

Sex Differences in Stroke Incidence, Prevalence, Mortality and Disability-Adjusted Life Years: Results from the Global Burden of Disease Study 2013

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Key Words

Sex differences · Stroke · Epidemiology · Burden · Global

Abstract

Background: Accurate information on stroke burden in men and women are important for evidence-based healthcare planning and resource allocation. Previously, limited research suggested that the absolute number of deaths from stroke in women was greater than in men, but the incidence and mortality rates were greater in men. However, sex differences in various metrics of stroke burden on a global scale have not been a subject of comprehensive and comparable assessment for most regions of the world, nor have sex differences in stroke burden been examined for trends over time. **Methods:** Stroke incidence, prevalence, mortality, disability-adjusted life years (DALYs) and healthy years lost due to disability were estimated as part of the Global Burden of Disease (GBD) 2013 Study. Data inputs included all available

information on stroke incidence, prevalence and death and case fatality rates. Analysis was performed separately by sex and 5-year age categories for 188 countries. Statistical models were employed to produce globally comprehensive results over time. All rates were age-standardized to a global population and 95% uncertainty intervals (UIs) were computed. **Findings:** In 2013, global ischemic stroke (IS) and hemorrhagic stroke (HS) incidence (per 100,000) in men (IS 132.77 (95% UI 125.34–142.77); HS 64.89 (95% UI 59.82–68.85)) exceeded those of women (IS 98.85 (95% UI 92.11–106.62); HS 45.48 (95% UI 42.43–48.53)). IS incidence rates were lower in 2013 compared with 1990 rates for both sexes (1990 male IS incidence 147.40 (95% UI 137.87–157.66); 1990 female IS incidence 113.31 (95% UI 103.52–123.40)), but the only significant change in IS incidence was among women.

Members of the GBD 2013 Writing Group and GBD 2013 Stroke Panel Experts Group are listed in the Appendix at the end of the paper.

Changes in global HS incidence were not statistically significant for males (1990 = 65.31 (95% UI 61.63–69.0), 2013 = 64.89 (95% UI 59.82–68.85)), but was significant for females (1990 = 64.892 (95% UI 59.82–68.85), 2013 = 45.48 (95% UI 42.427–48.53)). The number of DALYs related to IS rose from 1990 (male = 16.62 (95% UI 13.27–19.62), female = 17.53 (95% UI 14.08–20.33)) to 2013 (male = 25.22 (95% UI 20.57–29.13), female = 22.21 (95% UI 17.71–25.50)). The number of DALYs associated with HS also rose steadily and was higher than DALYs for IS at each time point (male 1990 = 29.91 (95% UI 25.66–34.54), male 2013 = 37.27 (95% UI 32.29–45.12); female 1990 = 26.05 (95% UI 21.70–30.90), female 2013 = 28.18 (95% UI 23.68–33.80)). **Interpretation:** Globally, men continue to have a higher incidence of IS than women while significant sex differences in the incidence of HS were not observed. The total health loss due to stroke as measured by DALYs was similar for men and women for both stroke subtypes in 2013, with HS higher than IS. Both IS and HS DALYs show an increasing trend for both men and women since 1990, which is statistically significant only for IS among men. Ongoing monitoring of sex differences in the burden of stroke will be needed to determine if disease rates among men and women continue to diverge. Sex disparities related to stroke will have important clinical and policy implications that can guide funding and resource allocation for national, regional and global health programs. © 2015 S. Karger AG, Basel

Introduction

Evidence before This Study

The burden of stroke in women was often underestimated until the early 1980s [1]. Although once considered to be primarily a disease affecting men, stroke is now recognized as a major public health problem in women as well [2]. Recent data have shown that 60,000 more women than men have a stroke each year in the US [3]. Globally, more women die of stroke than men [4].

Although there is also increasing evidence of sex-specific differences in stroke symptoms, diagnosis, peri-procedural risk, treatment and preventive interventions [5–11], controversies regarding differences in stroke epidemiology between men and women continue [12–17], making this an area worthy of further investigation.

Knowledge Gap

The data on sex-specific stroke burden have remained scarce [18–20]. In the Greater Cincinnati-Northern Kentucky Stroke Study (GCNKSS) [21], apart from higher

incidence in women aged ≤ 34 years, incidence rates were lower for women aged 45–74 years, but higher in those aged ≥ 75 years. This is possibly a reflection of the open-ended age category. Projections of GCNKSS rates on the 2000 US population gave an estimated 82,000 incident stroke events in women and 49,000 events in men, and in 2050, an estimated 198,000 events in women compared with 129,000 events in men [22]. Total number of deaths was higher for women but the cause-specific mortality rates were lower, possibly because women tend to be more affected by multi-morbidity.

Other authors have reported lower incidence rates of stroke in women than in men except in older age (75+ years) where incidence in women exceeded that in men [23, 24]. Examination of the Framingham Study data by Petrea et al. [25] showed that stroke incidence increased with each decade of life in both women and men with no significant sex difference in stroke subtypes, severity or case fatality rates. Data from the Framingham Study further suggested that 1 in 5 women and 1 in 6 men reaching the age of 55 years free of stroke will develop a stroke event during their remaining lifetime [26]. The major methodological limitations of the literature available are the lack of national representativeness in terms of generalizability, as well as potential bias issues, such as study population selection and study time periods [7]. Epidemiologic studies reveal a clear age–sex interaction in stroke with premenopausal women experiencing fewer strokes than similarly aged men but having higher rates in postmenopausal women than similarly aged men [27]. Generally, any data on stroke epidemiology are scarce in developing countries.

Study Aim

While the above provides an indication of sex differences in stroke epidemiology, comprehensive and comparable assessments of stroke incidence, prevalence, mortality and disability trends over time have not been produced by sex for most regions of the world. Our aim was to estimate the global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life years (DALYs) and mortality of stroke in men and women as part of the 2013 Global Burden of Disease Study (GBD 2013).

Methods

Methods for determining incidence, all-cause mortality, cause-specific mortality, disability and disease prevalence in the GBD 2013 study have been previously described [28, 29], including the approach to stroke disease modeling [30]. Briefly, all available mor-

Table 1. Global number of women and men with stroke (in millions) by stroke type in 1990 and 2013 (95% UIs are in brackets)

| | | Female | | Male | |
|----|-----------|------------------|------------------|------------------|-------------------|
| | | 1990 | 2013 | 1990 | 2013 |
| IS | Incident | 2.14 (1.96–2.33) | 3.28 (3.06–3.52) | 2.17 (2.05–2.33) | 3.62 (3.43–3.85) |
| | Prevalent | 4.86 (4.56–5.19) | 8.66 (8.32–9.00) | 5.18 (4.93–5.46) | 9.65 (9.27–10.05) |
| HS | Incident | 0.86 (0.79–0.92) | 1.53 (1.42–1.63) | 1.03 (0.96–1.09) | 1.84 (1.72–1.94) |
| | Prevalent | 1.78 (1.67–1.87) | 3.36 (3.23–3.51) | 2.11 (2.02–2.22) | 4.00 (3.81–4.17) |

tality data were compiled. Non-specific cause codes were redistributed based on expert opinion and statistical methods. The total for all cause-specific deaths was fit to an envelope for all-cause mortality. Deaths were compiled into 240 causes, including ischemic stroke (IS) and hemorrhagic stroke (HS). Stroke was defined based on the World Health Organization (WHO) clinical criteria [31]. For stroke death estimates, GBD defined stroke ICD-10 codes as IS, HS or non-specific as to type. The parent category of cerebrovascular disease was based on the mapping of the detailed causes. Deaths coded as due to G45 (transient ischemic attack) were coded as IS and deaths coded as due to unruptured aneurysms (ICD code I67.0) were coded as HS. Non-specific codes, including I64, I67.9, I68.8, I69.4–I69.9, were redistributed to IS or HS using a regression model. An ensemble model was used to estimate a continuous time series for mortality by age, sex, country and year. Country-level covariates were incorporated into the model, and out-of-sample validity testing was used to assess model performance. Uncertainty intervals (UIs) were estimated using 1,000 draws from the posterior distribution for each age–sex–country group, with the interval taken as the 2.5 and 97.5 percentiles of the resulting distribution. Disease prevalence was estimated using the DisMod-MR disease modeling software [32]. All available estimates of stroke incidence, prevalence and case fatality from systematic reviews of the scientific literature, population surveys and stroke registries were used. IS and HS were modeled separately. Adjustments were made to account for incidence estimates specifying first-ever or any stroke. Disability due to acute stroke was considered to last for up to 28–30 days while chronic stroke lasted from 30 days until death [29]. YLDs were calculated as the product of a disability weight and prevalent cases of stroke. DALYs were calculated as the sum of years of life lost prematurely, based on maximum observed global longevity, and YLDs. Countries were stratified by development status (i.e. developed and developing).

Results

Incidence and Prevalence

Table 1 shows overall trends in the number of women and men with stroke by stroke type in 1990 and 2013. While the number of women and men with IS was similar in 1990 and increased over time, this increase was more marked for men. Non-overlapping 95% UIs show that the

increase over time in numbers of incident IS and HS was significant for both women and men. The number of women with HS was lower than that of men, though with a similar proportional increase over time to men.

Figure 1 presents the incidence rates of HS and IS broken down into 5-year age bands for men and women in 1990 and 2013. The age-related patterns of incidence for men and women remain relatively similar across time and stroke types. The global age-adjusted incidence of IS showed a trend to decline in both men and women, but no significant change was detected as UI overlapped between 1990 and 2013 (table 2). For HS, there was little change detected in incidence over time.

Stroke prevalence rates for both stroke types were significantly higher for men compared with women in both 1990 and remained so in 2013. The increase in number of prevalent cases of stroke between 1990 and 2013 despite significant declines in incident stroke are consistent with change due to population growth, population ageing and, for some regions, decreases in stroke-related mortality (table 3). Therefore, there were no detectable change in age-standardized prevalence rates for IS from 1990 to 2013. In contrast to IS rates, HS age-standardized prevalence rates increased over time for both sexes.

Mortality, DALYs and YLDs

The age-standardized death rate (table 4) from IS declined at a similar rate for men and women, although absolute values were higher in men. Mortality due to HS also declined over time in both sexes. While mortality in women with HS was slightly lower than that of men in 1990, it was higher than that of men in 2013, with no overlap of UIs.

DALYs due to IS in men rose significantly from 1990 to 2013 while among women the trend toward an increase was not significant (table 4). DALYs related to HS were higher in men than in women, though increases from 1990 to 2013 were not significant for either sex.

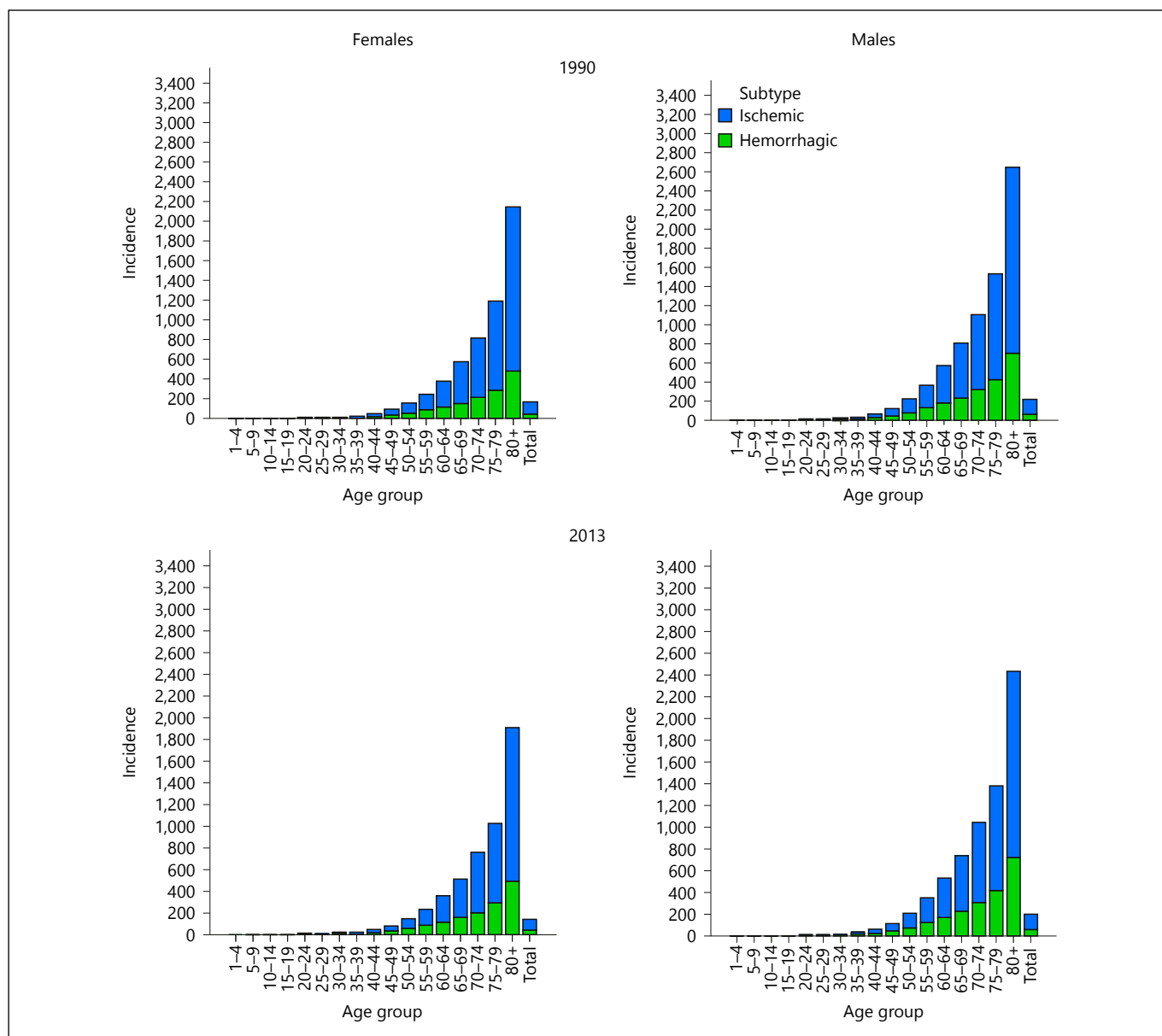


Fig. 1. Incidence per 100,000 of IS and HS in females and males by 5-year age bands in 1990–2013.

YLDs related to IS remained similar for women and for men over time. While YLDs also remained stable over time for women with HS, there was a significant rise in YLD for men from 1990 to 2013.

The number of deaths, DALYs and YLDs increased, while the age-standardized rates of deaths and DALYs per 100,000 decreased (table 3). The increase in number of IS deaths was significantly greater among men than women. There was a trend toward a greater increase among men for HS though the UI in percentage change overlapped.

Current Country Specific DALYs, YLDs and Mortality Online supplementary Web Appendix A (for all online suppl. material, see www.karger.com/doi/10.1159/000441103). shows country-specific stroke burden in 1990 and 2013 for women and men; whilst online supplementary Web Appendix B presents this information by stroke type (IS and HS). Overall death rates in 2013 ranged from a low of 28.6 per 100,000 (95% UI 19.9–34.4) in Israel to 357.9 (95% UI 297.8–432.0) in Madagascar. Death rates in men exceeded those in women in the majority ($n = 138$,

Table 2. Age-standardized incidence and prevalence rates per 100,000 persons by sex in 1990 and 2013 globally (95% UIs are in brackets), with prevalence rates by country development status

| | Females | | Males | |
|-------------------|-------------------------|--|--|--|
| | 1990 | 2013 | 1990 | 2013 |
| <i>Global</i> | | | | |
| IS | Incidence Prevalence | 113.31 (103.52–123.40) 253.60 (237.19–271.50) | 98.85 (92.11–106.62) 260.40 (249.97–271.03) | 147.40 (137.87–157.66) 346.08 (332.43–360.57) |
| HS | Incidence Prevalence | 44.25 (40.78–47.36) 89.18 (83.63–93.97) | 45.48 (42.43–48.53) 99.90 (95.98–104.26) | 64.89 (59.82–68.85) 136.65 (130.41–142.37) |
| <i>Developed</i> | | | | |
| IS | Prevalence | 396.74 (364.28–437.18) | 500.62 (474.62–526.94) | 678.544 (646.93–713.21) |
| HS | Prevalence | 84.02 (74.60–93.41) | 125.64 (116.01–135.80) | 134.15 (122.03–145.32) |
| <i>Developing</i> | | | | |
| IS | Prevalence | 131.706 (125.238–138.710) | 130.494 (122.616–139.06) | 185.15 (173.51–197.20) |
| HS | Prevalence | 93.51 (88.72–97.53) | 91.57 (87.55–96.13) | 139.87 (133.10–146.74) |

Table 3. Global median percent change in number and age-standardized rate per 100,000 persons for deaths, DALYs and YLDs from 1990 to 2013 by stroke type and sex

| | DALYs | | | Deaths | | | YLDs | | | Prevalence | | |
|--------|--------|-----------|----------|-----------|-------|----------------|--------|------------|----------|--------------|------|------------|
| | number | rate | % change | number | rate | % change | number | rate | % change | number | rate | % change |
| IS | | | | | | | | | | | | |
| Male | 51.6 | 71.1–36.8 | -16.3 | 84.4–48.4 | -15.4 | -5.6 to -22.8 | 86.1 | 99.5–73.2 | 2.8 | 9.9 to -4.7 | 85.9 | 98.8–3.9 |
| Female | 27.4 | 35.7–15.3 | -26.0 | 49.5–28.7 | -23.2 | -17.8 to -29.3 | 78.0 | 94–64.1 | 3.3 | 12.7 to -4.9 | 77.7 | 93.7–3.4 |
| HS | | | | | | | | | | | | |
| Male | 23.9 | 42.1–12.3 | -25.6 | 63.4–25.1 | -23.0 | -8.1 to -30.6 | 88.7 | 101–75.5 | 8.5 | 16.4 to 0.9 | 89.3 | 101.6–77.0 |
| Female | 7.9 | 20–0.9 | -33.8 | 41.4–13.3 | -29.1 | -18.5 to -34.8 | 88.1 | 103.6–76.5 | 12.1 | 21.4 to 5.1 | 88.4 | 103.4–77.4 |

Table 4. Age-standardized DALYs, YLDs and death rates per 100,000 persons with 95% UIs by stroke type and sex in 1990 and 2013

| | Female | | Male | |
|-----------|---------------------------|-----------------------|---------------------------|---------------------------|
| | 1990 | 2013 | 1990 | 2013 |
| <i>IS</i> | | | | |
| DALYs | 919.3 (740.1–1,063.2) | 675.8 (539.2–774.9) | 1,101.5 (894.3–1,288.4) | 922.1 (758.1–1,061.5) |
| YLDs | 36.3 (25.3–48.4) | 37.5 (26.3–49.6) | 48.5 (33.9–63.7) | 49.8 (35.4–65.3) |
| Mortality | 69.0 (55.7–78.7) | 52.9 (42.5–60.3) | 73.4 (60.6–85.3) | 62.1 (51.1–71.7) |
| <i>HS</i> | | | | |
| DALYs | 1,259.7 (1,041.5–1,500.3) | 835.8 (703.9–1,001.4) | 1,613.8 (1,368.4–1,870.7) | 1,212.5 (1,052.7–1,477.0) |
| YLDs | 13.1 (9.2–17.4) | 14.8 (10.3–19.5) | 18.6 (12.8–24.6) | 61.0 (52.4–75.3) |
| Mortality | 63.9 (52.2–76.1) | 45.7 (39.0–56.6) | 77.9 (64.9–90.6) | 20.2 (13.8–26.5) |

73.8%) of countries. Overall, DALYs for 2013 ranged from a low of 380.7 (95% UI 288.0–443.8) in Israel to a high of 6,559.5 per 100,000 (95% UI 5,243.0–8,169.3) in Madagascar.

Of those countries where women had higher death rates than men, listed in parentheses, many of which (indicated with*) also had higher DALYs in women than in men (Afghanistan*, Algeria*, Australia, Bahrain*, Bangladesh*, Belize, Brunei, Burundi*, Central African Republic*, Canada, Chad*, Comoros, Democratic Republic of Congo, Djibouti*, Eritrea*, Ethiopia*, Guatemala*, Guinea*, Haiti*, Indonesia, Iran*, Iraq*, Israel, Jamaica*, Jordan, Kuwait*, Laos, Lebanon*, Libya*, Malawi*, Maldives, Mali*, Mauritania*, Morocco*, New Zealand, Niger*, Nigeria*, Pakistan*, United Arab Emirates, United Kingdom, Uganda*, Tunisia*, The Gambia*, Somalia*, Senegal*, Saint Vincent and the Grenadines, Qatar*, Uzbekistan, Yemen*, Zimbabwe*, Zambia*). Aside from Canada, New Zealand and the United Kingdom, where the difference in death rate between males and females was minimal (in the order of 3–5 per 100,000), the majority of these countries are developing and/or have recent negative historical events (e.g. warfare, natural disaster). YLDs ranged from a low of 2.3 (95% UI 1.5–3.3) in Libya to a high of 127.5 (95% UI 90.0–178.4) in Canada. Men had higher YLD than women in all countries.

Discussion

Main Findings

Over time, the global burden of stroke has been increasing for both men and women but the increases have been greater among men. There is a trend toward a de-

creased incidence of IS in women from 1990 to 2013, with no significant change detected for men. Improved vascular risk factor control and better healthcare interventions are likely explanations for reductions in stroke incidence over this period seen for both sexes. It is possible that differences between men and women in the extent of improvement are partly explained by women in some countries being more sensitive to health information, having better health-seeking behavior and having better access to primary prevention [33, 34]. An alternative explanation is that neurovascular risk factors are more frequent and severe in men and have declined faster in women, for example, tobacco [35, 36].

Comparison with Previous Research

These findings are in contrast to those previously reported in which the reduction in incidence rates was more marked in men than in women. For example, in a review of 56 population-based studies, data from high-income countries revealed a 42% decrease overall in worldwide stroke incidence rates from 163 per 100,000 person-years in the period 1970–1979 to 94 per 100,000 person-years in the period 2000–2008 [37], a faster decline was observed for men. One explanation for difference between those findings and the present are that they were from a relatively smaller study catchment. Our inclusion of all countries leads to greater UIs which blunts our ability to detect trends in some subgroups. Our uncertainty for prevalence and incidence was considerably greater than for mortality because there is data on deaths from almost all countries but data on incidence and prevalence from a limited number of countries. In their 2008 comprehensive review of literature, Reeves et al. [22] showed that women have more stroke events than men but age-specific stroke rates are higher in men, and there

were little sex differences in stroke subtypes (except subarachnoid hemorrhage). Our findings demonstrated that the risk (rate of stroke) and absolute number of IS and HS events (both incident and prevalent strokes) in 2013 was significantly greater in men than in women, suggesting changes in the sex distribution of stroke burden in the world.

Similarly, sex-specific data from the Framingham Heart Study showed decreases in stroke incidence of 30.3% for men and 17.8% for women from 1950 to 2004 [38], though the study periods are not the same. One possible contributing factor is the increase in the 'smoking epidemic' in women which, according to Lopez et al. [39], occurs 10–20 years later than in men.

The decline in IS incidence and mortality rates over the past decades represents a major improvement in population health and is observed for both sexes and across age groups [40]. These significant improvements are concurrent with cardiovascular risk factor control interventions. An American study concluded that efforts in arterial hypertension control initiated in the 1970s appeared to have had the most substantial influence on the accelerated decline in stroke risk and mortality. Although implemented later, control of diabetes mellitus and dyslipidemia and smoking cessation programs, particularly in combination with treatment of hypertension, were also implicated in contributing to the decline in stroke incidence and mortality [40]. A history of hypertension, current smoking, waist-to-hip ratio, diet, physical activity, diabetes mellitus, alcohol intake, psychosocial stress and depression, cardiac causes and ratio of apolipoproteins B to A1 was estimated to account for 88.1% of the population-attributable risk for all stroke [41]. However, sex interacts with these risk factors. For example, women with diabetes have a higher risk of death from cardiovascular disease than men with diabetes, and after menopause, blood pressure and cholesterol levels rise drastically [42].

In contrast to IS, there were no major changes in HS incidence for women or men. Prior studies suggested the risk for intracerebral hemorrhage (ICH) to be marginally greater in men than in women. This differential risk by sex might be driven by an excess of deep hemorrhage in men [43, 44], although it is well known that the risk of subarachnoid hemorrhage (about 5% of all HS) is much greater in women than in men. HS incidence rates are reportedly slightly higher in Eastern Asia, where ICH has historically accounted for a larger percentage of all strokes than in Western populations, possibly due to the increased prevalence of hypertension [45–48]. Studies of incidence trends for HS in recent decades have produced

mixed results. There was a trend toward a reduced ICH incidence in Oxfordshire between 1981 and 2006 [49], and during the 1990s in several Chinese cities [45]. Other studies observed a decline of HS only in women aged <60 years in the period between 1985 and 2005 [50], or do not report such declines [51, 52]. Also, ICH has a high mortality rate, especially with increased age. There are some reports that suggest that withdrawal of aggressive care practices may be different between sexes (this may also vary by region and culture), and this may account for some of the mortality differences in sex in ICH [53]. Women with strokes have also been found to present with non-traditional stroke symptoms more often than men [54]. Delays in presentation, evaluation, diagnosis and treatment of women with ICH may contribute to the association between female sex and more severe stroke.

The increasing global population over time, even in the context of declining incident stroke rate, will lead to an increasing number of strokes. Population aging will also increase the number of strokes, and this has implications on the burdens faced by healthcare systems. The number of deaths, DALYs and YLDs increased for both men and women since 1990 for both stroke subtypes, with these increases being much higher in men [55].

In 2013, women had higher number of deaths and DALYs, which in examining country-level statistics, seems to be driven by developing countries and countries with recent histories of adversity (e.g. war, natural disaster). Otherwise, men have greater deaths, YLDs and DALYs both as absolute numbers and rates. One possible explanation for this is the differential smoking rate, with men having a much greater prevalence of smoking than women [56]. Although the overall number of adult smokers has decreased during the last 20 years, the number of women in their 10s and 20s who smoke has increased. This increases the risk of stroke in young women. It must also be noted here that there is no data from some of countries, so the results are purely modeled by the geo-spatial model. As such, any conclusions drawn about these particular data points must be tentative at the best. It is also possible that women from some countries might be 'outside the statistics' because they are not admitted to hospital, though this is more likely when there is no national healthcare system.

Alternatively, this may have a direct relationship to accessing care. More specifically, it is possible that the global trends in IS for women, especially in the Middle East, where the rates did not mirror global rates may be due to ascertainment and diagnosis patterns that may be different in men compared to women. For example, an

Egyptian study of acute myocardial infarction found significant sex differences in presentation and treatment with women less likely to receive aspirin upon admission or aspirin or statins at discharge, and had poorer in-hospital mortality rates [57]. Similarly, stroke mortality rate may also be influenced by access to emergency services, with elderly women possibly living alone and thus potentially having more difficulty accessing emergency medical services.

The WHO assessed sex-specific mortality rates across 39 countries in Europe and Central Asia [58] and reported an excess of total deaths because of stroke among women compared with men, of which 60% occurred in those over 75 years and 4% among those <55 years. The Centers for Disease Control and Prevention WONDER database in the United States suggests that men and women <45 years of age show similar stroke mortality rates. While women aged 45–74 years have lower stroke mortality compared with age-matched men, this advantage declines with advancing age [22]. A strong sex-by-age interaction was also reported by the WHO, as the male/female stroke mortality rate was greater in men than women aged <65 years but greater in women than men among those aged ≥75 years, possibly reflecting compounding disability in the older age range.

Strengths and Limitations

There are limitations to the GBD methods. These include the extrapolation of data from subnational regions to the whole country and missing data overall, in particular from low-income countries. Strengths include the use of consistent methods to enable comparison between subtypes of stroke and between diseases, the ability to highlight regions where stroke is a particular problem. This highlights the importance of studies being clear on how stroke and its subtypes are defined (e.g. TOAST criteria [59]) and their confirmation using gold standard methods such as by CT scans.

Implications for Research, Policy and Practice

While age-adjusted incidence and death rates from stroke have been declining since the late 20th century, the global stroke burden measured as the absolute numbers of people affected by stroke, disabled due to stroke or deaths from stroke are increasing for both men and women, with larger increases in men. This increasing burden is a reflection of population growth and aging and lifestyle and environmental changes. That women tend to survive longer and experience stroke at an older age suggests that in the future, alongside the aging of the population, we

can expect a dramatic increase of stroke in older women. To combat this, it is important that preventive efforts and guidelines for treatment reflect sex differences in the profile of stroke.

Specifically, women have strokes associated with a higher prevalence of arterial hypertension, atrial fibrillation and pre-stroke disability but a lower prevalence of heart disease, peripheral vascular disease, smoking and alcohol use than men, and these will need to be taken into account [22]. In terms of treatment, women are less likely to receive intravenous alteplase treatment and lipid testing while in hospital in some countries [22]. These disparities suggest the need to explore whether differential strategies are required to target primary and secondary prevention of stroke in women and to determine if treatment protocols must also accommodate sex differences. Further strategies are particularly needed to lower high case fatality. These could include investment in pre-hospital and acute care in some regions and could perhaps include better home care provided in treatment and monitoring of blood pressure. Also, with extension of the average length of life and increase in ratios of atrial fibrillation, the prevalence of atrial fibrillation is increasing especially in developed countries, and atrial fibrillation is a strong risk factor for IS [60, 61]. The anticoagulant warfarin has been conventionally used for prophylaxis of cerebral infarction with atrial fibrillation. In particular, the prescription rate of warfarin increased after 2000. Recently, new oral anticoagulants have been used as alternatives to warfarin anticoagulation in non-valvular atrial fibrillation. There is a particular need to focus future efforts on obtaining data by sex from undeveloped regions.

Conclusion

Age-adjusted incidence rates for IS appear to be declining worldwide at a faster rate in women than in men. The reasons for this decline may reflect better risk factor control and healthcare. Despite the reduction in the occurrence of stroke, burden is still increasing. In line with the World Stroke Organization's initiative 'I am woman: stroke affects me' that was launched at the World Stroke Congress in Istanbul (October 22–25, 2014), more research on stroke epidemiology, including both indices of occurrence and burden, is required to provide better estimates, particularly for developing countries where the data remain sparse. Countries whose estimates were entirely based on statistical modeling should be a focus of efforts to improve data availability by designing, imple-

menting and reporting population-based studies of chronic disease including stroke. Guidelines for achieving good quality studies in stroke epidemiology are recently available [62].

Research into factors that potentially contribute to the causes of sex differences in risk and outcomes is also required. In addition, there is adequate evidence of differences in stroke incidence and burden between the sexes to support the need for well-designed stroke intervention trials that are equally powered for men and women to examine effectiveness of primary care, risk factor management strategies and hospital services.

Disclosure Statement

All the authors declare that they have no conflicts of interest.

Disclaimer

The views expressed in this article are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; National Institutes of Health or the US Department of Health and Human Services.

Appendix

GBD 2013 Writing Group (in Alphabetical Order)

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