The burden of neurological diseases in Europe: an analysis for the Global Burden of Disease Study 2017

Gunther Deuschl, Ettore Beghi, Franz Fazekas, Timea Varga, Kalliopi A Christoforidi, Eveline Sipido, Claudio L Bassetti, Theo Vos, Valery L Feigin

Summary

Background Neurological disorders account for a large and increasing health burden worldwide, as shown in the Global Burden of Diseases (GBD) Study 2016. Unpacking how this burden varies regionally and nationally is important to inform public health policy and prevention strategies. The population in the EU is older than that of the WHO European region (western, central, and eastern Europe) and even older than the global population, suggesting that it might be particularly vulnerable to an increasing burden of age-related neurological disorders. We aimed to compare the burden of neurological disorders in the EU between 1990 and 2017 with those of the WHO European region and worldwide.

Methods The burden of neurological disorders was calculated for the year 2017 as incidence, prevalence, mortality, disability-adjusted life-years (DALYs), years of life lost, and years lived with disability for the countries in the EU and the WHO European region, totally and, separately. Diseases analysed were Alzheimer’s disease and other dementias, epilepsy, headache (migraine and tension-type headache), multiple sclerosis, Parkinson’s disease, brain cancer, motor neuron diseases, neuroinfectious diseases, and stroke. Data are presented as totals and by sex, age, year, location and socio-demographic context, and shown as counts and rates.

Findings In 2017, the total number of DALYs attributable to neurological disorders was 21·0 million (95% uncertainty interval 18·5–23·9) in the EU and 41·1 million (36·7–45·9) in the WHO European region, and the total number of deaths was 1·1 million (1·09–1·14) in the EU and 1·97 million (1·95–2·01) in the WHO European region. In the EU, neurological disorders ranked third after cardiovascular diseases and cancers representing 13·3% (10·3–17·1) of total DALYs and 19·5% (18·0–21·3) of total deaths. Stroke, dementias, and headache were the three commonest causes of DALYs in the EU. Stroke was also the leading cause of DALYs in the WHO European region. During the study period we found a substantial increase in the all-age burden of neurodegenerative diseases, despite a substantial decrease in the rates of stroke and infections. The burden of neurological disorders in Europe was higher in men than in women, peaked in individuals aged 80–84 years, and varied substantially with WHO European region and country. All-age DALYs, deaths, and prevalence of neurological disorders increased in all age measures, but decreased when using age-standardised measures in all but three countries (Azerbaijan, Turkmenistan, and Uzbekistan). The decrease was mostly attributed to the reduction of premature mortality despite an overall increase in the number of DALYs.

Interpretation Neurological disorders are the third most common cause of disability and premature death in the EU and their prevalence and burden will likely increase with the progressive ageing of the European population. Greater attention to neurological diseases must be paid by health authorities for prevention and care. The data presented here suggest different priorities for health service development and resource allocation in different countries.

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Introduction

Neurological disorders are an important source of premature mortality and transient or permanent disability in survivors. According to WHO, in 2006, neurological disorders were identified as one of the greatest public health problems, accounting for 6·3% of total disability-adjusted life-years (DALYs).

A report by the Global Burden of Disease (GBD) 2015 Neurological Disorders Collaborator Group estimated that neurological disorders have become a leading cause of disability in the world, with attributable DALYs reaching 11·6%, and ranked second in terms of deaths after cardiovascular diseases, reaching 16·5% of all deaths.

Given that the prevalence of most neurological disorders increases with age, their burden is expected to rise in countries with with ageing populations. In Europe, the population is rapidly ageing, therefore, this region is an important setting for the assessment of the dynamics of the burden of neurological disorders. Some European countries continue to strengthen their cooperation around health strategy and so knowledge about the similarities and disparities in the burden of neurological diseases across European countries could inform political decision making.

We aimed to calculate incidence, prevalence, mortality, DALYs, and their components (years of life lost [YLLs],
Research in context

Evidence before this study
We searched PubMed on Feb 10, 2019, and March 3, 2020, for articles focusing on the incidence, prevalence, mortality, and overall burden of neurological disorders in Europe using the search terms (“Burden of disease” OR “Epidemiology” OR “Costs”) AND (“Neurology” OR “Neurologic disease”) AND ("Europe") with no language or time restrictions. Despite the publication of numerous studies on the frequency and outcome of neurological disorders in Europe, we found only a few and older reports on the burden of disease on a national basis or in selected age groups, and virtually no studies comparing various clinical conditions and different countries. The economic costs of disorders of the brain in Europe were calculated by the European Brain Council, but the corresponding burden was not measured. Worldwide and country-specific data on the burden of neurological disorders, in general and by type, have been provided only by the Global Burden of Diseases (GBD) studies. During the period 1990–2016, neurological disorders accounted for an increasing number of disability-adjusted life-years (DALYS). However, no data from the 27 EU countries plus the UK (EU28) were highlighted. As the population of EU28 is ageing and the prevalence of neurological disorders increases with age, the corresponding burden will increase even further in that area. Additionally, because the growth, ageing, and sociodemographic characteristics of the European population differ between the EU28 and the other countries in the larger WHO region, the burden of neurological disorders is expected to differ.

Added value of this study
This study updates the previous investigation covering the period 1990–2016 by providing data for the year 2017. In the EU28, neurological disorders were the third most common source of DALYS, after cardiovascular diseases and cancer. Comparing data from the EU28 to the three WHO European regions (western, central, and eastern Europe), substantial differences were found across countries in the burden of neurological disorders, which might reflect not only the structure of the underlying populations, but also the different approaches of the local health-care facilities in the introduction of prevention and treatment measures. This difference was particularly true for neurodegenerative diseases for which robust preventive measures and disease-modifying treatments are not available. During the study period, the burden of headache was unchanged, whereas the burden of stroke decreased and the burden of Alzheimer’s disease and other dementias increased, but at different paces in the EU28 and the WHO European regions.

Implications of the available evidence
Because of the ageing of the European population, the EU28 is facing an increasing burden attributable to neurological disorders, presenting the governments with an increasing demand for acute care, rehabilitation, and support services. The growing numbers of affected individuals and the corresponding numbers of neurological DALYS and deaths should call for action to address these diseases. Particularly neurodegenerative diseases that are still in need of robust preventive measures and disease-modifying treatments. The results of this study can be used by the health authorities and local governments to consider the burden of neurological disorders that could be addressed with preventive and therapeutic measures.

Methods

Overview
The GBD Collaborator Group is a network of scientists producing estimates of the burden of 328 diseases and injuries including 13 neurological disorders (stroke, Alzheimer’s disease and other dementias, Parkinson’s disease, epilepsy, multiple sclerosis, brain and nervous system cancer, encephalitis, meningitis, tetanus, headache [migraine and tension-type headache], motor neuron diseases, and other neurological diseases). The guiding principle of GBD is to assess health loss due to premature mortality and disability, intended as any deviation from full health. The methodological basis of the GDB studies is described in detail elsewhere.2

The analyses in the current study follow the GBD methodology. The data provided here are for 1990–2017. Population-based measures are taken from the related GBD standards.3 For the purposes of this study, data on GBD outcomes from the countries included in the EU28 were isolated and compared with the WHO European region and with global data. According to WHO, the European region includes, in addition to the 28 European countries that were part of the EU28 in 2017, another 22 countries (appendix p 9). WHO divides the European region into three subregions: western, central, and eastern Europe (appendix p 15).

In our analysis we included 13 neurological disorders. We chose to exclude traumatic brain injury and spinal cord injury because post-traumatic disorders were outside the scope of our investigation. The burden of neurological disorders was calculated as incidence, prevalence, mortality, DALYS, YLLs, and YLDs, totally and, separately, for each disorder.

DALYS, YLLs, and YLDs
To compare deaths and non-fatal outcomes within and between diseases, a unique indicator was used, DALYS, which is the sum of YLLs and YLDs. YLLs are the product of the number of deaths multiplied by the standard life...
expectancy at the age of death. Standard life expectancy is obtained from the lowest observed age-specific rates of mortality among populations in the world greater than 5 million. YLDs are the product of the prevalence of individual sequelae of each disease multiplied by a disability weight, quantifying the severity of a sequela as a number between 0 (representing full health) and 1 (representing death). Disability weights were estimated in nine US population surveys and an open-access internet survey in which respondents were asked to choose the healthier option between random pairs of health states that were presented with a short description of the main features.

Non-fatal estimates were obtained from systematic reviews of published and unpublished reports, records of health claims, survey microdata, registries, and disease surveillance systems. These data have been included in a single repository, the Global Health Data Exchange. Non-fatal data were analysed using DisMod-MR 2.1, a Bayesian meta-regression tool that adjusts datapoints for variations in study methods among different sources and enforces consistency between data obtained from different measures, such as incidence and prevalence. A different model was used for brain cancer according to the respective GBD analysis. For each disease, a parsimonious set of sequelae was selected that best described the different aspects of the various consequences of a disease. Each sequela is estimated separately (appendix).

**Mortality estimates**

All-cause mortality rates were estimated from vital registration data in countries with complete coverage. For other countries, the probabilities of death before age 5 years and between ages 15 years and 60 years were estimated from verbal autopsies. Using model life tables, these probabilities were converted into age-specific death rates by sex, year, and location. The cause of death was classified using subsequent versions of the International Classification of Diseases (or bespoke classifications in some countries). When coded data were less informative or in the absence of a specific diagnosis, causes of death were redistributed to more precise codes. Each death was assigned a single underlying cause. The mortality attributable to each cause is the product of the attributable fraction and the mortality due to the underlying disease. Causes of death were analysed using the cause of death ensemble model, a highly systematised tool running many different models on the same data and choosing an ensemble of models that best reflects the available input data. To enforce consistency, the sum of all cause-specific mortality rates was scaled to all-cause mortality rates in each category defined by age, sex, location, and year.

**Socio-demographic index**

Data were stratified by socio-demographic index (SDI), a composite indicator of sociodemographic development reflecting the geometric mean of normalised values of a location’s income per capita, the average number of years of educational attainment in the population aged 15 years and over, and the total fertility rate. Countries and territories were grouped into five quintiles of high, high-middle, middle, low-middle, and low SDI on the basis of their 2017 values.

DALYs were computed for the entire world, for the EU28, WHO Europe, the three WHO European subregions, and for each European country separately, and analysed by age, sex, and year.

With reference to the measure of sociodemographic development, European countries were stratified into two groups: high-SDI countries (Andorra, Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Russia, Slovakia, Slovenia, Sweden, Switzerland, and the UK) and high-middle-SDI countries (Armenia, Azerbaijan, Belarus, Bulgaria, Georgia, Hungary, Israel, Kazakhstan, Macedonia, Montenegro, Portugal, Romania, Serbia, Spain, Turkey, and Ukraine). Only Moldova was classified as a middle-SDI country.

**Standardisation and uncertainty measures**

Unless otherwise specified, all rates were age-standardised using the GBD standard (appendix p 45). The uncertainty of all estimates was propagated throughout all the calculations by creating 1000 values for each estimate of the burden and aggregating across causes and locations at the level of each of the 1000 values for all intermediate steps in the calculation. The lower and upper bounds of the 95% uncertainty intervals (UIs) were the 25th and 975th values of the ordered 1000 values. Significant differences were established if 975 or more of the ordered 1000 values of difference were on either side of zero. Definitions, imputation procedures and modelling strategies for major neurological disorders are described in the appendix (pp 47–147).

**Role of the funding source**

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. EB and GD had access to all raw data. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

**Results**

In 2017, the total population in the EU28 was 512.4 million and the population of WHO Europe region was 925.6 million. In the same year, 307.9 million neurological diseases were counted in the EU28, 74.5 million of which were newly diagnosed (table 1). In the WHO Europe region 540.3 million neurological diseases were counted, 133.0 million of which were...
newly diagnosed (table 1). The total number of DALYs in
patients with neurological disorders was 21·0 million
(95% UI 18·5–23·9) in the EU28 and 41·1 million
(36·7–45·9) in the WHO European region and the total
number of deaths was 1·1 million (1·09–1·14) in
the EU28 and 1·97 million (1·95–2·01) in the WHO
European region (table 1). In 2017, the worldwide
burden of neurological disorders accounted for 280·0 million
(251·4–312·2) DALYs. In the EU28, neurological
disorders ranked third for DALYs (after cancer and

|                | EU28                               | WHO European region | Global                       |
|----------------|------------------------------------|---------------------|------------------------------|
|                | Total age standardised rate per 100,000 | Total age standardised rate per 100,000 | Total age standardised rate per 100,000 |
| **All neurological diseases** |                                   |                     |                              |
| DALYs          | 7314978                            | 691                 | 18831007                     | 1198 | 1326516 | 1857 |
| (683270-776518) | (634-737)                          | (866400-137506)     | (126486-600-137506)         | (1126-1256) | (129-1326) | (129-1326) |
| Deaths         | 476003                            | 38                  | 1078620                      | 61  | 616792  | 80   |
| (46100-50451)  | (37-40)                            | (60-63)             | (60-63)                      | (60-63)  | (60-63)  | (60-63)  |
| Prevalence     | 9321098                           | 971                 | 1825495                      | 1196 | 10417840 | 1301 |
| (898668-1002454) | (921-1021)                      | (1129-1262)         | (1129-1262)                  | (1129-1262) | (1129-1262) | (1129-1262) |
| Incidence      | 1102677                           | 1072                | 2060660                      | 131  | 1193166 | 151  |
| (1030004-1178459) | (101-115) | (123-141) | (123-141) | (123-141) | (123-141) | (123-141) |
| DALYs          | 569357                            | 530                 | 15256228                     | 983  | 11315594 | 1423 |
| (554360-595058) | (516-552)                       | (965-1016)          | (965-1016)                   | (965-1016) | (965-1016) | (965-1016) |
| **Alzheimer’s disease and other dementias** |                                   |                     |                              |
| DALYs          | 5271564                           | 399                 | 7686392                      | 410  | 35052481 | 413  |
| (493455-5645197) | (372-427)                        | (383-438)           | (383-438)                    | (383-438)  | (383-438)  | (383-438)  |
| Deaths         | 501678                            | 35                  | 700355                       | 36   | 2514619 | 35   |
| (461100-5520705) | (34-36)                           | (35-36)             | (35-36)                      | (35-36)  | (35-36)  | (35-36)  |
| Prevalence     | 7744081                           | 594                 | 1137585                      | 612  | 44987890 | 605  |
| (686169-8531917) | (531-657)                       | (541-681)           | (541-681)                    | (541-681)  | (541-681)  | (541-681)  |
| Incidence      | 1249178                           | 98                  | 1851602                      | 101  | 7306645  | 97   |
| (118954-1390849) | (88-108)                       | (90-112)            | (90-112)                     | (90-112)  | (90-112)  | (90-112)  |
| DALYs          | 1165391                           | 88                  | 1694270                      | 90   | 6570378  | 89   |
| (832669-1516059) | (63-114)                          | (64-118)            | (64-118)                     | (64-118)  | (64-118)  | (64-118)  |
| Incidence      | 4106246                           | 311                 | 5392121                      | 320  | 2395105  | 324  |
| (1982651-2420304) | (301-320)                        | (312-327)           | (312-327)                    | (312-327)  | (312-327)  | (312-327)  |
| **Parkinson’s disease** |                                   |                     |                              |
| DALYs          | 839916                            | 70                  | 1226579                      | 70   | 5380212  | 72   |
| (766256-940813)  | (63-78)                          | (64-78)             | (64-78)                      | (64-78)  | (64-78)  | (64-78)  |
| Deaths         | 68612                            | 5                   | 84599                       | 5     | 340639  | 5    |
| (55722-67793)   | (4-5)                            | (4-5)               | (4-5)                        | (4-5)    | (4-5)    | (4-5)    |
| Prevalence     | 1215045                           | 105                 | 1828098                      | 107  | 8325404 | 109  |
| (996237-1457870) | (86-125)                       | (88-128)            | (88-128)                     | (88-128)  | (88-128)  | (88-128)  |
| Incidence      | 156667                            | 13                  | 225529                       | 13     | 1025939 | 13  |
| (124575-180761) | (11-16)                         | (11-16)             | (11-16)                      | (11-16)  | (11-16)  | (11-16)  |
| DALYs          | 170916                            | 15                  | 257986                       | 15     | 1121872 | 16   |
| (117642-233979) | (10-20)                        | (10-21)             | (10-21)                      | (10-21)  | (10-21)  | (10-21)  |
| Incidence      | 669000                            | 55                  | 968593                       | 55     | 4361241 | 57   |
| (612867-764328)  | (51-63)                         | (52-62)             | (52-62)                      | (52-62)  | (52-62)  | (52-62)  |

(Table 1 continues on next page)
| Health Condition                        | EU28 WHO European region | Global |
|----------------------------------------|--------------------------|--------|
| **Total**                              | Age-standardised rate per 100 000 | Age-standardised rate per 100 000 | Age-standardised rate per 100 000 |
| **Motor neuron disease**               |                          |        |                              |
| DALYs                                  | 252 987                  | 31     | 314 523                       | 24     | 878 518                       | 11 |
| Deaths                                 | 11 495                   | 1      | 13 410                        | 1      | 34 068                        | 0  |
| Prevalence                             | 42 937                   | 6      | 51 711                        | 4      | 237 053                       | 3  |
| Incidence                              | 13 010                   | 1      | 15 728                        | 1      | 67 322                        | 1  |
| YLDs                                   | 64 921-12 227            | 1      | 10 998                        | 1      | 50 416                        | 1  |
| YLLs                                   | 56 080-16 537            | 1      | 303 526                       | 1      | 828 102                       | 11 |
| **Multiple sclerosis**                 |                          |        |                              |
| DALYs                                  | 282 785                  | 39     | 391 078                       | 32     | 1 084 757                      | 13 |
| Deaths                                 | 56 306                   | 1      | 741                            | 1      | 20 655                        | 0  |
| Prevalence                             | 522 674                  | 77     | 699 238                       | 59     | 1 761 078                      | 22 |
| Incidence                              | 11 847                   | 3      | 17 544                        | 2      | 54 895                        | 1  |
| YLDs                                   | 91 319                   | 1      | 178 020                       | 15     | 456 556                       | 6  |
| YLLs                                   | 43 038-171 558           | 1      | 213 509                       | 17     | 628 202                       | 8   |
| **Brain and nervous system cancer**    |                          |        |                              |
| DALYs                                  | 964 964                  | 140    | 1 668 047                     | 147    | 8 744 765                     | 112 |
| Deaths                                 | 35 917                   | 4      | 56 246                        | 4      | 247 143                       | 3   |
| Prevalence                             | 330 074                  | 55     | 462 982                       | 45     | 1 795 702                      | 22 |
| Incidence                              | 70 026                   | 10     | 102 219                       | 9      | 405 218                       | 5   |
| YLDs                                   | 30 368                   | 5      | 43 489                        | 4      | 166 947                       | 3   |
| YLLs                                   | 93 596                   | 135    | 1 624 558                     | 143    | 8 572 818                     | 110 |
| **Meningitis**                         |                          |        |                              |
| DALYs                                  | 84 550                   | 20     | 288 614                       | 38     | 20 370 870                    | 293 |
| Deaths                                 | 20 333                   | 0      | 5 483                         | 1      | 288 021                       | 4   |
| Prevalence                             | 183 511                  | 33     | 505 430                       | 51     | 10 572 886                    | 139 |
| Incidence                              | 92 542                   | 22     | 222 423                       | 30     | 5 045 411                     | 71  |
| YLDs                                   | 17 079                   | 4      | 45 301                        | 5      | 9 313 935                     | 13  |
| YLLs                                   | 67 471                   | 17     | 243 313                       | 33     | 19 436 936                    | 281 |

(Continued from previous page)
| EU28 | WHO European region | Global |
|------|---------------------|--------|
|      | Total | Age-standardised rate per 100,000 | Total | Age-standardised rate per 100,000 | Total | Age-standardised rate per 100,000 |
|      |       |                                |       |                                |       |                                |
| **Encephalitis** |      |                                |       |                                |       |                                |
| DALYs | 57720 | 11 | 270736 | 34 | 5112280 | 71 |
|       | (50302–63183) | (10–12) | (226953–292768) | (30–38) | (4541340–5764967) | (63–79) |
| Deaths | 1729 | 0 | 5953 | 1 | 92370 | 1 |
|       | (1337–1829) | (0–0) | (4631–6266) | (0–1) | (83134–1017936) | (1–1) |
| Prevalence | 142435 | 22 | 315202 | 29 | 6764882 | 86 |
|       | (74374–234773) | (12–35) | (173810–507091) | (17–46) | (3731161–10760385) | (48–137) |
| Incidence | 47411 | 9 | 110769 | 12 | 2280535 | 30 |
|       | (46409–48414) | (9–9) | (108844–112873) | (12–12) | (2289100–2225245) | (29–30) |
| YLDs | 9372 | 2 | 22772 | 3 | 524154 | 7 |
|       | (6386–12593) | (1–2) | (15561–30309) | (2–3) | (385488–691266) | (5–9) |
| YLLs | 48348 | 10 | 247963 | 33 | 4588167 | 65 |
|       | (41387–51476) | (8–11) | (214185–261772) | (28–36) | (4059515–5230709) | (57–73) |
| **Tetanus** |      |                                |       |                                |       |                                |
| DALYs | 649 | 0 | 2127 | 0 | 2449433 | 35 |
|       | (558–755) | (0–0) | (1880–2770) | (0–0) | (1736263–3201172) | (25–46) |
| Deaths | 39 | 0 | 82 | 0 | 38134 | 1 |
|       | (33–46) | (0–0) | (72–100) | (0–0) | (25893–48771) | (0–1) |
| Prevalence | 4 | 0 | 160 | 0 | 59583 | 1 |
|       | (3–5) | (0–0) | (133–187) | (0–0) | (58762–62572) | (1–1) |
| Incidence | 68 | 0 | 164 | 0 | 79192 | 1 |
|       | (58–82) | (0–0) | (140–205) | (0–0) | (53360–105261) | (1–1) |
| YLDs | 1 | 0 | 4 | 0 | 1695 | 1 |
|       | (0–1) | (0–0) | (3–7) | (0–0) | (10656751–2511498) | (1–1) |
| YLLs | 649 | 0 | 2122 | 0 | 2447740 | 36 |
|       | (558–754) | (0–0) | (1856–2765) | (0–0) | (1734885–3199044) | (25–47) |
| **Epilepsy** |      |                                |       |                                |       |                                |
| DALYs | 781549 | 140 | 1479134 | 158 | 1473945 | 196 |
|       | (5124583–1168936) | (90–211) | (1063428–2050641) | (113–220) | (1141768–18991487) | (151–252) |
| Deaths | 9526 | 1 | 15370 | 1 | 130237 | 2 |
|       | (7286–10097) | (1–1) | (12663–16443) | (1–1) | (119680–195774) | (2–2) |
| Prevalence | 2244668 | 399 | 3742828 | 385 | 2728268 | 359 |
|       | (1496976–2977225) | (266–529) | (2718716–4823770) | (280–497) | (2157600–3144826) | (284–441) |
| Incidence | 189497 | 37 | 309286 | 35 | 2470759 | 33 |
|       | (114648–164471) | (25–50) | (2125139–329256) | (25–46) | (1296545–3062903) | (26–41) |
| YLDs | 523009 | 96 | 942629 | 100 | 9538880 | 124 |
|       | (259741–908273) | (48–166) | (528597–152164) | (57–160) | (5380607–12551498) | (72–166) |
| YLLs | 258546 | 44 | 556505 | 58 | 6222666 | 83 |
|       | (219592–274228) | (40–47) | (490237–585052) | (53–64) | (5079753–7289706) | (76–97) |
| **Migraine** |      |                                |       |                                |       |                                |
| DALYs | 4231019 | 770 | 7401471 | 735 | 47245390 | 597 |
|       | (2740462–6048715) | (495–1115) | (4810162–10539348) | (473–1056) | (2998062–68669318) | (378–866) |
| Prevalence | 11220762 | 2064 | 195794407 | 19650 | 133164642 | 16828 |
|       | (104739016–119973469) | (19324–22225) | (1826737–209186190) | (18270–21082) | (123719358–1433357249) | (15638–18119) |
| Incidence | 7506784 | 1724 | 1366499 | 1641 | 112933149 | 1477 |
|       | (6829187–817362) | (1568–1883) | (1246755–14861052) | (1493–1789) | (10289120–12899843) | (1344–1667) |
| YLDs | 4231019 | 770 | 7401471 | 735 | 47245391 | 597 |
|       | (2740462–6048715) | (495–1115) | (4810162–10539348) | (473–1056) | (2998062–68669319) | (378–866) |

(cardiovascular diseases) and deaths (after cardiovascular diseases and cancer). These diseases comprised 13·4% (10·3–17·1) of global DALYs and 19·3% (18·0–21·3) of deaths. In the WHO European region, neurological disorders ranked third for DALYs and deaths (after cardiovascular diseases and neoplasms). The proportion of total DALYs attributable to neurological disorders was 13·1% (12·8–13·5) and the proportion of deaths was 19·0% (19·0–19·1). The percentage of DALYs attributable to neurological disorders was lowest in western Europe (14·0% [12·7–15·2]) and highest in central Europe (15·1% [13·9–16·2]). The proportion of

Table 1 continues on next page)
neurological disorders in the WHO European region, accounting for the largest proportion of DALYs in the EU28 (table 1; figure 1; appendix p 17). Stroke also predominated in central Europe (55% [50·3–59·5]) with 3·3 million DALYs (3·1–3·5) and eastern Europe (62% [57·3–66·7]) with 8·2 million (7·8–8·5). All the other neurological disorders accounted for lower numbers and rates (appendix p 17).

In the EU28, the total number of DALYs was higher in women (12·0 million [9·9–14·5]) than in men (9·1 million [7·6–10·8]). The major contributors to the burden of neurological disorders were dementia and stroke, the attributable proportions of which increased substantially with age both for the number of DALYs and for DALY rates (figure 2). We found substantial sex differences in the number of DALYs and in age-standardised DALY rates in all age groups for dementia, migraine, and multiple sclerosis (that were higher in women) and for stroke and Parkinson’s disease (that were higher in men; appendix p 10). DALYs and DALY rates for epilepsy and brain cancer were also higher in men than in women. Findings were similar in the WHO European region for both sexes and for women and men separately (appendix p 12). In the EU28 the peak in the number of DALYs and DALY rates was in people aged 80–84 years for both sexes. By contrast, in the WHO European region the burden peaked in women aged 80–84 years and in men aged 75–79 years.

Dementia, stroke, and headache differed when comparing findings in western, central, and eastern Europe. In western Europe, the leading contributor was stroke (7·3 million [95% UI 6·7–7·9]; 35% [35–38]), followed by dementia (5·3 million [4·9–5·6]; 25% [23–28]), and headache (migraine and tension-type headache combined; 4·8 million [4·4–5·0]). Stroke also predominated in central Europe (7·7 million, 7·1–8·3]; 18·7% [17·3–20·2]). In eastern Europe (appendix p 12).

The changes in all-age and age-standardised DALY rates of neurological disorders in the EU28 and WHO European region between 1990 and 2017 are shown in table 1 (Continued from previous page).
of burden was also observed for encephalitis, meningitis, and tetanus (appendix p 19). We found a 53% increase (3 to 64) in deaths for epilepsy and 43% (0 to 54) in deaths for brain cancers. Brain cancers showed an 161% (98 to 192) increase in prevalence. A 41% (39 to 44) increased prevalence was also found for multiple sclerosis. With some exceptions, in the EU28 all measures differed only slightly from those in the WHO European region but significantly from the global estimates (appendix p 19).

In the EU28 and WHO European region, age-standardised DALY rates showed a significant decrease for stroke and infections and a modest, but still significant, decrease for dementia. We found a significant increase only for motor neuron disease in the EU28 (table 2). Findings were similar for deaths (appendix p 19), whereas prevalence (all age and age standardised) increased for all clinical conditions apart from headache, although at a variable speed between regions (appendix p 19).

In 1990, in high-SDI European countries stroke was the leading disease, accounting for 1286 age-standardised DALYs per 100000 (95% UI 1228 to 1341), followed by migraine (676 [433 to 975]), and dementia (430 [403 to 458]; tables 3). Migraine, stroke, and dementia ranked first, second, and third in 2017, while the age-standardised DALY rate for stroke was substantially lower in comparison to 1990 levels, at 650 (597 to 703; 49% decrease [–52 to –47]), the age-standardised DALY rate for migraine and dementia remained similar at 674 (431 to 970; unchanged) and 399 (373 to 426; 7% decrease; –9 to –5; table 3), respectively. In high-middle-SDI countries, stroke and dementia ranked first and third both in 1990 and in 2017, but the age-standardised rate of stroke decreased by 37% (–40 to –35) from 3196 (3097 to 3294) in 1990, while the decrease in the age-standardised rate of dementia was only 6% (–8 to –3; table 3). Epilepsy showed a 6% (–23 to 14) non-significant decrease only for motor neuron disease in the EU28 (appendix p 19). We found a 53% increase (3 to 64) in deaths for epilepsy and 43% (0 to 54) in deaths for brain cancers. Brain cancers showed an 161% (98 to 192) increase in prevalence. A 41% (39 to 44) increased prevalence was also found for multiple sclerosis. With some exceptions, in the EU28 all measures differed only slightly from those in the WHO European region but significantly from the global estimates (appendix p 19).

In the EU28 and WHO European region, age-standardised DALY rates showed a significant decrease for stroke and infections and a modest, but still significant, decrease for dementia. We found a significant increase only for motor neuron disease in the EU28 (table 2). Findings were similar for deaths (appendix p 19), whereas prevalence (all age and age standardised) increased for all clinical conditions apart from headache, although at a variable speed between regions (appendix p 19).

During the study period, all-age DALY numbers, deaths, and prevalence of neurological disorders varied across countries (appendix p 27), with increases in Albania, Andorra, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Bulgaria, Georgia, Greece, Lithuania, Macedonia, Malta, Moldova, Montenegro, Romania, Russia, Serbia, Turkmenistan, Ukraine, and Uzbekistan, and no change or decrease in the other countries. By contrast, age-standardised DALY and death rates decreased in all WHO European region countries, except for Azerbaijan, Turkmenistan, and Uzbekistan, where both measures increased, and Albania and Bosnia and Herzegovina, where prevalence increased but DALYs decreased. Table 2 gives a table of the % increase in the top 10 countries of all measures for strokes and other neurological disorders in the EU28. The appendixes give similar data for the SDI countries and show for all regions, in thousand SDI and high-SDI countries, that for all measures except headache, the % increase was higher in the SDI countries than in the EU28. For example, the % increase was 28% (22 to 34) in strokes DALYs in the EU28, whereas in the SDI countries it was 78% (62 to 94), in deaths, it was 24% (18 to 30) in the EU28 and 89% (73 to 106) in the SDI countries, and in prevalence it was 14% (9 to 19) in the EU28 and 49% (39 to 59) in the SDI countries.

Figure 1: Contribution of each disease to the overall burden of neurological disorders in the EU28, western, central, and eastern Europe in 2017

Table 2 gives a table of the % increase in the top 10 countries of all measures for strokes and other neurological disorders in the EU28. The appendixes give similar data for the SDI countries and show for all regions, in thousand SDI and high-SDI countries, that for all measures except headache, the % increase was higher in the SDI countries than in the EU28. For example, the % increase was 28% (22 to 34) in strokes DALYs in the EU28, whereas in the SDI countries it was 78% (62 to 94), in deaths, it was 24% (18 to 30) in the EU28 and 89% (73 to 106) in the SDI countries, and in prevalence it was 14% (9 to 19) in the EU28 and 49% (39 to 59) in the SDI countries.

Table 2: Contribution of each disease to the overall burden of neurological disorders in the EU28, western, central, and eastern Europe in 2017

| Disease                                      | EU28 | Western Europe | Central Europe | Eastern Europe |
|----------------------------------------------|------|----------------|----------------|----------------|
| Stroke                                       | 12%  | 20%            | 6%             | 6%             |
| Migraine                                     | 13%  | 16%            | 12%            | 10%            |
| Tension-type headache                        | 5%   | 7%             | 3%             | 5%             |
| Encephalitis                                 | 5%   | 3%             | 8%             | 4%             |
| Tetanus                                      | 2%   | 2%             | 2%             | 2%             |
| Motor neuron disease                         | 3%   | 3%             | 3%             | 3%             |
| Multiple sclerosis                           | 1%   | 1%             | 2%             | 1%             |
| Other neurological disorders                 | 1%   | 1%             | 1%             | 1%             |
| Epilepsy                                     | 2%   | 2%             | 2%             | 2%             |
| Alzheimer’s disease and other dementia       | 4%   | 4%             | 4%             | 4%             |
| Parkinson’s disease                          | 1%   | 1%             | 1%             | 1%             |
| Brain and nervous system cancer              | 4%   | 4%             | 4%             | 4%             |
| Tetanus                                      | 2%   | 2%             | 2%             | 2%             |
| Meningitis                                   | 2%   | 2%             | 2%             | 2%             |
| Other neurological disorders                 | 1%   | 1%             | 1%             | 1%             |
Herzegovina, where death rates were unchanged. We found a modest increase in age-standardised prevalence rates of neurological disorders in Azerbaijan, Bosnia and Herzegovina, Lithuania, Montenegro, the Netherlands, and Switzerland. We found an almost universal decrease in standardised DALY rates in all countries (maximally represented by a reduction in YLLs and, only to a lesser extent, by a reduction in YLDs), the only exceptions being Azerbaijan, Turkmenistan, and Uzbekistan. By contrast, except for Estonia, Latvia, and Ukraine, where a decrease of all raw numbers was also observed, prevalent cases, deaths, DALYs, YLLs, and YLDs all increased in Azerbaijan, Cyprus, Finland, France, Greece, Iceland, Israel, Kazakhstan, Macedonia, Malta, Montenegro, the Netherlands, Tajikistan, Turkmenistan, and Uzbekistan (appendix p 27).

Discussion

In 2017, neurological disorders were among the most common sources of health loss in the EU28 and the WHO European region. Although globally neurological disorders were the second largest contributor to DALYs and the second largest cause of death, in both European regions neurological disorders ranked third for DALYs and deaths.
### EU28 Stroke

| Age-standardised rate, 1990 | Age-standardised rate, 2017 | Change from 1990 to 2017 | Total, 1990 | Total, 2017 | Change from 1990 to 2017 | WHO European region |
|---------------------------|---------------------------|--------------------------|------------|------------|--------------------------|-------------------|
| DALYs                     |                           |                          |            |            |                          |                   |
| (1434 to 1538)            | (643 to 737)              | (-56 to -52)             | 10,446.307| 7,314.978  | (-30 to -27)             | 21,991.312        |
| Deaths                    | (85 to 87)                | (-58 to -54)             | 619.264   | 476.903    | (-23 to -19)             | 1,207.823         |
| Prevalence                | (921 to 1021)             | (-16 to -10)             | 7,692.547| 9,521.098  | (25 to 30)               | 12,870.522        |
| YLDs                      | (118 to 204)              | (-16 to -9)              | 1,621.402| 1,619.216  | (22 to 34)               | 2,245.049         |
| YLLs                      | (516 to 552)              | (-62 to -58)             | 5,665.377| 5,685.527  | (-38 to -35)             | 15,162.263        |
| Alzheimer’s disease and other dementias |            |                          |            |            |                          |                   |
| DALYs                     | (416 to 473)              | (-10 to -8)              | 3,240.658| 5,271.564  | (63% to 68%)             | 4,774.771         |
| Deaths                    | (38 to 39)                | (-8 to -7)               | 260.244   | 501.678    | (93% to 88%)             | 376.119           |
| Prevalence                | (34 to 36)                | (-11 to -10)             | 4,788.372| 7,740.481  | (62% to 67%)             | 7,074.259         |
| YLDs                      | (343 to 367)              | (-11 to -10)             | 706.265   | 1,165.301  | (65% to 79%)             | 1,036.646         |
| YLLs                      | (301 to 320)              | (-13 to -9)              | 2,534.204| 4,106.264  | (62% to 66%)             | 3,741.105         |
| Parkinson’s disease       |                           |                          |            |            |                          |                   |
| DALYs                     | (68 to 82)                | (2% to 17)               | 522.567   | 829.916    | (61% to 69)              | 781.347           |
| Deaths                    | (4 to 6)                  | (-2% to 19)              | 342.36    | 60.812     | (78% to 40%)             | 49.050            |
| Prevalence                | (86 to 125)               | (11% to 15)              | 704.533   | 1,215.045  | (72% to 100%)            | 1,123.483         |
| YLDs                      | (47 to 79)                | (11% to 17)              | 99.431    | 170.916    | (72% to 64%)             | 158.046           |
| YLLs                      | (51 to 63)                | (-22% to 6)              | 422.835   | 669.000    | (58% to 23%)             | 623.301           |
| Motor neuron disease      |                           |                          |            |            |                          |                   |
| DALYs                     | (26 to 29)                | (12% to 20)              | 157.904   | 252.987    | (60% to 49%)             | 203.830           |
| Deaths                    | (29 to 32)                | (29% to 37)              | 60.34     | 11.495     | (91% to 75%)             | 7.076             |

(The table continues on next page)
### EU28

| Age-standardised rate, 1990 | Age-standardised rate, 2017 | Change from 1990 to 2017 | Total, 1990 | Total, 2017 | Change from 1990 to 2017 | Age-standardised rate, 1990 | Age-standardised rate, 2017 | Change from 1990 to 2017 | Total, 1990 | Total, 2017 | Change from 1990 to 2017 |
|-----------------------------|-----------------------------|--------------------------|-------------|-------------|--------------------------|-----------------------------|-----------------------------|--------------------------|-------------|-------------|--------------------------|
| Prevalence                  |                             |                          |             |             |                          |                             |                             |                          |             |             |                          |
| (Continued from previous page) |                             |                          |             |             |                          |                             |                             |                          |             |             |                          |
| Deaths                      |                             |                          |             |             |                          |                             |                             |                          |             |             |                          |
| YLDs                         |                             |                          |             |             |                          |                             |                             |                          |             |             |                          |
| YLLs                         |                             |                          |             |             |                          |                             |                             |                          |             |             |                          |

### Multiple sclerosis

| DALYs | 39 (32 to 46) | 39 (32 to 46) | 0% (-16 to 12) | 226 945 (195 825 to 260 163) | 282 765 (233 418 to 328 139) | 25% (1 to 57) | 33 (28 to 38) | 32 (26 to 37) | -5% (-15 to 11) | 326 058 (279 079 to 372 431) | 391 078 (327 333 to 453 473) | 20% (5 to 38) |

### Brain and nervous system cancer

| DALYs | 153 (136 to 171) | 140 (117 to 153) | -9% (-28 to 5) | 823 616 (748 909 to 932 285) | 964 964 (879 495 to 1 030 050) | 17% (-11 to 28) | 158 (141 to 175) | 147 (130 to 163) | -7% (-20 to 5) | 1 435 491 (1 289 242 to 1 584 211) | 1 668 047 (1 439 524 to 1 979 509) | 16% (11 to 28) |

### Meningitis

| DALYs | 75 (71 to 81) | 70 (68 to 73) | -74% (-76 to -72) | 278 620 (261 680 to 295 462) | 84 550 (77 757 to 91 340) | -70% (-72 to -68) | 172 (1 15 to 203) | 38 (35 to 41) | -78% (-81 to -75) | 1 182 458 (1 118 688 to 1 247 097) | 288 814 (267 659 to 314 772) | -76% (-79 to -71) |

(Continued on next page)
### EU28

| Articles | Prevalence | Deaths | DALYs | YLDs | YLLs |
|----------|------------|--------|-------|------|------|
| Articles | 0          | 1      | 763   | 0    | 597  |
| (Continued from previous page) | (0 to 0)    | (0 to 1) | (1 to 1) | (0 to 0) | (0 to 0) |

#### Encephalitis

| DALYs | Prevalence | Deaths | YLDs | YLLs |
|-------|------------|--------|------|------|
| DALYs | 0          | 0      | 0    | 0    |
| (1 to 1) | (12 to 15) | (6 to 9) | (0 to 0) | (0 to 0) |

#### Tetanus

| DALYs | Prevalence | Deaths | YLDs | YLLs |
|-------|------------|--------|------|------|
| DALYs | 0          | 0      | 0    | 0    |
| (1 to 1) | (0 to 0)    | (0 to 0) | (0 to 0) | (0 to 0) |

#### Epilepsy

| DALYs | Prevalence | Deaths | YLDs | YLLs |
|-------|------------|--------|------|------|
| DALYs | 0          | 0      | 0    | 0    |
| (1 to 1) | (1 to 1)   | (1 to 1) | (1 to 1) | (1 to 1) |

#### Migraine

| DALYs | Prevalence | Deaths | YLDs | YLLs |
|-------|------------|--------|------|------|
| DALYs | 0          | 0      | 0    | 0    |
| (1 to 1) | (1 to 1)   | (1 to 1) | (1 to 1) | (1 to 1) |

(Continued from previous page)

| YLLs | 18 | 10 | 657 | 0 |
| YLDs | 2 | 2 | 18 | 0 |
| YLLs | 18 | 10 | 657 | 0 |

| Encephalitis | YLLs | 18 | 10 | 657 | 0 |
| YLDs | 2 | 2 | 18 | 0 |
| YLLs | 18 | 10 | 657 | 0 |

(Continued from previous page)

| YLLs | 18 | 10 | 657 | 0 |
| YLDs | 2 | 2 | 18 | 0 |
| YLLs | 18 | 10 | 657 | 0 |

(Continued from previous page)

| YLLs | 18 | 10 | 657 | 0 |
| YLDs | 2 | 2 | 18 | 0 |
| YLLs | 18 | 10 | 657 | 0 |

(Continued from previous page)

| YLLs | 18 | 10 | 657 | 0 |
| YLDs | 2 | 2 | 18 | 0 |
| YLLs | 18 | 10 | 657 | 0 |

(Continued from previous page)

| YLLs | 18 | 10 | 657 | 0 |
| YLDs | 2 | 2 | 18 | 0 |
| YLLs | 18 | 10 | 657 | 0 |

(Continued from previous page)

| YLLs | 18 | 10 | 657 | 0 |
| YLDs | 2 | 2 | 18 | 0 |
| YLLs | 18 | 10 | 657 | 0 |

(Continued from previous page)

| YLLs | 18 | 10 | 657 | 0 |
| YLDs | 2 | 2 | 18 | 0 |
| YLLs | 18 | 10 | 657 | 0 |
The high proportion of DALYs and deaths attributable to neurological disorders can be explained in part by the long life expectancy in Europe and, despite an overall decrease in age-standardised rates, by the increasing incidence and the increasingly long duration of age-related diseases. Population growth could also be implicated. The total population of Europe was 721 million in 1990 and rose to 916 million by 2016. The increase in the most common clinical conditions with age is most strongly explained in part by neurological disorders. The high proportion of DALYs and deaths attributable to neurological disorders when comparing the EU28, western, central, and eastern Europe, but with different numbers according to age. Whereas in western Europe dementia and stroke were the largest contributors to the burden of neurological disorders after age 70 years in both sexes, stroke was the strongest contributor between age 40 years and 89 years in central Europe and between age 50 years and 89 years in eastern Europe. National and regional differences in population age structure (for dementia), implementation of preventive and therapeutic measures (for stroke), and attention to diseases and access to health-care facilities are possible explanations.

This study has shown differences among WHO subregions in the proportion of DALYs, deaths, and
prevalence attributable to the commonest neurological disorders. Stroke was the largest contributor to the total DALYs in eastern Europe, followed by central and western Europe, whereas dementia showed the opposite gradient.

Stroke was the leading source of burden attributable to neurological disorders in the EU28 and the WHO European region. The age-standardised DALY rate for stroke was significantly higher in high-middle SDI than in high-SDI countries. Stroke is the overall leading contributor of DALYs and deaths worldwide. However, the declining all-age and age-standardised DALYs attributable to stroke is an important finding. As the prevalence of stroke showed a substantial increase, possibly due to the ageing of the society and the increasing detection of less severe cases, we found a corresponding decrease in DALYs, both absolute and relative. Preventive medicine and lifestyle changes are the most likely explanations and underscore the effects of increasing control of preventable risk factors (blood pressure control and smoking cessation) affecting mainly the prevalence. Previous reports from the GBD collaborators showed that more than 90% of the stroke burden was attributable to modifiable risk factors.

Another notable disease with a large increase in prevalence and DALYs was Parkinson’s disease. The global burden of Parkinson’s disease more than doubled during the study period. The growth of the burden of Parkinson’s disease surpassed that of Alzheimer’s disease and other dementias. This increase has been attributed to the ageing of the European population, the reduction of rural populations, occupational exposures, and the declining smoking rates. Although increased attention towards the disease might partially explain the increasing incidence observed, Parkinson’s disease is still underdiagnosed, as shown in the USA and by an online European survey that found that 40% of respondents had never seen a Parkinson’s disease specialist.

A substantial increase in all the measures of burden has been observed in Europe for motor neuron disease, another ageing-related disease. However, contrary to the other neurodegenerative diseases, we found a parallel increase of age-standardised rates, which can be explained by an increasing diagnostic accuracy rather than a true increase of the incidence of the disease.

Primary headache (migraine and tension-type headache) was the most prevalent neurological disorder and the second highest source of burden both in high-SDI and in high-middle SDI countries. Headache is a major public health concern worldwide. Based on the results of the GBD Study 2016, almost 3 billion individuals were estimated to have repeated migraine or tension-type headache attacks, accounting for a total of 52.3 million YLDs. In the WHO European region, migraine and

| Table 3: Age-standardised DALY rates by SDI in the EU28 and WHO European region from 1990 to 2017 |
|-----------------------------------------------|-----------------------------------------------|
| 1990 | 2017 | Change | 1990 | 2017 | Change |
|-----------------------------------------------|-----------------------------------------------|
| Stroke | 1286 (1228 to 1341) | 650 (597 to 703) | -49% (-52 to -47) | 3196 (3097 to 3294) | 1998 (1900 to 2104) | -37% (-40 to -35) |
| Alzheimer’s disease and other dementias | 430 (403 to 458) | 399 (373 to 426) | -7% (-9 to -5) | 466 (436 to 497) | 439 (410 to 472) | -6% (-8 to -3) |
| Parkinson’s disease | 63 (58 to 74) | 67 (59 to 73) | 6% (-16 to 31) | 78 (72 to 86) | 74 (68 to 83) | -4% (-10 to 0) |
| Motor neuron disease | 28 (27 to 29) | 31 (30 to 32) | 11% (6 to 16) | 8 (7 to 12) | 10 (9 to 11) | 17% (-22 to 43) |
| Multiple sclerosis | 33 (28 to 28) | 34 (29 to 40) | 6% (-12 to 10) | 14 (12 to 16) | 11 (10 to 13) | -21% (-31 to -1) |
| Brain and nervous system cancer | 125 (112 to 139) | 114 (99 to 124) | -9% (-25 to 3) | 148 (113 to 169) | 132 (117 to 147) | -11% (-22 to 16) |
| Meningitis | 62 (58 to 66) | 19 (17 to 22) | -70% (-72 to -63) | 201 (144 to 227) | 46 (40 to 49) | -77% (-80 to -71) |
| Encephalitis | 14 (13 to 15) | 10 (9 to 12) | -27% (-34 to -12) | 54 (46 to 64) | 32 (28 to 38) | -41% (-54 to -16) |
| Tetanus | 1 (1 to 1) | 0 (0 to 0) | -89% (-90 to -86) | 43 (33 to 54) | 2 (1 to 3) | -95% (-97 to -91) |
| Epilepsy | 125 (88 to 171) | 118 (77 to 173) | -6% (-23 to 14) | 175 (138 to 223) | 127 (91 to 177) | -27% (-42 to -9) |
| Migraine | 676 (433 to 975) | 674 (431 to 970) | 0% (-1 to 1) | 55 (46 to 64) | 55 (46 to 64) | 0% (-1 to 1) |
| Tension-type headache | 125 (112 to 139) | 114 (99 to 124) | -9% (-25 to 3) | 148 (113 to 169) | 132 (117 to 147) | -11% (-22 to 16) |
| Other neurological disorders | 61 (54 to 70) | 61 (52 to 72) | 0% (-10 to -10) | 46 (37 to 56) | 45 (37 to 57) | -2% (-18 to 21) |

Data are n (95% UI) or % (95% UI). DALY=disability-adjusted life-year. EU28=the 27 EU countries plus the UK. SDI=socio-demographic index. UI=uncertainty interval.
tension-type headache were the second most common source of burden attributable to neurological disorders (the third in the EU28). In this study, headache was in line with the worldwide burden of the disease and, by definition, accounted for a substantial health loss in terms of YLDs, with premature mortality virtually absent. Despite the abundance of symptomatic drugs available to treat headache, we found a modest increase in the absolute measures of burden of headache, suggesting that interventions should be directed towards increasing public knowledge of and decreasing exposure to modifiable risk factors, such as obesity, smoking, air pollution, low physical activity, blood pressure, and stress.26

Contrary to other neurological disorders and in spite of a slight increase in prevalence and deaths, epilepsy showed a reduction in all-age and age-standardised DALYs in Europe. The increasing number of deaths might be due to the ageing of the European population. This finding is not unexpected because epilepsy incidence is age related, with a first peak in the young but a steady increase in the older population and thereby an increase in mortality in an ageing society.27 The decreasing burden might be instead a reflection of improved management. The differences between high-SDI countries (showing a slight increase) and high-middle-SDI countries (showing a significant decrease) can be explained by the contrasting effects of ageing and quality of care, with a negative balance in countries with top economies (where the management of epilepsy could not further improve despite the increasing number of affected individuals) and a positive balance in growing economies (where the quality of care might be rapidly improving).

Multiple sclerosis is less frequent than other neurological disorders. The increasing prevalence, and the consequent burden, when comparing the first and the last year of the study period, could be due to the changing classifications of the disease. The disease can now be diagnosed earlier than was possible at the start of the study. Patients with clinically isolated syndromes showing one attack and evidence of two or more T2 or gadolinium-enhancing lesions have been included since 2010.28 Therefore, the incidence of the disease might not be truly increasing, but the expansion of the diagnostic boundaries might be a source of increasing burden and, consequently, of expenditures for the propensity of the caring physicians to anticipate the onset of treatment with disease-modifying drugs in the attempt to improve the disease course.29

In line with the global decrease of absolute numbers and age-standardised rates,29 CNS infections and tetanus showed a significant decrease in the EU28 and the WHO European region. The increase in prevalence and YLDs and, to a lesser extent, the increase of deaths attributable to brain tumours can be explained by better diagnostic ascertainment; the role of environmental risk factors is controversial.30,31

All the other neurological disorders accounted for a low proportion of the overall burden, due to low prevalence or a less remarkable effect on life expectancy or functional abilities.

The standardised DALY rates for all neurological diseases varied across countries but, with few exceptions, we found an overall decrease, mostly driven by a reduction in premature mortality. Given the predominant role of stroke in terms of attributable proportion, we infer that the decrease in DALYs overall is in large part explained by the improved prevention of stroke deaths.

The major strength of the study is the collection of epidemiological data worldwide using the same methodology and modelling measures. This methodology allowed us to document major differences between the EU28 and the WHO European region and within European countries in the burden of neurological disorders. Our study was able to highlight geographical trends in the burden of stroke within Europe and suggests that prevention and treatment are still deficient in several European countries. These results can be helpful for local authorities to address the burden of preventable and treatable neurological disorders. Other strengths are the continuous refinement of the available data, adding new original sources and the use of more sophisticated statistical methods when available, which allowed us to compare the European situation with the spectrum of the global situation.

This study also has limitations. First, because original epidemiological data were not available for all countries, Bayesian statistical models were used to estimate deaths and disease prevalence for countries where information was missing. For this reason, the inclusion in future of new primary data from countries with little data could lead to more precise estimates that might vary from current predicted values. Second, the disability weights used for the calculation of YLDs might not be uniform across populations and sociodemographic strata. However, a systematic variation in disability weights across populations, or within the same population as a function of education, was not detected by population surveys.32 Third, the 95% Uls are frequently wide, reflecting the low precision of the estimates and potentially limiting the ability to detect smaller differences across countries. Additional data on the proportions influencing the sequelae of neurological disorders might reduce uncertainties in future analyses. Fourth, neurological diseases can be correlated with other somatic and psychiatric comorbidities and injuries. Here, the correction for comorbidity was based on the assumption that diseases and their sequelae are independent. Future improvements of the GBD modelling should include dependent comorbidity. Fifth, disease rankings that are based on age-standardised rates can be influenced by the choice of the standard population. Sixth, the use of medical claims data could be biased because people who are not treated or are excluded from health insurance would not be counted. Seventh, the results reflect the study period and the...
quality of the sources. Additionally, the variable quality and completeness of the information available can partly explain the differences found when comparing the different European countries. Eighth, the definition of causes of death reflects the quality and completeness of the sources. Finally, several highly prevalent neurological diseases are not yet included in the GBD database, such as sleep disorders, essential tremor, or restless legs syndrome.

This study has shown the huge burden of neurological disorders in Europe. The numbers of citizens affected and the numbers of neurological DALYs and deaths call for action regarding this disease group. The major challenge for all countries is the increasing number of neurological diseases even if the DALYs per patient are decreasing for some conditions. Despite many similarities, the most prevalent diseases differ considerably in different regions or even countries and thus policy and actions needed might differ. Strategic planning in European countries might use this information to customise plans to efficiently deal with this burden. However, to improve the precision of our estimates, new studies are awaited to provide original data in countries where the information regarding the incidence, prevalence, and mortality of the target diseases is not yet available. The inclusion of these data in our models can correct the present findings and provide a more accurate estimate of the burden of neurological diseases and trends.

Contributors
EB, GD, and TV analysed the data and prepared the first draft. All other authors provided data, developed models, reviewed results, provided guidance on methodology, or reviewed and approved the final version of the manuscript.

Declaration of interests
GD reports grants from Medtronic; and personal fees from Boston Scientific, Cavion, Functional Neurorudimization, and Thieme publishers, outside of the submitted work. GD receives funding for his research from the German Research Council (SFB 1261, B5). EB reports grants from the Italian Ministry of Health and the Swedish Orphan Biovitrum, and American ALS Association; and personal fees from Arvelle Therapeutics, outside of the submitted work. All other authors declare no competing interests.

Data sharing
Data collected within the framework of this study are accessible to interested parties by contacting the corresponding author.

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