Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

GBD 2016 Stroke Collaborators

Summary

Background Stroke is a leading cause of mortality and disability worldwide and the economic costs of treatment and post-stroke care are substantial. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) provides a systematic, comparable method of quantifying health loss by disease, age, sex, year, and location to provide information to health systems and policy makers on more than 300 causes of disease and injury, including stroke. The results presented here are the estimates of burden due to overall stroke and ischaemic and haemorrhagic stroke from GBD 2016.

Methods We report estimates and corresponding uncertainty intervals (UIs), from 1990 to 2016, for incidence, prevalence, deaths, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life-years (DALYs). DALYs were generated by summing YLLs and YLDs. Cause-specific mortality was estimated using an ensemble modelling process with vital registration and verbal autopsy data as inputs. Non-fatal estimates were generated using Bayesian meta-regression incorporating data from registries, scientific literature, administrative records, and surveys. The Socio-demographic Index (SDI), a summary indicator generated using educational attainment, lagged distributed income, and total fertility rate, was used to group countries into quintiles.

Findings In 2016, there were 5·5 million (95% UI 5·3 to 5·7) deaths and 116·4 million (111·4 to 121·4) DALYs due to stroke. The global age-standardised mortality rate decreased by 36·2% (–39·3 to –33·6) from 1990 to 2016, with decreases in all SDI quintiles. Over the same period, the global age-standardised DALY rate declined by 34·2% (–37·2 to –31·5), also with decreases in all SDI quintiles. There were 13·7 million (12·7 to 14·7) new stroke cases in 2016. Global age-standardised incidence declined by 8·1% (–10·7 to –5·5) from 1990 to 2016 and decreased in all SDI quintiles except the middle SDI group. There were 80·1 million (74·1 to 86·3) prevalent cases of stroke globally in 2016; 41·1 million (38·0 to 44·3) in women and 39·0 million (36·1 to 42·1) in men.

Interpretation Although age-standardised mortality rates have decreased sharply from 1990 to 2016, the decrease in age-standardised incidence has been less steep, indicating that the burden of stroke is likely to remain high. Planned updates to future GBD iterations include generating separate estimates for subarachnoid haemorrhage and intracerebral haemorrhage, generating estimates of transient ischaemic attack, and including atrial fibrillation as a risk factor.

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Introduction Globally, stroke is a leading cause of mortality and disability and there are substantial economic costs for post-stroke care.1 Results from the 2015 iteration of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) showed that although the age-standardised death rates and prevalence of stroke have decreased over time, the overall burden of stroke has remained high.2 As populations age, and low-income and middle-income countries go through the epidemiological transition from infectious to non-communicable diseases as the predominant cause of morbidity, together with concomitant increases in modifiable risk factors, it is expected that the burden of stroke will further increase until effective stroke prevention strategies are more widely implemented.3

Although estimates of disease burden for stroke have been produced by other research groups by meta-analysing data in the literature on incidence and deaths,4–6 GBD is unique in its approach to generating estimates for all locations, including those with scarce or no epidemiological data, by using all available data from the literature, administrative hospital and medical claims records, and cause of death records. Additionally, the methods used by GBD allow unspecified stroke to contribute to both fatal and non-fatal estimates. These methods allow GBD to document disease burden from stroke in the most comprehensive way over time and to provide the necessary information for priority setting and planning of health services. The results provided here are the most up-to-date estimates of death,
The study was compliant with GATHER guidelines. (UIs) were the 25th and 975th values of the ordered draws. For overall stroke, we included verbal autopsy studies to include results through 2016. The results presented here are also the source data for the recently published estimates of the lifetime risk of stroke.

Added value of this study
There were several important updates to this iteration of GBD, enabling generation of improved estimates. First, we developed new approaches for our inpatient hospital data processing, which allowed us to include data for several locations that had previously been excluded because of insufficient information about the catchment population. Second, we extended the terminal age group of 80 years and older into 80–84 years, 85–89 years, 90–94 years, and 95 years and older. We updated prevalence, incidence, and disability for overall stroke and the pathological types of ischaemic and haemorrhagic stroke, using the standard GBD metrics of deaths, prevalence, incidence, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life-years (DALYs).

Methods
Overview
Methods used to generate estimates of stroke incidence, mortality, prevalence, YLDs, YLLs, and DALYs have been described in previously; additional details are in the appendix. Sources included in all models can be accessed via the GBD 2016 Data Input Sources Tool. For all models, point estimates were calculated from the mean of 1000 draws from the posterior distribution by age, sex, location, and year. 95% uncertainty intervals (UIs) were the 25th and 975th values of the ordered draws. The study was compliant with GATHER guidelines.

Case definition
Stroke was defined according to WHO criteria as rapidly developing clinical signs of focal (at times global) disturbance of cerebral function lasting more than 24 h or leading to death with no apparent cause other than that of vascular origin. Data on transient ischaemic attack were not included because of the very short period of disability and no associated mortality for these events.

We modelled acute and chronic stroke separately. Stroke cases were considered acute from the day of incidence of a first-ever stroke through day 28 after the event. Chronic stroke included the sequelae of an acute stroke and all recurrent stroke events. 28 days was selected as the cutoff between acute and chronic stroke because this corresponds to the period of early case fatality.

Incident strokes were defined as the occurrence of first-ever stroke on the basis of a clinical diagnosis by a physician according to the WHO criteria described above. Ischaemic strokes were defined as all atherosclerotic and thromboembolic events that resulted in compromised blood flow to brain tissue and subsequent infarction. Haemorrhagic strokes were defined as all non-traumatic events due to subarachnoid or intracerebral haemorrhage identified by neuroimaging.

Mortality
Standard Cause of Death Ensemble modelling (CODEm) methods were used to estimate cause-specific mortality. The International Classification of Diseases (ICD) 9 and 10 codes that we used are listed in the appendix. For overall stroke, we included verbal autopsy data in addition to vital registration data; for the stroke type models, we used vital registration data only because accurate assessment of stroke type requires imaging.
## Incidence rates, 1990–2016

| Region           | Deaths (95% uncertainty interval) | Incident cases (95% uncertainty interval) | DALYs (95% uncertainty interval) |
|------------------|-----------------------------------|--------------------------------------------|----------------------------------|
|                  | (2016 counts)                     | (Percentage change in age-standardised rates, 1990-2016) | (2016 counts)                     | (Percentage change in age-standardised rates, 1990-2016) |
| Global           | 5 528 232 (5 334 609 to 5 734 681) | -36.2% (-39.3 to -33.6)                    | 1 676 761 (1 623 488 to 1 692 806) | -8.1% (-10.7 to -5.5)                              |
|                  | (Austria) 3888                     |                                            | (Australia) 13 480                 |                                           |
|                  | (Western Europe) 310 011           |                                            | (South Korea) 31 011               |                                           |
|                  | (High-income Asia) 4 526 544       |                                            | (Low-income South Asia) 1 124 081  |                                           |
|                  | (High-middle SDI) 1 082 392        |                                            | (Low-income Africa) 160 610        |                                           |
|                  | (High SDI) 721 049                 | -51.9% (-53.5 to -50.4)                    | (New Zealand) 2589                 | -20.8% (-22.7 to -18.8)                     |
|                  | (674 268 to 701 105)               |                                            | (USA) 371 762                      | -17.2% (-21.7 to -12.6)                    |
|                  | (High-middle SDI) 1 082 392        | -51.9% (-53.5 to -50.4)                    | (112 199 to 1 124 145)            | -17.2% (-21.7 to -12.6)                    |
|                  | (High SDI) 721 049                 | -51.9% (-53.5 to -50.4)                    | (Low-income South America) 26 753 | -17.2% (-21.7 to -12.6)                    |
|                  | (674 268 to 701 105)               |                                            | (New Zealand) 2589                 | -17.2% (-21.7 to -12.6)                    |
|                  | (High-middle SDI) 1 082 392        | -51.9% (-53.5 to -50.4)                    | (USA) 371 762                      | -17.2% (-21.7 to -12.6)                    |
|                  | (High SDI) 721 049                 | -51.9% (-53.5 to -50.4)                    | (112 199 to 1 124 145)            | -17.2% (-21.7 to -12.6)                    |
|                  | (674 268 to 701 105)               |                                            | (Low-income South America) 26 753 | -17.2% (-21.7 to -12.6)                    |
|                  | (High-middle SDI) 1 082 392        | -51.9% (-53.5 to -50.4)                    | (High-income Asia) 4 526 544       | -17.2% (-21.7 to -12.6)                    |
|                  | (High SDI) 721 049                 | -51.9% (-53.5 to -50.4)                    | (Western Europe) 310 011           | -17.2% (-21.7 to -12.6)                    |
|                  | (674 268 to 701 105)               |                                            | (High-income Asia) 4 526 544       | -17.2% (-21.7 to -12.6)                    |
|                  | (High-middle SDI) 1 082 392        | -51.9% (-53.5 to -50.4)                    | (Western Europe) 310 011           | -17.2% (-21.7 to -12.6)                    |
|                  | (High SDI) 721 049                 | -51.9% (-53.5 to -50.4)                    | (High-income Asia) 4 526 544       | -17.2% (-21.7 to -12.6)                    |
|                  | (674 268 to 701 105)               |                                            | (Western Europe) 310 011           | -17.2% (-21.7 to -12.6)                    |
|                  | (High-middle SDI) 1 082 392        | -51.9% (-53.5 to -50.4)                    | (High-income Asia) 4 526 544       | -17.2% (-21.7 to -12.6)                    |
|                  | (High SDI) 721 049                 | -51.9% (-53.5 to -50.4)                    | (Western Europe) 310 011           | -17.2% (-21.7 to -12.6)                    |
|                  | (674 268 to 701 105)               |                                            | (High-income Asia) 4 526 544       | -17.2% (-21.7 to -12.6)                    |
|                  | (High-middle SDI) 1 082 392        | -51.9% (-53.5 to -50.4)                    | (Western Europe) 310 011           | -17.2% (-21.7 to -12.6)                    |
|                  | (High SDI) 721 049                 | -51.9% (-53.5 to -50.4)                    | (High-income Asia) 4 526 544       | -17.2% (-21.7 to -12.6)                    |
| Country          | 2016 counts (1990-2016) | Percentage change in age-standardised rates | 2016 counts | Percentage change in age-standardised rates | 2016 counts | Percentage change in age-standardised rates |
|------------------|-------------------------|--------------------------------------------|-------------|--------------------------------------------|-------------|--------------------------------------------|
| Greece           | 15 891                  | -54.7% (-58.9 to -50.3)                    | 34 149      | -27.5% (-31.5 to -23.2)                    | 200 543     | -51.6% (-55.4 to -47.7)                    |
| Iceland          | 163                     | -42.8% (-48.9 to -36.5)                    | 603         | -16.0% (-20.5 to -11.4)                    | 234         | -46.2% (-51.1 to -41.2)                    |
| Israel           | 1915                    | -60.8% (-65.8 to -55.0)                    | 746         | -30.4% (-34.3 to -26.5)                    | 316 531     | -58.4% (-63.2 to -53.5)                    |
| Malta            | 52 377                  | -59.3% (-62.2 to -53.1)                    | 166 015     | -22.2% (-25.8 to -18.3)                    | 641 405     | -58.7% (-62.3 to -55.1)                    |
| Switzerland      | 334                     | -69.0% (-72.7 to -65.2)                    | 1074        | -37.7% (-40.9 to -34.2)                    | 4966        | -66.7% (-70.0 to -63.1)                    |
| Norway           | 250                     | -60.5% (-66.7 to -53.1)                    | 892         | -30.7% (-34.4 to -26.7)                    | 4105        | -59.2% (-64.7 to -52.9)                    |
| Sweden           | 780                     | -39.8% (-47.0 to -34.6)                    | 24 807      | -15.5% (-16.0 to -6.6)                     | 10 2126     | -42.3% (-47.7 to -36.2)                    |
| Switzerland      | 4439                    | -61.9% (-67.7 to -61.1)                    | 19766       | -10.3% (-13.0 to -6.0)                     | 63 410      | -56.9% (-63.6 to -49.4)                    |
| UK               | 48 628                  | -52.6% (-54.3 to -50.9)                    | 134 979     | -26.9% (-29.4 to -24.2)                    | 667 392     | -52.7% (-54.7 to -50.9)                    |
| Southern Latin America | 35 357 (23 341 to 38 404) | -53.2% (-57.0 to -48.8)                | 95 250 (87 970 to 102 544) | -33.3% (-36.4 to -29.7)                | 666 622 (607 737 to 724 526) | -54.1% (-57.7 to -50.0)                |
| Argentina        | 22 010                  | -54.5% (-58.5 to -50.1)                    | 59 608      | -35.4% (-39.1 to -31.3)                    | 434 748     | -55.2% (-59.0 to -51.0)                    |
| Chile            | 3869                    | -51.9% (-61.5 to -40.6)                    | 28 412      | -28.3% (-33.2 to -24.2)                    | 395 748     | -53.1% (-64.3 to -43.5)                    |
| Uruguay          | 3478                    | -45.3% (-49.4 to -40.6)                    | 7123        | -15.3% (-18.3 to -9.8)                     | 57 244      | -46.3% (-50.0 to -41.9)                    |
| Eastern Europe   | 461 418                 | -29.0% (-31.4 to -23.2)                    | 962 562     | -13.8% (-15.0 to -11.0)                    | 8 235 892   | -24.8% (-28.8 to -20.9)                    |
| Belorus          | 14 437                  | -26.8% (-38.0 to -15.3)                    | 37 939      | -13.8% (-19.0 to -7.9)                     | 281 651     | -26.9% (-37.4 to -16.4)                    |
| Estonia          | 1200                    | -74.3% (-78.0 to -68.1)                    | 4610        | -37.3% (-41.6 to -32.5)                    | 231 79      | -68.5% (-73.0 to -63.0)                    |
| Latvia           | 4512                    | -46.8% (0.0 to -39.3)                      | 12 188      | -16.0% (-22.7 to -7.6)                     | 73 098      | -43.7% (-49.8 to -36.6)                    |
| Lithuania        | 4435                    | -20.3% (-27.7 to -12.4)                    | 15 035      | -1.3% (-7.3 to 5.0)                        | 77 247      | -24.1% (-30.3 to -17.3)                    |
| Moldova          | 5590                    | -34.0% (-41.8 to -25.2)                    | 12 925      | -17.2% (-21.6 to -12.5)                    | 119 356     | -29.6% (-37.8 to -20.4)                    |
| Russia           | 345 861                 | -26.5% (-43.5 to -4.8)                     | 676 846     | -14.6% (-20.4 to -8.3)                     | 6 082 727   | -22.4% (-39.4 to -0.5)                     |
| Ukraine          | 85 383                  | -37.8% (-49.4 to -23.4)                    | 203 018     | -19.0% (-24.5 to -13.0)                    | 1 578 664   | -31.4% (-43.1 to -16.7)                    |

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| Country          | Deaths (95% uncertainty interval) | Incident cases (95% uncertainty interval) | DALYs (95% uncertainty interval) |
|------------------|----------------------------------|-------------------------------------------|----------------------------------|
|                  | 2016 counts                      | Percentage change in age-standardised rates, 1990-2016 | 2016 counts                      | Percentage change in age-standardised rates, 1990-2016 |
| Central Europe   | 177 467 (166 446 to 191 258)     | -43.8% (-46.6 to -40.7)                   | 467 197 (432 780 to 499 536)     | -14.9% (-18.6 to -11.1)                                      |
|                  | 297 660 (270 447 to 317 163)     | -44.4% (-47.0 to -41.6)                   |                                  |                                                         |
| Albania          | 4751 (4108 to 5374)              | -8.7% (-20.7 to 3.1)                      | 8436 (768 to 9130)               | 0.5% (-4.2 to 5.5)                                         |
|                  |                                  |                                            |                                  |                                                         |
| Bosnia and Herzegovina | 6446                           | -37.9% (-47.8 to -26.4)                  | 16 687 (15 103 to 18 272)        | -1.8% (-7.5 to 3.7)                                        |
| Herzegovina      | 5608 to 7434                    |                                            |                                  |                                                         |
| Bulgaria         | 20 458 (17 924 to 23 249)        | -34.4% (-43.3 to -24.6)                  | 38 368 (34 899 to 41 894)        | -14.8% (-19.9 to -9.7)                                     |
| Croatia          | 3585 (6608 to 8547)             | -43.2% (-51.1 to -35.0)                  | 20 469 (19 234 to 21 532)        | -10.4% (-15.8 to -4.3)                                     |
| Czech Republic   | 10 169 (9 355 to 11 037)        | -70.6% (-73.0 to -67.8)                  | 38 959 (35 267 to 42 806)        | -20.0% (-34.7 to -24.3)                                    |
| Hungary          | 13 188 (11 698 to 14 703)       | -55.8% (-60.0 to -50.3)                  | 40 003 (36 296 to 43 822)        | -26.0% (-30.7 to -20.8)                                    |
| Macedonia        | 4596 (4085 to 5567)             | -22.2% (-29.4 to -14.9)                  | 8147 (7377 to 8881)              | -15.0% (-19.9 to -10.2)                                    |
| Montenegro       | 1500 (1319 to 1662)             | -12.1% (-24.0 to 1.4)                    | 2346 (2162 to 2556)              | -6.1% (-10.3 to -1.8)                                      |
| Poland           | 35 815 (31 974 to 40 055)       | -49.1% (-54.4 to -43.4)                  | 124 540 (113 864 to 132 877)     | -7.4% (-13.8 to 0.2)                                       |
| Romania          | 40 042 (44 527 to 54 190)       | -27.0% (-33.8 to -19.6)                  | 103 102 (93 806 to 112 993)      | -11.3% (-17.4 to -3.8)                                     |
| Serbia           | 17 992 (14 972 to 20 989)       | -34.5% (-42.0 to -26.2)                  | 39 275 (37 480 to 41 089)        | -14.6% (-20.1 to -8.7)                                     |
| Slovakia         | 5056 (4456 to 5673)             | -49.5% (-56.2 to -42.4)                  | 20 560 (18 662 to 22 686)        | -4.0% (-10.5 to 3.7)                                       |
| Slovenia         | 1 767 (1 469 to 2 079)          | -68.1% (-72.7 to -63.2)                  | 2604 (23 829 to 65 991)          | -34.3% (-38.0 to -30.5)                                    |
| Central Asia     | 73 150 (68 710 to 78 547)       | -25.6% (-29.9 to -20.7)                  | 141 713 (131 302 to 151 650)     | -14.1% (-17.0 to -10.9)                                    |
|                  |                                  |                                            |                                  |                                                         |
| Armenia          | 2355 (2097 to 2615)             | -48.6% (-54.5 to -42.4)                  | 6639 (616 840 to 132 877)        | -20.5% (-24.9 to -16.1)                                    |
| Azerbaijan       | 8222 (6720 to 9484)             | -22.4% (-34.0 to -8.4)                   | 17 221 (15 765 to 18 656)        | -3.0% (-7.3 to 2.1)                                       |
| Georgia          | 8978 (7770 to 10 276)           | -27.4% (-38.0 to -15.4)                  | 39 275 (37 480 to 41 089)        | -10.9% (-15.4 to -6.0)                                     |
| Kazakhstan       | 17 699 (15 216 to 20 895)       | -25.6% (-38.6 to -11.6)                  | 35 810 (32 918 to 38 755)        | -15.2% (-19.7 to -9.8)                                     |
| Kyrgyzstan       | 4588 (4180 to 5023)             | -35.6% (-41.0 to -29.3)                  | 8133 (7483 to 8759)              | -24.6% (-28.4 to -20.4)                                    |
| Mongolia         | 3338 (2918 to 3785)             | 55.7% (32.8 to 84.7)                     | 4495 (4161 to 4837)              | 22.3% (17.5 to 27.4)                                       |
| Tajikistan       | 4801 (4214 to 5562)             | -10.3% (-21.7 to 4.4)                    | 8791 (8109 to 9465)              | -10.7% (-15.0 to -6.3)                                     |
| Torkmenistan     | 4145 (3843 to 4436)             | -12.3% (-19.0 to -4.9)                   | 6850 (6306 to 7389)              | -0.2% (-4.3 to 3.4)                                       |
| Uzbekistan       | 19 223 (16 854 to 22 305)       | -25.5% (-34.7 to -16.4)                  | 39 275 (36 323 to 42 740)        | -15.0% (-19.2 to -11.0)                                    |
| Central Latin American | 60 687              | -42.6% (-45.9 to -39.4)                  | 210 120 (191 977 to 227 671)     | -13.5% (-16.6 to -10.2)                                    |
|                  |                                  |                                            |                                  |                                                         |
| Colombia         | 11 830 (10 388 to 13 213)       | -54.4% (-60.0 to -48.6)                  | 42 277 (38 454 to 46 181)        | -25.4% (-29.0 to -21.1)                                    |
|                  |                                  |                                            |                                  |                                                         |
|                  | (Table continues on next page)  |                                            |                                  |                                                         |
| Country                   | 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 |
|---------------------------|-------------|-------------------------------------------------------|-------------|-------------------------------------------------------|-------------|-------------------------------------------------------|
| Costa Rica                | 989         | (-52.2 to -47.0)                                       | 4696        | (-13.7 to -8.6)                                        | 19 996      | (-47.2 to -42.1)                                       |
| El Salvador               | 1330        | (-67.1 to -62.6)                                       | 5 109       | (-25.3 to -20.6)                                       | 29 666      | (-68.8 to -64.6)                                       |
| Guatemala                 | 3 397       | (-20.5 to -16.0)                                       | 10 008      | (-2.7 to -2.0)                                         | 87 714      | (-26.6 to -22.1)                                       |
| Honduras                  | 2 698       | (-39.3 to -35.3)                                       | 6 283       | (-12.7 to -8.8)                                        | 81 255      | (-47.5 to -43.2)                                       |
| Mexico                    | 27 738      | (-36.4 to -32.7)                                       | 104 877     | (-6.5 to -2.4)                                         | 626 688     | (-34.3 to -30.5)                                       |
| Nicaragua                 | 1 232       | (-37.8 to -34.0)                                       | 4 641       | (-31.4 to -26.8)                                       | 28 456      | (-40.0 to -36.2)                                       |
| Panama                    | 1 448       | (-47.1 to -43.1)                                       | 3 996       | (-24.5 to -20.0)                                       | 26 905      | (-46.8 to -42.8)                                       |
| Venezuela                 | 9 922       | (-39.4 to -35.6)                                       | 28 233      | (-18.1 to -14.4)                                       | 220 376     | (-39.9 to -36.1)                                       |
| Andean Latin America      | 14 122      | (-54.9 to -49.9)                                       | 49 970      | (-20.5 to -16.7)                                       | 330 016     | (-57.1 to -53.2)                                       |
| Bolivia                   | 4 214       | (-49.6 to -44.8)                                       | 10 149      | (-18.2 to -14.3)                                       | 96 482      | (-53.5 to -49.7)                                       |
| Ecuador                   | 4 535       | (-49.3 to -44.3)                                       | 13 309      | (-21.6 to -17.2)                                       | 93 289      | (-52.0 to -48.3)                                       |
| Peru                      | 5 873       | (-60.8 to -55.6)                                       | 26 212      | (-31.0 to -26.8)                                       | 140 244     | (-61.6 to -57.2)                                       |
| Caribbean                 | 33 297      | (-28.3 to -23.1)                                       | 63 459      | (-15.6 to -12.4)                                       | 659 354     | (-34.9 to -31.2)                                       |
| Antigua and Barbuda       | 46          | (-51.6 to -46.8)                                       | 110         | (-7.0 to -3.0)                                         | 930         | (-50.3 to -46.3)                                       |
| The Bahamas               | 246         | (-26.9 to -22.1)                                       | 515         | (-15.0 to -11.0)                                       | 5048        | (-30.8 to -26.8)                                       |
| Barbados                  | 272         | (-42.8 to -37.9)                                       | 533         | (-22.9 to -18.7)                                       | 4429        | (-40.6 to -36.7)                                       |
| Belize                    | 118         | (-61.7 to -56.7)                                       | 255         | (-7.1 to -3.0)                                         | 266         | (-15.7 to -12.3)                                       |
| Bermuda                   | 31          | (-66.0 to -60.6)                                       | 81          | (-35.2 to -31.4)                                       | 516         | (-62.9 to -58.4)                                       |
| Cuba                      | 9 684       | (-23.0 to -17.6)                                       | 21 416      | (-13.2 to -9.5)                                        | 161 069     | (-30.6 to -26.8)                                       |
| Dominica                  | 50          | (-28.3 to -23.0)                                       | 97          | (-13.1 to -9.5)                                        | 883         | (-26.8 to -22.4)                                       |
| Dominican Republic        | 5 395       | (-30.7 to -24.8)                                       | 11 365      | (-16.6 to -12.1)                                       | 101 780     | (-37.4 to -33.2)                                       |
| Grenada                   | 92          | (-31.3 to -25.6)                                       | 141         | (-18.8 to -15.0)                                       | 1686        | (-32.5 to -28.8)                                       |
| Guyana                    | 688         | (-38.9 to -33.3)                                       | 953         | (-26.7 to -22.3)                                       | 26 360      | (-45.2 to -41.8)                                       |
| Haiti                     | 994         | (-31.4 to -25.8)                                       | 10 982      | (-23.0 to -19.2)                                       | 246 846     | (-38.3 to -35.2)                                       |
| Jamaica                   | 3 021       | (-17.4 to -12.0)                                       | 4 568       | (-14.4 to -9.9)                                        | 48 039      | (-26.7 to -23.5)                                       |
| Puerto Rico               | 1 917       | (-18.0 to -12.6)                                       | 3 568       | (-0.1 to -0.0)                                         | 30 944      | (-22.1 to -18.6)                                       |
| Saint Lucia               | 124         | (-48.6 to -43.9)                                       | 252         | (-26.3 to -22.0)                                       | 233         | (-47.9 to -43.3)                                       |

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Deaths (95% uncertainty interval)  
| Country | 2016 counts | Percentage change in age-standardised rates, 1990-2016 |
|---------|-------------|------------------------------------------------------|
| Saint Vincent and the Grenadines | 91 | -16.2% (-24.5 to -6.3) |
| Suriname | 482 | -0.2% (-9.3 to 9.8) |
| Trinidad and Tobago | 1002 | -43.7% (-48.9 to -38.1) |
| Virgin Islands | 95 | -25.2% (-35.4 to -13.2) |

Incident cases (95% uncertainty interval)  
| Country | 2016 counts | Percentage change in age-standardised rates, 1990-2016 |
|---------|-------------|------------------------------------------------------|
| Vietnam | 275,943 | -19.8% (-29.9 to -7.4) |
| Seychelles | 47 | -37.7% (-46.5 to -28.0) |
| Timor-Leste | 507 | -32.2% (-47.8 to -5.2) |
| Vietnam | 107,745 | -33.0% (-43.2 to -19.7) |

DALYs (95% uncertainty interval)  
| Country | 2016 counts | Percentage change in age-standardised rates, 1990-2016 |
|---------|-------------|------------------------------------------------------|
| Vietnam | 7,452,659 | -18.6% (-30.0 to -5.3) |

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| Country                | Deaths (95% uncertainty interval) | Incident cases (95% uncertainty interval) | DALYs (95% uncertainty interval) |
|------------------------|-----------------------------------|------------------------------------------|----------------------------------|
|                        | 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 | 2016 counts                       | Percentage change in age-standardised rates, 1990-2016 |
| American Samoa         | 27                                | -33·3% (–43·7 to –20·3)                  | 76                               | -12·4% (–16·0 to –8·2)                  |
|                        | (23 to 32)                        |                                          | (69 to 82)                       |                                          |
| Federated States of Micronesia | 100                             | -17·5% (–34·7 to 3·7)                   | 123                              | -8·9% (–12·6 to –4·5)                   |
|                        | (79 to 125)                       |                                          | (113 to 133)                     |                                          |
| Fiji                   | 569                               | -21·3% (–40·4 to 3·4)                   | 1176                             | -6·5% (–10·8 to –2·2)                   |
|                        | (449 to 710)                      |                                          | (1069 to 1280)                   |                                          |
| Guam                   | 121                               | -9·0% (–22·6 to 6·7)                    | 294                              | 1·6% (–2·7 to 6·5)                     |
|                        | (107 to 138)                      |                                          | (271 to 320)                     |                                          |
| Kiribati               | 113                               | -14·0% (–25·3 to –0·7)                  | 139                              | -8·7% (–12·5 to –4·7)                   |
|                        | (99 to 128)                       |                                          | (128 to 150)                     |                                          |
| Marshall Islands       | 42                                | -18·6% (–30·6 to –4·4)                  | 69                               | -5·4% (–9·5 to –1·1)                    |
|                        | (35 to 50)                        |                                          | (63 to 74)                       |                                          |
| Northern Mariana Islands | 25                             | -36·7% (–49·5 to –20·3)                 | 80                               | -14·5% (–17·9 to –10·6)                 |
|                        | (20 to 31)                        |                                          | (72 to 89)                       |                                          |
| Papua New Guinea       | 6620                              | -18·1% (–31·3 to –0·3)                  | 7867                             | -8·5% (–12·1 to –4·8)                   |
|                        | (5320 to 7980)                    |                                          | (7271 to 8436)                   |                                          |
| Samoa                  | 136                               | -29·0% (–40·9 to –16·6)                 | 234                              | -11·9% (–15·6 to –7·9)                  |
|                        | (112 to 159)                      |                                          | (217 to 253)                     |                                          |
| Solomon Islands        | 572                               | -13·1% (–26·3 to 3·4)                   | 625                              | -8·7% (–12·2 to –4·8)                   |
|                        | (481 to 703)                      |                                          | (577 to 671)                     |                                          |
| Tonga                  | 57                                | -21·8% (–35·5 to –5·1)                  | 115                              | -4·9% (–8·7 to –1·2)                    |
|                        | (50 to 165)                       |                                          | (106 to 124)                     |                                          |
| Vanuatu                | 287                               | -32·4% (–38·0 to –3·5)                  | 345                              | -15·5% (–15·4 to –7·4)                  |
|                        | (232 to 352)                      |                                          | (218 to 372)                     |                                          |
| North Africa and Middle East | 228 747 | -23·8% (–29·3 to –15·9) | 586 080 | -6·0% (–9·0 to –2·9) | 5 655 638 | -26·8% (–31·3 to –20·8) |
|                        | (219 467 to 259 910)              |                                          | (535 384 to 637 793)             |                                          |
| Afghanistan            | 23 132                            | 1·9% (–9·7 to 18·1)                     | 27 042                           | -3·3% (–7·5 to 1·3)                     |
|                        | (18 798 to 27 674)                |                                          | (24 921 to 29 329)               |                                          |
| Algeria                | 16 682                            | -31·2% (–39·5 to –21·4)                 | 44 590                           | -12·9% (–17·2 to –8·3)                  |
|                        | (14 193 to 19 374)                |                                          | (40 627 to 48 799)               |                                          |
| Bahrain                | 139                               | -53·1% (–61·9 to –42·3)                 | 937                              | -16·7% (–21·0 to –12·3)                 |
|                        | (114 to 159)                      |                                          | (834 to 1041)                    |                                          |
| Egypt                  | 52 093                            | -26·8% (–36·9 to –13·3)                 | 107 854                          | -1·2% (–6·2 to 4·3)                     |
|                        | (44 633 to 60 475)                |                                          | (98 457 to 117 547)              |                                          |
| Iran                   | 28 786                            | -28·2% (–42·4 to –9·8)                  | 82 516                           | -15·8% (–20·0 to –11·3)                 |
|                        | (24 530 to 33 892)                |                                          | (74 457 to 90 102)               |                                          |
| Iraq                   | 17 080                            | -16·4% (–32·9 to 2·3)                   | 33 390                           | -8·8% (–13·0 to –3·3)                   |
|                        | (14 064 to 20 294)                |                                          | (30 583 to 36 358)               |                                          |
| Jordan                 | 1991                              | -42·1% (–56·4 to –26·8)                 | 6302                             | -18·0% (–22·9 to –12·9)                 |
|                        | (1573 to 2518)                    |                                          | (5729 to 6895)                   |                                          |
| Kuwait                 | 445                               | -17·7% (–16·0 to 46·1)                  | 2655                             | 14·8% (8·7 to 21·8)                     |
|                        | (335 to 580)                      |                                          | (2361 to 2952)                   |                                          |
| Lebanon                | 1174                              | -68·1% (–76·7 to –55·9)                 | 6745                             | -19·3% (–23·8 to –14·2)                 |
|                        | (895 to 1453)                     |                                          | (6698 to 7450)                   |                                          |
| Libya                  | 1914                              | -12·7% (–25·6 to 1·5)                   | 6526                             | 7·8% (2·5 to 13·7)                      |
|                        | (1582 to 2353)                    |                                          | (5890 to 7122)                   |                                          |
| Morocco                | 15 730                            | -25·4% (–36·3 to –6·1)                  | 42 777                           | -4·1% (–8·4 to 0·5)                     |
|                        | (12 655 to 19 431)                |                                          | (38 074 to 46 792)               |                                          |
| Oman                   | 755                               | -46·4% (–57·9 to –33·3)                 | 3049                             | -6·5% (–10·2 to –2·6)                   |
|                        | (670 to 839)                      |                                          | (2750 to 3383)                   |                                          |
| Palestine              | 2240                              | 20·3% (3·8 to 41·3)                     | 3580                             | 17·8% (11·0 to 24·5)                    |
|                        | (2076 to 2407)                    |                                          | (3288 to 3882)                   |                                          |

(Table continues on next page)
| Country                  | Deaths (95% uncertainty interval) | Incident cases (95% uncertainty interval) | DALYs (95% uncertainty interval) |
|-------------------------|-----------------------------------|-------------------------------------------|---------------------------------|
|                         | 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 |
|                         |                                   |                                           |                                 |                                           |                                 |                                           |
| Southern sub-Saharan Africa | 33 545 (31 364 to 35 758) | -3.8% (–11.4 to –6.0)                     | 62 096 (66 947 to 6 170) | -4.6% (–7.1 to –2.2)                     | 773 257 (720 981 to 823 722) | -7.3% (–14.7 to –1.8) |
| Botswana                | 910 (453 to 1 287)                | -25.2% (–61.6 to –6.8)                    | 1565 (148 953 to 172 601)       | -11.4% (–15.5 to –5.9)                    | 2 871 080 (2 572 931 to 3 206 620) | -22.5% (–33.4 to –8.7) |
| Lesotho                 | 1 752 (1 298 to 2 277)            | -16.3% (–13.4 to 53.4)                   | 1 610 (1 472 to 1 748)          | -4.9% (–9.9 to 0.9)                      | 36 219 (26 956 to 47 080)       | -19.3% (–32.1 to 61.2) |
| Namibia                 | 937 (628 to 1 217)                | -42.8% (–60.8 to –28.3)                  | 1588 (1 453 to 1 731)           | -21.6% (–30.4 to –9.4)                   | 19 827 (13 523 to 25 659)       | -47.2% (–61.1 to –32.2) |
| South Africa            | 23 906 (22 357 to 25 503)         | -0.3% (–8.7 to 9.7)                      | 48 260 (44 245 to 52 262)       | -2.1% (–0.5 to 4.9)                      | 511 038 (478 470 to 543 233)    | -10.8% (–18.3 to 3.1) |
| Swaziland               | 581 (380 to 819)                  | -23.0% (–45.5 to 3.5)                    | 920 (746 to 901)                | -6.9% (–11.1 to 4.5)                     | 12 717 (8 431 to 17 898)        | -23.0% (–46.1 to 5.4) |
| Zimbabwe                | 5 459 (4 438 to 6 613)            | -11.3% (–23.3 to 37.1)                   | 8 251 (7 308 to 9 895)          | -5.1% (0.5 to 9.7)                       | 172 751 (144 782 to 204 756)    | 9.6% (–15.8 to 73.3) |
| Western sub-Saharan Africa | 105 939 (96 170 to 114 435)    | -18.2% (–26.0 to –10.0)                  | 202 647 (185 544 to 220 626)    | -5.7% (–8.7 to –2.3)                     | 2 890 623 (2 631 129 to 3 124 294) | -20.6% (–28.0 to –13.2) |
| Benin                   | 4 065 (3 493 to 4 629)            | -5.0% (–17.3 to 8.8)                     | 6 181 (5 680 to 6 685)          | -3.1% (–7.4 to 1.5)                      | 109 438 (94 370 to 124 933)     | -8.0% (–19.5 to 4.6) |
| Burkina Faso            | 4 134 (3 615 to 5 012)            | -11.3% (–5.3 to 33.7)                    | 7 985 (7 260 to 8 772)          | 9.8% (5.1 to 14.8)                       | 117 917 (94 938 to 136 783)     | 4.6% (–10.6 to 25.4) |
| Cameroon                | 9 091 (6 846 to 11 638)           | -3.6% (–24.2 to 20.2)                    | 12 801 (11 739 to 13 890)       | -3.5% (–8.1 to 1.0)                      | 234 925 (175 652 to 302 530)    | 1.2% (–23.2 to 24.0) |
| Cape Verde              | 216 (185 to 2 461)                | -35.4% (–44.4 to –25.7)                  | 426 (391 to 464)                | -4.1% (–18.0 to 9.7)                     | 447 (381 404 to 513 414)        | -38.2% (–47.3 to –27.7) |
| Chad                    | 4 259 (3 544 to 5 002)            | -11.2% (–24.5 to 4.5)                    | 6 947 (6 344 to 7 512)          | -2.0% (–6.2 to 2.7)                      | 121 399 (101 074 to 143 343)    | -11.9% (–24.6 to 2.5) |

(Continued from previous page)
| Country                          | 2016 counts (2013 to 2015) | Percentage change in age-standardised rates, 1990–2016 | 2016 counts (2013 to 2015) | Percentage change in age-standardised rates, 1990–2016 | 2016 counts (2013 to 2015) | Percentage change in age-standardised rates, 1990–2016 |
|--------------------------------|-----------------------------|-------------------------------------------------------|-----------------------------|-------------------------------------------------------|-----------------------------|-------------------------------------------------------|
| Côte d’Ivoire                  | 10 788                      | (-4.0% to -1.4%)                                       | 14 502                      | (-7.3% to -2.9%)                                       | 306 552                    | (-4.3% to -1.7%)                                       |
| The Gambia                     | 477                         | (-14.0% to -1.4%)                                      | 992                         | (-3.0% to -1.1%)                                      | 13 083                     | (-15.8% to -12.6%)                                     |
| Guinea-Bissau                  | 1145                        | (-10.8% to -5.6%)                                      | 1323                        | (-7.6% to -3.5%)                                      | 31 694                     | (-13.4% to -9.6%)                                      |
| Saudi Arabia                   | 1647                        | (-4.9% to -1.6%)                                       | 2500                        | (-8.9% to -5.5%)                                      | 42 873                     | (-5.0% to -1.6%)                                       |
| Guinea-Bissau                  | 1111                        | (-40.3% to -15.2%)                                     | 2444                        | (-19.0% to -14.9%)                                     | 28 170                     | (-43.3% to -38.3%)                                     |
| Nigeria                        | 6315                        | (-9.7% to -5.1%)                                       | 10 280                      | (-2.5% to -1.9%)                                      | 149 767                    | (-34.7% to -29.7%)                                     |
| Mozambique                     | 5259                        | (-0.1% to -0.6%)                                       | 8966                        | (-2.1% to -1.9%)                                      | 721 086                    | (-40.9% to -36.1%)                                     |
| Sao Tome and Principe          | 270                         | (-39.4% to -26.7%)                                     | 419                         | (-1.2% to -0.8%)                                      | 142 598                    | (-24.7% to -20.8%)                                     |
| Senegal                        | 529                         | (-11.6% to -13.5%)                                     | 8220                        | (-4.4% to -4.8%)                                      | 126 173                    | (-12.6% to -10.6%)                                     |
| Sierra Leone                   | 2499                        | (5.8% to 13.6%)                                        | 3870                        | (4.7% to 9.6%)                                        | 76 263                     | (0.0% to 1.4%)                                         |
| Togo                           | 2775                        | (-8.5% to -6.4%)                                       | 4213                        | (-3.9% to 0.5%)                                       | 76 969                     | (-8.4% to 1.1%)                                        |

Table continues on next page.
Non-fatal disease modelling

We used DisMod-MR 2.1, a Bayesian meta-regression tool, to model the non-fatal burden of stroke. Estimates were generated using a two-stage modelling approach. In the first stage, we ran four models (acute ischaemic, chronic ischaemic, acute haemorrhagic, and chronic haemorrhagic stroke) using only incidence, prevalence, and excess mortality data as inputs. The four models were then re-run using the stroke deaths estimated in CODEm into acute and chronic cause-specific mortality estimated by these models to divide the ischaemic-specific and haemorrhagic-specific mortality data as inputs. We then used the ratio of acute to chronic disease incidence and case fatality data from registries and inpatient hospital data sources listed in the appendix. First-ever, type-specific (ischaemic vs haemorrhagic) data from stroke registries were the reference. Datapoints that included recurrent stroke, did not report type-specific data, or only included hospital admissions, were adjusted in DisMod. Prevalence data from surveys, along with the incidence of those surviving the first 28 days calculated from the acute models were included as input data for the chronic models. Counts of data points and covariates and model settings for DisMod are in the appendix. Detailed descriptions of health states, lay descriptions, distributions of functional and cognitive disability, and disability weights for stroke sequelae in GBD 2016 are in the appendix.

Socio-demographic Index (SDI)

SDI was developed for GBD 2015 as a metric of overall development that positions all locations on a spectrum of socioeconomic development, using educational attainment, lagged distributed income, and total fertility rate. For GBD 2016, this index was updated such that minimum scores are the lowest observed level of GDP per capita or educational attainment or highest observed level of total fertility rate in known datasets. Maximum scores are now plateaus in the relationships between the component parts of the index and selected mortality or health outcomes, indicating no additional benefit to increases in education or lagged distributed income or decreases in

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The ICD codes used for data from stroke for each combination of sex, age group, and geographic location. The ICD codes used for data from

| Deaths (95% uncertainty interval) | Incident cases (95% uncertainty interval) | DALYs (95% uncertainty interval) |
|----------------------------------|------------------------------------------|---------------------------------|
| 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 |
| Tanzania | 14 647 | -30.4% | (11 980 to 17 354) | 26 556 | -8.7% | (24 222 to 28 845) | 344 995 | -32.3% | (285 299 to 407 059) |
| Uganda | 10 409 | -38.8% | (8 568 to 12 321) | 15 359 | -20.0% | (14 022 to 16 747) | 247 499 | -42.3% | (205 349 to 293 208) |
| Zambia | 5 572 | 2.7% | (4 267 to 69 74) | 8 080 | -1.8% | (7 360 to 88 16) | 133 977 | 5.2% | (103 666 to 167 385) |

**Table:** Deaths, Incident cases, and DALYs for stroke in 2016 and percentage change of age-standardised rates for 1990–2016, by location

**Continued from previous page**

| Location | Deaths (95% uncertainty interval) | Incident cases (95% uncertainty interval) | DALYs (95% uncertainty interval) |
|----------|----------------------------------|------------------------------------------|---------------------------------|
| Central sub-Saharan Africa | Central African Republic | Democratic Republic of the Congo | Equatorial Guinea | Gabon |
| Tanzania | Uganda | Zambia | 47 427 | (40 448 to 53 380) | -17.2% | (-25 8 to -7.5) | 62 468 | (57 344 to 67 591) | -11.2% | (-14.5 to -7.9) | 1 116 581 | (970 039 to 1 241 311) | -20.7% | (-28.7 to -11.6) |
| Angola | 7 656 | -29.0% | (5 201 to 10 190) | -45.4 to -6.8 | 12 096 | (-13.9 to -11.9) | 190 746 | -33.5% | (144 242 to 252 969) |
| Central African Republic | 4 110 | -7.5% | (3 178 to 5 045) | -34.9 to -9.9 | 3 772 | (-13.4 to -4.7) | 97 526 | -8.4% | (76 289 to 120 239) |
| Congo Brazzaville | 2 139 | -41.7% | (1 678 to 2 635) | -54.6 to -27.1 | 2 978 | -25.2% | (272 632 to 3 239) | 48 013 | -45.3% | (37 480 to 59 329) |
| Democratic Republic of the Congo | 32 497 | -9.0% | (26 643 to 3 7 036) | -20.0 to -3.6 | 4 181 | -7.2% | (38 416 to 45 399) | 75 216 | -12.3% | (63 668 to 86 958) |
| Equatorial Guinea | 190 | -70.7% | (112 to 287) | -81.2 to -56.9 | 5 10 | -31.1% | (461 560) | 4 553 | -73.7% | (282 71 to 65 07) |
| Gabon | 834 | -37.8% | (671 to 1 008) | -49.6 to -22.6 | 1 297 | -24.0% | (1 189 to 1 419) | 16 518 | -41.3% | (13 375 to 19 884) |

DALYs=disability-adjusted life-years. SDI=Socio-demographic Index.
total fertility rate. Gaussian process regression was used to establish the average relationship between cause-specific, age-standardised DALY rates and SDI for all locations from 1990 to 2016. These rates were used as the expected values for DALYs in comparisons between observed and expected rates.

Risk factor estimation
The comparative risk assessment framework developed for GBD was used to estimate levels and trends in attributable burden of stroke due to risk factors that satisfied the criteria of sufficient evidence of a causal relationship, availability of exposure data, and potential for modification. Four components were incorporated into estimating attributable burden using this approach: (1) burden estimates for stroke; (2) exposure levels for each risk factor; (3) relative risk of stroke as an outcome of exposure to the risk factor; and (4) theoretical minimum risk exposure level—ie, the level of exposure that minimises risk for each individual in the population. The population attributable fraction, estimated independently for each risk factor, is the proportion of the cause that would be decreased if the exposure to the risk factor in the past had been reduced to the counterfactual level of the theoretical minimum risk exposure level. Estimates of attributable burden for each risk–outcome pair were established by multiplying the relevant cause measure by the population attributable fraction. All estimates of attributable burden are generated at the most detailed level and estimates for risk groupings or all risk factors combined are generated via an aggregation process that accounts for the fact that the effect of one risk factor might be partly or completely mediated through the effect of another. This mediation analysis is informed by individual-level data from prospective cohort studies on the joint effects of combinations of risk factors.

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
GBD stroke estimates for 1990–2016 are available for download from the GBD Results Tool at the Global Health Data Exchange. In 2016, stroke was the second largest cause of death globally (5.5 million [95% UI 5.3–5.7] deaths) after ischaemic heart disease (table). Fewer women died as a result of stroke (2.6 million [2.5–2.7] deaths) than did men (2.9 million [2.8–3.0] deaths). The number of global deaths due to ischaemic stroke (2.7 million [2.6–2.8]) was slightly lower than the number...
due to haemorrhagic stroke (2·8 million [2·7–2·9] deaths; appendix). Stroke was also the second most common cause of global DALYs (116·4 million [111·4–121·4]), an increase from 1990 (95·3 million [91·6–100·6]). Women had fewer stroke DALYs (50·8 million [47·6–53·7]) than men (65·6 million [63·1–68·2]). The number of DALYs due to ischaemic stroke (51·9 million [47·9–55·6]) was lower than the number due to haemorrhagic stroke (64·5 million [62·6–66·5]; appendix). There were 80·1 million (74·1–86·3) prevalent cases of stroke globally in 2016: 41·1 million (38·0–44·3) prevalent cases in women and 39·0 million (36·1–42·1) prevalent cases in men. Of the total number of prevalent strokes, 84·4% (82·1–86·4) were ischaemic. There were 13·7 million (12·7–14·7) new stroke cases in 2016.

The highest age-standardised incidences of stroke were observed in east Asia, especially China (354 [95% UI 331–378] per 100,000 person-years), followed by eastern Europe, ranging from 200 (181–218) per 100,000 person-years in Estonia to 335 (301–369) per 100,000 person-years in Latvia (figure 1). The lowest incidences were in central Latin America, especially El Salvador (97 [88–105] per 100,000 person-years). Age-specific stroke incidence was similar between men and women younger than 55 years, but significantly greater for men than women at ages 55–75 years (figure 2).

Age-standardised incidence declined from 1990 to 2016 globally (8·1% [–10·7 to –5·5]), in all SDI groups except the middle SDI group, and in most regions (table; appendix). The region with the largest decrease in age-standardised stroke incidence was southern Latin America (33·3% [–36·4 to –29·7]) and the region with the largest increase was east Asia (4·9% [1·3 to 8·1]). For ischaemic stroke, the largest decrease was in southern Latin America (38·0% [–39·4 to –36·6]), and the largest increase was in east Asia (17·5% [15·8 to 19·2]; appendix). For haemorrhagic stroke, incidence decreased in all regions. The largest decrease was in high-income Asia Pacific (–32·5% [–33·7 to –31·2]), and the smallest decrease was in southern sub-Saharan Africa (–5·1% [–6·2 to –4·0]; appendix).

Globally, the age-standardised rate of deaths due to stroke decreased by 36·2% (–39·3 to –33·6) from 1990 to 2016, with decreases in all five SDI groups. These death rates also declined for all but one region from 1990 to 2016, with the largest decrease in the high-income Asia Pacific region (–66·3% [–68·8 to –63·4]; and no significant change in southern sub-Saharan Africa (–3·8% [–11·4 to 6·0]; table). These results were similar for ischaemic stroke and haemorrhagic stroke, with the largest decrease for both in the high-income Asia Pacific region (70·2% [72·3 to –67·8] for ischaemic stroke and –59·8% [63·1 to –56·1] for haemorrhagic stroke; appendix). Death rates for neither ischaemic nor haemorrhagic stroke changed significantly between 1990 and 2016 in southern sub-Saharan Africa (0·6% [–7·9 to 11·9] for ischaemic stroke and –7·2 [–15·1 to 2·2] for haemorrhagic stroke).

Age-standardised DALY rates for stroke also declined from 1990 to 2016 globally (34·2% [–37·2 to –31·5]) for all SDI quintiles, and for all regions, again with the largest change occurring in high-income Asia Pacific (–61·5% [–64·9 to –58·1]) and the smallest in southern sub-Saharan Africa (–7·3% [–14·7 to 1·8]; table). Southern Latin America was the region with the largest decrease for ischaemic stroke (–63·7% [–66·8 to –60·6]; appendix) and high-income Asia Pacific was the region with the largest decrease for haemorrhagic stroke (–59·9% [–63·4 to –55·8]; appendix). Southern sub-Saharan Africa had no change in ischaemic stroke (–1·9% [–9·9 to 7·4]) and a decrease in haemorrhagic stroke (–10·2% [–17·9 to –1·1]).

Rates of YLLs and YLDs were very low for the younger age groups (<40 years) and then increased substantially with age, with YLLs increasing much more rapidly than YLDs (figure 3) because of the high mortality burden of stroke.

After an increase in expected DALY rates at the lower end of the SDI scale, these rates decline rapidly for SDI values of 0·35 and higher (figure 4). For most regions, the burden of stroke decreased with increases in SDI over time. However, central and eastern Europe and central Asia saw increased DALY rates in the early 1990s after the dissolution of the Soviet Union, followed by subsequent decreases as SDI increased. Stroke DALY burden in southern sub-Saharan Africa showed a similar pattern, with an initial spike in rates with increasing SDI, followed by a steady decrease. DALY rates were higher than expected early in the time series for eastern and central sub-Saharan Africa and high-income Asia Pacific but have decreased with increasing SDI. Eastern Europe, central Europe, central Asia, Oceania, and east Asia had higher stroke-related DALY rates than would be expected on the basis of comparisons of SDI for all years. Conversely, rates for Latin America, western Europe, Australasia, south Asia, and southern and western sub-Saharan Africa were lower.
than expected for all timepoints. Although DALY rates in southeast Asia were initially lower than expected, they were in most recent years slightly higher than expected.

Under the comparative risk assessment framework, most stroke DALYs (88·8% [95% UI 86·5–90·9]) can be attributed to risk factors measured in GBD; this percentage is similar for both stroke types (87·9% for ischaemic stroke [84·1–91·6] and 89·5% for haemorrhagic stroke [87·1–91·6]). Metabolic risks (high systolic blood pressure, high body-mass index, high fasting plasma glucose, high total cholesterol, and low glomerular filtration rate) accounted for 72·1% (66·4–77·3) of stroke DALYs. Behavioural factors (smoking, poor diet, and low physical activity) accounted for 66·3% (59·3–73·1) of attributable DALYs, and environmental risks (air pollution and lead exposure) for 28·1% (25·3–30·9). As the effect of many of these risk factors are mediated partly or wholly through another risk factor, the crude sum of the groups is expected to exceed 100%. The aggregation process to generate estimates of overall attributable burden accounts for joint effects of a combination of risk factors, thus the final estimate is less than 100%. The remaining burden is due to unknown or unmeasured risk factors, genetic factors, or the effect of gene–environment interactions.

Population attributable fractions and UIs for the top ten risk factors for each stroke subtype by sex in 1990 and 2016 are in the appendix.

Discussion

Our estimates indicate that the global burden of stroke is high, with more than 80 million stroke survivors in 2016. Age-standardised death rates from stroke have decreased in all regions from 1990 to 2016, whereas incidence has decreased in most regions but increased in east Asia and southern sub-Saharan Africa. The overall burden of stroke, as quantified by age-standardised DALY rates, decreased from 1990 to 2016, but the absolute number of DALYs due to stroke increased over that same period. The increase in absolute numbers is largely due to population growth and ageing resulting in a greater number of people with stroke despite declining incidence and improved stroke survival leading to higher prevalence of chronic stroke.

Studies have shown that much of the burden due to stroke can be attributed to modifiable atherosclerotic risk factors. INTERSTROKE, a case-control study done at 32 locations, found that the risk factors for stroke in low-income and middle-income countries were similar to those in high-income countries, although the relative contribution of each differed between regions. The high burden of stroke worldwide suggests that primary prevention strategies are either not widely implemented or not sufficiently effective. In addition to targeting behavioural risk factors, effective screening for conditions that increase stroke risk, such as hypertension, atrial fibrillation, and diabetes mellitus, is essential. Many screening strategies use the predicted absolute risk of cardiovascular disease to identify individuals at high risk of cardiovascular disease events and to define therapeutic thresholds for specific interventions. However, these approaches have limitations, including low efficiency and missing data for people with low to moderate
cardiovascular disease risk, in whom about 80% of strokes occur.\textsuperscript{4,5} Preliminary evidence suggests that strategies via mobile technologies are effective for healthy lifestyle modification and primary stroke prevention.\textsuperscript{6,10} Treatment with statins and blood pressure medications has been shown to be effective and cost-effective for both primary and secondary prevention of stroke.\textsuperscript{11-22} Healthy lifestyle modification and better adherence to recommended medications via an affordable multidrug polypill containing blood pressure and lipid-lowering medications could potentially also enable cost-effective prevention of stroke globally, potentially halving stroke incidence and mortality.\textsuperscript{12,23,24}

In addition to prevention efforts, appropriate acute and long-term treatment is essential, given the high recurrence rate of stroke. Highly effective treatments for stroke have been developed over the past few decades and are now considered the standard of care where available.\textsuperscript{23-28} To assist countries in identifying gaps in stroke care, a survey has been done in collaboration with the World Stroke Organization and WHO to obtain data on facilities and providers for acute stroke care and rehabilitation; results from the survey will be available soon.\textsuperscript{27} Studies are also underway to assess different approaches to treatment when the closest medical facilities do not have the resources to provide advanced stroke care (NCT02795962).

Although the attributable burden for most of the risk factors identified for stroke has been quantified in GBD, the effect of atrial fibrillation has not yet been estimated. Atrial fibrillation increases the risk of stroke up to five fold, largely through an increased risk of thrombotic events leading to ischaemic stroke.\textsuperscript{29} Antithrombotic therapy with vitamin K antagonists, antiplaude drugs, or novel oral anticoagulants have been shown to reduce this risk by up to 60% in a meta-analysis of clinical trials.\textsuperscript{30} Improved diagnosis of and treatment for atrial fibrillation is thus likely to have a substantial impact on stroke burden.

GBD faces several measurement challenges for estimating cause-specific mortality and non-fatal burden of stroke. Although GBD employs spatiotemporal methods that use patterns across time and geographic regions to inform estimates for locations with sparse data, these approaches cannot completely overcome issues when data are missing for some large geographic regions. Although much stroke data is available for some regions, data on incidence, stroke type, and stroke severity is sparse in many low-income and middle-income countries. Adding new sources of data is an ongoing effort of GBD, but we are limited to locations where representative studies have been done or where there is access to administrative data. To ensure that inpatient hospital data capture all events, adjustments are made to these data using correction factors derived from medical claims data, to which we only had access for the USA in GBD 2016. The generalisability of claims data and the derived correction factors have been questioned.\textsuperscript{30-32} However, data from administrative sources provide essential information for capturing burden in many locations, and we are able to estimate and adjust the amount of stroke burden due to subarachnoid haemorrhage and intracerebral haemorrhage separately; however, future iterations of GBD will. We also do not generate estimates for transient ischaemic attacks; however, incidence estimates for these events would be useful for health planning purposes.\textsuperscript{33} The new ICD 11 classifications, which include imaging criteria, could be used along with the original clinical WHO diagnostic criteria in future estimates.\textsuperscript{34}

Our findings with regard to stroke burden and modifiable risk factors are consistent with those from GBD 2015 and emphasise the need for effective prevention strategies. Although age-standardised deaths due to stroke have been decreasing, the overall burden of stroke remains high, continues to increase, and is unlikely to decrease without interventions to address stroke risk factors. Stroke has been identified as one of the priorities for WHO and the UN in their actions to reduce the burden of non-communicable diseases; global estimates such as those generated by GBD are essential in appropriately targeting efforts.\textsuperscript{35}

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Declaration of interests

Results, provided guidance on methods, or reviewed the manuscript. All other authors provided data, developed models, reviewed results and edited the first draft and final versions of the manuscript. A list of all contributors is provided in the Supplementary Material.

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Contributors

COJ analysed the data and prepared the first draft. GAR, VLF, and TVo reviewed results and edited the final draft and final versions of the manuscript. All other authors provided data, developed models, reviewed results, provided guidance on methods, or reviewed the manuscript.

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