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Are Stroke Occurrence and Outcome Related to Weather Parameters? Results from a Population-Based Study in Northern Portugal

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Key Words

Epidemiology of stroke · Seasonal variation · Poisson model · Stroke incidence · Weather

Abstract

Background: Changes in meteorological parameters have been associated with cardiovascular mortality and stroke. The high incidence of stroke in Portugal may be modelled by short- or long-term weather changes whose effect may be different across stroke types and severity. ***Methods:*** Data include all patients with a first-ever-in-a-lifetime stroke registered in a population of 86,023 residents in the city of Porto from October 1998 to September 2000. Specific stroke types were considered and ischaemic stroke (IS) subtype was defined according to the Oxfordshire Community Stroke Projet classification and the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria. Information on daily temperature, humidity and air pressure was obtained from the National Meteorological Office. The Poisson distribution was used to model the daily number of events as a function of each weather parameter measured over different hazard periods, and the binomial model to contrast effects across subgroups. Differential effects of meteorological parameters and hazard periods upon stroke occurrence and outcome were analysed in a stepwise model. ***Results:*** Among the 462 patients registered, 19.6% had a primary intracerebral haemorrhage (PICH) and 75.3% an IS. Among patients with IS, 21.6% were total anterior circulation infarcts (TACIs), 19.8% partial anterior circulation infarcts (PACIs), 19.5% posterior circulation infarcts (POCIs) and 39.1% were lacunar infarcts (LACIs). The aetiology of IS was large artery atherosclerosis in 6.9%, cardioembolism in 23.3% and small artery occlusion in 35.6%. The incidence of PICH increased by 11.8% (95% CI: 3.8–20.4%) for each degree drop in the diurnal temperature range in the preceding day. The incidence of IS increased by 3.9% (95% CI: 1.6–6.3%) and cardioembolic IS by 5.0% (95% CI: 0.2–10.1%) for a 1 °C drop in minimum temperature in the same hazard period. The incidence of TACIs followed the IS pattern while for PACIs and POCIs there were stronger effects of longer hazard periods and no association was found for LACIs. The relative risk of a fatal versus a non-fatal stroke increased by 15.5% (95% CI: 6.1–25.4%) for a 1 °C drop in maximum temperature over the previous day. ***Conclusions:*** Outdoor temperature and related meteorological parameters are associated with stroke occurrence and severity. The different hazard periods for temperature effects and the absence of association with LACIs may explain the heterogeneous effects of weather on stroke occurrence found in community-based and hospital admission studies. Emergency services should be aware that specific weather conditions are more likely to prompt calls for more severe strokes.

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Introduction

The association between temperature and mortality from all causes was described in a cross-country European study, showing that Portugal has the highest coefficient of seasonal variation in mortality among 14 countries despite having the highest mean winter temperature (–3.5 to 13.5°C) [1]. Deaths from acute myocardial and cerebral infarction contribute to the excess winter mortality [2–4], but routine mortality statistics may over-report the number of stroke deaths [5, 6] confounded by post-stroke complications. On the other hand, the incidence of stroke in most countries has a seasonal pattern, peaking during winter [7–9], with a lesser frequency in spring [10, 11], autumn [12] or summer months [13]. These seasonal/monthly effects are important to adopt preventive measures and to estimate the overall hospital and/or stroke units' workload, but fell short of demonstrating meteorological factors underlying and triggering stroke occurrence, in particular a first-in-a-lifetime stroke.

Irrespective of a seasonal effect, an association between weather parameters and hospital admissions for stroke was found in several studies [14–18], pointing out the short-term effects of temperature, atmospheric pressure as well as their short-term variations (24–48 h). In prospective community-based incidence studies, heterogeneous results concerning the effect of outdoor temperature on the incidence of stroke have been reported [12, 19, 20]. The high incidence of stroke in Portugal [5] may in part be explained by exposure to aggressive meteorological conditions. Moreover, it has been suggested that mortality increases to a greater extent during falls in temperature in regions with warm winters and in populations with cooler homes [21]. Portugal, and in particular the city of Porto, with its maritime climate and traditionally unheated homes, represents a 'natural experimental environment' to test whether outdoor temperature or other meteorological parameters are associated with the occurrence of stroke. Since different aetiological mechanisms/risk profiles are present in specific stroke types, we may hypothesize that these effects will be different according to stroke type and severity. Moreover, the effects of each parameter may be different according to the hazard period.

Materials and Methods

Identification and Classification of Stroke Patients

All first-ever-in-a-lifetime strokes registered in a population of 86,023 residents in the city of Porto between October 1998 and September 2000 were included. Case ascertainment methods included direct referrals by general practitioners and hospital admissions as well as routine checking contacts with nursing homes, private hospitals/practices and review of death certificates/autopsy findings. Details on methods for identification of patients have been provided elsewhere [5]. All patients were examined by neurologists, and CT scans were performed; for those who died soon after the event or were identified by death certificates, information was given by relatives or an eye witness. Stroke was defined according to the WHO as 'rapidly developing clinical symptoms and/or signs of focal, and at times global loss of cerebral function (patients in deep coma or cerebral haemorrhage), with symptoms lasting more than 24 h or leading to death, with no apparent cause other than of vascular origin' [22]. Pathological types of stroke were defined according to Sudlow and Warlow [23] and the ischaemic stroke (IS) subtype by the Oxfordshire Community Stroke Project (OCSP) classification [24] and the aetiology according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria [25]. For patients identified away from the event onset, classification relied primarily on medical record documentation. A stroke was considered to be fatal if death occurred within 28 days.

Meteorological Characteristics and Data

The city of Porto is situated on the right bank and very close to the mouth of the river Douro, in northern Portugal, and had a population of about 250,000 in the 2001 Census, comprising 15 administrative divisions. The study evolved in 10 of these divisions, the catchment area of the Hospital de Santo António. Porto has a Mediterranean climate, with warm dry summers and mild rainy winters, but unlike the coastal south of Europe, it is often windy and usually cooler in winter with rainy weather for long periods. Daily maximum (T_{max}) and minimum temperature (T_{min}) (°C), relative humidity (%), atmospheric pressure at sea level (hPa), and total precipitation (mm/m^2) at the Observatório da Serra do Pilar were obtained from the National Meteorological Office. This weather station provides data representative of the southeast Porto catchment area. Besides the crude values of meteorological data available we have also considered temperature variations within 1 day, i.e. diurnal temperature range (DTR), since it has been described to be associated with acute stroke death [26].

Statistical Analysis

The description of stroke types and IS subtypes includes the daily mean of events and the respective 95% confidence interval (95% CI), stratified by season. Case fatality by season is also described. The Poisson distribution was used to model the daily number of events as a function of each weather parameter using a log-link function [27]. Generalized additive Poisson models were used alternatively, to check whether explanatory variables should enter the model as linear terms or smoothed functions with varying degrees of freedom (d.f.), enabling some flexibility in the shape of the function describing the relation. For ascertaining the effect of meteorological variables on daily stroke occurrence, a series of models were considered for exposure at different hazard periods before the event – the previous 24-hour value and the averaged values for the previous 7- and 14-day periods. Using a stepwise procedure, the final model for the specific event was built, considering as predictors the values for the three periods, besides the seasonal effect. Finally, the binomial distribution (logistic model) was used to estimate the relative risk of a fatal stroke

Table 1. Distribution of patient characteristics and vascular risk factors by types and subtypes of IS

Diagnosis/prognosis	All		Age ≥65 years		Women	
	n	%	n	%	n	%
All strokes	462		331	71.6	287	62.1
Fatal stroke[1]	78	16.9	65	83.3	54	69.2
Pathological types						
PICH	78	16.9	46	59.0	48	61.5
IS	348	75.3	259	74.4	215	61.8
OCSP classification						
TACI	75	21.6	66	88.0	59	78.7
PACI	69	19.8	60	87.0	47	68.1
LACI	136	39.1	86	63.2	74	54.4
POCI	68	19.5	47	69.1	35	51.5
TOAST criteria						
Large artery atherosclerosis	24	6.9	18	75.0	14	58.3
Cardioembolism	81	23.3	76	93.8	56	69.1
Small artery occlusion	124	35.6	78	62.9	69	55.6
Other determined/undetermined	119	34.2	87	73.1	76	63.9

[1] Death within 28 days from onset.

under different weather conditions. The effects (General Linear Model coefficients) are presented as the rate ratio for a unit drop in the temperature parameters (T_{max}, T_{min}, DTR) and unit increase in the other parameters for Poisson models and as the odds ratio for binomial models, with the respective 95% CI. The likelihood ratio χ^2 was used for comparing the fitted models against the intercept-only model. All analyses were done with the PASW Statistics 17.0 and by R statistical software Version 2.8.1. For statistical tests, a value <0.05 was used to indicate a significant association. For all analyses, we assumed a stable population at risk throughout the study period and so no adjustment for deaths and births were made.

Results

Patients' Characteristics

Based on a detailed clinical examination, including CT scans (97.4% of the patients and 83.5% within the first 48 h) and/or autopsy or lumbar puncture findings, a total of 462 patients were diagnosed with a first stroke. The stroke was fatal in 78 patients (16.9%) and 83.3% of them were ≥65 years old. The distribution according to pathological types and subtypes is described in table 1. Patients with primary intracerebral haemorrhage (PICH) were younger than those with IS (χ^2 = 7.5, d.f. = 1, p = 0.006) and those with a lacunar (LACI) or posterior circulation infarct (POCI) were younger than those with total circulation (TACI) or partial circulation infarct (PACI) (χ^2 = 22.9, d.f. = 3, $p < 0.001$). TACIs were more frequent in women compared with the remainder (χ^2 = 16.4, d.f. = 3, $p < 0.001$) and cardioembolism was more frequent in the oldest (χ^2 = 24.8, d.f. = 3, $p < 0.001$).

Seasonal Patterns in Weather Parameters and the Incidence of Stroke

Weather parameters varied across seasons as expected, low values of T_{max}, T_{min} and relative humidity and high values of atmospheric pressure in winter contrasting with high temperatures in summer, high relative humidity in summer and autumn and low atmospheric pressure in summer and spring (table 2). Precipitation attains the highest values in spring and autumn. There was no seasonality in the overall number of strokes, PICH or IS in spite of the increasing trend from summer to spring in the number of POCI (χ^2 = 8.8, d.f. = 3, $p < 0.04$). There was seasonality in case fatality from PICH, higher in summer (62.5%) compared to the remaining seasons (χ^2 = 8.0, d.f. = 3, $p < 0.05$). The overall trend in PICH, IS and the incidence of fatal stroke throughout the study period are shown in figure 1 together with the values of the meteorological parameters. T_{max} and T_{min} (not shown) were highly correlated (r = 0.78) as well as relative humidity and DTR (r = –0.63); DTR increased with T_{max} (r = 0.38) and decreased with precipitation (r = –0.45), while relative humidity increased with precipitation (r = 0.31). The

Table 2. Description of weather parameters, incident events and case fatality by season

Weather and population characteristics	All (n = 731)		Summer (n = 188)		Autumn (n = 178)		Winter (n = 181)		Spring (n = 184)	
	mean	95% CI	mean	95% CI	mean	95% CI	mean	95% CI	mean	95% CI
Weather parameters										
Temperature, °C										
Maximum	19.0	18.6–19.3	23.7	23.2–24.1	17.7	17.2–18.2	15.5	14.9–16.0	18.9	18.3–19.5
Minimum	10.3	10.0–10.6	14.7	14.4–15.0	9.1	8.5–9.7	6.2	5.7–6.7	10.9	10.4–11.4
Diurnal range	8.7	8.5–8.9	8.9	8.5–9.4	8.6	8.2–9.0	9.3	8.8–9.7	8.0	7.5–8.4
Relative humidity, %	77.0	76.2–77.9	78.1	76.6–79.5	78.8	77.3–80.3	74.2	72.2–76.2	77.1	75.6–78.6
Precipitation, mm/m^2	3.1	2.6–3.7	2.0	1.1–2.9	3.6	2.4–4.8	2.1	1.4–2.9	4.6	3.4–6.1
Rainy days, %	43.6	40.0–47.2	20.7	14.9–26.6	55.6	48.8–63.5	43.6	36.4–50.9	54.9	47.6–62.2
Atmospheric pressure (above 1,000 hPa)	19.4	18.9–19.9	16.3	15.8–16.9	21.5	20.5–22.5	23.8	22.8–24.9	16.2	15.3–17.1
Daily incident events[1]										
All strokes	7.3	6.6–8.0	5.9	4.8–7.2	7.4	6.0–8.8	7.9	6.5–9.3	8.1	6.7–9.5
PICH	1.3	0.9–1.5	1.1	7.6–1.6	1.3	0.8–2.0	1.2	0.7–1.9	1.5	0.9–2.2
IS	5.6	5.0–6.2	4.3	3.4–5.5	5.8	4.7–7.2	5.9	4.8–7.3	6.0	4.9–7.4
LACI	2.2	1.7–2.6	2.1	1.4–2.9	2.0	1.4–2.9	2.2	1.5–3.0	2.4	1.7–3.3
TACI	1.2	0.9–1.5	0.8	0.7–1.9	1.7	1.2–2.6	0.9	0.6–1.6	1.2	0.7–1.9
PACI	1.1	0.8–1.4	0.8	0.5–1.4	1.2	0.7–1.7	1.5	0.9–2.2	0.9	0.6–1.5
POCI	1.1	0.8–1.4	0.6	0.2–1.1	0.9	0.5–1.5	1.4	0.8–2.1	1.5	0.9–2.2
Case-fatality, %										
All strokes	16.9	13.5–20.3	21.9	13.6–30.1	14.0	7.7–20.4	14.6	8.4–20.9	17.8	11.2–24.4
PICH	33.3	22.9–43.8	62.5	38.8–86.2	30.0	9.9–50.1	22.2	3.0–41.4	25.0	7.7–42.3
IS	10.9	7.6–14.2	8.6	2.0–15.1	9.0	3.0–14.9	9.7	3.7–15.7	15.6	8.4–22.9

[1] Incidence per 1,000,000 population.

relative peaks in PICH (fig. 1) and fatal strokes closely followed the constant drop and relative trough in T_{max} and DTR.

Meteorological Parameters and the Incidence and Outcome of Stroke

The incidence of PICH was associated with DTR and precipitation; for 1°C drop in DTR over the preceding 24 h, the incidence increased by 11.8%, and for each millimetre of precipitation it increased by 3.1%, reaching 5.7% (95% CI: 0.7–11.1%) when considering the average 14-day period (table 3). The incidence of IS, on the other hand, was associated with both Tmax and T_{min} for the three hazard periods considered; for a 1°C drop in temperature, the incidence increased between 3.3 and 4.3%. There were nevertheless different hazard periods for the effects of T_{max} and T_{min} according to IS subtype; the incidence of TACI increased by 5.9% for a 1°C drop in T_{max} over the preceding 24 h, the incidence of PACI increased by 6.6% after a 1°C drop in T_{min} over the previous 24 h or 7-day period and that of POCI increased between 5.8 and 7.4% when T_{max}/T_{min} drops over different hazard periods. The incidence of LACI was not associated with any meteorological parameter. According to aetiology, only the incidence of cardioembolic IS increased by 5.0% (95% CI: 0.2–10.1%) for a 1°C drop in T_{min}. In the stepwise models, the most important predictors of PICH and IS were DTR and T_{min} in the previous 24 h, respectively (table 4). A 24-hour short-term effect of T_{min} and relative humidity was only associated with the incidence of TACI, while for PACI and POCI only the average 7/14 days effect of DTR, relative humidity and T_{max} were included in the model. Despite the effects of relative humidity in the incidence of LACI, the fit was no better than for the intercept-only model. Using the binomial model, the odds of a fatal versus non-fatal stroke increased by 15.5% (6.1–25.4%) after a 24-hour drop in T_{max}, and no significant differences were found across age and gender for IS. The contrasting short-term effects of DTR and T_{min} on the incidence of PICH and IS are displayed in figure 2a, b, and the effects of T_{max} on fatal and non-fatal strokes are displayed in figure 2c.

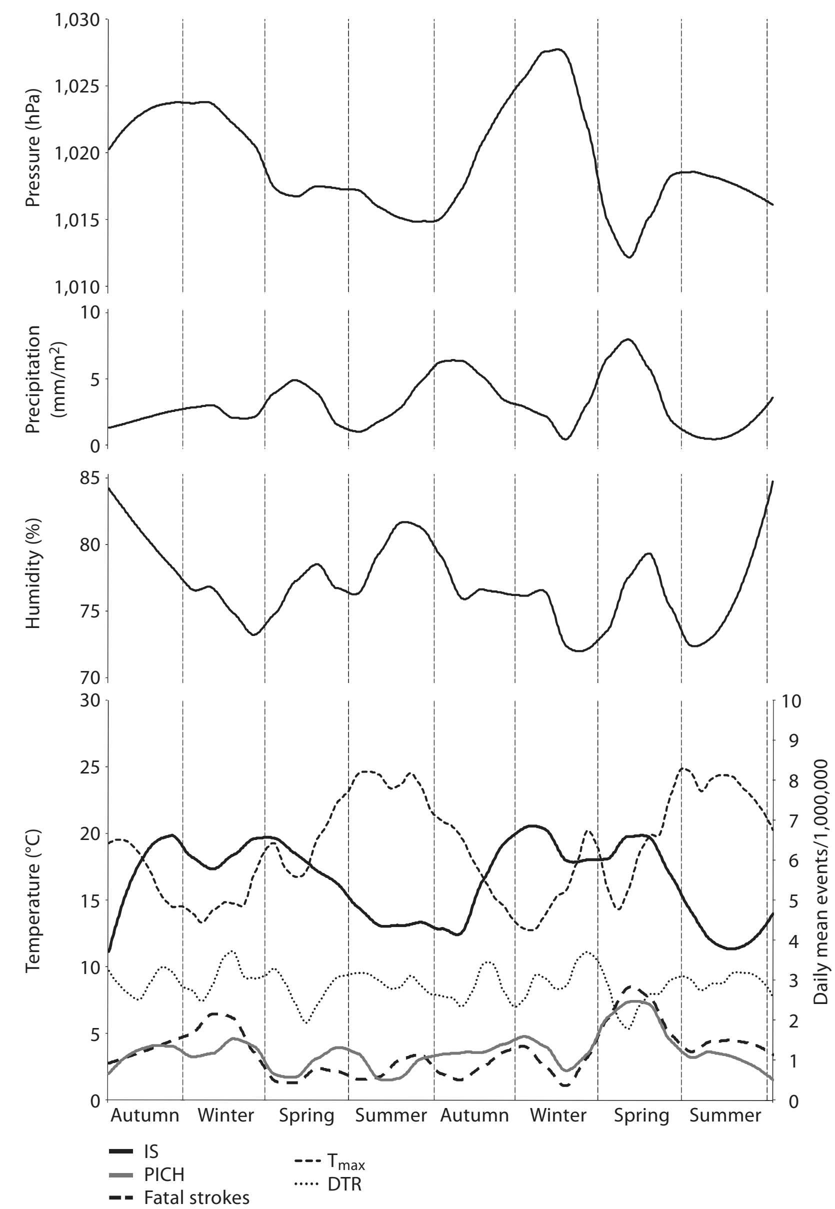

Fig. 1. LOWESS smoothed values of daily incidence of events (per million per day) and meteorological parameters (T_{max}, DTR, relative humidity, atmospheric pressure and precipitation) at Porto during the study period.

Discussion

This study shows that the high incidence of a first-ever-in-a-lifetime stroke in Portugal may be related to adverse effects of meteorological conditions. Moreover, irrespective of seasonal variations, these effects varied according to pathological type. The incidence of PICH was associated with precipitation and DTR while the incidence of IS was associated with temperature (T_{max}/T_{min}) and relative humidity. Moreover, the relative importance of the hazard period was associated with stroke severity and the OCSP classification. The predominant effects after a 24-hour hazard period were observed in the incidence of PICH, TACI, cardioembolic IS and fatal strokes. The effect of DTR and relative humidity was more important after a 7-day hazard period for PACI and after a 14-

Table 3. Association between incident stroke events and meteorological parameters according to exposure period

Weather parameter/ hazard period	PICH		IS									
			all		TACI		PACI		LACI		POCI	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Season												
Autumn	1.32	0.68–2.55	1.34*	0.98–1.84	2.04†	1.07–3.88	1.28	0.63–2.60	0.99	0.61–1.62	1.64	0.71–3.80
Winter	1.17	0.60–2.29	1.38†	1.01–1.88	1.11	0.54–2.31	1.71	0.88–3.32	1.07	0.66–1.73	2.42†	1.11–5.29
Spring	1.53	0.81–2.89	1.40†	1.03–1.91	1.39	0.70–2.77	1.10	0.53–2.27	1.18	0.74–1.88	2.73†	1.27–5.86
Temperature, ↓ 1°C												
Maximum												
Previous 24 h	1.05*	1.00–1.10	1.03‡	1.01–1.06	1.06†	1.01–1.12	1.03	0.98–1.08	1.02	0.98–1.06	1.04	0.98–1.09
Mean 7 days	1.04	0.98–1.10	1.04‡	1.01–1.07	1.04	0.98–1.10	1.04	0.98–1.11	1.02	0.98–1.07	1.07†	1.01–1.14
Mean 14 days	1.04	0.99–1.11	1.04‡	1.01–1.07	1.03	0.97–1.10	1.06*	1.00–1.13	1.02	0.98–1.07	1.07†	1.00–1.14
Minimum												
Previous 24 h	1.00	0.95–1.05	1.04§	1.02–1.06	1.04	0.99–1.09	1.07†	1.01–1.12	1.02	0.98–1.05	1.06†	1.01–1.11
Mean 7 days	1.02	0.96–1.08	1.04‡	1.01–1.07	1.02	0.97–1.08	1.07†	1.01–1.13	1.02	0.98–1.06	1.07†	1.01–1.14
Mean 14 days	1.03	0.98–1.09	1.04‡	1.02–1.07	1.03	0.97–1.09	1.06*	1.00–1.13	1.03	0.99–1.07	1.07†	1.00–1.13
Diurnal range												
Previous 24 h	1.12‡	1.04–1.20	0.99	0.95–1.02	1.04	0.96–1.12	0.92†	0.85–1.00	1.01	0.96–1.07	0.96	0.88–1.03
Mean 7 days	1.10	0.98–1.23	1.00	0.94–1.05	1.06	0.94–1.20	0.89*	0.78–1.01	1.02	0.94–1.12	0.98	0.86–1.11
Mean 14 days	1.07	0.92–1.24	0.98	0.91–1.05	1.02	0.88–1.19	0.97	0.83–1.14	0.95	0.84–1.06	0.99	0.84–1.16
Relative humidity, %												
Previous 24 h	1.02	0.99–1.04	1.00	0.99–1.01	1.03†	1.00–1.05	1.00	0.98–1.02	1.00	0.98–1.01	1.00	0.98–1.02
Mean 7 days	1.01	0.98–1.04	1.01	1.00–1.02	1.01	0.98–1.04	1.01	0.98–1.04	1.01	0.98–1.03	1.01	0.98–1.05
Mean 14 days	1.00	0.96–1.04	1.00	0.99–1.02	1.01	0.97–1.05	1.02	0.98–1.06	0.99	0.96–1.01	1.02	0.98–1.06
Precipitation, mm/m^2												
Previous 24 h	1.03‡	1.01–1.05	1.00	0.99–1.02	0.99	0.96–1.03	1.00	0.97–1.03	1.00	0.98–1.02	1.02	1.00–1.05
Mean 7 days	1.04*	1.00–1.08	1.00	0.98–1.03	1.01	0.97–1.06	0.97	0.91–1.03	1.01	0.97–1.04	1.02	0.97–1.07
Mean 14 days	1.06†	1.01–1.11	1.00	0.97–1.03	1.02	0.96–1.08	0.97	0.91–1.04	0.98	0.93–1.03	1.03	0.97–1.09
Atmospheric pressure, hPa												
Previous 24 h	1.00	0.97–1.03	1.01	0.99–1.02	1.02	0.98–1.05	1.02	0.98–1.05	1.00	0.98–1.02	1.01	0.97–1.04
Mean 7 days	1.00	0.97–1.04	1.01	0.99–1.03	1.01	0.98–1.05	1.03	0.99–1.08	1.00	0.98–1.02	1.02	0.98–1.06
Mean 14 days	0.99	0.97–1.01	1.01	0.99–1.02	1.00	0.98–1.02	1.04*	0.99–1.08	1.00	0.98–1.02	1.03	0.99–1.07

* $p < 0.1$, † $p < 0.05$, ‡ $p < 0.01$, § $p < 0.001$, otherwise $p > 0.1$; ↓ = decrease; RR = rate ratio

day period for POCI. No association was found for LACI, irrespective of the hazard period.

Despite an overall increase from summer to spring in the incidence of stroke, there was no evidence for a seasonal effect in our region, either for PICH or for IS. This pattern of variation has been previously described in other population-based studies undertaken in England, Italy, France and Russia [12, 19, 20, 28], while most studies based on registers of hospital admissions found evidence of seasonality [10, 11, 14]. This may reflect the fact of being 'community-based' thus including events, some of them reported by general practitioners, that otherwise would be excluded. Moreover, they report only associations for a first-ever-in-a-lifetime event, usually with low proportions of severe cases compared to hospital admission studies or emergency transport events, the latter also being more subject to misclassification bias [29–31]. The lack of seasonality in community-based studies may also result from the different seasonal effects on PICH and OCSP subtypes and their case mix in different populations. The incidence of PICH and TACI, peaking in spring and autumn compared to summer, points to the apparently steepest variation in T_{max}/T_{min} in these seasons whilst the incidence of PACI peaks in autumn and winter, pointing to possibly less acute effects of temperature. In addition, there appears to be a seasonal pattern in POCI and complete absence of seasonality in LACI, which represents as much as 39% of IS in this study.

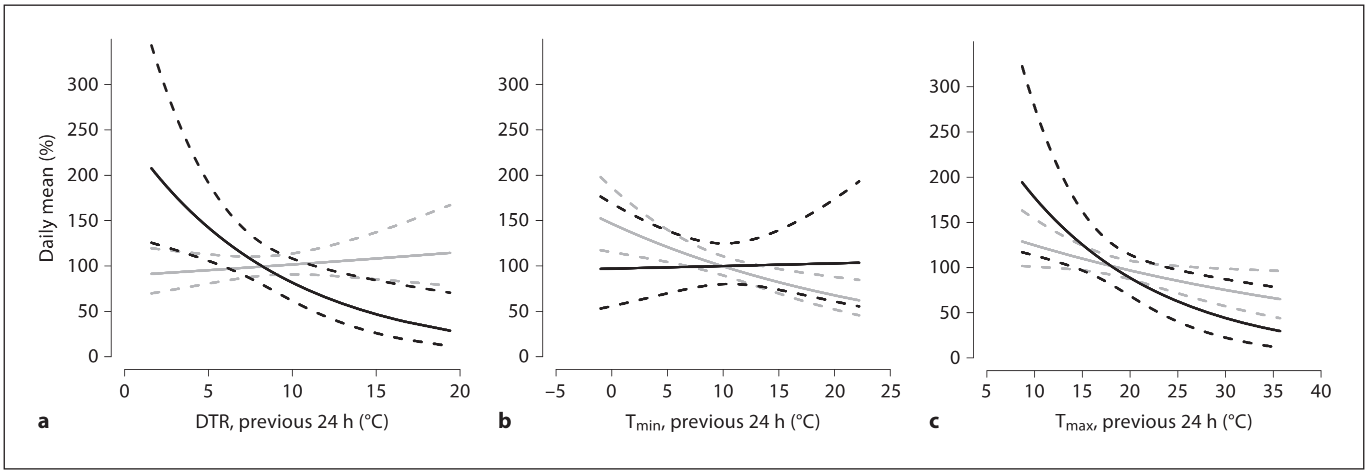

Fig. 2. Fitted number of PICH (black) and IS (grey) (scaled to be a percentage of mean daily strokes) plotted against DTR (**a**) and T_{min} (**b**); fitted number of fatal (black) and non-fatal (grey) strokes plotted against T_{max} (**c**). (Poisson models for the specific events). Dashed lines represent 95% CI.

Table 4. Association between incident stroke events and meteorological parameters according to exposure period (multiple-regression models)

Stroke type/weather parameter	RR	95% CI	p
PICH			(0.003)[1]
DTR – previous 24 h	1.12	1.04–1.20	0.003
IS			(0.001)
T_{min} – previous 24 h	1.04	1.02–1.06	0.001
IS subtype			
TACI			(0.011)
T_{min} – previous 24 h	1.05	1.00–1.11	0.045
RH – previous 24 h	1.03	1.01–1.06	0.018
PACI			(0.006)
DTR – mean 7 days	0.78	0.66–0.92	0.003
RH – mean 7 days	1.05	1.00–1.10	0.034
Tmax – mean 14 days	1.07	1.00–1.14	0.037
LACI			(0.061)
RH – mean 7 days	1.04	1.00–1.08	0.029
RH – mean 14 days	0.95	0.91–0.99	0.018
POCI[2]			(0.016)
DTR – mean 14 days	0.80	0.64–1.00	0.045
RH – mean 14 days	1.06	1.00–1.12	0.037
Fatal stroke[2]			(0.001)
T_{max} – previous 24 h	1.17	1.08–1.26	0.0001
Nonfatal stroke[2]			(0.004)
RH – mean 7 days	1.02	1.01–1.04	0.010
DTR – mean 14 days	0.88	0.81–0.96	0.005

For temperature (T_{max}, T_{min}, DTR), the coefficients are for a 1°C drop. RH = Relative humidity; RR = rate ratio.
[1] (value of p for the overall model).
[2] Coefficients adjusted for seasonal effect.

It was hypothesized that the effect of meteorological parameters would be evidenced in specific stroke types since the prevalence of different risk factors varies according to aetiology and clinical type [32, 33]. Despite the reduced number of events, PICH and TACI are more closely related to temperature in shorter hazard periods. Since their prognosis is worst, it is not surprising that a cold diurnal temperature (T_{max}) is associated with the likelihood of a fatal stroke. The fact that T_{min} (nocturnal) rather than T_{max} is a better predictor of overall and in particular cardioembolic IS, the incidence of IS may be related to the already reported circadian rhythm of IS, peaking in the morning and closely following the morning surge in blood pressure [34, 35]. Other factors that can trigger a stroke after cold exposure, such as activation of coagulation-related factors [36], haemoconcentration and increased blood viscosity [37] may have a greater impact in cardioembolic IS, the more frequent aetiological mechanism of TACI and PACI. On the other hand, the incidence of PICH is consistently associated with precipitation, increasing with the hazard period (24 h, 7 and 14 days). This is the empirical evidence of a fact already mentioned by neurologists at emergency departments all over the country – why do we see more strokes on rainy days? Our data confirm this hypothesis, but when considering the effect of all-weather parameters, DTR in the previous day seems to explain this effect. This triggering effect of drops in DTR, characteristic of spring months might be explained by the concurrence of other atmo-

spheric parameters since they coincide with rises in precipitation, relative humidity and steepest drops in T_{max} (inversely correlated with DTR) and atmospheric pressure (fig. 1). An inverse relationship with atmospheric pressure was found in Siberia [19] as well as an increase in the incidence associated with a mild ambient temperature. In our study, this effect was found when T_{max} approached T_{min}, characterizing spring time with cold days but not so cold nights. These extreme climate features were apparent in the second spring of the study period and not so marked in the first year, a pattern also found in the incidence of PICH. When dealing with weather effects on health events, it is important to look for unusual combinations of meteorological parameters and sometimes characterize the days based on these combinations, as in the study undertaken in Israel [29]. These triggering exposures were rare and usually concentrated, and their effects might be detected by an adequate data smoothing of events as shown in figure 1. They may be overlooked when dealing with extended time series data. Indeed, this fact might explain why contradictory findings on the effects of meteorological parameters have been reported in several studies, most of them finding an inverse relation between incidence and temperature, others a direct relation [15, 31] and both direct and indirect relations across different regions within the country [30]. The right answer is probably given by an Australian study [28] reporting an increase in incidence for extreme temperature values.

Until now, few community-based studies have examined the relation between first-ever-in-a-lifetime stroke and weather parameters. In England [20] and Italy [28], only the incidence of specific events increased with falls in temperature, PICH and fatal stroke, respectively, while in Russia [19] the relation was present for both PICH and IS. From previous reports, we know that the incidence of first-ever stroke is higher in Russia and Portugal compared to England. Population characteristics, mainly the endemic level of vascular risk factors already related to weather changes [38, 39], as well as housing and environmental features, may explain these contradictory findings. Hypertension has a high prevalence in Portugal linked to the excess salt intake, i.e. almost twice as high as that recommended by the WHO [40] as well as a high prevalence of vascular risk factors in general [41]. Therefore, extreme values in environmental temperature, either during daytime or night-time would more likely trigger cardiovascular events. On the other hand, the surrounding conditions for the effect of temperature to be felt cannot be disregarded. The Eurowinter Group, with data from Finland, Germany, the Netherlands, the UK, Italy and Greece [21], has shown that high indices of cold-related mortality were associated with high mean winter temperatures, low living-room temperatures, limited bedroom heating, a low proportion of people wearing protective clothes and inactivity. In the region of the city under study, i.e. the old part of the city near the river bank, most of these conditions prevail and thus we may conclude that in Porto we had conditions for an almost 'experimental' environmental study, excluding in general possible effect modifiers such as eating/conditioning systems.

The major limitation of this study is the reduced number of events, especially when the analysis involves stratification by IS subtypes or overall case fatality. However, the reduced study power for comparing incident strokes according to the OCSP or TOAST classification using the binomial model (that excludes days with no events), had no influence on our conclusion that the effects of cold days on outcome (fatal and non-fatal events) are different. The conclusions of most studies rely on subgroup analysis and although they concluded that there was an effect, some of them did not attempt to verify whether subgroups behave differently [33]. Another important analysis would be to investigate subgroups according to circumstances associated with the onset and time to maximum deficit, as has already been done for myocardial infarction [42]. We have also assumed that meteorological conditions are homogeneous in the study area and the risk to be similar across different environments and circumstances, which might not be true. The data specification included the day when stroke occurred without specifying the hour of the day, and so the 24-hour exposure to meteorological parameters also refers to the preceding calendar day. This means that the value of T_{min} (usually during night-time) might by more distant from the event onset than T_{max} (usually during daytime). It would be rather difficult to know the 'exact' event time since patients might not remember the exact time and more importantly this is impossible when symptoms are felt when awakening.

Our results point out two major conclusions: stroke type and IS subtypes must be considered when studying the effects of weather on incidence, confirming and corroborating the different aetiological mechanisms of stroke. Moreover, it is not only exposure (intensity) that matters, but also the hazard period involved. Since the trigger effect is associated with severity/outcome, emergency services (either dial emergency number or hospital emergency departments) should be aware that specific

weather conditions are more likely to prompt calls for more severe strokes. Further studies with larger data sets involving time trends may be useful to show whether the effects remain after all recent developments in stroke prevention and treatment.

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References

1 Healy JD: Excess winter mortality in Europe: a cross country analysis identifying key risk factors. J Epidemiol Community Health 2003;57:784–789.
2 Sheth T, Nair C, Muller J, Yusuf S: Increased winter mortality from acute myocardial infarction and stroke: the effect of age. J Am Coll Cardiol 1999;33:1916–1919.
3 Eng H, Mercer JB: Mortality from cardiovascular diseases and its relationship to air temperature during the winter months in Dublin and Oslo/Akershus. Int J Circumpolar Health 2000;59:176–181.
4 Diaz J, Garcia R, Lopez C, Linares C, Tobias A, Prieto L: Mortality impact of extreme winter temperatures. Int J Biometeorol 2005; 49:179–183.
5 Correia M, Silva MR, Matos I, Magalhaes R, Lopes JC, Ferro JM, Silva MC: Prospective community-based study of stroke in Northern Portugal: incidence and case fatality in rural and urban populations. Stroke 2004; 35:2048–2053.
6 Vemmos KN, Bots ML, Tsibouris PK, Zis VP, Grobbee DE, Stranjalis GS, Stamatelopoulos S: Stroke incidence and case fatality in southern Greece: the Arcadia stroke registry. Stroke 1999;30:363–370.
7 Wang Y, Levi CR, Attia JR, D'Este CA, Spratt N, Fisher J: Seasonal variation in stroke in the Hunter Region, Australia: a 5-year hospital-based study, 1995–2000. Stroke 2003;34: 1144–1150.
8 Jakovljevic D, Salomaa V, Sivenius J, Tamminen M, Sarti C, Salmi K, Kaarsalo E, Narva V, Immonen-Raiha P, Torppa J, Tuomilehto J: Seasonal variation in the occurrence of stroke in a Finnish adult population. The FINMONICA Stroke Register. Finnish Monitoring Trends and Determinants in Cardiovascular Disease. Stroke 1996;27: 1774–1779.
9 Myint PK, Vowler SL, Woodhouse PR, Redmayne O, Fulcher RA: Winter excess in hospital admissions, in-patient mortality and length of acute hospital stay in stroke: a hospital database study over six seasonal years in Norfolk, UK. Neuroepidemiology 2007; 28:79–85.
10 Turin TC, Kita Y, Murakami Y, Rumana N, Sugihara H, Morita Y, Tomioka N, Okayama A, Nakamura Y, Abbott RD, Ueshima H: Higher stroke incidence in the spring season regardless of conventional risk factors: Takashima Stroke Registry, Japan, 1988–2001. Stroke 2008;39:745–752.
11 Karagiannis A, Tziomalos K, Mikhailidis DP, Semertzidis P, Kountana E, Kakafika AI, Pagourelias ED, Athyros VG: Seasonal variation in the occurrence of stroke in Northern Greece: a 10 year study in 8204 patients. Neurol Res 2010;32:326–331.
12 Laaidi K, Minier D, Osseby GV, Couvreur G, Besancenot JP, Moreau T, Giroud M: Seasonal variation in strokes incidence and the influence of the meteorological conditions (in French). Rev Neurol (Paris) 2004;160:321–330.
13 Anlar O, Tombul T, Unal O, Kayan M: Seasonal and environmental temperature variation in the occurrence of ischemic strokes and intracerebral hemorrhages in a Turkish adult population. Int J Neurosci 2002;112: 959–963.
14 Jimenez-Conde J, Ois A, Gomis M, Rodriguez-Campello A, Cuadrado-Godia E, Subirana I, Roquer J: Weather as a trigger of stroke. Daily meteorological factors and incidence of stroke subtypes. Cerebrovasc Dis 2008;26:348–354.
15 Dawson J, Weir C, Wright F, Bryden C, Aslanyan S, Lees K, Bird W, Walters M: Associations between meteorological variables and acute stroke hospital admissions in the west of Scotland. Acta Neurol Scand 2008; 117:85–89.
16 Morabito M, Crisci A, Vallorani R, Modesti PA, Gensini GF, Orlandini S: Innovative approaches helpful to enhance knowledge on weather-related stroke events over a wide geographical area and a large population. Stroke 2011;42:593–600.
17 Ohshige K, Hori Y, Tochikubo O, Sugiyama M: Influence of weather on emergency transport events coded as stroke: population-based study in Japan. Int J Biometeorol 2006; 50:305–311.
18 Chang CL, Shipley M, Marmot M, Poulter N: Lower ambient temperature was associated with an increased risk of hospitalization for stroke and acute myocardial infarction in young women. J Clin Epidemiol 2004;57: 749–757.
19 Feigin VL, Nikitin YP, Bots ML, Vinogradova TE, Grobbee DE: A population-based study of the associations of stroke occurrence with weather parameters in Siberia, Russia (1982–92). Eur J Neurol 2000;7:171–178.
20 Rothwell PM, Wroe SJ, Slattery J, Warlow CP: Is stroke incidence related to season or temperature? The Oxfordshire Community Stroke Project. Lancet 1996;347:934–936.
21 Keatinge WR, Donaldson GC: Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. The Eurowinter Group. Lancet 1997;349:1341–1346.
22 Hatano S: Experience from a multicentre stroke register: a preliminary report. Bull World Health Organ 1976;54:541–553.
23 Sudlow CL, Warlow CP: Comparing stroke incidence worldwide: what makes studies comparable? Stroke 1996;27:550–558.
24 Bamford J, Sandercock P, Dennis M, Burn J, Warlow C: Classification and natural history of clinically identifiable subtypes of cerebral infarction. Lancet 1991;337:1521–1526.
25 Adams HP, Jr., Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, Marsh EE, III: Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 1993;24:35–41.
26 Chen G, Zhang Y, Song G, Jiang L, Zhao N, Chen B, Kan H: Is diurnal temperature range a risk factor for acute stroke death? Int J Cardiol 2007;116:408–409.
27 Gelman A, Hill J: Data Analysis Using Regression and Multilevel/Hierarchical Models, ed 3. Cambridge, Cambridge University Press, 2007.
28 Carolei A, Marini C, De Matteis G, Di Napoli M, Baldassarre M: Seasonal incidence of stroke. Lancet 1996;347:1702–1703.
29 Berginer VM, Goldsmith J, Batz U, Vardi H, Shapiro Y: Clustering of strokes in association with meteorologic factors in the Negev Desert of Israel: 1981–1983. Stroke 1989;20: 65–69.
30 Ebi KL, Exuzides KA, Lau E, Kelsh M, Barnston A: Weather changes associated with hospitalizations for cardiovascular diseases and stroke in California, 1983–1998. Int J Biometeorol 2004;49:48–58.

31 Bull GM: Meteorological correlates with myocardial and cerebral infarction and respiratory disease. Br J Prev Soc Med 1973;27:108–113.
32 Jackson CA, Hutchison A, Dennis MS, Wardlaw JM, Lindgren A, Norrving B, Anderson CS, Hankey GJ, Jamrozik K, Appelros P, Sudlow CL: Differing risk factor profiles of ischemic stroke subtypes: evidence for a distinct lacunar arteriopathy? Stroke 2010;41:624–629.
33 Matsumoto M, Ishikawa S, Kajii E: Cumulative effects of weather on stroke incidence: a multi-community cohort study in Japan. J Epidemiol 2010;20:136–142.
34 Giles T: Relevance of blood pressure variation in the circadian onset of cardiovascular events. J Hypertens Suppl 2005;23:S35–S39.
35 Stergiou GS, Vemmos KN, Pliarchopoulou KM, Synetos AG, Roussias LG, Mountokalakis TD: Parallel morning and evening surge in stroke onset, blood pressure, and physical activity. Stroke 2002;33:1480–1486.
36 Woodhouse PR, Khaw KT, Plummer M, Foley A, Meade TW: Seasonal variations of plasma fibrinogen and factor VII activity in the elderly: winter infections and death from cardiovascular disease. Lancet 1994;343:435–439.
37 Keatinge WR, Coleshaw SR, Cotter F, Mattock M, Murphy M, Chelliah R: Increases in platelet and red cell counts, blood viscosity, and arterial pressure during mild surface cooling: factors in mortality from coronary and cerebral thrombosis in winter. Br Med J (Clin Res Ed) 1984;289:1405–1408.
38 Alpérovitch A, Lacombe JM, Hanon O, Dartigues JF, Ritchie K, Ducimetière P, Tzourio C: Relationship between blood pressure and outdoor temperature in a large sample of elderly individuals: the Three-City study. Arch Intern Med 2009;169:75–80.
39 Yeh CJ, Chan P, Pan WH: Values of blood coagulating factors vary with ambient temperature: the Cardiovascular Disease Risk Factor Two-Township Study in Taiwan. Chin J Physiol 1996;39:111–116.
40 Polonia J, Maldonado J, Ramos R, Bertoquini S, Duro M, Almeida C, Ferreira J, Barbosa L, Silva JA, Martins L: Estimation of salt intake by urinary sodium excretion in a Portuguese adult population and its relationship to arterial stiffness. Rev Port Cardiol 2006;25:801–817.
41 Nunes B, Silva RD, Cruz VT, Roriz JM, Pais J, Silva MC: Prevalence and pattern of cognitive impairment in rural and urban populations from Northern Portugal. BMC Neurol;10:42.
42 Moller J, Ahlbom A, Hulting J, Diderichsen F, de Faire U, Reuterwall C, Hallqvist J: Sexual activity as a trigger of myocardial infarction. A case-crossover analysis in the Stockholm Heart Epidemiology Programme (SHEEP). Heart 2001;86:387–390.