Impact of smoke-free legislation on acute myocardial infarction and stroke mortality: Tianjin, China, 2007–2015

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ABSTRACT

Background Smoke-free legislation is an effective way to protect the population from the harms of secondhand smoke and has been implemented in many countries. On 31 May 2012, Tianjin became one of the few cities in China to implement smoke-free legislation. We investigated the impact of smoke-free legislation on mortality due to acute myocardial infarction (AMI) and stroke in Tianjin.

Methods An interrupted time series design adjusting for underlying secular trends, seasonal patterns, population size changes and meteorological factors was conducted to analyse the impact of the smoke-free law on the weekly mortality due to AMI and stroke. The study period was from 1 January 2007 to 31 December 2015, with a 3.5-year postlegislation follow-up.

Results Following the implementation of the smoke-free law, there was a decline in the annual trends of AMI and stroke mortality. An incremental 16% (rate ratio (RR): 0.84; 95% CI: 0.83 to 0.85) decrease per year in AMI mortality and a 2% (RR: 0.98; 95% CI: 0.97 to 0.99) annual decrease in stroke mortality among the population aged ≥35 years in Tianjin was observed. Immediate postlegislation reductions in mortality were not statistically significant. An estimated 10 000 (22%) AMI deaths were prevented within 3.5 years of the implementation of the law.

Conclusion The smoke-free law in Tianjin was associated with reductions in AMI mortality. This study reinforces the need for large-scale, effective and comprehensive smoke-free laws at the national level in China.

INTRODUCTION

Exposure to secondhand smoke (SHS) increases the risk of morbidity and premature mortality due to cardiovascular and cerebrovascular diseases.[1] Given the evidence of the adverse health effects of SHS, the WHO Framework Convention on Tobacco Control (WHO FCTC) requires each member state to adopt effective legislative measures to protect people from exposure to tobacco smoke in workplaces and public areas.[2] As of 2017, 55 countries had implemented a comprehensive smoke-free law covering all public places and workplaces.[3 4]

China is the largest consumer and producer of tobacco, with over 300 million smokers who smoke approximately one-third of the cigarettes in the world.[5 6] Additionally, approximately 740 million non-smokers, including 180 million children, in China are routinely exposed to SHS which is responsible for approximately 230 000 deaths annually.[7–9] The results from nationally representative surveys showed that 54% of indoor employees smoke or were exposed to SHS at worksites, 57% of youth were exposed to SHS inside enclosed public spaces and 44% were exposed at home.[10 11]

Despite the high prevalence of smoking and SHS exposure, China lags behind other countries in revising tobacco control legislation at the national level as required by the WHO FCTC and is the only country from the BRICS (Brazil, Russia, India, China, South Africa) group that has not passed a national smoke-free law.[12 13] However, one encouraging step undertaken by the Chinese government in the lead-up to the national prohibition of smoking in public places is the enactment and implementation of smoke-free legislation in major cities. Since 2008, at least 18 cities in China have taken promising steps to enact laws or regulations promoting smoke-free public places.[13 14]

Tianjin, the third largest city (area 11 860 km^2, population 15.6 million) of China, first implemented the smoke-free law on 31 May 2012. The law prohibits smoking in select places, including indoor government offices, schools, healthcare facilities, supermarkets and all public transportation. The law also bans smoking in other indoor workplaces and public places including bars, restaurants, hotels and other entertainment venues unless they have designated smoking rooms with an effective separate ventilation system. The smoke-free law specifies strong penalties for violations and a clear set of responsibilities for enforcement agencies.

Following the implementation of the smoke-free law in Tianjin, studies demonstrated reductions in SHS exposure and indoor particulate concentrations, increases in smoke-free signage in indoor public areas and public awareness of the health hazards of smoking and passive smoking.[13 15 16] However, the evidence generated in these studies is insufficient for understanding the health effects of implementing the smoking ban. The aim of this study was to assess the impact of the municipal smoke-free legislation on acute myocardial infarction (AMI) and stroke mortality in Tianjin. This study is intended to fill the impact evaluation gap in Tianjin and pave the way for similar evaluations to be adopted in other areas that have enacted or are in the process of enacting smoke-free laws.

METHODS

Data

Subjects of the mortality analysis include all cases of AMI and stroke deaths among Tianjin permanent residents (with Tianjin Hukou). Mortality data from January 2007 to December 2015 for Tianjin were obtained from the all-cause mortality surveillance system which monitors the entire residential population of the city. This system was established in 1984 and has been maintained by the local Centers for Disease Control and Prevention (CDC). The records include the date of death, underlying causes of death, age, sex, residential address and whether the death occurred in a hospital setting or elsewhere.[17] The cause of death classification for the study period was based on the International Classification of Disease, 10th Revision. The underlying causes of death selected for analysis included AMI (I21) and stroke (I60-I64).

The recording process and quality control of the data have been described elsewhere.[18 19] Death certificates filled out by practising clinicians from hospitals or community clinical centers are required by law to be reported. Non-hospital deaths are ascertained through records from the police department and the government mortuary, as well as community clinicians. The underlying causes of non-hospital deaths are investigated through interviews with the deceased's relatives by trained community clinicians on a door-to-door basis. The district and municipal CDCs oversee and check the quality of death certificates at the primary and secondary levels, respectively. The municipal CDC also provides technical training and support to staff involved in the surveillance process.[19]

Data related to meteorology were obtained from the local Meteorological Bureau and Environmental Monitoring Station. Meteorology data used as covariates include the average daily temperature and relative humidity of Tianjin for the study period. Missing temperature or relative humidity values were replaced with values predicted from single regression imputation. Single-year population estimates by sex and age were taken from the Residence Registry Section of the Municipal Bureau of Public Security.

Statistical analysis

Poisson regression with interrupted time-series analysis was used to examine the impact of smoke-free legislation. The analysis was restricted to mortality events in the population aged 35 years and above to reflect the population at risk for smoking-related mortality. The outcome of each model was the weekly number of deaths due to AMI or stroke by sex and age group. An indicator variable was used in the model to define smoke-free legislation, with a value of zero given to the weeks before law implementation and a value of one given to the weeks after implementation. An interaction term between the smoke-free law and the time since the law took effect was included in the regression to estimate the change in the slope of the secular trend in the postlegislation period compared with that in the prelegislation period. The sex- and age-specific population was included as an offset in the models. The long-term secular trend was adjusted by including a homogeneous linear term along the week series, as an initial exploration of the form of the long-term trend suggested that the linear assumption was appropriate. The linear time trend was used to quantify changes in population risk factors, treatment and other secular trends. A seasonal pattern was modelled by annual sine and cosine terms. The study period was from 1 January 2007 to 31 December 2015, including a postban follow-up of approximately 3.5 years. All models were adjusted for temperature and relative humidity.

The Poisson model equation estimating weekly events was expressed as follows:

$$log\,(Y) = offset\ log\,(P) + \beta_0 + \beta_1\,T + \beta_2\,Ban + \beta_3\,(Ban * T') + \beta_4 cos\left(\frac{2T*\pi}{52}\right) + \beta_5\,sin\left(\frac{2T*\pi}{52}\right) + \beta k\,(TM,\ RH) + \varepsilon$$

where Y denotes the response (weekly events), P is the age group and sex-specific population, T is the time elapsed since the start of the study, T' is the time elapsed since the implementation of the smoke-free law, β_0 represents the baseline level at T=0, β_1 is the model coefficient for the weekly secular trend (the underlying prelegislation trend), β_2 is the coefficient of the indicator variable Ban (coded 0 for preban period and 1 for postban period) denoting the level/instantaneous change following the law, β_3 indicates the slope/gradual change following the smoke-free law and β_κ denotes the coefficients for a set of covariates of interest (TM: temperature, RH: relative humidity).

The estimated immediate relative change (in percentage) in the mortality rate from the prelegislation to postlegislation periods was quantified as $100(\exp(\beta_2)-1)$. The annual relative change was quantified as $100(\exp(52*\beta_3)-1)$. Each sex and age group (≥35, 35–64, 65–84, ≥85) was analysed separately. For further validation that the final models were detecting true ban impact, two additional models were fitted with false smoke-free law implementation dates at 6 months and 1 year prelegislation.

The number of averted deaths associated with the city-level smoke-free law was calculated as the regression-based prediction of the number of deaths from 1 January 2007 to 31 December 2015, subtracted from the predicted number of deaths without the influence of the law. All analyses were conducted using R V.3.3.2, and statistical modelling was conducted with the glm function.

RESULTS

There were approximately 86 300 AMI deaths and 99 900 stroke deaths among permanent residents aged 35 years and older in Tianjin (from 1 January 2007 to 31 December 2015) which constituted a crude mortality rate of 162 (male 183, female 143) and 188 (male 218, female 160) deaths per 100 000 population per year for AMI and stroke, respectively. From 2007 to 2015, an overall increase in the crude AMI mortality rate was observed, with the upward trend becoming less pronounced and turning into a downward trend in the postlegislation period (figure 1). In contrast, the stroke mortality rate showed a decreasing trend for all three age groups. The mean age at AMI death was 73.8, and mean age at stroke death was 73.1. The proportion of all stroke deaths under age 65 increased from 20.7% in 2007 to 24.0% in 2015 ($p<0.001$).

The distribution of death locations stratified by sex and age group is shown in table 1. The percentage of AMI deaths that occurred at home increased from 70.9% in 2007 to 77.3% in 2013 ($p<0.001$; death locations for deaths occurring in 2014 and 2015 are not available). For both AMI deaths and stroke deaths, the percentage that occurred at home is higher in older age groups and women.

Results of mortality regressions

The overall, sex- and age group-specific postban results of Poisson regressions for mortality in Tianjin are reported in table 2. Following the implementation of smoke-free legislation, a 16% decrease in mortality per year was observed in AMI (rate ratio (RR): 0.84; 95% CI: 0.83 to 0.85). Likewise, a

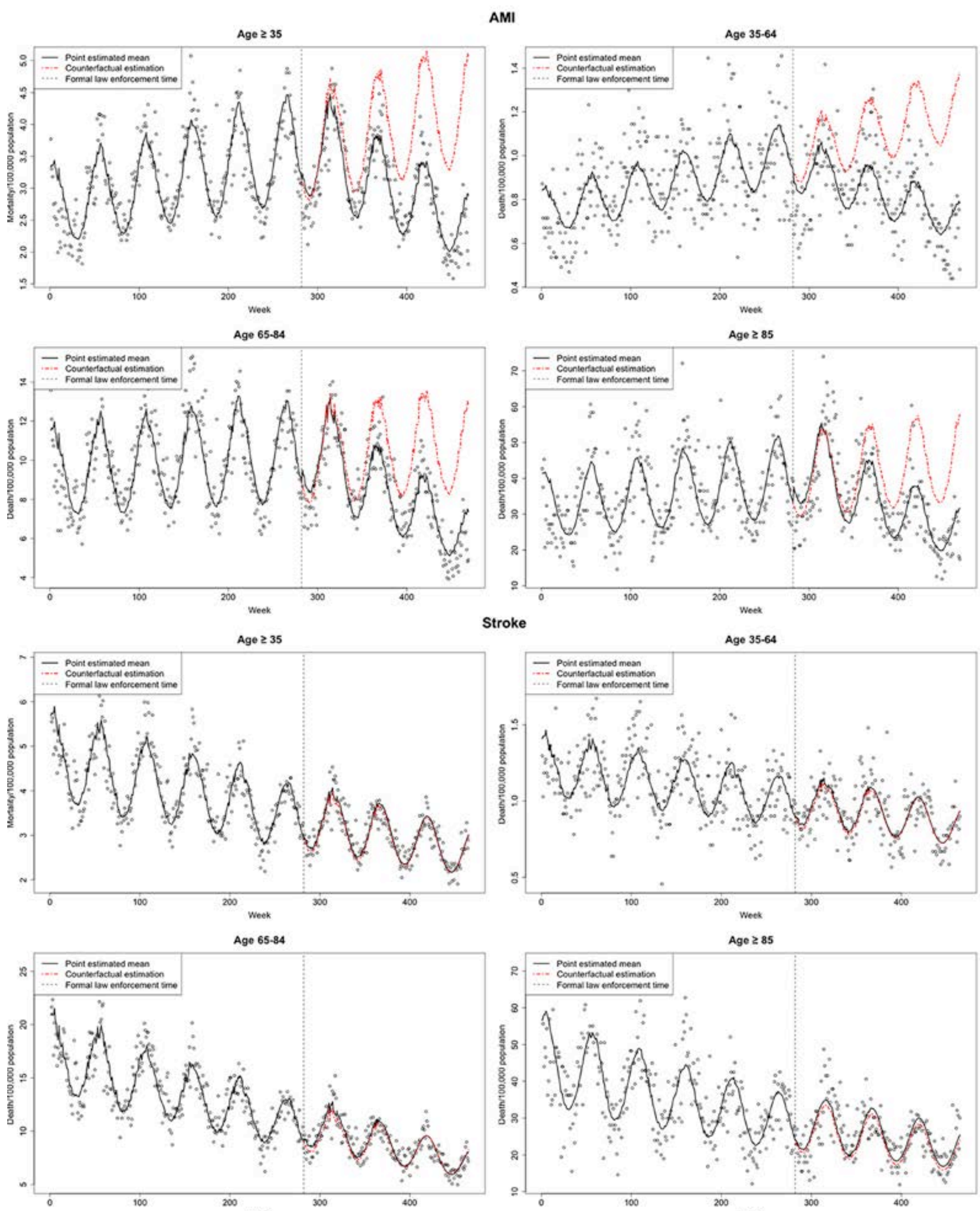

Figure 1 Observed and predicted weekly acute myocardial infarction (AMI) and stroke mortality rates in Tianjin (2007–2015). Observed (circles) and predicted (solid and dot dash lines) mortality rates. black solid line, pre- and post-legislation trends; red dot dash line, counterfactual scenario; dashed line, law enforcement date.

gradual 2% reduction per year was observed in stroke mortality (RR: 0.98; 95% CI: 0.97 to 0.99). Annual trend effects in AMI mortality were observed in both men (RR: 0.85; 95% CI: 0.83 to 0.86) and women (RR: 0.84; 95% CI: 0.82 to 0.85), and this difference in magnitude was not statistically significant. Decreases in the annual trend of stroke mortality were observed in both sexes as well but were smaller in magnitude than the annual trend effects in AMI mortality.

The immediate effect, measured by whether the trend line shifted down at the time the law was implemented, was observed only in AMI mortality among the 35–64 age group, although the decrease was not statistically significant (RR: 0.96; 95% CI: 0.90 to 1.02). For the age group 35–64, the 4% immediate postlegislation decrease in AMI mortality was followed by a gradual 13% decrease each postlegislation year. This resulted in a net postlegislation decrease of 25% in the 3.5 years of follow-up. For the age group 65–84, an immediate 10% increase in AMI mortality was observed (RR: 1.10; 95% CI: 1.06 to 1.14), followed by a 17% decrease per year, resulting in a net postlegislation decrease of 25%. Similarly, a net postlegislation decrease of 21% in AMI mortality was observed for the age group ≥85. In contrast, the net decrease in stroke mortality is non-significant, as the annual trend decrease was offset by the immediate postlegislation increase. There was no significant negative association between stroke mortality and smoke-free legislation.

For illustration, figure 1 presents the observed and expected trends by age group of weekly mortality of AMI and stroke among permanent residents of Tianjin from 2007 to 2015. A strong seasonal pattern in AMI and stroke mortality was

Table 1 The trend of place of death stratified by age group and sex

	Age 35–64				Age ≥65			
	Male		Female		Male		Female	
	2007	2013	2007	2013	2007	2013	2007	2013
AMI death, N (%)	1131	1635	498	601	3030	4427	2789	4274
Home	719 (63.6)	1099 (67.2)	346 (69.4)	449 (74.7)	2129 (70.2)	3433 (77.5)	2090 (74.9)	3471 (81.2)
Hospital (excluding emergency department)	156 (13.7)	146 (8.9)	73 (14.7)	64 (10.6)	491 (16.2)	493 (11.1)	397 (14.2)	433 (10.8)
Emergency department	120 (10.6)	236 (14.4)	41 (8.2)	59 (9.8)	197 (6.5)	312 (7.0)	148 (5.3)	230 (5.4)
On the way to health facilities	79 (7.0)	67 (4.1)	25 (5.0)	16 (2.6)	108 (3.6)	94 (2.1)	77 (2.8)	46 (1.1)
Stroke death, N (%)	1771	1726	925	698	5548	4148	4752	3638
Home	1047 (59.1)	1064 (61.6)	648 (70.1)	490 (70.2)	4309 (77.7)	3220 (77.6)	3824 (80.4)	2863 (78.7)
Hospital (excluding emergency department)	531 (30.0)	481 (27.8)	207 (22.4)	153 (21.9)	850 (15.3)	698 (16.9)	655 (13.8)	595 (16.4)
Emergency department	103 (5.8)	122 (7.1)	33 (3.6)	43 (6.2)	136 (2.5)	128 (3.1)	102 (2.1)	110 (3.0)
On the way to health facilities	49 (2.8)	22 (1.3)	22 (2.4)	6 (0.9)	111 (2.0)	26 (0.6)	90 (1.9)	16 (0.4)

AMI, acute myocardial infarction.

detected, with the largest number of events occurring in autumn and winter. The estimated health effect, under the interrupted time series Poisson regression, is visible in the discontinuity of the line at the beginning of the implementation and the change in the secular trends in mortality after the implementation of the law. The net effect on AMI mortality for those aged 35 and above, visible as the distance from the red line (predicted rate) to the blue line (estimated rate for counterfactual scenario in which the law was not implemented), was estimated as a 12% drop during the first year and continuing exponential declines, reaching approximately 41% in December 2015. Similar patterns are observed in all of the other three age groups.

We conducted additional sensitivity analyses to investigate the impact of varying a range of model assumptions. Overdispersion was considered and found to be very limited. Residual autocorrelation is non-problematic because seasonality that largely explains autocorrelation was controlled using circular distributions. The testing of false law implementation dates showed that gradual trend effects were smaller in magnitude than the actual effects. None of these sensitivity analyses led to systematic changes in the results reported.

In the absence of municipal-level smoke-free legislation, an estimated 10 000 (95% CI: 9312 to 10 688) additional AMI deaths would have occurred from 31 May 2012 to

Table 2 Multivariate analysis* of overall, sex- and age group-specific postban effects on mortality rates, Tianjin, 2007–2015

	Overall		Male		Female	
	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)
Tianjin						
AMI mortality						
All-age	1.05 (1.02 to 1.08)	0.84 (0.83 to 0.85)	1.06 (1.02 to 1.10)	0.85 (0.83 to 0.86)	1.05 (1.01 to 1.08)	0.84 (0.82 to 0.85)
35–64	0.96 (0.90 to 1.02)	0.87 (0.85 to 0.89)	0.96 (0.90 to 1.03)	0.87 (0.84 to 0.90)	0.96 (0.85 to 1.07)	0.84 (0.82 to 0.86)
65–84	1.10 (1.06 to 1.14)	0.83 (0.82 to 0.85)	1.13 (1.07 to 1.18)	0.84 (0.82 to 0.86)	1.08 (1.02 to 1.14)	0.83 (0.81 to 0.85)
≥85	1.16 (1.09 to 1.22)	0.81 (0.79 to 0.83)	1.18 (1.08 to 1.29)	0.8 (0.77 to 0.83)	1.15 (1.06 to 1.24)	0.82 (0.79 to 0.85)
Stroke mortality						
All-age	1.05 (1.02 to 1.08)	0.98 (0.97 to 0.99)	1.05 (1.02 to 1.09)	0.98 (0.96 to 0.99)	1.04 (0.99 to 1.08)	0.99 (0.97 to 1.01)
35–64	1.05 (0.99 to 1.11)	0.98 (0.95 to 1.00)	1.06 (0.99 to 1.14)	0.97 (0.94 to 1.00)	1.02 (0.92 to 1.13)	0.99 (0.94 to 1.03)
65–84	1.09 (1.05 to 1.12)	0.96 (0.95 to 0.98)	1.07 (1.02 to 1.12)	0.95 (0.93 to 0.97)	1.11 (1.05 to 1.17)	0.97 (0.95 to 0.99)
≥85	1.06 (0.99 to 1.13)	0.99 (0.96 to 1.02)	1.13 (1.02 to 1.25)	0.98 (0.94 to 1.02)	1.00 (0.91 to 1.09)	1.00 (0.96 to 1.04)

*Adjusted for time trend, population, seasonality, temperature and relative humidity.
AMI, acute myocardial infarction.

31 December 2015. No deaths were prevented in association with stroke mortality.

DISCUSSION

In an analysis based on cause-specific mortality data for a permanent population of approximately 10 million people over 9 years, we found that the implementation of the municipal smoke-free law prohibiting smoking in enclosed worksites and selected public places was associated with AMI mortality reduction in the population aged 35 and above but had no significant impact on the stroke mortality rate.

There are two main pathways linking smoke-free law to health benefits, including directly reducing environmental SHS exposure among non-smokers and indirectly reducing active smoking or encouraging quitting.[20] Using population-level data on changes in smoking status and exposure to SHS, two studies have suggested that approximately 1% of the smoking ban effects on ischemic heart disease (IHD) events are due to decreases in active smoking,[17 21] while a Scottish study showed a 14% reduction in admissions for acute IHD among smokers.[22] As there has been no evidence of a decrease in active smoking after legislation, the effects observed in Tianjin may have been predominantly attributed to the change in the SHS exposure prevalence (65% in 2012 and 43% in 2014) and the decrease in particulate matter 2.5 ($PM_{2.5}$) concentrations in public venues.[15 23]

AMI mortality rates showed a downward trend after legislation which is contrary to the upward trend that has accelerated since 2004 in both urban and rural populations in China.[24] Decreases in AMI mortality are usually triggered by reductions in preventable behavioural, biological and environmental risk factors as well as improvements in medical care.[24–28] In addition to the smoke-free legislation, other potential explanations for the observed decrease in the AMI mortality rate after 2013 in Tianjin include the implementation of the Maintaining of Normal Blood Pressure and Bodyweight project in 2004,[19] the Healthy Lifestyle for All project in 2008[29] and gradual establishment of Chest Pain Centers in 2014.[29] However, these prevention and control interventions were not implemented extensively,[19 29] and their timing was not consistent with the observed decrease in AMI mortality rates which indicates that the decreases were more likely associated with the smoke-free law. In contrast to the downward trend in AMI mortality rate, AMI incidence rate increased in the postlegislation period[15 30]; however, this could be explained by improved completeness of incident case ascertainment due to embedding the incidence reporting component into the Hospital Information System of hospitals at all levels in Tianjin starting in 2010.

The lack of immediate reduction in AMI mortality may be explained by the fact that we examined mortality rates rather than incidence rates or hospital admissions. As less than 30% of patients who experience heart attack die within 12 months, the effect on AMI deaths may be delayed compared with that on admissions.[31] The progressive enforcement of the smoke-free law in Tianjin since the implementation in May 2012 might have further delayed the effects.[32] For instance, smoking was observed in 96% of government agencies and 38% of hotels in the season before law enforcement. Drops of 18.2% and 3.1% in the proportion were observed for government agencies and hotels, respectively, in the first year of law enforcement, and then further decreases of 70.5% and 23.9%, respectively, were observed in the second year of enforcement.[23 33 34] Low public awareness and unreliable compliance with the law at the initial implementation stage are also potential contributing factors.[15 16] In a survey conducted 6 months after the law went into effect, smoking was observed in 68.5% of restaurants, 50% of entertainment venues and 79.2% of internet bars.[33] Immediate increases in mortality rates for the 65–84 age group detected by the models were most likely due to uncontrolled risk factors, including air pollutants.

No significant effect of the smoke-free law on stroke mortality was observed in Tianjin. In comparison with AMI, relatively few published original studies have examined the impact of smoke-free laws on stroke. Our results are consistent with those of previous studies conducted in New York, New Zealand and Hong Kong[35–37] but contrary to those of studies conducted in Ireland, Scotland and Arizona and a meta-analysis.[17 38–41] As stated in the United States Surgeon General's report, the evidence for a causal link between smoke-free law and reductions in stroke events is relatively weak,[42] so the implementation of such laws may less-directly affect stroke. In addition, compared with AMI, a higher proportion of stroke incidence is non-fatal.[43] Therefore, the effect of smoke-free law on stroke may be restricted to non-fatal events, especially when the law has not been fully enforced.

Our results showed that reductions in mortality following the smoke-free law did not decline with age which is consistent with findings from similarly designed studies in Hong Kong and Ireland.[17 37] The US Surgeon General's report attributed the decline in effect with age to the possible lower exposure of older people to bars and similar venues where smoking was allowed before the legislation.[1] In Tianjin, older people are unlikely to frequent bars, but most of them use public transportation, go to grocery stores and/or eat out with family at restaurants. The relatively higher exposure of seniors in Tianjin may explain why our findings are contrary to those of some studies showing that smoke-free laws affected coronary or cerebrovascular events only in younger people.[31 38 41 44]

We detected similar reductions in AMI mortality among men and women. Although many studies have not examined impacts stratified by sex,[31 35 37 45–48] the absence of an impact on women has been found in England and Italy.[21 49 50] This was mainly attributed to lower prelegislative levels of and reductions in exposure to SHS among women.[49] Another potential reason is that higher prevalence of smoking among men allows for a larger percentage to quit. In contrast, studies conducted in Scotland[38] and the Piedmont region of Italy[51] have found a larger effect in women, suggesting that exposure to SHS and/or smoking decreased more among women. Although the prevalence of smoking was much lower among women (3%) than that among men (50%) in China,[52] the prevalence of SHS exposure prelegislation in public places or worksites among female non-smokers was as high as that among male non-smokers (72% vs 74%),[53] and the reduction in exposure to SHS after the Tianjin Act of Tobacco Control is similar for women and men.[15]

Several limitations of our study should be noted. Inaccuracies may exist due to the use of ill-defined causes of deaths as a measure of death from AMI or stroke. It is difficult to measure misclassification of the two diagnoses in Tianjin's mortality data with the existing data and resources. Because of the compensatory patterns of misclassification, studies conducted among representative rural and urban populations of China have shown that population-level estimates of mortality from IHD and stroke are only mildly affected.[54 55] On the other hand, the extent of over-representation or under-representation of AMI and stroke deaths caused by misclassification in all-cause mortality data was most likely not associated with smoke-free legislation status and therefore may not bias the results.

Despite adjusting for underlying time trends and other covariates, some other population-level variables not controlled for, such as concentration of air pollutants, obesity prevalence, population cholesterol levels and influenza outbreaks, may have influenced our results. Like other ecological studies, we also lack information on variables at the individual level, such as smoking status and SHS exposure. Further research is needed to estimate the extent to which the reduction in mortality is caused by quitting/reducing smoking among smokers or reduced SHS exposure among non-smokers.

Among the strengths of our study, the two major ones are that the data come from mortality surveillance that covers a considerably large and relatively closed population and that the dataset spans a long period (470 weeks/time points in total, with 280 weeks prelegislation period). Using this population-based dataset, we were able to offer greater statistical power to detect secular trends and assess the health impact.

CONCLUSIONS

The results of this study, which was carried out on a large population-based dataset over a long follow-up period, suggest that the smoke-free law is associated with a gradual reduction in the trend of coronary disease mortality. As a result of the law, our analysis estimated that approximately 10 000 or one in five AMI deaths were likely prevented in a 3.5-year period. This finding has critical implications for informing the effective development and enforcement of future policy.

What this paper adds

- This is the first study to measure the specific health impact of the smoke-free laws passed in major cities of mainland China excluding Hong Kong and Macau.
- With surveillance data spanning a long period and covering a large and relatively closed population, the study has high statistical power to detect secular trends and assess the impact on myocardial infarction and stroke events.
- Following the implementation of the smoke-free legislation, 10 000 (22%) acute myocardial infarction (AMI) deaths were likely prevented in 3.5 years. This study reinforces the need for large-scale, effective and comprehensive smoke-free laws at the national level in China.
- This study added evidence of reductions in AMI mortality risk among women and older people following smoke-free legislation.
- The study filled the evaluation gap in Tianjin and paved the way for similar studies assessing smoke-free legislation using the interrupted time series design in other cities or regions of China.

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Contributors HX designed the study, contributed to data collection, completed the analysis and wrote the first draft of the manuscript. GhY and XW conceived the study, managed the data collection, supervised the analysis and contributed to the interpretation of the data. MN supervised the analysis and contributed to the interpretation of the data. GJ managed the data collection and contributed to the interpretation of result. HZ, DW, CS and YZ contributed to data collection. All authors contributed to and have approved the final manuscript.

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