Epidemiology of stroke in Europe and trends for the 21st century

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Summary
Despite major improvements in primary prevention and acute treatment over the last decades, stroke is still a devastating disease. At the beginning of the 21st century, the age-standardized incidence of stroke in Europe ranged from 95 to 290/100,000 per year, with one-month case-fatality rates ranging from 13 to 35%. Approximately 1.1 million inhabitants of Europe suffered a stroke each year, and ischemic stroke accounted for approximately 80% of cases. Although global stroke incidence is declining, rates observed in young adults are on the rise, thus suggesting a need for strategies to improve prevention. In addition, because of the ageing population, the absolute number of stroke is expected to dramatically increase in coming years: by 2025, 1.5 million European people will suffer a stroke each year. Beyond vital prognosis, stroke patients are also at increased risk of poor outcome within the first year of the event including re-hospitalisation (33%), recurrent event (7 to 13%), dementia (7 to 23%) mild cognitive disorder (35 to 47%), depression (30 to 50%), and fatigue (35% to 92%), all of them contributing to affect health related quality of life. Given these observations, an urgent development of acute care provision, as well as resources for post-stroke therapeutic strategies, is needed.

Introduction
It is essential to evaluate the epidemiology of stroke so as to organize health policy in order to improve stroke prevention and management, by determining needs with regard to the implementation of dedicated services, and to guide and evaluate future priorities. In a context of ongoing major demographic changes, this article aims to provide contemporary data about the epidemiology of stroke in Europe with regard to incidence, global burden, and patients' outcomes, and to show expected trends for coming years.

Incidence of stroke in Europe
Global incidence of stroke
Reliable information about the incidence of stroke in Europe comes from population-based stroke registries. These registries are the most relevant tools to study the epidemiology of stroke on
condition that they comply with well-defined quality criteria so as to ensure both the quality and exhaustiveness of case-ascertainment, and the reliable interpretation of collected data, thus allowing international comparisons between studies \[1,2\]. Based on recently published studies, the age-standardized (to European standard population) incidence of stroke in Europe at the beginning of the 21st century ranged from 95 to 290/100,000 per year (figure 1) \[3–19\]. An East-West and North-South gradient was observed with higher incidence rates in eastern countries and lower rates in southern countries. Such a gradient was already reported in the 1990s, although it vanished with time \[17,20\]. Geographical variations could be related to environmental, meteorological, and genetic factors, differences in the distribution of vascular risk factors and local health care policies.

Given that population-based stroke registries are time consuming and expensive, only limited data are available. In addition, these studies are mainly conducted within urban areas, where stroke incidence rates have been shown to differ from those observed in rural areas, essentially because of variations in the distribution of vascular risk factors \[21,22\]. Furthermore, population-based stroke registries cover relatively small populations that may not reflect the composition of the entire population of a country in terms of socioeconomic level of the population or access to medical services. Therefore, the true incidence of stroke may be underestimated and generalization of the findings of these registries may be hazardous. To overcome these limitations, the Global Burden of Disease Study (GBD) developed a model to provide nationwide estimates of the incidence of stroke \[23,24\]. Estimations were shown to correctly correlate with true incidence rates provided by population-based registries, and confirmed that the highest incidence rates were observed in Eastern Europe \[24\]. In the early 2000s, approximately 1.1 million inhabitants of Europe suffered a stroke each year \[24\]. In France, nationwide estimates obtained from the French Hospital Discharge Database (Programme de médicalisation des systèmes de santé [PMSI]), indicated that the absolute number of hospitalisations for acute cerebrovascular events in France was 138,601 in 2009, including 106,927 strokes and 31,674 TIA's \[25\].

**Specific stroke incidence**

Stroke incidence in a defined area is largely influenced by the structure of the population in terms of age and sex distribution. Hence, incidence rates increase by a factor of 100 between the age of forty and eighty, thus justifying the need for standardization to compare rates from one study to another (figure 2).
addition, population-based studies have demonstrated that age-adjusted incidence rates were 1.2 to 2 times higher in men than in women in all European countries (figure 3), consistently with findings from outside Europe [3-19]. This excess in stroke incidence in men was observed after 55–60 years old, and could be due to a greater prevalence of traditional vascular risk factors. However, since life expectancy in women is greater, and incidence rates increase with age, more women suffered from stroke, in terms of absolute number.

**Incidence of transient ischemic attack**

Because of methodological difficulties, the incidence of transient ischemic attack (TIA) has been poorly investigated and is probably underestimated. Population-based studies indicated that TIA incidence age-adjusted to the European population ranged from 28 to 59/100,000/year [15,26,27].

**Recent trends in incidence rates of stroke**

Only a few European population-based registries maintained their case-ascertainment procedures over a long period of time so as to provide temporal trends in incidence. Diverging findings were observed: one registry reported a stable incidence (Dijon, France from 1985 to 2006) [17], others observed decreasing incidence rates (Oxfordshire, UK between 1985-1984 and 2002-2004) [15], Tartu, Estonia, between 1991-1992 and 2001-2003 [6], Valley d’Aosta, Italy, between 1989 and 2005 [19], and Novosibirsk, Russia from 1982 to 1992 [28], and another reported increasing stroke incidence (Lund-Orup, Sweden between 1983-1985, 1993-1995, and 2001-2002) [12]. The Global Burden of Disease Study reported a 12% decrease in the age-standardised incidence of overall stroke in high-income countries including European countries [23]. Recently, it has been demonstrated that ischemic stroke incidence is on the rise in young adults in high-income countries, including Europe, as well as in developing countries [18,23,28-30]. In the Dijon Stroke Registry, the incidence of ischemic stroke in individuals aged < 55 years old rose from 8.1/100,000/year in 1985-1993 to 10.7/100,000/year in 1994-2002, and to 18.1/100,000/year in 2003-2011 [18]. Similar trends were observed when considering hospitalization rates for stroke and TIA, which increased by approximately 6% between 2000 and 2007 in people aged < 65 years old at a nationwide level in France [29]. Moreover, a rise in the incidence of hospitalization for stroke in individuals aged 30 to 65 years old was noted in Sweden between 1989-1991 and 1998-2000 [30]. Several explanations for these trends have been proposed, including a rise in the prevalence of diabetes, hypercholesterolemia, obesity, cigarette smoking, alcohol abuse, and the use of illicit drugs in young adults.

**Distribution of stroke subtypes**

Huge differences in the distribution of stroke subtypes were observed in contemporary population-based registries. Ischemic stroke was the most frequent subtype, accounting for 55 to 90% of overall cases, whereas intracerebral haemorrhage represented 10 to 25%, and subarachnoid haemorrhage accounted for 0.5 to 5% (figure 4) [4,5,7-12,14-19]. Several reasons could
explain these discrepancies such as a different distribution of risk factors, especially hypertension, between-study populations and the efficacy of their management. Another reason for between-study differences in stroke subtype distribution is the availability of acute access to brain imaging, leading to a proportion of undetermined strokes ranging from 1% to 10%. As stroke incidence studies differ with regard to the organization of health care systems in terms of cost and accessibility, and patients’ attitudes toward seeking medical attention, the identification of patients with minor strokes, most of which are ischemic, may substantially diverge, resulting in marked discrepancies in reported stroke incidence. Of note, a higher proportion of undetermined stroke was noted in Eastern European countries.

Ischemic stroke is a heterogeneous disease. Etiological subtypes are usually classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification [31]. However, only scarce data from European population-based studies are available and their results show large differences in the distribution of these subtypes (figure 5) [7,11,15,16,32-34]. Several explanations for these differences are possible. Firstly, the age structure of the study population is of major importance since the frequency of ischemic subtypes differs according to age. For example, the proportion of cardioembolic strokes increases sharply with age because of the rise in the prevalence of atrial fibrillation in elderly people [35]. Conversely, the “other cause” category is more frequent in young people given the high proportion of cervical dissection at this age [36]. Secondly, race/ethnic discrepancies may also account for between-study variations in ischemic stroke subtype distribution, explained by differences in the prevalence of vascular risk factors, and in socioeconomic and environmental status [32]. Finally, as the TOAST classification requires the use of diagnostic procedures, discrepancies in access to medical resources can account for differences in the findings of studies. Consistent with this remark, the proportion of ischemic strokes of undetermined cause...
cause ranged from 22 to 45%. This category includes patients with insufficient diagnostic investigations.

**Post-stroke prognosis**

**Case-fatality rates**

At the beginning of the 21st century, one-month case-fatality rates in population-based studies ranged from 13 to 35% [4,7–12,14,15,17–19,37] (figure 6). Huge variations were observed according to the subtype of stroke. Indeed, intracerebral haemorrhage was associated with one-month case-fatality rates ranging from 25 to 61%, which was similar to those for subarachnoid haemorrhage (26 to 48%). In contrast, better prognosis was noted in patients with ischemic stroke, with case-fatality rates ranging from 9 to 19%. The prognosis of patients with ischemic stroke is heterogeneous, and greatly depends on the underlying etiological subtype. In several studies, worse survival was observed in patients with ischemic stroke, with case-fatality rates ranging from 9 to 19%. The prognosis of patients with ischemic stroke is heterogeneous, and greatly depends on the underlying etiological subtype. In several studies, worse survival was observed in patients with cardioembolic stroke (from 40 to 55% at 2 years), and to a lesser degree in those with stroke from large artery atherosclerosis (from 58 to 80% at 2 years), as compared with patients with lacunar stroke (from 80 to 90% at 2 years) [34,38–40]. Although most of the studies demonstrated a decrease in early case-fatality after stroke, variations in the level of acute care may account for differences in the magnitude of the improvement [41]. In addition, the decrease in stroke case-fatality rates was attributed to the better management of ischemic stroke, whereas case-fatality for intracerebral haemorrhage appeared to be stable between 1980 and 2008 in one meta-analysis [42].

**Stroke recurrence**

Data about stroke recurrence are limited. Globally, the cumulative risk of recurrence after a first-ever stroke ranged from 1 to 4% at 1 month, from 7 to 13% at one year, and reached almost 40% at 10 years [43–45]. Similar recurrence rates were observed for ischemic stroke and ICH, whereas patients with subarachnoid haemorrhage had a lower risk of stroke recurrence (less than 10% at 10 years) [43]. Concerning ischemic stroke, the etiological subtype influenced the risk of recurrence. A meta-analysis of population-based studies, most of which were performed in European populations, revealed that 3-month recurrences were more frequent in ischemic stroke from large artery atherosclerosis (14.3%) than in cardioembolic stroke (7.7%), lacunar stroke (2%), and ischemic stroke from undetermined cause (5.6%) [46]. When considering TIA patients, the risk of subsequent stroke was estimated at 5% at 7 days, and population-based studies demonstrated an annual risk ranging from 2 to 5% (although very early recurrences were excluded in these studies) [47]. Beyond the risk of subsequent stroke, stroke patients may also suffer from other vascular diseases. The risk of myocardial infarction was estimated at 2.2%, and that of non-stroke vascular death at 2.1% in a meta-analysis [48]. Of note, similar numbers are observed when considering TIA patients [47].

**Other outcomes**

Stroke patients were shown to have a high risk of subsequent readmission to hospital. The risk of all-cause readmission within the first year following stroke was approximately 33% [49], with adverse consequences in terms of its effect on the well-being of patients, and the induced socioeconomic costs. Several other aspects of post-stroke outcomes have recently been explored. Given the ageing population, post-stroke dementia now appears to be a major issue to be dealt with. Its prevalence was estimated at between 7 and 23% of patients within the first year following a first-ever stroke [50,51], and a history of stroke conferred a two-fold risk of dementia in the population aged > 65 years [52]. Beyond dementia, stroke patients are also at increased risk of mild cognitive disorder. Studies suggested that the prevalence of cognitive impairment...
after stroke is high, ranging between 35 and 47%\cite{53–56}. Moreover, the vascular contribution to the burden of cognitive decline is certainly underestimated since these studies only considered patients with symptomatic stroke. Silent brain lesions of vascular origin including territorial infarcts, lacunes, white matter lesions, or microbleeds also largely contribute to vascular cognitive impairment\cite{56}.

Finally, stroke patients also have an increased risk of depression (30–50% of patients during the first year)\cite{57}, and fatigue (35% to 92% of patients)\cite{58}, both contributing to impairment of the perceived quality of life.

**Stroke prevalence in Europe**

Only a few dedicated studies on stroke prevalence have been conducted in Europe, and none of them came from Eastern European countries. In these studies, stroke prevalence rates ranged from 5% in people aged less than 75 years old to more than 10% in those older than 80 years old\cite{24}. Consistent results were found when considering GBD estimates. The global prevalence rate of stroke in Europe at the beginning of the 21st century was 1.34%, which corresponded to 6 million prevalent stroke events annually\cite{59}.

![Observed cases and projections of cerebrovascular events (stroke and TIA) in the population of Dijon, France, 1985–2055](image_url)

**Figure 7**

Observed cases and projections of cerebrovascular events (stroke and TIA) in the population of Dijon, France, 1985–2055

Europe is currently facing the ageing of the population, and this phenomenon is expected to grow in coming years. Since the incidence of stroke is closely related to age, the absolute number of patients who will suffer a stroke each year will inevitably continue to rise over the next decades. Figure 7 illustrates this trend. Hence, in Dijon, France, despite stable global incidence rates, the absolute number of cases of cerebrovascular events (including both stroke and TIA) increased by 70% between 1985 and 2014. On the basis of a stable trend in incidence and demographic projections, this number will further increase by 80% by 2055. Of note, the proportion of patients aged more than 75 years old was 60% in the 90s. This proportion will reach 75% after 2050. Similar trends are expected in Europe. Projections indicate that according to a scenario of stable incidence rates, the ageing population would lead to an increase in the absolute number of stroke cases from 1.1 million per year in 2000 to more than 1.5 million per year in 2025\cite{24}. On the basis of a 2% decrease in stroke incidence over 5 years, the number of events would increase to 1.4 million annually. In the worst scenario of an increase in incidence of 2% over 5 years, the number of cases would reach 1.7 million per year.

**Conclusion**

Stroke remains a devastating disease in Europe despite major improvements in management over recent decades, which has contributed to better outcomes in patients. Although the incidence has been stable or has decreased, the ageing population will lead to a dramatic increase in the absolute number of cases during the first half of the 21st century. These data clearly indicate the urgent need for the better identification and understanding of risk factors so as to improve both primary and secondary prevention, and the development of acute care provision as well as resources for post-stroke therapeutic strategies, especially for the elderly.

**Disclosure of interest:** the authors declare that they have no competing interest.

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