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Manuel Correia, Mário R. Silva, Ilda Matos, Rui Magalhães, J. Castro Lopes, José M. Ferro and M. Carolina Silva

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# Prospective Community-Based Study of Stroke in Northern Portugal

## Incidence and Case Fatality in Rural and Urban Populations

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**Background and Purpose**—Mortality statistics indicate that Portugal has the highest stroke mortality in Western Europe.

Data on stroke incidence in Northern Portugal, the region with the highest mortality, are lacking. This study was designed to determine stroke incidence and case fatality in rural and urban populations in Northern Portugal.

**Methods**—All suspected first-ever-in-a-lifetime strokes occurring between October 1998 and September 2000 in 37 290 residents in rural municipalities and 86 023 living in the city of Porto were entered in a population-based registry. Standard definitions and comprehensive sources of information were used for identification of patients who were followed-up at 3 and 12 months after onset of symptoms.

**Results**—During a 24-month period, 688 patients with a first-ever stroke were registered, 226 in rural and 462 in urban areas. The crude annual incidence was 3.05 (95% CI, 2.65 to 3.44) and 2.69 per 1000 (95% CI, 2.44 to 2.93) for rural and urban populations, respectively; the corresponding rates adjusted to the European standard population were 2.02 (95% CI, 1.69 to 2.34) and 1.73 (95% CI, 1.53 to 1.92). Age-specific incidence followed different patterns in rural and urban populations, reaching major discrepancy for those 75 to 84 years old, 20.2 (95% CI, 16.1 to 25.0) and 10.9 (95% CI, 9.0 to 12.8), respectively. Case fatality at 28 days was 14.6% (95% CI, 10.2 to 19.3) in rural and 16.9% (95% CI, 13.7 to 20.6) in urban areas.

**Conclusions**—Stroke incidence in rural and urban Northern Portugal is high compared to that reported in other Western Europe regions. The high official mortality in our country, which could be explained by a relatively high incidence, was not because of a high case fatality rate. (*Stroke*. 2004;35:2048-2053.)

**Key Words:** epidemiology ■ fatal outcome ■ incidence ■ stroke

Among the 28.1 million deaths caused worldwide by noncommunicable disease in 1990, stroke accounted for 4.4 million, being the second leading cause of death after ischemic heart disease.<sup>1</sup> Portugal ranked the highest among Western Europe countries in stroke mortality during the period from 1985 to 1994.<sup>2</sup> Despite a significant decline in mortality in this period, stroke was still the leading cause of death in 1999, accounting for 20% of all deaths,<sup>3</sup> and age-standardized mortality was 170 per 100 000 for men and 142 per 100 000 for women. Besides the relatively high mortality, the recently reported incidence in western central Portugal was also high, 240.2 per 100 000.<sup>4</sup>

Unlike Western European countries, but similar to Eastern European countries, Portugal (particularly the Northern region) has a marked contrast between urban and rural populations; stroke mortality ranges from 254 to 298 per 100 000 in the Northeast predominantly rural areas to 164 per 100 000

in Porto.<sup>3</sup> Comparing incidence of stroke in these populations may add important knowledge about cause and prevention. A community-based prospective register of stroke was thus initiated in Northern Portugal, including urban and rural populations. This article presents incidence and case fatality data for a 2-year registration period.

### Subjects and Methods

The Neurological Attacks prospective community register (ACINrhc project) was a community-based study of incidence and outcome of first-ever-in-a-lifetime stroke and transient focal neurological symptoms and signs. The study was designed to meet the criteria proposed by Malmgren et al<sup>5</sup> and Sudlow and Warlow<sup>6</sup> for “ideal” population-based studies.

### Study Area and Population

The study population comprised everyone registered at 3 health centers in Porto, where 71 general practitioners (GPs) provide care

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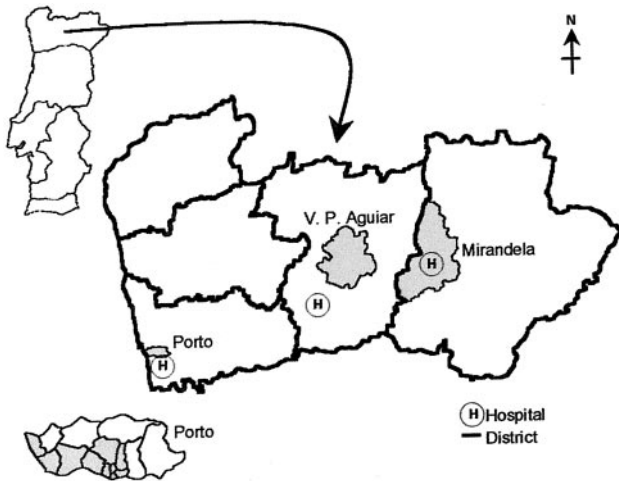
From Serviço de Neurologia (M.C., J.C.L.), Hospital Geral de Santo António, Porto, Portugal; Serviço de Neurologia (M.R.S.), Hospital de S. Pedro, Vila Real, Portugal; Serviço de Neurologia (I.M.), Hospital Distrital de Mirandela, Mirandela, Portugal; Departamento de Estudos de Populações (R.M., M.C.S.), Instituto de Ciências Biomédicas de Abel Salazar, Universidade do Porto, Porto, Portugal; Serviço de Neurologia (J.M.F.), Hospital de Santa Maria, Lisboa, Portugal.

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**Figure 1.** Map of Portuguese northern region showing urban and rural areas included in the study (shaded).

for the residents in 10 city administrative divisions, and at 2 health centers (29 GPs) from the rural municipalities of Miranda and Vila Pouca de Aguiar (VPAguiar) in the northeast region (Figure 1).

The Portuguese National Health Service (NHS) is assumed to have universal coverage through a network of health centers and hospitals, providing free medical care to all inhabitants. Since 1998, patient registration involves the assignment of a unique identification number, which constituted an accurate age–sex register to estimate the size of the study population on the September 30, 1999 (mid-study period). The main reason for studying these populations was the NHS network established within the northern region. The Hospital Geral de Santo António (HGSA) receives all patient referrals from this part of the city and from the 2 northeast districts. The 2 district hospitals with neurological care, emergency departments, and computed tomography (CT) scan facilities are connected with the health centers at Miranda and VPAguiar.

Based on the 2001 census, the study involved  $\approx 36\%$  of the city population, those inhabiting the old part of Porto, covering an area of 13.6 km<sup>2</sup> where the population density is 7028 per kilometer<sup>2</sup>. This is an aged population, with 20.4% being older than 64 years. In contrast, the 2 municipalities in the northeastern districts include 2 rural towns and surroundings covering a wider area, 878 km<sup>2</sup>, and the population density is  $\approx 40$  per kilometer<sup>2</sup>; 19% of the population is older than 64 years.

### Case Ascertainment and Follow-Up

Before starting the study, authorization from the Northern Region Health Authorities was sought. The objectives and study design were then explained to the directors of the collaborating health centers. To ensure complete registration, at each health center a doctor/nurse team was assigned to be study coordinators.

Patients were identified by using overlapping sources of information: GP reports from routine appointments, home visiting, and from the 24-hour emergency service at the VPAguiar health center; reports from neurologists at the hospital outpatient clinics and emergency departments and reports of patients admitted to hospital who had a stroke during their hospital stay. In rural areas, GPs also provided information about patients in nursing homes, whereas in Porto a regular contact was established. Information from private practice patients was sought by contacting neurologists from other hospitals.

A study neurologist examined all suspected patients, and a CT scan was performed soon after the event. Patients from Porto were examined at a special study outpatient clinic or during their hospital stay. Patients from rural areas were examined at the district hospitals, and those from VPAguiar also at the health center ward visited by a study neurologist once per week.

Indirect sources of information were sought: daily checks of admissions to emergency departments, discharge records from study

hospitals *International Classification of Disease, Ninth Revision*, codes 430 to 438, 342, 781); death certificates indicating that the main or secondary cause of death registered was stroke, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, cerebral thrombosis, cerebral atherosclerosis, senile dementia, dementia, senility, or unknown; registers from out-of-hospital emergency care; head CT scan and cerebral angiography lists at the radiology and neuroradiology departments and autopsies performed at the pathology department or at the Medical Forensic Institute in Porto. For this “cold pursuit” of cases, the hospital and/or GP medical records were reviewed to check details of any previous stroke events and risk factors.

If a patient died soon after the event, we attempted to obtain additional information from an eyewitness. For patients unable to communicate or those identified by death certificate, we interviewed close relatives or other suitable informants.

Registration of patients began on October 1, 1998, and continued until September 30, 2000. Surveillance of all sources of information continued for a further 2 months to ensure full registration. Study neurologists at the outpatient clinics assessed all patients at 3 and 12 months after the event. At one city health center, patients were only contacted by telephone 1 year after the event.

The principal investigator reviewed the information collected for each patient. Throughout the study period, GPs received a report on their patients registered in the study, and every 2 months a periodic newsletter with the updated results was sent to all collaborators.

The Ethics Committee of HGSA, where the study Coordination Centre was located, approved the study. Informed consent was obtained from each participant or from the next of kin, when appropriate, before any clinical assessment.

### Definitions

Stroke was defined according to the WHO definition as “rapidly developing clinical symptoms and/or signs of focal, and at times global (applied to patients in deep coma and to those with subarachnoid hemorrhage), loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin.”<sup>7</sup> Pathological types of stroke were classified according to Sudlow and Warlow standard definitions.<sup>8</sup> Strokes were classified as of undetermined pathological type when there was no brain CT scan performed within 30 days, no autopsy, and no lumbar puncture or angiography in case of suspected subarachnoid hemorrhage.

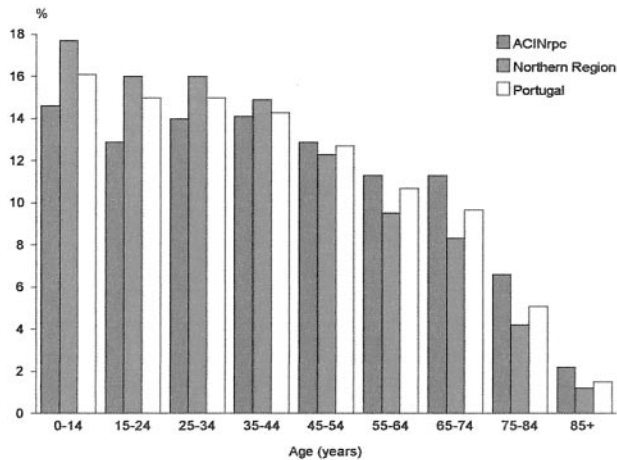
### Statistical Methods

Incidence is reported as crude rates and age-standardized rates to the Portuguese and standard European populations.<sup>9</sup> The 95% CIs for incidence were calculated using the Poisson distribution. Case fatality was assessed at 28 days and 3 and 12 months after onset, and the corresponding CIs were calculated by the Wilson “score” method.<sup>10</sup>

### Results

The study population comprised 123 112 individuals registered at 5 health centers on September 30, 1999, 37 089 from rural areas, and 86 023 from Porto. In the 2001 census, the population living in the study areas was 130 004, with a slightly lower female/male ratio than the study population in rural (1.1) and urban areas (1.2). Twenty percent of the study population was aged 65 years or older compared with 14% in the Northern Region and 16% in the entire country (Figure 2).

During the study period, 802 patients were notified with suspected stroke and 1229 with transient focal symptoms. After clinical assessment, a first stroke was confirmed in 688 patients, with 643 correctly identified and 45 out of those suspected of having transient focal symptoms. Recurrent events or incorrect diagnoses were the main reasons for excluding 159 patients.



**Figure 2.** Age structure of study population in rural and urban areas compared with the 2001 census results.

From “hot-pursuit,” 535 patients (77.8%) were included in the study; this proportion is higher in rural areas, mainly because of an early referral from GPs (Table 1). Out of the 399 patients with a hospital-based notification, 19 had the first stroke during their hospital stay for another reason. Based on “cold-pursuit,” a further 153 patients were included. Of 477 scrutinized death certificates, 315 had stroke as first cause of death; of these, only 27% were correctly classified. Furthermore, the corrected cause of death was a stroke in 6 of the 162 death certificates stating other causes. Overall, 92 patients who died from a stroke were identified, 20 because of a recurrent event and 32 not yet found by previous methods.

The included patients were more often women (58.7%). In general, patients from rural areas were older than those from urban areas. A study neurologist examined 656 patients, and 80.3% of these were examined within the first 48 hours after onset of symptoms. CT scan was performed in 96.9% of patients, and in 1.5% of these, CT was performed >30 days after onset (1 with a magnetic resonance imaging scan). Fifteen patients out of the 21 without CT were identified from death certificates. Most of the strokes were ischemic (76.2%), 16.1% were primary intracerebral hemorrhage.

The crude overall annual incidence of a first stroke per 1000 population was 2.79 (95% CI, 2.59 to 3.00). Adjusting for the Portuguese population, it was 2.34 (95% CI, 2.14 to 2.53) and 1.81 (95% CI, 1.64 to 1.97) adjusted to the European standard population (Table 2). The crude annual incidence was 3.04 for men and 3.05 for women in rural areas; in urban areas, it was 2.35 and 2.94, respectively. The overall incidence increased with age in the rural and urban populations, but with a somewhat different pattern. Whereas in rural areas there was a sharp increase from 3.1 to 20.2 between 55 and 84 years, stabilizing afterward, in urban areas there was a steady but slower increase from 6.8 for those aged 65 to 74 years to 16.9 in the eldest. These patterns were the same in men and women.

The overall 28-day case fatality was 16.1% (95% CI, 13.6% to 19.1%), increasing to 22.1% (95% CI, 19.2% to 25.3%) at 3 months and to 29.4% (95% CI, 26.1% to 32.9%) at 12 months (Table 3). For all 3 time periods, there was a

**TABLE 1. Assessment of Patients Included in the Rural and Urban Areas**

	Rural, % (n=226)	Urban, % (n=462)
<b>First Source of Information</b>		
Direct	94.7	69.5
Health center	48.7	5.6
Hospital	46.0	63.9
Indirect*	5.3	30.5
Women	51.8	62.1
<b>Age, y†</b>		
All	74 (67–80)	72 (63–81)
Men	72 (66–78)	69 (60–76)
Women	76 (70–81)	74 (65–83)
<b>Patient Assessment</b>		
Emergency services	91.2	92.0
In-patient admission	52.2	57.8
<b>Delay Between Onset and Assessment, h‡</b>		
0–24	75.9	69.3
25–48	7.3	9.6
>48	16.8	21.1
CT scanning performed	96.0	97.4
<b>Delay Between Onset and CT Scanning, h</b>		
0–24	65.4	69.1
25–48	14.7	14.4
>48	19.8	16.4
<b>Type of Stroke</b>		
Cerebral infarction	77.9	75.3
Primary intracerebral hemorrhage	14.6	16.3
Subarachnoid hemorrhage	2.7	3.7
Undetermined	4.9	4.1

\*Emergency records, hospital discharge list, death certificate, others.

†Median and interquartile range.

‡Excluding 6 rural and 26 urban patients identified by death certificate.

stable increase in case fatality with age until 75 to 84 years, followed by a significant increase in the eldest, which was more marked in rural than in urban areas.

## Discussion

The ACINrpc project presents the first epidemiological evidence on stroke incidence and case fatality in Portugal, focusing the urban–rural dichotomy. Very few studies comparing rural and urban populations were performed, restricted either in age range or in population denominators.<sup>11,12</sup> Because it is a population-based study prospectively designed fulfilling the standard recommended criteria, it provides high-quality data for an accurate measurement of incidence and case fatality.

Because the NHS has universal coverage, differences in the distribution of registered patients and those of the population residing in the corresponding geographical area were irrelevant, and even though detailed socioeconomic data of the study population were unavailable, it is likely that they were

**TABLE 2. Age- and Sex-Specific Annual Incidence per 1000 for Stroke in Rural and Urban Areas in Northern Portugal (1999–2000)**

Sex/Age	Rural			Urban		
	N/N at Risk	Rate	95% CI	N/N at Risk	Rate	95% CI
<b>Men</b>						
0–14	0/3032	0	—	0/6101	0	—
15–24	0/2840	0	—	0/4850	0	—
25–34	1/2491	0.20	0.01–1.12	2/5227	0.19	0.02–0.69
35–44	1/2518	0.20	0.01–1.11	10/5276	0.95	0.45–1.74
45–54	3/2056	0.73	0.15–2.13	17/5168	1.64	0.96–2.63
55–64	18/1931	4.66	2.76–7.37	34/4202	4.05	2.80–5.65
65–74	44/1950	11.28	8.20–15.15	57/3916	7.28	5.51–9.43
75–84	36/859	20.95	14.67–29.01	42/1991	10.55	7.60–14.26
≥85	6/226	13.27	4.87–28.89	13/519	12.52	6.67–21.42
Total	109/17903	3.04	2.47–3.62	175/37250	2.35	2.00–2.70
ASRP		2.99	2.43–3.56		2.23	1.89–2.56
ASRE		2.22	1.77–2.78		1.79	1.48–2.09
<b>Women</b>						
0–14	0/2996	0	—	1/5871	0.09	0–0.47
15–24	0/2845	0	—	1/5383	0.09	0–0.52
25–34	1/2641	0.19	0.01–1.05	1/6921	0.07	0–0.40
35–44	3/2468	0.61	0.13–1.78	12/7127	0.84	0.43–1.47
45–54	6/2124	1.41	0.52–3.07	21/6582	1.60	0.99–2.44
55–64	8/2262	1.77	0.76–3.48	32/5590	2.86	1.96–4.04
65–74	35/2225	7.87	5.48–10.94	76/5856	6.49	5.11–8.12
75–84	48/1217	19.72	14.54–26.15	87/3915	11.11	8.90–13.68
≥85	16/408	19.61	11.21–31.84	56/1528	18.32	13.84–23.80
Total	117/19186	3.05	2.50–3.60	287/48773	2.94	2.60–3.28
ASRP		2.53	2.03–3.04		2.13	1.84–2.42
ASRE		1.84	1.45–2.33		1.67	1.41–1.93
<b>All</b>						
0–14	0/6028	0	—	1/11972	0.04	0–0.23
15–24	0/5685	0	—	1/10233	0.05	0–0.27
25–34	2/5132	0.19	0.02–0.70	3/12148	0.12	0.03–0.36
35–44	4/4986	0.40	0.11–1.03	22/12403	0.89	0.56–1.34
45–54	9/4180	1.08	0.49–2.04	38/11750	1.62	1.14–2.22
55–64	26/4193	3.10	2.02–4.54	66/9792	3.37	2.61–4.29
65–74	79/4175	9.46	7.49–11.79	133/9772	6.81	5.65–7.96
75–84	84/2076	20.23	16.14–25.05	129/5906	10.92	9.04–12.81
≥85	22/634	17.35	10.88–26.27	69/2047	16.85	13.11–21.33
Total	226/37089	3.05	2.65–3.44	462/86023	2.69	2.44–2.93
ASRP		2.74	2.37–3.13		2.18	1.96–2.40
ASRE		2.02	1.69–2.34		1.73	1.53–1.92

ASRP indicates age-standardized rate of the Portuguese population, 1999; ASRE, age-standardized rate of the European population.

representative of urban and rural populations from Northern Portugal.

The inclusion of transient focal symptoms in the study scope avoided under-reporting of patients and the information network established permitted most patients to be assessed at hospital soon after symptom onset, improving the reliability

of results. However, despite our efforts to contact all clinical staff involved, direct notification was achieved for only 77.8% of patients, with a first notification from GPs for 6% of the city and 49% in rural settings. These heterogeneous values and those reported in other studies,<sup>13,14</sup> ranging from 6% to 84.6%, may reflect regional differences in health

**TABLE 3. Case Fatality After Stroke by Age and Time Period in Rural and Urban Areas in Northern Portugal (1999–2000)**

Period/Age (y)	Rural			Urban		
	N	%	95% CI	N	%	95% CI
<b>28 Days</b>						
≤64	4	9.8	3.9–22.6	13	9.9	5.9–16.2
65–74	9	11.4	6.1–20.3	18	13.5	8.7–20.4
75–84	10	11.9	6.6–20.5	25	19.4	13.5–27.1
≥85	10	45.5	26.9–65.3	22	31.9	22.1–43.6
Total	33	14.6	10.2–19.3	78	16.9	13.7–20.6
<b>3 Month</b>						
≤64	4	9.8	10.6–22.6	16	12.2	7.7–18.9
65–74	14	17.7	10.9–27.6	24	18.1	12.4–25.5
75–84	16	19.1	12.1–28.7	35	27.1	20.2–35.4
≥85	15	68.2	47.3–83.6	28	40.6	29.8–52.4
Total	49	21.7	16.8–27.5	103	22.3	18.7–26.3
<b>12 Months</b>						
≤64	5	12.2	5.3–25.5	22	16.8	11.4–24.1
65–74	17	21.5	13.9–31.8	30	22.6	16.3–30.4
75–84	25	29.8	21.0–40.3	49	38.0	30.1–46.6
≥85	16	72.7	51.9–86.9	38	55.1	43.4–66.2
Total	63	27.9	22.4–34.1	139	30.1	26.1–34.4

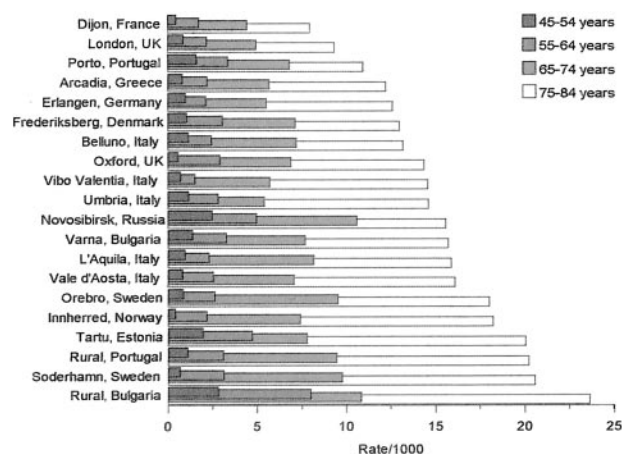
service organization and accessibility. Overall, 4.7% of patients were discovered from review of death certificates, a value within the range of those reported in other studies<sup>14,15</sup> (2% to 6%).

Most incidence studies have high admission rates, 80% in Tartu<sup>16</sup> and 92% in L'Aquila,<sup>13</sup> but rates similar to ours (56%) were found in Varna,<sup>12</sup> Oxfordshire,<sup>14</sup> and Novosibirsk.<sup>17</sup> It is sometimes not clear what is meant by "admitted to hospital," whether it is only attendance at the hospital emergency service, a 24-hour stay in a ward, or a more prolonged inpatient stay. This could be the explanation for the reported variation.

Compared with studies included in a recent systematic review,<sup>18</sup> ours has higher (97%) and quicker frequency of CT scan. The distribution of stroke types is similar to others reported elsewhere.<sup>19,14</sup>

The age-standardized incidence of a first stroke in Porto, 1.73 per 1000, was higher than that reported in Dijon, London, and Erlangen,<sup>19</sup> ranging from 1.00 to 1.36 per 1000. Figure 3 shows the higher incidence in the 45- to 64-year-old age groups in Porto compared with these cities. Only in Eastern European countries<sup>12,16,17</sup> are these age-specific incidences higher than in Portugal. For those aged 65 to 74 years, the incidence of stroke in Portugal is similar to those reported in Denmark,<sup>20,21</sup> Bulgaria,<sup>12</sup> Greece,<sup>22</sup> Italy,<sup>13,23–26</sup> and United Kingdom.<sup>14</sup> For the oldest, the cleavage is apparent between incidence reported in rural populations in Norway,<sup>27</sup> Portugal, Sweden,<sup>28,29</sup> and Bulgaria,<sup>12</sup> and that reported in urban populations.

The overall 28-day case fatality (16.1%) was close to that reported in most studies<sup>14,19,27</sup> but lower than that in Arca-



**Figure 3.** Age-specific stroke incidence in European community-based studies. Studies are ranked by increasing incidence in the 75- to 84-year-old age group.

dia,<sup>22</sup> L'Aquila,<sup>13</sup> and Novosibirsk<sup>17</sup> (>22%). The relatively high incidence of stroke in the younger age groups and/or the different death risks attributed to specific subtypes of ischemic stroke<sup>21</sup> may account for this result.

The differences in stroke incidence in rural and urban Northern Portugal are in accordance with official stroke mortality rates. However, the high official mortality, partially explained by a relatively high incidence, was not caused by a high case fatality rate. Death certificate inaccuracies may explain the differential between the death rate in our cohort and official rates. Stroke was confirmed in only 27% of death certificates indicating it as the underlying cause of death, which is proportionally lower than that confirmed in the Arcadia<sup>22</sup> or Melbourne<sup>15</sup> studies (53%).

In summary, the first-year results of the ACINrpc project show a relatively high incidence of stroke compared with similar Western European regions, although case fatality is close to those reported in these regions. This calls for attention from the Portuguese health planners to act on stroke risk factors to reduce the individual social and economic burden of stroke.

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