

The Global Burden of Ischaemic Stroke an overview of the findings of The Global Burden of Diseases, Injuries, and Risk Factors (GBD 2010) Study

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ABSTRACT

Background and objectives: To summarize the findings of The Global Burden of Diseases, Injuries, and Risk Factors (GBD 2010) Study for ischaemic stroke (IS) and report the impact of tobacco smoking on IS burden in specific countries.

Methods: 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 (MI) ratio and disability-adjusted life years (DALYs) lost, including 95% uncertainty intervals (UI).

Findings: 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 DALYs lost due to IS (64% in LMIC). From 1990-2010, 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 DALYs lost due to IS (18% increase). Age-standardised IS incidence, DALYs lost, mortality, and MI ratios in HIC declined by about 13% (95% UI 6-18%), 34% (95% UI 16-36%), and 37% (95% UI 19-39%), 21% (95% UI 10-27%), respectively. However, in LMIC there was a modest 6% increase in the age-standardised incidence of IS (95% UI -7%; 18%) despite modest reductions in mortality rates, DALYs lost, and MI 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.

Conclusions: Although age-standardized IS mortality rates have declined over the last two decades, the absolute global burden of IS is increasing, with the bulk of DALYs 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.

Introduction

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 health care planning. Ischemic stroke (IS) is the most common subtype world-wide, but there has been little information on the global and regional IS incidence, mortality, disability-adjusted life-years (DALYs) lost in high-income countries (HIC) compared with low- and middle-income countries (LMIC). The Global Burden of Diseases, Injuries, and Risk Factors (GBD 2010) Study ranked stroke as the second most common cause of death¹ and the third leading cause of disability in 2010². The aim of this report is to summarize the key findings of GBD 2010 study for IS incidence, mortality, mortality to incidence (MI) ratio and DALYs 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 versus LMIC).³ This report will review region-specific data on incidence, mortality and DALYs lost for IS for the 21 GBD regions. The burden of IS attributable to tobacco, one of the leading preventable risk factors⁴ associated with IS was also investigated.

Methods

A systematic review was conducted in order 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 analysed only for studies that had head computed tomography, magnetic-resonance imaging, or brain autopsy findings available for at least 70% of stroke cases. Only first-ever-in-a-lifetime ischaemic stroke events were analysed 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-years⁷. The cause of death model (CODEm) used ensemble models to estimate region- and country-level IS mortality rates per 100,000 person-years^{8 9}. Years lived with disability (YLD) due to nonfatal IS and years of life lost due to IS were summed to equal the summary measure of disease burden,

disability-adjusted life years (DALYs) lost. IS deaths and DALYS lost per 100,000 people by age groups (<75 years; ≥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 WHO standard population as a reference population. Box and whisker plots were used in order 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.

Mortality to incidence (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 vs LMIC and age < 75 versus age ≥75 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 DALYs 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 1000 times from the posterior distributions of these parameters. This was done for mortality and disability parameters separately from attributable burden and also 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 DALYs 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-standardised incidence rates (per 100,000 person-years) of IS ranged from 51.88 (Qatar; 95% UI 36.92-70.28) to 433.97 (Lithuania; 95% UI 369.12-505.59). Age-standardised mortality rates (per 100,000 person-years) of IS ranged from 9.17 (Qatar; 95% UI 7.71-10.60) to 137.70 (Russia; 95% UI 108.71-150.90), and for DALYs lost - from 163.89 (Israel; 95% UI 132.32-207.45) to 2032.11 (Afghanistan; 95% UI 1,576.6-2,886.65).

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 (Figure 1A). There was considerable amount of heterogeneity among countries within GBD regions for age-standardized IS incidence rates, mortality rates, and DALYs lost in 2010. The largest variation in incidence rates was seen in East Asia (Lower quartile [Q1]: 144.75, Upper quartile [Q3]: 205.95), whilst the smallest variation was seen in Australasia [Q1: 76.27, Q3: 79.45](Figure 1A). In 2010 the lowest IS incidence rate was seen in Australasia and the highest was in Eastern Europe (Figure 1A). Considering mortality rates the largest variation was seen in Central Asia [Q1: 36.88, Q3: 86.97](Figure 1B) whilst 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 (Figure 1B). Finally for DALYs, 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] (Figure 1C). In 2010 the lowest DALYs lost were in Australasia and North America and the highest DALYs lost were in Eastern Europe.

FIGURE 1 HERE

Table 1 presents the median and interquartile ranges (IQR) for age-standardized incidence, mortality per 100, 000 person-years and DALYs 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 DALYs 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 DALYs 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 DALYs lost (IQR) in 1990 was 127.65 (13.31), 39.10 (16.37), and 516.51 (194.33) respectively. In 2010 these 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 time period the estimates in 1990 were: 136.36 (6.63), 57.85 (12.96), and 964.04 (144.73) respectively and in 2010 were: 166.69 (6.26), 53.07 (18.51) and 831.72 (145.72) respectively.

TABLE 1 HERE

One of the key findings of the GBD 2010 study was that in HIC, age-standardized IS incidence rates, mortality rates, DALYs, and MI ratios were statistically significantly reduced: by 13% (95% UI 6-18%), 37% (95% UI 19-39%), 34% (95% UI 16-36%) and 21% (95% UI 10-27%), respectively, between 1990 – 2010. These reductions were statistically significant for both younger (<75 years) and older (≥75 years) age groups. In LMIC there was a statistically non-significant 6% increase (95% UI -7%, 18%) in age-standardized IS incidence. In addition mortality rates, DALYs lost and MI ratios for IS were reduced by 14% (95% UI 9%, 19%), 17% (95% UI -11%, 19%) and 16% (95%CI -12%, 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 five years older in HIC compared to 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, 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%, 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 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 USA and Japan had improved between 1990 and 2010 they were still ranked 6th and 5th in 2010 with 2.6% and 3.4% of all IS deaths attributable to tobacco consumption.

FIGURE 2A AND 2B HERE

Discussion

A key finding of the GBD 2010 study was that in the last two 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 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 DALYs 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 improvements¹¹, however this needs confirmation in non-ecological 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 al⁴ found that risk for IS was 54% higher (95% UI: 1.21 – 1.96) in female current smokers and 53% higher in male current smokers (95%

UI: 1.28 – 1.82) compared to men and women that did not smoke. We noted that China, Russia, India, USA, and Japan were the top ranked countries for IS deaths attributable to tobacco consumption in 1990. However, two decades later the USA 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 men¹² and women.¹³ In recent decades there have been significant reductions in smoking in HIC (such as the U.S.A.) due to political interventions (such as smoking free policies¹⁴ higher taxes and/or higher prices)¹⁵, smoking cessation programs¹⁶, and clinical guidelines.¹⁷ Several of these approaches have been implemented in HIC at the start of the 21st century and could also be utilized in LMIC settings.¹⁸ The World Health Organization Framework Convention on Tobacco Control (WHO FCTC) has been monitoring smoke-free environments, tobacco taxation levels, and smoking cessation services in countries around the world (http://www.who.int/tobacco/surveillance/policy/country_profile/en). In addition the WHO FCTC monitors anti-tobacco 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 of between 35% - 46%, and all have varying levels of support for smoking cessation programs [such as those provided by health clinics or primary care facilities] (http://www.who.int/tobacco/surveillance/policy/country_profile/en).

Conclusion

Although age-standardized mortality rates for IS have decreased in the past two decades, the absolute number of DALYs 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 LMICs. 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, (two 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 non-communicable diseases.

Contributions

DAB 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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Conflict of interest

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

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Figure Legends

Figure 1

Box and whisker plots of (A) age-standardized ischaemic stroke incidence rates; (B) age-standardized ischaemic stroke mortality rates; and (C) DALYs lost; by each of the 21 GBD regions. 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.

Figure 2A

Top ranked countries for ischaemic stroke deaths attributed to tobacco consumption in 1990. Values outside of the piechart are mean absolute numbers of ischaemic 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 ischaemic stroke deaths attributable to tobacco.

Figure 2B

Top ranked countries for ischaemic stroke deaths attributed to tobacco consumption in 2010. Values outside of the piechart are mean absolute numbers of ischaemic 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 ischaemic stroke deaths attributable to tobacco.

Table 1: Age-standardized incidence, median (IQR) mortality, and DALY rates by twenty-one GBD regions

GBD region	Median (IQR) Incidence, Mortality and DALY rates by twenty-one GBD region between 1990 and 2010								
	1990			2005			2010		
	Incidence	Mortality	DALYs	Incidence	Mortality	DALYs	Incidence	Mortality	DALYs
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)

Figure 1A: Age-standardized incidence rates per 100,000 person-years by GBD region in 2010

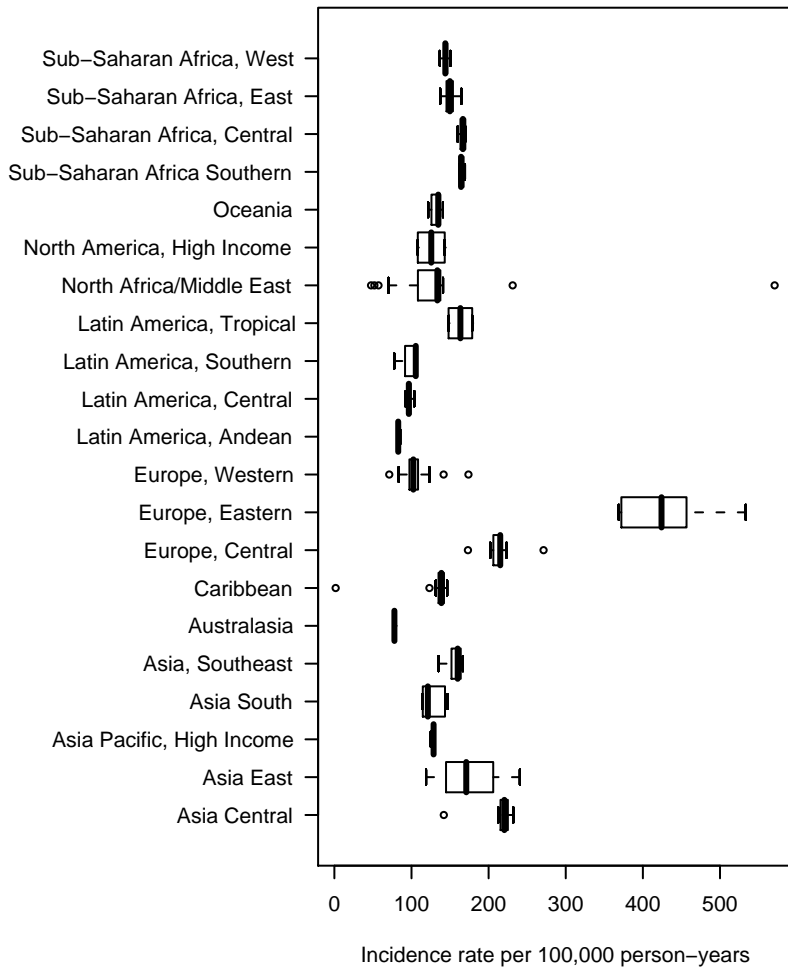


Figure 1B: Age-standardized mortality rates per 100,000 person-years by GBD region in 2010

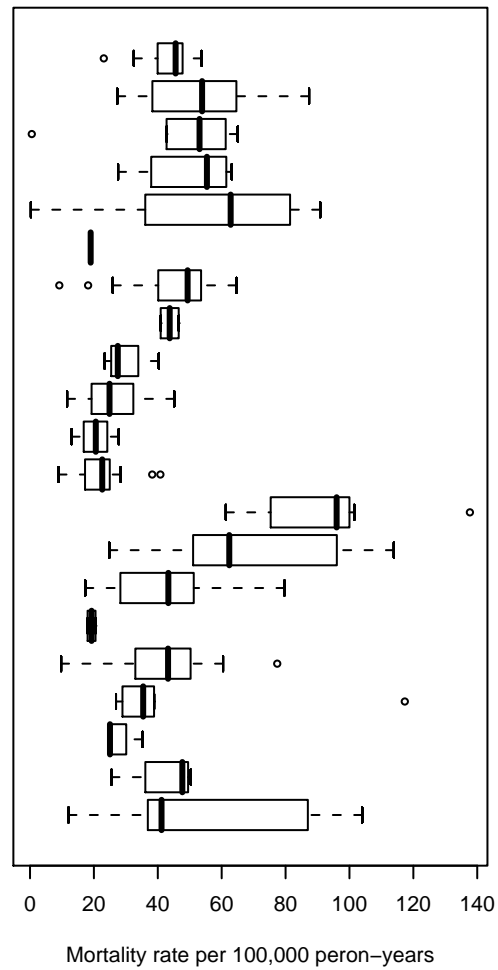


Figure 1C: Age-standardized DALYs per 100,000 people by GBD region in 2010

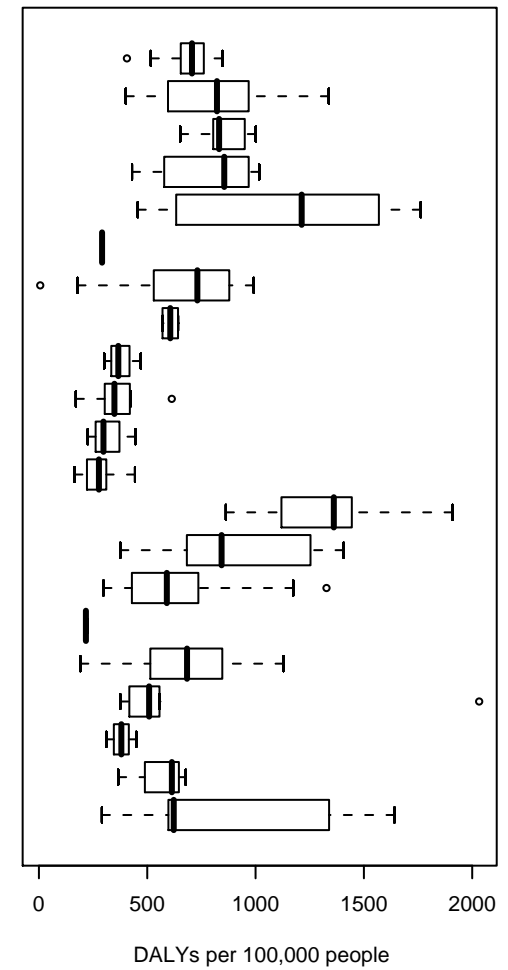


Figure 2A: The top countries for all ischaemic deaths due to tobacco in 1990

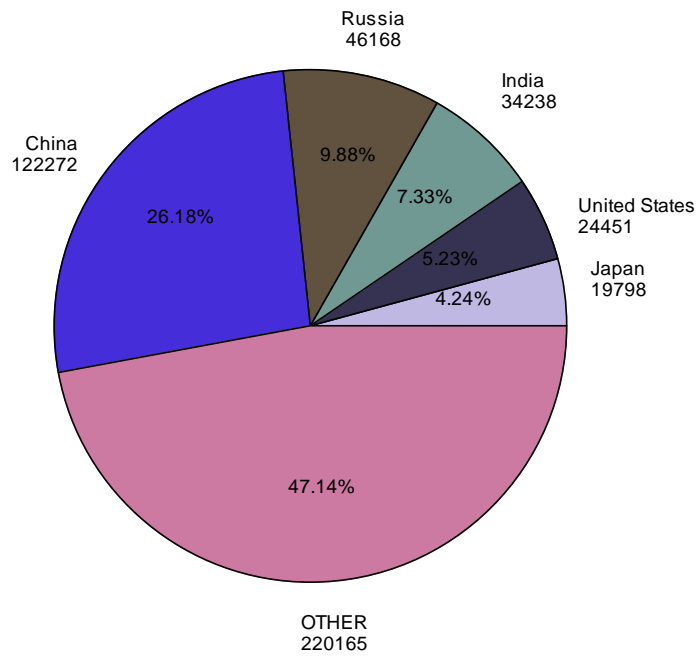


Figure 2B: The top countries for all ischaemic deaths due to tobacco in 2010

