Part I

Foundations

Chapter 1

Stroke: The Size of the Problem

Graeme J. Hankey

The global and regional burden of stroke during 1990–2015 has been estimated by the Global Burden of Disease (GBD) studies of 2010, 2013, and 2015 (Krishnamurthi et al., 2013, 2015; Feigin et al., 2014, 2015; GBD 2015 Neurological Disorders Collaborator Group, 2017).

The GBD 2010 study group undertook a systematic review which identified 119 relevant studies (58 from high-income countries [HIC] and 61 from low- and middle-income countries [LMIC]) that were published between 1990 and 2010 and from which regional and country-specific estimates of the incidence, prevalence, mortality, and disability-adjusted life-years (DALYs) lost by age group (<75 years, ≥75 years, and in total) and country income level of first-ever ischaemic and haemorrhagic stroke in all 21 regions of the world for 1990, 2005, and 2010 could be calculated (Feigin et al., 2014). Pathological subtypes of stroke were confirmed by brain imaging or autopsy in at least 70% of cases.

The GBD estimates of stroke incidence in all regions were therefore obtained using a systematic approach which allows comparison across disease states. Complementary estimates of stroke incidence, based on epidemiological studies of stroke incidence using ideal methods, and also adjusted to the World Health Organization (WHO) world population figures, are provided by Thrift and Kim and colleagues (2020).

Incidence

In 2010, the age-standardized incidence rate of stroke was 258 (234–284) per 100,000 person-years (Feigin et al., 2014) (Table 1.1).

The absolute number of people who experienced a first stroke was 16.9 million in 2010; 68.6% were resident in LMIC and 62% were aged younger than 75 years (Feigin et al., 2014) (Table 1.1). In 2013, there were 10.3 million new strokes (67% ischaemic stroke [IS]) (Feigin et al., 2015).

Ischaemic Stroke

In 2010, the age-standardized incidence of IS was 176 (161–192) per 100,000 person-years (Bennett et al., 2014) (Table 1.1).

In 2010, there were approximately 11,569,000 incident IS events (63% in LMIC) (Bennett et al., 2014).

Haemorrhagic Stroke

In 2010, the overall age-standardized incidence rate of haemorrhagic stroke (HS) (intracerebral and subarachnoid haemorrhage) was 81.52 (95% confidence interval [CI]: 72.27–92.82) per 100,000 person-years globally.

In 2010, there were 5.3 million cases of HS; 80% were in LMIC (Krishnamurthi et al., 2013, 2014).

There were significant regional differences in incidence rates of HS, with the highest rates in LMIC regions such as sub-Saharan Africa and East Asia, and lowest rates in high-income North America and Western Europe.

The overall age-standardized incidence rates of HS per 100,000 person-years were 48.41 (95% CI: 45.44–52.13) in HIC and 99.43 (95% CI: 85.37–116.28) in LMIC. Hence, LMIC had a 40% higher incidence of HS than did HIC.

Trends in Stroke Incidence Rates

From 1990 to 2010, the age-standardized incidence of stroke per 100,000 person-years remained fairly stable, being 251 (95% CI: 230–273) in 1990 and 258 (95% CI: 234–284) in 2010 (Feigin et al., 2014) (Table 1.1).

However, from 1990 to 2010, the absolute number of people with a first stroke increased significantly by 68%, from 10 million to 16.9 million.

From 1990 to 2010, the age-standardized incidence of stroke per 100,000 person-years significantly decreased by 12% (95% CI: 6–17) in HIC, and increased by 12% (95% CI: –3–22) in LMIC, albeit non-significantly.

Table 1.1 Age-adjusted annual incidence and mortality rates (per 100,000 person-years), prevalence (per 100,000 people), and disability-adjusted life-years (DALYs) lost (number, and per 100,000) for all stroke, ischaemic stroke, and haemorrhagic stroke, in 1990, 2005, 2010, and 2015

All Stroke	1990		2005		2010		2015		Change from 1990–2015	
	Number of events	Rate (95% CI) per 100,000	Number of events	Rate (95% CI) per 100,000	Number of events	Rate (95% CI) per 100,000	Number of events	Rate (95% UI) per 100,000	Number of events	Rate (95% UI) per 100,000
Incidence	10,078,935	251 (230–273)	14,734,124	256 (232–284)	16,894,536	258 (234–284)	Not reported	Not reported	68%↑ (to 2010)	12% (6–17%) ↓ HIC (to 2010) 12% (–3–22%) ↑ LMIC (to 2010)
Prevalence	17,915,338	435 (389–497)	28,495,582	490 (437–558)	33,024,958	502 (451–572)	42,431,000 (42.068 m – 42.767 m)	627 (621–631)	59.2% (58–60%) ↑	9.8% (9–10%) ↓
DALYs lost	86,010,384	2063 (1950–2280)	101,951,696	1750 (1569–1831)	102,232,304	1554 (1374–1642)	118,627,000 (114.862 m – 111.627 m)	1777 (1721–1835)	21.7% (18–26%)↑	32.3% (30–34%) ↓
Deaths	4,660,449	117 (112–130)	5,684,970	99 (89–104)	5,874,182	88 (80–94)	6,326,000 (6.175 m – 6.493 m)	101 (99–104)	36.4% (32–41%) ↑	30% (28–32%) ↓

Ischaemic stroke								
Incidence	7,238,758	181 (167–196)	10,097,297	175 (160–192)	11,569,538	176 (161–192)	37% ↑	13% (6–18%) ↓ HIC 6% (–7–18%) ↑ LMIC
DALYs lost	32,128,220	796 (734–906)	38,571,908	668 (617–774)	39,389,408	598 (560–692)	18% ↑	34% (16–36%) ↓ HIC 17% (–11–19%) ↓ LMIC
Mortality	2,241,077	58 (54–64)	2,701,873	47 (44–54)	2,835,419	42 (40–49)	21% ↑	37% (19–39%) ↓ HIC 14% (9–19%) ↓ LMIC
Haemorrhagic stroke								
Incidence	2,840,177	69 (62–77)	4,636,828	80 (71–92)	5,324,997	82 (72–93)	47% ↑	18.5% ↑ globally 8% (1–15%) ↓ HIC 22% (5–30%) ↑ LMIC
DALYs lost	53,882,164	1267 (1068–1484)	63,379,792	1081 (935–1234)	62,842,896	956 (828–1104)	14% ↑	39% (32–44%) ↓ HIC 25% (7–38%) ↓ LMIC
Mortality	2,419,372	60 (51–70)	2,983,097	52 (45–59)	3,038,763	46 (40–53)	20% ↑	38% (32–43%) ↓ HIC 23% (–7–36%) ↓ LMIC

Source: Adapted from Krishnamurthi et al., 2013, 2014; Feigin et al., 2014; Bennett et al., 2014, and GBD 2015 Neurological Disorders Collaborator Group, 2017.
CI: confidence interval. HIC: high-income countries. LMIC: low- and middle-income countries. UI: uncertainty interval.

Ischaemic Stroke

From 1990 to 2010, the age-standardized incidence of IS per 100,000 person-years remained fairly stable, being 181 (95% CI: 167–196) in 1990 and 176 (95% CI: 161–192) in 2010

From 1990 to 2010, there was a significant increase in the absolute number of people with incident IS from 7.2 million to 11.6 million (37% increase).

Age-standardized IS incidence in HIC declined by about 13% (95% uncertainty interval [UI]: 6–18%). However, in LMIC there was a modest 6% increase in the age-standardized incidence of IS (95% UI: –7–18%).

Haemorrhagic Stroke

The age-standardized incidence of HS increased by 18.5% worldwide between 1990 and 2010, from 69 (62–77) to 82 (72–93) per 100,000 person-years.

From 1990 to 2010, there was a 47% increase worldwide in the absolute number of HS cases, from 2.8 million to 5.3 million.

In HIC, there was a reduction in incidence of HS by 8% (95% CI: 1–15%) in the past 2 decades. However, in low-income and middle-income countries there was a significant increase in the incidence of HS by 22% (95% CI: 5-30%), which is one rate that has increased over the past two decades, particularly in people younger than 75 years (19% increase in HS in past two decades, 95%CI: 5–30% increase).

Prevalence

In 2010, the prevalence of stroke survivors was 502 (451–572) per 100,000 people and the absolute number of stroke survivors was 33 million.

In 2015, the prevalence of stroke survivors was 627 (95% UI: 621–631) per 100,000 people and the absolute number of stroke survivors was 42.431 million (95% UI: 42.068–42.767 million) (GBD 2015 Neurological Disorders Collaborator Group, 2017).

Ischaemic Stroke

In 2013, in younger adults aged 20–64 years, the global prevalence of IS was 7.258 million cases (95% UI: 6.996–7.569 million) (Krishnamurthi et al., 2015).

Haemorrhagic Stroke

In 2013, in younger adults aged 20–64 years, the global prevalence of HS was 3.725 million cases (95% UI: 3.548–3.871 million) (Krishnamurthi et al., 2015).

Trends in Prevalence

From 1990 to 2010, the absolute number of stroke survivors increased significantly by 84%, from 18 million to 33 million (Feigin et al., 2014).

Between 1990 and 2015, the absolute number of stroke survivors increased globally by 59.2% (58.4–59.9%), whereas the age-standardized prevalence rate of stroke fell by 9.8% (9.4–10.3% reduction) (GBD 2015 Neurological Disorders Collaborator Group, 2017).

Ischaemic and Haemorrhagic Stroke

Between 1990 and 2013, there were significant increases in absolute numbers and prevalence rates of both HS and IS for younger adults globally (Krishnamurthi et al., 2015).

Mortality

In 2010, the age-standardized mortality rate of stroke was 88 (80–94) per 100,000 person-years, and the absolute number of stroke-related deaths was 5.9 million (Feigin et al., 2014)

In 2015, the age-standardized mortality rate of stroke was 101 (99–104) per 100,000 person-years, and the number of stroke deaths was 6.3 million (95% UI: 6.2–6.5 million) (GBD 2015 Neurological Disorders Collaborator Group, 2017).

The percentage of estimated total global mortality due to stroke in 2013 was 11.3%, which exceeds that of HIV/AIDS, tuberculosis, and malaria combined (7.2%) by more than 50% (GBD 2013 Mortality and Causes of Death Collaborators, 2015).

Ischaemic Stroke

In 2010, the age-standardized mortality rate of IS was 42 (40–49) per 100,000 person-years, and there were approximately 2.835 million deaths from IS (57% in LMIC) (Bennett et al., 2014).

Haemorrhagic Stroke

In 2010, the age-standardized mortality rate of HS was 46 (40–53) per 100,000 person-years, and there were 3.0 million deaths due to HS.

Hence, HS caused more than half (51.7%) of the 5.9 million stroke-related deaths in 2010, despite causing less than one-third of all strokes.

The largest proportion of HS deaths occurred in LMIC countries. Low- and middle-income countries had a 77% higher mortality from HS than did HIC.

The highest mortality rates in 2010 were in low-income Central Asia, Southeast Asia, and sub-Saharan Africa, whereas the lowest mortality rates were in high-income North America, Australasia, and Western Europe.

In 2013, in younger adults aged 20–64 years, the number of deaths from HS (1.047 million [95% UI: 0.945–1.184 million]) was significantly higher than the number of deaths from IS (0.436 million [95% UI: 0.354–0.504 million]) (Krishnamurthi et al., 2015).

Trends in Stroke Mortality Rates

From 1990 to 2010, mortality rates decreased significantly from 117 (112–130) to 88 (80–94) per 100,000. The fall was in both HIC (37%, 31–41) and LMIC (20%, 15–30). However, the absolute number of stroke-related deaths significantly increased by 26%, from 4.7 million to 5.9 million.

Between 1990 and 2015, the absolute number of stroke deaths increased globally by 36.4% (32.4–40.8%), whereas the age-standardized mortality rate of stroke fell by 30% (27.7–32.0% reduction) (GBD 2015 Neurological Disorders Collaborator Group, 2017).

Ischaemic Stroke

From 1990 to 2010, mortality rates due to IS decreased by one-fifth, from 58 (54–64) to 42 (40–49) per 100,000.

However, the absolute number of deaths from IS increased from 2.24 million to 2.84 million (21% increase).

Age-standardized mortality in HIC declined by about 37% (95% UI: 19–39%).

In LMIC, there were modest reductions in mortality rates.

Haemorrhagic Stroke

From 1990 to 2010, mortality rates due to HS decreased from 60 (51–70) to 46 (40–53) per 100,000.

There was a significant reduction in HS mortality by 38% (95% CI: 32–43%) in HIC and by 23% (95% CI: –3–36%) in LMIC .

However, the number of deaths globally from HS increased by 20% from 2.4 million to 3.0 million.

DALYs Lost

In 2010, the rate of DALYs lost due to stroke was 1554 (1374–1643) per 100,000, and the absolute number of DALYs lost was 102 million.

In 2015, the rate of DALYs lost due to stroke was 1777 (1721–1835) per 100,000 and the absolute number of DALYs lost was 118.627 million (114.862–122.627 million) (GBD 2015 Neurological Disorders Collaborator Group, 2017; GBD 2016 DALYs and HALE Collaborators, 2017).

Ischaemic Stroke

In 2010, there were approximately 39.4 million DALYs lost due to IS (64% in LMIC) (Bennett et al., 2014).

Haemorrhagic Stroke

In 2010, there were 62.8 million DALYs lost (86% in LMIC) due to HS.

Consequently, HS caused three-fifths (61.5%) of the 102.2 million DALYs lost due to stroke throughout the world.

Low- and middle-income countries had 65% higher DALY rates of HS than did HIC.

Trends in DALYs Lost

From 1990 to 2010, the age-standardized rate of DALYs lost per 100,000 decreased from 2063 (1950–2280) to 1554 (1374–1642), but the absolute number of DALYs lost increased by 12% from 86 million to 102 million.

Between 1990 and 2015, the age-standardized rate of DALYs lost per 100,000 decreased by 32.3% (30.0–34.4% decrease), but the absolute number of DALYs lost increased by 21.7% (17.8–25.7%) (GBD 2015 Neurological Disorders Collaborator Group, 2017).

Ischaemic Stroke

From 1990 to 2010, the age-standardized rate of DALYs lost per 100,000 decreased from 796 (734–906) to 598 (560–692), but the absolute number of DALYs lost due to IS increased by 18%, from 32 million to 39 million.

Age-standardized DALYs lost in HIC declined by about 34% (95% UI: 16–36%).

The bulk of DALYs lost were in LMIC.

Haemorrhagic Stroke

From 1990 to 2010, the age-standardized rate of DALYs lost per 100,000 decreased from 1267 (1068–1484) to 956 (828–1104). In HIC, there was a reduction in DALYs lost due to HS by 39% (95% CI: 32–44%), and in LMIC countries, there was a reduction in DALYs lost by 25% (95% CI: 7–38%).

However, from 1990 to 2010, the absolute number of DALYs lost due to HS increased by 14% from 54 million to 63 million.

Special Populations

Low- and Middle-Income Countries

In 2010, most of the burden of IS and HS was in LMIC, which accounted for

- 63% of incident IS and 80% of HS,
- 57% of deaths due to IS and 84% of deaths due to HS, and
- 64% of DALYs lost due to IS and 86% due to HS (Krishnamurthi et al., 2013).

The average age of incident and fatal IS and HS was 6 years younger in LMIC than in HIC.

The greater burden of stroke in LMIC is not simply because a larger proportion of the world's population lives in LMIC. The rates (i.e. number per 100,000 population) of stroke incidence, DALY loss, and mortality due to stroke are higher in LMIC, correlating inversely with country-level macroeconomic status indicators. Thus, not only are individuals in LMIC more likely to have strokes, but these strokes are also more likely to lead to death and disability.

The disproportionate stroke burden in LMIC is also not mediated by a greater prevalence of cardiovascular risk factors in LMIC. Cardiovascular risk is actually lower in low-income countries. However, national per capita income correlates inversely with stroke mortality and DALY loss rates independent of cardiovascular risk. It is therefore likely that suboptimal resources in LMIC to invest in stroke prevention, treatment, and rehabilitation have contributed to, and perpetuate, substantial inequities in stroke incidence and outcomes, beyond the burden of stroke risk factors.

People Younger than 75 Years of Age

In 2010, much of the burden of stroke was borne by people younger than 75 years, who accounted for

- 62.0% of new strokes,
- 69.8% of prevalent strokes,
- 45.5% of deaths from stroke, and
- 71.7% of DALYs lost because of stroke (Feigin et al., 2014) (Table 1.2).

People younger than 75 years also accounted for

- 62% of incident IS and 78% of HS, and
- 63% of DALYs lost due to IS and 83% due to HS.

Children and Young Adults

In 2010, 5.2 million (31%) strokes occurred in children (aged <20 years) and young and middle-aged adults (20–64 years).

Children from LMIC contributed almost 74,000 (89%) strokes, and young and middle-aged adults from LMIC contributed almost 4.0 million (78%) strokes.

In 2013, in younger adults aged 20 to 64 years, there were 1.483 million (95% UI: 1.340–1.659 million) stroke deaths globally (Krishnamurthi et al., 2015). The total DALYs from all strokes in those aged 20–64 years was 51.429 million (95% UI: 46.561–57.320 million) (Krishnamurthi et al., 2015).

Among younger adults, death rates for all strokes declined significantly between 1990 and 2013, in both developing countries, from 47 (95% UI: 42.6–51.7) in 1990 to 39 (95% UI: 35.0–43.8) in 2013, and in developed countries, from 33.3 (95% UI: 29.8–37.0) in 1990 to 23.5 (95% UI: 21.1–26.9) in 2013 (Krishnamurthi et al., 2015).

Summary

- In 2010, an estimated 16.9 million strokes occurred worldwide, or 1 every 2 seconds, at an incidence rate of 258 (234–284) per 100,000 persons per year. Approximately 70% of these strokes occurred in low- and middle-income countries (LMIC). The 16.9 million incident strokes were added to a pool of 33 million prevalent stroke survivors (502 [451–572) per 100,000 people). There were 5.9 million stroke-related deaths, at a rate of 88 (80–94 per 100,000 person-years), and 102 million disability-adjusted life-years (DALYs) lost due to stroke at a rate of 1554 (1374–1642) per 100,000 people.
- In 2010, stroke was the second leading cause of death and the third leading cause of DALYs worldwide.
- In 2010, most of the global burden of stroke was due to haemorrhagic stroke (HS), and most of the burden of HS was borne by LMIC. Although HS was

Table 1.2 Burden of stroke in 2010 globally, and by low and middle-income countries and people younger than 75 years. Age-adjusted annual incidence and mortality rates (per 100,000 person-years), prevalence (per 100,000 people), and disability-adjusted life-years (DALYs) lost (number, and per 100,000) for all stroke, ischaemic stroke, and haemorrhagic stroke, in 2010

All stroke	Global		Low- and middle-income countries			Age <75 years		
	Number of events	Rate (95% CI)	Number of events	%	Rate (95% CI)	Number of events	%	Rate (95% CI)
Incidence	16,894,536	258 (234–284)	11,590,294	68.6%	281 (244–322)	10,469,624	62.0%	169 (152–187)
Prevalence	33,024,958	502 (451–572)	17,238,778	52.2%	393 (330–483)	23,052,804	69.8%	367 (328–420)
DALYs lost	102,232,304	1554 (1374–1642)	79,411,312	77.7%	1821 (1589–1925)	73,293,552	71.7%	1163 (1011–1232)
Mortality	5,874,182	88 (80–94)	4,164,293	70.9%	105 (91–112)	2,668,499	45.5%	43 (38–45)
Ischaemic stroke								
Incidence	11,569,538	176 (161–192)	7,316,281	63%			67%	
DALYs lost	39,389,408	598 (560–692)	25,137,666	64%			63%	
Mortality	2,835,419	42 (40–49)	1,625,339	57%				
Haemorrhagic stroke								
Incidence	5,324,997	82 (72–93)	4,274,013	80%	99 (85–116)		78%	
DALYs lost	62,842,896	956 (828–1104)	54,273,644	86%			83%	
Mortality	3,038,763	46 (40–53)	2,538,954	84%	62 (53–72)			

Adapted from Krishnamurthi et al., 2013, 2014; Feigin et al., 2014; Bennett et al., 2014.

only half as common as ischaemic stroke (IS), constituting a third (31.5%) of the 16.9 million incident stroke events (20% in the high-income countries [HIC] and 37% in LMIC), HS caused more than half (51.7%) of the 5.9 million stroke-related deaths, and three-fifths (61.5%) of the 102.2 million DALYs lost throughout the world. The number of years of life lost were greater with HS because it affected people at a younger age (mean 65.1 years [standard deviation (SD) 0.11]) than did IS (73.1 years [0.10]) and had a higher case fatality (57% vs 25%).

- In the preceding two decades, between 1990 and 2010, the global incidence rate of stroke has remained stable but the absolute number of incident strokes has increased by 68% (from 10 million to 16.9 million); the prevalence rate has increased modestly (from 435 to 502 per 100,000), yet the absolute number of stroke survivors has nearly doubled (81% increase from 17.9 million to 33 million); the rate of DALYs lost due to stroke has decreased (from 2063 [1950–2280] to 1554 [1374–1642] per 100,000), but the absolute number of DALYs lost has increased by 12% (from 86 million to 102 million); and the age-standardized rates of stroke mortality have decreased (from 117 [112–130] to 88 [80–94] per 100,000 person-years), but the absolute number of stroke-related deaths has increased by 26% (from 4.7 million to 5.9 million).
- Over the past 2 decades (1990–2010), the worldwide burden of HS has increased in terms of absolute numbers of HS incident events. Whilst the absolute number of people with IS stroke has increased significantly by 37%, the absolute number of people with incident HS has increased by 47%.
- Although age-standardized IS mortality rates have declined over the past 2 decades, the absolute global burden of IS is increasing, with the bulk of DALYs lost occurring in LMIC. Between 1990 and 2010, there has been an increase in the number of deaths due to IS by 21% and HS by 20%, and the number of DALYs lost due to IS by 18% and HS by 14%.
- The increase in absolute numbers has arisen despite a reduction in the age-standardized incidence rates of IS by 13% and HS by 19%, a reduction in the mortality rates of IS by 37% and HS by 38%, and a reduction in DALYs lost due to IS by 34% and HS by 39%.
- The reduction in rates probably shows improved education, prevention, diagnosis, treatment, and rehabilitation of stroke. The increase in absolute numbers, despite a reduction in rates, is presumably because global population growth and increasing life expectancy have increased the denominator by a greater proportion than the increasing number of stroke events has increased the numerator.
- Most of the burden of stroke is in LMIC, which bear 63% of incident IS and 80% of IS, 57% of deaths due to IS and 84% due to HS, and 64% of DALYs lost due to IS and 86% due to HS. The average age of incident and fatal IS and HS was 6 years younger in LMIC than in HIC.
- The higher burden of stroke in LMIC is not simply because a larger proportion of the world's population lives in LMIC, as the *rates* of stroke incidence, DALY loss, and mortality due to stroke per 100,000 are higher in LMIC. It is also not mediated by a greater prevalence of cardiovascular risk factors but more so by the lower national per capita income realizing suboptimal resources to invest in stroke prevention, treatment, and rehabilitation.
- Most of the burden of IS and HS is also borne by people younger than 75 years, who bear 62% of incident IS and 78% of HS, and 63% of DALYs lost due to IS and 83% due to HS.
- Overall, despite stable age-standardized incidence rates of stroke and decreasing age-standardized mortality rates due to stroke worldwide in the past 2 decades, the global burden of stroke is great and increasing due to increases in the absolute number of (a) people who have a stroke every year, (b) stroke survivors, (c) DALYs lost due to stroke, and (d) stroke-related deaths.

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