Seasonal variation in incidence of stroke in a general population of 1.4 million Japanese: the Shiga Stroke Registry

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Short Title: Seasonal variation in stroke incidence in Japan

Number of Tables: 2 tables and 1 supplemental table.

Number of Figures: 1 figure.

Word count: 2246 words.

Key words: stroke, seasonal variation, incidence, community based, epidemiology of stroke.

Abstract

Introduction: The purpose of this study was to investigate seasonal variation in stroke incidence using data from a large-scale stroke registry of general population in current Japan.

Methods: Shiga Stroke Registry [SSR] is an ongoing population-based registry of stroke that occurred in the Shiga Prefecture in central Honshu, Japan. A total 6,688 cases of first-ever stroke, with onset dates ranging from 1 January 2011 to 31 December in 2013 were included in this study. Incidence rates of first-ever stroke in each season were estimated using the person-year approach and adjusted for age and sex using the Poisson regression models.

Results: From 2011 to 2013, we identified a total of 6,688 stroke cases (3,570 men, 3,118 women), of which 4,480 cases had ischemic stroke (2,518 men, 1,962 women), 1,588 had intracerebral hemorrhage (857 men, 731 women) and 563 had subarachnoid hemorrhage (166 men, 397 women). Age- and sex-adjusted incidence rates of total stroke were 151 (95% confidence interval [CI] 144-160, p=<0.001 vs summer) in spring, 130 (95% CI 122-137) in summer, 141 (95% CI 133-149, p=0.020 vs summer) in autumn and 170 (95% CI 161-179, p=<0.001 vs summer) in winter. Seasonal variation was more pronounced in intracerebral hemorrhage than in ischemic stroke.

Conclusion: In the present large-scale stroke registry of general population, incidence rates of stroke were highest in winter and lowest in summer in current Japan.

Introduction

Lifetime risk of stroke is estimated to be 25% [1] and stroke affects 12 million people worldwide [2]. Stroke is also leading causes of premature death affecting 6.2 million people worldwide annualy [3]. In addition, many stroke survivors suffer from physical, cognitive and communication deficits, placing burden on family and community [4-7]. Effective prevention of stroke requires strategies based on up-to-date knowledge of stroke risk factors [8].

A number of epidemiological studies reported seasonal variation in incidence of stroke [9-16]. However, current evidence is mainly derived from Western populations [9,10]. There are some epidemiological studies which showed seasonal variation in stroke incidence among Japanese, but they were based on population-based data obtained during 1960s-2000s [11,12] or based on hospital-based populations [13-16]. Therefore, it is not quite clear whether current evidence is applicable to general population in current Japan.

The purpose of this study was to investigate seasonal variation in stroke incidence using data from a large-scale stroke registry of general population (Shiga Stroke Registry [SSR] as a part of the Shiga Stroke and Heart attack Registry Study [SSHR]) in current Japan [17-22].

Methods

Study design

SSHR is an ongoing population-based registry of stroke and coronary artery disease that occurred in the Shiga Prefecture in central Japan. As a part of SSHR, we have established a population-based registry study of stroke (SSR) designed to build a complete information system regarding acute ischemic and non-traumatic hemorrhagic stroke management in Shiga Prefecture, Japan. The design of SSR has been described elsewhere in detail. In brief, the SSR uses central and local coordination and monitoring, combined with remote data collection and quality control systems, to create an integrated surveillance system involving the registration of cases among a network of all acute-care hospitals with neurology/neurosurgery facilities and smaller hospitals with rehabilitation facilities in Shiga Prefecture. Information on the death certificates of all deceased residents is also collected to help detect all cases of stroke, including those leading to rapid death outside hospital, with the approval of the Ministry of Health, Labour and Welfare [17-22].

Definition of stroke

A total 6,688 cases of first-ever stroke, with onset dates ranging from 1 January 2011 to 31 December in 2013 were included in this study. Diagnosis of stroke was defined as a sudden onset of focal neurological deficits persisting for more than 24 hours, according to the Monitoring Trends and Determinants in Cardiovascular Disease (WHO-MONICA) Project [23]. Stroke was classified into ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage and other/unclassified stroke. The present study was approved by the Institutional Review Board of Shiga University of Medical Science (R2011-186).

Temperature data

Information on average, maximum and minimum temperature at the Hikone Meteorological Observatory, which located in the center of the Shiga Prefecture, in each month during the study period (2011-2013) was obtained from website of the Japan Meteorological Agency [24].

Statistical analysis

Incidence rates of first-ever stroke in each month during the study period (2011-2013) were estimated using the person-year approach. The number of residents in the Shiga Prefecture was obtained by sex and 10-year age groupings from the national population estimates data on 30th June 2012 [25]. Age- and sex-adjusted incidence rates were estimated and compared using the Poisson regression models.

Age- and sex-adjusted incidence rates in spring (March-May), summer (June-August), autumn (September-November) and winter (December-February) were also estimated and compared using the Poisson regression models. A P value less than 0.05 was considered statistically significant. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, US).

Results

Temperature characteristics of the Shiga Prefecture was shown in Table 1. Average temperature was lowest (<5°C) in January/February and highest (>25°C) in July/August.

From 2011 to 2013, we identified a total of 6,688 stroke cases (3,570 men, 3,118 women), of which 4,480 cases had ischemic stroke (2,518 men, 1,962 women) (1,042 lacunar infarction, 1,333 Large artery infarction and 1,235 cardioembolic infarction), 1,588 had intracerebral hemorrhage (857 men, 731 women) and 563 had subarachnoid hemorrhage (166 men, 397 women). Figure 1 shows monthly variation in average temperature (top part of Figure 1) and age- and sex-adjusted incidence rates of total stroke in the Shiga Prefecture (Figure 1A). Incidence rates of total stroke tended to be low in summer (June-August) high in winter and (December-February). When age- and sex-adjusted incidence rates of total stroke were estimated by season with pooling of data from 2011 to 2013, incidence (per 100,000 person-years) was lowest in summer (130, 95% confidence interval [CI] 122-137) (Table 2). Compared with summer, age- and sex-adjusted incidence rates of total stroke was significantly higher in winter (170, 95% CI 161-179, p<0.001), in autumn (141 95% CI 133-149, p=0.020) and in spring (151 95% CI 144-160, p=<0.001). Stratified analysis by age and sex demonstrated similar seasonal patterns in 4 groups (men aged <70 years, men aged ≥70 years, women aged <70 years and women aged ≥70 years) (Supplemental Table 1).

Similar patterns were observed for ischemic stroke (Figure 1B), intracerebral hemorrhage (Figure 1C) and subarachnoid hemorrhage (Figure 1D) but seasonal variation was more evident for intracerebral hemorrhage than ischemic stroke. Age- and sex-adjusted incidence rates of ischemic stroke were 88 (95% CI 82-94, p=0.004 vs summer) in spring, 78 (95% CI 72-83) in summer, 80 (95% CI 74-86, p=0.549 vs summer) in autumn and 90 (95% CI 84-97, p=<0.001 vs summer) in winter (Table 2). When ischemic stroke was classified into subtypes, there were no clear seasonal variation in incidence rates of lacunar infarction (Table 2). In contrast, incidence rates of large artery infarction were highest in winter (26 per 100,000 person-years) (P=0.008 vs. summer) (Table 2). Incidence rates of cardioembolic infarction were also highest in winter (18 per 100,000 person-years) and spring (18 per 100,000 person-years) (P<0.001 for both winter and spring versus summer) (Table 2). Age- and sex-adjusted incidence rates of intracerebral hemorrhage were 39 (95% CI 35-43, p=<0.001 vs summer) in spring, 30 (95% CI 27-34) in summer, 38 (95% CI 34-42, p=0.002 vs summer) in autumn and 52 (95% CI 47-57, p=<0.001 vs summer) in winter (Table 2). Age- and sex-adjusted incidence rates of subarachnoid hemorrhage were 16 (95% CI 13-19, p=0.170 vs summer) in spring, 13 (95% CI 11-16) in summer, 16 (95% CI 14-19, p=0.129 vs summer) in autumn and 20 (95% CI 17-23 p=0.002 vs summer) in winter (Table 2).

Discussion

In the present large-scale stroke registry of general population, incidence rates of stroke were high in winter and low in summer in current Japan. Seasonal variation was more evident for intracerebral hemorrhage than for ischemic stroke.

Some prior epidemiological studies have investigated seasonal variation in stroke incidence in Japan [11-16]. A hospital-based stroke registry in Akita investigated 2,168 stroke patients from 1983 to 1985 and demonstrated higher risks of total stroke and intracerebral hemorrhage in winter than in summer, but did not report clear seasonal variation for ischemic stroke [13]. Hospital-based stroke registry in Kyoto investigated 13,788 stroke patients from 1999 to 2009 and demonstrated increased incidence rates of total stroke, intracerebral hemorrhage and subarachnoid hemorrhage in winter and spring compared with those in summer, but no clear seasonal variation was observed for ischemic stroke [15]. Another nation-wide hospital-based stroke registry (Japanese Standard Stroke Registry) investigated 35,631 stroke patients admitted to 163 acute stroke hospitals from 1999 to 2007 and demonstrated increased risks of hemorrhagic stroke and cardioembolic infarction in winter, while the risks of non-cardioembolic infarction were higher in summer than winter [14]. A recent hospital-based observational study of 2,965 acute ischemic stroke patients admitted to an acute stroke hospital from 2011 to 2015 demonstrated no clear seasonal variation in incidence rates of ischemic stroke, while the risks of cardioembolic infarction were highest in winter [16]. However, findings from hospital-based studies might be affected by seasonal variation of stroke patients' intention to visit acute-care hospitals or by capacity of each hospital. With regard to population-based study, the Hisayama Study investigated 311 stroke patients during follow-up duration from 1961 to 1985 and showed higher incidence of intracerebral hemorrhage and ischemic stroke in winter than in summer [11]. A population-based stroke registry (Takashima Stroke Registry) investigated 1,665 stroke patients from 1988 to 2001 and reported highest risks of total stroke, intracerebral hemorrhage and ischemic stroke in spring and lowest risks in summer [12]. The results of the present large-scale population-based study of 6,688 stroke patients were comparable with those of some prior studies and this study clearly demonstrated that incidence rates of total stroke and its subtypes including ischemic stroke were higher in winter than in summer in current Japan.

Exposure to the cold provokes a range of physiological responses, predominantly as a consequence of activation of the sympathetic nervous system, including elevation in blood pressure and heart rate [26,27]. In fact, several observational studies reported seasonal variation of BP levels (i.e. higher BP levels in winter than those in summer) [28-34]. Cold weather was also reported to be associated with increased risks of arrhythmia including atrial fibrillation [35-38]. Framingham study also reported decreased endothelial function in the cold weather [39]. Other possible mechanisms involve seasonal variation in serum lipids, fibrinogen and viscosity, [40,41] which are reported to be risk factors of ischemic stroke [42-45]. Influenza and influenza-like symptoms, which are more likely to strike in winter than other seasons, have also been shown to be associated with stroke [46,47]. Exacerbation of air pollution including gaseous pollutants (such as ozone) and particulate matter (such as PM2.5) in winter and spring in East Asia [48] might also be attributable to seasonal variation of stroke, as exposure to air pollution has been reported to be associated with admissions to hospitals for stroke [49]. These mechanisms might be in part attributable to seasonal variation in incidence rates of stroke.

Although this is a large-scale, comprehensive, population-based registry in current Japan, several limitations should be discussed. First, we could not examine the association between seasonal variation in incidence of transient ischemic attack due to no information on the patients with transient ischemic attack. Another limitation is that we do not have information on environmental temperature of patients at the time of stroke onset. Third, our findings might not be generalizable to other regions of Japan where climate conditions and cardiovascular risk factors of residents are different from those in the Shiga Prefecture.

Conclusion

In the present large-scale stroke registry of general population, incidence rates of stroke were high in winter and low in summer in current Japan.

Acknowledgments

We are deeply grateful to all investigators, participating hospitals, study staff at the Shiga Stroke Data Center, Shiga Medical Association, Shiga Prefecture Hospital Association, Biwako Brain and Heart attack Consortium(BIWA-BHAC), Department of Public Health Care and Welfare, Shiga prefecture government.

Statement of Ethics

The present study was approved by the Institutional Review Board of Shiga University of Medical Science (R2011-186) and the president of Shiga University of Medical Science gave the waiver for written informed consent.

Conflict of Interest Statement

Arima H is an associate editor of the journal Cerebrovascular Disease. The other authors have no conflicts of interest to declare.

Funding Sources

Shiga Stroke and Heart Registry is supported by Shiga Prefecture and the Japan Agency for Medical Research and Development (grant number 17ek0210090)

Data Availability Statement

Research data are not publicly available on ethical grounds.

Author Contributions

Nozaki K, Kita Y and Takashima N contributed to the conception of this study and Nozaki K, Kita Y, Takashima N, Miyamatsu N and Miura K contributed to the design of this study. Fujii T, Takashima N, Kita Y, Tanaka-Mizuno S, Shitara S, Miyamatsu N, Miura K and Nozaki K contributed to the acquisition of data. Fujii T and Arima H contributed to analysis of this study, and Fujii T, Takashima N, Kita Y, Tanaka-Mizuno S, Urushitani M, Miura K and Nozaki K contributed to interpretation of data. Fujii T drafted the manuscript for the work and Arima H supervised the writing of the manuscript. And all authors revised the manuscript, approved the manuscript to be published, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Figure legends

Figure 1 Monthly variation in average temperature and age- and sex-adjusted incidence rates of (A) total stroke, (B) ischemic stroke, (C) intracerebral hemorrhage and (D) subarachnoid hemorrhage: Shiga Stroke Registry 2011-2013.

The top part of the figure shows average temperature at the Hikone Meteorological Observatory, which located in the center of the Shiga Prefecture, in each month from 2011 to 2013. The lower parts of the figure show incidence rates of (A) total stroke, (B) ischemic stroke, (C) intracerebral hemorrhage and (D) subarachnoid hemorrhage in each month from 2011 to 2013, which was estimated using the person-year approach and standardized for age and sex using the Poisson regression models.

Table 1. Temperature characteristics of the Shiga Prefecture from 2011 to 2013

2011												
Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Average (°C)	2.0	4.8	5.5	10.8	17.4	23	27.3	28.1	24.3	17.8	13.1	6.0
Maximum (°C)	8.3	15.8	15.6	26.6	27.2	35.2	35.2	35.9	33	25.4	23.1	16.2
Minimum (°C)	-3.9	-2.9	-1.1	0.7	8.4	15	20.8	22.2	13.7	9.4	3.9	-0.3
2012												
Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Average (°C)	3.4	3.1	6.8	12.4	16.9	21.3	26.5	28.5	25.3	17.9	10.9	4.9
Maximum (°C)	9.7	10.5	19.4	26.2	27.6	29.9	35.8	35.5	33.5	27.4	20.2	12.1
Minimum (°C)	-1.9	-3.8	-1.6	1.4	8.6	15.3	19.3	22.6	16.6	8.8	1.8	-2.0
2013												
Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Average (°C)	3.3	3.4	7.9	11.7	17.2	22.7	27.1	28.3	23.5	19.3	11.2	6.0
Maximum (°C)	10.9	13.1	19.8	24.0	28.7	31.8	36.2	35.6	32.2	32.1	20.5	14.7
Minimum (°C)	-3.7	-2.4	-1.9	2.4	4.7	15.9	19.3	20.5	13.1	7.1	2.1	-1.2

Table shows average, maximum and minimum temperature at the Hikone Meteorological Observatory, which located in the center of the Shiga Prefecture, in each month from 2011 to 2013.

Table 2. Seasonal variation in age- and sex- adjusted incidence rates of stroke and its subtypes: Shiga Stroke Registry 2011-2013

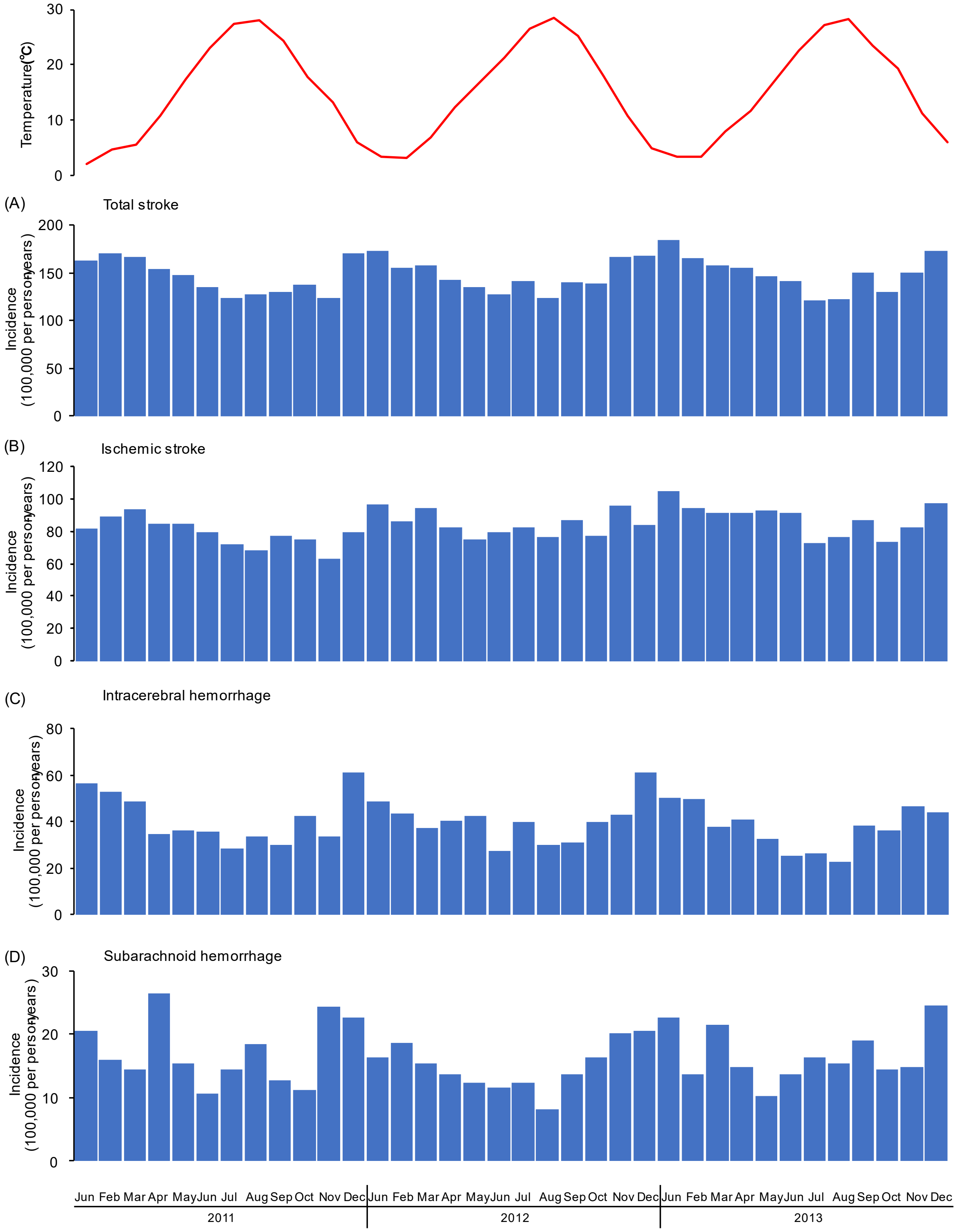
	Age- and sex-adjusted incidence rate, per 100,000 person-years	(95% confidence interval)	P value (versus summer)
Total stroke			
Spring	151	(144 to 160)	<0.001
Summer	130	(122 to 137)	Reference
Autumn	141	(133 to 149)	0.020
Winter	170	(161 to 179)	<0.001
Ischemic stroke			
Spring	88	(82 to 94)	0.004
Summer	78	(72 to 83)	Reference
Autumn	80	(74 to 86)	0.549
Winter	90	(84 to 97)	<0.001
Lacunar infarction			
Spring	20	(17 to 23)	0.478
Summer	21	(19 to 25)	Reference
Autumn	23	(20 to 27)	0.325
Winter	21	(18 to 24)	0.815
Large artery infarction			
Spring	25	(22 to 28)	0.031
Summer	21	(18 to 24)	Reference
Autumn	20	(18 to 23)	0.661
Winter	26	(23 to 30)	0.008
Cardioembolic infarction			
Spring	18	(12 to 18)	<0.001
Summer	13	(9 to 13)	Reference
Autumn	14	(9 to 14)	0.517
Winter	18	(12 to 18)	<0.001
Intracerebral hemorrhage			
Spring	39	(35 to 43)	<0.001
Summer	30	(27 to 34)	Reference
Autumn	38	(34 to 42)	0.002
Winter	52	(47 to 57)	<.0001
Subarachnoid hemorrhage			
Spring	16	(13 to 19)	0.170
Summer	13	(11 to 16)	Reference
Autumn	16	(14 to 19)	0.129
Winter	20	(17 to 23)	0.002

Incidence rates in spring (March-May in 2011-2013), summer (June-August in 2011-2013), autumn (September-November in 2011-2013) and winter (December-February in 2011-2013) were estimated using the person-year approach and standardized for age and sex using the Poisson regression models.
Age- and sex- adjusted incidence rates were compared to the reference group of summer using the Poisson regression models.

Supplemental Table 1. Seasonal variation in incidence rates of total stroke according to age and sex: Shiga Stroke Registry 2011-2013

	Age- and sex-adjusted incidence rate, per 100,000 person-years (95% confidence interval)		P value (versus summer)
Male, Age <70 years			
Spring	109	(99 to 121)	0.444
Summer	103	(93 to 114)	Reference
Autumn	115	(104 to 127)	0.138
Winter	138	(126 to 151)	<0.001
Male, Age ≥70 years			
Spring	732	(671 to 799)	0.016
Summer	625	(568 to 687)	Reference
Autumn	659	(601 to 723)	0.422
Winter	807	(742 to 878)	<0.001
Female, Age <70 years			
Spring	57	(50 to 66)	0.414
Summer	53	(46 to 61)	Reference
Autumn	59	(51 to 68)	0.283
Winter	62	(54 to 71)	0.124
Female, Age ≥70 years			
Spring	659	(610 to 712)	<0.001
Summer	515	(471 to 562)	Reference
Autumn	559	(514 to 609)	0.184
Winter	698	(646 to 753)	<0.001

Figure 1



Temperature(℃)
30
20
10
0
(A)
Total stroke
Incidence
(100,000 per person-years)
200
150
100
50
0
(B)
Ischemic stroke
120
100
80
60
40
20
0
(C)
Intracerebral hemorrhage
80
60
40
20
0
(D)
Subarachnoid hemorrhage
30
20
10
0
Jun Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec
2011
2012
2013