primary CNS cancer. Our results show that the global burden of CNS cancer increased between 1990 and 2016, as evidenced by an increase in incident cases, deaths, and DALYs. However, despite increasing age-standardised incidence rates, age-standardised DALYs and age-standardised death rates decreased between 1990 and 2016 (albeit the change was not significant), possibly due to improved treatment and timelier, accurate diagnosis. Also, for most regions, the mortality to incidence ratio decreased with improvements in SDI and over time, which can be seen as a surrogate for improved survival. Our estimates are in line with other major efforts to quantify CNS cancer incidence and related deaths worldwide. The GLOBOCAN study estimated 256 213 incident cases and 189 382 deaths in the year 2012. GBDb estimates 287 893 incident cases (95% UI 256 282–300 541) and 208 163 deaths (95% UI 188 461–219 882) for the same year. The GBD and GLOBOCAN are also consistent in showing large regional variation in the age-standardised incidence rates of CNS cancer, with the highest rates occurring in Europe and North America and the lowest rates occurring in Africa and parts of Asia.

Perhaps the most substantial global health challenge related to CNS cancer is the requirement of highly specialised medical and surgical care for diagnosis and long-term management. No simple, population-wide screening test is available for CNS cancer to allow for early, uniform detection; moreover, symptoms such as headache or seizure are often too common and non-specific to signal the need for further radiological testing. Headaches are the most common form of neurological morbidity worldwide, but few patients with headaches have CNS cancers. Patients with CNS cancer often present with a spectrum of non-specific symptoms and signs and progress to life-threatening conditions before definitive radiological diagnosis. Diagnosis and subsequent treatment planning require the use of advanced and costly imaging modalities not readily accessible in many areas. However, over the time period studied, such technologies were becoming more widely disseminated. Despite efforts in GBD to correct for underascertainment, ascertainment bias could partly explain the increased incidence of CNS cancer during this time, but the degree to which this bias contributes to overall increase in age-standardised incidence rates requires further study.

Optimal treatment paradigms for primary CNS cancer consist of multidisciplinary approaches that combine biopsy or aggressive surgical resection with postoperative radiation and chemotherapy, when appropriate. Patients require access to neurosurgical services, intensive care units, and highly specialised radiation and neuro-oncology services that are mainly located in urban areas and in countries with advanced health-care systems. Moreover, the relative infrequency of CNS cancer compared with other cancers in adults makes them a low priority for low-resource settings. As such, the disparity in access to these services is amplified across the sociodemographic spectrum. However, our analysis shows that mortality to incidence ratios decrease with improvements in socioeconomic development, which can be interpreted as improved survival with higher SDI. This result is consistent with the improved survival for CNS cancer over time, observed by the National Cancer Institute’s Surveillance, Epidemiology, and End Results programme (relative 5-year survival probability increased from 26–8% for people diagnosed in 1990 to 36–1% for those diagnosed in 2009). This result is also consistent with findings from the CONCORD-3 study, which included aggregated data from 37·5 million patients across 15 years from 322 population-based cancer registries in 71 countries. Survival for CNS cancer was stable across that time period but did improve by 3–10% in several higher SDI regions, including high-income North America (USA, Canada), western Europe (Iceland, Norway, Sweden, the UK, Denmark, France, Switzerland), and high-income Asia Pacific (South Korea, Singapore).
On a global scale, the age-standardised incidence rate of CNS cancer is increasing but DALYs are decreasing. This relationship is also true for higher SDI quintiles but is inverted for the low-middle and low SDI quintiles. These findings show that DALYs related to CNS cancer are disproportionately represented in lower SDI regions and are likely to be reflective of a lack of access to the highly specialised services needed to treat these complex diseases. These disparities are likely to result in both a delay in diagnosis and an inability to effectively implement treatment regimens that would prevent or delay mortality. The heterogeneity observed in CNS cancer incidence probably reflects a combination of multiple factors, including genetic predisposition, environmental exposures, and the above-mentioned effects of access to health care. Previous studies have suggested that CNS cancer, in particular glioma, is more common in white populations than Asian or African populations. Our data support this finding. The highest incidence rates were in western and central Europe, and the lowest rates were in Africa. Evidence suggested this pattern was independent of SDI. For example, in the highest SDI regions, the incidence of CNS cancer and associated DALYs was more than three times higher in central Europe than in high-income Asia Pacific. Broad-scale genetic susceptibilities could account for the difference in incidence across various populations, particularly when considering that regions of similar SDI should have equal access to necessary diagnostic and treatment modalities.

It is also important to note, however, that environmental factors and exposures are likely to be highly variable across these populations. A positive association with ionising radiation and negative association with atopic conditions are the only risk factors that are consistently supported by evidence. However, incidence of atopic conditions is generally higher in high SDI countries, in which we found higher CNS cancer incidence rates. Explanations for this finding are that atopic conditions might not be causal factors for considerable proportions of CNS cancer or, more probably, the association is true at the individual but not necessarily the population level. The degree to which environmental factors are responsible for regional variance in incidence requires further study. Unfortunately, detailed analysis of the relative effects of various other epidemiological risk factors in populations has not supported any causative relationships. Perhaps by identifying the large heterogeneities in incidence, the GBD study can help direct research to identify risk factors or genetic predispositions.

The largest limitation for the GBD estimates of CNS cancer is the aggregation of all malignant CNS tumours into a single group. Given the large heterogeneity in outcomes between low-grade and high-grade brain tumours, and between gliomas, tumours of the meninges, and...
other CNS tumour histologies, the analyses of CNS cancer as a single group should be seen as a first step until more detailed analyses can be done. With increasing availability of diagnostic tools, cancer registry data quality is improving. However, the unavailability of advanced imaging and radiologists, neurologists, oncologists, and neurosurgeons in many locations will clearly affect the diagnostic accuracy and therefore also the registry and death certificate data. Coding of CNS metastases as primary CNS tumours and inclusion of benign tumours in the malignant category are examples of data deficiencies that make it difficult to distinguish between measurement error and true variation. A strength in the GBD estimation is the use of predictive covariates in the estimation process. However, given the absence of known strong environmental and genetic risk factors for CNS cancer, only covariates that are predictive of clinical outcomes (eg, access to medical care for diagnosis and treatment) should be used rather than covariates, such as alcohol consumption, that have not been found to be linked to CNS cancer incidence or mortality.

We present a detailed account of the distribution of CNS cancer across the globe and we explore associations between incidence, DALYs, mortality to incidence ratio, and various demographic factors. The global burden of CNS cancer has increased over the past 25 years. However, the relationship between the mortality to incidence ratio and SDI suggests that access to early detection and treatment leads to improved outcomes. This analysis can be used to inform resource allocation and strategic planning on a global scale and highlights the need for further research into underlying risk factors and associations with genetic susceptibilities that could explain the large heterogeneity in CNS cancer incidence.

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Educação e Ciência) under the Partnership Agreements PT2020 UID/FEDER/007728 and POCI/01/0145/FEDER/007265) and National Funds support from the European Union (FEDER funds POCI/01/0145/01/0145/FEDER/007265) and National Funds (FCT/MEC, Fundação para a Ciência e a Tecnologia and Ministério da Educação e Ciência) under the Partnership Agreements PT2020 UID/MULTI/04718/2013 and PT2020 UID/QUI/50006/2013.

MJ acknowledges the Ministry of Education Science and Technological Development of the Republic of Serbia, which has co-financed the Serbian component of this project (grant OI 175 014). Publication of results was not contingent upon the Ministry’s censorship or approval. YJK received support from the Office of Research and Innovation, Xiamen University, Malaysia. AMS was supported by the Egyptian Fulbright Mission Program. RT-S was supported in part by grant number PROMETEOI/2015/021 from Generalitat Valenciana and the national grant F17/00719 from ISCIII-FEDER. KBT acknowledges funding support from the Maurice Wilkins Centre for Biodiscovery, Cancer Society of New Zealand, Health Research Council, Gut Cancer Foundation, and the University of Auckland.

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