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1 **Title: The Burden of Stroke in Europe: An analysis of the Global Burden of Disease study**
2 **findings from 2010 to 2019**

3

4 From Carlota F. Prendes^{1*}, GBD 2019 Europe Stroke Collaborators

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23 **ABSTRACT (max. 300 words)**

24 **Background:** While most European Regions perform well in global comparisons, large
25 discrepancies within stroke epidemiological parameters exist across Europe. The objective of
26 this analysis was to evaluate stroke burden across European regions and countries in 2019,
27 and its difference to 2010.

28 **Methods:** GBD 2019 analytical tools were used to evaluate regional and country-specific
29 estimates of incidence, prevalence, deaths and disability-adjusted life-years (DALYs) of
30 stroke for the 53 countries making up the WHO European Region (EU-53) and for EU-28,
31 between 2010 and 2019. Results were analysed at a regional, subregional and country level.

32 **Results:** In EU-53, the absolute number of incident and prevalent strokes increased by 2%
33 (UI, 0 to 4%), from 1,767,280 to 1,802,559, and by 4% (UI, 3 to 5%) between 2010 and 2019,
34 from 10,731,496 to 11,245,368, respectively. While the absolute number of incident strokes
35 remained stable in EU-28, the absolute number of prevalent strokes and stroke-related deaths
36 increased by 4% (UI, 2 to 5%), from 5,775,590 to 5,989,161, and by 7%, from 354,658 to
37 370,467 (UI, 2 to 12%), respectively. All-stroke age-standardized mortality rates, however,
38 decreased by 18% (UI, -22 to -14%), from 82 to 67/100,000 people in EU-53, and by 15%
39 (UI, -18 to -11%), from 49.3 to 42.0/100,000 people, in EU-28. Despite most countries
40 presenting age-adjusted incidence, prevalence, mortality and DALY rate reductions, these
41 were 1.4x, 1.2x, 1.6x and 1.7x higher in EU-53 in comparison to EU-28. There was
42 significant variation between countries, with the largest discrepancies observed across age-
43 standardized death rates (e.g. 206.6/100,000 in Montenegro versus 21.8/100,000 in
44 Switzerland).

45 **Conclusion:** EU-53 showed a 2% increase in incident strokes, while they remained stable in
46 EU-28. Age-standardized rates were consistently lower for all stroke-burden parameters in

47 EU-28 in comparison to EU-53, and huge discrepancies in incidence, prevalence, mortality
48 and DALY rates were observed between individual countries.

49

50 **Funding:** Bill & Melinda Gates Foundation

51 **Introduction**

52 Although substantial efforts have been made in primary stroke prevention, treatment
53 and tertiary prevention strategies, stroke remains the second-leading cause of death and third-
54 leading cause of burden of disease worldwide (1). The Global Burden of Disease, Injuries,
55 and Risk Factors Study (GBD) 2019 stroke analysis reported a sharp decrease in age-
56 standardised stroke mortality rates between 1990 to 2019 (2). However, despite reductions in
57 age-standardised rates, absolute numbers of incident, prevalent and mortality cases secondary
58 to strokes have increased by 70%, 85% and by 43%, between 1990 and 2019 worldwide (2).

59 In the European Union, stroke is the second most frequent cause of death and the
60 leading cause of adult disability, with thirty-year projections of absolute numbers of
61 incidence, prevalence, deaths and DALYs estimating a 27% increase by 2047 (3). In 2006, the
62 Helsingborg Declaration on European Stroke Strategies was adopted (4). One of their aims
63 was for all stroke patients in Europe to have access to a stroke unit by 2015, however, the
64 2020 Stroke Alliance for Europe Report found that only 30% of stroke patients across Europe
65 currently have access to acute stroke unit care (4,5,6). They also found high discrepancies in
66 stroke burden exist across Europe, with age-standardized death rates in Bulgaria, Romania,
67 Serbia, Latvia, Lithuania, Croatia, Hungary, and Slovakia 7x times higher than in France,
68 Spain, Luxembourg, Austria, and Belgium (6).

69 The European Stroke Organisation (ESO) and the Stroke Alliance for Europe (SAFE)
70 created the European Stroke Action Plan (ESAP) for the years 2018 to 2030 (7,8). Their
71 pursued targets for 2030 are *i*) reduction of absolute number of strokes in Europe by 10%, *ii*)

72 treatment of at least 90% of stroke patients in dedicated stroke units as the first level of care,
73 *iii*) implementation of national plans for stroke management, and *iv*) implementation of
74 national strategies for multisector public health interventions (7). Implementation of ESO
75 guidelines and 2018-2030 ESAP strategies across all European countries could lead to
76 standardization of stroke care across Europe, improving and homogenising the burden of
77 stroke across different European countries (7-10). However, studies analysing the burden of
78 stroke throughout Europe, considering both the European Union (EU-28), as well as Europe
79 according to the 2019 World Health Organisation definition (EU-53) are lacking.

80 The aim of this study was to compare the burden of stroke during the last 10 years in
81 EU-28 (the 27 member countries of the EU plus the UK) and in EU-53, including a regional
82 and country-specific analysis.

83

84 **Methods**

85 *Global Burden of Disease 2019*: The GBD 2019 study effort has quantified the
86 burden of 369 diseases and injuries in 204 countries and territories worldwide, analysing data
87 from 3686 vital registration sources, 147 verbal autopsy sources, 368 incidence sources, 117
88 prevalence sources, 229 excess mortality sources, 7753 risk factor exposure sources, and 2733
89 risk factor relative risk sources (see <http://ghdx.healthdata.org/> for further details) (1, 11-16). It
90 is a landmark effort, updated annually, designed to allow for consistent comparison over time
91 starting from 1990 to 2019, by age and sex, socio-demographic index, World Bank country
92 income, and across locations. (1,11) It produces standard epidemiological measures such as
93 incidence, prevalence, and death rates as well as summary measures of health, including
94 DALYs (1, 11), reported in compliance with Guidelines for Accurate and Transparent Health
95 Estimates Reporting (GATHER) guidelines (17). All of their results are publically available,
96 and can be found using the GBD Results Tool and GBD Compare website (1, 10, 11).

97 The GBD classifies causes into four levels, from the broadest (Level 1; eg, non-
98 communicable diseases), to the most specific (Level 4; eg, ischaemic stroke [IS]). Stroke is
99 categorized as a level 3 cause, and has 3 level 4 subtypes. Definitions and International
100 Classification of Diseases codes used categorization are described in **Supplementary Table 1**
101 (18, 19). Vital registration and verbal autopsy data are used as inputs into the Cause of Death
102 Ensemble modelling (CODEm) framework to estimate deaths due to stroke and stroke
103 subtypes (1,2). CODEm is a flexible modelling tool that utilises geospatial relationships and
104 information from covariates to produce estimates of death for all locations across the time
105 series (1990–2019). Deaths from vital registration systems coded to impossible or
106 intermediate causes of death or unspecified stroke are reassigned using statistical methods
107 (1,2,20,21). Methods used for assigning cause of death to stroke and stroke subtypes in
108 regions where neuroimaging is not available have been previously described in detail (1,11-
109 13).

110 ***Study Design:*** This study has analysed the burden of stroke using GBD data for all
111 countries included in EU-53 (WHO definition of Europe), its three subregions (Central,
112 Eastern and Western Europe), EU-28 (countries included in the European Union in 2019 plus
113 the United Kingdom) and all 53 individual countries making up EU-53 for both 2019 and
114 2010 (**Supplementary Table 2**). Epidemiological estimates for incidence, prevalence, deaths,
115 DALYs, YYLs and YLD for *i*) all stroke, *ii*) ischemic stroke (IS), *iii*) intracerebral
116 haemorrhage (ICH) and *iv*) subarachnoid haemorrhage (SAH) were calculated and analysed.
117 Standard life expectancy of the individual countries has been obtained using the lowest
118 observed age-specific rates of mortality among populations in the world greater than 5
119 million. (1, 16, 20, 21) Absolute numbers, age-standardized rates per 100,000
120 population/year, age-standardized rates by gender, rates for the population under the age of 70
121 years of age and for the population ≥ 70 years of age (70+) for incidence, prevalence, death
122 and DALYs for the years 2010 and 2019 have been presented, as well as the difference

123 between 2010 to 2019, given as percentage. Stroke-deaths attributable to risk factors for
124 countries included in EU-53 and EU-28 were extracted from the GBD results tool and
125 provided for both 2010 and 2019 in visual form. The exact methodology of how this was
126 performed has been explained in detail previously (22). All estimates are given with a 95%
127 uncertainty interval (UI), derived from the 25th and 975th ordinals of 1000 draws of the
128 posterior distribution at each step of the burden estimation process (1). An increase in the
129 absolute number or rate from 2010 to 2019 has been defined as a positive change between
130 2010 and 2019, wherein 0 can be in the limits of the UI interval, but cannot be included inside
131 the UI interval (ie. [UI, 0 to +13%] has been considered a significant increase, but [UI, -3 to
132 +13%] would not be considered a significant increase). Similarly, a decrease in the absolute
133 number or rate between 2010 and 2019 is considered as any negative change between 2010
134 and 2019, in which the UI does not cross the zero line. Negative changes between 2010 and
135 2019 have been represented throughout the tables with a (-) sign.

136

137 **Results**

138 **1. Incidence (Figure 1)**

139 - **EU-53:** There was a 2% (95% UI, 0 to 4%) increase in the total number of incident strokes
140 between 2010 and 2019, from 1,767,280 to 1,802,560 total incident strokes in 2019, 70% of
141 which were attributable to IS (**Figure 1A, Supplementary Table 3**). Absolute numbers of IS
142 and SAH increased by 3%, while ICH decreased by 4% (**Supplementary Table 4**). Age-
143 adjusted incidence rates, however, decreased by 10% (UI, -12 to -8%) from 132.3 to 118.7 per
144 100,000 people, with consistent reductions in all stroke subtypes (**Figure 1B**). Despite a
145 higher total number of incident strokes in women (1,029,427 vs. 773,133 in men, 2019), both
146 genders presented similar age-adjusted incidence rates (116.9 in women vs. 118.8 in men, per
147 100,000, 2019) (**Figures 1A and 1B**). Between 2010 and 2019, all EU-53 countries showed

148 either stability or reduction of age-standardized incidence rates, with the largest reductions
149 observed in Norway, Austria and Israel (**Figure 1C**). The lowest age-standardized incidence
150 rate was observed in Switzerland, with 58.9 new cases per 100,000 (**Figure 1D**). Other
151 countries with incidence rates under 65 included Ireland, France, Luxembourg and the UK.
152 Overall, however, there were large discrepancies, with multiple countries presenting incidence
153 rates higher than 230 per 100,000, including Turkmenistan, Montenegro and Bulgaria. Of EU-
154 53 countries, Northern Macedonia presented the highest age-adjusted incidence rate, at 259.3
155 per 100,000, 4.4x times higher than Switzerland (**Figure 1D**). An 8% (UI, -11 to -5%)
156 reduction in incidence rates was observed in the population 70+, whilst remaining stable in
157 those < 70 (**Figure 1E**). Finally, when analysing EU-53 by subregions, Eastern Europe
158 reported the highest absolute number of incident strokes (629,928), followed by Western and
159 Central Europe, with stable rates between 2010 and 2019 in all subregions (**Supplementary**
160 **Table 5**). Age-standardized incidence rates, however, decreased consistently across all
161 subregions (**Figure 1F**), except for those <70 in Eastern and Central Europe, where they
162 remained stable. The highest age-standardised incidence rate was observed in Eastern Europe,
163 which was 2.75x higher than in Western Europe, despite all subregions presenting significant
164 rate reductions over the last 10 years.

165

166 - **EU-28**: In contrast to EU-53, the absolute number of incident strokes in EU-28 remained
167 stable during this period (**Figure 1A**), with a total of 844,239 incident strokes in 2019. Age-
168 adjusted incidence rates for all-stroke decreased by 12% (UI, -14 to -10%) between 2010 and
169 2019, from 95.4 to 83.9 per 100,000. In 2019, these were 0.71x lower in EU-28 in comparison
170 to EU-53 (**Figure 1C**). In EU-28, age-standardized rates for women and men showed an
171 11% (UI, -14 to -8%) and a 13% (UI, -16 to -11%) reduction for all-stroke. In contrast to EU-
172 53, all-stroke in EU-28 showed a reduction of rates not only for the 70+ population (-11
173 reduction, UI -14 to -7), but also for the population < 70 (-3% reduction, UI -7 to 0%) (**Figure**

174 **1E**). Except Switzerland, countries presenting lowest incidence rates were part of EU-28. In
175 EU-28, countries with the highest age-standardized incidence rates were Bulgaria, with
176 236.24 new cases per 100,000, Romania (184.4) and Latvia (183.6) (**Figure 2**).

177

178

179 **2. Prevalence (Figure 3):**

180 - **EU-53**: The total number of prevalent strokes increased by 4% (UI, 3 to 5%) between 2010
181 and 2019, from 13,701,815 to 14,261,365 total prevalent cases in 2019 (**Figure 3A**). Ischemic
182 strokes accounted for 78.9% of prevalent strokes, while ICH accounted for 14.4% and SAH
183 for 10.6%. The largest increase in absolute prevalence numbers was observed for IS
184 (**Supplementary Table 4**). Age-adjusted prevalence rates, however, decreased by 6% (UI, -7
185 to -5%) for all-stroke between 2010 and 2019, from 1,056 to 989 per 100,000 people, a
186 decrease that was consistent for all stroke subtypes and for both men and women (**Figure 3B**).
187 Women presented both significantly larger absolute prevalence numbers, but also 1.2 - 1.3x
188 higher age-adjusted prevalence rates for all-stroke (1,067.6 vs 899.2), IS (831.6 vs 689.6), and
189 for SAH (129.8 vs 97.2). All EU-53 countries showed either stability or reduction of the age-
190 standardized prevalence rates, with the most significant reductions between 2010 and 2019
191 observed in Denmark, Kyrgyzstan and Kazakhstan (**Figure 3C**). Switzerland presented the
192 lowest age-standardized prevalence rate in 2019, with 608 prevalent cases / 100,000 people.
193 Other countries with age-standardized prevalence rates below 650 were Italy, France and
194 Ireland. In contrast, Northern Macedonia and Bulgaria had the highest age-adjusted
195 prevalence rates, both over 1,600 per 100,000 people (**Figure 3D**). Stroke prevalent cases in
196 the population 70+ showed an 8% (UI, -10 to -6%) decrease. However, in the population <70,
197 in contrast to incidence rates, they increased by 4% (UI, 2 to 5%) (**Figure 3E**). Finally, when
198 analysing EU-53 by subregions, absolute prevalence numbers increased in Western and

199 Central Europe, while remaining stable in Eastern Europe. Overall, age-standardized
200 prevalence rates decreased for all subgroups (**Figure 3F**). However, there was a 4 and 5%
201 increase in age-standardized prevalence rates for the population <70 in Eastern and Central
202 Europe. The highest age-standardised prevalence rate was observed in Eastern Europe, which
203 was 1.89x higher than in Western Europe.

204 - **EU-28**: The absolute prevalence also increased by 4% (UI, 2 - 5%) between 2010-2019,
205 from 7,099,527 to 7,350,739 prevalent cases in 2019 (**Figure 3A**). IS and SAH absolute
206 prevalent cases increased by 4% (UI, 2-6%) and 6% (UI, 4 – 8%), respectively, while ICH
207 cases decreased by -2% (UI, -3 – 0%). Age-standardized prevalence rates, however, decreased
208 by 6% (UI, -8 to -5), from 848 to 795 per 100,000 (**Figure 3B**). Although both EU-53 and
209 EU-28 showed significant decreases in age-standardised prevalence rates, these were 0.80x,
210 0.82x, 0.68x and 0.87x times lower for all-stroke, IS, ICH and SAH in EU-28. Similar to EU-
211 53, prevalent cases in the population < 70 also increased (2%, UI, 0 to 4%). Finally, the
212 majority of countries with low prevalence rates were part of EU-28. Here, countries with the
213 highest age-standardized incidence rates were Bulgaria, with 1605.2 prevalent cases per
214 100,000, Romania (1327.7) and Hungary (1236.6) (**Figure 2**).

215 Age-standardized incidence and prevalence rates for each of the 53 countries included in EU-
216 53, for both sexes, men and women can be found in **Supplementary Table 6**.

217

218 **3. Deaths (Figure 4):**

219 - **EU-53**: The total number of all-stroke deaths remained stable between 2010 and
220 2019 (**Figure 4A**), with 1,176,328 deaths due to stroke registered in 2019. Of these, 70%,
221 24.5% and 5.5% were accounted for by IS, ICH and SAH, respectively (**Supplementary**
222 **Table 4**). Age-standardized mortality rates saw a significant reduction, decreasing by 18%

223 (95% UI, -22 to -14%) between 2010 and 2019, from 81.5 to 66.8 per 100,000 (**Figure 4B**).

224 Despite a higher absolute number of deaths in women, age-adjusted mortality rates were

225 0.87x lower in women than in men (61.9 vs. 71.3). In 2019, stroke was the leading cause of

226 death in Montenegro, North Macedonia and Portugal (**Supplementary Figures 1**). Countries

227 presenting the largest reductions in age-adjusted mortality rates between 2010 and 2019 were

228 Luxembourg, Armenia and Kyrgyzstan (**Figure 4C**). In 2019, Switzerland, Iceland and

229 Andorra presented the lowest age-adjusted mortality rate, with < 25 deaths per 100,000; while

230 Northern Macedonia and Montenegro had the highest rates, with > 200 deaths per 100,000

231 people (**Figure 4D**). Death rates in Montenegro were 12.5x higher than in Switzerland. In this

232 regard, significant discrepancy in stroke-deaths attributable to risk factors exist throughout

233 EU-53 (**Figure 5A and B**). Death rates in the population 70+, similarly to incidence rates,

234 decreased by 11% (UI, -15 to -7%), whilst remaining stable in those <70 years (**Figure 4E**).

235 Finally, when looking at the three subregions, the absolute number of stroke-related deaths

236 increased by 9% (UI, 6-12%) in Western Europe, while remaining stable in Eastern and

237 Central Europe. The highest age-adjusted mortality rate, but also biggest decrease between

238 2010 and 2019, was observed in Eastern Europe (167 to 131, 21% decrease [95% UI, -28 to -

239 15%]), followed by Central Europe (116 to 95, 18% decrease [95% UI, -26 to -9%]) and lastly

240 by Western Europe (37 to 32, 13% decrease [95% UI, -15 to -10%]) (**Figure 4F**).

241 - **EU-28**: In contrast to EU-53, a 6% (UI, 1 to 10%) increase in the number of stroke-related

242 deaths was observed in EU-28, from 507,628 to 535,742 deaths in 2019, mainly attributable

243 to a 7% increase of deaths caused by IS and SAH (UI: 2-12% for IS, and 1-12% for SAH)

244 (**Figure 4A**). Age-adjusted mortality rates, however, decreased by 15% (95% UI, -18 to -

245 11%) from 49 to 42 per 100,000 (**Figure 4B**), with the greatest reduction observed for ICH

246 mortality (from 13 to 11, -16% decrease [95% UI, -20 to -12%]). Although the age-adjusted

247 mortality rate reduction was smaller for EU-28 in comparison to EU-53, age-adjusted

248 mortality rates for all stroke, IS, ICH and SAH were 0.62, 0.61, 0.64 and 0.76 lower in EU-28

249 than in EU-53, respectively. Reduction of age-adjusted rates was similar in both women and
250 men. In contrast to EU-53, mortality rates in the population <70 in EU-28 also showed a 9%
251 reduction (UI, -16 to -3%) between 2010 and 2019 (**Figure 4E**). In EU-28, the country with
252 the lowest age-standardized mortality rates was France, with 24.54 deaths per 100,000, whilst
253 the country with the highest rate, 7.8x higher than France, was Bulgaria, with 191.54 deaths
254 per 100,000 (**Figure 2**). Although there is also significant discrepancy in stroke-deaths
255 attributable to risk factors, its distribution is more consistent than in EU-53 (**Figure 5B**), with
256 Bulgaria and Romania passing 250 deaths per 100,000 attributable to risk-factors. In the
257 majority of countries, however, this rate was under 100. The rate of stroke-deaths attributable
258 to risk factors for 2010 can be found in **Supplementary Figures 2 and 3**.

259

260 **4. DALYs**

261 - **EU-53**: The total number of DALYs decreased by 7% (UI, -12 to -3%), from
262 22,043,161 to 20,501,446 in 2019, of which 62.3%, 29% and 8.1% were accounted by IS,
263 ICH and SAH, respectively (**Figure 6A, Supplementary Table 3 and 4**). Of all age-adjusted
264 rates evaluated in EU-53, DALYs showed the largest reduction, with a 19% decrease between
265 2010 and 2019 (**Figure 6B**). IS was the stroke subtype with the largest reduction (-23%, UI, -
266 19 to -16%). Despite higher absolute numbers of stroke DALYs in women, age-adjusted rates
267 were 0.79x, 0.88x, 0.63x and 0.86 lower in women than men, for all-stroke, IS, ICH and
268 SAH, respectively. Countries with the largest decrease in age-standardized DALYs between
269 2010 and 2019 were the Republic of Moldova and Kyrgyzstan, followed by Luxembourg and
270 Armenia (**Figure 6C**). In 2019, Switzerland presented the lowest DALY rates, at 372 per
271 100,000 people. Other countries with rates below 450, were Iceland and Andorra. In contrast,
272 Northern Macedonia, Uzbekistan and Turkmenistan presented rates of over 3500
273 DALYs/100,000 people (**Figure 6D**). Stroke was the leading cause of death and DALYs in

274 Montenegro, North Macedonia and Portugal. Regarding EU-53 subregions, the absolute
275 number of DALYs remained stable in Central and Eastern Europe, while it decreased by 15%
276 (UI, -22 to -7) in Eastern Europe. Despite larger reductions observed in Eastern and Central
277 Europe age-adjusted DALY rates, significant discrepancies exist between regions, with rates
278 being 4.5x higher in Eastern Europe in comparison to Western Europe (**Figure 6F**).

279 Interestingly, despite Eastern Europe presenting the highest incidence, prevalence, death and
280 DALY age-standardized rates of the three European subregions, Central-Europe presented the
281 highest stroke prevalence rate in the population 70+.

282 - **EU-28**: In comparison, the total number of DALYs remained stable, with 8,155,623 DALYs
283 attributable to stroke in 2019 (**Figure 6A**). Here, too, age-standardized DALYs showed the
284 biggest reduction in EU-28 of all evaluated parameters (16% decrease; 95% UI, -19 to -12%)
285 (**Figure 6B**). Although the age-adjusted DALY rate reduction was smaller for EU-28 in
286 comparison to EU-53, age-adjusted DALYs for all stroke, IS, ICH and SAH were 0.58, 0.57,
287 0.55 and 0.74 lower in EU-28 than in EU-53, respectively. Reduction of age-adjusted rates
288 was similar in both women and men, with women having an age-adjusted DALY rate 0.90x,
289 0.87x, 0.63x lower than men for all-stroke, IS and ICH in 2019, respectively. In EU-28, the
290 country with the lowest age-standardized DALY rates was France, with 453.6 DALYs per
291 100,000, whilst the country with the highest rate, 7.5x higher than France, was Bulgaria, with
292 3390.2 DALYs per 100,000 (**Figure 2**).

293 Age-standardized death and DALY rates for each of the 53 countries included in EU-53, for
294 both sexes, men and women can be found in **Supplementary Table 7**.

295

296 **Discussion**

297 This study reflects significant geographic variations in the burden of stroke across EU-
298 53, EU-28, Western, Central and Eastern Europe, as well as between individual countries.

299 While similar general trends were observed across EU-53 and EU-28, there were considerable
300 discrepancies between individual countries. Comparison of age-adjusted mortality and DALY
301 rates in countries with the lowest versus highest stroke burden showed some countries
302 presenting rates up to 12x higher. These differences were more evident across EU-53
303 countries, however, relevant discrepancies were also observed across EU-28 countries, with
304 Bulgaria, Hungary, Latvia, Lithuania, Romania and Slovakia presenting the highest incidence
305 and prevalence rates. Interestingly, while Bulgaria, Latvia and Romania presented equiparable
306 death and DALY rates, Hungary, Lithuania and Slovakia had death and DALY rates similar
307 to the rest of EU-28 countries (**Figure 2**).

308 Absolute numbers of first-ever-in-a-lifetime-strokes and stroke prevalence increased
309 throughout Europe, with the highest increase in EU-28 and Western Europe. These findings
310 may be explained by the long life-expectancy in these countries, alongside a rising incidence
311 of age-related diseases. Europe's population is also continuously growing, with an estimated
312 930 million people living in EU-53 in 2019, 35 million more than in 2010 (3.7% increase)
313 (23). Most EU-53 countries saw a population increase (**Supplementary Figure 4**), with
314 Tajikistan, Luxembourg and Kyrgyzstan presenting the largest population growth (24%, 21%
315 and 18%, respectively) between 2010 and 2019 (23). Eighteen countries, however, presented
316 a population decline, with Latvia and Lithuania suffering the largest reductions (- 10 and -
317 11%, respectively). During the same period, the estimated population in EU-28 grew only by
318 1.9%, from 503 to 512 million in 2019 (23) (**Supplementary Table 8**). Despite a lower
319 population growth in EU-28, the median age was higher (41.9 vs. 38.6 years in EU-28 and
320 EU-53, respectively). (23). In order to achieve a 10% reduction in the absolute number of
321 strokes by 2030 and reach the target proposed by the European Stroke Action Plan (7),
322 approximately 84,000 strokes would need to be prevented over 2020-2029 in EU-28. The
323 population in EU-28 is projected to remain relatively stable, with estimates suggesting 512.48

324 million people in 2027 (3). Assuming this, an annual 0.08% reduction in stroke incidence
325 would be necessary to achieve a total number 760,000 of strokes in 2030.

326 In contrast to absolute numbers, age-adjusted incidence, prevalence, death and DALY
327 stroke rates, have decreased consistently in both EU-53 and EU-28, and European subregions.
328 However, although EU-53, and especially Eastern Europe showed considerable improvements
329 in stroke burden within the last decade, its rates remain considerably higher than other
330 European subregions. Interestingly, Kyrgyzstan was one of the countries with the largest
331 reductions in age-adjusted prevalence, death and DALY rates between 2010-2019. Similar to
332 previous publications, more than 90% of the stroke burden remains attributable to modifiable
333 risk factors, especially high blood pressure. (**Figure 5**) (1, 24-26). Here, again, there are
334 significant discrepancies between countries, with Bulgaria and Romania showing very high
335 rates of high blood pressure, dietary risks and tobacco consumption, similar to other Central
336 and Eastern European countries which are not part of EU-28 (**Figure 5**).

337 Finally, alongside risk-factor prevention, nationwide implementation of stroke units
338 could substantially improve acute stroke management and post-stroke rehabilitation.
339 Unfortunately, there is no Europe-wide accepted definition of what a “stroke unit” should
340 actually be, and here again, large disparities can be observed between countries (6). For
341 example, although significant improvement has been made in the amount of resource
342 allocation for stroke unit creation in Spain, stroke units tend to be concentrated in highly
343 populated areas, so that autonomous regions like Madrid, Catalunya and the Vasque Country
344 have significantly more stroke units, while poorer but more extensive areas, such as Andalucia
345 have less stroke units, making access for the population in this area more difficult (27). French
346 data indicates that only 50% of stroke patients are treated in stroke units (28), while 73% of
347 Finnish patients that live within a specific catchment area of a stroke unit are treated in stroke
348 units, compared to only 9% of patients treated in stroke units when they live outside a catchment
349 area (29). These findings suggest large within-country and national variations in the quality and

350 accessibility of stroke treatment. Similarly, there are also significant variations regarding
351 intravenous thrombolysis (IVT) and endovascular therapy (EVT) (30, 31). Country-level data
352 shows that access to and delivery of acute stroke care are poor or totally lacking in many
353 countries (32), with under 20% of patients with acute ischaemic stroke being provided with
354 IVT, and an overall rate of IVT in incident IS of only 7.3% (29).

355 *Limitations of this study:* This study has chosen to focus on the epidemiological
356 burden of stroke, looking specifically at differences observed between different European
357 definitions, regions and country. However, an analysis of risk-factor prevalence and
358 causalities have not been performed, so causative conclusions cannot be drawn from this
359 analysis. Stroke unit accessibility and treatments used have also not been investigated, so that
360 a deeper understanding into stroke treatment and mortality cannot be made. Lastly, it is
361 possible that reporting quality is not the same for all 53 included countries, so that direct
362 comparisons between e.g. Sweden, which has a nation-wide stroke register and Tajikistan
363 may be susceptible to reporting errors.

364

365 **Conclusion**

366 Although a substantial effort has been made regarding stroke management in Europe,
367 this analysis shows increasing absolute numbers of first-ever-in-a-lifetime-strokes and stroke
368 prevalence in the last 10 years. Furthermore, the disparity of stroke burden across individual
369 European countries, subregions and EU definitions (EU-28 vs EU-53) is significant and
370 warrants further analysis.

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372

373 **Disclosures:** None

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395 [for-europe-sap-e-a-major-initiative-to-reduce-the-burden-of-stroke-in-europe/](https://eso-stroke.org/eso-and-safe-kick-off-the-implementation-of-the-stroke-action-plan-for-europe-sap-e-a-major-initiative-to-reduce-the-burden-of-stroke-in-europe/) (accessed
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482 **FIGURE LEGENDS AND TABLE TITLES:**

483 **Figure 1:** Changes in stroke incidence rates in EU-53 and EU-28. Trend-diagrams of the (A)
484 absolute numbers and (B) age-standardized rates of incident strokes. (C) Heatmap of age-
485 standardized annual percentage difference in stroke-incidence rates between 2010 and 2019.
486 (D) Age-standardized incidence rates in 2019 in all EU-53 countries. Trend-diagrams of
487 incident stroke rates in (E) the population 70+ and <70 and (F) by EU-53 subregion.

488

489 **Figure 2:** Age-standardized (A) incidence, (B) prevalence, (C) death and (D) DALY rates for
490 all 28 countries included in EU-28 in 2019, per 100,000 and for both sexes.

491

492 **Figure 3:** Changes in stroke prevalence rates in EU-53 and EU-28. Trend-diagrams of the (A)
493 absolute numbers and (B) age-standardized rates of prevalent stroke cases. (C) Heatmap of
494 the age-standardized annual percentage difference in stroke-prevalence rates between 2010
495 and 2019. (D) Age-standardized prevalence rates in 2019 in all EU-53 countries. (E). Trend-
496 diagrams of prevalent stroke rates in (E) the population 70+ and <70 and (F) by EU-53
497 subregion.

498

499 **Figure 4:** Changes in stroke deaths rates in EU-53 and EU-28. Trend-diagrams of the (A)
500 absolute numbers and (B) age-standardized rates of stroke deaths. (C) Heatmap of the age-
501 standardized annual percentage difference in stroke-death rates between 2010 and 2019. (D)
502 Age-standardized death rates in 2019 in all EU-53 countries. (E). Trend-diagrams of death
503 rates in (E) the population 70+ and <70 and (F) by EU-53 subregion.

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505 **Figure 5:** Stroke-deaths attributable to risk factors in 2019, age-standardized and for both
506 sexes, for (A) the 25 countries in the EU-53, which are not part of EU-28, and (B) the 28
507 countries included in the EU-28. Note the difference in scales (600 per 100,000 in panel A
508 and 400 per 100,000 in panel B).

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510 **Figure 6:** Changes in stroke DALYs in EU-53 and EU-28. Trend-diagrams of (A) absolute
511 numbers and (B) age-standardized DALY stroke rates. (C) Heatmap of the age-standardized
512 annual percentage difference in stroke-DALY rates between 2010 and 2019. (D) Age-
513 standardized DALYs in 2019 in all EU-53 countries (E). Trend-diagrams of age-standardized
514 DALY rates in (E) the population 70+ and <70 and (F) by EU-53 subregion.

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531 **SUPPLEMENTARY MATERIAL:**

532 **Supplementary Table 1:** Definitions, level causes and international classification codes used
533 for categorization of stroke and its subtypes by the GBD and in this study.

534 **Supplementary Table 2:** List of included countries in EU-53 region, European subregions
535 and EU-28.

536 **Supplementary Table 3:** Absolute and relative measures of the burden of stroke in EU-53
537 and EU-28 for all stroke in 2010, 2019 and the difference between 2010 and 2019.

538 **Supplementary Table 4:** Absolute and relative measures of the burden of stroke in EU-53
539 and EU-28 for stroke subtypes in 2010, 2019 and the difference between 2010 and 2019.

540 **Supplementary Table 5:** Absolute and relative measures of the burden of stroke in the three
541 EU-53 European subregions for all stroke in 2010, 2019 and the difference between 2010 and
542 2019.

543 **Supplementary Table 6:** Age standardized incidence and prevalence rates for all stroke.

544 **Supplementary Table 7:** Age standardized death and DALY rates for all stroke.

545 **Supplementary Table 8:** Population estimates for 2010 and 2019 for all EU-53 countries.

546

547 **Supplementary Figure 1:** Heat diagram showing the distribution of level 3 causes of death in
548 2019, for both sexes and all ages, for EU-53 countries.

549 **Supplementary Figure 2:** Stroke-deaths attributable to risk factors in 2010, age-standardized
550 and for both sexes, for the 25 countries in EU-53, which are not part of EU-28.

551 **Supplementary Figure 3:** Stroke-deaths attributable to risk factors in 2019, age-standardized
552 and for both sexes, for EU-28 countries.

553 **Supplementary Figure 4:** Population change (%) between 2010 and 2019 in EU-53
554 countries.

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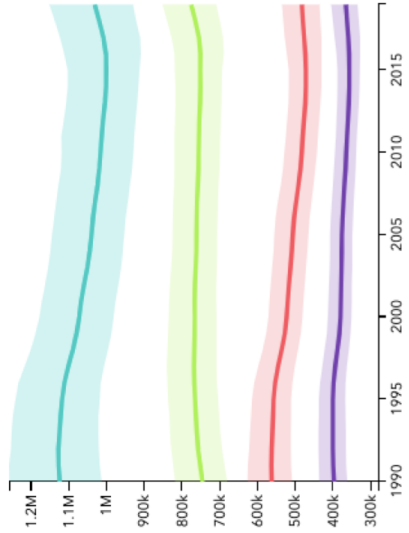
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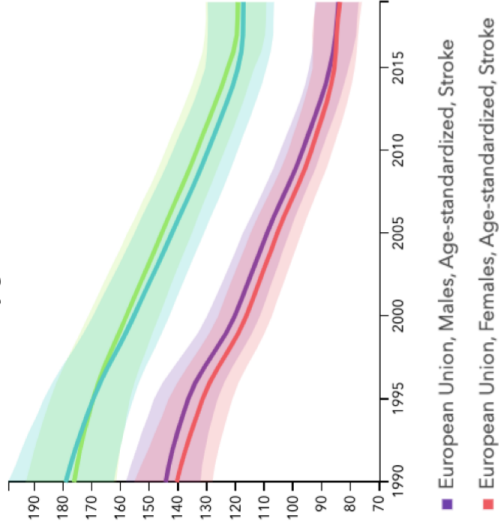
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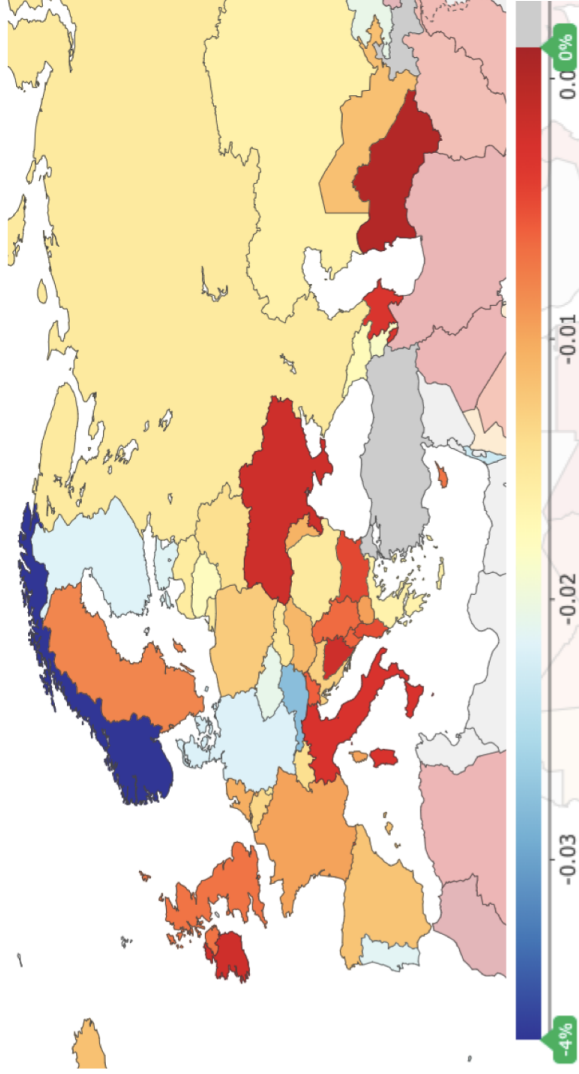
A. Absolute incident cases, by gender



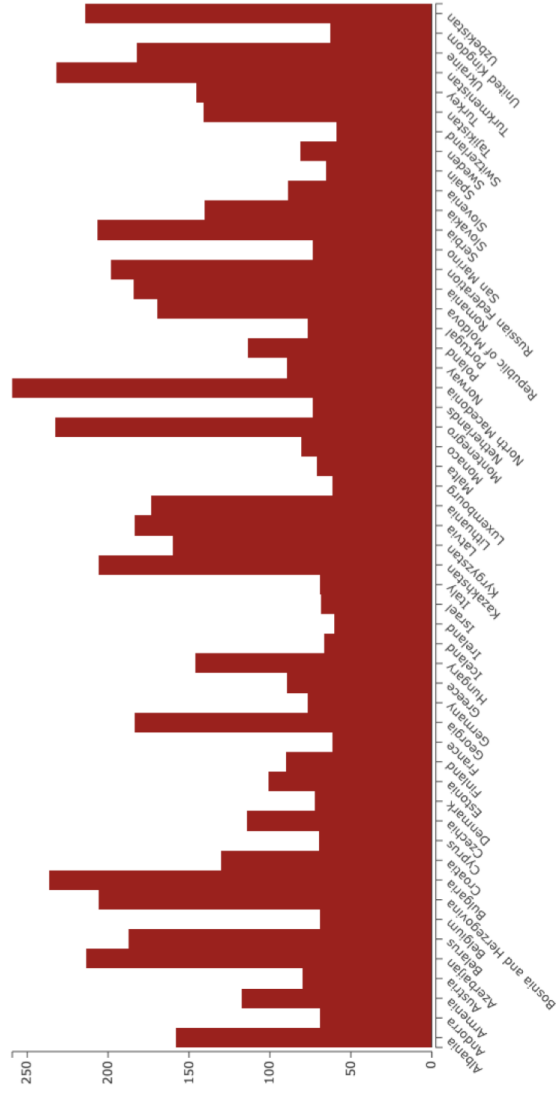
B. Age-standardized incident rates, by gender



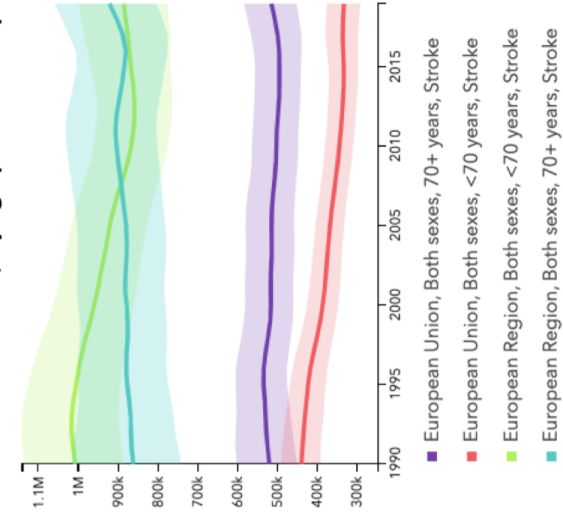
C. Age-standardized incidence annual % difference between 2010-2019



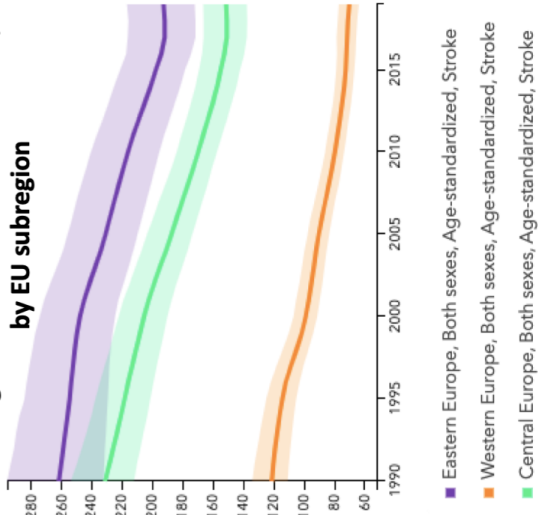
D. Age-standardized incidence rates per 100,000 in 2019, for both sexes, per country



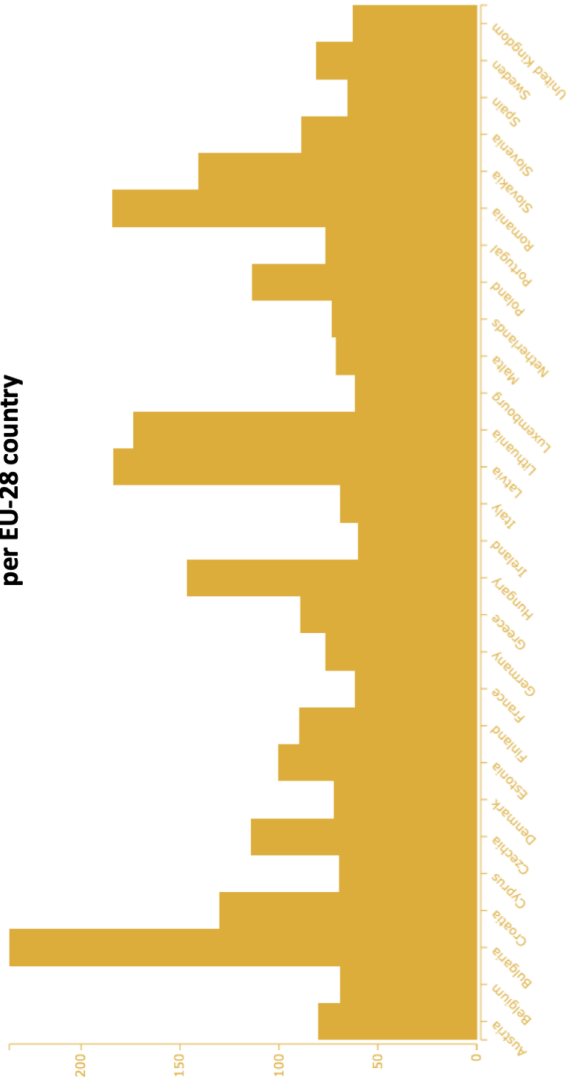
E. Incident cases, by age (70+ and <70)



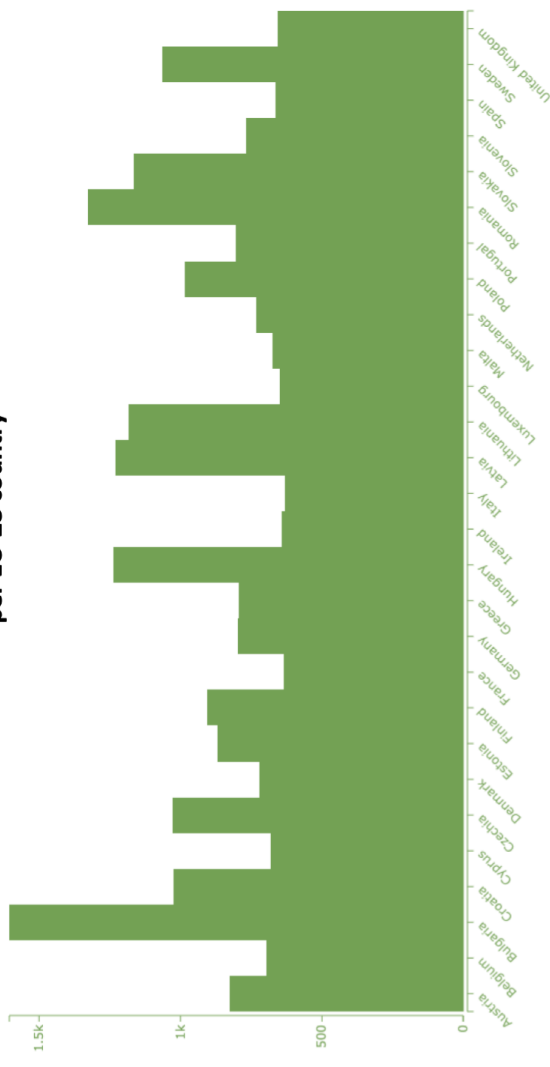
F. Age-standardized incidence rates, by EU subregion



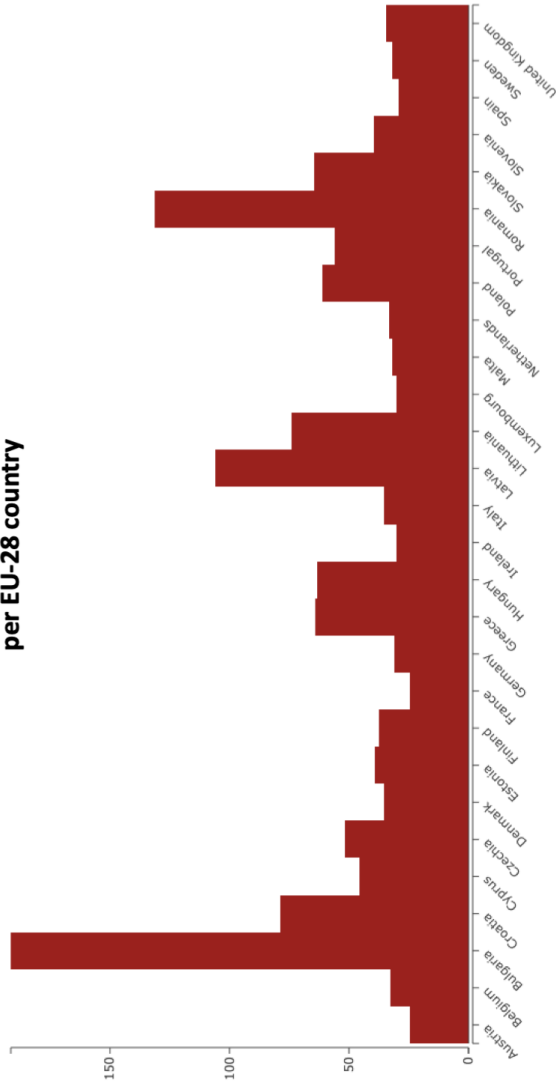
A. Age-standardized incidence rates per 100,000 in 2019, for both sexes, per EU-28 country



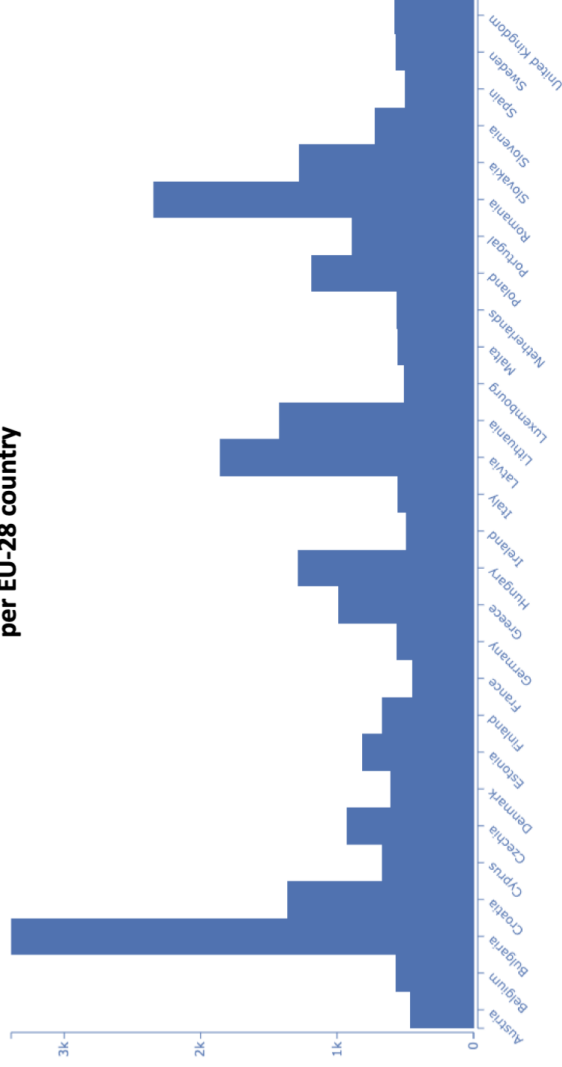
B. Age-standardized prevalence rates per 100,000 in 2019, for both sexes, per EU-28 country



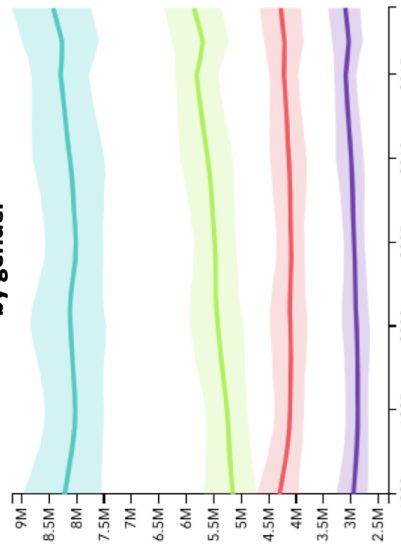
C. Age-standardized death rates per 100,000 in 2019, for both sexes, per EU-28 country



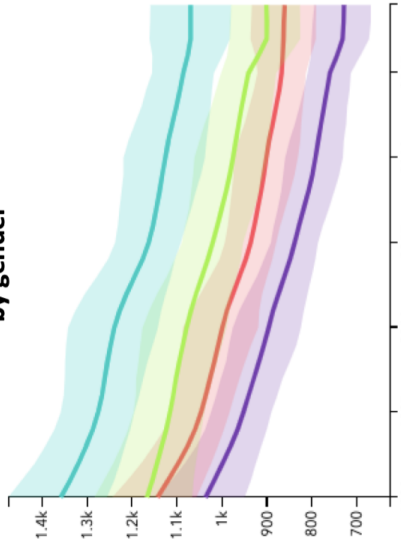
D. Age-standardized DALY rates per 100,000 in 2019, for both sexes, per EU-28 country



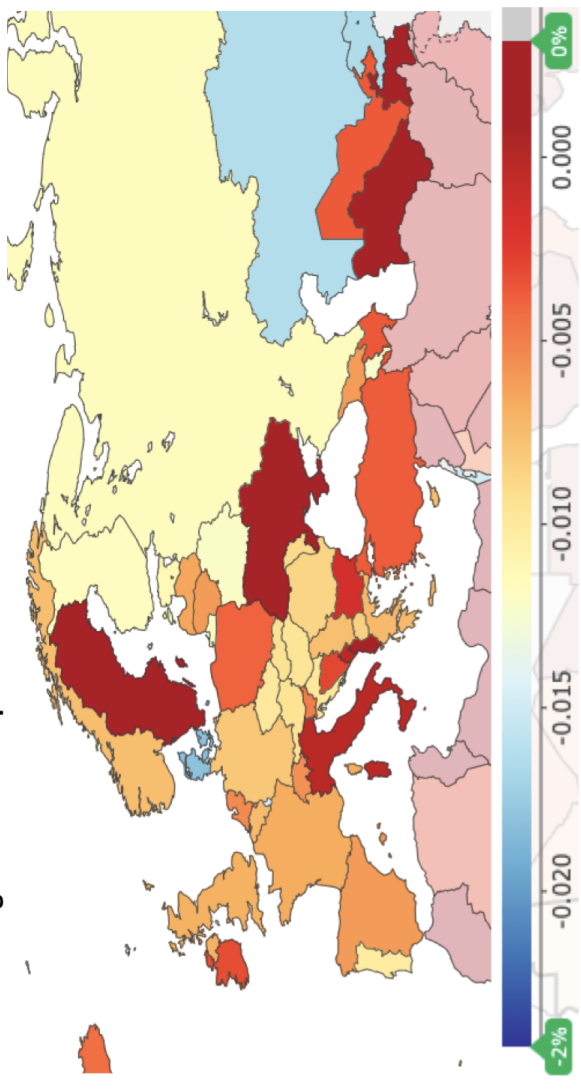
A. Absolute prevalent cases, by gender



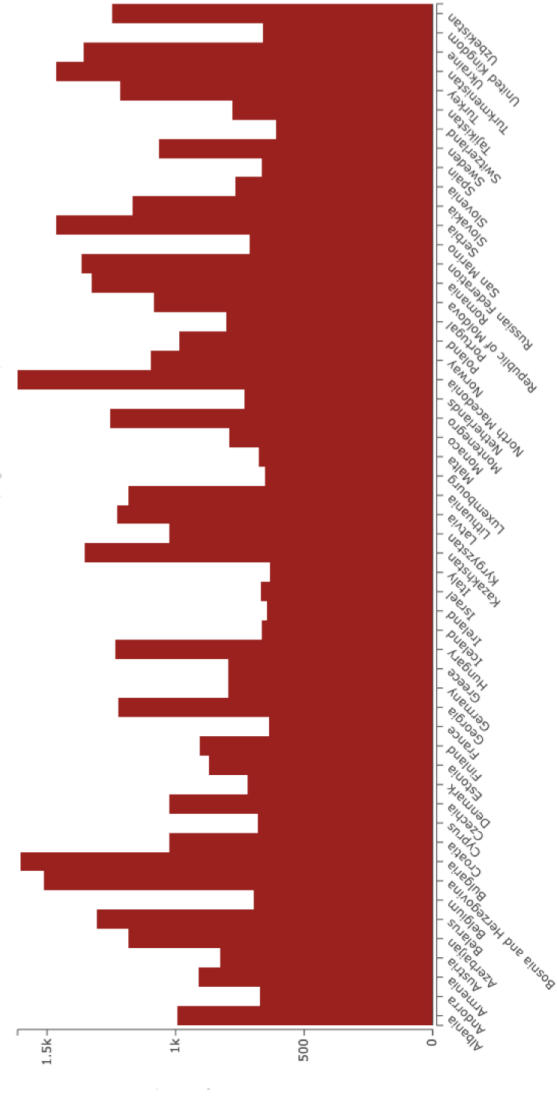
B. Age-standardized prevalence rates, by gender



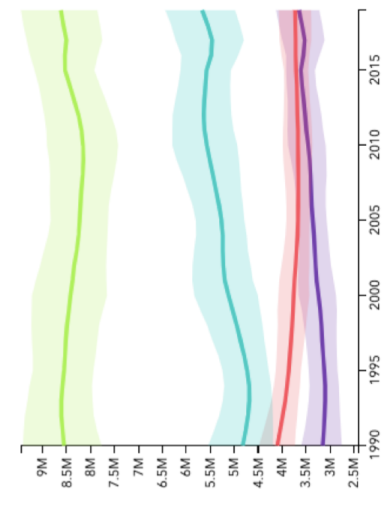
C. Age-standardized prevalence annual % difference between 2010-2019



D. Age-standardized prevalence rates per 100,000 in 2019, for both sexes, per country

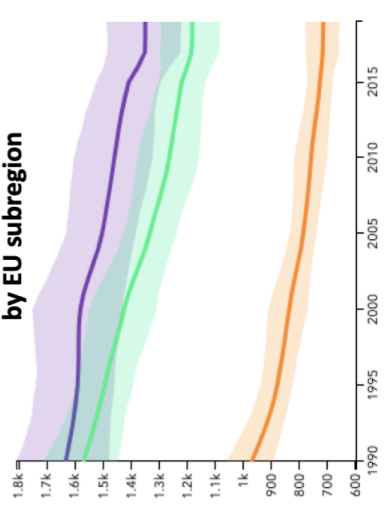


E. Prevalent cases, by age (70+ and <70)



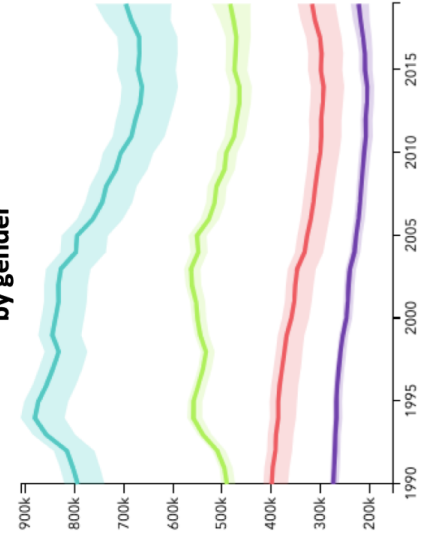
- European Union, Both sexes, 70+ years, Stroke
- European Union, Both sexes, <70 years, Stroke
- European Region, Both sexes, <70 years, Stroke
- European Region, Both sexes, 70+ years, Stroke

F. Age-standardized prevalence rates, by EU subregion

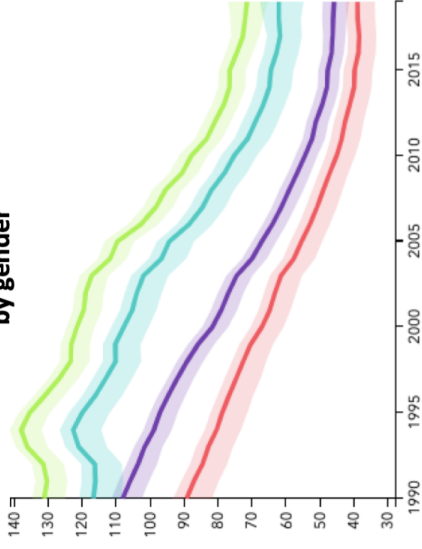


- Eastern Europe, Both sexes, Age-standardized, Stroke
- Western Europe, Both sexes, Age-standardized, Stroke
- Central Europe, Both sexes, Age-standardized, Stroke

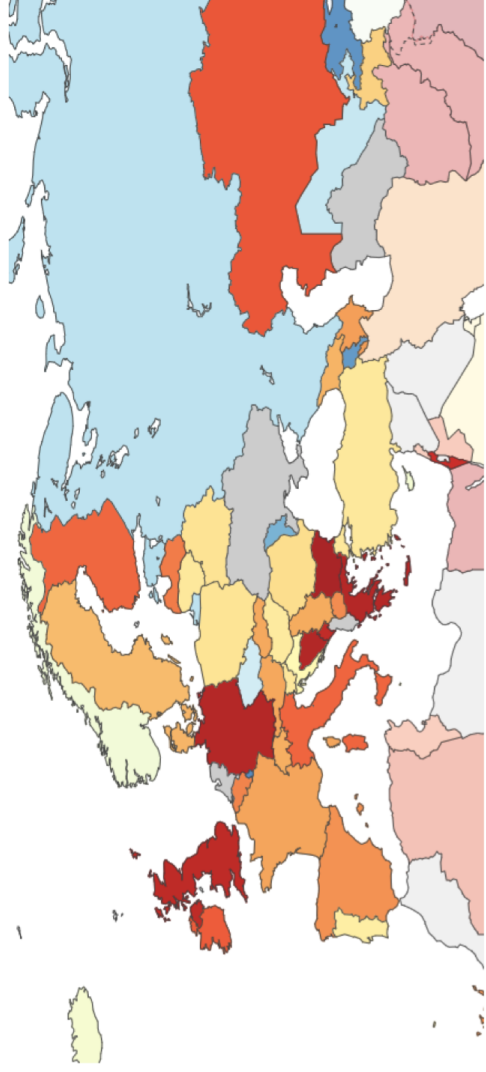
A. Absolute stroke deaths, by gender



B. Age-standardized death rates, by gender



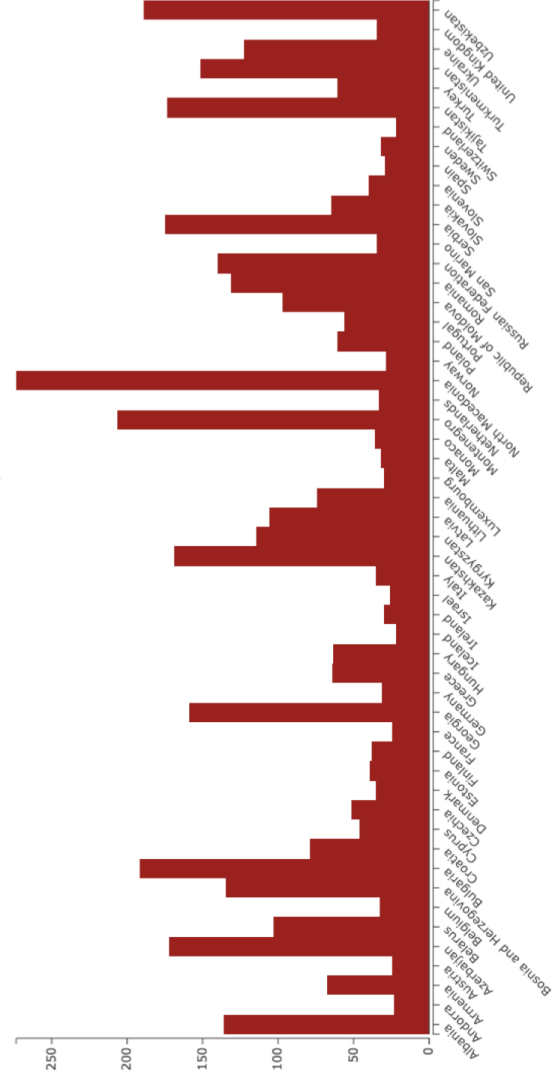
C. Age-standardized death annual % difference between 2010-2019



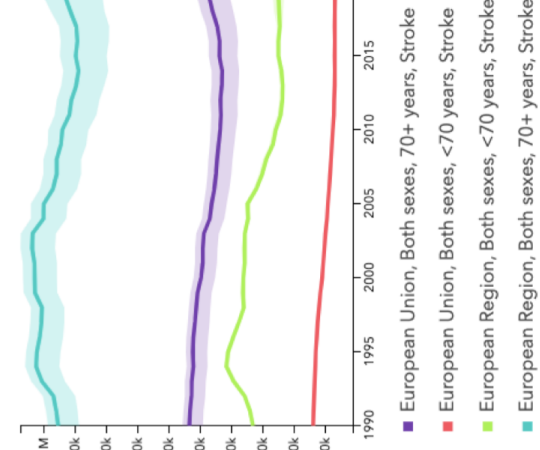
■ European Region, Males, Age-standardized, Stroke
■ European Region, Females, Age-standardized, Stroke

■ European Union, Males, Age-standardized, Stroke
■ European Union, Females, Age-standardized, Stroke

D. Age-standardized death rates per 100,000 in 2019, for both sexes, per country

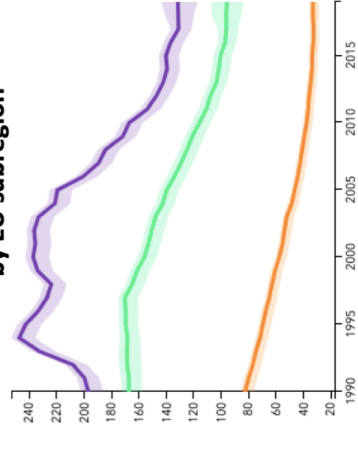


E. Deaths per 100,000, by age (70+ and <70)



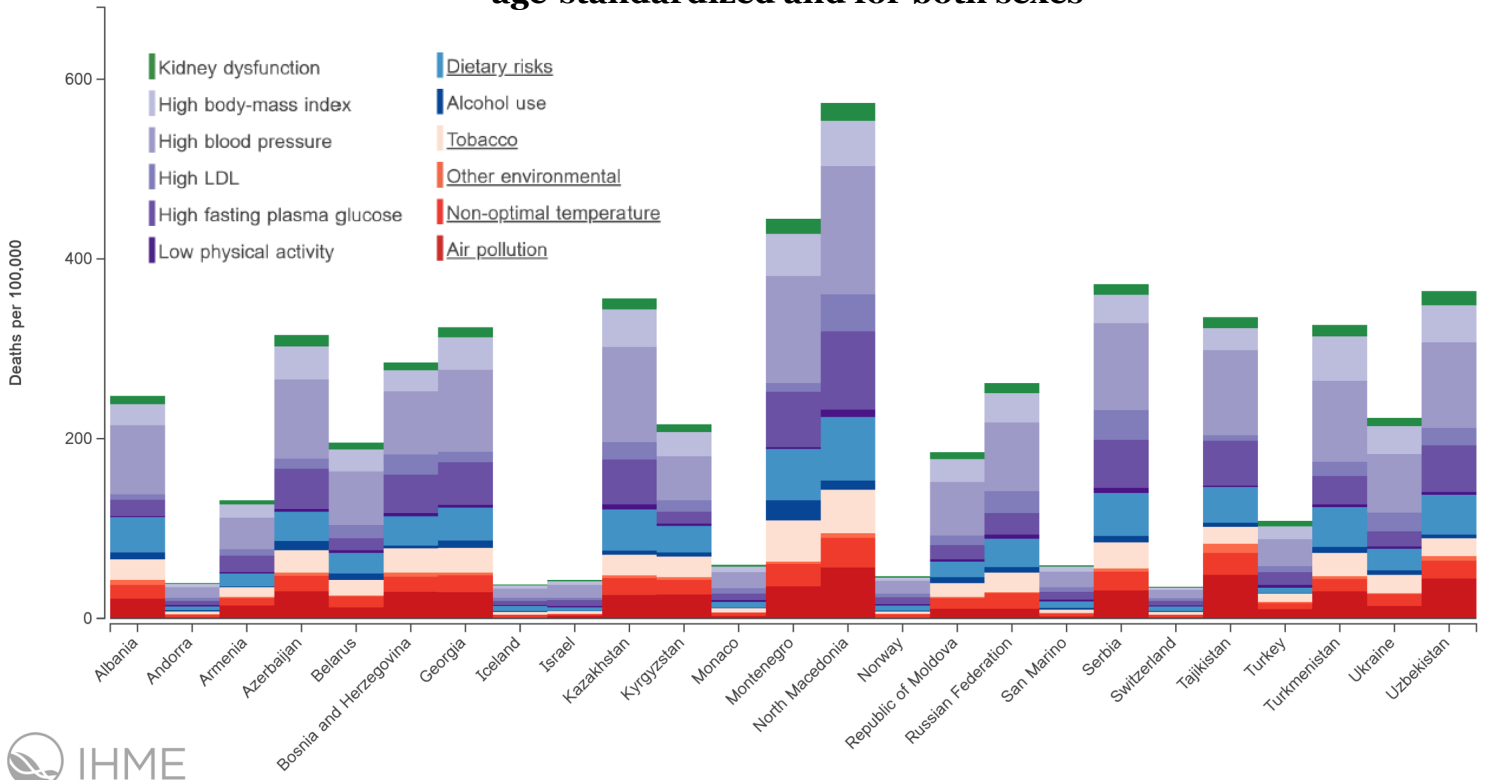
■ European Union, Both sexes, 70+ years, Stroke
■ European Union, Both sexes, <70 years, Stroke
■ European Region, Both sexes, <70 years, Stroke
■ European Region, Both sexes, 70+ years, Stroke

F. Age-standardized death rates, by EU subregion

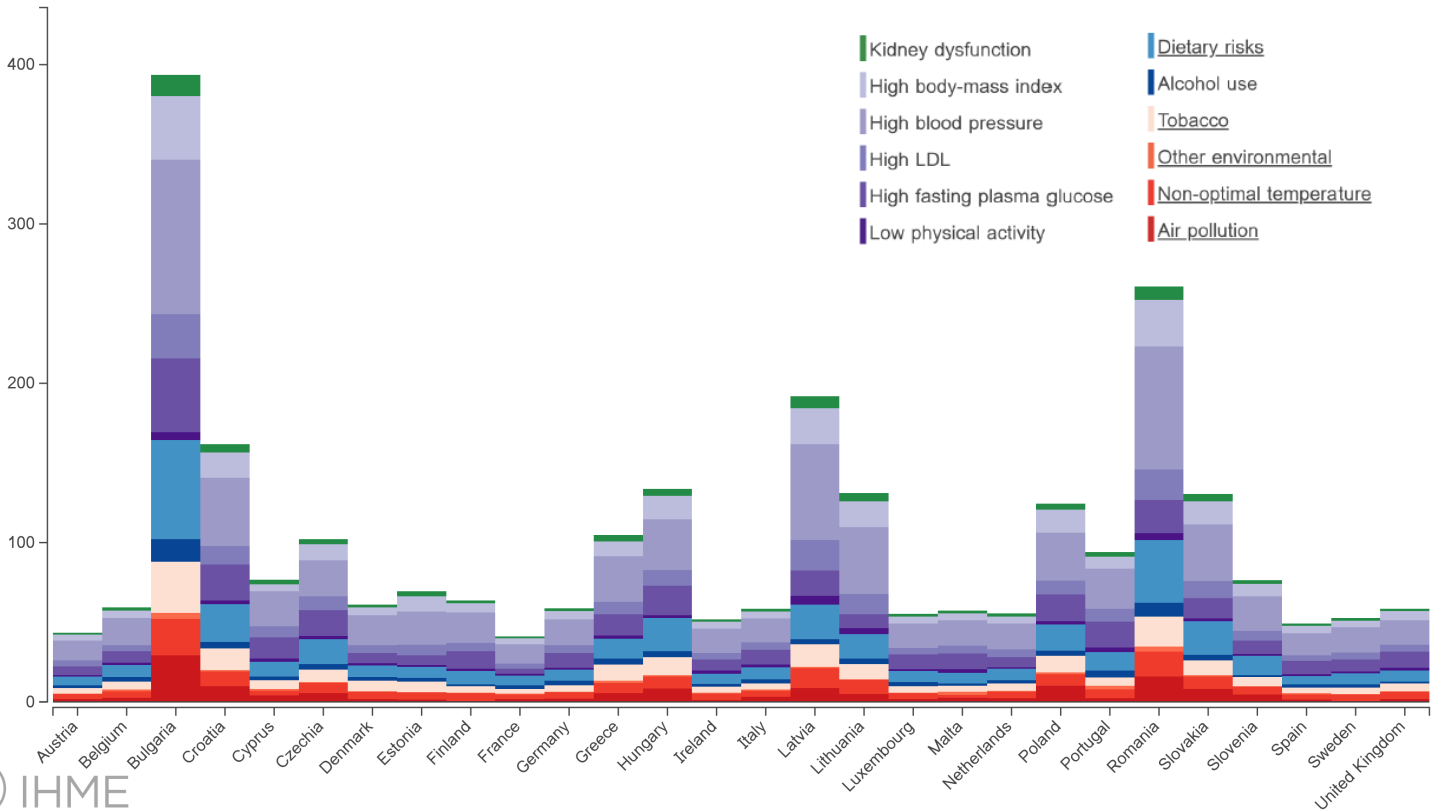


■ Eastern Europe, Both sexes, Age-standardized, Stroke
■ Western Europe, Both sexes, Age-standardized, Stroke
■ Central Europe, Both sexes, Age-standardized, Stroke

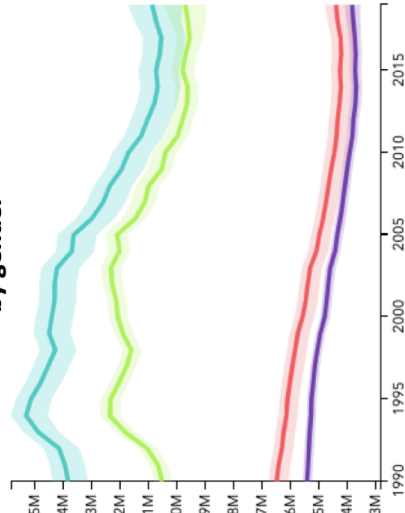
A. Stroke-deaths attributable to risk factors in 2019 for the 25 additional countries in the EU-53 (and not part of the EU-28), age-standardized and for both sexes



B. Stroke-deaths attributable to risk factors in 2019 for countries in EU-28, age-standardized and for both sexes

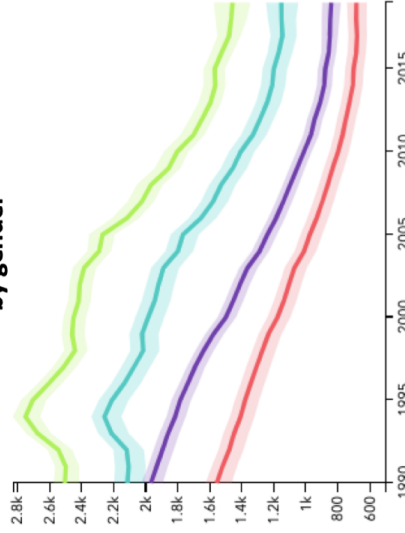


A. Absolute DALY cases, by gender



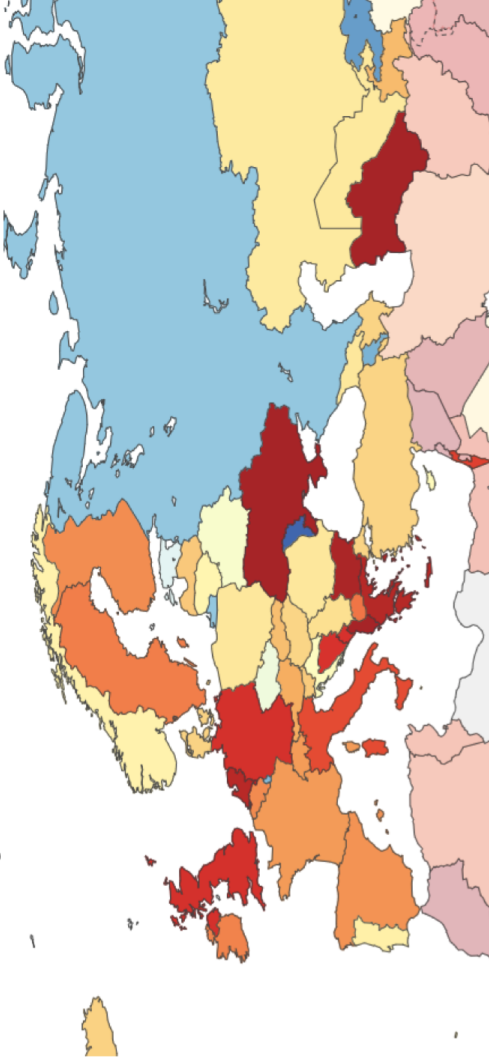
■ European Region, Males, Age-standardized, Stroke
 ■ European Region, Females, Age-standardized, Stroke

B. Age-standardized DALY rates, by gender

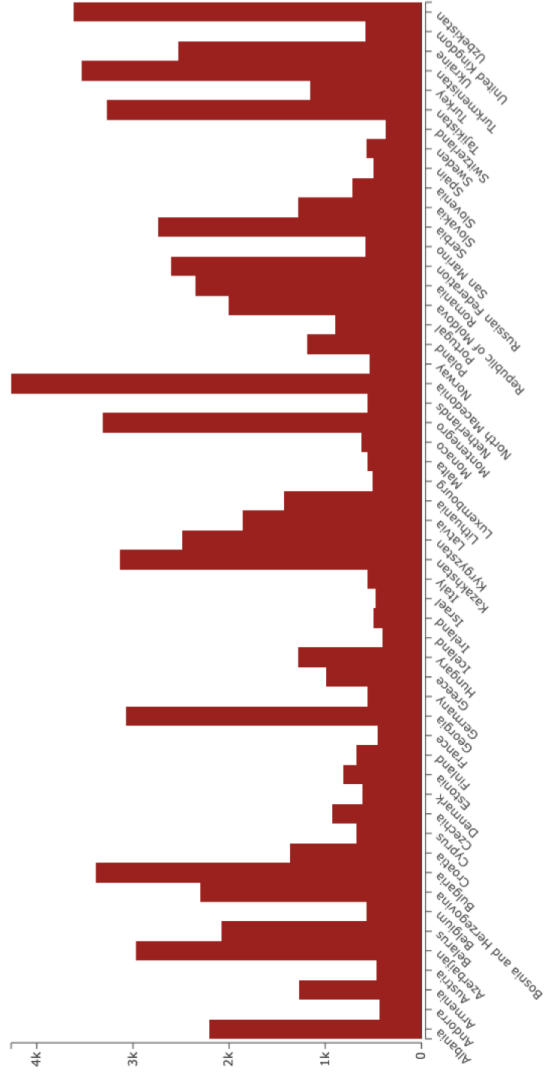


■ European Union, Males, Age-standardized, Stroke
 ■ European Union, Females, Age-standardized, Stroke

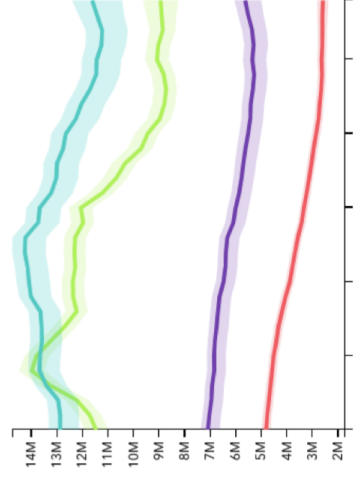
C. Age-standardized DALY annual % difference between 2010-2019



D. Age-standardized DALY rates per 100,000 in 2019, for both sexes, per country

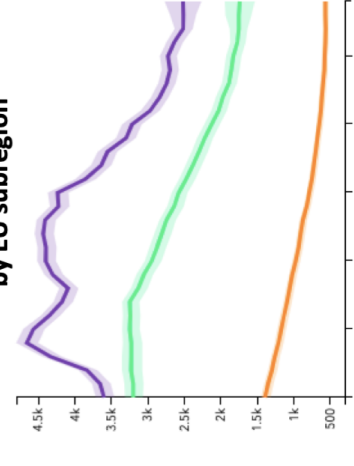


E. DALYs per 100,000, by age (70+ and <70)



■ European Union, Both sexes, 70+ years, Stroke
 ■ European Union, Both sexes, <70 years, Stroke
 ■ European Region, Both sexes, <70 years, Stroke
 ■ European Region, Both sexes, 70+ years, Stroke

F. Age-standardized DALY rates, by EU subregion



■ Eastern Europe, Both sexes, Age-standardized, Stroke
 ■ Western Europe, Both sexes, Age-standardized, Stroke
 ■ Central Europe, Both sexes, Age-standardized, Stroke