

Chapter

Global Burden of Stroke: Insights and Trends from GBD 2021

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Abstract

Stroke represents a major global health challenge, being one of the leading causes of death worldwide. In developed countries, while both the incidence and prevalence of stroke have generally declined, these nations now face the growing burden of stroke-related disability and the demands of post-stroke rehabilitation, exacerbated by an aging population and increasing life expectancy. In contrast, developing countries are confronting an even more challenging situation, as stroke rates are rising not only among the elderly but also among younger individuals, driven by the detrimental effects of modern lifestyles and environmental factors. Additionally, these nations struggle with significant challenges in managing and treating stroke, largely due to limited healthcare resources. This chapter aims to provide a comprehensive analysis of the global burden of stroke, highlighting the disparities in prevention, treatment, and care strategies, as well as the long-term impacts of the disease in both developed and developing nations.

Keywords: stroke, epidemiology, global burden disease, mortality, risk factor, LMICs

1. Introduction

Stroke, defined as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin” [1], remains one of the leading causes of death worldwide. According to data from the Global Burden of Disease (GBD). In 2021 there were 93.8 million (95% Uncertainty Interval [UI]: 89.0–99.3) stroke survivors, 11.9 million (10.7–13.2) new stroke events, 7.3 million (6.6–7.8) deaths attributed to stroke, and 160.5 million (147.8–171.6) Disability-Adjusted Life Years (DALYs) lost due to stroke. These figures accounted for 10.7% (9.8–11.3) of all deaths and 5.6% (5.0–6.1) of total DALYs from all causes, ranking stroke as the third leading cause of death, and the fourth leading cause of DALYs, after COVID-19 and ischemic heart disease. Notably, 83.3% of incident strokes, 76.7% of prevalent strokes, 87.2% of stroke-related deaths, and 89.4% of stroke-related DALYs occurred collectively in low- and middle-income countries (LMICs) [2]. A global meta-analysis conducted in 2011 estimated the pooled cumulative risks of stroke recurrence as 3.1% (95% CI: 1.7–4.4) at 30 days, 11.1% (95% CI: 9.0–13.3) at 1 year, 26.4% (95% CI:

20.1–32.8) at 5 years, and 39.2% (95% CI: 27.2–51.2) at 10 years following the initial stroke event [3]. Given the high mortality rates, substantial DALYs, and notable recurrence risk, stroke profoundly impacts individual health and results in enduring psychological, social, and economic consequences. These severe outcomes escalate pressures on social development and healthcare systems, particularly within countries that have limited resources.

In 2019, the global value of lost welfare (VLW) due to stroke was estimated at US\$2059.67 billion, corresponding to 1.66% of global Gross domestic product (GDP) [4]. The economic impact is particularly severe in Central European, Eastern European, and Central Asian regions, where the VLW-to-GDP ratio reached 3.01% [4]. Beyond direct costs related to emergency services, acute care, and rehabilitation, indirect costs, including productivity loss, long-term disability, and informal caregiving, account for approximately 32% of the total economic burden of stroke and are projected to increase further with the population aging and improved post-stroke survival [5]. Notably, lifetime indirect costs per patient have been estimated to reach as high as US\$54,067, with informal caregiving accounting for up to 80% of these costs. Stroke survivors often face persistent disabilities impairing mobility, communication, and self-care, leading to long-term dependence on caregivers [5]. A study of 22,929 patients revealed that 70–79% were either deceased or dependent at five years post-stroke [6]. Moreover, psychological sequelae are highly prevalent, with cognitive impairment affecting 30.0% of survivors, depression at 39.1%, and anxiety at 34.9%, further diminishing quality of life [7].

2. Current burden of stroke

2.1 Global burden

In 2021, stroke was the third leading cause of death globally. Among the primary subtypes, ischaemic stroke accounted for the largest share of new cases (65.3% [62.4–67.7]), followed by intracerebral hemorrhage (28.8% [28.3–28.8]) and sub-arachnoid hemorrhage (5.8% [5.7–6.0]) [8]. Ischemic strokes result from blood vessel blockage, commonly due to large artery disease, arteriolosclerosis, or cardioembolism while hemorrhagic strokes occur due to blood vessel rupture, leading to intracerebral bleeding. Deep hemorrhages are typically associated with hypertension, while lobar hemorrhages may be related to amyloid angiopathy or vascular malformations.

Although hemorrhagic strokes are less common, they generally have a poor prognosis and account for a greater proportion of stroke-related DALYs (79.5 million, or 49.6%) than ischaemic stroke (70.4 million, or 43.8%) [9]. The risk of death from hemorrhagic stroke is up to four times higher in the first week, 2.5 times higher after 1 week, and 1.5 times higher after 3 weeks compared to ischemic stroke [10]. Significant geographic variation was observed in age-standardized stroke metrics. For instance, the lowest incidence was reported in Luxembourg (57.7 per 100,000 [95% UI: 53.5–62.1]), while the highest was observed in the Solomon Islands (355.0 per 100,000 [95% UI: 332.7–378.1]). Stroke prevalence was highest in Ghana (2045.8 per 100,000) and lowest in Cyprus (521.5 per 100,000), whereas age-standardized death rates ranged from 14.2 per 100,000 in Singapore to 277.4 per 100,000 in North Macedonia. The highest stroke burden, as measured by age-standardized incidence, prevalence, mortality, and DALYs, occurred in East Asia, Central Asia, and sub-Saharan Africa, and was lowest in high-income regions such as North America, Australasia, and Latin America [9].

Between 1990 and 2021, there was a significant global reduction in age-standardized stroke metrics: incidence decreased by 21.8% (95% UI –23.7 to –19.8), prevalence by 8.5% (–9.7 to –7.3), mortality by 39.4% (–44.0 to –34.6), and DALYs by 38.7% (–43.4 to –34.0). However, during the same period, the absolute number of stroke cases and outcomes increased: new stroke events rose by 70.2% (65.9 to 74.6), stroke survivors by 86.1% (83.0 to 89.4), stroke-related deaths by 44.1% (32.3 to 56.0), and stroke-related DALYs by 32.2% (21.7 to 42.7). Notably, the pace of decline in age-standardized stroke incidence slowed in recent years: –1.8% (–2.8 to –0.6) during 2019–2021, compared to –3.1% (–4.2 to –2.0) across 2010–2021 [9].

Among individuals aged ≥ 70 years, there were substantial reductions in stroke incidence (–18.2% [–21.3 to –14.6]), mortality (–34.2% [–39.4 to –29.3]), and DALY rates (–35.6% [–40.2 to –30.8]) from 1990 to 2021, while prevalence remained relatively unchanged (–1.0% [–3.1 to 1.2]). In contrast, among individuals aged < 70 years, the stroke incidence increased by 4.1% (0.9 to 7.6), and prevalence rose by 14.8% (13.1 to 16.8). Death and DALY rates in this younger group decreased by 17.4% (–25.0 to –8.9) and 19.0% (–26.0 to –11.6), respectively. These trends were consistent across ischaemic stroke subtypes. However, the prevalence of subarachnoid hemorrhage in people under 70 years increased slightly by 3.4% (1.3 to 5.5), while the incidence, prevalence, mortality, and DALYs associated with intracerebral hemorrhage and subarachnoid hemorrhage declined in both age groups [9].

The observed divergence between declining age-standardized stroke rates and rising absolute numbers of stroke events, deaths, and DALYs reflects the complex interplay between epidemiological transition and demographic change. On one hand, substantial progress in primary prevention, such as improved blood pressure control, reductions in tobacco use, healthier diets, and expanded access to acute stroke care, has contributed to notable decreases in stroke incidence and mortality at the individual level. However, these gains are offset by rapid global population growth, particularly in LMICs [11], and by marked population aging worldwide. As the ≥ 70 -year-old age group, those at highest risk for stroke, expands in both absolute and relative terms, the total number of stroke events continues to increase despite lower individual risk. Moreover, advances in acute stroke management have improved survival, resulting in a growing number of stroke survivors who live with long-term disability, thereby sustaining or increasing total DALYs. This trend does not signify failure in stroke prevention, but rather highlights a shifting public health challenge: an aging population that is living longer, but with greater post-stroke care needs. The implications are particularly profound for LMICs, which face the dual burden of rising non-communicable diseases and limited health system capacity to manage long-term sequelae [12].

2.2 Low-and middle-income countries

Stroke remains a leading cause of death and disability globally, but its epidemiological burden and the quality of stroke care differ substantially between the high-income countries (HICs) and LMICs. Over recent decades, LMICs have accounted for the majority of new stroke events, stroke-related deaths, and DALYs lost globally [13–16]. According to the GBD Study 2021, LMICs contributed to 83.3% of incident strokes, 76.7% of prevalent stroke cases, 87.2% of stroke-related deaths, and 89.4% of total stroke DALYs. Significant differences in stroke subtype distributions also exist; ischemic stroke accounted for 74.9% (95% UI 72.3–84.1) of incident strokes in HICs, compared with only 63.4% (53.6–73.7) in LMICs. Conversely, intracerebral

hemorrhage comprised a higher proportion of strokes in LMICs (31.1% [30.2–31.3]) than in HICs (17.8% [17.3–17.9]), reaching its highest proportion in low-income countries (36.9% [36.5–37.1]). Subarachnoid hemorrhage was more common in HICs (7.3% [7.2–8.3]) than LMICs (5.5% [5.4–5.7]) [2].

Socioeconomic status and health-system capacity significantly influence stroke outcomes. Individuals with lower socioeconomic status typically experience reduced access to high-quality acute and rehabilitation stroke care compared to their counterparts with higher socioeconomic status, resulting in poorer clinical outcomes [17]. Access to comprehensive stroke care, including stroke units, acute treatments, and rehabilitation services, varies substantially between HICs and LMICs. For instance, stroke units are available in approximately 91% of HICs, compared to only 18% of low-income countries. Similarly, the availability of acute stroke therapies is substantially greater in HICs (approximately 60%) than in low-income settings (approximately 26%) [18]. Furthermore, rehabilitation care, including inpatient and community-based services, is considerably less accessible in LMICs.

These disparities are clearly evident within continents, particularly across five major regions: Africa, South Asia, Southeast Asia, Oceania, and South America. In Africa, stroke incidence and prevalence remain consistently high, with annual incidence rates reaching up to 316 per 100,000 and prevalence up to 1460 per 100,000 [19]. Stroke fatality rates are alarmingly elevated, often exceeding 80% at 3 years post-stroke. Strokes in African populations occur at younger ages, amplifying their socioeconomic impact. Moreover, this burden is growing, driven by escalating rates of non-communicable diseases and inadequate control of hypertension [20]. South Asia and Southeast Asia, including India, have among the highest global age-standardized incidence, mortality, and DALY rates associated with stroke. Major risk factors in these regions include hypertension, diabetes, and tobacco use, with considerable inter-country variability observed. In South America, the stroke burden remains high yet highly heterogeneous, characterized by marked disparities in incidence rates and outcomes across countries. In Oceania, while comprehensive data are scarce, available evidence indicates significant within-region disparities [21]. Even within individual continents, stroke incidence, mortality, and disease burden remain substantially higher in LMICs compared with their neighboring high-income countries. In Africa, for instance, Nigeria reports a stroke prevalence of approximately 1.14 per 1000 population, with 30-day case fatality rates reaching as high as 40% [22]. The disability and mortality from stroke in Nigeria impose significant socioeconomic impacts, reflected by a stroke-related DALYs burden nearly sevenfold higher than in high-income regions [23]. Similarly, in South Asia, stroke ranks as the fourth leading cause of death and fifth leading cause of disability in India, with incidence rates ranging from 105 to 172 per 100,000 people annually, and prevalence between 26 and 757 per 100,000 [24]. One-month stroke case fatality rates in India vary from 18 to 42%, with hospitalization costs reaching up to INR 50,000, imposing substantial financial burdens and chronic disability on affected families [25]. Within Southeast Asia, stroke remains a major public health concern. In Vietnam had a considerably higher age-standardized stroke mortality rate of 196.56 per 100,000 (95% UI: 164.21–226.77). Despite this high burden, from 1990 to 2021, Vietnam experienced gradual reductions in stroke incidence, mortality, and DALYs, with average annual percentage changes (AAPCs) of -0.34% , -0.49% , and -0.61% , respectively [26].

2.3 HIC versus LMICs

Although stroke is a global public health crisis, its burden is unequally distributed with LMICs bearing a disproportionately high share of cases, deaths, and disability. Approximately 86% of all stroke deaths and 89% of stroke-related DALYs occur in LMICs [27]. Over the past four decades, LMICs have experienced more than a two-fold increase in stroke incidence, in stark contrast to a 42% decline observed in HICs during the same period [28]. Furthermore, patients in LMICs typically experience stroke at significantly younger ages (63 years) compared to their HIC counterparts (69 years), resulting in a greater loss of productive life years and amplifying socioeconomic consequences [18]. The health system challenges in LMICs are profound when prehospital emergency systems are often underdeveloped, leading to delayed hospital arrival, and stroke units remain scarce, with only 18% of LMICs reporting dedicated stroke rehabilitation services compared to over 90% in HICs [29]. Access to essential acute interventions such as intravenous thrombolysis and mechanical thrombectomy remains severely restricted in LMICs, with thrombolysis administered to approximately 3% of eligible patients in these settings, in stark contrast to usage rates as high as 30–40% in advanced stroke centers within high-income countries [30]. Post-acute care is equally inadequate. Most LMIC stroke survivors lack formal rehabilitation services. They are cared for by family members without professional support, leading to higher rates of long-term disability and dependency [31]. As a result, stroke survivors in LMICs frequently endure persistent severe disabilities, poor quality of life, and perpetuate cycles of poverty and social isolation.

3. Risk factors for stroke

The factors influencing stroke risk can be broadly categorized into three major groups: behavioral factors, including genetic predisposition, ethnicity, lifestyle, and health-related behaviors; metabolic factors, encompassing underlying medical conditions such as hypertension and diabetes, as well as the capacity and responsiveness of the healthcare system; and environmental or occupational factors, such as air pollution and climate change, in which nonmodifiable risk factors for stroke include age, sex, race–ethnicity, and genetic predisposition. Stroke is predominantly a disease of aging, and national health systems should leverage these factors to identify vulnerable populations for targeted screening programs. However, these nonmodifiable factors should not be the central focus of stroke prevention strategies. Instead, greater attention must be directed toward modifiable risk factors. Evidence indicates that approximately 90% of the global stroke burden is attributable to a small number of potentially modifiable risk factors, and a growing body of research demonstrates that addressing these factors can lead to a substantial reduction in stroke incidence [32]. The INTERSTROKE study, a large international case–control investigation, identified ten modifiable risk factors significantly associated with ischemic stroke including hypertension, current smoking, elevated waist-to-hip ratio, poor dietary patterns, physical inactivity, diabetes mellitus, binge alcohol consumption, psychosocial stress and depression, cardiac disease, and an elevated apolipoprotein B to A1 ratio. For intracerebral hemorrhage, key modifiable risk factors included hypertension, smoking, high waist-to-hip ratio, unhealthy diet, and heavy alcohol use [33].

Although the importance of modifiable risk factors is consistently emphasized across all major stroke prevention guidelines worldwide, the real-world control

of these factors remains suboptimal, particularly in LMICs, where healthcare systems often lack adequate capacity. Globally, in 2019, only approximately 23% of women and 18% of men with hypertension had their blood pressure controlled (<140/90 mmHg), with the highest rates (>50%) observed in high-performing countries such as South Korea, Canada, and Iceland. In contrast, many LMICs reported control rates below 10% [34]. Contributing barriers include poor hypertension detection, inadequate or insufficient therapy, limited access to medications, physician inertia, and low adherence among patients. The COVID-19 pandemic further disrupted screening and management efforts, exacerbating existing gaps in care [35, 36]. To address this, proposals have included the creation of a Global Hypertension Care Taskforce and the implementation of an “80–80–80” strategy, aiming for 80% of adults screened, 80% of those diagnosed receiving treatment, and 80% of treated patients achieving blood pressure control [37].

Similarly, while the global pooled rate of diabetes control improved from 16% before 2000 to 22% after 2010, significant disparities remain. Control rates are higher in high-income countries, whereas they remain as low as 16% in low-income settings [38]. Poor control of diabetes in LMICs can largely be attributed to the demanding nature of effective glycemic management, which requires strict medication adherence along with sustained dietary and physical activity modifications, practices that are difficult to maintain in contexts where health literacy is low and care-seeking behavior is predominantly symptom-driven. Furthermore, individuals in LMICs often face considerable financial and logistical barriers to accessing newer antidiabetic and antihypertensive agents, which have demonstrated superior efficacy and lower side-effect profiles compared to older treatments. Addressing these challenges will require a multifaceted response, including strengthening public health education and expanding government and global health support programs that improve access to affordable, effective therapies in resource-limited settings.

Another key determinant that contributes not only to stroke risk but also to the broader landscape of metabolic risk factors is the category of intrinsic factors, encompassing individual-level characteristics such as dietary habits, tobacco use, physical inactivity, and alcohol consumption. In 2010, the global mean sodium intake was estimated at 3.95 grams per day, with regional averages ranging from 2.18 to 5.51 grams. Sodium consumption above the recommended threshold was associated with approximately 1.65 million cardiovascular deaths annually (95% uncertainty interval: 1.10–2.22 million), accounting for 9.5% of all cardiovascular mortality worldwide. Among these, 61.9% occurred in men and 38.1% in women; notably, 84.3% of these deaths occurred in LMICs, and 40.4% occurred before the age of 70 [39]. Tobacco use remains a substantial public health concern, particularly in LMICs, which now account for the majority of the world’s smokers. Smoking prevalence varies markedly across regions, from 13.5% in Africa to 32.2% in Asia [40], and a significant proportion in LMICs, between 7.5 and 38.4% of current smokers, are classified as “hardened smokers,” defined as long-term daily users with low motivation to quit [41]. However, a range of tobacco control strategies have demonstrated real-world effectiveness in reducing tobacco use. Among these, fiscal measures, particularly taxation and price increases, are consistently identified as the most impactful interventions globally, with robust evidence supporting their role in curbing tobacco consumption and improving population-level health outcomes [42]. In parallel, legislative measures such as comprehensive bans on smoking in public places and workplaces have been shown to significantly reduce both smoking prevalence and exposure to secondhand smoke, and are widely endorsed as effective tools for governmental action [43].

Importantly, multi-component tobacco control programs that integrate taxation, regulatory policies, mass media campaigns, and cessation support are associated with greater reductions in tobacco use than single-strategy interventions, underscoring the value of comprehensive policy frameworks [44]. In addition, urbanization in LMICs is also contributing to a rise in sedentary behavior, particularly in densely populated urban centers [45]. Meanwhile, global obesity rates are accelerating more rapidly in LMICs than in high-income countries, especially among women and children [46]. While high-income countries have seen reductions in alcohol consumption driven by regulatory and public health measures, LMICs are experiencing a rise in alcohol use [47]. Heavy alcohol consumption contributes to elevated blood pressure, cardiac arrhythmias, and cardiomyopathy, all of which heighten the risk of stroke. Moreover, alcohol alters platelet function and coagulation pathways, thereby increasing the likelihood of both ischaemic and haemorrhagic events [48].

Environmental air pollution, particularly fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2), is a well-established risk factor for both ischaemic and haemorrhagic stroke. Air pollution may precipitate cerebrovascular events through mechanisms involving inflammation, oxidative stress, and vascular dysfunction [49]. Both short-term and long-term exposures have been shown to increase stroke risk. Exposure to both fine ($PM_{2.5}$) and coarse (PM_{10}) particulate matter has been consistently associated with higher rates of stroke incidence, hospital admissions, and mortality. The association is particularly strong for $PM_{2.5}$ (OR = 1.008; 95% CI: 1.005–1.011) [50]. It is estimated that approximately 16.9% of the nearly 15 million strokes that occur annually worldwide can be attributed to air pollution, with both short- and long-term exposure contributing to increased risk, especially for strokes caused by atherosclerosis [51]. This burden is particularly pronounced in LMICs, where $PM_{2.5}$ concentrations are significantly higher. The annual mean exposure to $PM_{2.5}$ between 2011 and 2017 was $48.42 \mu g/m^3$ in LMICs, compared to $20.02 \mu g/m^3$ in HIC. $PM_{2.5}$ levels in many LMICs have been found to exceed WHO air quality standards and affect regions that collectively account for approximately 40% of the global population [52]. Effective air pollution control policies include comprehensive national plans such as China's Air Pollution Prevention and Control Action Plan, which set phased targets and cross-sector measures [53]; sector-specific interventions focusing on transportation, energy, and industry such as promoting public transit, transitioning to cleaner fuels, tightening emission standards [54], a combination of incentive-based and punitive approaches, including free public transportation, subsidies for clean household energy, and congestion pricing for vehicles [55]. These policies have contributed to significant reductions in $PM_{2.5}$, PM_{10} , and SO_2 levels, along with public health gains.

A growing environmental determinant of stroke risk, particularly in LMICs, is exposure to extreme ambient temperatures, which contribute to approximately 13% of cardiovascular deaths and 5.2% of global stroke mortality [56, 57]. A multinational analysis involving data on 3,443,969 ischemic and 2,454,267 hemorrhagic stroke deaths across 522 cities in 25 countries demonstrated a U-shaped association, indicating elevated stroke mortality at both temperature extremes [58]. Specifically, extreme cold significantly increased hemorrhagic stroke risk (RR = 1.49, 95%CI 1.40–1.58) compared to ischemic stroke (RR = 1.34, 95% CI 1.27–1.41), whereas extreme heat was predominantly associated with ischemic stroke (RR = 1.13, 95%CI 1.06–1.20) rather than hemorrhagic stroke (RR = 1.02, 95% CI 1.00–1.05). Socioeconomic context further modified these relationships: countries with lower GDP per capita experienced higher risks of heat-related hemorrhagic stroke mortality (RR = 1.08, 95%CI 1.02–1.15), whereas ischemic stroke risk due to heat was comparable across

income levels. Mechanistically, cold exposure promotes vasoconstriction, hypertension, cholesterol crystallization, plaque instability, and hypothermia-associated bleeding, thereby increasing stroke risks [59, 60]. Conversely, heat exposure induces dehydration, hemoconcentration, sympathetic activation, and systemic inflammation via heat shock proteins, all exacerbating thrombotic and ischemic events [61, 62].

The distribution and control of stroke risk factors differ markedly between HICs and LMICs, driving much of the global disparity in stroke incidence and outcomes. Hypertension, the most significant modifiable risk factor for stroke globally, is particularly poorly controlled in LMICs, where it affects up to 64% of stroke patients and is a principal driver of the higher proportion of hemorrhagic strokes (about 20% in LMICs versus 10% in HICs) [31]. LMICs are experiencing a rapid increase in other vascular risk factors, including diabetes and obesity, driven by urbanization, dietary transitions toward high-salt and high-fat foods, and reduced physical activity [31]. Environmental exposures such as ambient and indoor air pollution further exacerbate stroke risk in these regions. Moreover, region-specific factors, including chronic infections such as HIV-associated vasculopathy in sub-Saharan Africa and genetic disorders like sickle cell disease, disproportionately affect younger individuals in LMICs, contributing to earlier stroke onset and greater loss of productive life years. The underdiagnosis and suboptimal treatment of atrial fibrillation and hypercholesterolemia in LMICs, partly due to limited healthcare infrastructure and lower awareness, also contribute to uncontrolled stroke risk [31].

4. Management and rehabilitation

Effective stroke management encompasses rapid prehospital recognition and response, timely hospital-based reperfusion therapies, organized stroke unit care, and comprehensive post-acute rehabilitation. While these components are routinely integrated into HICs, their implementation remains severely limited in LMICs, contributing to higher mortality and disability rates. In LMICs, public awareness of stroke symptoms is generally low, and emergency medical services (EMS) are often fragmented or underdeveloped, resulting in delayed hospital arrival. This delay is a major barrier to the use of reperfusion therapies. Intravenous thrombolysis, a cornerstone intervention shown to improve functional independence by up to 30%, is administered to only ~3% of eligible patients in LMICs, compared to up to 30–40% in HICs. Access to mechanical thrombectomy, which offers an additional 14–25% improvement in favorable outcomes for large vessel occlusions, is nearly absent in LMICs [28, 63]. In many countries LMICs, the treatment rate is below 1% due to a lack of essential infrastructure such as angiographic suites and trained neurointerventionalists [30].

Once patients reach hospital care, the availability of stroke units, a critical intervention shown to reduce mortality by 14% and improve functional outcomes, is extremely limited, reported in only 18% of LMIC hospitals versus over 90% in HICs [64]. The computed tomography scan (CTs) capabilities, essential for differentiating ischemic and hemorrhagic stroke, are often limited to urban tertiary centers in LMICs. Rural and peripheral hospitals frequently lack both CTs and MRI, leading to reliance on clinical assessment alone and increasing the risk of mismanagement. In-hospital care in LMICs often lacks essential supportive measures such as early mobilization, dysphagia screening, and prevention of complications, resulting in higher rates of preventable in-hospital morbidity and mortality [28].

Addressing these deficiencies requires targeted investment in health system infrastructure, including the development of EMS networks, expansion of stroke unit capacity, and provision of affordable neuroimaging. Capacity-building efforts should prioritize training multidisciplinary teams, including stroke neurologists, nurses, physiotherapists, and speech therapists. Innovative, cost-adapted approaches such as telemedicine networks, mobile stroke units, and regional stroke referral pathways are promising strategies to overcome geographical and resource barriers. Moreover, policy-level commitment is needed to subsidize critical therapies such as thrombolysis and thrombectomy and integrate stroke into national non-communicable disease strategies. Improving acute stroke management in LMICs is essential to reducing early mortality, minimizing disability, and alleviating the long-term socioeconomic burden of stroke.

In recent years, stroke diagnosis has undergone significant advancements driven by rapid progress in imaging technologies, molecular biology, and the integration of artificial intelligence, all aiming to optimize classification, management, and prognostication in stroke patients. One of the most notable developments is the widespread implementation of CT angiography (CTA) and CT perfusion (CTP) imaging, which enables the early identification of large-vessel occlusion and delineation of salvageable brain tissue. Landmark trials such as DAWN and DEFUSE-3 have demonstrated that patient selection based on perfusion imaging allows safe extension of the mechanical thrombectomy window up to 6–24 hours after symptom onset, with markedly superior functional outcomes at 90 days compared to medical therapy alone (49% with 13%) [65]. Similarly, the EXTEND trial showed that intravenous thrombolysis remains effective up to 9 hours from onset in patients selected by CTP [66]. These findings have been incorporated into international clinical guidelines since 2019–2021, establishing CTA and CTP as standard tools for assessing late-presenting stroke. Advanced MRI techniques such as diffusion-weighted imaging (DWI) and FLAIR have also contributed to extending treatment eligibility; notably, the WAKE-UP trial demonstrated that DWI–FLAIR mismatch can reliably identify patients with wake-up stroke suitable for thrombolysis [67]. In parallel, blood-based biomarkers, especially glial fibrillary acidic protein (GFAP), are emerging as promising tools for rapid differentiation between ischemic and hemorrhagic stroke. A prospective study involving 353 acute stroke patients revealed that GFAP levels <30 pg./mL had a negative predictive value of 100% for excluding intracerebral hemorrhage, while levels >200 pg./mL strongly suggested hemorrhagic stroke, with a positive predictive value of 90–95% [68]. These findings have direct clinical implications: a negative GFAP test may support the safe initiation of early thrombolytic therapy, whereas a positive result necessitates urgent blood pressure control or reversal of anticoagulation. In addition, AI is increasingly being applied as an effective supportive tool in the early diagnosis of stroke, helping to shorten alert times, accelerate inter-hospital transfers, and significantly reduce ‘door-in-door-out’ time. A study utilizing Canon Medical’s AI platform on 100 stroke CT cases demonstrated that the AI system could process CTA images in just 60 seconds, much faster than the average interpretation time by radiologists, which is 395 seconds, with a sensitivity of 77% for detecting large vessel occlusions, compared to 87% for radiologists [69]. However, algorithmic transparency and medicolegal issues related to diagnostic errors remain unresolved challenges. Taken together, these innovations pave the way for faster and more targeted therapeutic decision-making.

Advances in diagnostic imaging have led to numerous therapeutic breakthroughs. Mechanical thrombectomy, once restricted to 6 hours post-onset, is now effective

up to 24 hours in selected patients, thanks to advanced imaging that identifies viable penumbral tissue, as demonstrated in the DAWN and DEFUSE-3 trials. DAWN reported a 49% rate of functional independence at 90 days versus 13% with standard medical therapy [66]. Intravenous thrombolysis has also seen expanded indications, with the EXTEND trial showing efficacy up to 9 hours post-onset in patients selected by CT perfusion imaging [70]. In hemorrhagic stroke, blood pressure management has been refined, guided by imaging predictors such as the CTA “spot sign,” which indicates risk of hematoma expansion. Surgical approaches have also advanced: early minimally invasive hematoma evacuation is under active evaluation in ICH, while aneurysm coiling and clipping in subarachnoid hemorrhage benefit from earlier and more precise CTA-based diagnosis [70]. Additionally, neuroprotective strategies, though historically unsuccessful, are experiencing renewed interest through trials targeting specific molecular pathways or patient subsets. These advances are undoubtedly beneficial for patients, but they may also contribute to the stark disparities in outcomes between HICs and LMICs. While patients in HICs benefit directly from these novel approaches, those in LMICs often face significant barriers to access and implementation due to technological limitations and financial constraints.

5. Policy suggestion for low- and middle-income countries

LMICs should prioritize the development of integrated and comprehensive stroke care systems. Public education campaigns are essential to enhance community recognition of early stroke symptoms, commonly summarized by the acronym FAST as facial drooping, arm weakness, speech difficulties, and the necessity of timely activation of emergency medical services. Such initiatives must emphasize the critical importance of seeking immediate medical attention to optimize the chances of receiving acute interventions within the therapeutic window. Concurrently, raising public awareness about the availability, efficacy, and safety of acute-phase interventions, particularly intravenous thrombolysis (tPA), may facilitate timely hospital presentation and improve patient eligibility for reperfusion therapies.

Robust emergency medical service systems, dedicated stroke units within regional hospitals, and affordable, accessible neuroimaging infrastructure are foundational components required for timely diagnosis and effective management. Additionally, implementing telemedicine programs and remote consultation networks can empower local healthcare providers to manage complex stroke cases efficiently, minimize delays associated with inter-hospital transfers, and enhance access to specialized neurological expertise in resource-constrained settings.

Governments play a pivotal role in facilitating these advancements through supportive health policy development, financial subsidies for essential diagnostic tools and treatments, and integration of stroke prevention strategies within national non-communicable disease frameworks. Efforts targeting modifiable risk factors must be embedded within primary healthcare systems and reinforced by evidence-based public health interventions promoting healthy lifestyle behaviors and addressing environmental determinants.

Establishing multidisciplinary stroke care teams, including neurologists, rehabilitation physicians, specialized nurses, physiotherapists, speech-language pathologists, and occupational therapists, in conjunction with telemedicine expansions and mobile stroke units is critical for addressing existing gaps in stroke management. Through the implementation of these comprehensive strategies, LMICs can substantially

reduce stroke morbidity and mortality, enhance functional patient outcomes, and alleviate the significant socioeconomic burdens posed by stroke.

Access to modern stroke therapies, particularly intravenous thrombolysis (tPA), remains a significant challenge in low- and middle-income countries (LMICs), mainly due to financial barriers and stringent post-treatment monitoring requirements [71, 72]. The standard protocol for blood pressure monitoring in the first 24 hours after intravenous rtPA bolus is highly intensive, involving up to 36 measurements, posing considerable strain on healthcare resources, which are typically limited in LMIC settings. Various LMICs have implemented financial-support policies and have reported substantial initial successes. In Thailand, the rate of tPA usage increased notably from 0.38% in 2007 to 6.5% in 2012 following its inclusion in the universal healthcare coverage program [73]. In Brazil, policies offering free tPA raised its use from 1.3% in 2009 to 12.5% in 2019 and reduced 30-day mortality rates [74]. In China, expansion of the “Green Channel” hospital network and enhanced insurance reimbursement led to thrombolysis rates exceeding 15% in tertiary hospitals [75]. Recently, the OTIMIST main study proposed a simplified blood pressure monitoring protocol for mild-to-moderate stroke patients (NIHSS <10), reducing measurement frequency from 36 to 18 times without adversely impacting treatment outcomes, thus alleviating healthcare system strain while maintaining patient safety [76].

The Mobile Stroke Unit (MSU) is an innovative pre-hospital care model that functions as a mobile stroke hospital. It is equipped with a 32-slice CT scanner, cerebral vascular imaging systems, and telemedicine technology that enables remote consultation with neurologists [77]. This approach facilitates early diagnosis and intervention during patient transport. Several LMICs have reported successful implementation of the MSU model. In Thailand, a study of 978 acute ischemic stroke patients showed that those treated by MSU had the shortest door-to-needle time (20 minutes), the highest reperfusion therapy rate (56.8%), and significantly better outcomes (adjusted OR 2.15, 95% CI: 1.39–3.32) [78]. By significantly shortening onset-to-treatment time, MSUs have shown improved clinical outcomes compared to conventional ambulance transport.

6. Conclusions

In conclusion, stroke poses a major public health challenge worldwide and particularly in LMICs, significantly contributing to global morbidity and mortality. Addressing this issue effectively requires integrated stroke care systems, improved community awareness, robust emergency services, and expanded diagnostic capabilities. Strategic investment in healthcare infrastructure, telemedicine programs, and multidisciplinary stroke care teams can bridge current service gaps. Through supportive government policies and targeted preventive measures, LMICs can substantially reduce stroke burden, enhance patient outcomes, and decrease associated socioeconomic consequences.

Conflict of interest

The authors declare no conflict of interest.

Notes/thanks/other declarations

None.

Acronyms and abbreviations

LMICs	low- and middle-income countries
HICs	high income countries
GBD	global burden of disease
DALYs	total disability-adjusted life years
VLW	the global value of lost welfare
GDP	gross domestic product
WHO	World Health Organization
EMS	emergency medical services
CTA	CT angiography
CTP	CT perfusion
GFAP	glial fibrillary acidic protein

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