

# The Global Burden of Ischemic Stroke

## Findings of the GBD 2010 Study

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### ABSTRACT

This study sought to summarize the findings of the GBD 2010 (Global Burden of Diseases, Injuries, and Risk Factors) study for ischemic stroke (IS) and to report the impact of tobacco smoking on IS burden in specific countries. The GBD 2010 searched multiple databases to identify relevant studies published between 1990 and 2010. The GBD 2010 analytical tools were used to calculate region-specific IS incidence, mortality, mortality-to-incidence ratio, and disability-adjusted life years (DALY) lost, including 95% uncertainty intervals (UI). In 2010, there were approximately 11,569,000 incident IS events (63% in low- and middle-income countries [LMIC]), approximately 2,835,000 deaths from IS (57% in LMIC), and approximately 39,389,000 DALY lost due to IS (64% in LMIC). From 1990 to 2010, there was a significant increase in global IS burden in terms of absolute number of people with incident IS (37% increase), deaths from IS (21% increase), and DALY lost due to IS (18% increase). Age-standardized IS incidence, DALY lost, mortality, and mortality-to-incidence ratios in high-income countries declined by about 13% (95% UI: 6% to 18%), 34% (95% UI: 16% to 36%), and 37% (95% UI: 19% to 39%), 21% (95% UI: 10% to 27%), respectively. However, in LMIC there was a modest 6% increase in the age-standardized incidence of IS (95% UI: -7% to 18%) despite modest reductions in mortality rates, DALY lost, and mortality-to-incidence ratios. There was considerable variability among country-specific estimates within broad GBD regions. China, Russia, and India were ranked highest in both 1990 and 2010 for IS deaths attributable to tobacco consumption. Although age-standardized IS mortality rates have declined over the last 2 decades, the absolute global burden of IS is increasing, with the bulk of DALY lost in LMIC. Tobacco consumption is an important modifiable risk factor for IS, and in both 1990 and 2010, the top ranked countries for IS deaths that could be attributed to tobacco consumption were China, Russia, and India. Tobacco control policies that target both smoking initiation and smoking cessation can play an important role in the prevention of IS. In China, Russia, and India, even modest reductions in the number of current smokers could see millions of lives saved due to prevention of IS alone.

Evaluating stroke burden by its major pathological subtypes and studying secular trends of stroke subtypes in different regions of the world is important for targeted region- and country-specific stroke prevention and healthcare planning. Ischemic stroke (IS) is the most common subtype worldwide, but there has been little information on the global and regional IS incidence, mortality, disability-adjusted life-years (DALY) lost in high-income countries (HIC) versus in low- and middle-income countries (LMIC). The GBD 2010 (Global Burden of Diseases, Injuries, and Risk Factors) study ranked stroke as the second most common cause of death [1] and the third leading cause of disability in 2010 [2]. The aim of this report is to summarize the key findings of the GBD 2010 study for IS incidence, mortality, mortality-to-incidence (MI) ratio, and DALY lost

for IS in 1990 and 2010. Prior GBD 2010 study publications have presented IS estimates by country, age group, and country income category (HIC vs. LMIC) [3]. This report will review region-specific data on incidence, mortality, and DALY lost for IS for the 21 GBD regions. The burden of IS attributable to tobacco, one of the leading preventable risk factors [4] associated with IS was also investigated.

### METHODS

A systematic review was conducted to identify suitable IS and total stroke epidemiological studies for inclusion in the GBD 2010 study. The literature search strategy, selection criteria, and full details of the methodology are reported elsewhere [5,6]. Pathological types of stroke were analyzed only for studies that had computed tomography or

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The sponsor of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The Writing and GBD Global Analysis Group had access to all data sources and has responsibility for the content of the report and the decision to submit for publication.

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, Department of Health and Human Services, or any other government entity.

This work was undertaken as a part of the Global Burden of Diseases, Injuries, and Risk Factors 2010 study. The results in this paper are prepared independently of the final estimates of the Global Burden of Diseases, Injuries, and Risk Factors study.

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magnetic resonance imaging of the head, or brain autopsy findings available for  $\geq 70\%$  of stroke cases. Only first-ever-in-a-lifetime IS events were analyzed in this report. Briefly, the GBD 2010 study analytical tool, DisMod-MR, a Bayesian mixed-effects negative binomial meta-regression model, was applied to calculate region- and country-specific estimates (including 95% uncertainty intervals [UI]) of IS incidence rates per 100,000 person-years [7]. The cause-of-death model used ensemble models to estimate region- and country-level IS mortality rates per 100,000 person-years [8,9]. Years lived with disability due to nonfatal IS and years of life lost due to IS were summed to equal the summary measure of disease burden, DALY lost. IS deaths and DALY lost per 100,000 people by age group ( $<75$  years,  $\geq 75$  years, total) and country income level (HIC and LMIC) are reported for 1990, 2005, and 2010. Incidence and mortality rates per 100,000 person-years and DALY estimates per 100,000 people were age-standardized using the direct method with World Health Organization (WHO) standard population as a reference population. Box and whisker plots were used to display the measure of spread (or dispersion) of the computed incidence, mortality, and DALY estimates by country within region. The bottom and top of the box are the first and third quartiles of the metric for countries within that region, and the band inside the box is the median value of the particular metric for country-specific estimates within that region. The ends of the whiskers represent the minimum and maximum values of the metric for countries within a particular region.

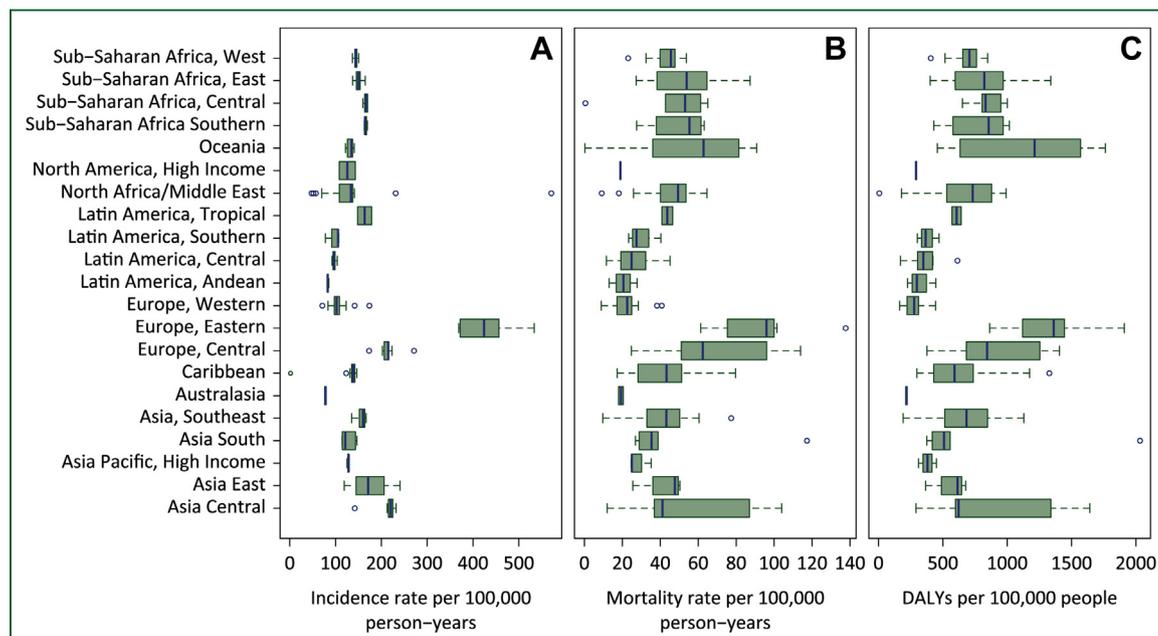
The MI ratio for each region/country is used as an indicator disease severity as well as the success or failure of stroke clinical management strategies in a particular region/country (MI ratio numbers were based on the total number of incident cases and deaths) were also calculated. The main GBD 2010 study results on HIC versus LMIC and age  $<75$  years versus age  $\geq 75$  years have been published in detail elsewhere and shall only be summarized here [3]. For IS deaths attributable to tobacco, the estimates were based on the GBD 2010 study generic approach to assess burden due to risk factors. In brief, the GBD 2010 study used the fraction of the population in each country, age, sex, and year exposed to the risk factor using all available published and unpublished data. These estimates, together with strength of association between risk factor exposure and IS (i.e., relative risks) and estimates of cause-specific deaths and DALY from the GBD 2010 study were used to calculate the burden attributable to each risk factor exposure compared with the theoretical-minimum-risk exposure (population-attributable fraction analysis). Uncertainty was incorporated into the estimates of disease burden, relative risks, and exposures by drawing 1,000 times from the posterior distributions of these parameters. This was done for mortality and disability parameters separately from attributable burden and for risk factor evaluation [10].

## RESULTS

The GBD 2010 study literature search identified 119 stroke studies that met the inclusion criteria for the systematic review, and these were included in the subsequent analyses. The GBD 2010 study estimated that in 2010 there were about 11,569,000 incident IS events (7,316,000 [63%] in LMIC), about 2,835,000 deaths from IS (1,625,000 [57%] in LMIC), and that the total number of DALY lost due to IS were about 39,389,000 (25,137,000 [64%] in LMIC). The GBD 2010 study estimated that in 2010, total age-standardized incidence rates (per 100,000 person-years) of IS ranged from 51.88 (Qatar; 95% UI: 36.92 to 70.28) to 433.97 (Lithuania; 95% UI: 369.12 to 505.59). Age-standardized mortality rates (per 100,000 person-years) of IS ranged from 9.17 (Qatar; 95% UI: 7.71 to 10.60) to 137.70 (Russia; 95% UI: 108.71 to 150.90), and for DALY lost from 163.89 (Israel; 95% UI: 132.32 to 207.45) to 2,032.11 (Afghanistan; 95% UI: 1,576.6 to 2,886.65).

In the first decade of the 21st century, the highest incidence rates of IS were seen in Eastern Europe, Central Asia, East Asia, and North Africa/Middle East (Fig. 1A). There was a considerable amount of heterogeneity among countries within GBD regions for age-standardized IS incidence rates, mortality rates, and DALY lost in 2010. The largest variation in incidence rates was seen in East Asia (lower quartile [Q1]: 144.75, upper quartile [Q3]: 205.95), whereas the smallest variation was seen in Australasia (Q1: 76.27, Q3: 79.45) (Fig. 1A). In 2010, the lowest IS incidence rate was seen in Australasia and the highest was in Eastern Europe (Fig. 1A). Considering mortality rates, the largest variation was seen in Central Asia (Q1: 36.88, Q3: 86.97) (Fig. 1B), whereas the smallest variation was seen in South Asia (Q1: 28.94, Q3: 38.83). In 2010, the lowest mortality rates for IS were observed in High Income North America and the highest mortality rates for IS were observed in Eastern Europe (Fig. 1B). Finally for DALY, in 2010, the largest variation was seen in Oceania (Q1: 633.65, Q3: 1569.27) and the smallest in North America High Income (Q1: 287.30, Q3: 295.76) (Fig. 1C). In 2010, the lowest DALY lost were in Australasia and North America and the highest DALY lost were in Eastern Europe.

Table 1 presents the median and interquartile ranges (IQR) for age-standardized incidence, mortality per 100,000 person-years and DALY lost per 100,000 people for IS by countries within each of the 21 GBD regions between 1990 and 2010. These results show that in general incidence, mortality and DALY lost have decreased in high-income regions (e.g., Western Europe) but were very variable in low- and middle-income regions (e.g., increased incidence, but decreased mortality and DALY lost in Sub-Saharan Africa). Specifically, for countries in Western Europe, the median age-standardized incidence rate (IQR), median age-standardized mortality rate (IQR), and median DALY lost (IQR) in 1990 was 127.65 (13.31), 39.10 (16.37), and 516.51 (194.33), respectively. In 2010, these



**FIGURE 1. Box and whisker plots of (A) age-standardized ischemic stroke incidence rates per 100,000 person-years; (B) age-standardized ischemic stroke mortality rates per 100,000 person-years; and (C) age-standardized DALY lost per 100,000 people by each of the 21 GBD regions in 2010.** The bottom and top of the box are the first and third quartiles, and the band inside the box is the median. The ends of the whiskers represent the minimum and maximum of the metric of interest for a particular region. Outliers are displayed as an open circle. DALY, disability-adjusted life years; GBD, Global Burden of Diseases, Injuries, and Risk Factors study.

were reduced to 102.39 (11.16), 22.61 (7.74), and 276.95 (89.36), respectively. Conversely, in Sub-Saharan Africa, Central during the same period, the estimates in 1990 were 136.36 (6.63), 57.85 (12.96), and 964.04 (144.73), respectively, and in 2010, they were 166.69 (6.26), 53.07 (18.51), and 831.72 (145.72), respectively.

One of the key findings of the GBD 2010 study was that in HIC, age-standardized IS incidence rates, mortality rates, DALY, and MI ratios were statistically significantly reduced by 13% (95% UI: 6% to 18%), 37% (95% UI: 19% to 39%), 34% (95% UI: 16% to 36%), and 21% (95% UI: 10% to 27%), respectively, between 1990 and 2010. These reductions were statistically significant for both younger (<75 years) and older ( $\geq$ 75 years) age groups. In LMIC, there was a statistically nonsignificant 6% increase (95% UI: -7% to 18%) in age-standardized IS incidence. In addition, mortality rates, DALY lost, and MI ratios for IS were reduced by 14% (95% UI: 9% to 19%), 17% (95% UI: -11% to 19%), and 16% (95% UI: -12% to 22%), although these reductions were not statistically significant. The GBD 2010 study also estimated that globally, the mean age of patients with incident and fatal IS was about 5 years older in HIC than in LMIC, and this differential remained constant between 1990 and 2010 [3].

Figures 2A and 2B show the countries with the largest absolute number of deaths from IS due to tobacco consumption. In 1990, the countries with the highest number

of IS deaths due to tobacco were China, Russia, India, the United States, and Japan. Of all the deaths attributed to tobacco consumption in 187 countries included in the GBD 2010 study in 1990, China accounted for 26.2%, Russia for 9.9%, India for 7.3%, the United States for 5.2%, and Japan for 4.2%. Two decades later, the countries with the most IS deaths attributable to tobacco were China (29.2%), Russia (11.7%), India (10.6%), and Indonesia (4.9%). IS deaths attributable to tobacco consumption in China, Russia, and India together in 2010 were more than the IS deaths attributable to tobacco consumption in all of the other 184 countries included in the GBD 2010 study combined. Worryingly, the estimated IS deaths attributable to tobacco consumption in China, Russia, and India had increased in the 20-year period. Even though the United States and Japan had improved between 1990 and 2010, they were still ranked sixth and fifth in 2010, with 2.6% and 3.4% of all IS deaths attributable to tobacco consumption.

## DISCUSSION

A key finding of the GBD 2010 study was that in the last 2 decades, the most striking increases in age-standardized IS incidence rates were observed in LMIC, especially in Eastern Europe, Central and East Asia, North and Sub-Saharan Africa/Middle East. There was a marked decrease

**TABLE 1.** Age-standardized incidence, mortality, and DALY rates, median (IQR), by 21 GBD regions

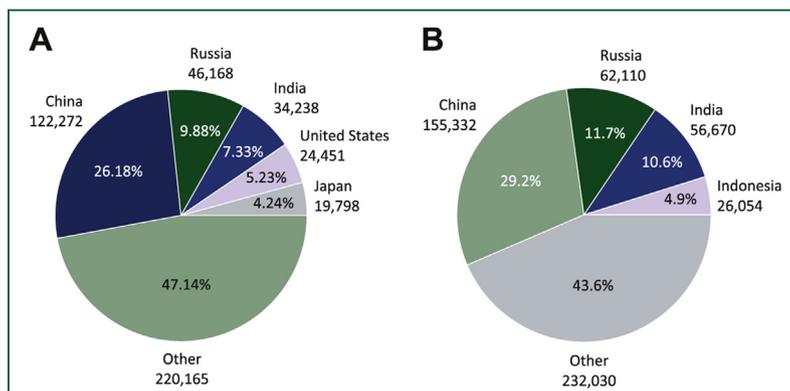
GBD region	Median (IQR) Incidence, Mortality and DALY Rates by 21 GBD Regions Between 1990 and 2010								
	1990			2005			2010		
	Incidence	Mortality	DALY	Incidence	Mortality	DALY	Incidence	Mortality	DALY
Asia Pacific, High Income	176.15 (11.88)	42.74 (12.70)	618.61 (158.97)	129.04 (5.67)	27.21 (12.78)	395.36 (135.79)	128.65 (4.21)	25.03 (10.59)	380.49 (138.35)
Asia Central	199.93 (6.12)	46.28 (45.36)	710.85 (591.53)	221.61 (9.34)	43.07 (73.67)	657.63 (836.61)	220.44 (9.51)	41.17 (50.09)	622.35 (741.69)
Asia, Southeast	137.82 (9.13)	46.30 (17.49)	766.77 (388.40)	154.73 (11.86)	42.24 (23.17)	760.08 (324.70)	159.90 (11.98)	43.22 (17.30)	683.79 (332.30)
Asia East	173.08 (33.60)	53.95 (47.29)	737.79 (628.77)	172.11 (62.60)	49.72 (15.93)	209.23 (542.80)	171.02 (61.17)	47.68 (13.38)	613.74 (156.91)
Asia South	104.69 (20.88)	32.81 (7.88)	484.76 (121.31)	113.58 (28.11)	36.95 (10.52)	533.15 (158.80)	121.22 (28.80)	35.43 (9.89)	508.73 (139.28)
Australasia	99.90 (3.58)	36.37 (5.36)	417.27 (31.43)	77.46 (3.15)	21.51 (1.38)	241.31 (3.77)	77.86 (3.18)	19.27 (2.48)	216.91 (10.74)
Caribbean	143.43 (6.24)	54.55 (25.92)	799.28 (433.03)	137.81 (8.42)	46.86 (28.18)	599.43 (375.45)	138.77 (8.57)	43.31 (27.56)	590.41 (364.05)
Europe, Central	224.83 (23.75)	109.95 (36.06)	1386.39 (484.82)	212.72 (12.41)	71.61 (50.09)	948.71 (660.85)	215.06 (10.01)	62.38 (44.99)	843.17 (570.74)
Europe, Eastern	374.97 (119.63)	123.71 (66.49)	1732.03 (536.98)	418.90 (114.59)	92.14 (53.87)	1643.70 (641.92)	424.19 (107.82)	95.98 (35.82)	1361.22 (542.26)
Europe, Western	127.65 (13.31)	39.10 (16.37)	516.51 (194.33)	101.68 (9.70)	25.81 (10.29)	319.53 (106.92)	102.39 (11.16)	22.61 (7.74)	276.95 (89.36)
Latin America, Andean	88.35 (3.47)	39.10 (22.25)	576.26 (329.63)	82.14 (2.62)	21.78 (15.49)	252.59 (312.92)	82.79 (3.61)	20.59 (14.77)	297.96 (220.07)
Latin America, Central	96.85 (3.64)	34.71 (18.45)	514.70 (221.23)	94.61 (2.77)	24.87 (10.56)	346.90 (93.16)	96.53 (4.41)	24.89 (13.08)	348.51 (116.05)
Latin America, Southern	143.59 (35.61)	54.49 (4.86)	657.01 (117.30)	106.06 (27.91)	29.91 (16.52)	402.49 (178.22)	105.54 (29.27)	27.48 (16.98)	366.44 (168.35)
Latin America, Tropical	170.47 (38.44)	57.43 (7.67)	835.83 (147.91)	161.32 (32.26)	44.37 (2.37)	621.82 (16.94)	163.40 (30.66)	43.73 (5.65)	606.31 (71.63)
North Africa/Middle East	114.43 (42.78)	59.43 (21.05)	909.18 (292.47)	131.29 (45.43)	52.36 (14.69)	750.95 (274.24)	133.55 (50.24)	49.34 (14.74)	731.38 (410.88)
North America, High Income	153.33 (40.56)	32.09 (1.79)	405.72 (1.72)	126.50 (33.38)	20.74 (0.75)	311.67 (18.72)	125.64 (34.94)	18.99 (0.15)	291.53 (8.46)
Oceania	164.67 (10.26)	83.11 (47.78)	1579.40 (456.11)	136.67 (13.16)	71.98 (43.39)	1381.83 (896.73)	134.71 (11.37)	62.81 (45.33)	1212.80 (935.62)
Sub-Saharan Africa, Central	136.36 (6.63)	57.85 (12.96)	964.04 (144.73)	153.81 (8.82)	52.96 (6.92)	820.33 (124.45)	166.69 (6.26)	53.07 (18.51)	831.72 (145.72)
Sub-Saharan Africa, East	131.44 (5.11)	61.17 (33.58)	919.26 (560.21)	142.11 (10.66)	49.70 (31.17)	796.69 (402.22)	149.77 (11.26)	53.87 (28.73)	821.87 (405.22)
Sub-Saharan Africa, Southern	150.42 (7.82)	57.20 (12.92)	888.74 (249.14)	159.25 (6.54)	54.71 (26.17)	905.70 (442.42)	164.23 (3.93)	55.38 (23.51)	855.45 (390.10)
Sub-Saharan Africa, West	125.24 (3.29)	45.10 (9.64)	748.54 (161.53)	137.99 (2.95)	41.89 (11.40)	672.43 (157.46)	143.86 (5.48)	45.58 (8.45)	706.46 (121.20)

in age-standardized IS incidence rates in North America as well as some other high-income regions. Compared with 1990, in 2010, MI ratios for IS were markedly reduced in Western Europe, Australasia, Central and Andean Latin America, but increased in North Africa/Middle East and Southeast Asia. Age-specific incidence rates of IS increased with age significantly in all GBD regions. Age-specific incidence, mortality rates, MI ratios, and DALY in LMIC for IS were overall greater than those in HIC [3]. It is quite likely that general improvements in primary and secondary prevention strategies for IS in HIC are driving these incidence and mortality improvements [11]; however, this needs confirmation in nonecological studies.

In this report, we presented new information by the 21 GBD regions and showed that there was considerable heterogeneity among countries within regions. Tobacco consumption is an extremely important preventable risk factor for IS. A recent report by Peters et al. [4] found that risk for IS was 54% higher (95% UI: 1.21 to 1.96) in female current smokers and 53% higher in male current smokers (95% UI: 1.28 to 1.82) than in men and women that did not smoke. We noted that China, Russia, India, the United States, and Japan were the top ranked countries for IS deaths attributable to tobacco consumption in 1990. However, 2 decades later, the United States and Japan have improved, whereas China, Russia, and India are still in the top ranked countries for IS deaths attributable to tobacco. The benefits of quitting smoking have been clearly demonstrated in large-scale long-term epidemiological studies of men [12] and women [13]. In recent decades, there have been significant reductions in smoking in HIC (such as the United States) due to political interventions (such as smoke-free policies [14], higher taxes, and/or higher prices) [15], smoking cessation programs [16], and clinical guidelines [17]. Several of these approaches have been implemented in HIC at the start of the 21st century and could also be used in LMIC settings [18]. The WHO Framework Convention on Tobacco Control (FCTC) has been monitoring smoke-free environments, tobacco taxation levels, and smoking cessation services in countries around the world [19]. In addition, the WHO FCTC monitors antitobacco mass media campaigns; health warnings on tobacco packages; and enforced bans on tobacco advertising, promotion, and sponsorship. The WHO FCTC has been adopted in LMIC but only to a limited extent. For example, the most recent data from 2012 shows that China and Russia have no smoke-free environment policies, but India does. China, Russia, and India have total taxation levels on cigarettes between 35% and 46%, and all have varying levels of support for smoking cessation programs (such as those provided by health clinics or primary care facilities) [19].

## SUMMARY

Although age-standardized mortality rates for IS have decreased in the past 2 decades, the absolute number of



**FIGURE 2. Top ranked countries for ischemic stroke deaths attributed to tobacco consumption in 1990 (A) and 2010 (B).** (A) Top ranked countries for ischemic stroke deaths attributed to tobacco consumption in 1990. Values outside of the pie chart are mean absolute numbers of ischemic stroke deaths attributable to tobacco consumption and numbers inside the pie chart are percentages for the top ranked countries as a percentage of the aggregate of all estimated mean ischemic stroke deaths attributable to tobacco. (B) Top ranked countries for ischemic stroke deaths attributed to tobacco consumption in 2010. Values outside of the pie chart are mean absolute numbers of ischemic stroke deaths attributable to tobacco consumption, and numbers inside the pie chart are percentages for the top ranked countries as a percentage of the aggregate of all estimated mean ischemic stroke deaths attributable to tobacco.

DALY lost is increasing, with most of the burden occurring in LMIC. The primary drivers for this increase include population growth and aging, as well as adverse risk factor trends. Policy and legislative interventions that target the prevention and control of risk factors can play an important role in addressing the growing IS burden in LMIC. Investments in locally acceptable and affordable primary and secondary prevention strategies for IS would be a step in the right direction. For example, tobacco control policies that target both smoking initiation and smoking cessation can play an important role in the prevention of IS particularly in China and India (2 of the world's most populous countries), where even modest reductions in the number of current smokers could prevent millions of deaths. Meaningful implementation of the WHO FCTC is a top priority not only for reducing IS burden but also the burden from other chronic noncommunicable diseases.

## CONTRIBUTIONS

D.A.B. wrote the first draft of the report. All members of the writing committee contributed to the critical revision of the manuscript for important intellectual content.

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