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



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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 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).¹ A report by the Global Burden of Disease (GBD) 2015 Neurological Disorders Collaborator Group² 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.² 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],

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See Correspondence page e523

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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.

and years lived with disability [YLDs]) as absolute numbers and rates attributable to neurological disorders in the so-called EU28 (the 27 member countries of the EU plus the UK), in general and by age, sex, year, and location for the period 1990–2017, and to compare the EU28 with the WHO Europe region and the rest of the world.

See Online for appendix

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.²⁻⁴

The analyses in the current study follow the GBD methodology. The data provided here are for 1990–2017.

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 diseasemodifying 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.

Population-based measures are taken from the related GBD standards.⁵ 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.⁶ 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.⁷

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.8 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.9 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.6 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.⁶

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 $21\cdot0$ million (95% UI $18\cdot5-23\cdot9$) in the EU28 and $41\cdot1$ million ($36\cdot7-45\cdot9$) in the WHO European region and the total number of deaths was $1\cdot1$ million ($1\cdot09-1\cdot14$) 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-standardided rate pe 100 000
All neurologica	al diseases					
DALYs	21 046 899	190	41 103 486	232	279 895 042	278
	(18 499 198-23 863 193)	(160–225)	(36 655 558-45 935 037)	(201–266)	(251 440 223-312 210 489)	(250–310)
Deaths	1116 038	8	1 974 840	10	9 927 123	12
	(1 094 328-1 142 613)	(8–8)	(1 947 870-2 012 204)	(10–10)	(9 771 333-10 100 744)	(12–12)
Prevalence	307 859 199	4137	540 277 716	4089	3 8 6 8 7 8 0 5 7 6	3791
	(291 599 989-327 023 248)	(3 900-4395)	(510 725 114-573 264 505)	(3856-4350)	(3 6 4 4 2 9 4 2 7 1 - 4 1 2 9 9 7 4 1 5 6)	(3569-4049)
YLDs	8 622 940	99	15 213 540	101	93 483 900	92
	(6 072 621-11 333 906)	(69–133)	(10 755 558-20 029 063)	(71–135)	(65 716 638-125 511 962)	(64–123)
YLLs	12 423 960	111	25 889 946	159	186 411 142	237
	(12 149 237-12 714 922)	(109–114)	(25 502 381-26 430 347)	(157-163)	(182 252 461-190 710 446)	(231–244)
Stroke						
DALYs	7314978	691	18 831 007	1198	132 051 366	1657
	(6833270-7768518)	(643-737)	(17 874 242-19 733 892)	(1136–1256)	(126 498 600-137 350 169)	(1587-1724)
Deaths	476 903	38	1 078 620	61	6167292	80
	(463 602-504 651)	(37-40)	(1 058 760-1 117 505)	(60-63)	(6044260-6327598)	(79-83)
Prevalence	9 531 098	971	18 254 959	1196	104178740	1301
	(8 958 668–10 024 854)	(921–1021)	(17 183 892-19 283 541)	(1129–1262)	(98453978-110124977)	(1229–1375)
Incidence	1102677	107	2 060 660	131	11 931 061	151
	(1030004-1178489)	(101–115)	(1 916 873-2 206 398)	(123–141)	(11 118 416-12 825 770)	(140–162)
YLDs	1621402	162	3 304 779	215	18 695 419	236
	(1191963-2036972)	(118–204)	(2 428 732-4 165 663)	(157-270)	(13 574 330-23 686 932)	(171–299)
YLLs	5 693 577	530	15 526 228	983	113 355 949	1423
	(5 543 620-5 958 058)	(516–552)	(15 235 982–16 036 397)	(965–1016)	(110 957 795-116 180 577)	(1392–1458)
Alzheimer's dis	sease and other dementias					
DALYs	5 271 654	399	7686392	410	30 521 481	413
	(4 915 486to 5 641 197)	(372-427)	(7175157-8205020)	(383-438)	(28 529 663-32 557 921)	(386-440)
Deaths	501 678	35	700 353	36	2 514 619	35
	(489 118-512 705)	(34–36)	(685 974-712 101)	(35–36)	(2 470 512-2 550 346)	(35–36)
Prevalence	7740 481	594	11 375 859	612	44 988 790	605
	(6 896 189-8 583 917)	(531-657)	(10 038 137-12 683 497)	(541-681)	(39 716 207-50 377 809)	(533–676)
Incidence	1249178	98	1851062	101	7300 645	97
	(1118954-1390849)	(88–108)	(1653033-2065251)	(90–112)	(6515 684-8133 403)	(87–109)
YLDs	1165391	88	1694270	90	6570378	89
	(832669-1516059)	(63–114)	(1209023-2212896)	(64-118)	(4678144-8588469)	(64-117)
YLLs	4106264	311	5 9 9 2 1 2 1	320	23 951 105	324
	(3982651-4213014)	(301–320)	(5 8 4 4 3 1 8 – 6 1 1 3 0 1 8)	(312–327)	(23 523 645-24 326 849)	(318–329)
Parkinson's dis						
DALYs	839 916	70	1226579	70	5 580 212	72
	(766 256-940 813)	(63–78)	(1126744-1363923)	(64-78)	(5 151 586-6 084 655)	(67–79)
Deaths	60 812	5	84599	5	340 639	5
	(55 723-67 973)	(4-5)	(80948-93079)	(4–5)	(324 378-355 089)	(4–5)
Prevalence	1 215 045	105	1838 098	107	8 525 404	109
	(996 237-1 457 870)	(86–125)	(1506 704-2 220 458)	(88–128)	(7 037 337–10 185 559)	(90-131)
incidence	150 667	13	225 529	13	1 025 939	13
	(124 575–180 761)	(11-16)	(185 864-271 669)	(11-16)	(854 090-1 229 873)	(11-16)
YLDs	170 916	15	257 986	15	1 218 972	16
	(117 642-233 979)	(10-20)	(178 581-354 467)	(10-21)	(823 711-1 662 213)	(11-22)
YLLs	669 000	55	968593	55	4361241	57
	(612 867–764 328)	(51-63)	(924800-1088287)	(52-62)	(4182792-4578722)	(55–60)
					(Tah	le 1 continues on next pag

	EU28		WHO European region		Global	
	Total	Age-standardised rate per 100 000	Total	Age-standardised rate per 100 000	Total	Age-standardised rate pe 100 000
(Continued fro	m previous page)					
Motor neuron	disease					
DALYs	252 987	31	314523	24	878 518	11
	(240 153-264 173)	(29–32)	(298 988-348 088)	(23–26)	(841 386-966 073)	(10–12)
Deaths	11 495	1	13 410	1	34068	0
	(10 900–12 020)	(1-1)	(12 728-14 790)	(1-1)	(32796-37053)	(0-0)
Prevalence	42 937	6	51711	4	237 053	3
	(38 970-47 145)	(5-7)	(46 991-56 707)	(4–5)	(211 191-264 106)	(3-3)
Incidence	13 010	1	15728	1	67322	1
	(12 311–13 767)	(1–2)	(14766-16723)	(1-1)	(60666-74311)	(1-1)
YLDs	9131	1	10 998	1	50 416	1
	(6492–12227)	(1–2)	(7 822-14720)	(1–1)	(35 744-67 546)	(1-1)
YLLs	243 856	29	303 526	23	828102	11
	(231168-254703)	(28–31)	(287 735 – 337 104)	(22–25)	(796699-917135)	(10–12)
Multiple sclero	osis					
DALYs	282765	39	391 078	32	1084757	13
	(233418-328839)	(32-46)	(327 333-453 473)	(26–37)	(942878-1237344)	(12–15)
Deaths	5601 (3954–6056)	1 (0-1)	7413 (5673-8395)	1 (0-1)	20 655 (17721-22 238)	0 (0-0)
Prevalence	522 674	77	699 238	59	1761078	22
	(473 413-579 422)	(69-85)	(635 288-772 355)	(53-65)	(1598226-1947909)	(20–24)
Incidence	11 847	3	17 544	2	54 895	1
	(10 861-13 042)	(2-3)	(16 068-19 308)	(2–2)	(50 054-60 812)	(1-1)
YLDs	132159	20	178 020	15	456 556	6
	(95038–171558)	(14–26)	(127 760-230 616)	(11–20)	(327 739 - 595 013)	(5–8)
YLLs	150 607	19	213 059	17	628 202	8
	(110 315-166 542)	(14–22)	(169 517-254 322)	(14–20)	(563 020-682 386)	(7–9)
Brain and nerv	ous system cancer					
DALYs	964 964	140	1668047	147	8744765	112
	(789 495-1 033 050)	(117–153)	(1439524-1799509)	(130–163)	(7652109-9554150)	(98-123)
Deaths	35 917	4	56 246	4	247 143	3
	(27 137-38 316)	(3-4)	(45 620-59 326)	(3-4)	(212 969-265 001)	(3–3)
Prevalence	330 074	55	462 982	45	1705702	22
	(270 005-360 630)	(46–62)	(398 536-511728)	(40–52)	(1470989-1894771)	(19–24)
Incidence	70 026	10	102219	9	405 218	5
	(54 549-75 620)	(8–11)	(86050-109460)	(8–10)	(351 030-442 624)	(4–6)
YLDs	30368	5	43 489	4	166 947	3
	(21160-40887)	(3–6)	(31 024-57 873)	(3–5)	(117 460-222 977)	(2-3)
YLLs	934596	135	1624558	143	8 577 818	110
	(766157-997931)	(113–148)	(1404505-1753504)	(127–158)	(7 527 040-9 359 303)	(97–121)
Meningitis						
DALYs	84550	20	288 614	38	20 370 870	293
	(77767-97340)	(18–24)	(267 659-324 772)	(35-43)	(17 800 140-23 356 670)	(254-337)
Deaths	2033	0	5 483	1	288 021	4
	(1947–2224)	(0–0)	(5 253-6 125)	(1-1)	(254 287-333 240)	(4-5)
Prevalence	183 151	33	505 430	53	10 572 886	139
	(153 769-216 836)	(28–39)	(430 502-591 790)	(45–62)	(8 836 735-12 552 236)	(116–165)
Incidence	92 542	22	232 423	30	5 0 4 5 4 1 1	71
	(82 041–105 206)	(19–25)	(205 684-266 898)	(26–35)	(4 4 3 5 0 7 3 - 5 8 7 7 8 4 1)	(62–83)
YLDs	17 079	4	45 301	5	933 935	13
	(12 032-22 999)	(3–5)	(31 73 8 – 60 745)	(4-7)	(652964–1255126)	(9-17)
YLLs	67 471	17	243 313	33	19 436 936	281
	(64 007-80 231)	(16–21)	(230 129-280 048)	(31–39)	(16 935 143-22 335 832)	(244–324)
						(Table 1 continues on next pa

	EU28		WHO European region		Global	
	Total	Age-standardised rate per 100 000	Total	Age-standardised rate per 100 000	Total	Age-standardised rate pe 100 000
(Continued from	n previous page)					
Encephalitis						
DALYs	57720 (50302-63183)	11 (10–12)	270736 (236953-292768)	34 (30–38)	5112280 (4541340-5764967)	71 (63–79)
Deaths	1729 (1337–1829)	0 (0-0)	5953 (4631-6266)	1 (0-1)	92370 (83134–107936)	1 (1-1)
Prevalence	142 435 (74 374-234 773)	22 (12–35)	315 202 (173 810–507 091)	29 (17–46)	6724882 (3731161-10760385)	86 (48–137)
Incidence	47 411 (46 409-48 414)	9 (9–9)	110769 (108844-112873)	12 (12–12)	2 220 535 (2 289 100-2 225 245)	30 (29–30)
YLDs	9 372 (6 386-12 593)	2 (1–2)	22773 (15651–30309)	3 (2–3)	524114 (365488-691266)	7 (5–9)
YLLs	48 348 (41 387-51 476)	10 (8–11)	247 963 (214 185–269 172)	33 (28–36)	4588167 (4059515-5230709)	65 (57–73)
Tetanus	640	•	2427		2.440.422	25
DALYs	649 (558–755)	0 (0–0)	2127 (1860–2770)	0 (0-0)	2 449 433 (1736 526-3 201 172)	35 (25–46)
Deaths	39 (33-46)	0 (0–0)	82 (72–100)	0 (0-0)	38134 (25893-48771)	1 (0-1)
Prevalence	(3-5)	0 (0-0)	160 (133–187)	0 (0-0)	59583 (56726-62572)	1 (1-1)
Incidence	68 (58–82)	0 (0-0)	164 (140–205)	0 (0-0)	79192 (53360-105261)	1 (1-1)
YLDs	(0-1)	0 (0-0)	(3-7)	0 (0-0)	1695 (1065–2541)	1 (1-1)
YLLs	649 (558–754)	0 (0-0)	2122 (1856–2765)	0 (0-0)	2 447 740 (1734 885-3 199 044)	36 (25-47)
Epilepsy DALYs	781549	140	1479134	158	14702045	196
	(512 4583-1168 936)	(90-211)	(1063428-2050641)	(113–220)	14793 945 (11417 678-18 991 487)	(151-252)
Deaths	9526 (7286-10097)	1 (1-1)	15370 (12663-16443)	1 (1-1)	130 237 (116 998-150 774)	2 (2-2)
Prevalence	2 2 4 4 6 6 8 (1 4 9 6 9 7 6 – 2 9 7 7 2 2 5)	399 (266–529)	3742 828 (2718 716 - 4 823 770)	385 (280-497)	27 288 268 (21 576 010–33 443 826)	359 (284-441)
Incidence	184 947 (124 646–244 171)	37 (25–50)	309 286 (221 551 – 399 256)	35 (25–46)	2 470 759 (1 905 450-3 062 903)	33 (26-41)
YLDs	523 003 (259 741 – 908 273)	96 (48–166)	942 629 (528 597–1 512 164)	100 (57–160)	8561880 (5380607–12551498)	114 (72–166)
YLLs	258 546 (219 592-274 228)	44 (40-47)	536 505 (490 237–585 052)	58 (53–64)	6 232 066 (5709 753-7 289 706)	83 (76–97)
Migraine	1221.010	770	7 101 171	725	472.45200	507
DALYs	4231019 (2740462-6048715)	770 (495–1115)	7 401 471 (4 810 162–10 539 348)	735 (473–1056)	47 245 390 (29 986 692 – 68 669 318)	597 (378–866)
Prevalence	112 207 672 (104739 016-119 973 469)	20 646 (19 234–22 225)	195794407 (182677431-209186190)		1331364642 (1237219585-1433357249)	16 828 (15 638–18 119)
Incidence	7506784 (6829187-8173362)	1724 (1568-1883)	13 669 490 (12 467 555-14 861 052)	1641 (1493-1789)	112 933 549 (102 829 920-122 899 843)	1477 (1344–1607)
YLDs	4231019 (2740461-6048715)	770 (495–1115)	7 401 471 (4 810 162–10 539 348)	735 (473–1056)	47245391 (29986693–68669319)	597 (379–866)

cardiovascular diseases) and deaths (after cardiovascular diseases and cancer). These diseases comprised $13\cdot4\%$ ($10\cdot3-17\cdot1$) of global DALYs and $19\cdot5\%$ ($18\cdot0-21\cdot3$) 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 $13\cdot1\%$ ($12\cdot8-13\cdot15$) and the proportion of deaths was $19\cdot0\%$ ($19\cdot0-19\cdot1$). The percentage of DALYs attributable to neurological disorders was lowest in western Europe ($14\cdot0\%$ [$12\cdot7-15\cdot2$]) and highest in central Europe ($15\cdot1\%$ [$13\cdot9-16\cdot2$]). The proportion of

	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
(Continued from	n previous page)					
Tension-type h	eadache					
DALYs	600 667	101	1163732	110	7 096 415	90
	(343 433-936 239)	(57–159)	(664951-1799904)	(63-173)	(4 044 590-11 213 525)	(51-142)
Prevalence	173 696 347	30 871	309 890 284	31 022	2 331 334 677	29 810
	(158 485 543-190 762 959)	(28 014-33 930)	(281758 135-340 323 834)	(28 086-34 097)	(2 110 373 311-2 575 461 450)	(27 057-32 943)
Incidence	63 611 672	11725	114411512	11805	882 441 388	11 371
	(57 147 715-69 565 055)	(10 423–12 971)	(102667592-125554761)	(10490-13036)	(783 241 228-975 064 340)	(10 058–12 591)
YLDs	600 667	101	1163732	110	7 096 415	90
	(343 433-936 239)	(57-159)	(664951-1799904)	(63–173)	(4 044 591-11 213 526)	(51–143)
Other neurolog	jical disorders					
DALYs	363 480	65	599 059	63	3 965 609	53
	(314 552-426 877)	(54 - 79)	(517 397–698 284)	(54-76)	(3 265 588-4 845 474)	(43-65)
Deaths	10 303	1	14052	1	53 946	1
	(9219-10 814)	(1-1)	(12762-14637)	(1-1)	(51 552-59 030)	(1-1)
Prevalence	2613	0	4364	0	38 870	1
	(1736–3517)	(0-1)	(2939–5868)	(0-1)	(25 596-53 211)	(0-1)
Incidence		0 (0-0)		0 (0-0)		0 (0-0)
YLDs	112 433	23	206 737	24	1961790	27
	(68 271-174 266)	(13–37)	(130 672-304 277)	(15–36)	(1276347-2823819)	(17–38)
YLLs	251 047	42	392 321	40	2 00 3 820	27
	(232 719-264 643)	(39-45)	(369 776-410 145)	(37-42)	(1856 755-2 269 519)	(25–31)

Data are n (95% UI). DALYs=disability-adjusted life-years. EU28=the 27 EU countries plus the UK. YLDs=years lived with disability. YLLs= years of life lost. UI=uncertainty interval.

Table 1: Comparison of DALYs, deaths, prevalence, YLDs, and YLLs for the EU28, WHO European region, and globally for all neurological diseases and each subcategory separately in 2017

deaths attributable to neurological disorders was $21\cdot8\%$ ($21\cdot6-22\cdot1$) in eastern Europe, $22\cdot6\%$ ($22\cdot3-23\cdot0$) in central Europe, and $21\cdot46\%$ ($21\cdot2-21\cdot9$) in western Europe (appendix p 16).

Stroke (7.3 million [95% UI 6.7–7.9]; 35% [35–38), dementia (5·3 million [4·9-5·6]; 25% [23-28]), and headache (migraine and tension-type headache combined; 4.8 million [3.1-7.1]; 23% [19-29]) were, in decreasing order, the three commonest sources of DALYs in the EU28 (table 1; figure 1; appendix p 17). Stroke also was the leading source of burden attributable to neurological disorders in the WHO European region, accounting for the largest proportion of DALYs (18.3 million [17.9-19.7]; 45.6% [42.0-49.0]), followedby headache (8.6 million [5.4-12.6]; 20.6% [14.7-27.2]) and dementia (7.7 million, 7.1-8.3]; 18.7% [17.3-20.2]). In western Europe, the leading contributor was stroke (28% [$25 \cdot 5 - 31 \cdot 5$]; figure 1), which accounted for 4.7 million DALYs (4.4-5.0). Stroke also predominated in central Europe (55% [50 \cdot 3–59 \cdot 5]) with 3 \cdot 3 million DALYs $(3 \cdot 1 - 3 \cdot 5)$ and eastern Europe $(62\% [57 \cdot 3 - 66 \cdot 7])$ 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 $(12 \cdot 0 \text{ million } [9 \cdot 9 - 14 \cdot 5])$ than in men $(9 \cdot 1 \text{ million } [7 \cdot 6 - 10 \cdot 8])$. 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 burden was predominantly represented by dementia and stroke after age 70 years in both sexes, whereas stroke was the strongest contributor in those aged 40–89 years in central Europe and 50–89 years 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

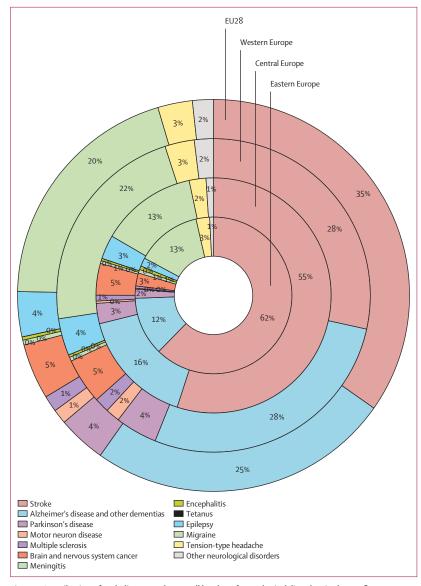


Figure 1: Contribution of each disease to the overall burden of neurological disorders in the EU28, western, central, and eastern Europe in 2017

Percentages represent proportion of DALYs. DALYs=disability-adjusted life-years. EU28=the 27 countries in the EU plus the UK.

table 2, and for global comparisons, in the appendix (p 19). In the EU28, dementia accounted for a 63% (95% UI 58 to 66) increase in DALYs and a 93% (88 to 97) increase in deaths. Similar changes were found for Parkinson's disease (61% increase [31 to 69]) and motor neuron disease (60% increase [49 to 69]), for which we found a 91% (75 to 102) increase in deaths. Modest increases in DALYs and other measures were observed for multiple sclerosis and, to a lesser extent, migraine and tension-type headache (appendix p 19). By contrast, a 30% decrease (–27 to –33) in stroke DALYs was observed despite a 25% (20 to 30) increase in prevalence and a 28% (22 to 34) increase in YLDs. A significant decrease in all measures

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 a 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, agestandardised 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 100 000 (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, but while the agestandardised 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 agestandardised rate of dementia was only 6% (-8 to -3; table 3). Epilepsy showed a 6% (-23 to 14) non-significant decrease in high-SDI countries and a 27% (-42 to -9) decrease in high-middle-SDI countries. Notably, the disease which showed the largest increase of prevalence and DALY rates, but only in high-SDI countries, was motor neuron disease (11% [6 to 16]). Parkinson's disease was next, showing a non-significant increase (6% [-16 to 11) in high-SDI countries but a significant decrease (-4% [-10 to 0) in high-middle SDI countries).

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

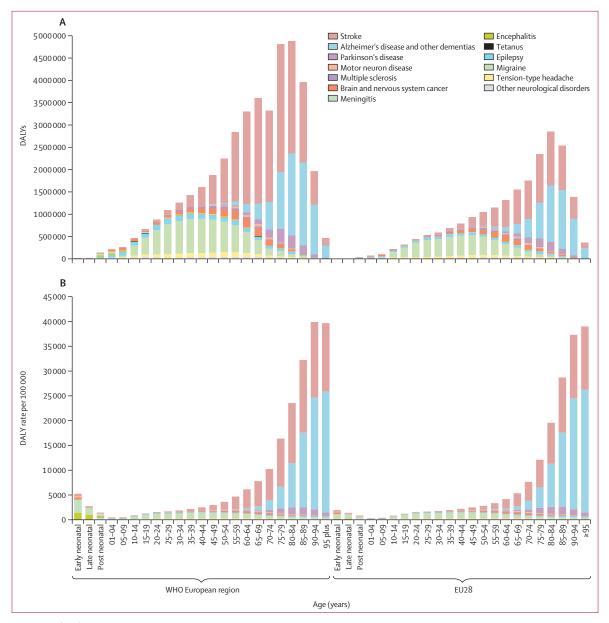


Figure 2: EU28 and WHO European region DALYs

Total number of DALYs (A) and age-standardised DALY rates (B) by age group including both sexes in 2017. DALYs=disability-adjusted life-years.

EU28=the 27 countries in the EU plus the UK.

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						WHO Europear	n region				
	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
Stroke												
DALYs	1489 (1434 to 1538)	691 (643 to 737)	-54% (-56 to -52)	10 446 307 (10 075 476 to 10 789 349)	7314978 (6833270 to 7768518)	-30% (-33 to -27)	2012 (1946 to 2075)	1198 (1136 to 1256)	-40% (-42 to -39)	21 991 312 (21 276 861 to 22 669 254)	18 831 007 (17 874 242 to 19 733 892)	-14% (-17 to -12)
Deaths	86 (85 to 87)	38 (37 to 40)	-57% (-58 to -54)	619 264 (611 400 to 627 766)	476 903 (463 602 to 504 651)	-23% (-25 to -19)	112 (111 to 113)	61 (60 to 63)	-45% (-47 to -44)	1207823 (1195003 to 1225524)	1078 620 (1058 760 to 1117 505)	-11% (-13 to -7)
Prevalence	1117 (1073 to 1167)	971 (921 to 1021)	-13% (-16 to -10)	7603547 (7294082 to 7947767)	9531098 (8958668 to 10024854)	25% (20 to 30)	1285 (1236 to 1345)	1196 (1129 to 1262)	-7% (-10 to -4)	13 870 323 (13 323 695 to 14 529 934)	18 254 959 (17 183 892 to 19 283 541)	32% (27 to 36)
YLDs	185 (135 to 232)	162 (118 to 204)	-13% (-16 to -9)	1266025 (925645 to 1584998)	1621402 (1191963 to 2036972)	28% (22 to 34)	229 (167 to 287)	215 (157 to 270)	-6% (-9 to -4)	2 475 049 (1797 028 to 3 105 300)	3304779 (2428732 to 4165663)	34% (29 to 38)
YLLs	1304 (1284 to 1321)	530 (516 to 552)	-59% (-61 to -58)	9 180 282 (9 044 047 to 9 307 537)	5 693 577 (5 543 620 to 5 958 058)	-38% (-40 to -35)	1783 (1761 to 1813)	983 (965 to 1016)	-45% (-46 to -43)	19516263 (19283622 to 19856420)	15 526 228 (15 235 982 to 16 036 397)	-20% (-22 to -18)
Alzheimer's	disease and ot	ther dementias	5									
DALYs	444 (416 to 473)	399 (372 to 427)	-10% (-12 to -8)	3 2 4 0 4 6 8 (3 0 3 8 7 8 9 to 3 4 5 3 5 5 2)	5 271 654 (4 915 486 to 5 641 197)	63% (58 to 66)	446 (418 to 476)	410 (383 to 438)	-8% (-10 to -7)	4774751 (4471802 to 5088817)	7 686 392 (7 175 157 to 8 205 020)	61% (58 to 63)
Deaths	38 (38 to 39)	35 (34 to 36)	-8% (-11 to -6)	260 244 (258 513 to 262 203)	501 678 (489 118 to 512 705)	93% (88 to 97)	38 (38 to 39)	36 (35 to 36)	-7% (-9 to -6)	376 119 (372 115 to 379 282)	700 353 (685 974 to 712 101)	86% (83 to 89)
Prevalence	654 (580 to 727)	594 (531 to 657)	-9% (-11 to -8)	4788372 (4216845 to 5360285)	7740 481 (6896 189 to 8583 917)	62% (57 to 67)	658 (580 to 734)	612 (541 to 681)	-7% (-8 to -6)	7 074 259 (6 222 667 to 7 942 113)	11 375 859 (10 038 137 to 12 683 497)	61% (57 to 65)
YLDs	97 (69 to 126)	88 (63 to 114)	-9% (-9 to -9)	706 265 (504 015 to 919 170)	1165391 (832669 to 1516059)	65% (59 to 71)	97 (69 to 126)	90 (64 to 118)	-7% (-8 to -5)	1033646 (741294 to 1345291)	1694270 (1209023 to 2212896)	64% (59 to 69)
YLLs	347 (345 to 349)	311 (301 to 320)	-10% (-13 to -9)	2 534 204 (2 517 343 to 2 553 205)	4106264 (3982651 to 4213014)	62% (57 to 66)	349 (346 to 352)	320 (312 to 327)	-8% (-10 to -7)	3741105 (3702678 to 3772727)	5 992 121 (5 844 318 to 6 113 018)	60% (57 to 63)
Parkinson's	disease											
DALYs	68 (63 to 82)	70 (63 to 78)	2% (-17 to 7)	522 267 (482 466 to 625 465)	839 916 (766 256 to 940 813)	61% (31 to 69)	69 (63 to 80)	70 (64 to 78)	2% (-10 to 5)	781347 (720120 to 908025)	1226579 (1126744 to 1363923)	57% (38 to 62)
Deaths	5 (4 to 6)	5 (4 to 5)	2% (-19 to 8)	34 236 (33 270 to 41 800)	60 812 (55 723 to 67 973)	78% (40 to 88)	4 (4 to 5)	5 (4 to 5)	2% (-13 to 6)	49 050 (47 428 to 57 737)	84599 (80948 to 93079)	72% (47 to 79)
Prevalence	94 (79 to 112)	105 (86 to 125)	11% (7 to 15)	704533 (584038 to 840424)	1 215 045 (996 237 to 1 457 870)	72% (65 to 80)	100 (82 to 119)	107 (88 to 128)	7% (5 to 10)	1 123 483 (925 451 to 1 344 223)	1838098 (1506704to 2220458)	64% (59 to 69)
YLDs	13 (9 to 18)	15 (10 to 20)	11% (7 to 16)	99 431 (68 796 to 134 551)	170 916 (117 642 to 233 979)	72% (64 to 80)	14 (10 to 19)	15 (10 to 21)	8% (5 to 11)	158 046 (107 768 to 215 467)	257 986 (178 581 to 354 467)	63% (57 to 69)
YLLs	55 (53 to 69)	55 (51 to 63)	-1% (-22 to 6)	422 835 (409 771 to 526 346)	669 000 (612 867 to 764 328)	58% (23 to 68)	55 (53 to 65)	55 (52 to 62)	0% (-14 to 4)	623 301 (601 534 to 744 574)	968593 (924800 to 1088287)	55% (33 to 62)
Motor neur												
DALYs	27 (26 to 29)	31 (29 to 32)	12% (4 to 20)	157 904 (151 812 to 164 075)	252 987 (240 153 to 264 173)	60% (49 to 69)	22 (19 to 26)	24 (23 to 26)	11% (-5 to 27)	203 830 (188 169 to 229 421)	314523 (298 988 to 348 088)	54% (38 to 75)
Deaths	1 (1 to 1)	1 (1 to 1)	29% (19 to 37)	6034 (5821 to 6282)	11 495 (10 900 to 12 020)	91% (75 to 102)	1 (1 to 1)	1 (1 to 1)	31% (20 to 43)	7 076 (6 773 to 7 536)	13 410 (12 728 to 14 790)	90% (76 to 103)
										(Tal	ble 2 continues o	n next page)

	EU28						WHO European region					
	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
(Continued	from previous p	age)										
Prevalence	4 (4 to 5)	6 (5 to 7)	42% (39 to 45)	23 986 (21 913 to 26 169)	42 937 (38 970 to 47 145)	79% (74 to 85)	3 (3 to 4)	4 (4 to 5)	35% (32 to 37)	30 603 (27 763 to 33 544)	51711 (46 991 to 56 707)	69% (64 to 74)
YLDs	1 (1 to 1)	1 (1 to 2)	42% (39 to 45)	5101 (3618 to 6809)	9131 (6492 to 12227)	79% (74 to 85)	1 (0 to 1)	1 (1 to 1)	35% (32 to 37)	6509 (4612 to 8693)	10 998 (7 822 to 14720)	69% (64 to 74)
YLLs	27 (25 to 28)	29 (28 to 31)	11% (3 to 19)	152 803 (146 985 to 158 391)	243 856 (231 168 to 254 703)	60% (48 to 69)	21 (19 to 25)	23 (22 to 25)	10% (-7 to 27)	197322 (181684 to 224050)	303 526 (287 735 to 337 104)	54% (37 to 75)
Multiple scl	erosis											
DALYs	39 (33 to 45)	39 (32 to 46)	0% (-16 to 12)	226 945 (195 825 to 260 163)	282765 (233418 to 328839)	25% (1 to 37)	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)
Deaths	1 (1 to 1)	1 (0 to 1)	-6% (-40 to 6)	4344 (3781 to 5021)	5601 (3954 to 6056)	29% (-21 to 41)	1 (1 to 1)	1 (0 to 1)	-11% (-35 to 8)	6104 (5202 to 6645)	7 413 (5673 to 8395)	21% (-14 to 43)
Prevalence	65 (59 to 71)	77 (69 to 85)	18% (16 to 21)	369 975 (336 977 to 407 130)	522 674 (473 413 to 579 422)	41% (39 to 44)	52 (47 to 58)	59 (53 to 65)	13% (11 to 14)	504 285 (457 958 to 555 895)	699 238 (635 288 to 772 355)	39% (37 to 41)
YLDs	17 (12 to 22)	20 (14 to 26)	18% (13 to 23)	94374 (67351 to 123083)	132 159 (95 038 to 171 558)	40% (34 to 46)	13 (10 to 18)	15 (11 to 20)	12% (9 to 16)	129 438 (92 358 to 168 926)	178 020 (127 760 to 230 616)	38% (33 to 42)
YLLs	22 (18 to 25)	19 (14 to 22)	-13% (-40 to 6)	132 570 (111 714 to 148 143)	150 607 (110 315 to 166 542)	14% (-25 to 34)	20 (16 to 21)	17 (14 to 20)	-16% (-34 to 10)	196 620 (162 235 to 206 779)	213 059 (169 517 to 254 322)	8% (-17 to 37)
Brain and n	ervous system	cancer										
DALYs	153 (136 to 171)	140 (117 to 153)	-9% (-28 to 5)	823 636 (748 909 to 932 285)	964 964 (789 495 to 1033 050)	17% (-11 to28)	158 (141 to 175)	147 (130 to 163)	-7% (-20 to 5)	1435491 (1289242 to 1584211)	1668047 (1439524 to 1799509)	16% (-1 to 28)
Deaths	4 (4 to 5)	4 (3 to 4)	2% (-25 to 9)	25 123 (23 238 to 28 753)	35 917 (27 137 to 38 316)	43% (0 to 54)	4 (4 to 4)	4 (3 to 4)	5% (-15 to 14)	39 568 (36 090 to 44 242)	56 246 (45 620 to 59 326)	42% (12 to 55)
Prevalence	24 (22 to 27)	55 (46 to 62)	127% (76 to 168)	126363 (114687 to 142588)	330 074 (270 005 to 360 630)	161% (98 to 192)	21 (19 to 24)	45 (40 to 52)	113% (76 to 150)	190 647 (174 163 to 212 101)	462 982 (398 536 to 511 728)	143% (97 to 176)
YLDs	3 (2 to 3)	5 (3 to 6)	84% (41 to 112)	13 971 (9 980 to 18 627)	30368 (21160 to 40887)	117% (61 to 142)	2 (2 to 3)	4 (3 to 5)	74% (43 to 101)	21 212 (15 112 to 28 018)	43 489 (31 024 to 57 873)	105% (64 to 128)
YLLs	150 (134 to 169)	135 (113 to 148)	-10% (-30 to 3)	809 666 (735 221 to 917 160)	934596 (766157 to 997931)	15% (-12 to 26)	156 (139 to 172)	143 (127 to 158)	-8% (-21 to 4)	1414279 (1271685 to 1561721)	1624558 (1404505 to 1753504)	15% (-2 to 27)
Meningitis												
DALYs	75 (71 to 81)	20 (18 to 24)	-74% (-76 to -69)	278 620 (261 680 to 296 452)	84 550 (77 767 to 97 340)	-70% (-72 to -65)	172 (115 to 203)	38 (35 to 43)	-78% (-81 to -64)	1182458 (811688 to 1378097)	288 614 (267 659 to 324 772)	-76% (-79 to -61)
Deaths	1 (1 to 1)	0 (0 to 0)	-74% (-76 to -69)	4937 (4360 to 5147)	2 033 (1 947 to 2 224)	-59% (-61 to -51)	2 (2 to 3)	1 (1 to 1)	-75% (-78 to -60)	16 633 (11721 to 18 979)	5 483 (5 253 to 6 125)	-67% (-71 to -50)
Prevalence	67 (59 to 76)	33 (28 to 39)	-51% (-54 to -47)	336120 (292854to 384061)	183 151 (153 769 to 216 836)	-46% (-50 to -41)	98 (85 to 112)	53 (45 to 62)	-46% (-49 to -42)	857183 (742594 to 983424)	505 430 (430 502 to 591790)	-41% (-45 to -37)
YLDs	7 (5 to 9)	3 (2 to 5)	-49% (-52 to -46)	31197 (21873 to 41791)	17 079 (12 032 to 22 999)	-45% (-49 to -42)	9 (6 to 12)	5 (4 to 7)	-44% (-46 to -41)	76 367 (53 464 to 102 765)	45 301 (31 738 to 60 745)	-41% (-43 to -38)
										(Ta	ble 2 continues o	on next page)

	EU28						WHO European	n region				
	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
(Continued	from previous p	page)										
YLLs	69 (65 to 75)	16 (15 to 20)	-76% (-79 to -71)	247 423 (231 164 to 263 632)	67 471 (64 007 to 80 231)	-73% (-75 to -67)	163 (107 to 193)	33 (31 to 39)	-80% (-83 to -66)	1106 091 (733 867 to 1300 227)	243313 (230129 to 280048)	-78% (-81 to -64)
Encephaliti												
DALYs	20 (14 to 21)	11 (10 to 12)	-44% (-50 to -16)	81788 (62092 to 87719)	57720 (50302 to 63183)	-29% (-36 to -6)	42 (38 to 48)	34 (30 to 38)	-19% (-34 to -4)	321230 (291041 to 359673)	270736 (236953 to 292768)	-16% (-29 to -4)
Deaths	0 (0 to 0)	0 (0 to 0)	-30% (-36 to -9)	1581 (1338 to 1648)	1729 (1437 to 1829)	9% (1 to 24)	1 (1 to 1)	1 (0 to 1)	-11% (-24 to -2)	5 433 (4 981 to 5 885)	5 953 (4 931 to 6 266)	10% (-5 to 17)
Prevalence	26 (14 to 41)	22 (12 to 35)	-16% (-18 to -15)	141 844 (76 154 to 230 446)	142 435 (74 374 to 234 773)	0% (-2 to 3)	34 (19 to 53)	29 (17 to 46)	-14% (-15 to -13)	311 615 (175 514 to 494 479)	315 202 (173 810 to 507 091)	1% (-1 to 3)
YLDs	2 (1 to 3)	2 (1 to 2)	-18% (-20 to -17)	9 989 (6 836 to 13 303)	9372 (6386 to 12593)	-6% (-8 to -4)	3 (2 to 4)	2 (2 to 3)	-15% (-17 to -14)	23 932 (16 651 to 31792)	22773 (15651 to 30309)	-5% (-7 to -3)
YLLs	18 (12 to 19)	10 (8 to 11)	-47% (-53 to -15)	71799 (52152 to 76731)	48348 (41387 to 51476)	-33% (-39 to -6)	40 (36 to 46)	32 (28 to 36)	-19% (-35 to -4)	297298 (266649 to 334872)	247 963 (214 185 to 269 172)	-17% (-30 to -4)
Tetanus												
DALYs	1 (1 to 1)	0 (0 to 0)	-90% (-92 to -88)	4809 (3793 to 5134)	649 (558 to 755)	-86% (-88 to -84)	11 (4 to 26)	0 (0 to 0)	-98% (-99 to -95)	69 067 (28 864 to 158 779)	2127 (1860 to 2770)	-97% (-99 to -93)
Deaths	0 (0 to 0)	0 (0 to 0)	-90% (-91 to -88)	240 (197 to 256)	39 (33 to 46)	-84% (-86 to -81)	0 (0 to 0)	0 (0 to 0)	-96% (-98 to -92)	1066 (612 to 2088)	82 (72 to 100)	-92% (-96 to -87)
Prevalence	0 (0 to 0)	0 (0 to 0)	-88% (-90 to -85)	26 (20 to 30)	4 (3 to 5)	-83% (-85 to -80)	0 (0 to 0)	0 (0 to 0)	-33% (-55 to -11)	214 (166 to 296)	160 (133 to 187)	-25% (-46 to -7)
YLDs	0 (0 to 0)	0 (0 to 0)	-90% (-91 to -88)	3 (2 to 5)	1 (0 to 1)	-85% (-87 to -82)	0 (0 to 0)	0 (0 to 0)	-77% (-88 to -58)	15 (8 to 28)	4 (3 to 7)	-72% (-84 to -54)
YLLs	1 (1 to 1)	0 (0 to 0)	-90% (-92 to -88)	4806 (3790 to 5131)	649 (558 to 754)	-86% (-88 to -84)	11 (4 to 26)	0 (0 to 0)	-98% (-99 to -95)	69 051 (28 852 to 158 748)	2122 (1856 to 2765)	-97% (-99 to -93)
Epilepsy												
DALYs	149 (105 to 208)	140 (90 to 211)	-7% (-30 to 24)	735793 (514 448 to 1023 814)	781549 (512458 to 1168 936)	6% (-20 to 41)	179 (137 to 235)	158 (113 to 220)	-12% (-29 to 9)	1507756 (1145663 to 1988615)	1 479 134 (1 063 428 to 2 050 641)	-2% (-21 to 21)
Deaths	1 (1 to 1)	1 (1 to 1)	3% (-28 to 11)	6223 (6106 to 6782)	9 526 (7286 to 10 097)	53% (3 to 64)	1 (1 to 2)	1 (1 to 1)	-8% (-26 to 8)	12 528 (11 675 to 13 504)	15 370 (12 663 to 16 443)	23% (-4 to 38)
Prevalence	358 (241 to 470)	399 (266 to 529)	11% (–19 to 50)	1794858 (1198133 to 2356841)	2 244 668 (1 496 976 to 2 977 225)	25% (-9 to 69)	352 (259 to 453)	385 (280 to 497)	9% (-15 to 35)	3 082 147 (2 254 550 to 3 960 937)	3742828 (2718716 to 4823770)	21% (-6 to 50)
YLDs	98 (53 to 156)	96 (48 to 166)	-2% (-37 to 49)	482 243 (264 069 to 770 314)	523 003 (259 741 to 908 273)	8% (-31 to 64)	104 (63 to 159)	100 (57 to 160)	-3% (-32 to 30)	894217 (541420 to 1373670)	942 629 (528 597 to 1 512 164)	5% (-25 to 44)
YLLs	52 (51 to 59)	44 (40 to 47)	-15% (-40 to -8)	253 550 (247 508 to 285 858)	258 546 (219 592 to 274 228)	2% (-30 to 10)	75 (65 to 84)	58 (53 to 64)	-23% (-35 to -4)	613 539 (549 291 to 680 608)	536 505 (490 237 to 585 052)	-13% (-28 to 5)
Migraine												
DALYs	763 (491 to 1106)	770 (495 to 1115)	1% (0 to 2)	3 947 343 (2 552 335 to 5 707 835)	4231019 (2740462 to 6048715)	7% (5 to 9)	737 (475 to 1059)	735 (473 to 1056)	0% (-1 to 1)	6702168 (4320439 to 9679278)	7401471 (4810162 to 10539348)	10% (9 to 12)
										(Ta	ble 2 continues c	on next page)

	EU28						WHO Europea					
	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
(Continued	from previous p	page)										
Prevalence	20543 (19061to 22105)	20646 (19234to 22225)	0% (0 to 1)	105746319 (98488927to 113530086)	112207672 (104739016 to 119973469)	6% (4to 8)	19697 (18304to 21171)	19650 (18270 to 21082)	0% (-1 to 1)	178317032 (166023492 to 191281010)	195794407 (182677431to 209186190)	10% (8 to 11)
YLDs	763 (491to1106)	770 (495 to 1115)	1% (0 to 2)	3947343 (2552335 to 5707835)	4231019 (2740462 to 6048715)	7% (5 to 9)	737 (475 to 1059)	735 (473 to 1056)	0% (-1 to 1)	6702168 (4320439to 9679278)	7401471 (4810162 to 10539348)	10% (9 to 12)
Tension-typ	e headache											
DALYs	102 (58 to 160)	101 (57 to 159)	0% (-2 to 1)	542038 (309633 to 850297)	600667 (343433 to 936239)	11% (8 to 14)	113 (64 to 176)	110 (63 to 173)	-2% (-3 to -1)	1043015 (596692 to 1625120)	1163732 (664951to 1799904)	12% (9 to 14)
Prevalence	31256 (28329to 34499)	30871 (28014to 33930)	-1% (-2 to 0)	162144987 (147265221to 178088317)	173696347 (158485543 to 190762959)	7% (5to10)	31858 (28899 to 35154)	31022 (28086 to 34097)	-3% (-3 to -2)	287861348 (261220814to 316795771)	309890284 (281758135 to 340323834)	8% (6to 10)
YLDs	102 (58 to 160)	101 (57 to 159)	0% (-2 to 1)	542038 (309633 to 850297)	600667 (343433 to 936239)	11% (8 to 14)	113 (64 to 176)	110 (63 to 173)	-2% (-3 to -1)	1043015 (596692 to 1625120)	1163732 (664951to 1799904)	12% (9 to 14)
Other neuro	ological disord	ers										
DALYs	66 (57to76)	65 (54to79)	-1% (-16 to 16)	313735 (277741to 360083)	363480 (314552 to 426877)	16% (3 to 30)	64 (55 to 75)	63 (54to76)	-1% (-14 to 15)	531078 (460688to 617442)	599059 (517397to 698284)	13% (0 to 28)
Deaths	1 (1to1)	1 (1 to 1)	-2% (-11 to 6)	7205 (6931 to 7450)	10303 (9219 to 10814)	43% (26 to 52)	1 (1 to 1)	1 (1 to 1)	1% (-8 to 10)	9941 (9424to 10402)	14052 (12762 to 14637)	41% (26 to 52)
Prevalence	0 (0 to 1)	0 (0 to 1)	7% (4 to 11)	2067 (1372 to 2855)	2613 (1736 to 3517)	26% (20 to 34)	0 (0 to 1)	0 (0 to 1)	4% (2 to 6)	3674 (2440 to 5020)	4364 (2939 to 5868)	19% (13 to 26)
YLDs	18 (11 to 28)	23 (13 to 37)	28% (-8 to 76)	84916 (54641to 126893)	112433 (68271to 174266)	32% (0to76)	19 (12 to 28)	24 (15to36)	24% (-6 to 61)	159965 (104111to 235740)	206737 (130672to 304277)	29% (1to 63)
YLLs	48 (45 to 52)	42 (39 to 44)	-12% (-24to-3)	228818 (218306 to 242385)	251047 (232719 to 264643)	10% (-2 to 20)	45 (39 to 50)	40 (37 to 42)	-12% (-24 to 3)	371114 (333652 to 403551)	392321 (369776 to 410145)	6% (-6 to 20)

Table 2: DALYs, death, prevalence, YLDs, YLLs, and rates of neurological disorders by category in the EU28 and WHO European region, with changes from 1990 to 2017

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 ageing-related diseases.¹⁰ Population growth could also be implicated. The total population of Europe was 721 million in 1990 and rose to 916 million by 2016.¹¹

While the substantial sex differences observed in the burden of neurological disorders reflect the differing distribution of each clinical condition in men and women, the increasing number of DALYs attributable to the most common clinical conditions with age is most likely linked with the ageing of the European population. The peak of DALYs observed in the oldest age groups reflects the predominance of ageing-related diseases in these older age groups. The predominance of dementia

in the oldest groups in the EU28 and in western Europe can be similarly explained.

Stroke, migraine, and dementia were the major contributors to the overall burden of 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

	1000	2017	Classia	1000	2017	Charan
	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 11)	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)	550 (350 to 800)	552 (351 to 804)	0% (-1 to 2)
Tension-type headache	93 (53 to 147)	93 (53 to 148)	0% (-1 to 1)	97 (55 to 151)	92 (52 to 145)	-5% (-6 to -3)
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 % (9	95% UI). DALY=disability-a	djusted life-year. EU2	8=the 27 EU countries p	lus the UK. SDI=socio-dem	ographic index. UI=uncert	ainty interval.

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.12 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. 13-16 Stroke unit care and thrombolysis have been proposed to have a role in ameliorating the outcome of ischaemic stroke17 and can explain the significant reduction in deaths and DALYs per patient. In the USA, the rate of use of r-TPA began to increase in 2001 and progressed steadily in the subsequent years.18 Similar trends are most likely present in Europe.

The increasing burden of Alzheimer's disease and other dementias observed since 1990 is in line with

increases in life expectancy, with burden increasing most rapidly in the population aged 60 years or older due to increasing longevity and declining birth rates.¹⁹

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 USA²³ and by an online European survey that found that 40% of respondents had never seen a Parkinson's disease specialist. 24,25

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 2016,²⁶ 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

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 of 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, ³⁰ 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.^{31,32}

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. 7.33 Third, the 95% UIs 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,³⁴ essential tremor,³⁵ or restless legs syndrome.³⁶

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 Neuromodulation, 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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References

- WHO. Neurological disorders. Public health challenges. Geneva: World Health Organization, 2006.
- 2 GBD 2015 Neurological Disorders Collaborator Group. Global, regional, and national burden of neurological disorders during 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Neurol* 2017; 16: 877-97.
- 3 Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL, eds. Global Burden of Disease and Risk Factors. Washington (DC): The International Bank for Reconstruction and Development/The World Bank and New York: Oxford University Press, 2006.
- 4 Lopez AD MC, Ezzati M, Jamison DT, Murray CLJ. Global Burden of disease and risk factors. Washington DC: The International Bank for Reconstruction and Development/The World Bank; New York: Oxford University Press, 2006.

- 5 GBD 2017 Population and Fertility Collaborators. Population and fertility by age and sex for 195 countries and territories, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; 392: 1995–2051.
- 6 GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; 390: 1151–210.
- 7 Salomon JA, Haagsma JA, Davis A, et al. Disability weights for the global burden of disease 2013 study. *Lancet Gliobal Health* 2015; 3: e712-23
- 8 Institute for Health Metrics and Evaluation. Global health data exchange. Seattle: University of Washington, 2016.
- 9 GBD 2017 Childhood Cancer Collaborators. The global burden of childhood and adolescent cancer in 2017: an analysis of the Global Burden of Disease Study 2017. Lancet Oncol 2019; 20: 1211–25.
- 10 Sorensen HT. Global burden of neurological disorders: challenges and opportunities with the available data. *Lancet Neurol* 2019; 18: 420–21.
- 11 Chow CK, Teo KK, Rangarajan S, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. *JAMA* 2013; 310: 959–68.
- 12 Feigin VL, Roth GA, Naghavi M, et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol* 2016; 15: 913–24.
- 13 Farzadfar F, Finucane MM, Danaei G, et al. National, regional, and global trends in serum total cholesterol since 1980: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3-0 million participants. *Lancet* 2011: 377: 578–86.
- Danaei G, Finucane MM, Lin JK, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. *Lancet* 2011; 377: 568–77.
- Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2·7 million participants. Lancet 2011; 378: 31–40.
- Finucane MM, Stevens GA, Cowan MJ, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9 · 1 million participants. Lancet 2011; 377: 557.
- Wardlaw JM, Murray V, Berge E, del Zoppo GJ. Thrombolysis for acute ischaemic stroke. Cochrane Database Syst Rev 2014; CD000213.
- 18 Kleindorfer D, de los Rios La Rosa F, Khatri P, Kissela B, Mackey J, Adeoye O. Temporal trends in acute stroke management. Stroke 2013; 44 (6 suppl 1): S129–31.
- 19 Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. Alzheimers Dement 2013; 9: 63–75.e2.
- 20 Collaborators GBDPsD. Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2018; 17: 039–53
- 21 Dorsey ER, Bloem BR. The Parkinson pandemic—a call to action. [AMA Neurol 2018; 75: 9–10.
- 22 Gunnarsson LG, Bodin L. Occupational exposures and neurodegenerative diseases—a systematic literature review and meta-analyses. *Int J Environ Res Public Health* 2019; 16: 337–53.
- 23 Willis AW SM, Evanoff BA, Perlmutter IS, Racette BA. Neurologist care in Parkinson disease: a utilization, outcome and survival study. 2011; 77: 851–57.
- 24 Schrag A, Khan K, Hotham S, Merritt R, Rascol O, Graham L. Experience of care for Parkinson's disease in European countries: a survey by the European Parkinson's Disease Association. Eur J Neurol 2018; 25: 1410–120.
- Willis AW, Schootman M, Evanoff BA, Perlmutter JS, Racette BA. Neurologist care in Parkinson disease: a utilization, outcomes, and survival study. Neurology 2011; 77: 851–57.

- 26 GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2018; 17: 954–76.
- 27 Forsgren L, Beghi E, Oun A, Sillanpaa M. The epidemiology of epilepsy in Europe—a systematic review. Eur J Neurol 2005; 12: 245–53.
- 28 Brownlee WJ, Hardy TA, Fazekas F, Miller DH. Diagnosis of multiple sclerosis: progress and challenges. *Lancet* 2017; 389: 1336–46.
- Comi G, Radaelli M, Soelberg Sorensen P. Evolving concepts in the treatment of relapsing multiple sclerosis. *Lancet* 2017; 389: 1347–56.
- 30 GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388: 1545–602.
- 31 Yang M, Guo W, Yang C, et al. Mobile phone use and glioma risk: a systematic review and meta-analysis. *PLoS One* 2017; **12**: e0175136.

- 32 Zumel-Marne A, Castano-Vinyals G, Kundi M, Alguacil J, Cardis E. Environmental factors and the risk of brain tumours in young people: a systematic review. *Neuroepidemiology* 2019; 53: 121–41.
- 33 GBD 2015 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388: 1603–58.
- 34 Lubetkin EI, Jia H. Burden of disease due to sleep duration and sleep problems in the elderly. Sleep Health 2018; 4: 182–87.
- 35 Hopfner F, Hoglinger GU, Kuhlenbaumer G, et al. Beta-adrenoreceptors and the risk of Parkinson's disease. Lancet Neurol 2020; 19: 247–54.
- 36 Innes KE, Selfe TK, Agarwal P. Prevalence of restless legs syndrome in North American and western European populations: a systematic review. Sleep Med 2011; 12: 623–34.