


Global trends in ischemic stroke burden attributable to high BMI

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Abstract

We aimed to assess the worldwide burden of ischemic stroke (IS) associated with high body mass index (BMI) using data from the Global Burden of Disease 2019. This study examined the impact of high BMI on IS-related age-standardized death rates (ASDR) and disability-adjusted life years (DALYs). Estimated annual percentage changes (EAPC) is estimated annual percentage change. Trends were assessed using EAPCs. Over the past 3 decades, there has been a declining trend in the global burden of IS associated with high BMI, especially in Western Europe (EAPC = -3.09 for DALYs) and high-income Asia Pacific (EAPC = -4.6 for ASDR). However, certain developing regions, notably Southeast Asia, have experienced significant increases in ASDR (EAPC = 3.7) and age-standardized DALY rates (EAPC = 3.64). The most substantial increase in burden was observed in Southeast Asia for both males (EAPC = 3.85) and females (EAPC = 3.53). Importantly, the burden was most pronounced in regions with low to middle sociodemographic index. The rising disease burden linked to high BMI is largely due to insufficient medical infrastructure and ineffective public health policies in the region. Urgent action is needed from decision-makers to improve these areas and implement effective interventions. This study reveals a consistent global decline in IS related to high BMI, with a more significant burden observed in males under the age of 65, particularly in Southeast Asia, where increases in IS associated with high BMI are notable. Public health officials and global policymakers need timely and reliable quantitative data. This information is essential for implementing effective behavioral interventions, such as monitoring diet and physical activity, to address identified risk factors and reduce the burden of high BMI.

Abbreviations: ASDR = age-standardized death rates, ASRs = age-standardized rates, BMI = body mass index, CI = confidence interval, DALYs = disability-adjusted life years, EAPCs = estimated annual percentage changes, GBD = Global Burden of Disease, ICD = International Classification of Diseases, IS = ischemic stroke, PAF = population attributable fractions, SDI = sociodemographic index, UI = uncertainty interval.

Keywords: adults, DALY, EAPC, global disease burden, global trend, high body mass index, ischemic stroke, sociodemographic index

1. Introduction

The landscape of global health is witnessing a significant shift, with noncommunicable diseases increasingly dominating in both developed and developing nations. Among these noncommunicable diseases, ischemic stroke (IS) emerges as a critical public health concern, representing approximately 70% of all strokes and carrying a high risk of long-term recurrence.^[1,2] The year 2019 saw a total of 3.29 million deaths attributed to IS, accounting for more than half of all stroke-related mortalities and 17.7% of deaths. This underscores the utmost importance of preventing IS.^[3,4]

A high body mass index (BMI) increases the risk of several chronic diseases, such as cardiovascular disease, type 2

diabetes, chronic kidney disease, various cancers, and musculoskeletal disorders. Consequently, these diseases have significantly increased the number of confirmed cases and deaths globally, placing a tremendous burden on individuals, families, and healthcare systems. There is a significant correlation between the rising rates of high BMI and the increasing incidence of ischemic stroke.^[5] This association is consistent across various countries and populations, irrespective of their economic or demographic characteristics.^[6-8] Furthermore, an analysis of stroke data from the Global Burden of Disease (GBD) 2019 database revealed a significant increase in strokes and stroke-related deaths from 1990 to 2019, despite a notable decrease in age-standardized rates during this period. This trend is particularly pronounced among those aged 70 years

The patients/participants provided their written informed consent to participate in this study.

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The datasets generated during and/or analyzed during the current study are publicly available.

This study is based on a publicly available database and does not require ethical approval.

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and older, those with low income, and those with high BMI.^[9,10] Studies indicate that people who are overweight or obese have a higher risk of ischemic stroke compared to those with normal weight. Research shows that obese patients experience greater permeability of the blood–brain barrier and have more infiltrating immune cells. This condition worsens inflammatory reactions and heightens the risk of ischemic brain injury. Thus, obesity can worsen ischemic brain injury, negatively impacting the prognosis of the nervous system. Moreover, obesity raises the risk of mortality in patients with ischemic stroke by nearly 40%. Consequently, effectively treating obesity and ischemic stroke presents a significant clinical challenge that must be urgently addressed.^[11] These findings emphasize the urgent need to address ischemic stroke, especially in relation to modifiable risk factors like BMI.

However, there is a lack of research on how high BMI affects IS, especially on a global scale. Most studies focus on the overall disease rather than its subtypes. Additionally, previous research has primarily focused on individual countries or regions, leaving evidence of future global trends unclear. Some studies have only reported the disease burden of stroke and other conditions related to high BMI. The lack of studies on the global burden of IS linked to high BMI worsens this knowledge gap. To fill this research gap and gain a better understanding of the changing patterns of IS related to high BMI, our study analyzed mortality rates and disability-adjusted life years (DALYs) of IS attributed to high BMI across different regions, age groups, and genders in 204 countries and territories. We hope to reveal the changing trend of IS attributed to high BMI worldwide, quantify the IS burden caused by these modifiable risk factors to help determine their impact on the population, and guide targeted interventions to reduce the global IS incidence rate.

2. Methods

2.1. Study data

This study is a component of the comprehensive GBD 2019 project, renowned for its extensive analysis comprising 369 diseases and injuries and 87 risk factors spanning from 1990 to 2019. GBD 2019 encompasses a wide geographical scope, incorporating data from 204 countries and territories across 21 regions. In this research, we obtained data pertaining to the disease burden associated with high BMI from the Institute for Health Metrics and Evaluation website's results tool (<http://ghdx.healthdata.org/gbd-results-tool>). The primary data sources for high BMI estimates can be accessed through the GBD 2019 Data Input Sources Tool (<https://vizhub.healthdata.org/gbd-results/>). This study utilizes a publicly available database that does not require ethical approval or participant consent, as the data is deidentified.

2.2. Definitions

A high BMI is classified as overweight (BMI between 25 and 30.0 kg/m²) or obese (BMI over 30 kg/m²) for individuals aged 20 years and older, according to the standards set by the International Obesity Task Force for children.^[12] The GBD 2019 utilized data on high BMI from a total of 2288 data sources, which can be explored further at <http://ghdx.healthdata.org/gbd-2017/data-input-sources>. A comprehensive account of the selection process and input data has been previously published.^[12]

IS in GBD 2019 was defined as a neurological dysfunction episode caused by a focal infarction in the cerebral, spinal, or retinal region. The category of unspecified strokes (International Classification of Diseases [ICD]-10 I64) was also further divided into IS. This classification aligns with the codes G45-G46.8,

I63-I63.9, I65-I66.9, I67.2-I67.3, I67.5-I67.6, I69.3 in the 10th version of the (ICD-10), and 433-435.9, 437.0-437.1, 437.5-437.8 codes in ICD-9.^[12]

The sociodemographic index (SDI) is a crucial tool used to assess development conditions. It classifies 204 countries and territories into 5 regions based on quintiles: low, low-middle, middle, high-middle, and high.^[13] This index plays a significant role in determining health outcomes as it is calculated as the geometric mean of 3 important factors: per capita income over time, total fertility rate among individuals under 25 years old, and average educational level of individuals aged 15 and above. The values of the index range from 0 to 1.^[14]

In view of the severe consequences frequently associated with IS, our study employs specific metrics to quantitatively assess its mortality and disability patterns. These metrics include the age-standardized death rate (ASDR) and the age-standardized DALYs, along with a 95% uncertainty interval (UI) for each. Additionally, estimated annual percentage changes (EAPC) serves as an indicator in linear regression models, linking the natural logarithm of a specific age group's rate to the model. We use the EAPC to analyze trends over time. We utilize the EAPC to examine temporal trends.^[15]

2.3. The measure of IS attributable to high BMI

Population attributable fractions (PAF) are employed to assess the contribution of specific risk factors to disease or mortality within an entire population, as well as the proportion by which mortality can be reduced if the population were at the theoretical minimum risk exposure level. The product of PAF with the disease's DALY and deaths represents the DALY and deaths attributed to that risk factor. The attributed standardized rates were used to measure the attributable disease burden of global IS risk factors.

$$PAF_{asly} = \sum_{x=1}^k RR_{asy}(x)P_{asly}(x) - \frac{1}{\sum_{x=1}^k RR_{as}(x)P_{asly}(x)}$$

where a is the age group, s is the sex, l is the location, and y is the year; PAF_{asly} is the PAF for the burden of diseases due to LPA; RR is the relative risks between exposure level x (from 1 to k) of LPA and the burden of diseases; and P is the proportion of the population exposed to low physical activity.

2.4. Statistical analysis

Age-standardized rates (ASRs, per 100,000 population) are calculated using the GBD world population age standard as a reference, following the methodology outlined by Ahmad et al direct standardization is employed in this process, yielding an age-adjusted rate that represents a weighted average of age-specific rates. These weights ensure that the relative age distribution in the population is accurately captured. The formula for calculating the direct ASR is as follows:

$$ASR = \frac{\sum_{i=1}^A a_i \omega_i}{\sum_{i=1}^A \omega_i} \times 10000$$

The computation of ASR signifies the rate that is specific to each age cohort while denoting the corresponding segment or "weight" in the reference population's age class. The computation of ASR signifies the rate that is specific to each age cohort while denoting the corresponding segment or "weight" in the reference population's age class. ASR trends play a crucial role in revealing dynamic risk factors and changes in patterns. The EAPC serves as a valuable metric for evaluating these trends in ASR. To calculate the EAPC from ASR, the calendar year is utilized as an independent variable to establish a regression line

based on the natural logarithm of ASR. The formula employed for this purpose is:

$$EAPC = 100 \times (e^\beta - 1)$$

In this expression, β is the estimated slope from the regression line. This formula is also used to calculate the 95% confidence interval (CI) of the fitted regression line. If both the EAPC and its lower 95% CI boundary are >0, it indicates an increasing trend in ASR. Conversely, if both the EAPC and its upper 95% CI boundary are below 0, it suggests a declining trend in ASR. Furthermore, if the EAPC is <0 but its upper 95% CI boundary is >0, or if the EAPC is >0 but its lower 95% CI boundary is <0, this implies a stable ASR trend, with the EAPC and its 95% CI range encompassing 0.

The stability and reliability of death registration, were taken into account when calculating the Pearson correlation coefficient for ASDR, age-standardized DALY rates, EAPC, and the SDI. A significant negative correlation between the 2 variables is indicated when the Pearson correlation coefficient is <0 and the P-value is .05 or below.

3. Results

3.1. Global trends in the distribution of disease burden of IS attributed to high BMI in different regions

The burden of IS attributed to high BMI has generally decreased over time in most countries. However, developing regions have experienced a higher burden of IS related to high BMI deaths compared to developed regions. It is important to note that a few developing countries, particularly those in Southeast Asia, have seen a significant increase in ASDR and age-standardized DALYs rate due to IS. In 2019, the highest ASDR and age-standardized DALY rate for IS attributed to high BMI were found in Eastern Europe, specifically in North Macedonia, with an ASDR of 28.87 per 100,000 (95% UI 14.99–46.95) and an age-standardized DALY rate of 579.67 per 100,000 (95% UI 344.21–859.54). These findings are summarized in Figures 1 and 2 and Tables 1 and 2.

From 1990 to 2019, the global rates of ASDR and age-standardized DALYs showed a decline in most countries and territories. However, there are still a few countries and territories, primarily in Southeast Asia, experiencing a significant upward trend in ASDR and age-standardized DALY rate. For instance, in Viet Nam, the EAPC for ASDR was 5.46 (95% CI 5.07–5.86), while the EAPC for the age-standardized DALY

rate was 5.39 (95% CI 5.02–5.75). Similarly, Mozambique also witnessed an upward trend, with an EAPC for ASDR of 5.28 (95% CI 4.95–5.62) and an EAPC for the age-standardized DALY rate of 5.33 (95% CI 5.01–5.65). These findings are presented in Tables 1 and 2, Table S1, Supplemental Digital Content, <http://links.lww.com/MD/N830>, Table S2, Supplemental Digital Content, <http://links.lww.com/MD/N830>, Figure S1, Supplemental Digital Content, <http://links.lww.com/MD/N830>, Figure S2, Supplemental Digital Content, <http://links.lww.com/MD/N830> and Figure 1. Importantly, all the observed upward trends in age-standardized DALY rates and ASDR were concentrated in regions characterized by middle or below SDI, namely middle SDI, low-middle SDI, and low SDI.

3.2. Characteristics of the distribution of IS attributed to high BMI disease burden in different sex and age groups

Age-specific analysis highlights significant variations in death and DALYs numbers attributed to high BMI-related IS, with notable differences observed across different age groups (Table S3, Supplemental Digital Content, <http://links.lww.com/MD/N830> and Table S4, Supplemental Digital Content, <http://links.lww.com/MD/N830>). Specifically, the 65 to 69-year age group exhibited the highest mortality rates. Similarly, the count of DALYs and age-adjusted rates increased progressively with age. Among both males and females, the greatest burden of DALYs was found in the 65 to 69-year age category (Fig. 3 and Figure S3, Supplemental Digital Content, <http://links.lww.com/MD/N830>).

In recent decades, the global death rate associated with high BMI and its connection to IS has increased across various age groups, impacting both males and females. Notably, deaths related to high BMI are more common in males compared to females. This disparity in DALYs for IS linked to high BMI is expected to widen further, as indicated in Tables S5 to S8, Supplemental Digital Content, <http://links.lww.com/MD/N830>. In 2019, male deaths reached 180,991 (95% UI: 97,720–283,782), while females accounted for 190,246 (95% UI: 105,319–299,021) in this regard. Similarly, both the ASDR and the age-standardized DALY rates were observed to be higher in males at both the global and regional levels, with females experiencing a more noticeable decline. In 2019, Eastern Europe had the highest figures for both genders (ASDR male = 20.44, 95% UI: 11.82–30.71; ASDR female = 16.39, 95% UI: 9.35–24.28; age-standardized DALY rate male = 508.48, 95%

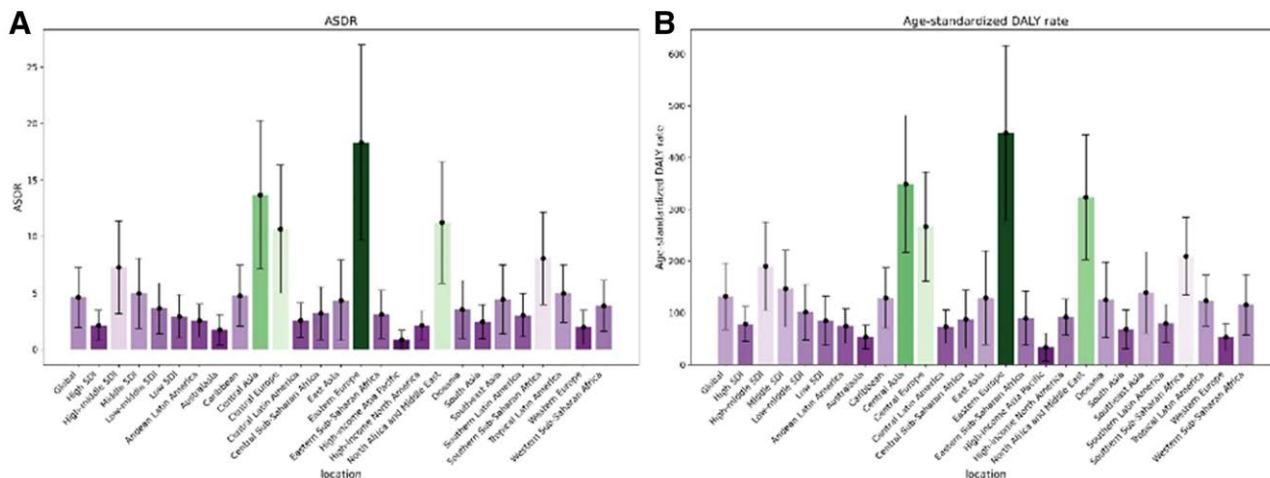


Figure 1. The ASRs of global burden of ischemic stroke attributed to high BMI by region: age-standardized DALY rate and ASDR in 2019. ASDR = age-standardized death rates, ASRs = age-standardized rates, BMI = body mass index, DALYs = disability-adjusted life years.

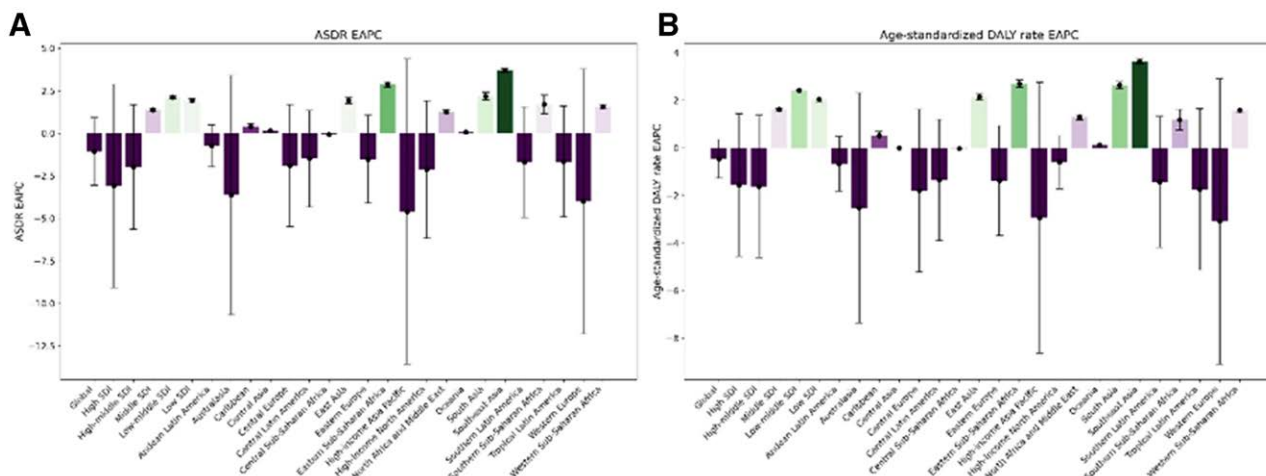


Figure 2. Trends in EAPCs of ischemic stroke attributed to high BMI by region: age-standardized DALY rate and ASDR, 1990–2019. ASDR = age-standardized death rates, BMI = body mass index, DALYs = disability-adjusted life years, EAPCs = estimated annual percentage changes.

Table 1

Deaths of ischemic stroke attributed to high BMI in 1990 and 2019 for both sexes and all regions.

Location	Numbers_1990	ASR_1990	Numbers_2019	ASR_2019	EAPC_CI	Numbers_change
Global	207,194 (107,687–328,397)	5.65 (2.77–9.15)	371,236 (206,106–579,834)	4.61 (2.5–7.29)	-1.06 (-1.19 to 0.92)	0.79 (0.59 to 1.03)
High SDI	48,163 (23,496–79,175)	4.51 (2.18–7.43)	42,923 (20,387–73,995)	2.12 (1.11–3.46)	-3.09 (-3.29 to 2.89)	-0.11 (-0.31 to 0.07)
High-middle SDI	112,022 (63,165–168,341)	11.04 (5.96–17.04)	147,290 (81,257–229,133)	7.28 (3.97–11.39)	-1.97 (-2.25 to 1.68)	0.31 (0.13 to 0.49)
Middle SDI	32,394 (14,314–57,034)	3.39 (1.43–6.13)	119,096 (65,740–188,267)	4.96 (2.64–8.07)	1.38 (1.29 to 1.47)	2.68 (1.85 to 4.01)
Low-middle SDI	10,679 (4050–20,466)	2 (0.72–3.98)	47,419 (25,503–74,700)	3.63 (1.9–5.87)	2.12 (2.06 to 2.19)	3.44 (2.36 to 5.73)
Low SDI	3849 (1429–7496)	1.76 (0.61–3.51)	14,312 (7433–22,937)	2.93 (1.47–4.86)	1.94 (1.86 to 2.03)	2.72 (1.89 to 4.62)
Andean Latin America	601 (315–959)	3.04 (1.52–4.99)	1402 (786–2172)	2.56 (1.42–4.01)	-0.73 (-0.96 to 0.5)	1.33 (0.68 to 2.28)
Australasia	1007 (502–1639)	4.27 (2.05–7.2)	972 (338–1803)	1.73 (0.7–3.09)	-3.63 (-3.85 to 3.41)	-0.03 (-0.47 to 0.31)
Caribbean	1142 (617–1780)	4.48 (2.36–7.16)	2475 (1361–3882)	4.76 (2.61–7.46)	0.4 (0.22 to 0.57)	1.17 (0.77 to 1.72)
Central Asia	5140 (2995–7567)	11.62 (6.68–17.3)	8977 (5645–12,747)	13.69 (8.16–20.26)	0.15 (-0.13 to 0.43)	0.75 (0.44 to 1.18)
Central Europe	23,681 (14,212–34,189)	16.43 (9.65–24.52)	23,828 (13,487–36,671)	10.66 (6.1–16.33)	-1.89 (-2.1 to 1.69)	0.01 (-0.21 to 0.21)
Central Latin America	2911 (1571–4479)	3.72 (1.93–5.91)	5892 (3130–9326)	2.58 (1.34–4.12)	-1.49 (-1.63 to 1.35)	1.02 (0.61 to 1.53)
Central Sub-Saharan Africa	596 (259–1080)	2.89 (1.18–5.32)	1479 (706–2520)	3.2 (1.45–5.54)	-0.08 (-0.4 to 0.25)	1.48 (0.9 to 2.56)
East Asia	21,374 (5206–46,532)	2.57 (0.6–5.7)	88,944 (37,414–157,506)	4.34 (1.78–7.9)	1.93 (1.76 to 2.1)	3.16 (1.9 to 7.12)
Eastern Europe	63,128 (37,854–91,039)	22.96 (13.41–34.04)	63,241 (36,199–93,871)	18.32 (10.58–26.98)	-1.52 (-1.98 to 1.06)	0 (-0.17 to 0.19)
Eastern Sub-Saharan Africa	1022 (344–2113)	1.49 (0.47–3.19)	4510 (2346–7336)	3.1 (1.55–5.22)	2.87 (2.71 to 3.03)	3.41 (2.13 to 6.43)
High-income Asia Pacific	4960 (1538–10,003)	2.62 (0.77–5.48)	4390 (1304–9322)	0.84 (0.28–1.69)	-4.6 (-4.83 to 4.38)	-0.12 (-0.41 to 0.23)
High-income North America	12,521 (6454–20,184)	3.38 (1.76–5.44)	14,468 (6818–24,209)	2.12 (1.07–3.45)	-2.13 (-2.35 to 1.91)	0.16 (-0.13 to 0.4)
North Africa and Middle East	13,455 (7875–19,915)	8.32 (4.63–12.83)	45,969 (29,818–65,073)	11.24 (6.95–16.62)	1.25 (1.14 to 1.37)	2.42 (1.73 to 3.33)
Oceania	91 (44–158)	3.15 (1.39–5.73)	239 (127–394)	3.53 (1.75–6.09)	0.07 (-0.12 to 0.26)	1.64 (1.16 to 2.39)
South Asia	6202 (1985–13,097)	1.27 (0.38–2.74)	33,174 (17,310–52,829)	2.46 (1.24–3.97)	2.19 (1.96 to 2.41)	4.35 (2.67 to 8.91)
Southeast Asia	4089 (1273–8603)	1.72 (0.51–3.77)	25,605 (13,561–41,528)	4.42 (2.25–7.47)	3.7 (3.58 to 3.81)	5.26 (3.32 to 10.95)
Southern Latin America	2135 (1034–3477)	4.71 (2.22–7.78)	2615 (1291–4270)	3.04 (1.52–4.95)	-1.69 (-1.82 to 1.56)	0.22 (-0.08 to 0.68)
Southern Sub-Saharan Africa	1390 (835–2057)	5.43 (3.12–8.32)	4014 (2608–5719)	8.06 (4.92–12.15)	1.7 (1.16 to 2.25)	1.89 (1.46 to 2.5)
Tropical Latin America	6944 (3610–10,940)	8.04 (4–13)	11,676 (6814–17,539)	4.95 (2.82–7.51)	-1.66 (-1.73 to 1.59)	0.68 (0.34 to 1.24)
Western Europe	32,778 (15,672–55,078)	5.44 (2.58–9.15)	20,650 (7439–38,666)	1.96 (0.85–3.46)	-4 (-4.21 to -3.78)	-0.37 (-0.6 to 0.22)
Western Sub-Saharan Africa	2025 (870–3688)	2.4 (0.98–4.53)	6717 (3865–10,312)	3.85 (2.09–6.11)	1.56 (1.48 to 1.65)	2.32 (1.43 to 4.31)

UI: 318.21–728.1; age-standardized DALY rate female = 397.81, 95% UI: 261.03–544.57). From 1990 to 2019, the decline in both ASDR and age-standardized DALY rates was more significant among females across most global regions. The largest

decrease in ASDR was observed in Australasian males (EAPC male = -4.09, 95% CI: -4.36 to -3.81) and high-income Asia Pacific females (EAPC female = -5.49, 95% CI: -5.78 to -5.2), while the most substantial reduction in age-standardized DALY

Location	Numbers_1990	ASR_1990	Numbers_2019	ASR_2019	EAPC_CI	Numbers_change
Global	5,586,433 (3,058,155–8,549,612)	138.76 (75.23–215.1)	10,951,021 (6,696,715–16,210,999)	132.05 (80.14–195.95)	-0.46 (-0.56 to 0.35)	0.96 (0.75 to 1.25)
High SDI	1,213,636 (672,069–1,850,322)	116.69 (65.12–177.52)	1,308,282 (805,722–1,905,135)	78.68 (50.8–112.42)	-1.56 (-1.69 to 1.43)	0.08 (-0.06 to 0.28)
High-middle SDI	2,853,808 (1,693,571–4,157,448)	262.39 (154.09–387.23)	3,862,879 (2,353,460–5,596,724)	190.21 (116.34–275.57)	-1.62 (-1.87 to 1.37)	0.35 (0.22 to 0.5)
Middle SDI	1,054,724 (495,851–1,800,160)	94.61 (43.23–163.8)	3,810,322 (2,279,844–5,686,050)	147.14 (86.75–221.28)	1.61 (1.55 to 1.66)	2.61 (1.88 to 3.84)
Low-middle SDI	332,084 (133,437–619,688)	52.15 (20.39–97.48)	1,465,748 (847,637–2,217,868)	101.57 (58.11–155.38)	2.41 (2.36 to 2.46)	3.41 (2.36 to 5.61)
Low SDI	129,773 (51,326–242,704)	49.67 (19.05–93.94)	497,755 (279,528–762,817)	85.1 (46.38–132.65)	2.04 (1.94 to 2.15)	2.84 (2.02 to 4.71)
Andean Latin America	19,309 (11,115–28,669)	86.15 (48.27–129.55)	43,053 (27,523–61,832)	74.67 (47.15–107.88)	-0.67 (-0.86 to 0.48)	1.23 (0.71 to 1.96)
Australasia	24,513 (14,157–36,430)	102.76 (58.8–153.78)	24,541 (14,817–36,012)	53.51 (33.99–76.39)	-2.52 (-2.73 to 0.23)	0 (-0.18 to 0.23)
Caribbean	31,907 (18,653–47,157)	118.18 (68.44–176.51)	66,726 (41,399–96,862)	129.17 (80.05–187.5)	0.52 (0.35 to 0.69)	1.09 (0.75 to 1.61)
Central Asia	148,512 (91,340–213,869)	310.73 (189.28–446.45)	267,790 (179,995–364,368)	349.31 (228.5–481.7)	0 (-0.28 to 0.28)	0.8 (0.52 to 1.21)
Central Europe	604,060 (383,567–843,788)	405.73 (256.98–569.62)	559,620 (362,343–785,889)	266.93 (174.24–372.25)	-1.79 (-1.96 to 1.63)	-0.07 (-0.21 to 0.07)
Central Latin America	92,921 (54,903–136,556)	102.32 (59.33–152.56)	176,204 (109,893–251,814)	73.44 (45.53–105.47)	-1.35 (-1.51 to 1.19)	0.9 (0.61 to 1.27)
Central Sub-Saharan Africa	19,469 (8871–34,307)	78.61 (34.87–139.54)	50,374 (26,202–80,726)	87.77 (44.31–143.73)	-0.03 (-0.37 to 0.31)	1.59 (1.06 to 2.52)
East Asia	677,489 (172,844–1,447,107)	71.77 (18.07–154.19)	2,770,469 (1,253,849–4,677,025)	129.49 (58.17–220.05)	2.14 (2.03 to 2.26)	3.09 (1.92 to 7.08)
Eastern Europe	1,554,539 (995,670–2,151,642)	546.92 (349.53–759.03)	1,513,971 (976,265–2,092,484)	447.53 (290.35–616.38)	-1.37 (-1.81 to 0.94)	-0.03 (-0.15 to 0.14)
Eastern Sub-Saharan Africa	38,289 (14,425–74,214)	44.73 (16.26–88.64)	165,890 (94,816–258,706)	89.71 (49.12–142.06)	2.7 (2.54 to 2.86)	3.33 (2.17 to 5.96)
High-income Asia Pacific	136,936 (46,396–258,961)	67.66 (22.71–129.86)	128,831 (51,022–237,661)	33.73 (13.79–60.76)	-2.93 (-3.11 to 2.76)	-0.06 (-0.2 to 0.2)
High-income North America	380,433 (226,518–557,481)	109.39 (66.58–159.32)	526,818 (334,871–743,153)	91.91 (59.59–126.86)	-0.6 (-0.68 to 0.52)	0.38 (0.22 to 0.61)
North Africa and Middle East	444,245 (276,867–641,775)	235.98 (142.27–344.39)	152,760 (105,5842–2,067,831)	323.44 (218.76–443.94)	1.29 (1.18 to 1.4)	2.44 (1.83 to 3.26)
Oceania	4006 (2140–6483)	111.68 (56.44–184.1)	10,608 (6163–16,570)	125.28 (69.92–198.28)	0.12 (-0.08 to 0.32)	1.65 (1.28 to 2.16)
South Asia	191,557 (65,130–391,382)	31.9 (10.52–65.25)	1,025,000 (574,710–1,595,447)	68.54 (37.56–106.13)	2.64 (2.49 to 2.79)	4.35 (2.76 to 8.5)
Southeast Asia	156,124 (53,308–310,671)	54.74 (18.32–110.69)	906,215 (521,138–1,401,404)	139.5 (78.8–218.13)	3.64 (3.53 to 3.74)	4.8 (3.12 to 9.24)
Southern Latin America	54,066 (28,080–84,120)	115.07 (59.19–181.87)	66,012 (38,807–96,662)	79.85 (47.37–116.54)	-1.43 (-1.53 to 1.32)	0.22 (0 to 0.63)
Southern Sub-Saharan Africa	48,223 (31,876–65,684)	160.77 (103.58–222.26)	120,790 (86,226–160,680)	209.41 (145.1–284.61)	1.18 (0.74 to 1.62)	1.5 (1.21 to 1.88)
Tropical Latin America	196,509 (109,182–300,820)	203.26 (109.34–315.48)	302,677 (198,463–420,408)	124.06 (81.08–173.08)	-1.74 (-1.83 to 1.65)	0.54 (0.28 to 1)
Western Europe	692,677 (372,812–1,060,187)	120.03 (65.53–182.24)	443,999 (240,271–693,654)	53.4 (31.26–79.53)	-3.09 (-3.28 to 2.91)	-0.36 (-0.46 to 0.26)
Western Sub-Saharan Africa	70,649 (32,660–122,133)	71.64 (32.8–125.11)	253,833 (158,372–375,251)	115.65 (70–174.04)	1.59 (1.51 to 1.67)	2.59 (1.71 to 4.51)

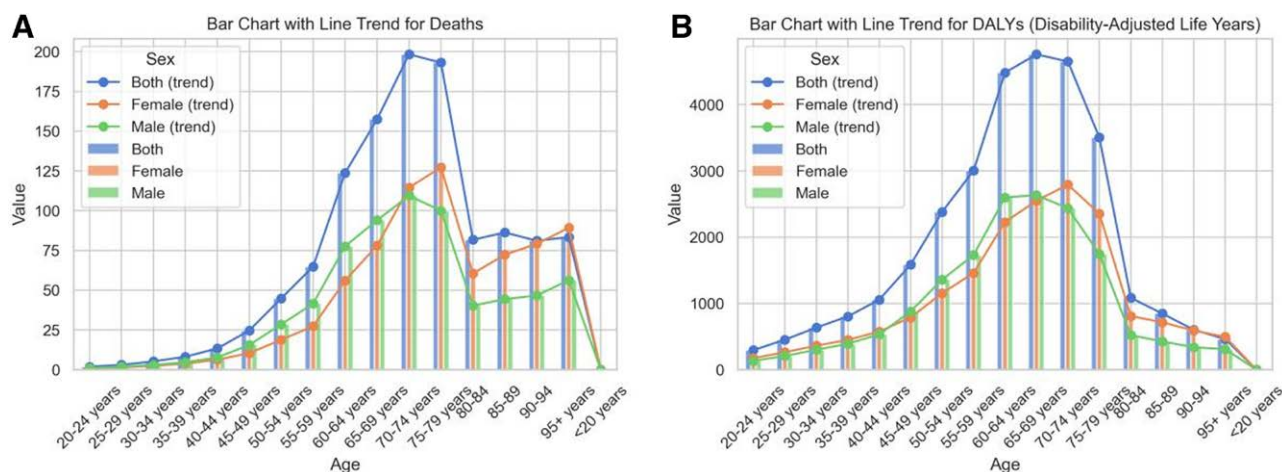


Figure 3. Bar chart with line trend of ischemic stroke attributed to high BMI 2019 by country and age group. BMI = body mass index.

rates occurred in females from high-income Asia Pacific (EAPC female = -3.23 , 95% CI: -3.47 to -3.00) and males from Western Europe (EAPC male = -3.36 , 95% CI: -3.53 to -3.18) (Table S5, Supplemental Digital Content, <http://links.lww.com/MD/N830>, Table S6, Supplemental Digital Content, <http://links.lww.com/MD/N830>, Table S7, Supplemental Digital Content, <http://links.lww.com/MD/N830>, and Table S8, Supplemental Digital Content, <http://links.lww.com/MD/N830>).

3.3. Distribution characteristics of IS attributed to high BMI disease burden in regions with different SDI levels

Among the 5 categories of SDI, the high-middle SDI territory showed the highest ASDR for IS due to elevated BMI, with a rate of 7.28 (95% UI: 3.97–11.39) per 100,000 individuals. This rate was higher than that of the middle SDI sector, which was 4.96 (95% UI: 2.64–8.07) per 100,000. From 1990 to 2019, a significant increase was observed in the low-middle SDI domain, with an EAPC of 2.12 (95% CI: 2.06–2.19), slightly higher than the EAPC of the low SDI stratum, which was 1.94 (95% CI: 1.86–2.03). Detailed information is provided in Table 1.

Among the 5 categories of SDI, the high-middle SDI bracket had the highest age-standardized DALYs rate for IS related to high BMI, at 190.21 (95% uncertainty interval [UI]: 116.34–275.57) per 100,000 population. Following closely was the median SDI group, with a rate of 147.14 (95% UI: 86.75–221.28) per 100,000. Over the period between 1990 and 2019, the low-middle SDI category experienced a significant increase, with an EAPC of 2.41 (95% CI: 2.36–2.46). The low SDI group had a slightly lower EAPC of 2.04 (95% CI: 1.94–2.15), as shown in Table 2.

Our analysis conducted in 2019 examined the patterns of ASDR and age-standardized DALY rates across different levels of SDI. The results of our analysis revealed a significant and direct correlation between SDI and both ASDR and DALY rates ($R = 0.244$, $P < .001$ for ASDR; $R = 0.233$, $P < .001$ for DALY rates). We observed that regions with higher SDI levels demonstrated a less pronounced increase in the burden of IS due to elevated BMI. This finding is illustrated in Figure S4, Supplemental Digital Content, <http://links.lww.com/MD/N830>.

In 2019, nationally, the data did not show a clear association between SDI and both ASDR and age-standardized DALYs rates for IS related to high BMI, nor their respective EAPC values ($R = 0.123$, $P = .1$ for ASDR; $R = 0.101$, $P = .18$ for DALY rates). This implies that the burden of disease from high BMI-related IS does not significantly vary with socioeconomic development, as illustrated in Figure S2, Supplemental Digital Content, <http://links.lww.com/MD/N830> and Figure S5, Supplemental Digital

Content, <http://links.lww.com/MD/N830>. However, there was a slight increase in this burden corresponding to socioeconomic progress up to an SDI threshold of approximately 0.7. Beyond this threshold, the burden decreased with further increments in SDI.

4. Discussion

This study represents the first comprehensive and systematic review of the disease burden of IS associated with high BMI based on the GBD 2019 study. It examines the global burden of IS across different levels of SDI, geographical regions, and demographic groups, covering the period from 1990 to 2019. While the total number of IS-related deaths linked to high BMI has increased worldwide, from around 207,194 in 1990 to 371,236 in 2019, there has been a consistent decline in ASDR and age-standardized DALY rates. This paradox suggests that the increase in the number of deaths is mainly due to population growth and aging, rather than an increased individual risk. This trend is consistent with the overall burden of cardiovascular diseases.

Globally and regionally, developing areas such as Southeast Asia show a significant rise in noncommunicable diseases linked to high BMI. This reveals major differences in health outcomes and resource access, indicating weak healthcare infrastructure and ineffective public health policies. In Eastern Europe, the rates of years of life lost, measured by ASDR and DALY, have increased, particularly in countries like North Macedonia. This emphasizes regional disparities in dietary habits, lifestyle changes, and how effectively healthcare systems address high BMI. These variations highlight unequal access to healthcare and differences in healthcare facility quality in developing countries, contributing to a poorer prognosis for patients with IS related to high BMI. Forecasts indicate a higher future burden of stroke in Eastern European nations compared to more developed European Union counterparts. Consequently, addressing the issue of premature deaths due to IS linked to high BMI in regions with low SDI requires reinforcing prevention strategies and providing feasible, effective, and affordable clinical management for at-risk populations.^[3,16–18]

The gender-specific analysis reveals that high BMI-related health issues have a greater impact on males compared to females, leading to a more substantial disease burden in males. This disparity aligns with previous studies indicating that men are more frequently affected by risk factors for high BMI and that conditions such as chronic inflammatory vascular diseases, like atherosclerosis, are more prevalent in men, thereby increasing the risk of IS.^[19] Several factors contribute to sex differences

in IS related to high BMI, including hormonal influences on fat deposition, body weight perceptions affecting weight management behaviors,^[20,21] and attitudes toward weight control.^[22] Biological, cultural, and socioeconomic factors may also play a role. Notably, in countries with lower SDI, the burden appears to be greater among females, potentially due to cultural perceptions associating larger body size with beauty and affluence, which may promote overweight and obesity.^[23] Moreover, in less developed nations, women often encounter greater inactivity and face significant cultural and socioeconomic barriers.^[24] Research indicates a clear social gradient in overweight and obesity rates among boys and girls from low socioeconomic backgrounds. Over time, obesity prevalence among children and adolescents from low socioeconomic families has been steadily increasing. This trend is not observed in children from middle to high socioeconomic families.^[25] Therefore, targeted interventions for both genders, considering their unique socioeconomic contexts, are essential. Age-specific analysis confirms that the highest disease burden is observed in the 65 to 69 age group, reflecting the cumulative effect of high BMI over an individual's lifespan. This heightened risk of IS in the elderly aligns with the patterns reported in demographic studies.

When examining the disease burden across different levels of SDI, it becomes apparent that regions with higher SDI levels show a smaller increase, and sometimes even a decline, in the burden of illness related to high BMI. This suggests that a higher socioeconomic status has a positive impact on health outcomes. However, the lack of a strong correlation between SDI and disease burden on a national scale in 2019 indicates that socioeconomic development alone cannot fully explain the variations in health outcomes. The observed trend, where the burden initially increases with socioeconomic development up to a certain threshold before decreasing, suggests that economic growth has a dual influence on health behaviors and healthcare systems^[26] (PMID: 34380492). This emphasizes the need for health policies that are tailored to the socioeconomic trajectories of specific regions.

Our study focuses on estimating the geographical and socioeconomic distribution pattern of the burden of IS related to high BMI, using comprehensive indicators such as deaths and DALYs. We conducted a thorough assessment across age, sex, and region in 204 countries from 1990 to 2019. In addition, we analyzed the impact of socioeconomic status using the SDI. Despite the extensive and systematic nature of our approach, it is important to acknowledge the limitations of this retrospective summary of the global burden of IS due to high BMI. One limitation is the potential underreporting or misclassification of data from less developed regions, which can degrade data quality, especially in countries lacking robust epidemiological studies linking IS to high BMI. Another limitation is that population data often fails to capture the interactions between risk factors and lacks control for confounding variables, which may restrict the alignment of our results with the actual situation. Furthermore, the calculation of DALYs using Bayesian meta-regression, based on population-based studies, may introduce bias. Additionally, our use of a BMI cutoff of $>25 \text{ kg/m}^2$, may not be applicable to all populations, as some research suggests varying BMI cutoffs.^[27-29] Furthermore, it is important to note that BMI does not account for gender-related differences in body composition. However, despite these limitations, our study makes use of the latest information available and contributes to a more comprehensive understanding of the trends in IS attributed to high BMI.

5. Conclusion

This study uncovered a consistent global decline of IS related to high BMI, with a higher burden observed in males below the age of 65. Nonetheless, gender disparities and disease burden differ across socioeconomic statuses, hence targeted

preventive strategies should be implemented within specific socioeconomic contexts. Implementing effective nationwide strategies to address high BMI can help reduce the prevalence of related diseases. Due to the varying impacts of high BMI-related diseases across different countries, it is important to develop and implement tailored prevention strategies based on each country's development status. For instance, digital health interventions for weight management, a balanced diet, and a healthy lifestyle can significantly reduce the risk of IS related to high BMI. Community-based interventions aim to modify the living conditions of socially and economically disadvantaged individuals, demonstrating greater effectiveness and sustainability. This study highlights the critical role of intensive dietary and lifestyle interventions, along with effective weight management, in reducing the risk of ischemic stroke associated with high BMI.

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References

- [1] Saceleanu VM, Toader C, Ples H, et al. Integrative approaches in acute ischemic stroke: from symptom recognition to future innovations. *Biomedicines*. 2023;11:2617.
- [2] Juli C, Heryaman H, Arnengsih, et al. The number of risk factors increases the recurrence events in ischemic stroke. *Eur J Med Res*. 2022;27:138.
- [3] Phipps MS, Cronin CA. Management of acute ischemic stroke. *BMJ (Clinical research ed)*. 2020;368:l6983.
- [4] Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: a report from the American Heart Association. *Circulation*. 2019;139:e56–e528.
- [5] Massie DC, Amaro A, Kaplan M. Patient well-being and the clinical and economic burdens associated with obesity in the United States. *Am J Manag Care*. 2022;28(15 Suppl):S279–87.
- [6] Wang W, Hu M, Liu H, et al. Global Burden of Disease Study 2019 suggests that metabolic risk factors are the leading drivers of the burden of ischemic heart disease. *Cell Metab*. 2021;33:1943–56.e2.
- [7] Song Y, Long Y, Long L, Zhang N, Liu Y. Polymorphism Ala54Thr of fatty acid-binding protein 2 gene is not associated with stroke risk in Han population of Hunan China. *Med Sci Monitor*. 2014;20:1751–7.
- [8] Tzoulaki I, Elliott P, Kontis V, Ezzati M. Worldwide exposures to cardiovascular risk factors and associated health effects: current knowledge and data gaps. *Circulation*. 2016;133:2314–33.
- [9] Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol*. 2021;20:795–820.
- [10] Kontis V, Mathers CD, Bonita R, et al. Regional contributions of six preventable risk factors to achieving the 25 × 25 non-communicable disease mortality reduction target: a modelling study. *Lancet Global Health*. 2015;3:e746–57.
- [11] Yawoot N, Govitrapong P, Tocharus C, Tocharus J. Ischemic stroke, obesity, and the anti-inflammatory role of melatonin. *BioFactors (Oxford, England)*. 2021;47:41–58.
- [12] Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet (London, England)*. 2018;392:1923–94.
- [13] Liu Q, He H, Yang J, Feng X, Zhao F, Lyu J. Changes in the global burden of depression from 1990 to 2017: findings from the global burden of disease study. *J Psychiatr Res*. 2020;126:134–40.

- [14] Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* (London, England). 2017;390:1260–344.
- [15] Li XY, Lv JJ, Zhao Y, et al. Global burden of stroke attributable to low physical activity/high body mass index among people aged 55 Years and Older. *Stroke*. 2024;55:2075–85.
- [16] Schröders J, Wall S, Hakimi M, et al. How is Indonesia coping with its epidemic of chronic noncommunicable diseases? A systematic review with meta-analysis. *PLoS One*. 2017;12:e0179186.
- [17] Stefler D, Brett D, Sarkadi-Nagy E, et al. Traditional Eastern European diet and mortality: prospective evidence from the HAPIEE study. *Eur J Nutr*. 2021;60:1091–100.
- [18] Wafa HA, Wolfe CDA, Emmett E, Roth GA, Johnson CO, Wang Y. Burden of stroke in Europe: thirty-year projections of incidence, prevalence, deaths, and disability-adjusted life years. *Stroke*. 2020;51:2418–27.
- [19] Libby P, Loscalzo J, Ridker PM, et al. Inflammation, immunity, and infection in atherosclerosis: JACC review topic of the week. *J Am Coll Cardiol*. 2018;72:2071–81.
- [20] Elmaleh-Sachs A, Schwartz JL, Bramante CT, Nicklas JM, Gudzone KA, Jay M. Obesity management in adults: a review. *JAMA*. 2023;330:2000–15.
- [21] van Baak MA, Mariman ECM. Obesity-induced and weight-loss-induced physiological factors affecting weight regain. *Nat Rev Endocrinol*. 2023;19:655–70.
- [22] Allnut AE, Smith DJ, Torrence WA, Alexander DS. Examining weight bias attitudes and obesity beliefs among undergraduate students. *J Am College Health*. 2024;72:1814–9.
- [23] Ajayi IO, Adebamowo C, Adami HO, et al. Urban-rural and geographic differences in overweight and obesity in four sub-Saharan African adult populations: a multi-country cross-sectional study. *BMC Public Health*. 2016;16:1126.
- [24] Shapira N. Women's higher health risks in the obesogenic environment: a gender nutrition approach to metabolic dimorphism with predictive, preventive, and personalised medicine. *EPMA J*. 2013;4:1.
- [25] Hoebel J, Waldhauer J, Blume M, Schienkiewitz A. Socioeconomic status, overweight, and obesity in childhood and adolescence—secular trends from the nationwide German Kiggs Study. *Deutsches Arzteblatt Int*. 2022;119:839–45.
- [26] Xu J, Zhao M, Vrosgou A, et al. Barriers to medication adherence in a rural-urban dual economy: a multi-stakeholder qualitative study. *BMC Health Serv Res*. 2021;21:799.
- [27] Midha T, Krishna V, Nath B, et al. Cut-off of body mass index and waist circumference to predict hypertension in Indian adults. *World J Clin Cases*. 2014;2:272–8.
- [28] Wu M, Li C, Yu Y, et al. Association between the triglyceride-glucose (TyG) index and stroke risk in Chinese normal-weight adults: a population-based study. *Diabetol Metab Syndr*. 2024;16:176.
- [29] Di Vincenzo O, Luisi MLE, Alicante P, et al. The assessment of the risk of malnutrition (undernutrition) in stroke patients. *Nutrients*. 2023;15:683.