

Stroke epidemiology, prevention, and management strategies at a regional level: Latin America and the Caribbean

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Stroke is a major health problem in Latin American and Caribbean countries. In this paper, we review the epidemiology, aetiology, and management of stroke in the region based on a systematic search of articles published in Spanish, Portuguese, and English. Stroke mortality is higher than in developed countries but rates are declining. Population-based studies show variations in incidence of strokes: lower rates of ischaemic stroke and similar rates of intracranial haemorrhages, compared with other regions. A significant proportion of strokes in these populations can be attributed to a few preventable risk factors. Some countries have published national clinical guidelines, although much needs to be done in the organisation of care and rehabilitation. Even though the burden of stroke is high, there is a paucity of information for implementing evidence-based management. The Global Stroke Initiative, the WHO STEPS Stroke surveillance, and WHO-PREMISE projects provide opportunities for surveillance at institutional and community levels.

Introduction

Stroke is the second commonest cause of death and the principal cause of adult disability in the world, and two-thirds of all stroke deaths occur in low-income and middle-income countries.^{1,2} About one in ten of all deaths in these communities are attributable to cerebrovascular disease and stroke is now a major health problem for many countries in Latin America and the Caribbean. According to WHO, in 2002 there were about 272 000 deaths from stroke in 27 selected Latin American countries. In 2000, stroke was the first or second cause of death in 25 countries in the region according to estimates from the WHO regional office.³ In these countries, the burden of stroke was 5–14 disability-adjusted life years lost per 1000 population (age standardised to 2002), which is higher than in most industrialised nations.⁴

The most informative way to estimate the burden of stroke is population-based epidemiology.⁵ Stroke epidemiology has been poorly studied in Latin America and the Caribbean.^{6,7} Methodological differences—such as case ascertainment, classification, definitions, and reference populations for standardisation—are some of the problems in the region.

Stroke is a heterogeneous disease with three main pathological subtypes: ischaemic stroke, intracerebral haemorrhage, and subarachnoid haemorrhage. Ischaemic stroke is further classified into different subtypes according to clinical syndromes and the presence of cardiac sources of embolism, atherosclerotic arterial disease, disease of small penetrating arteries, or various rarer causes.⁸ The prognosis and treatment differ according to the subtype. The incidence and distribution of stroke subtypes have moderate geographical variations that are probably related to prevalence of cardiovascular risk factors (eg, tobacco use, blood pressure, diet, and physical activity), social structure, and ethnic differences. The identification of the subtypes and cardiovascular

risk factors depends largely on whether the setting is hospital or community based⁹ and on the availability and access to health-care resources. The stroke component of the MONICA (WHO Monitoring Trends and Determinants in Cardiovascular Disease) project confirmed that the quality of stroke care makes a difference to the individual and, by extension, at the population level.¹⁰ In this paper, we review the epidemiology, risk factors, and management of stroke in Latin America and the Caribbean.

Search strategy and selection criteria

References for this review were identified by electronic searches of MEDLINE, Lilacs, Scielo, and searches of references from relevant papers. No date limit was set, and we included papers published up to September 2006. Publication types were reviews, meta-analyses, cohort studies, population-based stroke registers, clinical trials, case series, and clinical guidelines. We systematically searched and reviewed papers published in English, Spanish, and Portuguese and used the same search terms in English and the comparable Spanish translations. First term: “Latin America”, “South America”, “Caribbean”, and each individual country. Second term: “stroke”, “cerebrovascular accident”, “cerebral attack”, “cerebrovascular disease”, “ischemic stroke”, “hemorrhagic stroke”, “transient ischemic attack”, “cerebral infarction”, “cerebral thrombosis”, “intracranial hemorrhage”, “parenchymal hemorrhage”, “subarachnoid hemorrhage”. Third term: “epidemiology”, “mortality”, “burden”, “incidence”, “prevalence”, “prognosis”, “case fatality”, “Rankin”, “Barthel”, “outcome”, “surveillance”, “etiology”, “risk factors”, “infarction subtypes”, “hypertension”, “diabetes”, “hypercholesterolemia”, “dyslipidemia”, “Chagas’ disease”, “cysticercosis”, “atrial fibrillation”, “mitral stenosis”, “carotid stenosis”, “syphilis”, “management”, “treatment”, “clinical guidelines”, “stroke units”, “thrombolysis”,

“carotid endarterectomy”, “heparin”, “oral anticoagulation”, “aspirin”, “CT scan”, “CAT scan”, “computed cerebral tomography”, “carotid ultrasonography”, “carotid doppler”, “carotid duplex”, “echocardiography”. We obtained articles from Argentina, Barbados, Brazil, Bolivia, Chile, Colombia, Costa Rica, Cuba, Ecuador, Honduras, Martinique, Mexico, Panama, Peru, Uruguay, Trinidad and Tobago, and Venezuela. On the basis of abstracts, one or more authors selected the papers for the review.

We did not do a statistical analysis or meta-analysis, because of the variability of the data sources and study methodologies. Other relevant papers covering reviews or studies in wider geographical areas were also reviewed.

Results

Epidemiology

Stroke mortality and burden in Latin America and Caribbean

The WHO MONICA study provides the most reliable source of comparable data on stroke incidence, case fatality, and mortality rates, but unfortunately none of the 18 countries involved were located in Latin America and the Caribbean. Data from the WHO mortality database suggest that stroke is the leading cause of death in Brazil, the largest country in the region,¹¹ with age-adjusted mortality rates for stroke being the highest of nine Latin American countries in a recent comparison.¹² The WHO Global Infobase comparison system shows that age-adjusted mortality rates for stroke in 2002 were even higher in several Caribbean countries (figure 1).¹³ The proportion of deaths attributable to stroke differs between countries in the region ranging from 3% of all deaths in Peru to 11% in Trinidad and Tobago.¹⁴ In an international comparative study, stroke mortality rates were twice as high in Argentina, Chile, and Uruguay compared with western Europe and the USA. Cuba, Venezuela, and Mexico had intermediate rates, but Trinidad and Tobago had very high mortality rates.¹⁵

Limitations associated with these comparisons relate to the fact that stroke mortality estimates are based on death certificates, and official mortality statistics are inaccurate in many cases. Stroke is commonly assigned to related complications.¹⁶ A recent study has shown that cerebrovascular disease mortality has been declining over the past 30 years in most Latin American countries (it is stable in Mexico and Venezuela). This decline has been less pronounced than that observed in Canada or the USA, resulting in stroke mortality being two to four times higher in Latin America in 2000. The reasons for the declining mortality are not understood, although they might be related to changes in stroke incidence associated with improved control of cardiovascular risk factors.¹⁷ Other reasons include improvements in socioeconomic rather than classic cardiovascular risk factors and an improvement in the quality of stroke care.¹⁰ In another study in Brazil, standardised mortality rates decreased consistently between 1980 and 2000, from 68.2 per

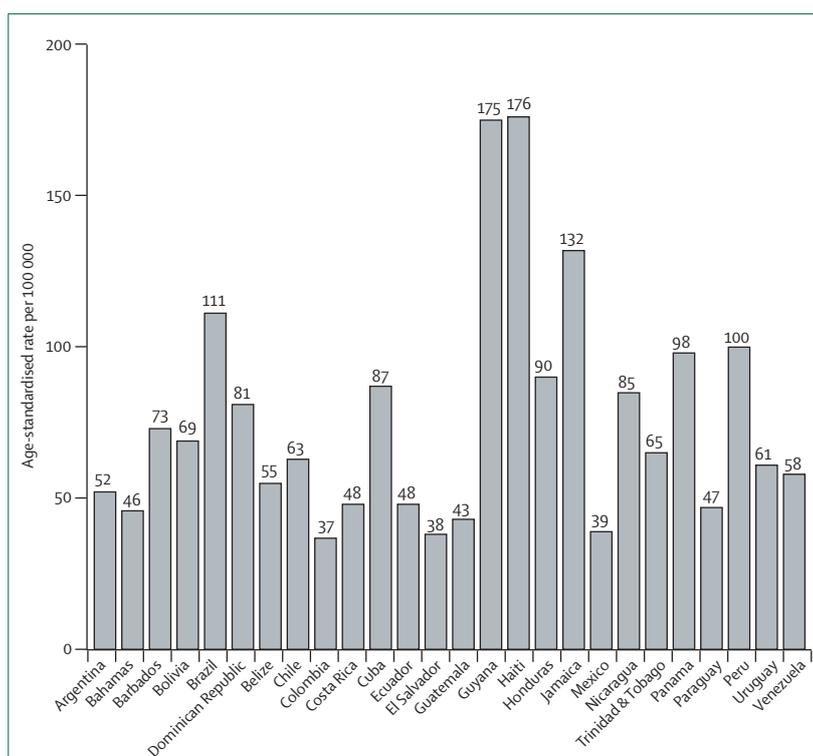


Figure 1: Mortality rates for stroke in all Latin American and Caribbean countries in 2002
Age standardised to the world population.

100 000 to 40.9 per 100 000, with regional variations. The reduction occurred in both sexes in all age groups and was highest in socioeconomically advanced regions, and risk of dying from stroke declined by 55%. This risk reduction is not entirely explained by classic risk-factor control in high-risk individuals, but may also reflect secular trends in general improvements in health conditions, technological advances, or improvement in acute stroke care.¹⁸

Incidence of total stroke

There are few well-designed, population-based, stroke-incidence studies in Latin American and Caribbean populations (table 1).^{19–22} The age-adjusted incidence of first-ever stroke was 140 per 100 000 per year (95% CI 124–156) in a community-based prospective study in a predominantly Hispanic Mestizo population in Iquique, Chile.¹⁹ Similar results were found in the Caribbean island of Martinique in a population of mostly African origin, in which the age-adjusted incidence of first-ever stroke was 151 per 100 000 per year (139–164).²⁰ In Barbados, a comparable population-based study reported an age-adjusted stroke incidence of 135 per 100 000 per year (112–158) in a predominately black English-speaking population.²¹ These three studies used standardised methods to ascertain all possible stroke cases, whether hospitalised or not, and had high rates of CT scanning, which decreases the likelihood of bias and aids the

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comparability of findings to other population-based studies.²³ In all three studies, incidence was higher in men than in women and, as was expected, increased significantly with each decade of life.

Other studies have investigated the incidence of stroke in different Latin American communities, although the methods did not meet the standards of ideal stroke studies.²⁴ In Joinville, Brazil, all hospitalised patients and all those dying from stroke in the community before hospital admission were prospectively ascertained.²² Surviving non-hospitalised patients were, however, not enumerated. The age-adjusted incidence of first-ever stroke was 156 per 100 000 per year (95% CI 96–217), which is similar to that in population-based studies. Similar incidences were found in another Brazilian hospital-based study in Salvador, Bahia.²⁵ Four other community-based studies reported incidence rates (unadjusted) of stroke, which were from 35–320 per 100 000 in Cuzco, Peru;²⁶ Sabanetta, Colombia;²⁷ Cienfuegos, Cuba;²⁸ and Amazonian, Bolivia.²⁹ These studies were essentially prevalence surveys that included self-report and subsequent screening of potential stroke survivors in the community. Many sources of bias might affect these studies, as only living patients were included, all diagnoses were clinical, and no CT scans were done; furthermore, the number of cases detected was under 15. The small numbers of cases produce such wide confidence intervals that it is difficult to interpret the data. The studies in Iquique, Martinique, and Barbados, showed that overall stroke incidence in these populations was lower than in other settings in Latin America and the Caribbean. However, hospitalisation rates were high in the Martinique and Joinville studies and could reflect under ascertainment of non-hospitalised cases; in the Iquique and Barbados studies, hospitalisation rates were low and incidence rates were similar to those in other countries in the region. Small geographical variations exist and are probably explained by methodological issues, including the small numbers of events.⁵

Stroke subtypes

The incidence of pathological subtypes (cerebral infarction, intracerebral haemorrhage, subarachnoid

haemorrhage) of stroke was investigated in the three community-based studies. The proportion that had CT scans ranged from 91% in Iquique to 96% in Barbados (table 1). Incidences were reported in two of the three studies. The age-adjusted incidence of cerebral infarction was higher in Barbados (120 per 100 000 per year, 95% CI 107–134) than in Iquique (87 per 100 000 per year, 75–100). The incidence of intracerebral haemorrhage was similar in the two populations: 27.6 per 100 000 per year (21.1–34.4) in Iquique and 18 per 100 000 per year (12–23) in Barbados. The incidence of subarachnoid haemorrhage was 6.2 per 100 000 per year (3.0–9.3) in Iquique¹⁹ and 3 per 100 000 per year (1–5) in Barbados.²¹ These findings are comparable with those reported in population-based studies elsewhere.⁵ Incidences were similar in hospital-based registries in the region.^{26,30,31} In population-based studies that reported all cases, irrespective of hospitalisation status, 63–81% of strokes were ischaemic; intracerebral haemorrhage made up 12–24% of strokes, and subarachnoid haemorrhage 2–5%. The proportion of intracerebral haemorrhage seems higher than in other populations, but this difference is attenuated after age adjustment and consideration of the precision of estimates (ie, confidence intervals).¹⁹ A study comparing hospitalised stroke patients in Boston, USA, and Buenos Aires, Argentina, found no difference in the proportion of intracerebral haemorrhage (19.4% and 21.0%, respectively).³² In a study of stroke in immigrants to Sweden, there was no higher risk for intracerebral haemorrhage in Chileans.³³ In hospital case series in Latin America, the proportion of stroke attributable to cerebral infarction and intracranial haemorrhage varies widely, largely due to methodological differences. Some hospital series include first-ever stroke, while others also include recurrent strokes. Some include intracerebral as well as subarachnoid haemorrhage although others only include intracerebral haemorrhage. Most importantly, the exclusion of non-hospitalised patients makes comparisons unreliable because of admission bias. The exclusion of very severe cases that die before hospital admission and of mild cases that do not seek medical attention as well as local clinical practice, socioeconomic, and geographical barriers to hospital admission are not

City, country	Years of observation	Number of strokes, population at risk	Mean age (years)	Hospital admission (%)	CT (%)	Incidence of total stroke ×1000	CI (%)	ICH (%)	SAH (%)	Undetermined stroke (%)
Iquique, Chile ¹⁹	2	292,396 712	65.5	71	91	1.40	63.3	23.6	5.1	7.8
Martinique, French West Indies ²⁰	1	580,360 000	71.2	93.5	92.8	1.51	79.8	14.3	3.4	2.4
Barbados, West Indies ²¹	1	352,268 000	72.5	69	96	1.35	83	12.9	2	4
Joinville, Brazil ^{22*}	1	320,319 219	65.2	91	97.7	1.56	73	18	8	..

CI=cerebral infarction. ICH=intracerebral haemorrhage. SAH=subarachnoid haemorrhage. *Semi-population based, surviving non-hospitalised cases not included in this study.

Table 1: Stroke incidence (per 1000) age-adjusted to the European population of first-ever stroke and proportion by pathological subtype in population-based studies in Latin America and the Caribbean

considered and can only be investigated in community-based prospective studies.^{32,34–39}

In summary, community-based studies show a slightly lower incidence of ischaemic strokes and similar rates of intracranial haemorrhages in Latin America and the Caribbean than in Europe and North America.

Incidence of ischaemic-stroke subtypes

The incidence of ischaemic-stroke subtypes according to the Oxfordshire Community Stroke Project classification⁴⁰ was reported in both the Iquique, Chile, and Barbados studies. The age and sex-adjusted incidence of first-ever lacunar infarction syndromes were high in both studies, being higher in Barbados (57 per 100 000 per year, 95% CI 50–65) than in Iquique (33 per 100 000 per year, 23–46) and could be attributed to an increased risk of small vessel disease in these populations. The incidence of partial anterior infarction and total anterior infarction were similar (27 and 14, respectively, in Barbados; and 20 and 14 in Iquique).^{19,41} The proportional incidence of ischaemic-stroke subtypes classified according to the Oxfordshire Community Stroke Project in population-based studies in the region compared with community studies in the UK (figure 2)^{19–21,40,41} showed a high proportion of lacunar infarction in Latin America and the Caribbean. The incidence of ischaemic-stroke subtypes in the community, according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification,⁴² in Latin America has only recently been described.⁴³ The incidence of transient ischaemic attacks in Iquique was lower than in other population-based studies.¹⁹ The frequency of previous transient ischaemic attack in patients with stroke was also low in this population. The low prevalence of carotid disease or non-presentation for medical attention, as well as under ascertainment factors, might be the cause of this low incidence.¹⁹

In hospital series, the proportion of ischaemic-stroke subtypes varies substantially.^{33,36–40,44,45} These differences might result from admission patterns, variation in clinical definitions of stroke, and differences in access to neurological and cardiac studies and limit the comparability of these data.

Prevalence of stroke and stroke-related disabilities

The prevalence of stroke is difficult to measure in a cross-sectional way because more than 30% of patients die in the first year and 20% are left without any disability. Prevalence studies have been done in both rural^{46–50} and urban populations^{27,28,51–56} in the region (table 2), but most studies have used different definitions and age groups to study neurological disorders (including stroke), making comparisons difficult, if not impossible.⁵⁷ The crude prevalence rates ranged from 1.7 per 1000 in rural Bolivia²⁹ to 9.6 per 1000 in urban Colombia,⁵² but the numbers of cases were too small to make meaningful comparisons. In people older than 60 years, the range increased from 19.3 to 48.0 per 1000. Prevalence studies generally

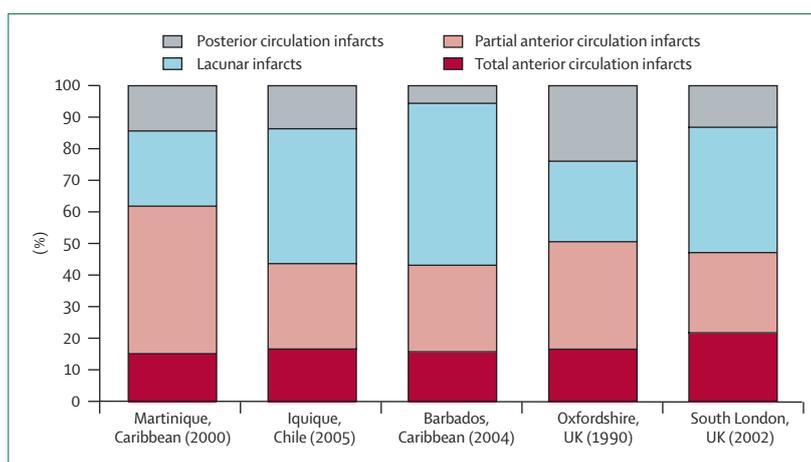


Figure 2: Proportion of ischaemic stroke subtypes

Classified according to the Oxfordshire Community Stroke Project classification (OCSF) in comparable population-based studies in Latin America, the Caribbean, and the UK.

	Age range	Population screened	Number of strokes	Prevalence ×1000			Prevalence ×1000 in elderly
				Men	Women	Total	
Salvador, Bahia, Brazil, ⁵³ 1982	≥15	810	5	9.0	4.0	6.2	..
Panama city, Panama, ⁵¹ 1986	..	955	7.5	..
Santiago, Chile, ⁵³ 1992	All	7175	43	4.1	5.8	6.0	25.0*
Cuzco, Peru, ²⁶ 1995	≥15	3246	21	8.1	5.1	6.2	..
Sabaneta, Colombia, ²⁷ 1997	All	13 588	76	5.7	5.4	5.6	46.7†
Cordillera, Bolivia, ²⁹ 1997	All	9955	16	2.5	1.0	1.7	19.3‡
Tegucigalpa, Honduras, ⁵⁴ 2003	All	1553	9	5.7	-
Atahualpa, Ecuador, ⁴⁷ 2004	≥15	1568	10	6.4	36.1†

*≥60 years. †>60 years. ‡≥65.

Table 2: Prevalence of stroke disability in Latin American populations by sex and older age groups.

exclude patients who recover completely because of the difficulty of follow-up or independent verification. Comparisons between studies are difficult because of the failure to publish age-specific rates in mid-decades.⁵⁸

The burden of stroke-related disabilities in this region was shown in a recent comparative study of functional limitations in populations over 60 years old in seven cities in Latin America and the Caribbean (Bridgetown, Barbados; Buenos Aires, Argentina; Havana, Cuba; Mexico City, Mexico; Montevideo, Uruguay; Santiago, Chile; and Sao Paulo, Brazil). Among other factors, difficulties in instrumental activities of daily living were independently associated with the presence of cerebrovascular disease.⁵⁹

Prognosis of stroke

The 30 day case-fatality rate of stroke reported in population-based studies (table 3) is very similar to the 22.9% cumulative case-fatality rate for other selected population-based studies.⁵ Case fatality was also similar for ischaemic stroke in Iquique and Martinique, and

	Cerebral infarction (%)	ICH (%)	SAH (%)	Undetermined (%)	Total (%)
Joinville, Brazil ²²	22.5 (53/235)	35.6 (22/61)	41.6 (10/24)	..	26.2 (84/320)†
Martinique, French West Indies ²⁰	15.8 (73/463)	37.3 (31/83)	25 (5/20)	21.4 (3/14)	19.3 (112/580)†
Barbados, West Indies ²¹	23.2 (64/276)	61 (25/41)	85.7 (5/6)	58.3 (7/12)	29.9 (101/335)†
Iquique, Chile ¹⁹	17.8 (33/85)	28.9 (20/69)	40.0 (6/15)	39.1 (9/23)	23.3 (68/292)

ICH=intracerebral haemorrhage. SAH=subarachnoid haemorrhage. *Semi-population based: surviving non-hospitalised cases not included. †Only percentages provided in text, number dead calculated.

Table 3: 30 day case-fatality rate for first-ever stroke and stroke pathological subtypes in comparable Latin American and Caribbean population-based studies

slightly higher in Barbados and Joinville.^{19–22} A greater variation in case fatality was seen for both intracerebral haemorrhage and subarachnoid haemorrhage in the studies in Iquique, Martinique, and Barbados, probably because of chance, since the number of cases are small and confidence intervals wide. In Barbados, the case-fatality rate at 3 months was 34.8%. Patients in Barbados had a poorer survival after stroke compared with similar patients in south London, especially if they were previously dependent, had untreated atrial fibrillation, were incontinent, or had dysphagia.⁶⁰

In Iquique, Chile, 33% were dead and 20% were dependent 6 months after a first-ever stroke. The rates of dependency and death increased with age and were highest for people with haemorrhagic stroke and total anterior-circulation infarcts.¹⁹ The main causes of death were neurological in the first month and chest infections or cardiovascular thereafter. These findings are similar to those in the few population-based studies looking at long-term prognosis.⁶¹ Survival 4 years after stroke was 23% in one study⁶² and 19.8% at 5 years in another.⁶³ The risk of death in this study was associated with older age, lack of rehabilitation, infections, and heart disease. Variations of outcomes after strokes in different countries were reported by the International Stroke Trial (IST) investigators, and this study included Argentina. Crude case-fatality rates and proportion of patients dead or dependent at 6 months were compared after adjusting

for prognostic factors. Sweden and Norway had the lowest case-fatality rates, whereas the UK, Argentina, and Poland had the highest rates. The researchers concluded that at least part of the difference could be accounted for by differences in the care process for acute stroke, including hospitalisation in stroke units, access to early CT scan, and use of aspirin at discharge.⁶⁴ There were no data on health care after discharge that could have influenced these findings.

Risk factors and causes

Cardiovascular risk factors

The distribution of cardiovascular risk factors can partly explain differences in risk of stroke and could influence the incidence of pathological types of stroke as well as the subtypes of ischaemic strokes across populations.⁶⁵ Population-based and hospital-based studies differ in the prevalence of risk factors: hospital-based studies are subject to selection bias and therefore to a higher prevalence of risk factors.⁹ Differences in population-based, risk-factor studies in Latin America and the Caribbean (table 4) are difficult to interpret because of differences in definitions and methods. Hypertension, defined differently in each study, was the most commonly cited risk factor in the three population-based studies. The high prevalence has been noted in other population-based studies as well. In comparison, diabetes is twice as common in patients with stroke in Iquique, Martinique, and Barbados as in many other populations.⁶⁶ In these populations, diabetes prevalence is high and hypercholesterolaemia and smoking are rare in patients with ischaemic stroke, and alcohol consumption is high in patients with intracerebral haemorrhage who have high alcohol consumption. Chance, bias, and confounding are likely to affect these observations.

A recent study compared black Caribbean and white European patients with stroke from two population-based registries in Barbados and south London that used the same methodology and definitions. The authors investigated the frequency of cardiovascular risk factors in stroke in both populations and found that hypertension, alcohol intake, smoking, and ischaemic heart disease were substantially less prevalent in the Caribbean population than in the south London population.⁴¹ These findings suggest that cardiovascular risk factors are dependent on geographical setting and that

	Iquique, Chile ¹⁹		Martinique, West Indies ^{20*}	
	Infarction	ICH	Infarction	ICH
Male sex	55	62
Mean age (SD)	66.5 (16.1)	58.5 (18.3)
Hypertension (%)	66.4	53.6	71.2	68.7
Diabetes (%)	23.2	15.9	31.8	24.1
Hypercholesterolaemia (%)	17.2	5.7	12.6	8.4
Atrial fibrillation (%)	12.4	10.1	15.1	3.6
Coronary heart disease (%)	8.6	5.7	6.1	3.6
PVD (%)	14.4	4.8
Smoking (%)	15.1	17.4	7.9	3.6
Alcohol (%)	10.8	18.8	12.2	21.7

ICH=intracerebral haemorrhage. PVD=Peripheral vascular disease. *No stratification by pathological subtype provided.

Table 4: Crude prevalence of cardiovascular risk factors in incident stroke patients stratified by pathological type in population-based studies in Latin America and the Caribbean

environmental factors might mediate the prevalence of cardiovascular risk factors and the incidence of stroke in migrant communities.

As previously noted, hospital-based case series are difficult to compare because of differences in reporting of risk factors for stroke and pathological subtypes, heterogeneity in definitions, lack of age and sex standardisation of rates, and biases in how patients are selected for admission. Wide variations in study results limit conclusions.

In Latin American and Caribbean populations, a significant proportion of the risk of stroke can be attributed to classic preventable cardiovascular risk factors, such as hypertension, diabetes, and smoking. Differences in their relative prevalences compared with those in other populations probably account for differences in the risk of pathological subtypes of strokes, especially a low risk of ischaemic strokes. The risk-factor profile of these communities could change in the future with economic development. Preventing these modifiable risk factors could have a substantial effect on life expectancy in the region.

Socioeconomic factors

Although recognised as an independent risk for stroke morbidity and mortality,⁶⁷ socioeconomic status measured as education level, occupation, and income has seldom been studied in Latin America and the Caribbean. There is consistent evidence of increased mortality and incidence of stroke in low socioeconomic groups in different populations.⁶⁸ Social inequalities are important in the region and therefore should affect incidence and prognosis of stroke. Such inequalities might be responsible for the higher stroke mortality rates found in socially deprived areas of Salvador, Brazil.^{69,70} In another study, a low educational level was associated with an increased risk of stroke in a sample of young women in five countries of this region.⁷¹ Socioeconomic status may modulate the risk of stroke through several mechanisms: poor knowledge, limited access to health care, unhealthy lifestyles, poor compliance with prevention strategies, inadequate water and housing conditions, increased stress, and underdiagnosis of severe cardiovascular diseases.⁶⁷ Improvements in these social factors could be responsible in part for the decline in stroke mortality rates observed in this region.

Ethnicity and race

Latin America and the Caribbean is a multiracial, multiethnic region whose population includes Amerindian, Mestizos, African-Americans, white Caucasians, Asians, and their various combinations. The term Hispanic has been used in the USA to denote people originally from Spanish-speaking countries in Latin America and the Caribbean. The search for a relation between stroke patterns and race-ethnicity has led to controversies among researchers mainly because

of difficulties in defining the race-ethnicity concept and because studies looking at ethnicity as a genetic variable have not controlled for confounders, such as socioeconomic status or any of its surrogate markers: access to quality health care, equity in stroke-care delivery, or attitudes towards physicians and preventive measures.^{32,72} The three population-based studies unbiased by access to health care examined different race-ethnic communities—two mainly black Caribbean and the other Hispanic-Mestizo—and had similar results in terms of overall incidence, frequency of pathological subtypes, and distribution of risk factors. Differences in stroke-mortality rates in Brazil between Afro-Brazilian and Caucasian men and women aged 40–69 years have been attributed to socioeconomic inequalities rather than ethnicity.⁷³ Ethnic disparities in stroke in Latin America and the Caribbean should be studied as interactions between environment and genes, socioeconomic status, and behaviour towards health, and population-attributable risks should be estimated.⁶⁷ The extrapolation of findings in immigrants in western industrialised countries to the Latin American and Caribbean countries should be done cautiously, because migrants have increased risk of cardiovascular disease and death.⁴¹

Stroke and infectious diseases in Latin America and Caribbean

In addition to the well-known causes of stroke in developed countries, some specific disorders are more common in low-income and middle-income countries, and in some cases almost exclusively in Latin America and the Caribbean.⁷⁴ American trypanosomiasis or Chagas' disease is an important cause of cardiomyopathy and cardioembolic stroke in South America. 16–18 million people have a chronic infection and 50 000 die each year.⁷⁵ The disease is produced by infection with *Trypanosoma cruzi*, a parasite in the infested faeces of a blood-sucking triatomine insect. The parasite is widely distributed from the north of Argentina and Chile to the south of Texas, USA, usually in rural and poor areas. The infection can also be transmitted through blood transfusions. More than 100 million people, 25% of the South American population, live in endemic areas. 8% of people in South America are seropositive for *T. cruzi*, but only 10–33% will develop a symptomatic disease, mainly Chagasic cardiomyopathy.^{76,77} In Latin America, Chagas' disease is a strong independent risk factor for all types of stroke, with an odds ratio of 5·4⁷⁸ and an increased risk of ischaemic embolic stroke and haemorrhagic stroke associated with anticoagulant use. Stroke associated with Chagas' disease cannot, however, be distinguished from other embolic strokes.

Neurocysticercosis, also endemic in South America, is the most common parasitic CNS infection.⁷⁹ Humans are infected by faecal-oral contamination with eggs of *Taenia solium*, and cysticercosis is caused by tissue infection with larval cysts, especially in muscle and brain. Cysticerci can be located in any area of the CNS, but most

commonly in the subarachnoid space, the ventricles, and the brain tissue. Mass lesions and seizures are the most common clinical symptom. Both lacunar and large-artery ischaemic strokes have been attributed to cerebral cysticercosis due to cerebral angitis at the base of the cranium.^{80–82} In large hospital series, this cause is seldom reported.

Sickle-cell disease, malaria, leptospirosis, snake bites, and viral haemorrhagic fevers are other prevalent disorders in some tropical areas of Latin America and the Caribbean that predispose to non-vascular stroke.⁷⁹ Sickle-cell disease, an inherited abnormality of haemoglobin, and cerebral malaria, an acquired parasitic disease, can cause ischaemic or haemorrhagic strokes through vascular damage produced by abnormal red blood cells. Leptospirosis is a spirochetal disease that may cause meningoencephalitis, and can cause cerebral haemorrhages secondary to coagulopathy and intracranial angitis that leads to the development of a moyamoya like phenomenon.⁸³ Snake bites can be very common in Amazonian regions. Snake venom can have procoagulant or fibrinolytic activity, producing either ischaemic or haemorrhagic strokes. Viral haemorrhagic fevers appear as epidemic outbreaks in different regions of Latin America and the Caribbean. Intraparenchymal or subarachnoid haemorrhage can occur as a manifestation of increased vascular permeability, disseminated intravascular coagulation, thrombocytopenia, and abnormal platelet function.

Cerebral sinus venous thrombosis seems common in young patients with strokes in Latin American countries, although probably due to hospitalisation bias.^{84,85} In Martinique only 0·6% of all ischaemic strokes were due to cerebral sinus venous thrombosis.²⁰

Management of stroke in Latin America and Caribbean

More than a decade ago, the Collaborative Group for Latin America published a paper about attitudes in the management of patients with stroke in seven Latin American countries. Many patients were treated with steroids if they had brain oedema and anticoagulation for strokes in evolution. Carotid doppler studies were rarely done and there were differences in access to CT scanning. Nevertheless the differences among countries and between socioeconomic levels were less than expected.⁸⁶ Practices have changed since then. In 2004, the presidents of the Iberoamerican Societies of Neurology met in Barcelona and declared stroke a catastrophic disease.⁸⁷ Furthermore, in several countries throughout Latin America, neurologists have formed stroke associations—study groups or societies that aim to improve the quality of care.⁸⁸ Early evidence-based guidelines or consensus statements were largely centred on acute treatment issues rather than policy issues related to the organisation of care or the provision of access to appropriate care.^{89–95} National management guidelines developed by the Chilean Ministry of Health guarantee a minimum level

of care to all with ischaemic stroke from July 2006 onwards. These guidelines include rapid neurological assessment, head CT, hospitalisation, neurorehabilitation, and secondary prevention strategies. Resources should be allocated for this purpose on a national basis.⁹⁶ In Cienfuegos, Cuba, a ten component fast-track approach to stroke management has been implemented with the emphasis on the word “early”: awareness of signs, medical contact, life support, referral, emergency treatment, imaging, admission, rehabilitation, education, and prevention. This approach has doubled hospital admission rates and halved case-fatality rates in Cienfuegos.⁹⁷

Hospitalisation of patients with acute stroke depends on access and cultural behaviour.⁹⁸ In population-based studies, 29% of patients with first-ever stroke were not hospitalised in Iquique, Chile, 31% in Barbados, and 6·5% in Martinique. Hospitalisation in stroke units lowers mortality and increases the chance of a good outcome.⁸ Stroke units have been organised in some institutions but they are not part of any national health-care policy in Latin America or the Caribbean.⁹⁹ The model of a comprehensive service through stroke units has been tested in Joinville, Brazil.¹⁰⁰ A different organisation of care has been adopted in some university hospitals with units that admit all acute patients with neurological disorders, with an emphasis on physiological monitoring and medical care and less on acute rehabilitation.¹⁰¹ Access to CT scans in patients with acute strokes is a potential marker of quality of care.⁶⁴ In the three community-based studies, the proportion of patients who had a CT scan before 30 days of onset was 91–96%. Another potential marker of quality of care is the proportion of patients discharged on long-term aspirin.⁶⁴ The WHO-PREMISE (Prevention of Recurrences of Myocardial Infarction and Stroke) project is a descriptive cross-sectional study that investigates current practice patterns of secondary prevention of stroke and cardiovascular diseases in ten countries (including Brazil) through an interview. This study found that among 160 consecutive patients with stroke recruited from primary, secondary, and tertiary settings in Porto Alegre, 58·8% were discharged receiving aspirin, 16·9% statins, 33·1% beta-blockers, and 44·4% angiotensin-converting-enzyme inhibitors, which shows a low penetration of secondary prevention medication.¹⁰² In Joinville, Brazil, the proportion of patients with known atrial fibrillation who had a cerebral infarction and who should have been treated with oral anticoagulants was studied; 50% could have avoided the event if warfarin had been used.¹⁰³ In another study in Sao Paulo, Brazil, a survey found that only 55% of high-risk patients with atrial fibrillation received dose-adjusted warfarin.¹⁰⁴ In Mexico City, 47% of patients with non-valvular atrial fibrillation and cerebral infarction were discharged with oral anticoagulants. Patients who were given antiplatelets had the worst prognosis. Patients were less likely to

receive warfarin if they were functionally impaired at discharge or if they lived in a rural area.¹⁰⁵ Intravenous thrombolysis has been used in the treatment of acute ischaemic stroke on small scale¹⁰⁶ but not on a national basis. The time from stroke onset to hospital arrival is crucial for thrombolysis to be effective and studies in Lima, Peru,¹⁰⁷ Montevideo, Uruguay,³⁸ and Joinville, Brazil,²² reported delays in hospital admission. Cost is also an issue, especially for public-health systems, which hampers planning of thrombolysis for a subgroup of patients with ischaemic stroke in Latin America.

Even though there have been advances, there are few data on the availability of stroke units, neuroimaging, neurologists, thrombolysis, rehabilitation programmes and secondary prevention strategies, and compliance with treatments in Latin American and Caribbean populations.

Discussion

Stroke is already the leading or second single cause of death in many Latin American and Caribbean countries, although the rates are declining. Prospective data from the three rigorous population-based studies in the region show only some geographical variations in the incidence of total stroke, pathological subtypes, and stroke prognosis, most of which are non-significant and comparable to most other populations. The frequency and distribution of cardiovascular risk factors is also similar among the different communities, with some small differences that could explain part of the slight geographical variations. Further comparable studies are needed, controlling for confounders such as age, sex, and socioeconomic and ethnic factors. The prevalence of the major cardiovascular risk factors has been increasing in Latin America and the Caribbean,¹⁰⁸ and in low-mortality developing regions, the risk-factor profiles were similar to those in higher-income regions. Latin America and the Caribbean is a very heterogeneous region and according to the World Bank, most countries are in the third stage of the epidemiological transition, but some are in the first. This means that for most of this region, deaths from chronic diseases exceed mortality from infections and malnutrition. Nevertheless residents in some countries and underserved areas in others are still at risk of morbidity and mortality from malnutrition and infectious diseases,¹⁰⁹ which may cause stroke.⁷ In the third stage of transition in most countries, cardiovascular diseases are the leading causes of death with an initial rise in stroke and later a preponderance of coronary heart disease—this pattern was shown in a study comparing four Latin American countries in different stages of the epidemiological transition.¹¹⁰ In this scenario, the burden of stroke is likely to increase in Latin America and the Caribbean and preventive measures should be similar to those in developed countries.¹¹¹ There are several local, regional, and global initiatives to deal with the problem of stroke. Some

regional and local neurological societies have already published clinical guidelines, and health ministries are beginning to incorporate stroke and other chronic diseases on their agendas and budgets.⁹⁵ A comprehensive approach to the prevention and management of cardiovascular diseases through strong government leadership and intersectoral policies is needed.¹¹² Special attention should be paid to the prevention and treatment of hypertension and diabetes as leading cardiovascular risk factors in the region. The provision of organised care for stroke patients should also be a priority, including the organisation of stroke units, stroke outpatient clinics, and rehabilitation centres. Prompt access to neuroimaging, cardiac and vascular studies, and secondary prevention drugs should be guaranteed to as many patients as possible.

Sustainable and context-specific evidence-based prevention and management strategies for stroke need to be pursued and implemented locally and nationally in Latin America and the Caribbean. Leading authorities in stroke should seek ways to push the stroke agenda to increase research funds, health provision for patients with stroke, and public awareness. Phase 2 of the WHO-PREMISE project plans to provide technical assistance to country teams in order to develop and implement strategies to narrow the gaps for the secondary prevention of stroke and cardiovascular disorders. The long-term objective is to replicate these measures on a national scale and to extend the programme to other low-income and middle-income countries. The Global Stroke Initiative, a collaboration between WHO, the International Stroke Society, and the World Federation of Neurology, has three objectives: to increase awareness of stroke; to generate better surveillance data; and to use such data to guide improved strategies for prevention and management.¹ National stroke days and other public information campaigns are being implemented in some Latin American countries to raise awareness. Stroke surveillance through WHO STEPS Stroke has been designed to help countries get started in the collection of standardised data on stroke to understand the magnitude of disease occurrence in populations over time, estimate future resources needed for prevention, and measure the effect of public-health initiatives. Several low-income countries are already participating in this initiative, including some Latin American countries, such as Honduras.³⁰ The WHO STEPS Stroke surveillance system, which offers countries a framework for continuous standardised data collection, is potentially an important tool for measuring the effect of efforts to prevent stroke locally or regionally in Latin America and the Caribbean.

In summary, stroke is a public-health problem in Latin America and the Caribbean that should be a significant part of the public-health agenda. Efforts need to be focused on better prevention and control of cardiovascular risk factors, population-based epidemiological studies

and surveillance, and improvement of health-service provision for patients with stroke.¹¹³

Contributors

PL wrote the epidemiology and cardiovascular risk factor section, to which JF, BL, and AJMH contributed substantially. CS wrote the tropical causes of stroke section, to which MM also contributed. AH wrote the management section with substantial input from JF, BL, PL, AJMH, JF, BL, and LJ, and RS did the literature search and selected the articles. MM reviewed the literature on Central America, and JF reviewed the Portuguese articles. PL wrote the first draft and AH edited it. All authors helped to write the summary, introduction, and discussion sections.

Conflicts of interest

PL and CS have been paid honoraria and received travel grants by Sanofi-Synthelabo Chile, Boehringer Ingelheim, and GlaxoSmithKline. AH has received travel honoraria from Bayer. AJMH, MM, JF, BL, LJ, and RS have no conflicts of interest.

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