Holiday Season and Weekend Effects on Stroke Mortality: A Nationwide Cohort Study Controlling for Stroke Severity

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Background**—**The effect of holiday season admission for stroke on mortality has not been investigated. Thus, we aimed to evaluate whether "holiday season" and "weekend" effects exist on mortality risk for stroke admission.

Methods and Results**—**A nationwide cohort study was conducted using Taiwan's National Health Insurance Research Database. We identified all patients admitted for stroke between 2011 and 2015 in Taiwan, and categorized them according to the admission date: holiday season (at least 4 days off) (n=3908), weekend (n=13 774), and weekday (n=49 045). We analyzed in-hospital, 7-day, and 30-day mortality using multivariable logistic regression, adjusting for stroke severity and other confounders. Compared with weekday admissions, holiday season admission for stroke was significantly associated with a 20%, 33%, and 21% increase in in-hospital, 7-day, and 30-day mortality, respectively. Compared with weekend admissions, holiday season admissions were associated with a 24%, 30%, and 22% increased risk of in-hospital, 7-day, and 30-day mortality, respectively. However, mortality did not differ significantly between weekend and weekday admissions. Subanalyses after stratification for age, sex, and stroke type also revealed similar trends.

Conclusions**—**We report for the first time a "holiday season effect" on stroke mortality. Patients admitted during holiday seasons had higher mortality risks than those admitted on weekends and weekdays. This holiday season effect persisted even after adjusting for stroke severity and other important confounders. These findings highlight the need for healthcare delivery systems with a consistent quality of round-the-clock care for patients admitted for stroke. **(*J Am Heart Assoc*. 2019;8:e011888. DOI: 10.1161/JAHA.118.011888.)**

Key Words: cohort study • holiday season • hospitalization • mortality • safety • stroke • weekend effect

Stroke is one of the leading causes of death and disability worldwide.[1] Previous studies have shown that hospital admission for stroke over the weekends, compared with that on weekdays, is associated with a higher mortality rate. This is called the "weekend effect" of stroke.[2–4] However, controversy still exists about the extent of this effect, whether it may reflect disparities in levels of staffing, availability of diagnostic tests or interventions, or access to emergency treatment for stroke between weekends and weekdays, and whether it exists at all.[5–8] Some authors have argued that the phenomenon of the weekend effect found in stroke patients is probably caused by differences in disease severity between those admitted on weekends and weekdays.[5,9]

The scarcity of healthcare resources, especially staff, is much more pronounced during holiday seasons. This aspect may strongly influence the quality of the care provided and consequently patient prognosis. However, although previous studies have examined and discussed the weekend effect on stroke prognosis,[2–9] studies evaluating a "holiday season effect" on mortality risk after stroke admission are still lacking, despite the considerable potential implications on public health.

In Taiwan, the annual holiday season for celebrating the Chinese New Year includes at least 4 days (from New Year's Eve to the third day of New Year) every January or February. Using the Chinese New Year holidays as an indicator of holiday season, we conducted a nationwide study to evaluate whether "holiday season" and "weekend" may affect the mortality risk for stroke admission in our Taiwanese cohort. We conducted an exhaustive investigation controlling for stroke severity and other potential confounders, overcoming the criticism associated with previous studies on the topic.

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Clinical Perspective

What Is New?

- We report for the first time a "holiday season effect" on stroke mortality: patients admitted for stroke during holiday seasons had higher in-hospital, 7-day, and 30-day mortality risks than those admitted on weekends and weekdays.
- Even after adjusting for stroke severity and other important confounders, the holiday season effect was observed.

What Are the Clinical Implications?

- Our findings highlight the urgent need of establishing healthcare delivery systems that provide a consistent quality of round-the-clock care for patients admitted for stroke.

Methods

The data set used in this study belongs to the Taiwan Ministry of Health and Welfare and thus is not available. However, researchers interested in accessing this data set can submit a formal request application to the Ministry of Health and Welfare (Taiwan Ministry of Health and Welfare, No. 488, Sec. 6, Zhongxiao E. Rd., Nangang Dist., Taipei City 115, Taiwan; phone: +886-2-8590-6825; e-mail: stcarolwu@mohw.gov.tw; website: https://dep.mohw.gov.tw/DOS/cp-2516-3591-113.html). All relevant data are within the article.

Data Sources

We conducted a nationwide cohort study to investigate the relationship between admission date and mortality risk in patients admitted for stroke, by retrieving data from Taiwan's National Health Insurance Research Database (NHIRD). The National Health Insurance (NHI) program in Taiwan is a mandatory single-payer program administered by the government and implemented since 1995. The NHI provides compulsory universal health insurance and covers comprehensive medical services, including outpatient, inpatient, and emergency services.[10] More than 99% of Taiwan's population is enrolled, and 97% of hospitals and clinics in Taiwan are contracted with NHI program. Taiwan's NHIRD is an administrative database containing medical records for research purposes, and is maintained by and made available through the Health and Welfare Data Science Center, Ministry of Health and Welfare, Taiwan. The NHIRD integrates detailed healthcare data from about 25 million enrollees, representing the Taiwan's entire population.[11] High quality of the information provided has been shown for prescription use, diagnoses, and hospitalizations.[12] The Tzu Chi General Hospital Research Ethics Committee approved this study (IRB106-106-C), and the need for informed consent was waived.

Study Cohort

Our study cohort included all adult patients, aged ≥20 years, who were admitted to acute care hospitals with a diagnosis of stroke in January and February each year, between 2011 and 2015, in Taiwan. The diagnosis of stroke was identified using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes 433, 434, and 436 (for ischemic stroke) and 430 to 432 (for hemorrhagic stroke). The diagnostic codes of stroke have been previously validated and shown to present high accuracy.[13–15] We defined the index date and hospitalization as the dates of stroke diagnosis and the corresponding hospitalization, respectively.

The admissions were categorized into 3 study groups based on the admission date: holiday season, weekend, and weekday admission groups. In this study, we used the Chinese New Year holidays as a reference for a holiday season period. This period typically includes at least 4 days each year during January or February, possibly extended if it encounters a Saturday and Sunday. The exact dates of the Chinese New Year holidays in each year were extracted according to Taiwan's national public holiday list. The weekend admission group was defined as admissions for stroke on Saturday and Sunday; the weekday group were defined as admissions on Monday through Friday, except during the period of Chinese New Year holidays. To reduce the influence of seasonal differences on disease and mortality rates, we excluded the admissions from March to December and included only the admissions happening in January and February for the weekend and weekday admissions.

Outcome Measures

We focused on 3 primary outcomes, including the all-cause in-hospital mortality and the all-cause mortality within 7 and 30 days. We obtained the patient vital status by combining information from the NHIRD with the National Register of Deaths in Taiwan. The in-hospital mortality was defined as death occurring during the index hospitalization; the 7- and 30-day mortality was defined as death occurring within 7 and 30 days after the index date, respectively. To examine whether both holiday season and weekend admissions may have an impact on mortality, we initially compared the mortality risk among our 3 study groups, using the weekday admission as the reference. Further, to evaluate whether the mortality risk differed between holiday season and weekend admissions, we directly compared these 2 groups, defining the weekend admission as the reference. Subgroup analyses after stratification for age, sex, and stroke type (ischemic or hemorrhagic) were further conducted.

Covariates and Estimation of Stroke Severity

The baseline characteristics and clinical details for all included cases were obtained from *ICD-9-CM* and procedure codes from the reimbursement claims of outpatient, inpatient, and emergency services. We defined preexisting comorbidity as disease diagnosed at least 1 time in an inpatient or 2 times in an outpatient service, within the year before the index date. We also calculated the Charlson comorbidity index, widely used to represent an individual's overall systemic health status and highly correlated with mortality risk, based on each patient's records.[16] Individuals' income was estimated from the income-related NHI premiums and categorized into 3 levels (New Taiwan dollars ≥40 000, 20 000–39 999, and <20 000). Hospitals for stroke admission were categorized into 3 levels according to their accreditation level (medical center, regional, or district). To eliminate the possible confounding effects associated with differences in stroke severity between different admission times,[5,9] we determined several stroke severity proxies and accounted for them in our analyses. We calculated the claims-based stroke severity index (SSI) to estimate the National Institutes of Health Stroke Scale (NIHSS) for each stroke inpatient. The claims-based SSI was specifically developed to deal with the lack of reliable stroke severity status information when using claims-based data from NHIRD.[17] The SSI has been validated previously and showed high correlation with the NIHSS and, consequently, functional outcomes after stroke.[17–19] After obtaining SSI for each stroke inpatient, the estimated NIHSS was then calculated from the SSI using the formula developed by Hsieh et al (estimated NIHSS=1.1722×SSI−0.7533), to predict stroke severity and neurologic deficit.[20] The detailed description for how to calculate the SSI and the estimated NIHSS can be found elsewhere.[17,20] In addition, other stroke severity proxies, such as diagnosis codes for hemiplegia and aphasia, operation/procedure codes for mechanical ventilation use, hospitalization in the intensive care unit, and head surgery, were retrieved from the records of the index hospitalization. Information on the use of intravenous thrombolysis was also retrieved.

Because the Charlson comorbidity index and some comorbidities were possibly collinear, potentially influencing results of the multivariable regression models, we further performed 2 sensitivity analyses, which did not include either the Charlson comorbidity index or the comorbidities in the regression models.

Statistical Analysis

We calculated the odds ratios and the respective 95% CIs for in-hospital, 7-day, and 30-day mortality in logistic regression models. The multivariable logistic regression model was performed, with adjustment for all covariates listed in Table 1. Interaction tests were performed for age, sex, and stroke type subgroups. A 2-sided probability value of <0.05 was considered statistically significant. Statistical analysis was performed using SAS 9.4 software (SAS Institute, Inc., Cary, NC).

Results

Patient Characteristics

We identified a total of 66 727 admissions for stroke in January and February between 2011 and 2015 in Taiwan. There were 3908 stroke patients admitted over the holiday season, 13 774 admitted on weekends, and 49 045 admitted on weekdays. The baseline characteristics of each of the study groups are shown in Table 1. The median duration of hospital stay in our study population was 9 days (interquartile range=14 days); the median time from admission to in-hospital death was 6 days (interquartile range=12 days) in patients who died during hospitalization.

Mortality Risks

Holiday season admission for stroke was associated with increased risk of mortality when compared with weekday admission in both the univariate and the multivariable analyses (adjusting for stroke severity and other relevant patient characteristics listed in Table 1). The holiday season admission group presented a 20% increased risk of in-hospital mortality (adjusted odds ratio [aOR], 1.20; 95% CI, 1.06–1.36; *P*=0.004), a 33% increased risk of 7-day mortality (aOR, 1.33; 95% CI, 1.15–1.54; *P*<0.001), and a 21% increased risk of 30-day mortality (aOR, 1.21; 95% CI, 1.08–1.36; *P*=0.001), when compared with that of the weekday admission group (Table 2).

Although patients admitted on weekends revealed significantly higher mortality risks than those admitted on weekdays in the univariate models, this weekend effect was not evident after adjusting for stroke severity and other patient characteristics in the multivariable logistic regression models (in-hospital mortality: aOR, 0.97; 95% CI, 0.90–1.05; *P*=0.497; 7-day mortality: aOR, 1.02; 95% CI, 0.93–1.12; *P*=0.681; 30-day mortality: aOR, 0.99; 95% CI, 0.93–1.07; *P*=0.876) (Table 2).

The 2 sensitivity analyses, which did not include either the Charlson comorbidity index or comorbidities in the multivariable regression models, revealed similar results.

Comparison Between Holiday Season and Weekend Admissions

In the univariate analysis, holiday season admission was associated with significantly higher mortality risk than

Table 1. Baseline Characteristics of Patients Admitted During the Holiday Season, Weekends, and Weekdays

	Holiday Season (n=3908)	Weekends (n=13 774)	Weekdays (n=49 045)
Age, y			
<40	86 (2.2%)	303 (2.2%)	1327 (2.7%)
40–59	871 (22.3%)	2947 (21.4%)	10 717 (21.8%)
60–79	1853 (47.4%)	6695 (48.6%)	23 289 (47.5%)
≥80	1098 (28.1%)	3829 (27.8%)	13 712 (28.0%)
Sex			
Male	2364 (60.5%)	8181 (59.4%)	29 619 (60.4%)
Female	1544 (39.5%)	5593 (40.6%)	19 426 (39.6%)
Charlson comorbidity index score			
0–2	2644 (67.7%)	8896 (64.6%)	30 755 (62.7%)
3–5	951 (24.3%)	3652 (26.5%)	13 692 (27.9%)
≥6	313 (8.0%)	1226 (8.9%)	4598 (9.4%)
Comorbidities			
Hypertension	2175 (55.7%)	7869 (57.1%)	28 541 (58.2%)
Diabetes mellitus	1175 (30.1%)	4254 (30.9%)	15 618 (31.8%)
COPD	438 (11.2%)	1618 (11.8%)	6172 (12.6%)
Heart failure	297 (7.6%)	1052 (7.6%)	3612 (7.4%)
Coronary artery disease	606 (15.5%)	2396 (17.4%)	8436 (17.2%)
Chronic kidney disease	313 (8.0%)	1306 (9.5%)	4451 (9.1%)
Chronic liver disease	209 (5.4%)	785 (5.7%)	2757 (5.6%)
Dementia	250 (6.4%)	862 (6.3%)	3311 (6.8%)
Malignancy	247 (6.3%)	1008 (7.3%)	3541 (7.2%)
Income level (NTD)			
<20 000	1259 (32.2%)	4548 (33.0%)	16 200 (33.1%)
20 000–39 999	2101 (53.8%)	7365 (53.5%)	25 969 (52.9%)
≥40 000	548 (14.0%)	1861 (13.5%)	6876 (14.0%)
Hospital level			
Level 1 (medical center)	1476 (37.8%)	5032 (36.5%)	16 517 (33.7%)
Level 2 (regional hospital)	1897 (48.5%)	6455 (46.9%)	22 610 (46.1%)
Level 3 (district hospital)	535 (13.7%)	2287 (16.6%)	9918 (20.2%)
Stroke type			
Ischemic stroke	2768 (70.8%)	10 020 (72.7%)	36 316 (74.0%)
Hemorrhagic stroke	1140 (29.2%)	3754 (27.3%)	12 729 (26.0%)
Stroke severity proxies			
Estimated NIHSS	11.57±7.52	11.33±7.41	10.80±7.05
Head surgery	333 (8.5%)	1079 (7.8%)	3150 (6.4%)
Aphasia	79 (2.0%)	241 (1.8%)	1029 (2.1%)
Hemiplegia	493 (12.6%)	1724 (12.5%)	6283 (12.8%)
ICU utilization	1461 (37.4%)	5008 (36.4%)	15 102 (30.8%)
Mechanical ventilation	800 (20.5%)	2599 (18.9%)	8118 (16.6%)
Intravenous thrombolysis	104 (2.7%)	305 (2.2%)	895 (1.8%)

Categorical variables between groups were compared using chi-square tests. COPD indicates chronic obstructive pulmonary disease; ICU, intensive care unit; NIHSS, National Institutes of Health Stroke Scale; NTD, New Taiwan dollars.

weekend admission. This effect persisted after adjusting for stroke severity and other patient characteristics. Holiday season admission was significantly associated with a 24% (aOR, 1.24; 95% CI, 1.08–1.42; P=0.002), 30% (aOR, 1.30; 95% CI, 1.11–1.53; P=0.001), and 22% (aOR, 1.22; 95% CI, 1.07–1.38; P=0.003) increased risk of in-hospital, 7-day, and 30-day mortality, respectively, when compared with that of weekend admission (Table 3).

Subanalyses After Stratification for Age, Sex, and Stroke Type

The subanalyses including stratification for age, sex, and stroke type revealed similar trends regarding the effect of holiday season admission. Although a few of the comparisons did not reach statistical significance, probably because of the decreased case numbers included in each group comparison after dividing the study's population into subgroups, holiday season admission still appeared to be associated with higher mortality than weekday admission, regardless of the subgroups (Table 4). In contrast, no difference in mortality risk between those patients admitted on weekends and weekdays was observed in the subanalyses after stratification (Table 4). Overall, the interaction tests for all age, sex, and stroke type subgroups did not reveal significant interactions in the analyses of the holiday season effect. The interaction tests for subgroups in the analyses of the weekend effect revealed similar results (Table 4).

Discussion

In this nationwide cohort study, we found that admissions for stroke during a holiday season were associated with increased mortality risk, when compared with that of both weekend and weekday admissions. Importantly, this effect was still evident after adjusting for stroke severity and other important confounders. To the best of our knowledge, our study is the first to report this phenomenon of "holiday season admission" effect on stroke mortality, an effect that seems to be more pronounced than the previously reported weekend effect and is unlikely to be driven by well-known confounders.

The existence of the so-called weekend effect, although reported in >1 study, has been under intense discussion. This study is one of a few studies aiming to replicate the weekend effect for stroke admissions taking into account stroke severity.[7–9,21–23] Although we could find evidence for a weekend effect in our univariate analysis, this effect disappeared after controlling for stroke severity and other confounders. Part of the previous criticism arose from the fact that most studies did not control for or consider the

Table 2. Mortality Risks for Patients Admitted for Stroke During the Holiday Season, Weekends, and Weekdays

	Holiday Season (n=3908)					Weekends (n=13 774)					Weekdays (n=49 045)				
	No. (%) of Deaths	Crude OR (95% CI)	P Value	aOR* (95% CI)	P Value	No. (%) of deaths	Crude OR (95% CI)	P Value	aOR* (95% CI)	P Value	No. (%) of Deaths	Crude OR (95% CI)	P Value	aOR* (95% CI)	P Value
In-hospital mortality	412 (10.5)	1.36 (1.22–1.51)	<0.001	1.20 (1.06–1.36)	0.004	1224 (8.9)	1.12 (1.05–1.20)	<0.001	0.97 (0.90–1.05)	0.497	3922 (8.0)	1.00	Ref.	1.00	Ref.
7-d mortality	265 (6.8)	1.49 (1.31–1.70)	<0.001	1.33 (1.15–1.54)	<0.001	730 (5.3)	1.15 (1.06–1.25)	0.002	1.02 (0.93–1.12)	0.681	2278 (4.6)	1.00	Ref.	1.00	Ref.
30-d mortality	464 (11.8)	1.34 (1.21–1.48)	<0.001	1.21 (1.08–1.36)	0.001	1398 (10.2)	1.12 (1.05–1.19)	<0.001	0.99 (0.93–1.07)	0.876	4492 (9.2)	1.00	Ref.	1.00	Ref.

aOR indicates adjusted odds ratio; OR, odds ratio; Ref., reference group.
*aOR was calculated using multivariable logistic regression model with adjustments for the stroke severity and other characteristics listed in Table 1.

Table 3. Comparison of Mortality Risks Between Patients Admitted for Stroke on the Holiday Season and Weekends

	Holiday Season (n=3908)					Weekends (n=13 774)				
	No. (%) of Deaths	Crude OR (95% CI)	*P* Value	aOR* (95% CI)	*P* Value	No. (%) of Deaths	Crude OR (95% CI)	*P* Value	aOR* (95% CI)	*P* Value
In-hospital mortality	412 (10.5)	1.21 (1.07–1.36)	0.002	1.24 (1.08–1.42)	0.002	1224 (8.9)	1.00	Ref.	1.00	Ref.
7-d mortality	265 (6.8)	1.30 (1.12–1.50)	<0.001	1.30 (1.11–1.53)	0.001	730 (5.3)	1.00	Ref.	1.00	Ref.
30-d mortality	464 (11.8)	1.19 (1.07–1.33)	0.002	1.22 (1.07–1.38)	0.003	1398 (10.2)	1.00	Ref.	1.00	Ref.

aOR indicates adjusted odds ratio; OR, odds ratio; Ref., reference group.
*aOR was calculated using multivariable logistic regression model with adjustments for the stroke severity and other characteristics listed in Table 1.

stroke severity during their analyses.[2,4,24–27] Indeed, a few studies adjusting for a stroke severity scale or similar proxies found a much smaller or even absence of effect.[7–9,21–23] Our study also revealed negative results after adjusting for important confounders such as stroke severity, supporting the hypothesis that this weekend effect may in fact be more of a statistical artifact rather than a true epidemiologic association. However, we note that a previous large-scale cohort study reported that stroke mortality is still higher for weekend admissions when compared with that of weekday admissions, even after adjustment for stroke severity and other important clinical factors.[3] The discrepancy between that study and ours may be related to differences in the healthcare system and hospital setting organization between different countries or regions. In Taiwan, the healthcare system is known for good accessibility, comprehensive coverage, short waiting times, low cost, and high quality.[10,28] In many clinical settings, such as emergency medicine departments and intensive care units, the differences in human and medical resources between normal weekends and weekdays are minimal and, in fact, most physicians do not take Saturday off routinely in Taiwan. This makes weekend resources much more like those of weekdays and is likely to explain why we did not observe the weekend effect in our Taiwanese cohort.

On the other hand, stroke patients admitted during the Chinese New Year holiday season had a higher mortality risk even after adjusting for stroke severity and other confounders. Interestingly, this effect is associated with much higher mortalities than those typically reported for the "weekend effect" (our study reported about a 30% increase in 7-day mortality, when compared with that of admissions during both weekends and weekdays). The causes underlying this holiday season effect remain elusive but are likely to be related to decreases in healthcare resources. In many clinical settings, health resources are particularly scarce during holiday periods, such as the Chinese New Year holiday season. As Christmas is to Western countries, so is Chinese New Year to Taiwan, as it is the time when families reunite. Particularly evident is the fact that medical staff are not as available as during periods with normal working hours. Further complicating this scenario, compared with weekends, these holiday season periods last much longer (at least 4 consecutive days) and are accompanied by a more significant decrease in the availability of medical staff. Unlike the typical weekends that physicians do not routinely take Saturday off in Taiwan as mentioned above, during Chinese New Year holiday, the medical staff including doctors are usually divided into 2 teams that take turns for having the holiday season off. These prolonged holiday periods, with decreased staffing levels and resources, and increased duty time of personnel (especially physicians), may influence the quality of care. In addition, human factors such as the physical and mental condition of the medical staff, who are fewer in number and have increased levels of sleep deprivation and fatigue due to the longer working hours and higher intensity of work, should be considered. Taken together, these factors may negatively impact the quality of the care provided and result in poorer outcomes for patients admitted in the holiday season. Another possible reason underlying the holiday season effect is the difference in disease severity. Our analyses for weekend admission found that the effect for increased mortality disappeared after controlling for stroke severity and other confounders, which suggests that our models can effectively consider major confounding factors in this issue. Although the effect size of the holiday season seemed to be mildly attenuated after adjusting for such confounders, the holiday season effect was still evident and significant. This implied that, rather than only disease severity, other important factors causing the holiday season effect remained, such as those discussed above.

Stroke, as one of the leading causes of death worldwide, is a high prevalence and incidence disease that requires hospitalization. Based on the high mortality rates of stroke patients observed in our study (6.8% and 4.6% of 7-day mortality for holiday season and weekday admissions, respectively), we can calculate that the absolute increased 7-day mortality risk for holiday season admission was 2.2%, when compared with that of weekday admissions. Thus, the estimated number needed to harm was about 45, which

Table 4. Subgroup Analyses for Mortality Risks Among Patients Admitted for Stroke on the Holiday Season and Weekends, Compared With Weekdays, After Stratification for Age, Sex, and Stroke Type

	Holiday Season			Weekends		
	aOR* (95% CI)	*P* Value	*P* for Interaction	aOR* (95% CI)	*P* Value	*P* for Interaction
In-hospital mortality						
Age subgroup			0.099			0.072
<65 y	1.41 (1.13–1.74)	0.002		1.09 (0.95–1.25)	0.233	
≥65 y	1.11 (0.95–1.30)	0.199		0.93 (0.85–1.02)	0.131	
Sex subgroup			0.717			0.403
Male	1.16 (0.98–1.38)	0.089		1.00 (0.90–1.11)	0.982	
Female	1.24 (1.03–1.49)	0.027		0.94 (0.81–1.08)	0.354	
Stroke type			0.625			0.170
Ischemic	1.12 (0.93–1.35)	0.217		0.89 (0.80–1.01)	0.052	
Hemorrhagic	1.27 (1.07–1.51)	0.007		1.06 (0.95–1.18)	0.272	
7-d mortality						
Age subgroup			0.186			0.244
<65 y	1.53 (1.20–1.95)	0.001		1.12 (0.95–1.32)	0.181	
≥65 y	1.24 (1.04–1.49)	0.020		0.98 (0.88–1.10)	0.752	
Sex subgroup			0.911			0.086
Male	1.33 (1.09–1.62)	0.004		1.10 (0.97–1.24)	0.146	
Female	1.31 (1.06–1.64)	0.015		0.94 (0.81–1.08)	0.354	
Stroke type			0.536			0.957
Ischemic	1.35 (1.08–1.69)	0.008		0.99 (0.85–1.14)	0.835	
Hemorrhagic	1.31 (1.08–1.59)	0.006		1.06 (0.94–1.20)	0.372	
30-d mortality						
Age subgroup			0.136			0.006
<65 y	1.39 (1.13–1.71)	0.002		1.17 (1.03–1.34)	0.020	
≥65 y	1.17 (1.02–1.34)	0.025		0.94 (0.86–1.02)	0.128	
Sex subgroup			0.947			0.125
Male	1.21 (1.03–1.41)	0.020		1.05 (0.95–1.15)	0.360	
Female	1.20 (1.01–1.43)	0.040		0.94 (0.84–1.05)	0.245	
Stroke type			0.837			0.176
Ischemic	1.22 (1.04–1.42)	0.015		0.93 (0.84–1.03)	0.149	
Hemorrhagic	1.25 (1.06–1.48)	0.010		1.08 (0.97–1.20)	0.171	

The aOR of mortality was calculated using the weekday admission as reference group. aOR indicates adjusted odds ratio.
*aOR was calculated using multivariable logistic regression model with adjustments for the stroke severity and other characteristics listed in Table 1.

indicates that 1 extra death within 7 days after stroke admission would occur for every 45 stroke admissions during this holiday season. Moreover, the estimated number needed to harm for 30-day mortality was up to 38. In other words, if the holiday season effect can be eliminated, 1 extra death within 30 days after stroke could be avoided for every 38 stroke admissions during holiday seasons. Since almost every country or region has its own national holiday season, not only the Chinese New Year holidays in Taiwan, the holiday season effect is likely to exist in other countries as well. The public health implications of this finding are substantial, and we call attention to the need for improving the healthcare delivery system to improve prognosis of stroke patients admitted during these periods. Further studies identifying the exact underlying causes are urgently needed. These studies may help to define and implement strategies to assure consistent quality of care can be provided to stroke patients, regardless of the period of admission.

This is the first study suggesting that patients with stroke admitted during a holiday season face a higher mortality risk. The main strength of our study is in its sample size and the richness of the data set gathered in terms of clinical information. Indeed, we opted for a nationwide study design, which covered all eligible patients in the entire Taiwan population. In addition, data on our study's outcome, mortality, were acquired using the Taiwan's National Register of Deaths, which is considered to be the most accurate source for retrieving mortality data.

Some limitations of this study should be acknowledged. First, similar to other studies based on administrative health data,[2–4,8,9,24,27] we could not access some detailed clinical information (such as lifestyle, alcohol consumption, smoking status, individual's mood, physical and psychiatric status, disability status, and image/laboratory examination reports). We could not retrieve information about access to resources and could not confirm the exact mechanisms beyond the observed holiday season effect. The information on quality of stroke management also could not be obtained directly from the claims-based data set. In addition, although the association between air quality and stroke incidence and mortality was reported previously,[29] air quality data was not accessible in our database. Thus, unmeasured or unknown confounders may still be present and may have biased our estimates. Second, previous available data have indicated that there is variation in the distribution of etiologic subtypes of stroke across ethnicities, which may be attributed to both genetic and environmental factors.[30] Thus, similar to other nontransnational studies, the results of this present study on an Asian population may not be directly generalizable to other ethnicities, and further studies evaluating the effect among different countries or ethnicities are still needed. Third, patient stroke severity was not directly accessed and was estimated using the claims-based data in the present study. Although previous studies have calculated the SSI to estimate the NIHSS using Taiwan's NHIRD (which showed a high correlation with the actual NIHSS) and, consequently, functional outcomes after stroke,[17–20] bias might still exist. Fourth, we could not obtain data on time from stroke onset to stroke diagnosis in the claims database, and thus we could not further adjust for this factor in the analyses. Finally, all information for personal identification was encrypted before we could access the database, and only deidentified data could be accessed. Therefore, we were not able to evaluating patients directly for confirming the accuracy of diagnosis. However, the patients who developed stroke were only identified as such if they were hospitalized for stroke. The diagnostic codes for stroke,[13–15] as well as for many other diseases,[31–34] in the NHIRD have been validated in previous studies. However, further studies that can directly evaluate individual data confirming the diagnostic codes are needed.

Conclusions

In this nationwide cohort study with a large sample, we found that patients admitted for stroke during holiday seasons present higher mortality risks than those admitted on weekends and weekdays. The findings persisted even after adjusting for stroke severity and other possible confounders. Further studies identifying the causes underlying this epidemiologic effect are urgently needed. Our findings highlight the urgent need of establishing healthcare delivery systems that provide consistent quality of round-the-clock care for patients admitted for stroke.

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Disclosures

None.

References

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Barker-Collo S, Bartels DH, Bell ML, Benjamin EJ, Bennett D, Bhalla K, Bikbov B, Bin Abdulhak A, Birbeck G, Blyth F, Bolliger I, Boufous S, Bucello C, Burch M, Burney P, Carapetis J, Chen H, Chou D, Chugh SS, Coffeng LE, Colan SD, Colquhoun S, Colson KE, Condon J, Connor MD, Cooper LT, Corriere M, Cortinovis M, de Vaccaro KC, Couser W, Cowie BC, Criqui MH, Cross M, Dabhadkar KC, Dahodwala N, De Leo D, Degenhardt L, Delossantos A, Denenberg J, Des Jarlais DC, Dharmaratne SD, Dorsey ER, Driscoll T, Duber H, Ebel B, Erwin PJ, Espindola P, Ezzati M, Feigin V, Flaxman AD, Forouzanfar MH, Fowkes FG, Franklin R, Fransen M, Freeman MK, Gabriel SE, Gakidou E, Gaspari F, Gillum RF, Gonzalez-Medina D, Halasa YA, Haring D, Harrison JE, Havmoeller R, Hay RJ, Hoen B, Hotez PJ, Hoy D, Jacobsen KH, James SL, Jasrasaria R, Jayaraman S, Johns N, Karthikeyan G, Kassebaum N, Keren A, Khoo JP, Knowlton LM, Kobusingye O, Koranteng A, Krishnamurthi R, Lipnick M, Lipshultz SE, Ohno SL, Mabweijano J, MacIntyre MF, Mallinger L, March L, Marks GB, Marks R, Matsumori A, Matzopoulos R, Mayosi BM, McAnulty JH, McDermott MM, McGrath J, Mensah GA, Merriman TR, Michaud C, Miller M, Miller TR, Mock C, Mocumbi AO, Mokdad AA, Moran A, Mulholland K, Nair MN, Naldi L, Narayan KM, Nasseri K, Norman P, O'Donnell M, Omer SB, Ortblad K, Osborne R, Ozgediz D, Pahari B, Pandian JD, Rivero AP, Padilla RP, Perez-Ruiz F, Perico N, Phillips D, Pierce K, Pope CA III, Porrini E, Pourmalek F, Raju M, Ranganathan D, Rehm JT, Rein DB, Remuzzi G, Rivara FP, Roberts T, De Leon FR, Rosenfeld LC, Rushton L, Sacco RL, Salomon JA, Sampson U, Sanman E, Schwebel DC, Segui-Gomez M, Shepard DS, Singh D, Singleton J, Sliwa K, Smith E, Steer A, Taylor JA, Thomas B, Tleyjeh IM, Towbin JA, Truelsen T, Undurraga EA, Venketasubramanian N, Vijayakumar L, Vos T, Wagner GR, Wang M, Wang W, Watt K, Weinstock MA, Weintraub R, Wilkinson JD, Woolf AD, Wulf S, Yeh PH, Yip P, Zabetian A, Zheng ZJ, Lopez AD, Murray CJ, AlMazroa MA, Memish ZA. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2095–2128.
2. Saposnik G, Baibergenova A, Bayer N, Hachinski V. Weekends: a dangerous time for having a stroke? *Stroke*. 2007;38:1211–1215.
3. Fang J, Saposnik G, Silver FL, Kapral MK. Association between weekend hospital presentation and stroke fatality. *Neurology*. 2010;75:1589–1596.
4. Tung YC, Chang GM, Chen YH. Associations of physician volume and weekend admissions with ischemic stroke outcome in Taiwan: a nationwide population-based study. *Med Care*. 2009;47:1018–1025.
5. Sorita A, Ahmed A, Starr SR, Thompson KM, Reed DA, Dabrh AM, Prokop L, Kent DM, Shah ND, Murad MH, Ting HH. Off-hour presentation and outcomes

in patients with acute ischemic stroke: a systematic review and meta-analysis. *Eur J Intern Med*. 2014;25:394–400.

6. Hoh BL, Chi YY, Waters MF, Mocco J, Barker FG II. Effect of weekend compared with weekday stroke admission on thrombolytic use, in-hospital mortality, discharge disposition, hospital charges, and length of stay in the Nationwide Inpatient Sample Database, 2002 to 2007. *Stroke*. 2010;41:2323–2328.
7. Albright KC, Savitz SI, Raman R, Martin-Schild S, Broderick J, Ernstrom K, Ford A, Khatri R, Kleindorfer D, Liebeskind D, Marshall R, Merino JG, Meyer DM, Rost N, Meyer BC. Comprehensive stroke centers and the 'weekend effect': the SPOTRIAS experience. *Cerebrovasc Dis*. 2012;34:424–429.
8. Inoue T, Fushimi K. Weekend versus weekday admission and in-hospital mortality from ischemic stroke in Japan. *J Stroke Cerebrovasc Dis*. 2015;24:2787–2792.
9. Hsieh CY, Lin HJ, Chen CH, Li CY, Chiu MJ, Sung SF. "Weekend effect" on stroke mortality revisited: application of a claims-based stroke severity index in a population-based cohort study. *Medicine (Baltimore)*. 2016;95:e4046.
10. Wu T-Y, Majeed A, Kuo KN. An overview of the healthcare system in Taiwan. *London J Prim Care (Abingdon)*. 2010;3:115–119.
11. Wu CY, Chen YJ, Ho HJ, Hsu YC, Kuo KN, Wu MS, Lin JT. Association between nucleoside analogues and risk of hepatitis B virus-related hepatocellular carcinoma recurrence following liver resection. *JAMA*. 2012;308:1906–1914.
12. Tsan YT, Lee CH, Ho WC, Lin MH, Wang JD, Chen PC. Statins and the risk of hepatocellular carcinoma in patients with hepatitis C virus infection. *J Clin Oncol*. 2013;31:1514–1521.
13. Hsieh CY, Chen CH, Li CY, Lai ML. Validating the diagnosis of acute ischemic stroke in a National Health Insurance claims database. *J Formos Med Assoc*. 2015;114:254–259.
14. Cheng CL, Kao YH, Lin SJ, Lee CH, Lai ML. Validation of the National Health Insurance Research Database with ischemic stroke cases in Taiwan. *Pharmacoepidemiol Drug Saf*. 2011;20:236–242.
15. Chang CH, Lin CH, Caffrey JL, Lee YC, Liu YC, Lin JW, Lai MS. Risk of intracranial hemorrhage from statin use in Asians: a nationwide cohort study. *Circulation*. 2015;131:2070–2078.
16. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383.
17. Sung SF, Hsieh CY, Kao Yang YH, Lin HJ, Chen CH, Chen YW, Hu YH. Developing a stroke severity index based on administrative data was feasible using data mining techniques. *J Clin Epidemiol*. 2015;68:1292–1300.
18. Sung SF, Hsieh CY, Lin HJ, Chen YW, Chen CH, Kao Yang YH, Hu YH. Validity of a stroke severity index for administrative claims data research: a retrospective cohort study. *BMC Health Serv Res*. 2016;16:509.
19. Hung LC, Sung SF, Hsieh CY, Hu YH, Lin HJ, Chen YW, Yang YK, Lin SJ. Validation of a novel claims-based stroke severity index in patients with intracerebral hemorrhage. *J Epidemiol*. 2017;27:24–29.
20. Hsieh CY, Huang HC, Wu DP, Li CY, Chiu MJ, Sung SF. Effect of rehabilitation intensity on mortality risk after stroke. *Arch Phys Med Rehabil*. 2018;99:1042–1048.e1046.
21. Kristiansen NS, Mainz J, Norgard BM, Bartels PD, Andersen G, Johnsen SP. Off-hours admission and acute stroke care quality: a nationwide study of performance measures and case-fatality. *Stroke*. 2014;45:3663–3669.
22. Jauss M, Oertel W, Allendoerfer J, Misselwitz B, Hamer H. Bias in request for medical care and impact on outcome during office and non-office hours in stroke patients. *Eur J Neurol*. 2009;16:1165–1167.
23. Kamitani S, Nishimura K, Nakamura F, Kada A, Nakagawara J, Toyoda K, Ogasawara K, Ono J, Shiokawa Y, Aruga T, Miyachi S, Nagata I, Matsuda S, Miyamoto Y, Iwata M, Suzuki A, Ishikawa KB, Kataoka H, Morita K, Kobayashi Y, Iihara K. Consciousness level and off-hour admission affect discharge outcome of acute stroke patients: a J-ASPECT study. *J Am Heart Assoc*. 2014;3:e001059. DOI: 10.1161/JAHA.114.001059.
24. Ogbu UC, Westert GP, Slobbe LC, Stronks K, Arah OA. A multifaceted look at time of admission and its impact on case-fatality among a cohort of ischaemic stroke patients. *J Neurol Neurosurg Psychiatry*. 2011;82:8–13.
25. Turin TC, Kita Y, Rumana N, Ichikawa M, Sugihara H, Morita Y, Tomioka N, Okayama A, Nakamura Y, Ueshima H. Case fatality of stroke and day of the week: is the weekend effect an artifact? Takashima Stroke Registry, Japan (1988–2003). *Cerebrovasc Dis*. 2008;26:606–611.
26. Reeves MJ, Smith E, Fonarow G, Hernandez A, Pan W, Schwamm LH. Off-hour admission and in-hospital stroke case fatality in the Get With the Guidelines-Stroke program. *Stroke*. 2009;40:569–576.
27. McKinney JS, Deng Y, Kasner SE, Kostis JB. Comprehensive stroke centers overcome the weekend versus weekday gap in stroke treatment and mortality. *Stroke*. 2011;42:2403–2409.
28. Ho Chan WS. Taiwan's healthcare report 2010. *EPMA J*. 2010;1:563–585.
29. Shah AS, Lee KK, McAllister DA, Hunter A, Nair H, Whiteley W, Langrish JP, Newby DE, Mills NL. Short term exposure to air pollution and stroke: systematic review and meta-analysis. *BMJ*. 2015;350:h1295.
30. Ornello R, Degan D, Tiseo C, Di Carmine C, Perciballi L, Pistoia F, Carolei A, Sacco S. Distribution and temporal trends from 1993 to 2015 of ischemic stroke subtypes: a systematic review and meta-analysis. *Stroke*. 2018;49:814–819.
31. Cheng CL, Chien HC, Lee CH, Lin SJ, Yang YH. Validity of in-hospital mortality data among patients with acute myocardial infarction or stroke in National Health Insurance Research Database in Taiwan. *Int J Cardiol*. 2015;201:96–101.
32. Su VY, Liu CJ, Wang HK, Wu LA, Chang SC, Perng DW, Su WJ, Chen YM, Lin EY, Chen TJ, Chou KT. Sleep apnea and risk of pneumonia: a nationwide population-based study. *CMAJ*. 2014;186:415–421.
33. Su VY, Yang KY, Yang YH, Tsai YH, Perng DW, Su WJ, Chou KT, Su KC, Yen YF, Chen PC. Use of ICS/LABA combinations or LAMA is associated with a lower risk of acute exacerbation in patients with coexistent COPD and asthma. *J Allergy Clin Immunol Pract*. 2018;6:1927–1935.e1923.
34. Cheng CL, Lee CH, Chen PS, Li YH, Lin SJ, Yang YH. Validation of acute myocardial infarction cases in the National Health Insurance Research Database in Taiwan. *J Epidemiol*. 2014;24:500–507.