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ARTICLE

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Trends of stroke attributable to high sodium intake at the global, regional, and national levels from 1990 to 2019: a population-based study

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ABSTRACT

Objectives: High sodium intake is associated with a higher risk of stroke. However, global patterns and trends in the stroke burden attributable to high sodium intake have not been systematically assessed.

Methods: We used the numbers and age-standardized mortality rate (ASMR), and disability-adjusted life years (DALYs) rate (ASDR) of the stroke burden attributable to high sodium intake by sex, socio-demographic index (SDI), and country, obtained from the Global Burden of Disease Study (GBD) 2019. We calculated the estimated annual percentage changes (EAPCs) to assess the trends of ASMR and ASDR of the disease burden attributable to high sodium intake between 1990 and 2019. We further calculated the contribution of changes in population growth, population aging, and mortality or DALYs to changes in total stroke deaths and DALYs.

Results: From 1990 to 2019, the global burden of stroke attributable to high sodium intake changed significantly, from a universal burden in Asia and Europe to one that mainly affected some countries in Asia and Oceania. This change was due to the combined effects of demographic changes and changes in mortality or DALY rates. For countries in Asia and Oceania, the effects of population aging and population growth outweighed the effects of declining mortality and DALY rates, resulting in an absolute increase in strokes attributable to high sodium intake.

Conclusion: Although the age-standardized global stroke burden attributable to high sodium intake has declined from 1990 to 2019, the burdens in some Asia and Oceania countries, particularly China, remain high.

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Sodium intake; stroke; GBD 2019; global; temporal changes

Introduction

Stroke is one of the leading causes of mortality and disability worldwide, with more than 13 million new cases each year [1]. Globally, the lifetime risk of stroke has almost one in four after the age of 25 [2], and its overall burden is still high and increasing [2], leading to substantial economic costs and social burdens, especially for low- and middle-income income countries. Increased sodium intake is associated with high blood pressure [3–6], which is a major risk factor for stroke, accounting for 62% of stroke events [7]. The causal relationship between high sodium intake and stroke mediated through systolic blood pressure is well established [8,9].

Although the minimum intake of sodium required for body function is not well defined, in many countries, sodium consumption exceeds the 2002 World Health Organization/Food and Agriculture Organization of the United Nations (WHO/FAO) joint recommendation of sodium 2 g/day (equivalent to salt 5 g/day) [10]. Understanding the global patterns and temporal trends in the stroke burden attributable to high sodium intake could provide evidence for policymakers to develop programs or legislation to reduce sodium intake levels and thus contribute to reducing the burden of stroke attributable to high sodium intake. However, comprehensive research in this area is limited. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), which assessed the burden of disease in 195 countries and territories worldwide, provides a unique opportunity to understand the landscape of disease burden attributable to high sodium intake.

Accordingly, we retrieved detailed information on the stroke burden attributable to high sodium intake from the GBD 2019. We hypothesized that high sodium intake was associated with a substantial stroke burden and the associated burden might change spatially and temporally. We aimed to investigate the spatial and temporal trends of the stroke burden attributable to high sodium intake from 1990 to 2019 at global, regional, and national levels, as well as to further exploration of the effects of demographic changes on stroke burden attributable to high sodium

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intake. The results can be used as scientific evidence for sodium reduction policy planning.

Material and methods

Study data

We retrieved data used in this study from GBD 2019 via the Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool). We obtained the number of cases and age-standardized rates of mortality and disability-adjusted life-years (DALYs) of stroke attributable to high sodium intake from 1990 to 2017 by sex, country, socio-demographic index (SDI) quintile, and GBD region. GBD 2019 divided countries and regions into five quintiles based on the SDI: low SDI, low-middle SDI, middle SDI, high-middle SDI, and high SDI. The SDI was calculated from a combination of per capita income, education rate, and fertility rate, and was similar to the human development index used by the World Bank [11,12]. Besides, GBD 2019 classified all countries and territories into 21 geographic regions based on epidemiological similarity and geographical proximity, such as east Asia, southeast Asia, and high-income Asia Pacific. Data are reported as numbers with 95% uncertainty intervals (UIs).

High sodium intake assessment

The assessment of high sodium intake has been detailed elsewhere [13]. Briefly, GBD 2019 collected 24-hour urinary sodium. To ascertain the optimal level of sodium intake, the level of sodium intake associated with the lowest risk of stroke mortality based on the studies included in the meta-analyses of the sodium relative risks was calculated. Then, the optimal level of sodium intake was estimated as the weighted mean of these numbers using the global proportion of stroke deaths as the weight. The uncertainty of the optimal level of sodium intake was also calculated based on a uniform distribution in the uncertainty estimation sampling. As a result, the optimal level of sodium intake and its uncertainty is 3 g (1,5) per day. High sodium intake is defined as an intake level higher than 3 g per day [13].

Stroke mortality and DALYs attributable to high sodium intake

We used age-standardized stroke mortality and DALYs rates (per 100,000 population) to quantify the stroke burden attributable to high sodium intake. Methods for estimating the disease burden have been detailed elsewhere [6,11]. In brief, GBD 2019 uses a comparative risk assessment framework to estimate levels in exposure, attributable deaths, and attributable DALYs, by age group, sex, year, and location for each risk from 1990 to 2019. Through a counterfactual scenario using theoretical minimum risk exposure level (TMREL), the portion of deaths and DALYs attributed to a given risk were estimated [11,14]. Particularly, to assess the stroke burden attributable to high sodium intake, GBD first estimates the relationship between urinary sodium and changes in systolic blood pressure, and then estimate the relationship between changes in systolic blood pressure and stroke.

Deaths were defined as the number of deaths in a population over a given period of time. DALYs were the sum of years lost due to premature death (YLLs) and years lived with disability (YLDs), where YLLs were multiplied by the number of deaths and the standard life expectancy at the age of death, and YLDs are the number of life-years lost to any short- or long-term health loss, weighted by severity by disability weights.

Statistical analysis

Differences in the age structure of the population may lead to heterogeneity in stroke burden quantified by mortality and DALY rates. To eliminate the effect of differences in population structure, we used the age-standardized mortality rate (ASMR) and age-standardized DALY rate (ASDR) [15]. Trends in ASMR and ASDR of stroke attributable to high sodium intake were estimated using estimated annual percentage change (EAPC), which takes into account the Gaussian distribution of age-standardized rates (ASR) over time intervals and is calculated using a generalized linear model [16]. We fitted the logarithm of ASR to the regression model: $\ln(ASR) = \beta_0 + \beta_1 X + \varepsilon$, where X was the calendar year and EAPC was calculated as $(\exp(\beta_1) - 1) \times 100$ [16]. If the lower boundary of its 95% confidence intervals (CIs) is above zero, the ASR is considered to be on the rise. Conversely, if the higher boundary of its 95% CIs is below zero, the ASR is considered to be in a downward trend. Otherwise, the ASR was considered to be stable.

We used Pearson's correlation coefficients to evaluate the relationship between SDI and different levels of ASR by fitting a Loess smoother to estimates the expected relation between SDI and mortality or DALY rates for all GDB regions between 1990 and 2019 [11,12].

Additionally, we used a recently developed algorithm [17] to calculate the contribution of changes of each of the three factors – population growth, population aging, and mortality change in 21 GBD regions between 1990 and 2019 – to changes in total stroke deaths and DALYs attributable to high sodium intake. All statistical analyses were performed using the R software (Version 3.5.3, R core team), and a 2-sided p-value of less than 0.05 was considered statistically significant.

Results

Global stroke burden attributable to high sodium intake

In 2019, the global ASMR of stroke attributable to high sodium intake was 12.05 (95% UI: 3.87–23.43) per 100,000 populations for males and 5.79 (95% UI: 1.-07–13.63) per 100,000 populations for females (**Table S1**); the global ASDR of stroke attributable to high sodium intake was 291.31 (95% UI: 106.80–539.34) per 100,000 populations for males and 140.88 (95% UI: 31.10–313.79) per 100,000 populations for females (**Table S2**). From 1990 to 2019, the global ASMR of stroke attributable to high sodium intake decreased by an average 1.67 % (95% CI: 1.56, 1.79) per year for males and 2.47% (95% CI: 2.35, 2.60) per year for females (**Table S1**); the global ASDR of stroke attributable to high sodium intake changed by an average −1.64% (95% CI: −1.74, −1.53) per year for males and −2.45% (95% CI: −2.57, −2.34) per year for females (**Table S2**).

Regionally, the ASMR and ASDR of stroke attributable to high sodium intake declined for both sexes in most GBD regions from 1990 to 2019 (Figure 1, **S1 and Tables S1, S2**), and decreased substantially in central Europe, east Asia, southeast Asia, high-income Asia Pacific, and eastern Sub–Saharan Africa. We found stroke burden attributable to sodium intake reduced from the approximate global level in 1990 to significantly lower than the global level in 2019. Although we also observed a significant reduction in East Asia, Southeast Asia and Central Europe, the stroke burden was still among some of the highest regions in the world in 2019. In Australasia, Western Europe, Caribbean, other sub-Saharan Africa regions, high−income North America, Latin America, and North Africa and the Middle East, however, there were little or no changes in the ASMR and ASDR of stroke attributable to high sodium intake.

In 2019, stroke attributable to high sodium intake caused 0.70 million (95% UI: 0.20–1.48) deaths and 17.67 million (95% UI: 5.76–34.92) DALYs globally. From 1990 to 2019, the global number of stroke deaths and DALYs attributable to high sodium intake increased by approximately 0.14 million and 3.0 million, respectively (**Tables S1, S2**). These increases were mainly the net results of decreases in countries in Europe and the Asia Pacific regions, and large increases in east Asia, south Asia, southeast Asia, and Oceania (Figure 2**, S2**). In particular, stroke deaths attributable to high sodium intake more than doubled in south Asia and Oceania and increased by more than 1.5-fold in southeast Asia. The number of DALYs attributable to high sodium intake increased more than 25% in east Asia, and more than doubled in south Asia and Oceania. Thus, by 2019, east Asia, southeast Asia, and south Asia accounted for more than four-fifths of stroke deaths and DALYs attributable to high sodium intake, compared with about two-thirds in 1990.

Effect of demography on the burden of stroke attributable to high sodium

Trends in total stroke deaths and DALY attributable to high sodium intake reflect the influence of changing mortality and DALY rate and demography. We calculated the contribution of changes in population growth, population aging, and mortality or DALY rate from 1990 to 2019 in 21 GBD regions according to the contributions of these three factors (**Figs S3, S4**). Most GBD regions experienced decreases in mortality rates. However, these decreases were offset by increases in population growth and population aging, with the effect of population aging being more pronounced in European and Asian countries. In contrast, population growth was more pronounced in Africa and Oceania. As a result, European countries experienced a net decrease in stroke attributable to high sodium intake. In contrast, in east Asia, south Asia, southeast Asia, and Oceania, population aging, and population growth led to a net increase in mortality, despite decreases in mortality rate.

The burden of stroke attributable to high sodium intake by SDI

All SDI quintiles showed a decrease in stroke ASMR attributable to high sodium intake (**Table S1**). In 2019, the ASMR was highest in the middle SDI and high-middle SDI quintiles, and lowest in the high SDI quintile than in the other quintiles. From 1990 to 2019, ASDR declined in all SDI quintiles, the high SDI quintile had the most significant decrease in ASMR, with a mean annual decrease of 3.91% (95% UI: 3.70, 4.11) (**Table S1**).

A similar pattern was observed for stroke ASDR attributable to high sodium intake, with the highest ASDR in the middle and high-middle SDI quintiles and the lowest in the high SDI quintile compared to other quintiles in 2019. From 1990 to 2019, the ASDR declined in all SDI quintiles, with the most pronounced decrease in the high SDI quintile (**Table S2**). All SDI quintiles except high SDI showed a net increase in the absolute number of deaths or DALYs attributable to high sodium intake from 1990 to 2019 (**Table S1, S2**), attributable to population growth and aging.

The correlation of the change in SDI and the change in ASMR or ASDR of stroke attributable to high sodium intake showed a negative correlation when SDI was above 0.67 and no correlation when SDI was lower than 0.67 (**Fig. S5**).

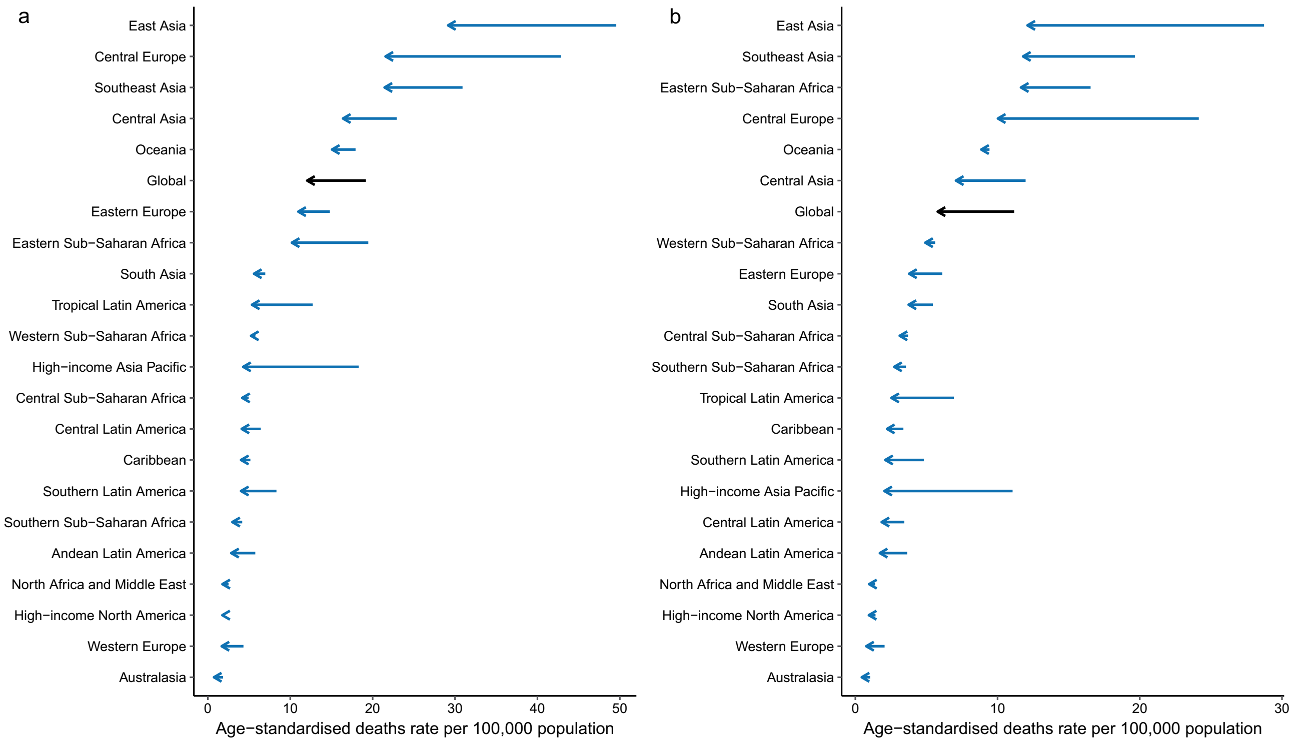

Figure 1. Change in age-standardized death rates of stroke attributable to high sodium intake between 1990 and 2019. A, age-standardized death rates of stroke attributable to high sodium intake for males. B, age-standardized death rates of stroke attributable to high sodium intake for females. The beginning of the arrow shows the age-standardized death rates of stroke attributable to high sodium intake in 1990, and the head indicates the value in 2019. Red corresponds to an increasing trend, while blue corresponds to a decreasing trend, and the global trend is shown in black.

The stroke burden attributable to high sodium intake by countries

There is considerable variation in the stroke burden attributable to high sodium intake across countries. In 2019, the ASMR varied more than 50-fold across countries (Figure 3), ranging from 0.85 (95% UI: 0.00, 5.90) in Australia to 47.63 (95% UI: 28.53, 67.60) in Macedonia for males, and from 0.94 (95% UI: 0.00, 3.07) in Lebanon to 35.04 (95% UI: 13.52, 58.87) in Macedonia for females. Overall, countries in east Asia, southeast Asia, central Asia, Oceania, and the Balkan Peninsula had higher ASMR of stroke attributable to high sodium intake. In contrast, the ASMR of stroke attributable to high sodium intake was relatively low in European, American, African, and Australian countries.

From 1990 to 2019, Estonia, South Korea, Japan, Singapore, Maldives, and the Czech Republic had the highest decrease in ASMR of stroke attributable to high sodium intake, with more than an average 6.0% decrease per year. In contrast, Ghana, Zimbabwe, Kuwait, Dominican Republic, Nepal, Pakistan, Philippines, and Bangladesh had the highest increase, with more than an average 1.0% increase per year (Figure 3). Most countries experienced a decline in ASMR of stroke attributable to high sodium intake. The countries with increased ASMR of stroke attributable to high sodium intake mainly located in south Asia, Africa, and north America.

Global stroke DALYs attributable to high sodium intake had a similar pattern with that of global stroke deaths attributable to high sodium intake (**Fig. S6**).

In 2019, with the highest ASMR and ASDR and large population, China had the most significant number of deaths or DALYs attributable to high sodium intake, approximately eight times higher than second-ranked India, followed by Indonesia and the Russian Federation.

Discussion

We performed a comprehensive estimation of the global spatial pattern and temporal trend in the burden of stroke attributable to high sodium intake from 1990 to 2019. Despite a general decline in ASMR and ASDR of stroke attributable to high sodium intake, the absolute number of mortality and DALYs increased in some countries and territories (east Asia, southeast Asia, south Asia, central Europe and Oceania), mainly due to population growth and aging.

Numerous studies have shown that high sodium intake was associated with increased blood pressure [3,5,18,19], whereas reduced sodium intake may lower blood pressure [3,6,8,18,20–22]. For example, a systematic review and meta-analysis including 133 randomized trials with 12,197 participants reported that every 50 mmol reduction in sodium excretion

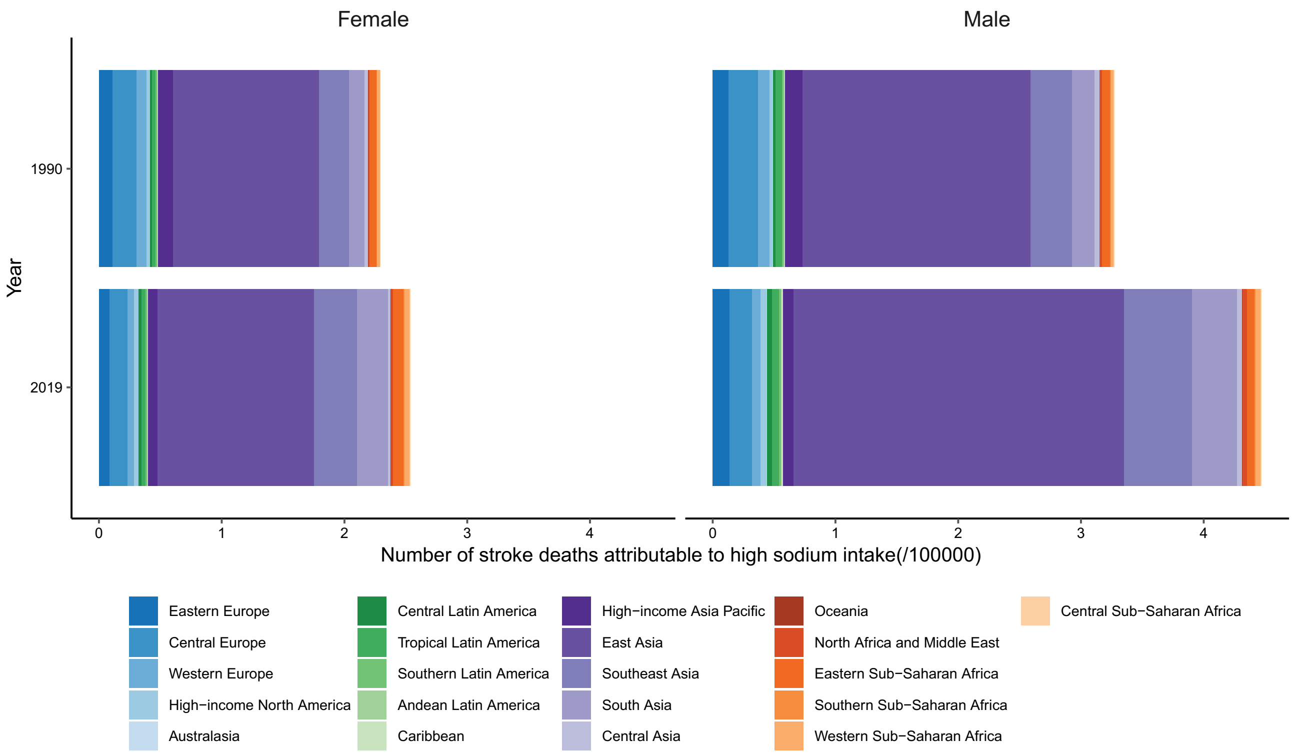

Figure 2. The number of stroke death attributable to high sodium intake in 21 GBD regions in 1990 and 2019 for females and males.

was associated with a 1.10 mm Hg reduction in systolic blood pressure and a 0.33 mm Hg reduction in diastolic blood pressure [6].

Our results demonstrate that the global burden of stroke attributed to high sodium intake, as quantified by ASMR and ASDR, has significantly decreased over the past three decades, but varies significantly among different countries and territories. Although significant declines of ASMR and ASDR have been recorded in east Asia, southeast Asia, central Europe and Oceania, the burden of stroke attributed to high sodium intake in these regions remains high because of their high level in 1990. Two possible reasons might explain the observed decreasing trends. First, the implementation of salt reduction measures. WHO has recommended a 30% reduction by 2025, with a long-term goal of fewer than five grams per day. Many high-income countries have already begun to implement action plans, mainly by setting salt reduction targets for processed foods, such as UK, where the average daily salt intake has fallen [22,23], it is estimated that from 2003 to 2015, salt reduction policies in UK prevented or delayed 52,000 cases of cardiovascular disease and 10,000 deaths from cardiovascular disease [22]. Although developing countries lagged behind, salt reduction programs have had some success [24,25] . For example, China is currently implementing a salt reduction program called the ‘Action on Salt China’, which has been in place since 2017. Second, the advances in primary and secondary stroke prevention, which have played a vital role in reducing stroke mortality and DALYs, resulting in a general decline in ASMR and ASDR of stroke in most parts of the world since 1990 [1].

Although the total burden of stroke attributable to high sodium intake as quantified by ASRs decreased in most parts of the world from 1990 to 2019, the absolute number of stroke deaths and DALYs attributed to high sodium intake did not generally decline over the same period. In particular, the absolute number of deaths and DALYs of stroke attributable to high sodium intake increased in east Asia, southeast Asia, south Asia, central Europe and Oceania. This study sheds light on the underlying reasons for the increase in absolute deaths and DALYs of stroke attributable to high sodium intake. Because stroke occurs predominantly in the elderly population, the decreases of stroke deaths and DALYs in these regions did not offset the effects of population aging and population growth, leading to a net increase in the number of stroke deaths and DALYs. Considering the fact that population aging is already occurring or will inevitably occur in the next decades, reducing mortality and DALY rates is crucial to reducing the absolute burden of stroke. In this regard, the high-income Asia-Pacific region has done well, although there is a severely aging population in the region, the decline in stroke deaths and DALYs has completely offset the impact of aging, resulting in a significant decline in stroke deaths and DALYs attributable to high sodium intake. In contrast,

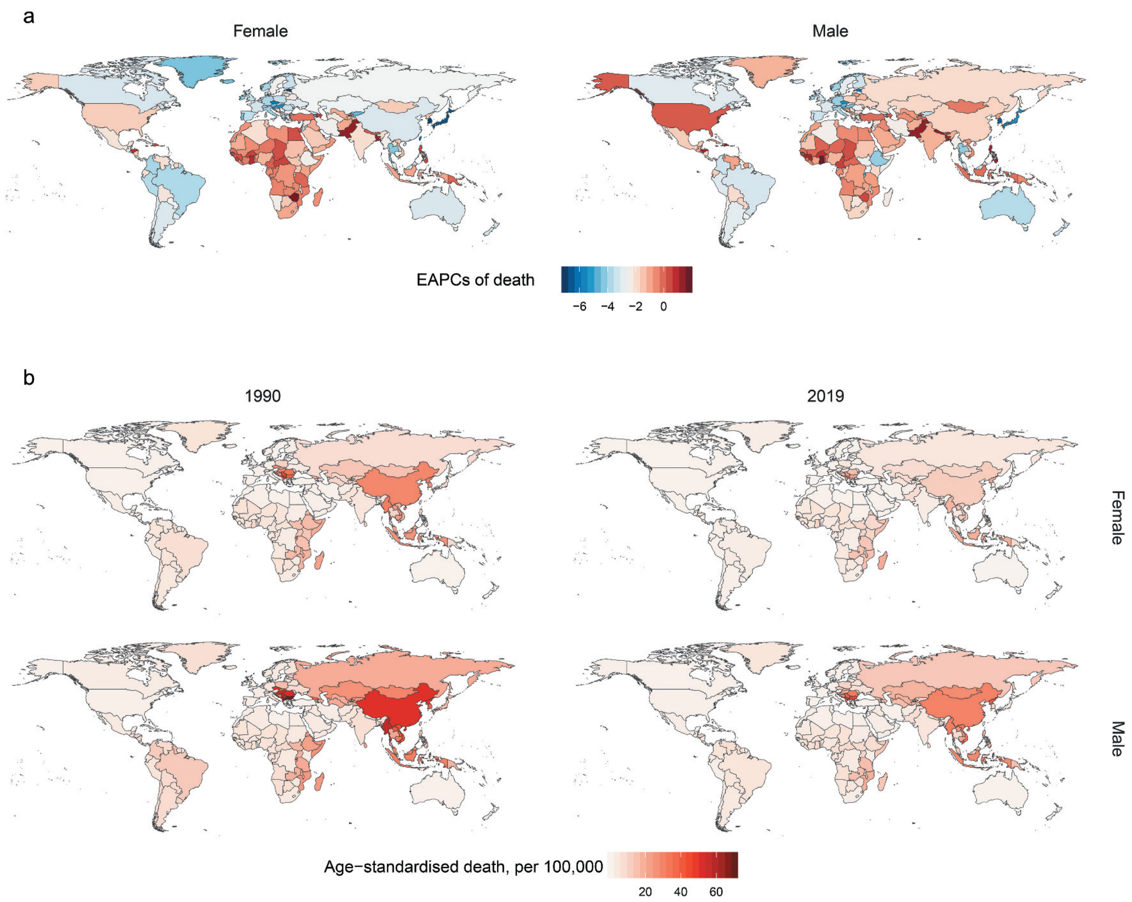

Figure 3. Age-standardized death rates of stroke attributable to high sodium intake and trends from 1990 to 2017. A, estimated annual percentage changes in age-standardized death rates of stroke attributable to high sodium intake by country between 1990 and 2019 for females and males. B, age-standardized death rates of stroke attributable to high sodium intake by country in 1990 and 2019 for females and males. Abbreviations: EAPC = estimated annual percentage change.

Oceania had the smallest reduction in stroke mortality and DALY, with little or no offsetting effect on population growth and aging, resulting in a significant net increase.

Our study reveals a negative correlation between SDI and stroke burden attributed to high sodium intake when SDI is greater than 0.67, suggesting that the pace of improvement in critical social, demographic, and economic conditions is a crucial factor in determining health progress [26].

Our research has three main implications for stroke prevention. First, countries around the world need to continue to promote salt reduction measures, especially for countries in east Asia, southeast Asia, south Asia, central Europe and Oceania. Second, it is crucial to strengthen stroke prevention, such as further promoting the use of statins and antihypertensive medicines, which has been shown to be practical and cost-effective for both primary and secondary prevention of stroke. At present, stroke prevention is still not widely implemented or sufficient enough in low- and middle-income countries [27,28]. Therefore, how to improve the effectiveness and coverage of stroke prevention measures in these low- and middle-income countries is also an issue that should be addressed. Third, the rapid population aging is likely to increase the burden of stroke even further by producing a more vulnerable population, so it is more urgent for countries with serious population aging to improve and change the current medical and healthcare system to make it more accessible and affordable to meet the increasing demand of an aging society.

There are a few potential limitations in this study. First, GBD did not collect sodium from spot urine samples, which might lead to lower data representativeness [16]. Second, GBD did not synthesize evidence on the direct effect of sodium on stroke, but only evaluated the effect of sodium on stroke through systolic blood pressure, which might introduce some degrees of data uncertainty [11,16,29]. Finally, the study is subject to other general limitations described by the GBD collaboration [29–31], such as assuming the distribution of dietary factors is independent, which may affect the accuracy of the estimates.

Conclusion

In summary, our study assessed the temporal and spatial variation in the stroke burden attributable to high sodium intake. Although the global age-standardized rate of stroke burden attributable to high sodium intake declined from 1990 to 2019, the burden remains high in some countries in east Asia, southeast Asia, central Asia, central Europe and Oceania. The findings highlight the urgency of accelerating salt reduction, continuing to advance stroke prevention measures, and improving medical services to better serve an aging population, which will bring substantial global health benefits.

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Disclosure of interests

The authors report no conflicts of interest.

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