

# **Incidence, prevalence and disability associated to neurological disorders in Italy between 1990 and 2019: an analysis based on the Global Burden of Disease Study 2019**

**Running head:** Incidence, prevalence and YLD of neurological disorders in Italy (GBD-2019)

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**ABSTRACT**

**Background.** Neurological conditions are highly prevalent and disabling, in particular in the elderly. The Italian population has witnessed sharp ageing and we can thus expect a rising trend in the incidence, prevalence and disability of these conditions.

**Methods.** We relied on the Global Burden of Disease 2019 study to extract Italian data on incidence, prevalence and years lived with a disability (YLDs) referred to a broad set of neurological disorders including, brain and nervous system cancers, stroke, encephalitis, meningitis, tetanus, traumatic brain injury, and spinal cord injury. We assessed changes between 1990 and 2019 in counts and age-standardized rates.

**Results.** The most prevalent conditions were tension-type headache, migraine, and dementias, whereas the most disabling were migraine, dementias and traumatic brain injury. YLDs associated with neurological conditions increased by 22.5%, but decreased by 2.3% in age-standardized rates. The overall increase in prevalence and YLDs counts was stronger for non-communicable diseases with onset in old age compared to young to adult-age onset ones. The same trends were in the opposite direction when age-standardized rates were taken into account.

**Conclusions.** The increase in YLDs associated with neurological conditions is mostly due to population ageing and growth: nevertheless, lived disability and, as a consequence, impact on health systems has increased. Actions are needed to improve outcome and mitigate disability associated with neurological conditions, spanning among diagnosis, treatment, care pathways and workplace interventions.

**KEY-WORDS:** Disability; Migraine; Stroke; Dementia; Multiple Sclerosis; Motor neuron disease

84

85 **INTRODUCTION**

86 The Global Burden of Disease (GBD) study aims to provide reliable information on global trends in the health  
87 status of populations and changes in the disease burden, measured by the disability-adjusted life years  
88 (DALYs), a metric which includes fatal outcomes, i.e. years of life lost (YLLs), and non-fatal health outcomes,  
89 i.e. years lived with disability (YLDs) [1]. The measurement of both YLLs and YLDs is of key relevance in  
90 the modern scenario of health outcomes, as the increase of populations disability is paradoxically a  
91 consequence of reduced premature deaths, but it also reflects the failure of health systems in maintaining high  
92 standards of health care. This is particularly true for non-communicable diseases (NCDs): based on 2019  
93 estimates, NCDs account for 64% of all-cause DALYs and 80% of all-cause YLDs (see  
94 [http://ghdx.healthdata.org/gbd-results-tool?params=gbd-api-2019-](http://ghdx.healthdata.org/gbd-results-tool?params=gbd-api-2019-permalink/25456ecb137f47b60482ce47135fd8a8)  
95 [permalink/25456ecb137f47b60482ce47135fd8a8](http://ghdx.healthdata.org/gbd-results-tool?params=gbd-api-2019-permalink/25456ecb137f47b60482ce47135fd8a8)). Over the 1990-2019 period, the share of NCDs over all-  
96 cause estimates have increased by 45% for DALYs and by 69% for YLDs (see [http://ghdx.healthdata.org/gbd-](http://ghdx.healthdata.org/gbd-results-tool?params=gbd-api-2019-permalink/1d45ef2f987f97ce8ec27e199b5ea9a2)  
97 [results-tool?params=gbd-api-2019-permalink/1d45ef2f987f97ce8ec27e199b5ea9a2](http://ghdx.healthdata.org/gbd-results-tool?params=gbd-api-2019-permalink/1d45ef2f987f97ce8ec27e199b5ea9a2)).

98 In a publication on the burden of neurological disorders in which GBD 2016 estimates were used [2], the group  
99 of neurological disease as defined by GBD – i.e. Alzheimer’s disease and other dementias, epilepsy, migraine,  
100 motor neuron diseases (MND), multiple sclerosis (MS), Parkinson’s disease (PD), and tension-type headache  
101 (TTH) – was complemented by other conditions that, although not included in the standard set of neurological  
102 diseases, have a clear impact on the central or peripheral nervous systems. These include two NCDs, namely  
103 stroke and brain and nervous system cancers, three communicable neurological diseases, namely encephalitis,  
104 meningitis, and tetanus, and two injuries, namely traumatic brain injury (TBI) and spinal cord injury (SCI).  
105 Taken as a whole, this broad group of neurological conditions accounted for 11.6% of all-cause DALYs in  
106 2016 [2]. The authors of this manuscript evidenced a consistently increasing trend for number of prevalent  
107 cases and disability, in addition to burden, for the selected neurological diseases, and hypothesized that the  
108 same indices are reasonably expected to further on increase in reason of population ageing and growth:  
109 however, no direct information was referred to YLDs associated to neurological disease by country. In  
110 addition, two recent publications addressed the burden of neurological and brain disorders in European  
111 countries, relying on GBD 2017 estimates. The first addressed the same set of neurological disorders used in  
112 the global-level GBD 2016 publication [2] and showed that neurological disorders accounted for 13.5% of all-  
113 cause DALYs and ranked third after cancers and cardiovascular diseases [3]. The second paper focused on  
114 brain disorders, i.e. the same set of enlarged neurological conditions (with the exclusion of SCI) together with  
115 mental health and substance abuse disorders: results showed that brain disorders ranked first among all NCDs  
116 in terms of prevalence (79.1%), YLDs (34.5%) and DALYs (26.9%) [4]. The common conclusion of these  
117 studies is that the burden of neurological and brain disorders is increasing, at global and European levels, and  
118 that a relevant part of such increase is driven by population ageing. The information reported by the three  
119 aforementioned manuscripts [2-4] largely refers to DALYs, with less attention to disability (i.e. YLDs), an

index that reflects what happens to people while they live with a disease, which is of importance for public health purposes in ageing populations.

Italy has the largest proportion of elderly population among European countries, with 21.4% of citizens being  $\geq 65$ , and 6.4%  $\geq 80$  years [5], and these rates are expected to rise in the forthcoming years. Such trend is due to reduced fertility, which will lead to a top-heavy age structure [6,7], and to the ongoing reduction of mortality at all ages, which will make Italians' lives longer: at present, Italy is in the top 10 countries globally for life and healthy life expectancy [8]. Nonetheless, the increase in life expectancy has relevant consequences at the societal level, in terms of increased old age dependency ratio (i.e. the number of people aged 65+ compared to those aged 15-64 [5]), and of the prevalence of chronic conditions that are typical of the old age, the so-called compression of morbidity.

Some neurological conditions, e.g. PD, stroke and dementias, are among those that are typical of old age: it is therefore likely that prevalence and disability associated with neurological diseases in Italy have increased in the last decades. Indeed, the recently published study on the global burden of neurological conditions has shown that DALY counts of neurological diseases in Italy have increased by approximately 10% between 1990 and 2016 in Italy [2]. Moreover, neurological disorders are associated with extensive care, including emergency room access, inpatient and outpatient care, surgery, rehabilitation, long term and palliative care. In fact, 37.0% to 43.6% of DALYs attributable to neurological disorders are due to YLDs [3,4] with important differences among diseases: the burden of headache disorders, is in fact represented by YLDs only, whereas for conditions such as brain and nervous system cancers or MND, less than 5% of DALYs are attributable to YLDs.

As the prevalence of neurological disorders is expected to rise due to population ageing, understanding the trend of disability associated with these diseases in the last decades is of paramount importance to inform policy making and enable cost-effective health-care planning and strategic resource allocation for the Italian health system. The aims of this article are therefore the following: to describe the incidence, prevalence and YLDs associated with a broad group of neurological disorders in Italy, and their variation between 1990 and 2019; to address the trends for those NCDs with typical onset in young to adult age (e.g. headache disorders) and for those with typical onset in old age (e.g. Alzheimer's disease and other dementias), as well as for neurological injuries and for communicable neurological diseases; to compare estimates referred to Italy to those of other Western Europe countries.

## **METHODS**

The Institute for Health Metrics and Evaluation (IHME) produces annual updates of the GBD study, including temporal and geographic trends since 1990. Each update incorporates new data and methodological improvements to provide policy makers with the most up-to-date information for health care planning and resource allocation. In this analysis, we relied on the GBD 2019 round estimates (available at <http://ghdx.healthdata.org/gbd-results-tool>) referred to Italy, and to the years 2019 and 1990. The Italian

156 population comprised 60.6 million in 2019, with a life expectancy at birth of 83.1 years (ranking third at  
 157 European level) and 71.0 years of healthy life expectancy years (ranking sixth at European level) [8].

158 The GBD taxonomy lists causes in a four-level scheme, from generic to narrow categories. For example,  
 159 Migraine is a Level 4 condition (code B.5.6.1), and it is included among “Headache disorders” (Level 3, code  
 160 B.5.6). In turn, headache disorders are among “Neurological disorders” (Level 2, code B.5), which are “Non-  
 161 communicable diseases” (Level 1, code B). In this analysis, we have aggregated the estimates for 14 diseases  
 162 and injuries outcomes that are generally cared for by neurological services. This broad group of neurological  
 163 conditions included both level 3 and level 4 conditions as presented in the GBD, specifically:

- 164 a) a set of Level 3 NCDs, namely Alzheimer’s disease and other dementias, brain and nervous system  
 165 cancers, epilepsy, MND, MS, PD and stroke, as well as two Level 4 ones, namely migraine and TTH;
- 166 b) three Level 3 communicable diseases whose sequelae affect the nervous system, namely meningitis,  
 167 encephalitis and tetanus;
- 168 c) two neurological injuries, namely TBI and SCI, that were taken from the “injury by nature”  
 169 categories at Level 1 (where they were identified as head and spinal injuries).

170 On the contrary, we did not include the residual category “Other neurological disorders”, in which the  
 171 remaining neurological diseases were included. The most common are expected to be ataxias, Huntington’s  
 172 disease, dystonia, sleep disorders, neuropathies, myasthenia gravis, myopathies, muscle dystrophy, cerebral  
 173 palsies, but many others, often rare, are included. For such disorders, estimates are not precise and poorly  
 174 informative, with incidence and prevalence information often being not reported from original studies due to  
 175 poor quality of estimates [2,3]. Non-fatal outcomes for the individual disorders included in this residual  
 176 category need to be approximated by assuming the same YLDs/YLLs ratios estimated for the main fatal  
 177 neurological disorders, which can be a precise approach for those conditions associated to relevant mortality  
 178 (e.g. Huntington’s disease), but not for those associated to little or no mortality (e.g. myasthenia gravis). For  
 179 the residual category, the most precise estimate is for mortality, which is based on vital registration, but that it  
 180 is not of interest for our study.

181 YLDs are estimated as the product of prevalence of individual consequences of diseases (or sequelae)  
 182 multiplied by their corresponding disability weights, which quantify the relative severity of sequelae as a  
 183 number between 0 (representing full health) and 1 (representing death) [9]. These estimates are based on  
 184 systematic reviews of published and unpublished documents, survey microdata, administrative records of  
 185 health encounters, registries, and disease surveillance systems that are catalogued in the Global Health Data  
 186 Exchange website (<http://ghdx.healthdata.org>). For each condition, disability weights are calculated through a  
 187 series of severity splits – typically defining sequelae as asymptomatic, mild, moderate, and severe – as  
 188 described in the main GBD 2019 paper [1]. Such a distinction is of great importance in consideration of the  
 189 broad severity spectrum of some conditions. For example, disability weights associated to meningitis vary  
 190 between 0.01 (95% uncertainty interval, UI: 0.004-0.019), which identifies mild hearing loss as a result of  
 191 meningitis, and 0.542 (95% UI: 0.37-0.702), which identifies severe motor plus cognitive impairments.  
 192 Asymptomatic MS disability weights are set to zero, whereas those of severe MS, which identifies patients

193 with slurred speech and difficulty swallowing, weak arms and hands, very limited and stiff leg movement, loss  
194 of vision in both eyes and urinary incontinence, are 0.719 (95% UI: 0.534-0.858).

195 To identify the NCDs with typical onset in young to adult age vs. old age we relied on the 2019 incidence rates  
196 for Italy, using both the five-years groups, and the five main age categories (below 5 years, 5-14, 15-49, 50-  
197 69, and 70+). For the purpose of this study, we defined conditions with typical onset in young to adult age  
198 those for which the peak of incidence rate was observed before 50 years of age and conditions with typical  
199 onset in old age those for which, on the contrary, the peak of incidence rate was observed after 70 years of age  
200 (see supplementary Figures 1-9).

201 For each condition and year, counts and age-standardized rates (the latter both for males and females) for  
202 incidence, prevalence, and YLDs, and their relative 95% UIs are presented, as well as the change in counts  
203 and in age-standardized rates between 1990 and 2019. We also extracted, for comparison, the age-standardized  
204 rates for the group of Western Europe countries as defined by the GBD, to address whether estimates for Italy  
205 are significantly different from those of other countries: estimates are considered different if the 95% UI  
206 referred to Italy do not overlap with that referred to Western Europe countries. Western Europe countries  
207 include: Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland,  
208 Israel, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United  
209 Kingdom (<http://ghdx.healthdata.org/countries>).

210 Changes over the period were also analysed at the group level, i.e. young to adult-age onset NCDs, older age  
211 onset NCDs, neurological injuries, and communicable neurological diseases.

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## 213 **RESULTS**

214 All-cause prevalence for neurological disorders in 2019 in Italy (60.6 million citizens) accounted for 58.2  
215 million cases and 8.96 million YLDs.

216 Our classification of NCDs in young to adult and old-age typical onset enabled to allocate migraine, TTH, MS  
217 and epilepsy to the first group; Alzheimer's disease and other dementias, brain and nervous system cancers,  
218 MND, PD and stroke were on the contrary allocated to the second.

219 Table 1 shows incidence, prevalence, and YLDs, both as counts and age-standardized rates, for selected  
220 neurological conditions referred to 1990 and 2019, as well as the change between 1990 and 2019. The most  
221 prevalent conditions in 2019 were migraine and TTH, with 12.5 and 23.2 million prevalent cases (28.5 million  
222 cases when combined), and an increase of 8.2% and 12.8% compared to 1990. The prevalent cases of  
223 Alzheimer's disease and other dementias were 1.37 million in 2019, more than doubled compared to 1990;  
224 stroke and TBI had estimates of 770 and 650 thousand prevalent cases. The same diseases were also leading  
225 causes for incidence. With regard to disability, migraine was the leading condition both in terms of YLD counts  
226 and age-standardized rates, followed by dementias, stroke, and TBI. TBI had fewer YLD counts than stroke  
227 and Alzheimer's disease and other dementias, but higher age-standardized YLD rates. YLDs due to migraine  
228 (almost 470 000, i.e. 754/100 000 age-standardized YLD rates) were higher than the sum of the YLDs  
229 associated with the remaining neurological disorders. Migraine in fact accounted for 5.2% of all-cause YLD

counts for Italy (8.96 million YLDs) and 7.0% of age-standardized YLD rates (10 747/100 000). Headache disorders combined accounted for almost 519 000 YLDs (828/100 000 age-standardized rates), which correspond to 5.8% of all-cause YLDs and 7.7% of all-cause age-standardized YLD rates.

Table 2 shows age-standardized rates for incidence, prevalence, and YLDs by sex for selected neurological conditions. Most of the differences are connected to incidence, with females showing higher rates for migraine and MS, whereas males showed higher incidence rates for MND, PD and TBI. With regard to prevalence, differences were found for migraine and MS, with females showing higher rates, and for both neurological injuries, with males showing higher rates. Finally, with regard to YLDs, higher age-standardized rates were observed in males only for TBI. It has to be noticed that a large gender difference exists for migraine-related YLDs with, however, large UIs.

Changes over time provide additional information (Tables 1-2 and Figure 1). With regard to incidence, a consistent decrease both for counts and age-standardized rates was observed for stroke, meningitis, tetanus and TBI, whereas a consistent increase both for counts and age-standardized rates was observed for TTH, MS, dementias and MND. For other conditions, the trend was not uniform: for encephalitis and PD, the trend was increasing when counts were taken into account, and decreasing in terms of age-standardized rates; the opposite was observed for migraine.

As for prevalence, a consistent decrease both for counts and age-standardized rates was observed for meningitis and tetanus, whereas a consistent increase both for counts and age-standardized rates was observed for migraine, TTH, MS and MND. For other disorders, the trend was not uniform: for PD, stroke, TBI and SCI the trend was increasing when counts were taken into account, and decreasing in age-standardized rates; for dementias and brain and nervous system cancers the trend was increasing for counts and stable in age-standardized rates; finally, for encephalitis, the trend was decreasing in age-standardized rates, and stable in counts.

With regard to YLDs, a consistent decrease both for counts and age-standardized rates was observed for meningitis and tetanus, whereas a consistent increase both for counts and age-standardized rates was observed for MS and MND. For PD, stroke, TBI and SCI the trend was increasing when counts were taken into account, and decreasing in age-standardized rates; for migraine, TTH and dementias and brain and nervous system cancers the trend was increasing when counts were taken into account, and stable in age-standardized rates; finally, for encephalitis, the trend was decreasing in age-standardized rates, and stable in counts.

Table 3 shows that, between 1990 and 2019, young to adult-age onset NCDs underwent a consistent increase for incidence, prevalence and YLDs, which denotes the joint effect of increasing trends and demographic change. The opposite can instead be seen for communicable neurological diseases. Old-age onset NCDs underwent the largest increase over the period in terms of counts, likely driven by the dramatic increase in dementias and MND, but such an effect was not paralleled by age-standardized rates, which denotes that the observed increase is due to population ageing together with population growth. Finally, a decrease was shown for the incidence of neurological injuries, whereas the increase observed in prevalence and YLD counts is due to the effect of changes in demographic composition. Taken as a whole, incidence and prevalence of selected



neurological conditions increased both in counts and in age-standardized rates, whereas YLDs increased only in counts.

Young to adult-age onset NCDs were the most incident and prevalent neurological diseases, both in terms of counts and age-standardized rates, with little or no variations between 1990 and 2019 (see supplementary figures 10 and 11). Figure 2 shows the share of young to adult-onset NCDs with regard to YLD counts and rates in 1990 and 2019: in terms of counts, a reduction of the share of young to adult-age onset NCDs and an increase of old-age onset NCDs can be seen; the opposite is observed when age-standardized YLD rates are taken into account.

Compared to the group of Western Europe countries as a whole, the most striking results were observed for age-standardized rate variations in the period 1990-2019. Compared to the other countries, Italy showed a significantly higher increase in incidence rates of dementias and MND, a higher increase in prevalence rates for migraine, TTH, MS and MND, and a higher increase in YLD rates of MND. Italy showed a significantly higher decrease in incidence rates for PD, stroke, encephalitis, meningitis and TBI, and a significantly higher decrease in prevalence and YLD rates of PD, encephalitis, meningitis, TBI and SCI. Please refer to Supplementary Table 1 for full details on the Italy-Western Europe Countries comparison.

**DISCUSSION**

This study pointed out five main results. First, the most common incident and prevalent neurological diseases are headache disorders. Second, there has been a dramatic increase in the counts and age-standardized rates of incidence and prevalence of some conditions with typical onset in old age, in particular for Alzheimer disease and other dementias, brain and nervous system cancers and MND. In contrast, for PD the increase was limited to counts whereas a decrease in age-standardized rates was observed, meaning that the variation over time was associated with population ageing and growth, and with a control on environmental risk factors. Third, most of the disability associated with neurological conditions is due to migraine: YLDs associated with migraine were higher than the sum of YLDs associated with the remaining conditions, and accounted for 7% of all-cause age-standardized YLDs for Italy. Fourth, sex differences were mostly observed for incidence and prevalence. Females showed higher incidence and prevalence for migraine and MS, whereas males showed higher incidence for MND, PD and TBI, and a higher prevalence for TBI and SCI. Fifth, and most relevant, YLDs associated with neurological diseases increased by 22.5% between 1990 and 2019. Among conditions with typical onset in the young to adult age the increase was by 10.0%, and for those with typical onset in old age by 57.4%. However, the increase in YLDs was due to a clear epidemiological change mostly for young to adult-onset conditions, for which age-standardized YLD rates increased by 5.0%, whereas for old-age onset disease the variation herein observed was mostly an effect of population ageing and growth as age-standardized YLDs rates decreased by 13.7%. We cannot, however, exclude the possible effect played by the inclusion of less severe disease forms: this is, for example, the case of clinically isolated syndromes within MS. A consistent increase in both YLD counts and age-standardized rates was observed only for MS (+60.9% and +33.8%) and for MND (+89% and +36.5%).



304

305 *Young to adult-age onset NCDs*

306 In Italy, headache disorders, and migraine in particular, were the leading incident, prevalent and disabling  
307 conditions. In 2019, they represented 49% of all-cause morbidity and accounted for 5.8% of YLDs, with  
308 migraine alone being responsible for 5.2% of all-cause YLDs. Such a finding is most likely due to the changing  
309 structure of the Italian population, which is undergoing a consistent ageing process, and where middle-aged  
310 people constitute the largest group. Unfortunately, migraine incidence and prevalence rates increased, and  
311 disability remained stable over time, despite the availability of a broad set of effective compounds for both the  
312 acute treatment [10] and prophylaxis [11-14]. It has to be considered that the estimates referred to 2019 still  
313 do not account for the effect of monoclonal antibodies for migraine prophylaxis, which have been approved in  
314 Italy on 2020. Very recently, some real-life studies (or open-label phases of previous RCTs) showed that such  
315 new compounds (specifically, erenumab, fremanezumab, galcanezumab and eptinezumab) produce long-term  
316 effect on disease course and patients' reported disability [15-19]. It is likely to presume that the effect of these  
317 new therapies will be observable in future estimates.

318 Migraine is much more common among women, with a slightly increasing trend, and mean YLDs show a large  
319 gender difference. Such a difference has however to be interpreted with caution in reason of the large UI in  
320 age-standardized YLDs, which can be interpreted as an indicator of the fleeting quality of such estimates and  
321 call for specific studies on the incidence, prevalence and disability features of migraine in the Italian  
322 population. A review highlighted some elements that might explain the reasons for such high disability levels  
323 [20]: among them, the peak age of migraine prevalence among women in the third and fourth decades of life,  
324 i.e. when many women are engaged in balancing professional duties together with family and social lives, the  
325 presence of several comorbidities and the fact that headaches themselves are common comorbidities of many  
326 diseases. The picture of headache-related disability is however incomplete and complicated by the difficulty  
327 in capturing the impact of headaches on sufferers' daily lives. Such an impact is variable in relation to the  
328 frequency and duration of attacks, and the person-level limitations with daily activities, which vary according  
329 to pain severity, accompanying symptoms and the individual's "activity profile" of different persons [21]. The  
330 lack of relevant differences in YLD rates by gender is likely associated with such activity profile and not with  
331 gender issues as traditionally shown also in other GBD publications [22]. Compared to Western Europe  
332 estimates, those for Italy show a higher increase in prevalence of both migraine and TTH. The scenario that  
333 likely explains this is referred to the modification of the Italian population structure, in which the middle aged  
334 ones constitute the largest group and, even more likely, to the increased awareness of headache disorders. A  
335 recent study showed that 53.2% of patients attending headache centers were aware of their condition [23].  
336 Although this figure might be considered low, it represents an improvement in awareness, in particular it is  
337 considered that data referred to 2009 showed that only 26.8% of Italian patients were aware of their condition  
338 [24].

339 Similar to headache disorders, YLDs due to epilepsy can be interpreted as the impact of seizures on daily living  
340 activities and the stigmatizing effects of the disease. First-line antiepileptic drugs offer good control on seizures

341 in the majority of patients, but approximately 20% of patients suffer from drug-resistant epilepsy [25], and  
342 some of them are candidates for invasive surgical approaches [26]. The trends over time of incidence,  
343 prevalence and YLDs of epilepsy remained substantially stable, with age-standardized rates showing a  
344 decrease, but the large UIs reflect the imprecision of estimates. The same trend was observed in the recent  
345 paper on the global burden of epilepsy [27], but the UIs of 2019 estimates are less wide than previous ones  
346 perhaps due to the larger amount of data [3,27].

347 Data referred to MS show a considerable increase of all indicators both for counts and age-standardized rates,  
348 which is a result of both population ageing and growth, inclusion of more disease forms, such as clinically  
349 isolated syndromes, as well as a change in the epidemiology of MS. Such a change can be a consequence of  
350 an improved diagnostic ability – updated diagnostic criteria (i.e., 2010 revision of McDonald’s criteria [28]) –  
351 along with more sophisticated neuroimaging techniques, which made it possible to include clinically isolated  
352 syndromes in the present version of MS estimates. Nonetheless, the most relevant change is the increased  
353 prevalence and YLDs associated with MS, which can be due to an increased disease duration and prolonged  
354 survival, in turn accompanied by long-term disability [29-32]. Such a result might appear controversial in  
355 consideration of the impact that new disease-modifying therapies – i.e. fingolimod, alemtuzumab, or  
356 natalizumab vs. glatiramer acetate or interferon beta – had on reduced disability progression in MS, generally  
357 defined in terms of lower hazard of conversion to secondary progressive MS, reduced relapse rates, or reduced  
358 risk of walking aid need [33,34]. However, this is likely the main cause for increased YLDs: these relatively  
359 new therapies, in fact, by reducing conversion into secondary progressive MS, determine a prolonged survival  
360 with MS, with the effect of increasing YLDs and YLD rates. Sex differences were also found, with women  
361 expectably showing higher incidence and prevalence rates, as well as higher YLDs rates, which were however  
362 partly overlapping. Higher YLD rates might be connected to social role issues, with women showing lower  
363 employment rates than men, as well as to higher comorbidity rates [35]. Finally, with regard to the higher  
364 increase observed for Italian MS prevalence estimates contrasted to Western European ones, it is likely to  
365 suppose that the reason lies again in the modification of the Italian population structure, in which the middle  
366 aged group constitute the largest one, but also in the possibility to obtain an adequate level of care, which is  
367 well rooted in the Italian territory. In fact, as reported by a recent descriptive study, there are 236 MS centers,  
368 which included almost 45,000 patients in a national registry in 2018 [36].

369

#### 370 *Old-age onset NCDs*

371 Incidence, prevalence and YLDs associated with Alzheimer’s disease and other dementias have more than  
372 doubled in Italy over the 1990-2019 period, but not in terms of age-standardized rates, where only for incidence  
373 a minor increase was found, suggesting that such an increase is a consequence of population ageing. Dementias  
374 are the second cause of disability among neurological disorders, and the main driver among old-age onset  
375 neurological NCDs. The overall impact of dementias in Italy is noteworthy, mostly in reason of its  
376 demographic composition. In fact, Italy is one of the countries with the highest rate of oldest old in Europe  
377 and worldwide; compared to the other Western Europe countries, Italy had lower mortality rates both in 2019

(387.9 vs 423.7) and 1990 (642.1 vs 679.1), higher life expectancy both in 2019 (83.1 vs 82.1) and 1990 (77.2 vs 76.4) [8], resulting in a higher proportion of people susceptible to develop dementias. As dementias have no cure to date, efforts aimed to reduce the impact of such conditions on the lives of sufferers and their caregivers is, and will be, more and more of importance. Likewise, it is important to reduce the impact of those pre-dementia conditions, such as hearing loss and hypertension in adulthood, depression and diabetes in older age, which collectively account for 16.3% of the weighted population attributable fractions associated to dementias [37]. GBD 2019 estimates show that, compared to Western Europe, the age-standardized prevalence rates in Italy for hearing loss among adults are 2% higher (6 680.1 vs 6 547.1) and those of hypertension are 92% higher (17.5 vs 9.1); among the oldest old, the prevalence rates for diabetes are 6.3% higher (29 668.6 vs 27 920.9). These factors are likely to contribute to the high prevalence of dementias in Italy, and should be specifically targeted to reduce the impact of these conditions.

Brain and nervous system cancers and MND were responsible for the lower share of incidence, prevalence and YLDs among old-age onset NCDs. As shown in recent studies, based on previous iterations of GBD studies, the burden of these two conditions is mostly due to premature mortality at both global and European level, with only 3-5% of DALYs being attributable to YLDs [3,4,38,39]. What our data add to this information is the specific increase between 1990 and 2019 in prevalence for both brain and nervous system cancers and MND and, for MND only, the increase in YLDs. A possible explanation is that enhanced disease-modifying and palliative treatments and overall management of these conditions enable patients to live longer after the diagnosis. Concerning brain and nervous system cancers, five-years survival in Italy increased by 4.7% between 2000-2004 and 2010-2014 [40], likely due to increased survival of gliomas, which can be achieved if patients are treated in high-specialty centres [41]. About MNDs, which are mostly represented by amyotrophic lateral sclerosis and spinal muscle atrophy, increased survival is likely due to the increasing use of mechanical ventilation [42] and to the availability, in the last few years, of new therapies for spinal muscle atrophy [43]. At present, however, such new therapies have proved effectiveness mostly on paediatric populations; thus the effect on YLDs can be hypothesized only on the younger groups of the population.

Globally, PD has been recognized as one of the most fast-growing conditions in terms of prevalence and burden [44]. This does not apply to Italy, where we found an increase in incidence, prevalence and YLDs only in counts but not in age-standardized rates, which decreased by 15-21%. Such a trend is similar to what was shown at the global level, where YLDs increased by 30.6%, but age-standardized YLD rates were stable (0.1% change, 95% UI -2.8 to 3.3%) [1]. Among the reasons for such a global-level rise, demographic (i.e. population ageing and increased life expectancy) and environmental causes (i.e. factors related to industrialization, such as exposure to pesticides, solvents or metals) have been considered as the most relevant. With regard to the Italian case, it can be hypothesized that increased incidence, prevalence and YLDs are associated with population ageing and not with industrialization, as Italy is in a radical deindustrialization phase [45].

Stroke is a leading burdensome condition. Globally, it accounts for 5.7% of all-cause DALYs and for 1.8% of all-cause YLDs [1] and much of its burden, as shown by the recent studies based on European estimates for 2017, is associated with premature mortality: in fact, YLDs accounted for approximately 20% of the total

burden of neurological disorders [3,4]. The estimates herein presented show a consistent decrease in stroke incidence, and an increase in prevalence and YLD, which are however associated with a decrease in age-standardized rates, which can be interpreted as the result of preventive measures. Stroke is a highly preventable disease [46], and the reduction of Italian rates, which for stroke incidence are broader compared to Western Europe countries, might be associated with better control of risk factors [47,48].

*Neurological injuries*

Our results show a significant decrease in incidence, prevalence and YLD rates for TBI and SCI, with trends that were wider than in Western Europe in general. With regard to TBI, these findings are consistent with data from regional Italian studies showing a 40% decrease in incidence between 1985 and 2000 [49,50] but are in contrast with the rising worldwide incidence. Such discrepancy could be attributed to the lack of rigorous high-quality data – in particular, the incomplete capture of mild cases which do not require extensive interventions or access to emergency setting and might therefore be not recorded – leading to an underestimation of TBI incidence [51,52]. On the other hand, SCI estimates from this study are in line with the global estimates and the results presented in a recent Italian epidemiological study [53].

Data on prevalence and YLDs of TBI and SCI point out a significant increase in counts and a significant decrease in age-standardized rates, indicating that the number of people living with the long-term sequelae of TBI and SCI is increasing. This increase is mostly due to the increased life expectancy after the acute events, which are mostly represented by falls and road accidents [54]. Altogether, these findings provide support for the need to invest in a rigorous granular collection of data for TBI and SCI and the planning of adequate public health initiatives aimed to reduce the long-term outcomes associated with these injuries, in particular in the elderly.

*Communicable neurological diseases*

Concerning meningitis and tetanus, the estimates herein presented show a consistent, and robust decrease for all indicators, whereas in the case of encephalitis incidence estimates were raised, prevalence and YLDs were stable, and age-standardized rates for the three indicators showed a significant decrease. Such a result is very likely due to improved public health actions such as sanitation and vaccine coverage [55] and is consistent with previous observations [2,45,56] and the global shift from communicable to non-communicable disorders generally observed in high-income countries [1,57]. It is finally noteworthy to observe that between 1990 and 2019, the reduction observed for incidence, prevalence and YLDs estimates was larger in Italy compared to the set of Western European countries particularly for meningitis and encephalitis.

*Limitations*

This study suffers from the general limitations of GBD studies. First, the adjustments of non-fatal outcomes to account for biases introduced by different case definitions, e.g. registries based on medical data vs. patients' reports. Second, the 95% UIs used to define the precision of the estimates are sometimes wide, reflecting the

overall uncertainty of the estimates. Third, the adjustment for comorbidities, which is made under the assumption of the independent distribution of comorbid conditions. This is critical in consideration of the high number of comorbidities that people with conditions typical of older age, such as PD or dementias, may have, as well as of the fact that headache disorders are comorbid to a great amount of conditions. Fourth, the estimates herein presented are not complete as we decided to exclude from our analysis the residual category “Other neurological disease”, which is aimed to address the burden of neurological disorders not explicitly attributable to the most relevant diseases. As previously stated, estimates for non-fatal outcomes of this residual category have little precision as they need to be approximated assuming the same YLDs/YLLs ratios estimated for the main fatal neurological disorders. For some of the conditions included in the residual category, such as nerve diseases and myasthenia gravis, mortality is very low [58-60], thus leading to imprecise YLDs estimation. Should these condition be included, we would have a minimal increase in YLDs (21.1, corresponding to 1.6% of the total age-standardized YLD rates reported for our group of conditions) and a negligible one for prevalence (0.9, corresponding to 0.002% of the total age-standardized prevalence rates), whereas incidence for the residual category was set to zero. Fifth, we used an ad-hoc approach to identify conditions with typical onset in young to adult vs. old age, i.e. addressing the peak for incidence before the age of 50 or after 70, which is not a common procedure in GBD-based studies. Other studies, using a different approach, might therefore produce different results.

469

## 470 *Conclusions*

In conclusion, we reported information on incidence, prevalence and disability associated with neurological disorders in Italy relying on the GBD 2019 estimates. Our results show that headache disorders are still the most prevalent and disabling conditions, and that epidemiological patterns have changed between 1990 and 2019. In particular, our work pinpoints a worrisome rise in incidence and prevalence for conditions with typical onset in older ages, particularly dementias and PD as an effect of population ageing; for MND, on the contrary, estimates suggest a consistent increase which cannot be explained by population ageing only, but also as an effect of prolonged survival.

Taken together, YLDs associated with this broad set of neurological conditions – where stroke, brain and nervous system cancers, TBI, SCI, encephalitis, meningitis, and tetanus were added to the standard set of neurological diseases – between 1990 and 2019 increased by 22.5% in counts whereas age-standardized rates decreased by 2.3%. Hence, the increase is mostly due to population ageing and growth, with the only exceptions of MND and MS (for which classification changes and the inclusion of less severe varieties can be also implicated), and points out the increased survival for many of these conditions.

Such a scenario calls for public health actions towards improving outcomes and mitigating disability associated with neurological diseases. These actions should involve different levels of care, from early diagnosis and targeted treatment, up to rehabilitation, as well as behavioural changes, modifications to public and private environment and workplace interventions.

488

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498             website of the Institute for Health Metrics and Evaluation: <http://ghdx.healthdata.org/gbd-results-tool>
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- 501         •     **Consent to participate.** Not applicable
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736 **Table 1:** Incidence, prevalence and years lived with a disability for selected neurological conditions in Italy, years 1990-2019, both sexes, counts  
737 and age-standardized rates, and percentage change over time

		Counts			Age-Standardised Rates			
		1990	2019	Change	1990	2019	Change	
Young to adult-age onset NCDs	Migraine	Incidence	761 737 (674 936 to 851 301)	693 328 (617 048 to 775 956)	-9.0% (-12.2 to -5.6%)	1 467.6 (1 297.0 to 1 638.4)	1 528.4 (1 354.4 to 1 709.3)	4.1% (1.8 to 6.7%)
		Prevalence	11 539 567 (10 071 697 to 13 244 875)	12 488 060 (10 866 465 to 14 382 675)	8.2% (2.9 to 13.8%)	18 823.3 (16 533.3 to 21 645.5)	20 337.7 (17 724.7 to 23 405.8)	7.5% (4.2 to 11.3%)
		YLDs	428 442 (60 294 to 999 838)	467 569 (69 422 to 1 085 192)	9.1% (2.3 to 17.0%)	699.0 (91.6 to 1 644.2)	754.0 (91.3 to 1 781.7)	7.7% (-1.0 to 12.8%)
	TTH	Incidence	6 924 922 (6 148 754 to 7 750 792)	7 399 179 (6 578 880 to 8 283 797)	6.8% (2.6 to 11.2%)	11 507.6 (10 191.2 to 12 864.6)	11 850.2 (10 463.6 to 13 286.3)	3.0% (0.4 to 5.6%)
		Prevalence	20 647 795 (18 432 606 to 22 872 626)	23 287 870 (20 931 617 to 25 813 025)	12.8% (8.4 to 17.0%)	33 199.0 (29 462.1 to 36 915.0)	35 514.3 (31 460.2 to 39 340.7)	7.0% (4.3 to 9.5%)
		YLDs	45 799 (12 898 to 163 750)	52 235 (14 845 to 188 815)	14.1% (3.3 to 21.7%)	71.0 (19.2 to 258.3)	73.9 (19.5 to 279.8)	4.1% (-4.5 to 9.3%)
	MS	Incidence	1 292 (1 109 to 1 487)	1 424 (1 204 to 1 658)	10.2% (4.3 to 17.0%)	2.2 (1.9 to 2.6)	2.8 (2.4 to 3.3)	26.3% (23.0 to 30.5%)
		Prevalence	45 114 (38 270 to 52 987)	73 486 (61 962 to 86 509)	62.9% (57.8 to 68.5%)	64.0 (54.2 to 75.4)	85.6 (71.7 to 102.2)	33.8% (30.7 to 38.4%)
		YLDs	11 353 (7 910 to 15 044)	18 268 (12 816 to 24 227)	60.9% (53.5 to 69.2%)	16.2 (11.2 to 21.5)	21.7 (15.2 to 29.0)	33.8% (27.1 to 40.9%)
	Epilepsy	Incidence	19 761 (12 835 to 26 832)	21 357 (13 553 to 28 891)	8.1% (-16.1 to 40.3%)	39.6 (24.9 to 54.7)	39.0 (24.1 to 55.1)	-1.5% (-24.0 to 25.4%)
		Prevalence	170 232 (113 351 to 222 536)	190 510 (124 111 to 254 479)	11.9% (-12.8% to 43.3%)	292.7 (196.0 to 387.1)	277.0 (178.5 to 377.8)	-5.4% (-26.1 to 21.4%)
		YLDs	41 518 (21 624 to 67 948)	40 423 (20 851 to 70 180)	-2.6% (-32.5 to 43.0%)	72.8 (37.9 to 121.0)	61.3 (31.1 to 105.9)	-15.8% (-42.4 to 24.8%)
Old-age onset NCDs	Alzheimer's disease and other dementias	Incidence	90 748 (74 769 to 106 630)	186 108 (156 694 to 214 287)	105.1% (95.8 to 117.0%)	100.9 (84.5 to 115.8)	103.7 (88.1 to 119.3)	2.8% (0.6 to 6.1%)
		Prevalence	649 189 (540 788 to 760 512)	1 369 006 (1 148 213 to 1 604 011)	110.9% (101.6 to 121.9%)	735.5 (615.3 to 845.5)	742.1 (627.4 to 862.2)	0.9% (-1.7 to 4.2%)
		YLDs	93 692 (65 580 to 126 413)	204 584 (141 692 to 276 418)	118.4% (107.5 to 130.5%)	106.5 (75.0 to 142.4)	108.7 (75.7 to 146.8)	2.0% (-0.7 to 5.5%)
	Brain and nervous	Incidence	4 471 (3 699 to 5 137)	6 056 (3 886 to 7 645)	35.5% (-15.9 to 67.6%)	6.3 (5.2 to 7.3)	6.1 (4.1 to 7.6)	-2.9% (-38.7 to 19.7%)

system cancers	Prevalence	11 439 (9 342 to 13 375)	18 878 (12 213 to 24 506)	65.0% (4.5 to 115.7%)	19.0 (15.5 to 22.6)	23.6 (15.7 to 29.9)	24.5% (-23.0 to 61.7%)
	YLDs	1 572 (1 068 to 2 104)	2 339 (1 388 to 3 458)	52.7% (-4.9 to 93.7%)	2.3 (1.6 to 3.1)	2.6 (1.5 to 3.7)	11.5% (-29.3 to 41.0%)
MND	Incidence	979 (909 to 1 052)	1 901 (1 798 to 1 999)	94.2% (88.1 to 100.5%)	1.3 (1.2 to 1.4)	1.5 (1.4 to 1.6)	26.1% (22.2 to 30.6%)
	Prevalence	4 119 (3 525 to 7 805)	7 785 (6 656 to 8 996)	89.0% (77.6 to 102.6%)	5.6 (4.5 to 6.5)	7.6 (6.6 to 8.8)	36.5% (30.1 to 44.5%)
	YLDs	875 (597 to 1 163)	1 655 (1 127 to 2 192)	89.0% (77.6 to 102.6%)	1.2 (0.8 to 1.6)	1.6 (1.1 to 2.1)	36.5% (30.1 to 44.5%)
	Incidence	16 426 (13 478 to 19 446)	22 405 (18 345 to 26 681)	36.4% (26.7 to 47.7%)	17.6 (14.7 to 20.7)	14.9 (12.4 to 17.6)	-15.4% (-19.5 to -11.3%)
PD	Prevalence	154 609 (127 896 to 184 618)	207 097 (168 366 to 251 061)	33.9% (25.6 to 42.9%)	166.1 (138.1 to 197.4)	131.4 (107.9 to 156.8)	-20.9% (-25.0 to -16.7%)
	YLDs	21 546 (14 762 to 29 515)	28 840 (19 618 to 39 472)	33.9% (24.5 to 42.7%)	23.2 (15.9 to 31.6)	18.6 (12.6 to 25.5)	-19.8% (-24.3 to -15.1%)
	Incidence	106 934 (90 775 to 128 136)	94 074 (83 223 to 106 720)	-12.0% (-18.9 to -5.5%)	124.4 (107.3 to 146.8)	68.9 (61.5 to 76.8)	-44.6% (-48.4 to -41.2%)
Stroke	Prevalence	732 828 (655 372 to 826 087)	772 098 (698 726 to 873 841)	5.3% (0.5 to 11.3%)	869.0 (780.9 to 968.4)	632.9 (569.2 to 703.1)	-27.2% (-30.2 to -23.9%)
	YLDs	109 993 (79 321 to 141 103)	121 126 (87 312 to 155 582)	10.1% (4.4 to 16.8%)	130.2 (94.1 to 165.3)	95.9 (68.8 to 122.0)	-26.3% (-29.5 to -23.0%)
	Encephalitis	Incidence	3 591 (3 083 to 4 078)	4 272 (3 793 to 4 737)	19.0% (11.2 to 27.6%)	6.5 (5.5 to 7.6)	6.1 (5.3 to 6.8)
Prevalence		9 677 (7 423 to 12 044)	9 977 (7 632 to 12 211)	3.1% (-1.3 to 7.6%)	15.0 (11.7 to 18.6)	12.5 (9.8 to 15.2)	-17.0% (-20.0 to -13.7%)
YLDs		1 033 (721 to 1 393)	1 035 (721 to 1 384)	0.2% (-4.0 to 4.4%)	1.7 (1.2 to 2.2)	1.4 (1.0 to 1.9)	-16.5% (-19.8 to -13.4%)
Meningitis	Incidence	6 677 (5 156 to 8 393)	2 962 (2 439 to 3 522)	-55.6% (-63.0 to -47.3%)	16.5 (12.3 to 21.4)	5.5 (4.5 to 6.6)	-66.8% (-71.6 to -60.3%)
	Prevalence	30 029 (24 656 to 36 444)	9 031 (7 879 to 10 375)	-69.9% (-73.1 to -66.6%)	50.8 (41.8 to 61.6)	12.3 (10.6 to 14.3)	-75.9% (-78.2 to -73.4%)
	YLDs	2 826 (1 917 to 3 865)	829 (578 to 1 095)	-70.7% (-73.2 to -68.1%)	5.0 (3.4 to 6.9)	1.2 (0.8 to 1.6)	-75.7% (-77.7 to -73.8%)
	Incidence	379 (308 to 466)	115 (82 to 165)	-69.6% (-77.0 to -57.7%)	0.4 (0.4 to 0.5)	0.1 (0.1 to 0.1)	-83.4% (-87.3 to -76.8%)
Tetanus	Prevalence	23 (18 to 29)	8 (6 to 11)	-64.5% (-71.8 to -53.5%)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	-74.9% (-80.7 to -67.9%)



		3	1	-68.9%	0.0	0.0	-82.2%	
YLDs		(2 to 4)	(1 to 1)	(-76.0to -57.3%)	(0.0 to 0.0)	(0.0 to 0.0)	(-85.9 to -75.8%)	
Neurolog ical injuries	TBI	Incidence	311 925	293 426	-5.9%	490.5	377.1	-18.3%
			(264 451 to 373 544)	(244 319 to 355 929)	(-11.2 to -0.3%)	(418.3 to 581.4)	(319.2 to 450.6)	(-20.0 to -16.5%)
		Prevalence	594 610	652 766	9.8%	808.3	657.0	-23.1%
			(561 364 to 626 824)	(614 279 to 691 707)	(7.9 to 12.1%)	(764.1 to 825.5)	(621.5 to 694.4)	(-26.1 to -20.0%)
	YLDs	86 061	93 736	8.9%	117.9	96.3	-18.7%	
		(60 155 to 116 787)	(66 044 to 126 346)	(6.8 to 11.5%)	(82.4 to 159.6)	(67.5 to 130.6)	(-20.0 to -17.3%)	
	SCI	Incidence	6 984	7 144	1.9%	10.2	7.8	-10.7%
			(5 309 to 9 235)	(5 225 to 9 725)	(-4.8 to 8.8%)	(8.0 to 12.9)	(6.1 to 9.8)	(-13.9 to -6.8%)
Prevalence		152 759	167 203	9.5%	218.3	192.6	-23.6%	
		(143 157 to 165 237)	(155 913 to 180 891)	(6.6 to 13.0%)	(204.3 to 235.2)	(179.3 to 207.6)	(-26.2 to -20.9%)	
YLDs	40 412	44 023	8.9%	58.6	52.3	-11.8%		
	(28 984 to 52 258)	(31 605 to 56 655)	(5.2 to 12.9%)	(41.6 to 76.2)	(37.5 to 67.6)	(-14.3 to -8.9%)		

Notes: NCDs, non-communicable diseases; YLDs, years lived with a disability; MND, motor neuron disease; MS, multiple sclerosis; PD, Parkinson's disease; SCI, spinal cord injury; TBI, traumatic brain injury; TTH, tension-type headache.

742 **Table 2:** Incidence, prevalence and years lived with a disability for selected neurological conditions in Italy, years 1990-2019, separately for males  
743 and females, age-standardized rates, and percentage change over time

		Males			Females			
		1990	2019	Change	1990	2019	Change	
Young to adult-age onset NCDs	Migraine	Incidence	1 010.2 (880.5 to 1 136.2)	1 066.8 (930.2 to 1 201.5)	5.6% (2.1 to 9.5%)	1 935.8 (1 715.0 to 2 157.6)	2 011.9 (1 778.9 to 2 251.1)	3.9% (0.8 to 7.0%)
		Prevalence	12 574.5 (10 884.4 to 14 677.0)	13 491.2 (11 607.8 to 15 761.4)	7.3% (2.6 to 12.4%)	25 196.2 (22 026.4 to 28 716.3)	27 289.6 (23 667.3 to 31 259.0)	8.3% (3.7 to 13.2%)
		YLDs	458.7 (59.6 to 1 057.9)	492.0 (59.0 to 1 132.0)	7.2% (-0.7 to 13.6%)	938.0 (122.3 to 2 212.2)	1 019.9 (122.5 to 2 499.1)	8.7% (-1.8 to 15.0%)
	TTH	Incidence	11 198.4 (9 885.7 to 12 550.5)	11 621.7 (10 247.6 to 13 031.6)	3.8% (0.1 to 7.4%)	11 793.8 (10 432.5 to 13 174.2)	12 070.4 (10 663.9 to 13 1565.6)	2.3% (-1.0 to 6.0%)
		Prevalence	32 340.7 (28 669.2 to 36 103.4)	35 617.1 (31 429.0 to 39 651.2)	10.1% (5.8 to 14.2%)	33 982.6 (30 255.1 to 37 767.3)	35 378.0 (31 485.9 to 39 176.7)	4.1% (1.2 to 7.3%)
		YLDs	57.7 (12.4 to 238.3)	61.5 (12.7 to 264.4)	6.6% (-5.3 to 13.2%)	83.8 (25.8 to 280.0)	86.2 (26.1 to 296.2)	2.9% (-5.5 to 8.2%)
	MS	Incidence	1.7 (1.4 to 2.0)	2.1 (1.8 to 2.4)	22.5% (18.5 to 27.3%)	2.8 (2.4 to 3.2)	3.6 (3.1 to 4.2)	29.4% (25.8 to 33.9%)
		Prevalence	46.2 (38.7 to 54.2)	61.2 (50.8 to 73.1)	32.6% (27.9 to 38.0%)	80.4 (68.1 to 94.8)	109.1 (91.6 to 129.9)	35.7% (32.1 to 40.6%)
		YLDs	12.0 (8.3 to 16.1)	15.8 (10.9 to 21.1)	31.4% (21.3 to 41.6%)	20.2 (14.1 to 26.7)	27.5 (19.1 to 36.8)	36.2% (28.1 to 44.7%)
	Epilepsy	Incidence	43.0 (27.3 to 59.5)	41.0 (25.7 to 58.2)	-4.6% (-26.72 to 22.4%)	36.2 (22.4 to 50.2)	37.1 (23.0 to 52.4)	2.3% (-20.9 to 30.9%)
		Prevalence	308.6 (205.1 to 408.1)	278.8 (179.4 to 380.1)	-9.7% (-29.9 to 15.5%)	278.1 (183.7 to 369.2)	276.0 (176.7 to 375.8)	-0.8% (-23.1 to 27.5%)
		YLDs	77.3 (40.6 to 128.1)	62.1 (31.5 to 108.0)	-19.7% (-45.4 to 19.5%)	68.6 (35.6 to 112.6)	60.7 (30.7 to 104.8)	-11.6% (-39.3 to 29.0%)
Old-age onset NCDs	Alzheimer's disease and other dementias	Incidence	84.1 (69.4 to 97.5)	88.4 (74.2 to 102.4)	5.1% (2.3 to 9.6%)	110.7 (93.4 to 126.9)	114.7 (97.9 to 131.6)	3.6% (1.2 to 7.0%)
		Prevalence	596.7 (493.3 to 697.9)	612.5 (513.3 to 715.9)	2.6% (-0.6 to 7.1%)	807.7 (681.8 to 936.7)	825.3 (699.8 to 954.7)	2.2% (-0.5 to 5.5%)
		YLDs	8.6 (60.6 to 116.6)	89.7 (62.3 to 121.3)	3.6% (0.1 to 8.3%)	116.7 (82.4 to 156.3)	120.7 (84.7 to 162.8)	3.4% (0.4 to -7.0%)
	Brain and nervous	Incidence	7.1 (5.3 to 8.1)	7.1 (4.6 to 9.4)	0.3% (-42.2 to 31.5%)	5.6 (4.2 to 7.0)	5.2 (2.8 to 7.0)	-7.4% (-44.4 to 28.7%)

system cancers	Prevalence	18.9 (14.1 to 22.3)	25.4 (16.5 to 34.2)	34.0% (-23.9 to 84.5%)	19.3 (14.1 to 25.1)	22.2 (12.1 to 31.4)	15.0% (-33.5 to 77.6%)	
	YLDs	2.5 (1.7 to 3.4)	2.9 (1.6 to 4.4)	16.7% (-32.9to 57.8%)	2.1 (1.4 to 3.0)	2.2 (1.1 to 3.4)	4.9% (-37.6 to 52.8%)	
MND	Incidence	1.5 (1.4 to 1.6)	2.0 (1.8 to 2.1)	27.9% (23.9 to 32.4%)	1.2 (1.1 to 1.3)	1.4 (1.3 to 1.5)	23.0% (18.4 to 27.9%)	
	Prevalence	6.2 (5.4 to 7.2)	8.5 (7.3 to 9.9)	36.6% (29.7 to 45.1%)	5.0 (4.3 to 5.9)	6.8 (5.9 to 7.9)	35.1% (27.6 to 43.6%)	
	YLDs	1.3 (0.9 to 1.8)	1.8 (1.2 to 2.4)	36.6% (29.7 to 45.1%)	1.1 (0.7 to 1.4)	1.4 (1.0 to 1.9)	35.1% (27.6 to 43.6%)	
PD	Incidence	21.1 (17.5 to 24.9)	18.6 (15.4 to 21.9)	-12.2% (-16.6 to -7.8%)	15.7 (13.0 to 18.5)	12.3 (10.1 to 14.5)	-22.0% (-27.5 to -16.6%)	
	Prevalence	176.5 (145.5 to 210.4)	150.9 (123.3 to 180.3)	-14.5% (-18.5 to -10.7%)	160.4 (132.3 to 190.9)	116.5 (95.2 to 139.1)	-27.4% (-32.7 to -22.1%)	
	YLDs	24.7 (16.9 to 34.0)	21.4 (14.5 to 29.4)	-13.5% (-17.9 to -8.6%)	22.3 (15.3 to 30.5)	16.4 (11.3 to 22.6)	-26.5% (-32.7 to -20.3)	
Stroke	Incidence	130.4 (112.4 to 153.9)	69.7 (62.7 to 77.7)	-46.5% (-50.6 to -43.0%)	119.0 (102.1 to 141.1)	67.8 (60.4 to 76.1)	-43.0% (-47.0 to -39.4%)	
	Prevalence	840.0 (750.0 to 947.2)	593.4 (532.2 to 662.8)	-29.4% (-32.5 to -26.0%)	896.0 (807.5 to 995.3)	668.8 (602.2 to 742.2)	-25.3% (-29.0 to -21.2%)	
	YLDs	119.8 (86.8 to 153.0)	85.7 (60.8 to 109.6)	-28.5% (-31.9 to -24.9%)	138.6 (100.0 to 175.7)	104.8 (75.7 to 133.8)	-24.4% (-28.1 to -20.5%)	
Communi cable diseases	Encephalitis	Incidence	6.8 (5.8 to 7.9)	6.4 (5.6 to 7.2)	-5.7% (-11.3 to -0.1%)	6.3 (5.3 to 7.3)	5.8 (5.0 to 6.5)	-7.9% (-12.7 to -2.5%)
		Prevalence	15.0 (11.5 to 18.6)	12.6 (9.8 to 15.3)	-16.3% (-19.6 to -12.8%)	15.0 (11.8 to 18.6)	12.4 (9.8 to 15.1)	-17.6% (-20.5 to -14.5%)
		YLDs	1.5 (1.1 to 2.1)	1.3 (0.9 to 1.8)	-13.4% (-16.9 to -9.9%)	1.8 (1.2 to 2.4)	1.4 (1.0 to 2.0)	-18.9% (-22.5 to -15.6%)
	Meningitis	Incidence	18.0 (13.4 to 23.4)	5.9 (4.8 to 7.1)	-67.2% (-72.1 to -60.6%)	15.0 (11.1 to 19.4)	5.1 (4.1 to 6.1)	-66.2% (-70.9 to -59.7%)
		Prevalence	53.8 (44.2 to 65.7)	12.9 (11.2 to 15.0)	-76.1% (-78.6 to -73.5%)	47.8 (39.6 to 58.1)	11.6 (10.1 to 13.5)	-75.6% (-77.8 to -73.2%)
		YLDs	5.0 (3.4 to 6.8)	1.2 (0.9 to 1.6)	-75.2% (-77.4 to -73.2%)	5.1 (3.4 to 7.0)	1.2 (0.8 to 1.6)	-76.1% (-78.2 to -74.2%)
	Tetanus	Incidence	0.3 (0.2 to 0.5)	0.1 (0.0 to 0.1)	-79.4% (-86.5 to -54.1%)	0.5 (0.4 to 0.6)	0.1 (0.1 to 0.1)	-85.1% (-89.0 to -79.8%)
		Prevalence	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	-69.9% (-78.6 to -46.0%)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	-7.0% (-82.8 to -70.6%)

		0.0	0.0	-78.1%	0.0	0.0	-83.8%	
		(0.0 to 0.0)	(0.0 to 0.0)	(-82.2 to -53.2%)	(0.0 to 0.0)	(0.0 to 0.0)	(-87.9 to -78.4%)	
Neurological injuries	TBI	Incidence	599.7 (514.1 to 705.4)	494.3 (420.9 to 589.5)	-13.7% (-15.5 to -11.7%)	362.7 (302.9 to 440.4)	251.6 (208.8 to 306.7)	-25.8% (-28.0 to -23.5%)
		Prevalence	1 027.3 (970.9 to 1 089.6)	884.7 (834.6 to 937.2)	-17.6% (-20.4 to -14.5%)	584.6 (548.2 to 618.3)	430.6 (403.5 to 457.3)	-30.6% (-34.4 to -27.0%)
		YLDs	151.1 (105.5 to 204.9)	130.4 (90.9 to 177.7)	-13.9% (-15.3 to -12.2%)	84.1 (59.1 to 113.9)	62.3 (43.7 to 84.4)	-26.3% (-27.8 to -24.6%)
		Incidence	10.7 (8.7 to 13.2)	8.9 (7.2 to 11.0)	-6.1% (-10.5 to -1.2%)	9.0 (6.7 to 12.0)	6.4 (4.8 to 8.4)	-17.1% (-21.3 to -12.1%)
	SCI	Prevalence	259.2 (241.8 to 280.5)	241.3 (224.3 to 261.8)	-16.6% (-19.4 to -14.0%)	175.1 (163.7 to 189.4)	143.3 (132.9 to 155.0)	-29.0% (-2.1 to -25.9%)
		YLDs	70.8 (50.3 to 91.9)	66.8 (47.4 to 86.1)	-6.9% (-9.8 to -3.5%)	45.9 (32.4 to 59.5)	38.0 (26.8 to 49.6)	-18.2% (-21.1 to -14.9%)

Notes: NCDs, non-communicable diseases; YLDs, years lived with a disability; MND, motor neuron disease; MS, multiple sclerosis; PD, Parkinson's disease; SCI, spinal cord injury; TBI, traumatic brain injury; TTH, tension-type headache.

749 **Table 3.** Change between 1990 and 2019 for prevalence, incidence and YLDs associated to neurological conditions in Italy by group in counts and  
750 age-standardized rates

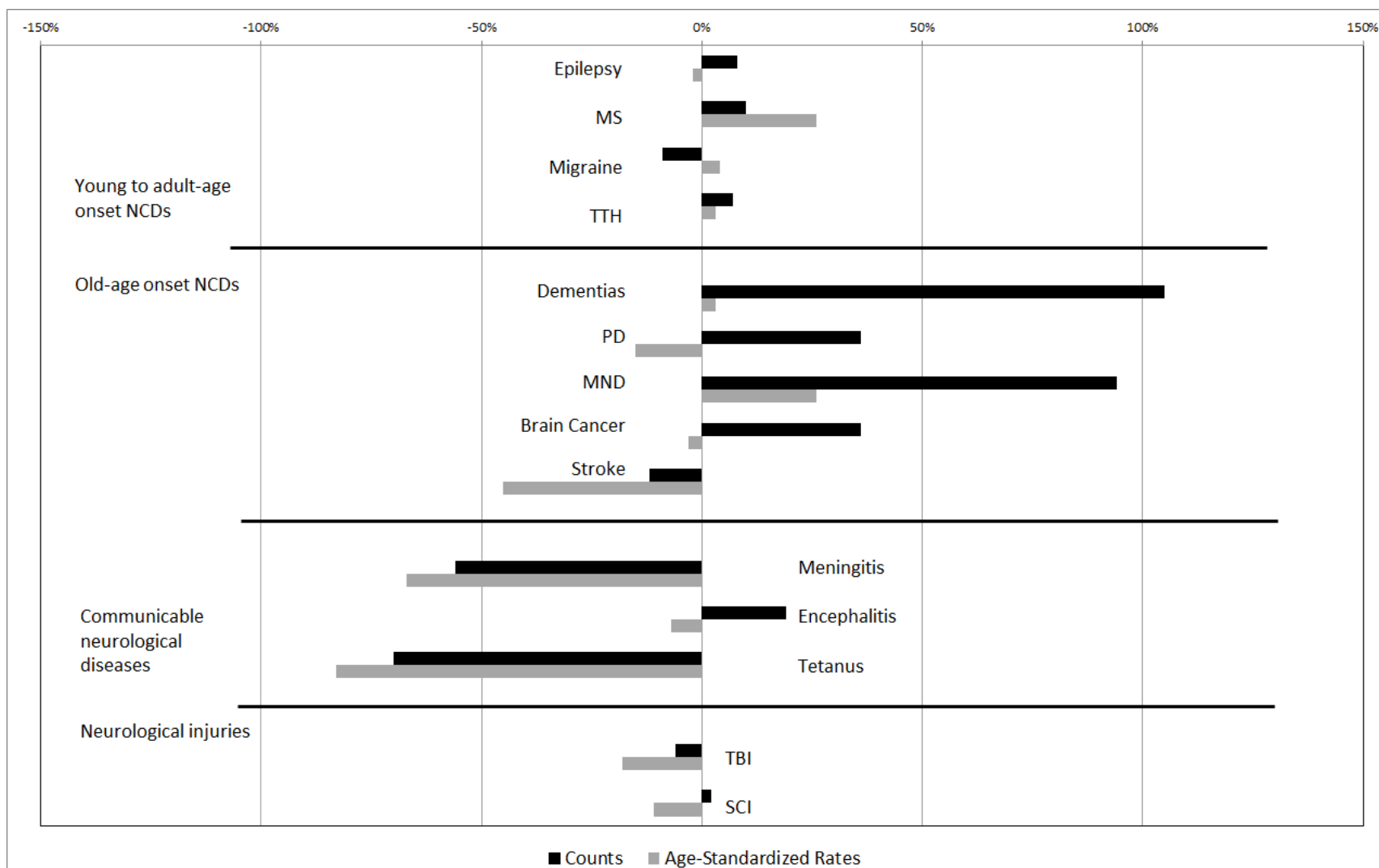
	Counts					Age-Standardized Rates				
	Young to adult-age onset NCDs	Old-age onset NCDs	Neurological injuries	Communicable diseases	All	Young to adult-age onset NCDs	Old-age onset NCDs	Neurological injuries	Communicable diseases	All
Incidence										
1990	7 707 712 (6 939 499 to 8 555 449)	219 557 (196 760 to 246 567)	318 909 (271 246 to 380 391)	10 648 (8 986 to 12 431)	8 256 825 (7 477 164 to 9 109 050)	13 017.0 (11 679.5 to 14 414.0)	250.6 (228.1 to 277.6)	500.6 (429.0 to 592.7)	23.5 (19.1 to 28.5)	13 791.7 (12 422.1 to 15 145.4)
2019	8 115 288 (7 296 914 to 8 986 042)	310 545 (280 665 to 339 830)	300 540 (250 968 to 363 563)	7 349 (6 669 to 8 095)	8 733 722 (7 908 181 to 9 603 751)	13 420.4 (12 052.7 to 14 863.8)	195.3 (178.2 to 211.6)	384.9 (326.9 to 459.1)	11.6 (10.4 to 13.0)	14 012.2 (12 654.9 to 15 457.8)
Change	5.3% (1.5 to 9.2%)	41.6% (31.9 to 9.4%)	-5.8% (-11.1 to -0.1%)	-30.7% (-38.7 to -22.5%)	5.8% (2.2 to 9.4%)	3.1% (0.8 to 5.3%)	-22.0% (-26.0 to -18.4%)	-23.1% (-26.1 to -20.1%)	-50.2% (-56.4 to -43.3%)	1.6% (-0.6 to 3.7%)
Prevalence										
1990	32 402 708 (29 594 987 to 35 193 536)	1 552 283 (1 409 416 to 1 639 210)	747 370 (706 276 to 788 018)	39 730 (33 913 to 47 149)	34 742 090 (31 923 175 to 37 542 380)	52 479.0 (47 774.0 to 57 084.3)	1 795.2 (1 643.7 to 1 948.9)	1 026.7 (973.7 to 1 084.4)	65.8 (56.0 to 78.4)	55 366.6 (50 705.4 to 59 994.4)
2019	36 039 926 (33 072 492 to 39 030 457)	2 374 864 (2 127 650 to 2 639 689)	819 968 (773 097 to 867 675)	19 016 (16 346 to 21 807)	39 253 775 (36 297 623 to 42 175 956)	56 214.6 (51 286.1 to 61 081.0)	1 537.6 (1 402.0 to 1 677.9)	849.6 (804.8 to 898.7)	24.7 (21.4 to 28.3)	58 626.5 (53 712.0 to 63 512.2)
Change	11.2% (7.9 to 14.4%)	53.0% (46.4 to 59.9%)	9.7% (7.9 to 11.9%)	-52.0% (-58.0 to -46.1%)	13.0% (9.8 to 16.0%)	7.1% (5.0 to 9.1%)	-14.3% (-16.7 to -11.9%)	-17.2% (-18.6 to -15.7%)	-62.3% (-66.6 to -58.1%)	5.9% (3.9 to 7.8%)
YLDs										
1990	527 294 (148 437 to 1 000 029)	227 678 (167 478 to 290 616)	126 472 (91 358 to 166 867)	3 862 (2 669 to 5 138)	885 124 (487 601 to 1 513 017)	860.0 (232.8 to 1 808.7)	263.4 (193.7 to 335.7)	176.4 (127.4 to 232.5)	6.7 (4.6 to 9.0)	1 3046.5 (668.2 to 2316.3)
2019	578 495 (162 446 to 1 217 794)	358 605 (260 663 to 462 172)	137 759 (99 629 to 182 356)	1 865 (1 318 to 2 453)	1 076 724 (622 962 to 1 772 153)	911.0 (222.6 to 1 964.7)	227.4 (165.7 to 291.9)	148.6 (108.1 to 196.5)	2.6 (1.8 to 3.4)	1 289.6 (596.8 to 2364.5)

Change	10.0% (3.3 to 17.3%)	57.4% (50.3 to 65.3%)	8.9% (6.8 to 11.5%)	-51.6% (-56.2 to -47.5%)	22.5% (15.5 to 31.8%)	5.0% (-5.5 to 11.2%)	-13.7% (-16.2 to -10.8%)	-15.8% (-17.4 to -13.9%)	-61.0% (-64.7 to -57.7%)	-2.3% (-11.8 to 4.3%)
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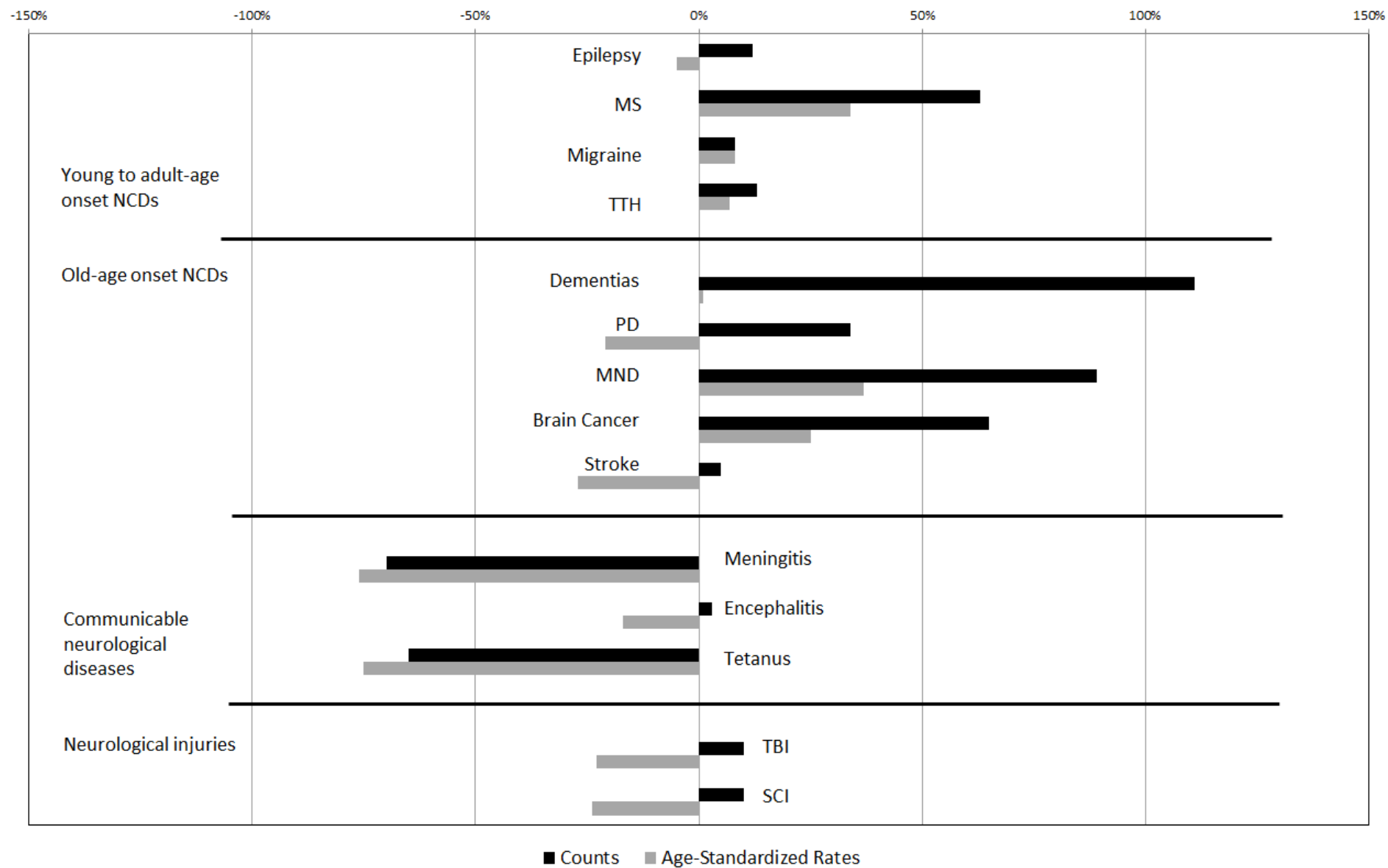
Notes: NCDs, non-communicable diseases; YLDs, years lived with a disability.

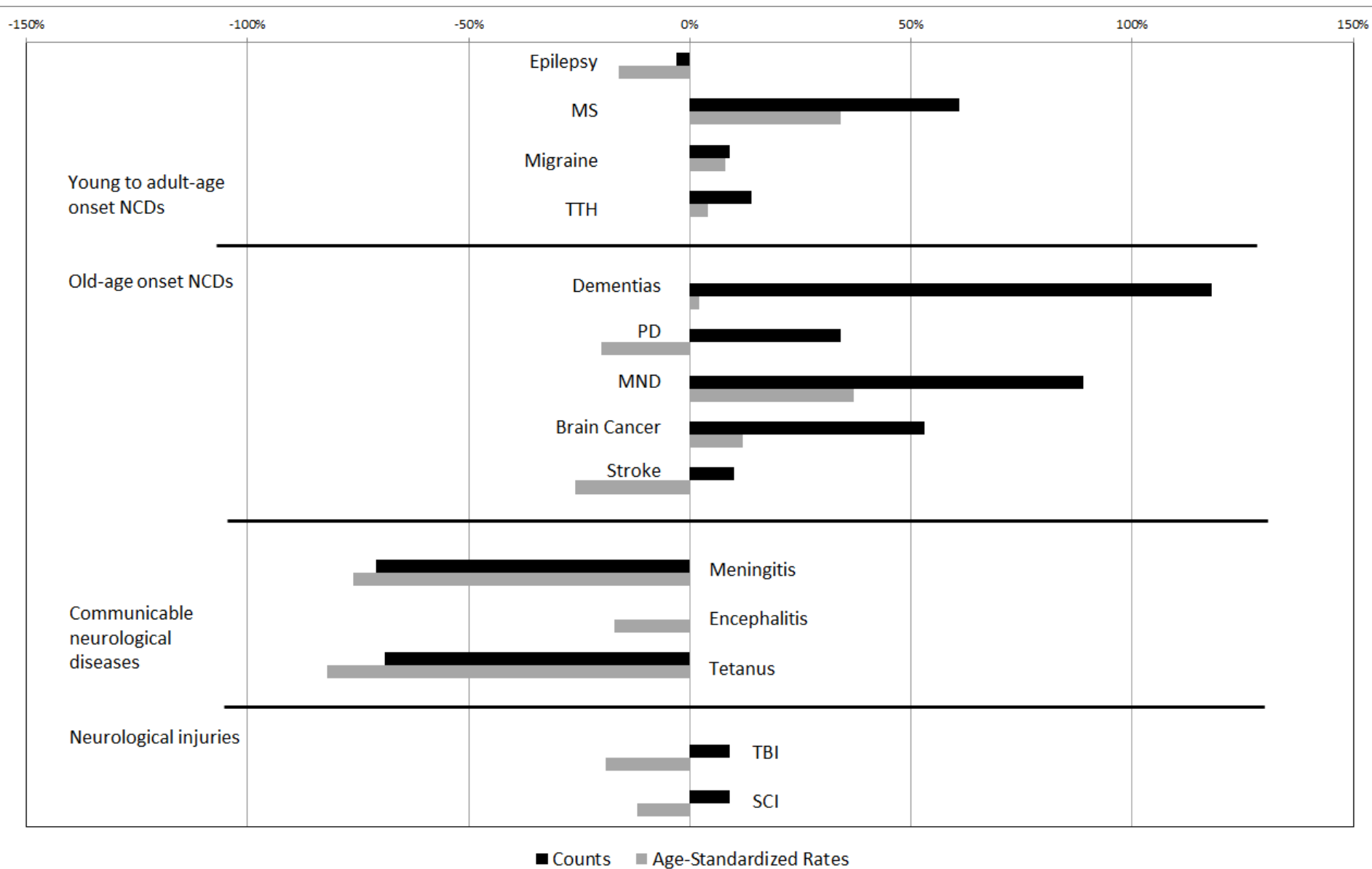
778 **Figure 1:** Percentage change between 1990 and 2019 in Italy for incidence, prevalence and YLDs associated to neurological conditions by sub-  
779 groups, counts and age-standardized rates  
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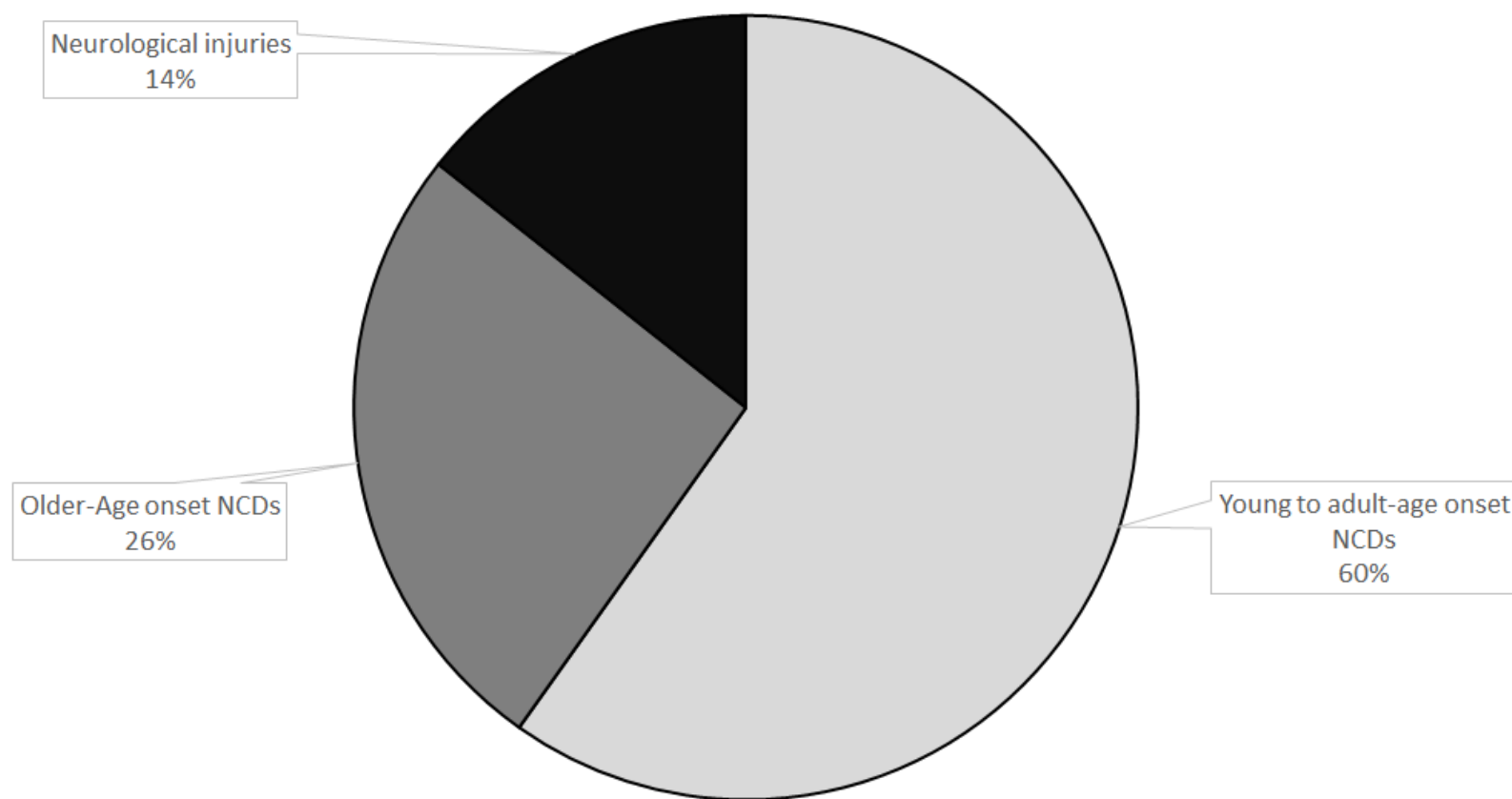


787 Notes. Figure 1.A, Incidence; Figure 1.B, Prevalence; Figure 1.C, YLDs. NCDs, non-communicable diseases; YLDs, years lived with a disability;  
788 MND, motor neuron disease; MS, multiple sclerosis; PD, Parkinson's disease; SCI, spinal cord injury; TBI, traumatic brain injury; TTH, tension-  
789 type headache.

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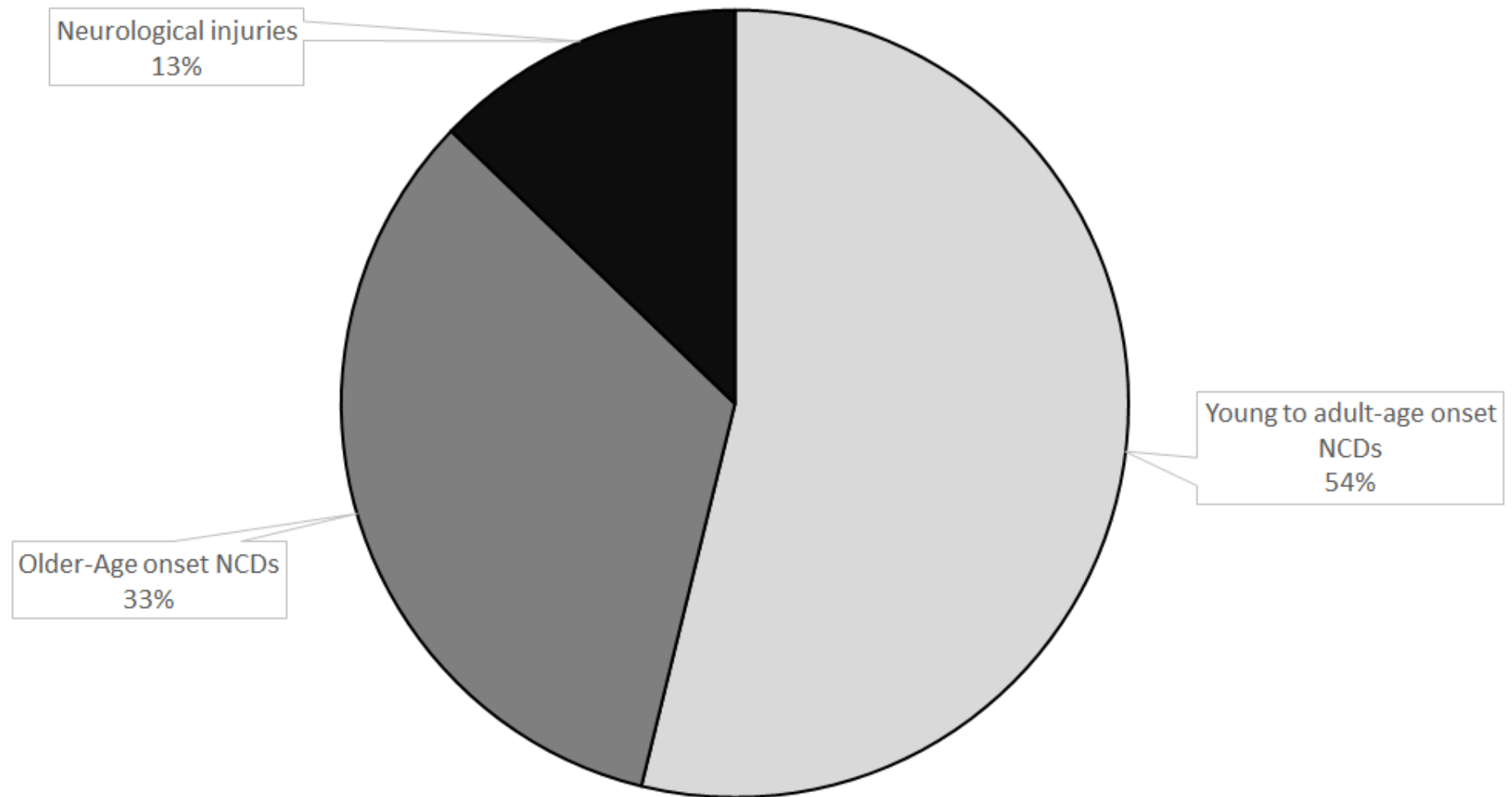
791 **Figure2.** Share of different disease groups on YLD counts and age-standardized rates in Italy, 1990 and 2019

792 2A

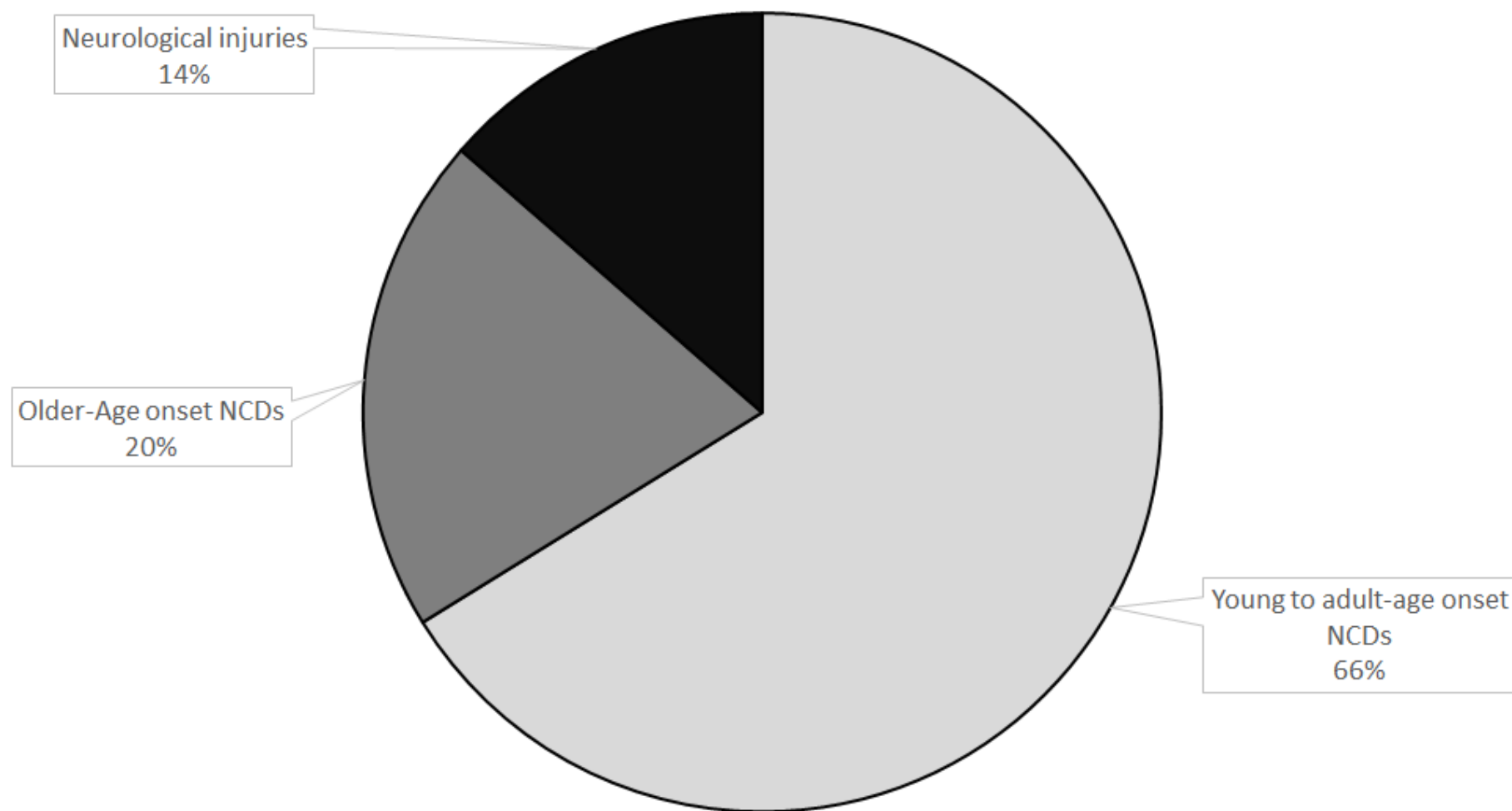


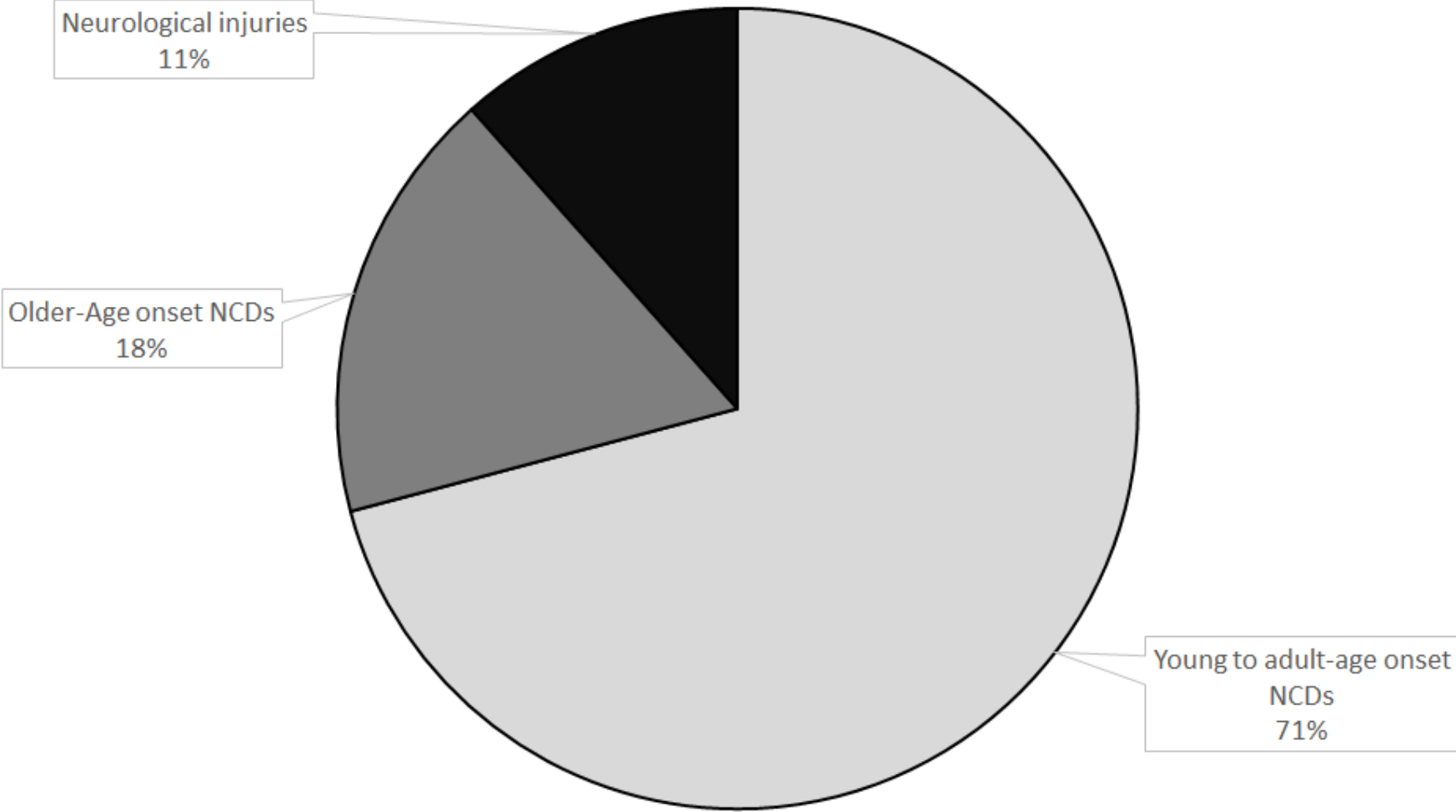
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794 2B  
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801 *Note.* Figure 2.A, YLD counts in 1990; Figure 2.B, YLD counts in 2019; Figure 2.C, age-standardized YLD rates in 1990; Figure 2.D, age-  
802 standardized YLD rates in 2019. Counts and rates for communicable neurological conditions were not included as their share was below 0.5%.