Original Article

# Impact of Smoke-Free Legislation on Acute Myocardial Infarction and Subtypes of Stroke Incidence in Shenzhen, China, 2012–2016: An Interrupted Time Series Analysis*

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**Abstract**

**Objective** This study assesses the impact of smoke-free legislation on the incidence rate for acute myocardial infarction (AMI) and stroke in Shenzhen.

**Methods** Data on ischemic ($n$ = 72,945) and hemorrhagic ($n$ = 18,659) stroke and AMI ($n$ = 17,431) incidence covering about 12 million people in Shenzhen from 2012 to 2016 were used. Immediate and gradual changes in incidence rates were analyzed using segmented Poisson regression.

**Results** Following the smoke-free legislation, a 9% (95% *CI*: 3%–15%) immediate reduction was observed in AMI incidence, especially in men (8%, 95% *CI*: 1%–14%) and in those aged 65 years and older (17%, 95% *CI*: 9%–25%). The gradual annual benefits were observed only in hemorrhagic and ischemic stroke incidence, with a 7% (95% *CI*: 2%–11%) and 6% (95% *CI*: 4%–8%) decrease per year, respectively. This health effect extended gradually to the 50–64 age group. In addition, neither the immediate nor gradual decrease in stroke and AMI incidence rates did not show statistical significance among the 35–49 age group ($P$ > 0.05).

**Conclusion** Smoke-free legislation was enforced well in Shenzhen, which would generate good experiences for other cities to enact and enforce smoke-free laws. This study also provided more evidence of the health benefits of smoke-free laws on stroke and AMI.

**Key words:** Smoke-free legislation; Second-hand smoke; Tobacco; Myocardial infarction; Stroke; Prevention

*Biomed Environ Sci, 2023; 36(6): 527-536* *doi: 10.3967/bes2023.064* *ISSN: 0895-3988*

*www.besjournal.com (full text)* *CN: 11-2816/Q* 

## INTRODUCTION

Tobacco use, including active smoking and exposure to secondhand smoke (SHS), is a leading cause of preventable diseases worldwide, especially for major non-communicable diseases[1]. Among them, the effect of SHS exposure on the public's health is substantial and extensive. Evidence indicates that the hazard of SHS exposure was nearly as large (80%–90%) as those of chronic active smoking[2]. Given the considerable disease burden caused by SHS exposure, the WHO

*This research was supported by the CAMS Innovation Fund for Medical Sciences [CIFMS; 2016-12M-3-001] and the China Medical Board (Strengthen Capacity of Study and Application on Burden of Disease in Health Care System of China – Establishment and Development of Chinese Burden of Disease Research and Dissemination Center [15-208].

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Framework Convention on Tobacco Control (WHO FCTC) requires each member state to protect the public by adopting effective legislative measures[3]. Until 2021, about 5.3 billion people have been covered by at least one of the six MPOWER tobacco control policy measures at the highest level of achievement[4].

China is the largest consumer and producer of tobacco products worldwide. More than 350 million smokers smoke more than 40% of the world's cigarettes[5] and approximately 740 million non-smokers to SHS[6]. Among more than one million Chinese people who die of tobacco-related diseases annually, SHS exposure is responsible for nearly 230,000 deaths[7,8]. Thus, China signed the WHO FCFC in 2003 and ratified it in 2005. However, it still does not have national smoke-free legislation that satisfies the WHO FCTC requirement[6].

Based on the WHO FCTC regulation, more and more cities in China have successively revised or enacted smoke-free regulations since 2010. More than 20 cities have implemented smoke-free regulations to ban smoking in public places, including Shenzhen. However, the implementation of smoke-free legislation has been quantitatively evaluated only in four cities (Hong Kong, Tianjin, Qingdao, and Beijing, China), using the hospital admission or mortality data for acute myocardial infarction (AMI) and stroke from hospitals or Diseases Surveillance Points System[9-12]. Numerous studies, mainly from North America and Europe, showed that the burden of cardiovascular and cerebrovascular diseases decreased sharply after implementing smoke-free legislation[9-16], especially for the AMI mortality rate or admission prevalence[10,11,17-21]. Meanwhile, only some studies focused on the subtypes of stroke, with inconsistencies among the results of some studies on stroke[9,11,12,22-24]. In addition, the relative risks (*RR*s) for ischemic and hemorrhagic strokes caused by SHS were different, highlighting the importance of considering these separately[25,26].

The city of Shenzhen, the first special economic zoom of China, enacted local smoke-free regulations in 1998, but with several exceptions and loopholes. The regulation was amended on March 01, 2014, to meet the requirements of the WHO FCTC, with deliberations for possible exemptions to the regulation (entertainment venues and leisure service establishments were only defined as restricted smoking places and were not 100% banned until 2017), because the local government thought that it would take several years between introducing the law and enacting it[27]. This law banned tobacco advertising, promotion, and sponsorship and supported various institutions in actively carrying out tobacco control publicity and education. It was expected to function under the WHO FCTC framework to reduce and prevent the harm of tobacco exposure. According to a questionnaire survey conducted in Shenzhen in 2016 using random and convenience sampling methods, only 9.9% of public places smokers were found smoking[28]. However, the implementation and the health benefit of this smoking ban need to be further evaluated. The interrupted time series (ITS) design is well-suited to address some unique characteristics of the interventions being studied and measured changes in outcomes longitudinally[29], which also has been widely used in the assessment of tobacco control policy implementation[9-12]. Thus, to promote the local smoke-free law implementation well, this study aimed to assess the implementation of Shenzhen's smoke-free legislation using AMI and major subtypes of stroke incidence and to estimate the health benefit of the legislation.

## MATERIALS AND METHODS

### *Data*

AMI incidence data were obtained from the Shenzhen AMI Registry System. This system was established in January 2012 and covered all Shenzhen permanent residents. Each AMI case was reported by all the secondary and tertiary hospitals in Shenzhen[30]. The Shenzhen Center for Chronic Disease Control assessed and checked the data quality since underreporting existed in the early stage of system establishment. Therefore, we analyzed the AMI incidence data starting from May 29, 2012, when the system was stable. Stroke incidence data were obtained from the Shenzhen Stroke Registry System, established in October 2002. Its reporting procedures were similar to the AMI Registry System[31]. Since the AMI incidence data started in 2012, this was used as the start date for the stroke data. Study subjects included in- and out-patients for AMI or stroke and ambulatory patients.

The structure of these two databases is similar. They record individual information, including a unique ID, age, sex, household type (urban or rural), dates of admission and primary diagnosis, and other relevant information. The classification of AMI and stroke was based on the International Classification of Diseases, Tenth Version (ICD-10). We identified all cases with a principal diagnosis of stroke (hemorrhagic stroke: I60–I62, ischemic stroke: I63) or AMI (I21). The incidence of AMI and stroke was calculated based on the number of events. Recurrence within 28 days was not included in incidence calculations, and recurrence after 28 days was considered a new case[10,11]. The sample was restricted only to the resident population aged ≥ 35 due to the low incidence of stroke and AMI among people aged < 35.

The meteorological data on the average daily temperature and relative humidity were obtained from the Shenzhen Meteorological Bureau. The daily particulate matter with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$) concentrations (μg/$m^3$) from 2015 to 2016 were obtained from the local Environmental Monitoring Center Station. $PM_{2.5}$ data from 2012 to 2014 were replaced with Tracking Air Pollution in China (TAP, http://tapdata.org.cn/) since the local Environmental Monitoring Center Station did not monitor $PM_{2.5}$ before 2015. This approach to tracking air pollution has been described elsewhere[32,33]. Single-year population estimates by gender and age were obtained from the Shenzhen Bureau of Statistics.

### *Statistical Analysis*

The crude incidence rate for all AMI, hemorrhagic stroke, and ischemic stroke was calculated as the number of annually diagnosed new cases divided by the resident population. We also calculated age-standardized incidence rates using the age structure of the Shenzhen population in 2017.

A Poisson regression model with interrupted time series was used to test the immediate and gradual changes in the crude incidence rate after the smoke-free legislation. All variables in the model were established as a time series in weeks. Multiple models were fitted by sex and age groups (35–49, 50–64, and ≥ 65 years) to evaluate the effect of the law on different subgroups. The response variable of each model was the weekly number of events for the selected diseases. An indicator variable was used to define the smoke-free legislation, with 0 given to the weeks before enforcing the law and 1 given to the weeks after enforcing it. An interaction term between legislation and weeks after the law implementation was included to estimate the change in the slope of the secular trend, and the weeks were set as 0 before enforcing the law. The age group and sex-specific resident population were included as an offset variable with a fixed coefficient of 1 in each model. A linear predictor, adjusted the long-term time trend, was included to quantify the changes in population risk factors, treatment, and other secular trends[10,11]. A Fourier series of sine and cosine terms was used to capture the seasonal pattern in the model. The study period for stroke and AMI was from January 01, 2012, to December 31, 2016, and from May 29, 2012, to December 31, 2016, respectively. In addition, the temperature (°C), relative humidity (%), and $PM_{2.5}$ were adjusted in all models[12,34]. The Poisson regression model is as follows:

$$\begin{aligned} \log(Y) &= \beta_0 + \beta_1 T + \beta_2 Law + \beta_3 (Law \times T') \\ &+ \beta_4 \cos\left(\frac{2T\pi}{52.1775}\right) + \beta_5 \sin\left(\frac{2T\pi}{52.1775}\right) \\ &+ \beta_k (Tem, Hum, PM_{2.5}) + offset \log(P), \end{aligned} \quad (1)$$

where $Y$ denotes weekly age- and sex-specific events (AMI, hemorrhagic stroke, and ischemic stroke), $P$ is the age- and sex-specific resident population every year, $T$ is the time variable during the study period (week, AMI: from 1 to 240, hemorrhagic stroke and ischemic stroke: from 1 to 261), $T'$ is the time variable (week) after law enforcement. *Law* represents the implementation of the smoke-free law (AMI: *Law* equals 0 before 93 weeks/1 after 93 weeks, stroke: *Law* equals 0 before 114 weeks/1 after 114 weeks). $\beta_0$ is the baseline level. $\beta_1$ represents the secular trend before law enforcement, $\beta_2$ represents the immediate effect of the ban, $\beta_3$ represents the gradual weekly effect of the ban, $\beta_4$ and $\beta_5$ represent seasonality in the model, $\beta_k$ denotes the coefficient for a set of covariates. Models were fitted separately for each age group and sex.

The effect of the smoke-free legislation was reflected by the immediate and gradual change in the incidence rate, respectively. The former was quantified as $100[\exp(\beta_2)-1]$, and the latter was quantified as $100[\exp(52.1775\times\beta_3)-1]$. In addition, the number of averted events (net post-legislation decrease) was calculated as the subtraction between the actual events and the predicted number of events without the influence of the law. All analyses were conducted in R V.4.1.0 (R Foundation for Statistical Computing, Vienna, Austria).

Ethical approval was not required as the data were deidentified, and results were presented at the group level.

## RESULTS

### *Basic Information*

Between January 01, 2012, and December 31, 2016, 72,945 incident ischemic strokes and 18,659 incident hemorrhagic strokes were identified among the resident population aged ≥ 35 years in Shenzhen. There were 17,431 cases of incident AMI from May 29, 2012, to December 31, 2016. The annual incidence rates were 398.9, 102.0, and 104.1 per 100,000 population for ischemic stroke, hemorrhagic stroke, and AMI, respectively. Overall, an annual increase in the age-standardized incidence rates for ischemic stroke and AMI was observed during the study period. A similar trend was also observed for hemorrhagic stroke. However, its standardized rates decreased in 2015 compared with previous years and then significantly increased rapidly in 2016 (Table 1). We calculated the average annual incidence rate of AMI and two stroke subtypes by age and gender during the study period (Table 2). Regardless of any disease, the incidence in men was higher than in women. In addition, the older the age group, the higher the incidence was. In particular, the incidence of ischemic stroke in the age group ≥ 65 years was about 48 times higher than in the age group 35–49 years.

### *Results of Incidence Regressions*

For incidence rates of hemorrhagic stroke and ischemic stroke, after the enforcement of the law, the relative risk (*RR*) values on immediate effects were 0.94 [95% confidence interval (*CI*): 0.89–1.00] and 1.03 (95% *CI*: 1.00–1.07), respectively. These values meant that the immediate changes were not statistically significant (Table 3). An immediate decrease was seen in the age group ≥ 50 for hemorrhagic stroke, with statistical significance only in the age group 50–64. The immediate reduction in ischemic stroke was not observed in all subgroups. Regarding long-term effects, there was a 7% (*RR*: 0.93; 95% *CI*: 0.89–0.98) and 6% (*RR*: 0.94; 95% *CI*: 0.92–0.96) decrease in the above two diseases, respectively, with statistical significance. These annual, gradual changes were also observed in both genders with statistical significance. Regarding different age groups, the decreasing trends for hemorrhagic stroke and ischemic stroke were also more pronounced in the older age groups, with the largest reduction of 12% (*RR*: 0.88; 95% *CI*: 0.81–0.96) and 9% (*RR*: 0.91; 95% *CI*: 0.88–0.94) among the age group ≥ 65, respectively. For the age

**Table 1.** Annual incidence rate (1/100,000) of AMI and stroke among the resident population aged 35 years and older in Shenzhen from 2012 to 2016

| Year | Ischemic stroke incidence | | | Hemorrhagic stroke | | | AMI | | |
|---|---|---|---|---|---|---|---|---|---|
| | Case, *n* | Crude annual rate (95% *CI*) | Standardized annual rate (95% *CI*) | Case, *n* | Crude annual rate (95% *CI*) | Standardized annual rate (95% *CI*) | Case, *n* | Crude annual rate (95% *CI*) | Standardized annual rate (95% *CI*) |
| 2012 | 10,891 | 311.1 (305.3, 317.0) | 281.8 (276.3, 287.4) | 3,084 | 88.1 (85.0, 91.2) | 83.6 (80.6, 86.6) | 1,484* | 72.7 (69.9, 75.5) | 69.6 (68.8, 72.4) |
| 2013 | 12,508 | 355.2 (349.0, 361.4) | 321.0 (315.1, 326.9) | 3,551 | 100.8 (97.5, 104.2) | 95.2 (92.0, 98.5) | 3,170 | 90.0 (86.9, 93.2) | 82.5 (79.5, 85.5) |
| 2014 | 14,693 | 412.5 (405.8, 419.1) | 372.8 (366.5, 379.2) | 3,716 | 104.3 (101.0, 107.7) | 98.7 (95.5, 102.0) | 3,616 | 101.5 (98.2, 104.8) | 93.1 (89.9, 96.3) |
| 2015 | 16,283 | 432.8 (426.2, 439.4) | 391.4 (385.1, 397.7) | 3,784 | 100.6 (97.4, 103.8) | 95.5 (92.4, 98.7) | 3,999 | 106.3 (103.0, 109.6) | 97.5 (94.4, 100.7) |
| 2016 | 18,570 | 471.5 (464.8, 478.3) | 427.2 (420.7, 433.6) | 4,524 | 114.9 (111.5, 118.2) | 108.7 (105.5, 112.0) | 5,162 | 131.1 (127.5, 134.6) | 120.1 (116.7, 132.5) |
| Total | 72,945 | 398.9 (392.5, 405.4) | - | 18,659 | 102.0 (98.8, 105.3) | - | 17,431 | 104.1 (100.8, 107.4) | - |

***Note.*** *Excluding the first 21 weeks of data.

group 35–49, the change in the annual incidence of either disease was not significant ($P > 0.05$).

After the implementation of the law, an analysis of its immediate effect showed a decrease in the AMI incidence rate, with a 9% (*RR*: 0.91; 95% *CI*: 0.85–0.97) reduction. The immediate reductions in incidence associated with the law were the highest in the age group ≥ 65, with reductions of 17% (*RR*: 0.83; 95% *CI*: 0.75–0.91). In addition, an annual change of 6% was also observed in the AMI incidence rate. However, this difference was not statistically significant (*RR*: 0.94; 95% *CI*: 0.89–1.00), which was the same for different age groups. In different genders, an annual 8% reduction (*RR*: 0.92; 95% *CI*: 0.86–0.99) was observed only among men, as detailed in Table 3.

***Protective Effect of the Law Against Incident Rates***

Figures 1–3 show the observed and predicted trends in the weekly incidence of AMI and the two subtypes of stroke among permanent residents of Shenzhen. The weekly variation incidence rate followed a seasonal pattern, with higher incidence rates in the winter and lower rates during the summer, particularly for AMI and hemorrhagic stroke (Figure 1 and Figure 2). The health effect of the smoke-free legislation can be seen in the difference in trends between the predicted incidence rates for the counterfactual scenario (red line) and the actual rate (blue line). In sum, during the whole smoke-free legislation period of 2.7 years, there were 2,422 incidents of AMI, 2,951 incidents of ischemic strokes, and 2014 incidents of hemorrhagic strokes that had been averted due to the implementation of the law. The net decrease in AMI incidence was estimated as 11.4% during the first year, reaching 16.7% by December 2016, which also was observed in all subgroups, except that the net

**Table 2.** Age and sex-specific incidence rates (1/100,000) of AMI and stroke in Shenzhen from 2012 to 2016

| Subgroups | Ischemic stroke | | | Hemorrhagic stroke | | | AMI | | |
|---|---|---|---|---|---|---|---|---|---|
| | Case, *n* | % | Average incidence (95% *CI*) | Case, *n* | % | Average incidence (95% *CI*) | Case, *n* | % | Average incidence (95% *CI*) |
| Age (years) | | | | | | | | | |
| 35–49 | 11,236 | 15.4 | 79.2 (75.9–82.5) | 6,539 | 35.0 | 46.1 (43.6–48.6) | 3,551 | 20.3 | 27.2 (25.3–29.2) |
| 50–64 | 24,536 | 33.6 | 787.7 (765.7–809.6) | 6,945 | 37.2 | 222.9 (211.2–234.7) | 5,391 | 30.8 | 188.3 (177.6–199.1) |
| ≥ 65 | 37,173 | 51.0 | 3782.0 (3697.7–3866.3) | 5,175 | 27.7 | 526.5 (494.5–558.5) | 7,005 | 40.0 | 775.6 (736.8–814.4) |
| Sex | | | | | | | | | |
| Men | 43,606 | 59.8 | 432.8 (423.7–441.9) | 12,097 | 64.8 | 120.1 (115.3–124.8) | 13,153 | 75.2 | 142.1 (136.9–147.3) |
| Women | 29,339 | 40.2 | 357.4 (348.3–366.5) | 6,562 | 35.2 | 79.9 (75.6–84.3) | 4,345 | 24.8 | 57.6 (53.9–61.3) |

**Table 3.** Multivariate analysis* of overall, sex-, and age-specific post-legislation effects on the incidence of AMI and two subtypes of stroke, Shenzhen

| Subgroups | Ischemic stroke incidence | | Hemorrhagic stroke incidence | | AMI incidence | |
|---|---|---|---|---|---|---|
| | Immediate effect | Gradual effect per annum | Immediate effect | Gradual effect per annum | Immediate effect | Gradual effect per annum |
| | *RR* (95% *CI*) | *RR* (95% *CI*) | *RR* (95% *CI*) | *RR* (95% *CI*) | *RR* (95% *CI*) | *RR* (95% *CI*) |
| Overall | 1.03 (1.00–1.07) | 0.94 (0.92–0.96) | 0.94 (0.89–1.00) | 0.93 (0.89–0.98) | 0.91 (0.85–0.97) | 0.94 (0.89–1.00) |
| Age (years) | | | | | | |
| 35–49 | 1.11 (1.02–1.20) | 1.00 (0.95–1.07) | 1.04 (0.94–1.15) | 1.00 (0.92–1.08) | 1.09 (0.94–1.26) | 0.99 (0.87–1.13) |
| 50–64 | 1.07 (1.01–1.13) | 0.95 (0.91–0.99) | 0.93 (0.84–1.03) | 0.91 (0.85–0.98) | 0.93 (0.83–1.05) | 0.91 (0.82–1.12) |
| ≥ 65 | 1.00 (0.96–1.04) | 0.91 (0.88–0.94) | 0.85 (0.76–0.96) | 0.88 (0.81–0.96) | 0.83 (0.75–0.91) | 0.94 (0.86–1.04) |
| Sex | | | | | | |
| Men | 1.02 (0.98–1.07) | 0.93 (0.91–0.96) | 0.95 (0.88–1.02) | 0.94 (0.89–0.99) | 0.92 (0.86–0.99) | 0.92 (0.86–0.99) |
| Women | 1.05 (1.00–1.11) | 0.95 (0.91–0.98) | 0.93 (0.84–1.03) | 0.92 (0.86–0.99) | 0.88 (0.77–1.01) | 1.01 (0.90–1.15) |

***Note.*** *Adjusted for time trend, population, seasonality, temperature, relative humidity, and $PM_{2.5}$.

post-legislation reductions in the age group 35–49 and women were not apparent. Similar patterns were seen in hemorrhagic stroke and all of its subgroups. In the 2.7 years following the legislation, there was a net reduction of 15.1% for hemorrhagic stroke and only 6.9% for ischemic stroke.

## DISCUSSION

By analyzing incidence data from two Disease Registry Systems covering about 12 million people in Shenzhen over 5 years, this study provided extensive longitudinal data and high-quality outcome assessments. Therefore, it could compare the implementation progress of smoke-free laws with other cities (such as Qingdao, Tianjin, and Beijing) in China and serve to motivate those cities without smoke-free laws to enact these laws as soon as possible. In addition, this study is the first to assess the health effects of the implementation of smoke-free legislation on major subtypes of stroke in China.

The implementation effect indicators of smoke-free legislation can be divided into short-term, medium-term, and long-term indicators[35]. Among them, the illegal smoking rate and SHS in non-smoking places can reflect the direct effects of enforcing the law. According to two surveys conducted in Shenzhen in 2015, the percentage of places where smokers were found was 9.9% after the policy, and the percentage of places where cigarette butts, the smell of smoke, or smokers were found was 20.6%[28]. More than 50% of residents learned about tobacco control through TV or the Internet[36]. 91.4% of managers and 81.0% of the public supported banning smoking in public places after the legislation, respectively[28]. Overall, these short-term and medium-term indicators all showed that the implementation of the smoke-free legislation had given Shenzhen residents a very high sense of identity with this law. Our study provided more evidence of the health benefits of smoke-free legislation on long-term indicators. We found that as time passed, the health effects were gained for the older population and gradually extended to the younger group.

In general, the smoke-free law was implemented

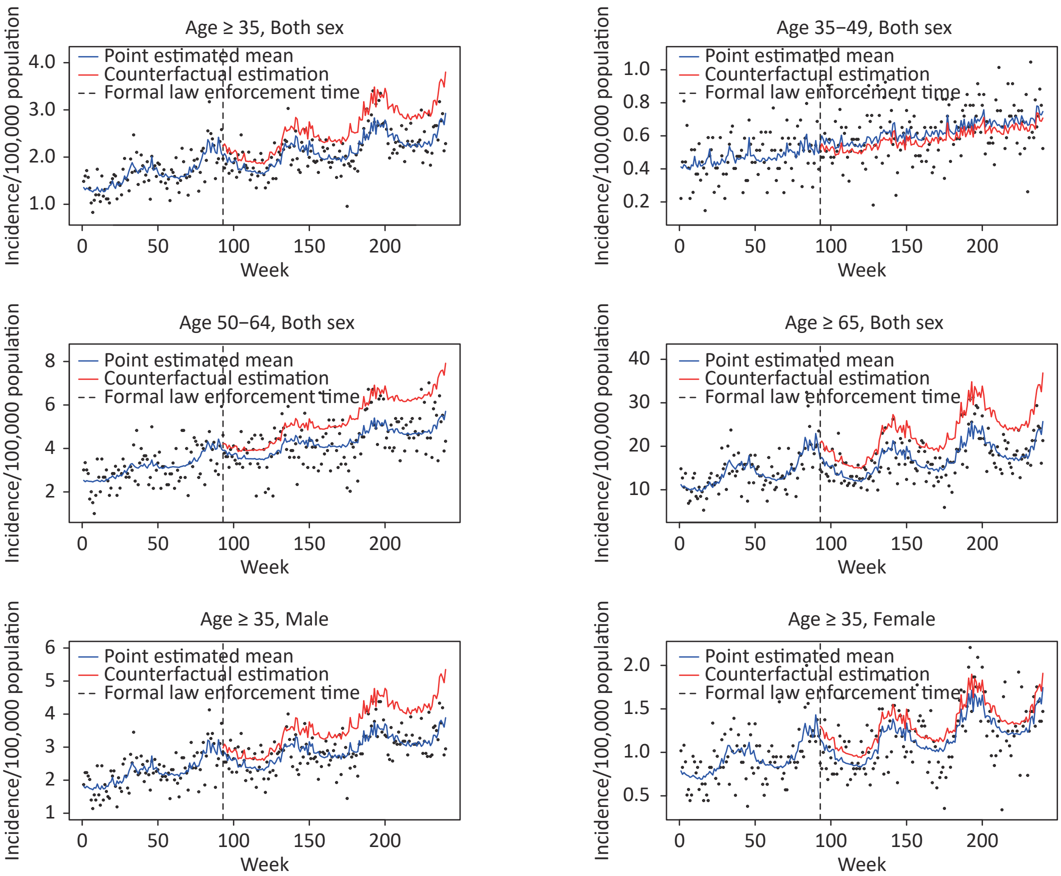


**Figure 1.** Observed and predicted weekly AMI incidence rates (1/100,000) in Shenzhen (2012–2016).

well in Shenzhen. Following the smoke-free law, immediate reductions were observed in AMI, especially in men and in those aged 65 years and older. The gradual annual benefits were only observed in hemorrhagic stroke and ischemic stroke incidence rates after the law, with the effect extending to those aged 50 years or older. However, no matter which disease it was, the age group 35–49 was not sensitive to the health benefits of the legislation. In our opinion, the most valuable experience learned from Shenzhen is that multi-agencies should implement an effective monitoring mechanism, including the Administration Department for Market Regulation, Bureau of Transportation, Bureau of Public Security, Bureau of Education in Shenzhen, and others[37]. The Tobacco Control Office of Shenzhen, called the administration department, charges legislation implementation. First, all the smoke-free organizations or departments referred to in the law were classified into different groups, and a designated agency administrated each group. The administration required all the agencies to perform the inspections as per their everyday activities. Random checks were implemented by the administration from time to time with live broadcasts by the media to enhance the deterrence of the law and social influence. One public place may be inspected several times until it implements the law well, which is called "wheel war" in Chinese. In addition, there was a volunteer team in Shenzhen. After the administration trained them, they also helped to inspect the policy implementation in all the public places during their daily life. Of course, Shenzhen's proximity to Hong Kong exposes its residents to many aspects of life in Hong Kong, including living in a smoke-free environment, which also helps the residents accept it and abide by the law. Therefore, we believe that other cities adjacent to Shenzhen will be impacted by this smoke-free environment in the near future.

Our results showed that the AMI incidence rates significantly decreased as immediate effects after

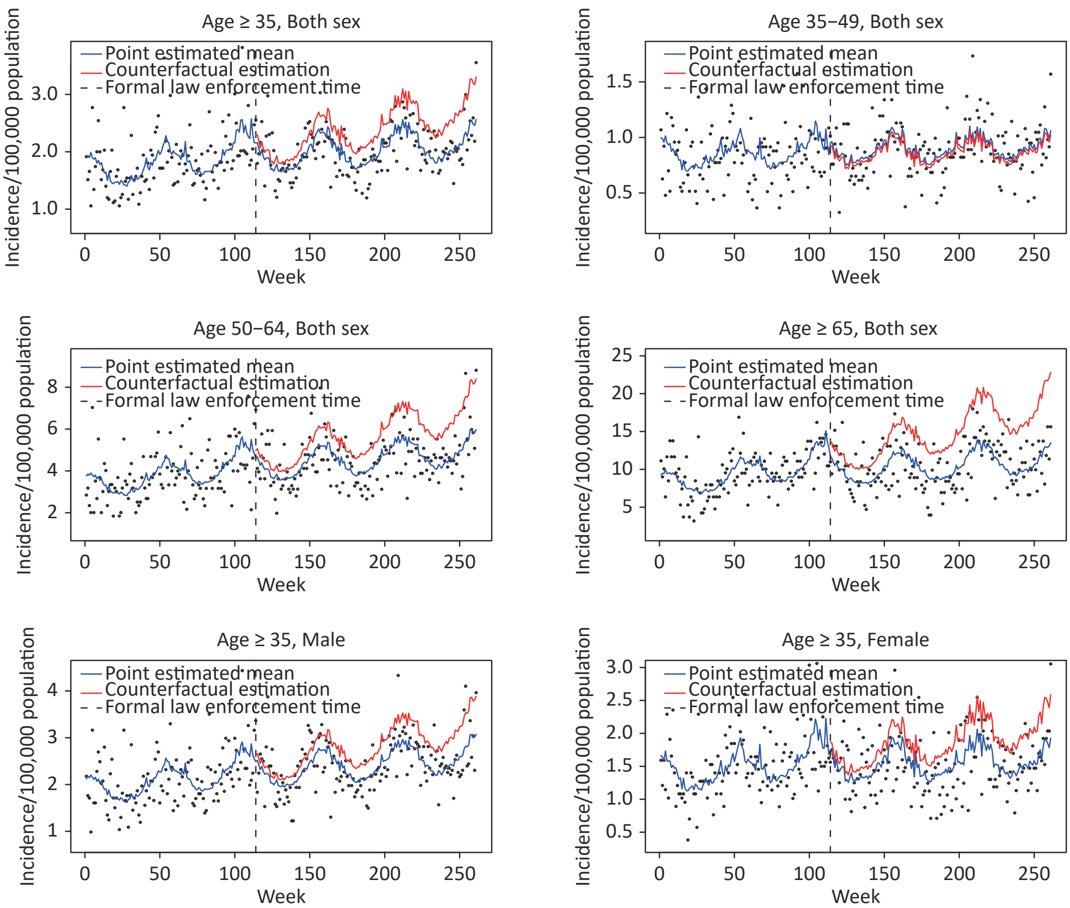


**Figure 2.** Observed and predicted weekly hemorrhagic stroke incidence rates (1/100,000) in Shenzhen (2012–2016).

the law (*RR*: 0.91; 95% *CI*: 0.85–0.97). Biological and disease mechanisms may explain this phenomenon, and even low-dose environmental tobacco exposure might result in platelet activation and aggregation. After endothelial dysfunction, the triggering of arterial vasoconstriction can increase the risk of AMI[38,39]. Although the AMI incidence decreased of gradual effect for each age group was observed, the changes were not statistically significant, which was inconsistent with studies in New York[40], Germany[41], Qingdao[11], and Tianjin[10]. The reason may be the high proportion of the young population in Shenzhen with low AMI cases or the limited follow-up period. In addition, our study also found that the immediate effect on AMI was not significant in women. Most previous studies found that women were more sensitive to policy implementation, which meant that they gained more health effects[42-44]. A study from the United Kingdom reported that the decrease in AMI admissions was not significant in women under 60[19], which was similar to our results.

In our study, we further analyzed the association between the enforcement of smoke-free legislation and the incidence decrease for two stroke subtypes. Significant annual decreases in ischemic and hemorrhagic stroke incidence rates were observed right after the law. However, the immediate effect of the law was not significant, except in the age group ≥ 65 on hemorrhagic stroke. One possible explanation for this issue is that the immediate reduction in ischemic stroke incidence post-legislation could have been offset by the effect of a tobacco control project in Shenzhen. In 2010, Shenzhen initiated a smoke-free environment promotion project in five important places, including hospitals, schools, government agencies, CDC, and public transportation[45], which may have generated a health effect for stroke. Overall, the gradual effect of the smoke-free law on stroke incidence in our study was similar to that found in Scotland[46], Florida[47], New York[47], Arizona[24], Qingdao[11], and Beijing[12]. Though previous studies found

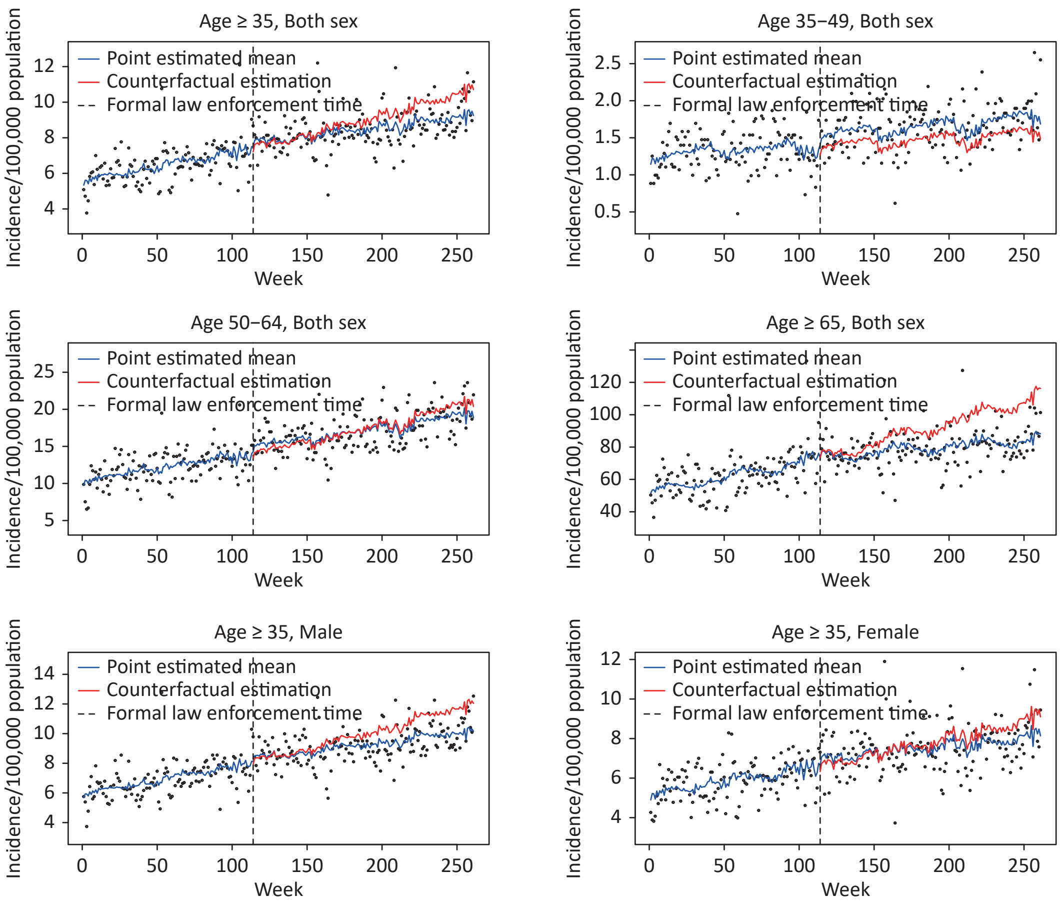


**Figure 3.** Observed and predicted weekly ischemic stroke incidence rates (1/100,000) in Shenzhen (2012–2016).

inconsistent results in the effect of the smoke-free law on stroke, our study added further evidence to support the health effects of the law on both ischemic and hemorrhagic stroke.

In the subgroup analysis, we found evidence of stronger associations between the smoke-free law and two subtypes of stroke among older adults, which was consistent with findings from Qingdao[11] and Beijing[12]. In contrast, some time series studies conducted in North American and European countries and two meta-analyses found that the decrease in cardiovascular and cerebrovascular events after enforcing the law was mainly due to younger people[14,21,46,48]. One possible explanation is that, in China, where the most concerned areas are on the legislation, most older people prefer to travel by public transportation and do physical exercises in communities or parks. Therefore, the levels of SHS exposure in these public places have dropped significantly after the legislation[28]. In contrast, most young people prefer to go to entertainment and internet cafes during their leisure time, such as bars, dance halls, bathing centers, and other indoor venues, which had not been involved in the legislation during the study period. These places were only defined as restricted smoking places and were not 100% banned areas until 2017. Thus, further health effects evaluation should be conducted with the data after 2017. We believed that more health effects would be gained with stricter law implementation in 2017.

Some limitations of our study should be noted. First, a series of tobacco control campaigns had been conducted before the legislation was implemented, which might have affected the true health effect evaluation. Second, the sensitivity analysis was not conducted due to the limited number of weeks before the legislation. Third, some subgroups were not analyzed in other categories due to the limited data collection. More data should be collected to increase insights into different subgroup combinations. Fourth, despite adjusting for highly relevant time-varying confounders (time trends, seasonality, $PM_{2.5}$, others), other time-varying confounders remained, and we were unable to control them (obesity prevalence, population cholesterol levels, and others). Fifth, individual information was unavailable on covariates (smoking status, BMI) due to this study's ecological design.

## CONTRIBUTORS

SHI Yu Lin completed the analysis and wrote the first draft of the manuscript. XIONG Jing Fan helped with data collection and cleaning and contributed to the interpretation of the data. PENG Ji was in charge of the data collection and data quality improvement. WAN Xia conceived the study, supervised the analysis, and contributed to the interpretation of the data. LIU Li Qun supervised the analysis and contributed to the interpretation of the data. ZHAO Zhi Guang managed the data collection, supervised the analysis, and contributed to the interpretation of the results. All authors contributed to and have approved the final manuscript.

Received: August 5, 2022;
Accepted: December 30, 2022

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