Incidence, 30-day case-fatality rate, and prognosis of stroke in Iquique, Chile: a 2-year community-based prospective study (PISCIS project)

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Summary

Background The epidemiology of stroke in Latin-American populations and variation of subtypes between communities are unclear. Our aim was to ascertain prospectively the incidence of first-ever stroke in the predominantly Hispanic-Mestizo population of Iquique, a city in the northern desert region of Chile.

Methods We prospectively identified all possible cases of stroke and transient ischaemic attacks between July 1, 2000, and June 30, 2002, from several overlapping sources. Patients were rapidly assessed by two field neurologists. Standard definitions for incident cases, stroke, transient ischaemic attack, pathological type, and infarction subtype were used. All cases identified were adjudicated by at least two stroke neurologists and followed up at 6 months. Incidence rates of first-ever strokes were calculated from the population of Iquique (214 526) according to the national census of 2002.

Findings Of 380 cases of stroke identified, 292 were incident. CT scans were done in 267 (91%) patients and the mean time to scan was 2·2 days. The hospital admission rate was 71% (207/292). The overall age-adjusted incidence rate of first-ever stroke was 140·1 per 100 000 (95% CI 124·0–156·2). The incidence rates per 100 000 according to pathological type were: infarcts 87·3, intracerebral haemorrhage 27·6, and subarachnoid haemorrhage 6·2. The 30-day and 6-month case-fatality rates were 23·3% and 33·0%, respectively.

Interpretation Our results show incidence rates of stroke similar to those reported in other community studies. Although the proportion of intracerebral haemorrhages was higher than reported in previous studies, the overall incidence was not, which could indicate a slightly lower incidence of ischaemic strokes in this population than in other countries. The prognosis was similar to that found in other population-based studies.

Introduction

Stroke was the second most common cause of death in Chile after acute myocardial infarction[1] in 2000, was the most frequent cause of admission in people older than 65 years in 1990,[2] and accounted for about 1% of all discharges in 2001.[3] However, the incidence of stroke in Chile is unknown. This information is much needed owing to major health reform in Chile[4] and progressive ageing of the population.[5] Stroke mortality trends are decreasing in Chile as well as in other countries in South America,[6] but mortality statistics have limitations and biases, especially for a disorder such as stroke for which a substantial proportion of cases are not fatal and diagnostic and coding methods have varied over time.[7] Incidence and case-fatality data are more informative than mortality statistics and when properly obtained can be used to compare rates, assess factors that explain ethnic and geographical differences, and thus improve knowledge about possible causes and prevention.[8] Previous studies in Chile and other Latin-American countries, based solely on hospital data banks, have reported high frequencies of intracerebral haemorrhage and lacunar infarction.[9–12] This pathological distribution is similar to that described in Hispanic, Native American, and African American population groups in the USA,[13] but such a comparison has been controversial because of the difficulties encountered in the definition of a population that is a mixture of ethnic groups with a Hispanic language and cultural background.[14] PISCIS (Proyecto Investigación de Stroke en Chile: Iquique Stroke Study) is a community-based, prospective study of stroke incidence in a predominantly Hispanic and Mestizo population in Latin America. The project is an epidemiological field study undertaken in the city of Iquique, Chile, to ascertain the incidence of stroke by age, sex, stroke subtype, and distribution of risk factors, the case-fatality rate, the recurrence rate, and outcome at 6 months. We report the incidence of first-ever stroke, 30-day case-fatality rates, previously known vascular risk factors, prognosis, and cause of death at 6 months.

Methods

We organised the study according to the criteria for studies of stroke incidence, proposed by Sudlow and Warlow.[15] We attempted to identify all cases of stroke, without bias towards hospital admission or outpatient referral, and to obtain brain CT or necropsy reports for every patient as soon as possible. A pilot study was undertaken for 6 months in 1999 to test the methods and feasibility.[16]

In 2000, the population of the northern city of Iquique was 181 984 according to the projections of the 1992 national census, and in 2002, it was 214 526 according to the 2002 national census. Iquique is a port surrounded by a desert and is 300 km from the nearest other city. Owing to this geographical isolation, patients with acute stroke are unlikely to seek medical attention elsewhere. There are a public general hospital with 350 beds, two small private hospitals with 20 beds each, four general outpatient clinics or primary-health centres, four military-service outpatient facilities, and two small private walk-in trauma centres. About 200 physicians work in the city and many have private practices. There are three CT scanners, one in the general hospital and two in the small private hospitals; two facilities for carotid duplex ultrasonography; one for trans-oesophageal echocardiography; one for conventional catheter angiography; and none for MRI.

We checked prospectively many cases from overlapping sources. Daily checks were done of emergency consultation and admission charts in the three hospitals and hospital admission and discharge lists (hot pursuit). Weekly checks were undertaken of intensive-care units, all relevant medical wards, and order forms for CT or carotid duplex ultrasonography, and monthly checks were undertaken of nursing homes, outpatient clinics, and death certificates (cold pursuit). Patients were identified between July 1, 2000, and June 30, 2002. Follow-up continued until Dec 31, 2002, for the last patient registered. This period was extended another 2 months for completion.

We encouraged the referral of all patients with any symptom potentially associated with stroke or transient ischaemic attack to be assessed by the two field neurologists (LP and AE). Regular meetings were held during the pilot phase, and every 3 months thereafter, with the general (family) practitioners of the four public outpatient clinics and with internists, ophthalmologists, neurosurgeons, neurologists, geriatricians, and cardiologists working in the city. Orders for CT and carotid duplex scans and death certificates were checked manually to ensure inclusion of all patients not seen or referred to the study neurologists. To identify all admitted patients, we did daily checks of admission and discharge lists for the general city hospital and weekly checks for the two private hospitals. Medical wards, intensive care units, and neurosurgical beds were checked weekly for any patients not referred to our study physicians. The National Statistic System Hospital Discharge Registry was checked to identify further cases on the basis of categories I61–I69 and G45 of the International Classification of Disease, tenth revision.

A public information campaign called “mind your brain” (“cuide su cerebro”) was launched to inform the public about symptoms of stroke and about the study. The campaign included interviews in the local newspaper and TV station, and flyers and posters distributed in public waiting rooms. Physicians were kept informed through a newsletter and a pocket-card that provided information about dedicated phone numbers for referrals and signs and symptoms of stroke. Local health authorities and city officials were notified of the project.

Patients who were admitted and those referred to outpatient clinics were examined as soon as possible by one of the two field investigators (LP or AE). A structured neurological examination and CT were done for all patients who were alive at the time of identification. An investigator (LP) or a study nurse (CT) reviewed the medical records of those patients identified through other sources, and relevant clinical and radiological information was extracted. Radiological data were reviewed in all cases by a radiologist who was aware of the clinical signs and symptoms.

All patients were followed up at 1 month and 6 months after the stroke by a trained study nurse who undertook an interview, directly or by telephone, with the patient or his or her next of kin with a standard questionnaire. Information about recovery, dependency, stroke recurrence, and cause of death were recorded. A modified Rankin score was obtained for all cases and clinical notes and death certificates were checked when appropriate.

All clinical data and radiological images were sent to the central adjudication committee where two to four cerebrovascular neurologists reviewed the data and categorised the patients by case, pathological subtype, infarct subtype, and cause, according to prespecified definitions. Cases were defined as individuals who had had a stroke and who had a permanent address in the city of Iquique during the study period, so that visitors were excluded. Cases of first ever in a lifetime stroke were defined as those without a clinical history of stroke independent of CT findings. Patients with a history of transient ischaemic attack who had a subsequent stroke were regarded as incident strokes, those with a history of stroke and a subsequent transient ischaemic attack were deemed recurrent cases, and those with incident stroke or recurrent stroke were categorised as any stroke.

A stroke was defined as rapidly developed signs of focal (or global) disturbances of cerebral function lasting longer than 24 h (unless interrupted by death), with no apparent non-vascular cause.[17] Transient ischaemic attack was defined as an acute loss of focal cerebral or ocular function with symptoms lasting less than 24 h that after adequate investigation was presumed to be a result of embolic or thrombotic vascular disease.[18]

Cases of stroke for which brain CT, undertaken on or before the 30th day from onset of symptoms, showed an area of low attenuation in a region compatible with the clinical picture or for which CT was normal but examination of the brain after death showed an area of cerebral infarction were regarded as infarction.[19] Intracerebral haemorrhage was categorised as cases of stroke for which brain CT undertaken less than 30 days from symptom onset showed an area of high attenuation in a region compatible with clinical signs and symptoms or for which post-mortem examination of the brain showed intracerebral haemorrhage.[19] Subarachnoid haemorrhage was regarded as cases with acute onset of severe headache, sometimes associated with loss of consciousness, seizures, or focal neurological signs not associated with trauma, and a brain CT scan showing subarachnoid or cisternal high attenuation, a non-traumatic lumbar puncture with more than 2×10^9 /L red blood cells or xanthochromic supernatant, or signs of subarachnoid haemorrhage at necropsy.[19] Uncertain cases were those with clinical features of stroke or subarachnoid haemorrhage, but without confirmation from investigations (mostly from death certificates), or with brain CT scans undertaken later than 30 days after symptom onset (mostly outpatients).[19]

Ischaemic strokes were further classified according to the Bamford classification.[20] Cardiovascular risk factors were: hypertension (a history of treated hypertension or current use of antihypertensive medication); diabetes (a history of diabetes or current treatment for diabetes mellitus); coronary-artery disease (history of angina, acute myocardial infarction, or coronary revascularisation); congestive heart failure (history of or current treatment for congestive heart failure); atrial fibrillation (known previous atrial fibrillation or current treatment for atrial fibrillation); hypercholesterolaemia (current treatment for hypercholesterolaemia); smoking (current smoker); and alcohol consumption (current moderate or heavy drinker was defined as >50 g per day, equivalent to 500 mL or two drinks of wine, 1000 mL of beer, or >5 units of spirits, or being intoxicated at least once a week).

Causes of death were divided into five categories. Neurological deaths resulted directly from the effects of the brain lesion—herniation, oedema, hydrocephalus, raised intracranial pressure, or a recurrent stroke. Complications of immobility included pneumonia and any chest infection leading to respiratory failure and death, urinary sepsis and other infections, pulmonary embolism, and pressure sores. Cardiac deaths included acute myocardial infarction, cardiac failure, and sudden death. Other deaths were from cancer and AIDS. Unknown deaths were those for which there was insufficient medical data for a conclusion as to the cause of death to be drawn.

When possible or clinically necessary, we measured blood-cell count, erythrocyte sedimentation rate, glucose concentration, blood urea, serum electrolytes, and blood lipids, and undertook electrocardiography, chest radiography, transthoracic echocardiography, or transoesophageal echocardiography, carotid duplex sonography, and catheter angiography, when appropriate. We recorded all relevant clinical, past medical, radiological, and laboratory investigations on precoded forms and entered them on an EPI-6 database (EpiInfo, version 6.04). We calculated incidence rates using the sum of the two populations as the denominator—ie, the projected population in Iquique in 2000, according to the 1992 national Census projections, plus the actual population of 2002, according to the 2002 national Census.[5] This calculation was done to account for immigration into the city. Incidence rates of first-ever strokes were adjusted to standard 2002 Chilean and Segis' European and world populations by the direct method. To enable comparison with other population-based studies, incidence was age-adjusted to those 55 years or older and those 45–84 years by use of Segis' world and European populations as standards, respectively.[21] We calculated CI for crude rates and for rates specific for age and sex on the assumption of a normal distribution

	Men		Women		Total population	
	Number of cases/ number at risk	Incidence rate (95% CI)	Number of cases/ number at risk	Incidence rate (95% CI)	Number of cases/ number at risk	Incidence rate (95% CI)
Age group, years						
0–24	7/91 608	7·6 (3–16)	1/87 445	1·1 (0·03–6·4)	8/179 054	4·5 (1·9–8·8)
25–34	3/34 096	8·7 (1·8–26·6)	1/32 167	3·1 (0·7–17·3)	4/66 462	6·0 (1·6–15·4)
35–44	10/31 394	31·8 (15·3–58·6)	4/30 905	12·9 (13·2–33·1)	14/62 300	22·5 (12·3–37·7)
45–54	27/22 190	121·6 (80·2–177)	16/20 984	76·2 (43·6–123·8)	43/43 174	99·6 (72·1–134·1)
55–64	50/11 819	423·0 (328·6–576·9)	23/11 862	193·9 (136·4–311·1)	73/23 682	308·2 (241·6–387·6)
65–74	31/6220	498·4 (338·6–707·4)	33/7619	433·1 (298·2–592·8)	64/13 838	462·5 (356·2–590·6)
75–84	28/2438	1148·5 (763·2–1659·9)	38/3928	967·4 (684·6–1327·8)	66/6366	1036·7 (801·8–1319·0)
≥85	8/500	1600 (690·8–3152·6)	12/1136	1056·3 (545·8–1845·2)	20/1836	1089·3 (665·4–1682·4)
All	164/200 466	81·8 (69·3–94·3)	128/196 046	65·3 (53·9–76·6)	292/396 712	73·6 (69·3–77·9)
Adjusted Chile*		103·2 (87·4–118·9)		86·5 (71·5–101·5)		97·4 (86·2–108·6)
Adjusted Europe†						140·1 (124·0–156·2)
Adjusted world ‡						108·2 (95·8–120·6)
Adjusted world §						94·1 (83·3–104·9)

*Total population of Chile according to 2002 census. †Segis' European population. ‡WHO world population. §Segis' world population.

Table 1: **Incidence rates per 100 000 population of first-ever stroke, by age and sex**

for counts greater than 100 and a Poisson distribution for counts less than 100. CI for age-adjusted rates were calculated according to the formula proposed by Keyfitz.[22] Proportions were compared by the χ^2 test or Fisher's exact test when appropriate, and the χ^2 test for linear trend in proportions was used to compare age-groups. All tests were two tailed.

The local ethics committee approved the study and, although informed consent was not obtained, no test beyond those of regular medical practice was done.

Role of the funding source

The sponsors had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

During the study period, 394 patients were identified as having had a stroke. Of these, 14 were later excluded by the adjudication committee. The reasons were lack of appropriate clinical data to establish diagnosis in 11 cases and brain metastasis, brain abscess, and hypoglycaemia in one case each. 292 patients were judged to have had a first-ever stroke, 20 a first-ever transient ischaemic attack, and 68 a recurrent stroke or a recurrent transient ischaemic attack. Of the patients with first-ever stroke, 196 (67%) were identified as such in the emergency department and 53 (18%) in outpatient clinics, 11 (4%) had strokes while in hospital for other reasons, 15 (5%) were identified through death certificates, and other sources provided information about 17 (6%) cases. For eight of those identified through death certificates, we were able to obtain clinical and imaging information; the other seven died at home and thus we based the diagnosis on the clinical judgment of the treating physician. The hospital admission rate was 71% (207/292).

Of the patients identified with first-ever stroke, 128 (44%) were women and 164 (56%) were men. The mean ages were 68·5 years (SD 14·6) and 61·2 years (16·6), respectively. 267 (91%) patients had brain CT within 30 days of symptom onset. The mean time from symptom onset to CT was 2·2 days (SD 4·6), and 211 (72%) underwent CT within 2 days of symptom onset. Many of the ambulatory patients were recruited from private practices where access to the two private CT scanners available in the city is quite fast. In one patient with subarachnoid haemorrhage, the diagnosis was made by lumbar puncture; in another case, the diagnosis was made at necropsy. All other cases without CT were labelled as undetermined (n=23). The reasons for not doing CT were rapid death (nine [39%]), refusal by the patient or family to undergo transfer to health facility (two [9%]), late consultation (five [22%]), and unknown or films unavailable for assessment by a study neurologist (seven [30%]).

	Infarction		Intracerebral haemorrhage		Subarachnoid haemorrhage	
	N	Incidence rate (95% CI)	N	Incidence rate (95% CI)	N	Incidence rate (95% CI)
Men						
0–24	2	2·2 (0·2–7·8)	5	5·5 (1·8–12·7)	0	–
25–34	1	2·9 (0·07–16·3)	1	2·9 (0·07–16·3)	1	2·9 (0·07–16·3)
35–44	4	12·7 (3·5–33)	4	12·7 (3·5–32·6)	1	3·9 (0·08–17·7)
45–54	12	54·1 (28–94·5)	9	40·6 (18·5–77·0)	4	18·0 (4·9–46·1)
55–64	32	271 (185–382)	14	118·4 (64·7–198·7)	2	16·9 (2–61)
65–74	26	418 (273–612)	4	64·3 (17·5–164·6)	0	–
75–84	21	861·4 (533–1317)	4	164·1 (44·7–420·1)	0	–
≥85	5	1000 (324–2334)	2	400 (48·4–1444·9)	0	–
All	103	51·4 (46·3–56·5)	43	21·4 (18·1–24·7)	8	4·0 (1·6–7·8)
Adjusted Chile		63·0 (50·8–75·1)		24·4 (17·1–31·7)		4·1 (1·3–6·9)
Women						
0–24	1	1·2 (0·03–6·4)	0	–	0	–
25–34	1	3·1 (0·08–17·8)	0	–	0	–
35–44	3	9·7 (2–28·4)	1	3·2 (0·08–18)	0	–
45–54	8	38·1 (14·4–75·1)	5	23·8 (7·7–55·6)	2	9·5 (1·2–34·4)
55–64	15	126·5 (70·7–208·6)	6	50·6 (18·6–110·1)	1	8·4 (0·2–46·9)
65–74	24	315·0 (201·8–468·7)	4	52·5 (14·3–134·4)	2	26·2 (3·2–94·8)
75–84	21	534·6 (330·9–817·2)	9	229·1 (104·7–434·9)	2	50·9 (6·2–183·9)
≥85	9	792·3 (362·3–503·9)	1	88·0 (2·2–490·5)	0	–
All	82	41·8 (33·3–51·9)	26	13·3 (8·6–19·4)	7	3·6 (1·4–7·3)
Adjusted Chile		52·0 (40·7–63·2)		16·1 (9·9–22·2)		4·2 (1·1–7·3)
Total Population						
0–24	3	1·7 (0·3–4·9)	5	2·8 (0·9–6·5)	0	–
25–34	2	3·0 (0·4–10·9)	1	1·5 (0·04–8·4)	1	1·5 (0·04–8·4)
35–44	7	11·2 (4·5–23·1)	5	8·0 (2·6–18·7)	1	1·6 (0·04–8·9)
45–54	20	46·3 (28·3–71·5)	14	32·4 (17·7–54·4)	6	13·9 (5·1–30·3)
55–64	47	198·5 (145·8–263·9)	20	84·4 (51·6–130·4)	3	12·6 (2·6–37)
65–74	50	361·3 (268·2–476·4)	8	57·8 (24·9–113·9)	2	14·4 (1·7–52·2)
75–84	42	659·7 (475·5–879·8)	13	204·2 (108·7–349·2)	2	47·1 (3·8–113·5)
≥85	14	762·5 (416·9–1279·4)	3	163·4 (33·9–477·5)	0	–
All	185	46·6 (39·8–53·3)	69	17·4 (13·5–22)	15	3·8 (21–6·2)
Chile*		59·6 (51·0–68·2)		20·0 (15·3–24·7)		4·5 (2·2–6·8)
Europe†		87·3 (74·7–99·9)		27·6 (21·1–34·1)		6·2 (3·0–9·3)
World‡		66·5 (56·9–76·1)		22·1 (16·9–27·3)		4·9 (2·4–7·3)

*Chile total population according to 2002 census. †Segis' European population. ‡Segis' world population.

Table 2: **Age-specific and sex-specific incidence rates per 100 000 of first-ever stroke, by pathological subtype**

The crude annual incidence of any stroke was 95·8 per 100 000 population (95% CI 86·2–105·4). The crude annual incidence of first-ever stroke was 73·6 per 100 000 (69·3–77·9) in Iquique and 97·4 per 100 000 (86·2–108·6) when adjusted to the Chilean population of 2002 (table 1). The age-adjusted incidence of any stroke was 168·4 per 100 000 (151·9–184·8) and the incidence rates of first-ever stroke were 140·1 per 100 000 and 94·1 per 100 000 when adjusted to the European and world populations, respectively. The crude annual incidence of

	Frequency (n=185)	Incidence rate (95% CI) (number at risk=396 712)	Case-fatality rate at 30 days	
			Deaths	Rate (95% CI)
TACI	31 (17%)	7·8 (5·3–11·1)	18	58·1 (34·4–91·8)
PACI	49 (27%)	12·3 (9·1–16·3)	6	12·2 (4·5–26·6)
LACI	79 (43%)	19·9 (15·8–24·8)	4	5·1 (1·4–13·0)
POCI	26 (14%)	6·5 (4·3–9·6)	5	19·2 (6·2–44·9)

TACI=total anterior circulation infarction; PACI=partial anterior circulation infarction; LACI=lacunar infarction; POCI=posterior circulation infarction.

Table 3: **Frequency, incidence, and case-fatality rate of first-ever infarction, by subtype**

	Number/ number at risk	Case-fatality rate (95% CI)
Infarction	33/185	17·8 (12·3–25·1)
Intracerebral haemorrhage	20/69	28·9 (17·7–44·8)
Subarachnoid haemorrhage	6/15	40·0 (14·7–87·1)
Undetermined	9/23	39·1 (17·9–74·3)
Total	68/292	23·3 (18·1–29·5)

Table 4: **Case-fatality rates of incident stroke, by pathological subtype**

recurrent stroke was 17·1 per 100 000 (13·3–21·7) and the age-adjusted rate was 32·6 per 100 000 (24·8–40·3). Table 2 shows the age-specific and sex-specific incidence rates for first-ever stroke by pathological subtype. Stroke incidence was higher in men than in women and increased progressively with each decade of life. The frequencies of stroke types in people aged 45–84 years were: ischaemic infarction 159 (65%), primary intracerebral haemorrhage 55 (23%), subarachnoid haemorrhage 13 (5%), and undetermined 17 (7%).

The crude incidence of first-ever transient ischaemic attack was 5 per 100 000 (95% CI 3·1–7·8) and the age-adjusted rate to the European population was 8 per 100 000 (4·5–11·5). Table 3 shows the incidence of ischaemic stroke subtypes according to the Oxfordshire Community Stroke Project (OCSP) classification.[20] Around 40% of incident strokes in this population were lacunar infarctions and a smaller proportion were partial infarctions of the anterior circulation or infarctions of the posterior circulation. Since severe strokes are usually over-represented in non-community studies, that the proportion of total anterior circulation infarctions or severe strokes in our study was 16·8%, with an incidence rate of 7·8 (95% CI 5·3–11·1), is noteworthy. 68 patients died during the first month of follow-up. The case-fatality rate at 30 days (table 4) did not differ between men (26·2% [95% CI 18·9–35·3]) and women (24·2% [16·4–34·4]). Case fatality was higher for intracerebral haemorrhage, subarachnoid haemorrhage, and undetermined stroke than for ischaemic stroke (table 4).

Table 5 shows the prevalence of known previous cardiovascular risk factors and use of antithrombotic agents. The prevalence of previous transient ischaemic attacks was low, although incidence was also low, which suggests that our finding is probably accurate. The prevalence of previous diabetes mellitus was consistently high for total strokes and for each pathological subtype compared with findings of previous studies.[23] The rates of previous hypertension, atrial fibrillation, myocardial infarction, and current smoking habit were all similar to those reported in previous population-based studies.[23] Previous heavy drinking was probably underestimated since many patients under-report their drinking habits. The distribution of risk factors in the incident-stroke population is similar to that of incident ischaemic stroke or intracranial haemorrhage. The only significant differences between pathological types were age and the proportion with hypercholesterolaemia, which were higher in ischaemic strokes. Previous hypertension was most prevalent in the ischaemic stroke subgroup and heavy drinking was most common in the intracerebral haemorrhage subgroup; however, these differences were not significant. The use of antithrombotic medication was reported in 20–25% of incident cases, probably associated with previous known cardiovascular disease.

Follow-up data were available for 282 (97%) incident cases. Ten patients were lost to follow-up because of wrong addresses (nine) or because they had moved out of the country (one). At 6 months after symptom onset, 93 (33% [95% CI 26·6–40·4%]) patients had died and 132 (47% [33·4–60·2%]) were living independently. There were no significant differences by sex, but the risk of a poor outcome rose with age (p=0·03) (table 6). The 6-month case-fatality rate was higher for patients with first-ever haemorrhagic stroke—subarachnoid (46·2%, 16·9–100%) or intracerebral (38·8%, 25·3–56·6%)—than for those with infarction (27·9%, 20·7–36·6%) (table 7). The same was true for patients with severe ischaemic strokes (TACI), which had the worse overall prognosis with 96·7% of patients dead or dependent at 6 months (table 7). Patients with lacunar infarction had

	Total strokes (%, 95%CI) (n=292)	Cerebral infarction (n=186)	Intracerebral haemorrhage (n=69)	p*
Base line characteristics				
Men	164 (56%; 50·2–61·9)	103 (55%)	43 (62%)	0·3
Mean (SD) age, years	64·4 (16·1)	66·5 (14·9)	58·5 (18·3)	0·0004
Premorbid risk factors				
Previous TIA	10 (3%; 1·6–6·3)	6 (3%)	1 (1%)	0·3
Hypertension	175 (60%; 54–65·5)	123 (66%)	37 (54%)	0·06
Diabetes mellitus	60 (21%; 15·7–26·4)	43 (23%)	11 (15%)	0·1
Hypercholesterolaemia	42 (14%; 10·4–19·3)	32 (17%)	4 (6%)	0·02
Atrial fibrillation	31 (11%; 7·2–15·1)	23 (12%)	7 (10%)	0·6
Myocardial infarction	25 (9%; 5·5–12·6)	16 (9%)	4 (6%)	0·3
Congestive heart failure	11 (4%; 1·8–6·7)	8 (4%)	3 (4%)	0·6
Current smoker	43 (15%; 10·6–19·8)	28 (15%)	12 (17%)	0·6
Heavy drinker	37 (13%; 8·9–17·5)	20 (11%)	13 (19%)	0·08
Premorbid antithrombotic use				
Antiplatelets	51 (18%; 13·0–22·9)	34 (18%)	13 (19%)	0·9
Anticoagulants	15 (5%; 2·8–8·4)	12 (7%)	3 (4%)	0·3

*Cerebral infarction versus intracerebral haemorrhage. TIA=transient ischaemic attack.

Table 5: **Premorbid cardiovascular risk factors and use of antithrombotic medication in patients with incident stroke, cerebral infarction, and intracerebral haemorrhage**

	mRankin 0–2		mRankin 3–5		mRankin 6	
	n	Rate (95% CI)	n	Rate (95% CI)	n	Rate (95% CI)
Sex						
Men (n=157)	79	50 (39·8–62·7)	25	16 (10·3–23·5)	53	34 (25·3–44·1)
Women (n=125)	53	42 (31·8–55·5)	32	26 (17·5–36·1)	40	32 (22·9–43·6)
Age-group, years						
0—44 (n=25)	9	36 (16·5–68·3)	6	24 (8·8–52·2)	10	40 (19·2–73·6)
45—64 (n=110)	67	61 (47·2–77·3)	17	15 (9·0–24·7)	26	24 (15·4–34·6)
65—84 (n=129)	51	40 (29·4–51·9)	32	25 (16·9–35·0)	46	36 (26·1–47·6)
≥85 (n=18)	5	28 (9·0–64·8)	2	11 (1·3–40·1)	11	61 (30·5–100·0)
Total (n=282)	132	47 (33·4–60·2)	57	20 (15·3–26·2)	93	33 (26·6–40·4)

Table 6: **Prognosis at 6 months after first-ever stroke, by sex and age-group**

the best outlook at 6 months compared with patients with other types of infarction. The main causes of death in the first month after stroke were neurological, followed by those related to complications of immobility, especially pneumonia, which accounted for 21% of all deaths within 30 days. After this time, the main causes of death were either unknown or cardiac related (table 8).

Discussion

According to the 2002 census, 11% of the population in Chile are 60 years or older. With a mean life expectancy of 76 years, the projection is that 18% of the population will be older than 60 years in 2025, thus incidence of stroke in Chile will probably rise. The 2002 census also showed that 334 337 (2%) inhabitants had some form of disability, of which 40% were physical and 30% were mental disabilities. Most of the physical disabilities are concentrated in those older than 65 years, and possibly many of these are the result of a stroke. Our study reported the incidence of first-ever stroke in a well-defined population in Latin America.

We made every effort to ensure that we identified all cases of stroke using the quality criteria for population-based studies of stroke proposed by Sudlow and Warlow in 1996.[8] Our data for yearly admission rates for stroke were checked against and accorded with the Chilean National Hospital Discharge Registry data, which reported 212 total strokes or transient ischaemic attacks in Iquique in 2001. Identification of stroke patients not admitted to hospital and of others by their death certificates ensured as near complete ascertainment of the stroke population as practicable with the resources available. Unfortunately, we did not look for cases in special high-risk groups such as vascular clinics, which were assessed in the OXVASC study;[23] however, our finding that 30% of stroke patients were not admitted to hospital was surprising because, although we do not have exact information, the general belief is that most stroke patients are admitted to hospital for treatment. Nevertheless, this finding has been commonly reported in other community-based studies.[24] Although we did not assess the probability of completeness of ascertainment either by direct or indirect methods, we used the supplementary search strategies used in OXVASC, which have been shown to identify 98% of incident strokes.[25]

Incidence rates of first-ever stroke, adjusted to the European population per 1000 person-years, are similar to those found in studies in Erlangen, Germany (1·3),[26] London, UK (1·3),[27] Auckland, New Zealand (1·4),[28] Martinique (1·6),[29] and Oxford, UK (1·62),[23] but are lower than with other population-based studies.[30–34] When age-standardised to people aged 55 years or older, the incidence rate per 1000 person-years of all strokes was 4·9, which is within the range of 4·2–6·5 reported in most studies analysed recently by Feigin and colleagues.[24] Incidence rates per 1000 person-years for stroke subtypes fell within the range of most population-based studies published after 1990, age-standardised to people older than 55 years, with the exception of ischaemic stroke, the rate of which was slightly under the lower range previously published, albeit with overlapping CI.[24] The same is true for comparison of rates age-standardised to people aged between 45 and 84 years, as proposed by Sudlow and Warlow[15] (table 9). These findings lend support to the notion that there are small geographical variations in incidence of all strokes and of pathological subtypes when comparable methods are used and when age standardisation includes the older age-groups in which most stroke events occur. Nevertheless, some cases of very mild ischaemic stroke or transient ischaemic attack could have been missed because some patients did not seek medical attention, and thus the proportion of haemorrhages or severe strokes might have increased as a result. The proportion of severe strokes, according to the OCSP classification, was similar to that reported by Bamford and colleagues.[20]

Stroke subtype	mRankin 0–2		mRankin 3–5		mRankin 6	
	n	Rate (95% CI)	n	Rate (95% CI)	n	Rate (95% CI)
Intracerebral haemorrhage (n=67)	22	33 (20·6–49·7	19	28 (17·1–44·3)	26	39 (25·3–56·6)
Subarachnoid haemorrhage (n=13)	6	46 (16·9–100)	1	8 (0·19–42·8)	6	46 (16·9–100)
Undetermined (n=20)	5	25 (8·1–58·3)	5	25 (8·1–58·3)	10	50 (23·9–91·9)
Infarction (n=183)	99	54 (43·9–65·9)	33	18 (12·4–25·3)	51	28 (20·7–36·6)
TACI (n=31)	1	3 (0–9·6)	10	32 (15·5–59·3)	20	65 (39·4–99·6)
PACI (n=48)	23	48 (30·4–71·9)	14	29 (15·9–48·9)	11	23 (11·4–41·0)
LACI (n=78)	61	78 (59·8–100)	9	12 (5·3–21·9)	8	10 (4·4–20·2)
POCI (n=25)	13	52 (27·7–88·9)	5	20 (6·5–46·7)	7	28 (11·3–57·7)

TACI=total anterior circulation infarction; PACI=partial anterior circulation infarction; LACI=lacunar infarction; POCI=posterior circulation infarction.

Table 7: **Outcome at 6-months after first-ever stroke, by pathological and infarction subtype**

	<30 days after stroke (n=68)	30 days to 6 months after stroke (n=26)	Total (n [%; 95% CI])
Neurological	43 (63%)	2 (8%)	45 (48%; 35·3-64·7)
Complications of immobility			
Pneumonia	14 (21%)	5 (20%)	19 (20%; 12·3-31·9)
Sepsis and other infections	3 (4%)	2 (8%)	5 (5%; 1·7-12·5)
Cardiac	2 (3%)	6 (23%)	8 (9%; 3·7-16·9)
Other	0	2 (8%)	2 (2%; 0·3-9·4)
Unknown	6 (9%)	8 (31%)	14 (15%; 8·2-25·2)
Total	68 (73%)	25 (27%)	93

Table 8: **Causes of death after stroke**

	All strokes	Ischaemic stroke	Intracerebral haemorrhage	Subarachnoid haemorrhage
Iquique: >55 year age-group*	4·9 (4·3–5·5)	3·3 (2·8–3·8)	0·90 (0·6–1·2)	0·16 (0·04–0·3)
Iquique: 45–84 year age-group†	3·5 (3·0–3·9)	2·2 (1·9–2·5)	0·68 (0·5–0·9)	0·16 (0·07–0·2)
Feigin:[24] >55 year age-group*	4·2–6·5	3·4–5·2	0·3–1·2	0·03–0·2
Sudlow:[15] 45–84 year age-group†	2·4–6·3	1·8–3·5	0·26–0·6	0·04–0·19

*Segis' world population, †Segis' European population.

Table 9: **Age-standardised annual incidence (95% CI) per 1000 strokes, by pathological subtypes, in Iquique Chile and other population-based studies**

The incidence of first-ever stroke in the younger age-groups was especially high for men younger than 65 years. The same was found in Arcadia, Greece,[31] and in the OXVASC study.[23] In Iquique, this finding was mainly due to a high incidence of intracerebral haemorrhage in men in this particular age-group, possibly associated with factors such as high alcohol consumption[35] and significantly raised systolic blood pressure in men compared with women.[36]

The incidence of first-ever transient ischaemic attack was very low, with a ratio to strokes of one in 15, compared with a ratio of stroke to transient ischaemic attack of one in six (43 per 100 000) in OCSP[37] and one in three (58 per 100 000) in OXVASC.[23] This low ratio has been a concern for many years in Chile. A study of the history of transient ischaemic attacks in patients admitted to hospital with ischaemic stroke reported a rate of 18% in patients with previous ischaemic strokes, which is not as low as our findings, but lower than that reported in many previous studies.[38] A low incidence of transient ischaemic attacks has also been recorded in Japan,[39] a country that shares many genetic characteristics and health risks (eg, gastric cancer incidence) with Chile. Another possible explanation could be non-presentation for medical attention, as has been previously reported[37] and also suggested by Sacks and co-workers[40] who, in a survey of patients attending emergency departments in Valparaíso, Chile, showed that only 12% of patients with mild acute focal neurological symptoms sought medical attention immediately. The low incidence could also be due to under-ascertainment of cases that were not suspected as transient ischaemic attacks. However, we checked orders for carotid Duplex ultrasonography, echocardiography, and CT to identify cases seen by other specialists and not referred to neurologists so that cases suspected as transient ischaemic attacks should have come to our attention.[25] A low incidence of carotid disease in Chilean populations could also affect the incidence of transient ischaemic attacks. In fact, in well-studied hospital series with 100% carotid ultrasonographic studies, only 14% of patients had symptomatic arterial stenosis,[41] which is significantly less than reported in previous studies.[42]

We were interested that we did not find an overall higher incidence of primary intracerebral haemorrhage (table 2), as has been reported previously in Latin-American populations.[43] Most previous data came from hospital case series and were based on the proportional frequency of stroke subtypes. Even though the distribution of subtypes of strokes in Iquique shows a higher proportion of intracerebral haemorrhage than in many studies, the rate is nevertheless similar to that reported in Belluno, Italy,[44] and London, UK.[27] This high proportion could be due to the slightly lower incidence of ischaemic strokes in Iquique as well as in other Latin-American populations than in other countries and thus could be a matter only of proportions and not of true incidence.

We did not record ethnic origin, although our study population was predominantly Hispanic-Mestizo, which is representative of most of Chile where there is a very low proportion of people of single ethnic origin, whether white, black, Native American, or Asian. In fact, according to the 2002 National Census, only 5·9% regarded themselves as Native Americans in the city of Iquique.[5] Most studies in north America that have reported differences in stroke incidence by ethnic origin have been hospital based,[45,46] were subject to selection bias, and did not meet many of the criteria of stroke-incidence studies set out by Sudlow and Warlow[8] and updated by Feigin and co-workers in 2004.[47] Data for place of death according to ethnic origin suggest that Hispanic-Americans of all ages who have had strokes have a higher risk of dying in hospitals than non-Hispanic whites who were more likely to die at home or in nursing homes. Thus, non-Hispanic white patients with severe haemorrhages could have died at home rather than in the hospital and might not be counted.[48] The same finding was reported in a community-based study in Leicester, UK,[49] which looked at differences and similarities between stroke patients in south-Asian and white populations. The researchers showed that many of the differences in stroke incidence could be explained by lower admission rates in white patients and better survival in Asian than in white patients.[49] Our data show high admission rates for stroke, in a pattern similar to that for Hispanic patients in north America and for south-Asian patients in the UK.

Another potential source of bias in population-based studies that can affect the incidence rates of intraparenchymal haemorrhages is the timing of brain CT.[50] Wardlaw and colleagues[51] noted that in patients with mild strokes, late CT could fail to identify intracerebral haemorrhages in more than 75% of cases and concluded that to identify most haemorrhages, CT should be done within 8 days of the index stroke.[51] In our study, the mean time from symptom onset to CT was 2·2 days (SD 4·6), and 72% of patients underwent CT within 2 days of onset. In most population-based studies the time to CT after stroke was beyond 20 days, except in a few.[26,31,32] Of note is the fact that two of the studies with early CT[31,32] reported higher incidence of haemorrhages than most other populations. In hospital-based studies describing differences by ethnic origin, the timing of CT in relation to symptom onset is seldom reported and no firm conclusions can be drawn, even though scans are likely to be undertaken earlier and thus more haemorrhages would be identified especially among patients admitted for strokes.

The overall 30-day case-fatality rate for first-ever incident stroke in our study is very similar to that found in most population-based studies.[34] We have shown the case-fatality rate by pathological subtypes in Iquique to be lower than in Arcadia[31] or Belluno[44] and slightly higher than in Erlangen[26] or the OCSP.[52] There does not seem to be an over-representation of severe strokes in our study since the proportion of total-anterior-circulation infarction is very similar to that recorded in OCSP[20] and lower than that in London.[53] Ethnic origin has been linked to high case-fatality rates in Hispanic,[45] black,[49] and Maori and Pacific people[54] admitted to hospital in community studies. The reasons for these differences are not well understood but could be related to risk-factor predisposition and distribution. Some of the differences in case-fatality could also be explained by differences in stroke management since all patients with strokes in Iquique are cared for in general medical wards instead of stroke units.

There are very few previous reports of the frequency of premorbid risk factors in population-based studies. The distribution of risk factors in our study shows a higher proportion of men and of patients with hypertension and diabetes mellitus than in OXVASC[23] and a lower frequency of previous transient ischaemic attacks and hypercholesterolaemia. The frequencies of atrial fibrillation, previous myocardial infarction, and smoking were similar to previously reported rates. Admission rates could account for some but not all of these differences because patients admitted to hospital have higher rates of premorbid hypertension and hypercholesterolaemia than non-admitted patients with ischaemic strokes.[55] The distribution of vascular risk factors is also significantly affected by ethnic origin, both in population-based studies and in patients admitted to hospital with strokes.[56] Hispanic and Native American patients with strokes who have been admitted have higher rates of hypertension and diabetes and lower rates of hypercholesterolaemia and coronary-artery disease than white populations.[13] This distribution could be a risk factor for the development of small-vessel lacunar disease and intracranial haemorrhage and could reduce atherothrombotic or cardioembolic diseases.[12] The differences in known risk factors between pathological subtypes of stroke in our study are similar to those of previous studies, with high rates of heavy drinking, low mean age, and lower rates of hypercholesterolaemia in intracerebral haemorrhage.[12,57]

The long-term prognosis of first-ever stroke has been described in only a few population-based studies. Bamford and colleagues, in the OCSP,[52] recorded a 31% case-fatality rate at 1 year with a distribution by pathological and ischaemic stroke subtype very similar to that reported here. Closely similar results were also reported at 1 year in Erlangen, Germany,[26] and Arcadia, Greece.[58] The main difference between our findings and these three studies was a lower case-fatality rate for primary intracerebral haemorrhage. The reason could be the prompt identification of less severe cases of intracerebral haemorrhage in Iquique since CT was undertaken in most cases within 72 h of symptom onset, reducing possible misclassification bias. The proportions of patients functionally independent at 6 months overall and by subtype did not differ in Iquique from those shown in the OCSP at 6 months.[59] Rates of dependency and death increased with age in Iquique. Similarly, age was shown to be independently associated with dependency at 1 year, together with atrial fibrillation and depressed consciousness on admission in Arcadia.[58]

The causes of death at 30 days and 6 months followed a similar pattern and proportion to what has been described in other unselected populations.[60] These findings are not surprising and lend support to the notion that even in the community, initial efforts should be directed at decreasing the extent of brain damage caused by strokes and later on at reducing the effects of impairments, such as dysphagia and aspiration pneumonia, as well as implementing secondary prevention measures for cardiovascular deaths.

Extrapolation of these data to other Latin-American populations should be done cautiously, and our findings need to be repeated in new community-based studies. Nevertheless, with these data we can estimate that there are about 15 000 patients with new strokes in Chile each year, 33% of whom die and 20% survive but are dependent at 6 months. The current health reform identifies stroke as a major health problem and will guarantee a minimum standard of health services based on evidence-based national clinical guidelines, which is a much-needed leap forward. Nevertheless, primary prevention efforts should be directed at decreasing this annual number of new strokes.

Contributors

P M Lavados and C Sacks were responsible for the literature search, planning, writing of the protocol, the information campaign, case adjudication, and analysis of data. F Araya, R Salinas, W Feuerhake, and G Alvarez participated in the planning and did most of the case adjudication. L Prina, A Escobar, and C Tossi identified and examined each case and did all the follow-up. M Galvez reviewed all the CT films. P M Lavados wrote the first draft and all authors helped to write the manuscript.

Conflicts of interest statement

P M Lavados and C Sacks have received honoraria and travel grants from Sanofi-Synthelabo Chile, Boehringer Ingelheim, and GlaxoSmithKline. F Araya and C Tossi have received honoraria by Sanofi-Synthelabo Chile. L Prina and A Escobar have received travel grants by Sanofi-Synthelabo Chile. G Alvarez, W Feuerhake, M Galvez, and R Salinas declare that they have no conflict of interest.

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