

Association between the extension of smoke-free legislation and incident acute myocardial infarctions in Singapore from 2010 to 2019: an interrupted time-series analysis

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To cite: Ho JSY, Ho AFW, Jou E, et al. Association between the extension of smoke-free legislation and incident acute myocardial infarctions in Singapore from 2010 to 2019: an interrupted time-series analysis. *BMJ Glob Health* 2023;**8**:e012339. doi:10.1136/bmjgh-2023-012339

Handling editor Lei Si

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjgh-2023-012339>).

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Received 18 March 2023
Accepted 30 July 2023



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ABSTRACT

Background We examined the association between smoke-free laws implemented in the outdoors and the common areas of residential apartment blocks and reported acute myocardial infarctions (AMI) in Singapore.

Methods We used an interrupted time-series design and seasonal autoregressive integrated moving average models to examine the effect of the smoke-free law extensions in 2013 (common areas of residential blocks, covered pedestrian linkways, overhead bridges and within 5 m of bus stops), 2016 (parks) and 2017 (educational institutions, buses and taxis) on the monthly incidence rate of AMIs per 1 000 000 population.

Results We included 133 868 AMI reports from January 2010 to December 2019. Post-2013, there was a decrease in the AMI incidence trend ($\beta = -0.6$ per month, 95% CI -1.0 to -0.29) and 2097 (95% CI 2094 to 2100) more AMIs may have occurred without the extension. There was a significant step-decline in male AMIs and a non-significant step-increase in female AMIs post-2013. Those 65 years and older experienced a greater decline to the postlegislation 2013 trend ($\beta = -5.9$, 95% CI -8.7 to -3.1) compared with those younger ($\beta = -0.4$, 95% CI -0.6 to -0.2), while an estimated 19 591 (15 711 to 23472) additional AMI cases in those 65 years and above may have occurred without the extension. We found a step-increase in monthly AMI incidence post-2016 ($\beta = 14.2$, 95% CI 3.3 to 25.0).

Conclusion The 2013 smoke-free law extension to residential estates and other outdoor areas were associated with a decline in AMIs and those above the age of 65 years and men appeared to be major beneficiaries. Additional epidemiological evidence is required to support the expanded smoke-free legislation to parks, educational institutions, buses and taxis.

INTRODUCTION

Tobacco use is the second greatest preventable cause of mortality globally, accounting for 10.8 million deaths in 2019.¹ Exposure to secondhand smoke, by being in close proximity to those smoking, is responsible for 1.3

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Many countries have enacted smoke-free laws and previous studies have reported associated respiratory and cardiovascular health benefits.
- ⇒ Evidence of the benefits of smoke-free laws was largely confined to those for indoor smoking bans and largely in non-Asian cities.
- ⇒ Evidence of the effects of expanding smoke-free laws to housing estates and outdoor areas where residents frequent is lacking.

WHAT THIS STUDY ADDS

- ⇒ This study found a reduction in the incidence of acute myocardial infarction following the introduction of smoke-free laws to the common areas of housing estates and outdoor areas, including covered pedestrian linkways, overhead bridges and within 5 m of bus stops.
- ⇒ Elderly populations appeared to benefit most from such smoke-free legislation expansion.
- ⇒ The expansion of smoke-free legislation to parks, educational institutions, buses and taxis did not appear to reduce the incidence of acute myocardial infarction.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ These study findings provide additional evidence for policymakers in other similar urban cities who are considering expanding their smoke-free laws to reduce the adverse consequences of population exposure to environmental tobacco smoke.
- ⇒ Additional epidemiological evidence is required to support the expanded smoke-free legislation to parks, educational institutions, buses and taxis.

million deaths annually.¹ Deaths attributed to secondhand smoking is most common due to ischaemic heart disease,² which manifests suddenly as acute myocardial infarction (AMI). Due to the significant burden of secondhand smoke and associated AMI on

mortality and morbidity, global attention has focused on this issue since the WHO Framework Convention on Tobacco Control (FCTC) in 2003. The FCTC recommended that countries adopt and implement measures that provide protection from 'exposure to tobacco smoke in indoor workplaces, public transport, indoor public places and, as appropriate, other public places'.³

Since 2003, 67 countries have introduced comprehensive smoke-free laws.⁴ Smoke-free laws have been reported to reduce AMI risk. A meta-analysis of 18 studies performed in Europe, North America and New Zealand demonstrated an overall reduction in risk of AMI by 13% after the implementation of smoke-free legislation but with evidence of heterogeneity, and differences in effectiveness of the smoke-free legislation on the risk of AMI between countries of study were observed.⁵ In these studies, the extent of smoking ban differed between countries, with most banning all indoor smoking in public spaces and workplaces, while others, such as Italy, allowing designated smoking areas and Canada extending the ban to outdoor seating in restaurants and licensed premises. The varying types of smoking exposure may contribute to the heterogeneity observed, which requires further investigation. Compliance with smoke-free laws may be different across settings and this could influence the impact of associated with health benefits.⁶ Smoking remains an unresolved epidemic in Asia and the majority of tobacco consumers are in Asia.⁷ Several Asian countries such as India,⁸ Malaysia⁹ and South Korea¹⁰ have implemented smoking laws but evidence of their effect on cardiovascular disease is limited. Furthermore, previous European, American and studies in the Pacific were also limited to smoking bans in indoor public areas and workplaces with or without inclusion of bars and restaurants.¹¹

Singapore has one of the most comprehensive and strictest tobacco control laws in the South East Asian region.¹² Under the Smoking (Prohibition in Certain Places)¹³ Act 1992 which has undergone several legislative amendments since 1970, it is an offence 'to inhale and expel the smoke of tobacco or any other substance and to hold any cigar, cigarette, pipe or any other form of tobacco product which is alight or emitting smoke' in specified places and vehicles.¹³ An individual who commits an offence of smoking in a prohibited place shall be guilty of an offence and shall be liable on conviction to a fine not exceeding 1000 Singapore Dollars. The present list of places where smoking is prohibited is listed in online supplemental annex 1. According to its Ministry of Health, public education on the harms of tobacco use, smoking cessation programmes, legislative measures, taxation and enforcement have contributed to a decline in smoking prevalence in the Singapore population from 13.9% in 2010 to 11.8% in 2017 and 10.1% in 2020.¹⁴

On 15 January 2013, the smoke-free law in Singapore was extended to all common areas of residential blocks, linkways, overhead bridges and within 5 m from bus stops. More than 80% of the population live in high-rise

residential apartment blocks. Common areas of residential blocks include sheltered but naturally ventilated spaces within the block and may be enclosed on at least two sides. Some examples include corridors leading to residential units, stairwells, void decks and community spaces. On 1 June 2016, it was further extended to all public, private residential estate and neighbourhood parks. On 1 October 2017, all educational institutions, passenger transportation buses and taxis were included in the list of areas and vehicles where smoking is prohibited.

Smoke-free laws in Singapore are very strict, with a sizeable enforcement branch to ensure compliance.¹⁵ For example, in 2020, more than 18 500 fines were issued by the National Environmental Agency for non-compliance with smoke-free laws.¹⁶ Effects of extensions of existing smoking ban laws in areas within and around housing complexes where residents frequent have not been evaluated.

In this study, we aimed to investigate the association between the extensions of smoke-free laws to common areas of public housing apartment blocks and outdoor areas and the incidence of AMI cases in a multiethnic Asian population in Singapore. We seek to inform the body of evidence surrounding the use of smoke-free law extensions in reducing the health burden of cardiovascular disease in urban populations.

METHODS

Study design

Our study adopted an interrupted time-series study design, which involves the assembly of a time-series of the outcome measure of interest and compares the trend before and after the introduction of the policy intervention being assessed.

Outcome

We obtained monthly reports of all AMI cases from January 2010 to December 2019 from the Singapore Myocardial Infarction Registry. The National Registry of Diseases Office (NRDO) maintains national registries for selected diseases in Singapore. AMI notifications to the NRDO are legally mandated under the National Registry of Diseases Act.¹⁷ The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 410 was used to identify AMI cases diagnosed from 2010 to 2011 while ICD-10 (Australian Modification) codes I21 and I22 were used for AMI cases diagnosed from 2012 onwards. We followed the WHO's Monitoring Trends and Determinants in Cardiovascular Disease framework for case management.¹⁸ Using this approach, an AMI was considered a separate case if it occurred 28 or more days after a previous AMI. Diagnoses were further centrally adjudicated by physicians based on medical records, clinical presentation and laboratory test results.¹⁹ Annual audits ensured data accuracy and inter-rater reliability of at least 95%. The monthly incidence of AMIs (per 1 000 000 population) was obtained by dividing

the total number of AMI reports from each month with the monthly population estimates interpolated from mid-year population census obtained from the Department of Statistics Singapore.²⁰

Factors associated with AMI risk

Obesity, hypertension, diabetes, hyperlipidaemia and smoking are risk factors for AMI.^{21 22} The prevalence of these risk factors was obtained from previous cross-sectional national population health surveys carried out in 2010, 2013, 2017 and 2019 to 2020.²³ Polynomial functions were fitted to obtain the interpolated monthly estimates of obesity (R^2 value=1.000), hypertension (R^2 value=1.000), diabetes (R^2 value=1.000), hyperlipidaemia (R^2 value=1.000) and smoking prevalence (R^2 value=0.999) from January 2010 to December 2019. To account for changes in tobacco retail prices, which may influence the consumption frequency and volume of tobacco use, we obtained the monthly average retail price of a 20 cigarette pack over the study period.

Statistical analysis

We analysed the association between each of the smoke-free law extensions with the postimplementation level-change and level-trend of monthly AMI incidence using segmented, seasonal autoregressive integrated moving average (SARIMA) models. We first inspected the autocorrelation functions (ACF) and the partial autocorrelation functions (PACF) of the time-series of AMI incidence. We then explored different SARIMA model specifications, using the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) values to inform our final choice of the core model. The core model comprised only the outcome, autoregressive and moving average terms. In univariate analysis, we then assessed the association between obesity, hypertension, diabetes, hyperlipidaemia, smoking prevalence and tobacco prices with AMI incidence in six separate core models. We then simultaneously added the significant factors into the core model in multivariable analysis. None of these factors was found to be associated with the outcome, therefore they were not included in our final models (see online supplemental annex 2).

We modelled the underlying time trend using a continuous variable, which took on consecutive values from 1 to 120. We modelled the step-change effect for each smoke-free legislation introduction on AMI incidence using a binary variable, which took on value of '1' when it was in effect and the value of '0' prior to its introduction. We also estimated the respective postlegislation introduction effect on the subsequent AMI incidence trend using a continuous variable, which took on consecutive values beginning with '1' in the month it was first introduced until the final month of the study duration. We used the Ljung-Box test of randomness on the residuals to assess the presence of any residual autocorrelation. Our final models (SARIMA (1,0,1) x (1,0,1)₁₂) took the following form:

$$Y_t = \beta_0 + \beta_1 t + \beta_2 X_{1t} + \beta_3 tX_{1t} + \beta_4 X_{2t} + \beta_5 tX_{2t} + \beta_6 X_{3t} + \beta_7 tX_{3t} + \beta_8 tX_{3t}$$

Where Y_t represents the AMI incidence at time interval t , β_0 represents the baseline AMI incidence at the beginning of the study, t represents time on a monthly timescale (the underlying pre-intervention trend), X_{1t} represents the level change following the introduction of the 2013 smoke-free legislation, tX_{1t} is an interaction term and represents the slope change following the introduction of the 2013 smoke-free legislation, X_{2t} represents the level change following the introduction of the 2016 smoke-free legislation, tX_{2t} is an interaction term and represents the slope change following the introduction of the 2016 smoke-free legislation, X_{3t} represents the level change following the introduction of the 2017 smoke-free legislation and tX_{3t} represents the slope change following the introduction of the 2017 smoke-free legislation and β_n represents the estimated coefficients for the respective terms in the equation.

To assess the effects of the smoke-free extensions on different subgroups, we stratified our analysis by sex and age (<65 years and ≥65 years) in separate regression models. Despite age being difficult to be universally defined due to it being contextually sensitive, we used 65 years to define strata because it is one common convention used in population health²⁴ and the United Nations refers to this age value when discussing ageing issues.²⁵ For each of these subgroups, we compared the 95% CIs for the stratum-specific estimates and where there was no overlap at all, considered that as potential effect modification. Finally, for each smoking law prohibition extension which was associated with a reduction in AMIs, we computed the corresponding additional number of AMI cases that might have occurred by subtracting the observed number of cases from the predicted number of cases without the influence of that specific smoking law extension. In sensitivity analysis, we relaxed our linearity assumption and modelled time as a non-linear (quadratic) effect on overall AMI incidence. We produced the graphical results from our final regression models with reference to the best practices for interrupted time-series analytical studies.²⁶ We used a threshold of ($p < 0.05$) to determine statistical significance level for all our model estimates. All analyses were carried out in Stata V.13 (Texas Corp).

Patient and public involvement

No patients were involved in the study design or conduct, though we seek to present our study findings to the community. We expect that the results of this study would be of interest to health policy-makers and members of the community, which could, in turn, benefit the review and implementation of future smoke-free legislation.

RESULTS

Descriptive statistics

Over the 10-year study period, there were 133 868 AMI cases (table 1). Of these, 87 763 (66%) were men and 80 597 (60%) were 65 years of age or older. The incidence

Table 1 Reported acute myocardial infarction cases in Singapore, January 2010 to December 2019

Category	AMI cases per 1 000 000 population			
	January 2010 to December 2012 (pre-trend)	January 2013 to May 2016 (2013 law extension)	June 2016 to Sep 2017 (2016 law extension)	October 2017 to December 2019 (2017 law extension)
Overall (n=133 868)	130.7	150.3	172.0	180.1
≥65 years (n=80 597)	991.2	1065.6	1172.1	1171.2
<65 years (n=53 271)	86.2	98.4	107.5	109.9
Male (n=87 763)	239.4	280.5	327.8	343.2
Female (n=46 105)	123.7	149.0	167.4	173.5

of AMI in those 65 years and older was approximately 10-fold that of those below 65 years of age. The incidence of men was almost double that in women. The overall AMI incidence generally rose over the study duration, though the rise from Oct 2017 appeared to be less substantial compared with previous time periods.

SARIMA model specification

Based on the ACF and PACF plots of the AMI incidence, we explored 13 potential models and selected the SARIMA (1,0,1) × (1,0,1)₁₂ as our final core model based on its lowest AIC (866.4) and BIC (883.1) values (see online supplemental annex 3). There was no evidence of departure from a white-noise series in our final core model (Ljung-Box test p value=0.603).

Effects of smoke-free legislation extensions on overall AMI incidence

The overall incidence of AMI increased by a rate of 0.9 (95% CI 0.7 to 1.1) per 1 000 000 population per month prior to the 2013 smoke-free legislation extension (figure 1).

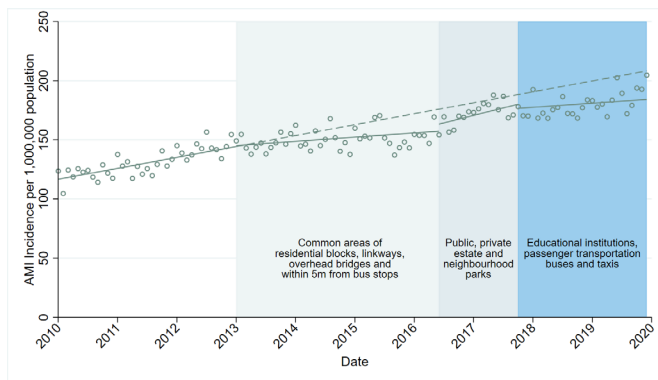


Figure 1 Monthly incidence of acute myocardial infarction in Singapore, January 2010 to December 2019. The hollow teal circles represent the incidence of AMI cases while the solid teal line represents de-seasoned incidence trend of AMI cases while the solid red line represents the smoothed trend of these numbers. The solid navy circles represent the counterfactual trend of AMI incidence in the absence of the smoke-free legislation introduced in 2013. The different coloured sections depict the respective extensions of the smoke-free legislation in January 2013, June 2016 and October 2017. AMI, acute myocardial infarction.

Although there was no evidence of a step-change ($\beta=-3.7$, 95% CI -11.8 to 4.4) after the implementation of the 2013 legislation, we did observe a decrease in the post-2013 overall AMI incidence trend ($\beta=-0.6$, 95% CI -1.0 to -0.3). In the absence of the 2013 extension, an estimated 2097 (95% CI 2094 to 2100) more AMIs may have occurred. We observed a step-change increase in the AMI incidence post-2016 ($\beta=14.2$, 95% CI 3.3 to 25.0) (table 2). No evidence of departure from a white-noise series was observed in our final model (Ljung-Box test p-value=0.456).

Sensitivity analysis

When we assumed a quadratic trend for time, we observed an increase in the overall incidence of AMI ($\beta=0.007$, 95% CI 0.006 to 0.009) per 1 000 000 population per month prior to the introduction of the 2013 extension. There was a step-decline in the AMI incidence post-2013 ($\beta=-10.3$, 95% CI -18.7 to -1.8) and a decrease in the post-2013 trend ($\beta=-0.02$, 95% CI -0.03 to -0.02). There was a step-increase in AMI incidence post-2016 ($\beta=23.0$, 95% CI 14.7 to 31.3). The direction of effect for these estimates was the same as those derived from using a linear assumption for the time in our original model, suggesting that our results were robust to model assumptions.

Age-stratified analysis

The 2013 smoke-free legislation extension was associated with a greater decline in the post-legislation trend in those aged 65 years and above ($\beta=-5.9$, 95% CI -8.7 to -3.1) compared with those younger than 65 years of age ($\beta=-0.4$, 95% CI -0.6 to -0.2) (figure 2). Had the 2013 extension not taken place, an estimated 19 591 (95% CI 15 711 to 23 472) additional AMI cases may have occurred in those aged 65 years and above compared with the 1325 (95% CI 1059 to 1590) additional cases in those under 65 years of age. We observed a step-change increase in the AMI incidence of those aged 65 years and older post-2016 ($\beta=114.4$, 95% CI 36.2 to 192.5) but not in those below 65 years ($\beta=6.4$, 95% CI -2.8 to 15.5).

Sex-stratified analysis

There was no difference in the post-2013 change to the AMI incidence trend between men ($\beta=-1.1$, 95% CI

Table 2 Associated effects of smoke-free legislation extensions on overall myocardial infarction incidence, stratified by age and sex

AMI incidence per 1 000 000 population	Overall	≥65 years	<65 years	Male	Female
Underlying trend					
β (95% CIs)	0.9 (0.7 to 1.1)	5.1 (3.3 to 7.0)	0.6 (0.4 to 0.8)	1.9 (1.5 to 2.4)	1.0 (0.6 to 1.3)
P value	0.001	0.001	0.001	0.001	0.001
2013 step-change					
β (95% CIs)	-3.7 (-11.8 to 4.4)	-14.6 (-78.9 to 49.7)	-4.2 (-9.3 to 0.8)	-14.5 (-28.0 to -1.0)	4.9 (-5.3 to 15.1)
P value	0.368	0.655	0.099	0.035	0.343
Post 2013-trend					
β (95% CIs)	-0.6 (-1.0 to -0.29)	-5.9 (-8.7 to -3.1)	-0.4 (-0.6 to -0.2)	-1.1 (-1.7 to -0.5)	-0.9 (-1.4 to -0.4)
P value	<0.001	<0.001	<0.001	<0.001	<0.001
2016 step-change					
β (95% CIs)	14.2 (3.3 to 25.0)	114.4 (36.2 to 192.5)	6.4 (-2.8 to 15.5)	28.6 (13.1 to 44.0)	17.3 (-11.1 to 45.6)
P value	0.011	0.004	0.175	<0.001	0.233
Post-2016 trend					
β (95% CIs)	0.2 (-1.0 to 1.3)	3.1 (-6.8 to 13.0)	-0.3 (-1.3 to 0.6)	-0.1 (-1.7 to 1.4)	0.19 (-2.2 to 2.6)
P value	0.788	0.537	0.497	0.852	0.875
2017 step-change					
β (95% CIs)	-7.2 (-18.2 to 3.7)	-71.4 (-198.6 to 55.8)	-0.8 (-10.1 to 8.5)	-8.0 (-26.4 to 10.4)	-12.5 (-30.1 to 5.2)
P value	0.195	0.272	0.868	0.392	0.166
Post-2017 trend					
β (95% CIs)	0.5 (-0.7 to 1.7)	1.0 (-9.7 to 11.8)	0.4 (-0.6 to 1.4)	0.4 (-1.2 to 2.0)	0.9 (-1.4 to 3.3)
P value	0.458	0.853	0.392	0.623	0.437
AIC	845.9	1368.4	776.2	1005.5	934.7
BIC	882.2	1401.8	812.4	1041.8	971.0

-1.7 to -0.5) and women ($\beta=-0.9$, 95% CI -1.4 to -0.4). However, there was a significant step-decline in the male AMI incidence ($\beta=-14.5$, 95% CI -28.0 to -1.0) and a non-significant increase in female AMI incidence post-2013 ($\beta=4.9$, 95% CI -5.3 to 15.1). An estimated 4748 (95% CI 4101 to 5394) additional male AMI cases and 3059 (95% CI 2395 to 3723) additional female AMI cases may have occurred in the absence of the 2013 smoking legislation introduction. We observed a step-change increase in the male AMI incidence post-2016 ($\beta=28.6$, 95% CI 13.2 to 44.0) though this was not statistically different from the average rise in women ($\beta=17.3$, 95% CI -11.1 to 45.6).

2017 effects

We observed a step-decline in the overall AMI incidence following the extension of the 2017 smoking legislation to all educational institutions, passenger transportation buses and taxis, though the effect was non-significant ($\beta=-7.2$, 95% CI -18.2 to 3.7). The step-decline had a consistent direction of effect in age-stratified and sex-stratified analysis, with those below 65 years of age potentially experiencing the greatest decline ($\beta=-71.4$, 95% CI -198.6 to 55.8) even though all the subgroup-specific estimates were also non-significant. We did not observe

any significant effects of the 2017 smoking legislation extension on the AMI incidence trend.

DISCUSSION

In this study, we found evidence of an independent association between the 2013 extension (smoke-free laws in common areas of residential apartments, covered pedestrian linkways, overhead bridges and within 5 m of bus stops) and a decline in the overall trend in AMI incidence. The protective effect of the 2013 extension on AMI incidence remained robust in sensitivity analysis, which assumed a non-linear time trend.

Studies that compared the risk of AMI before and after the enactment of smoke-free laws have reported reductions in the postlegislation enactment period,²⁷⁻⁴² including studies across Italy, USA, Canada, UK, Panama, Uruguay, Switzerland, Spain, Hong Kong⁴³ and New Zealand. In New Zealand, smoking bans in indoor public workplaces and hospitality venues in 2003 were associated with a 5% reduction in AMI admissions.⁴⁴ Greater effects were observed in studies in the USA, where smoking bans in all public places but not bars and bowling alleys resulted in a 39% reduction in coronary artery disease

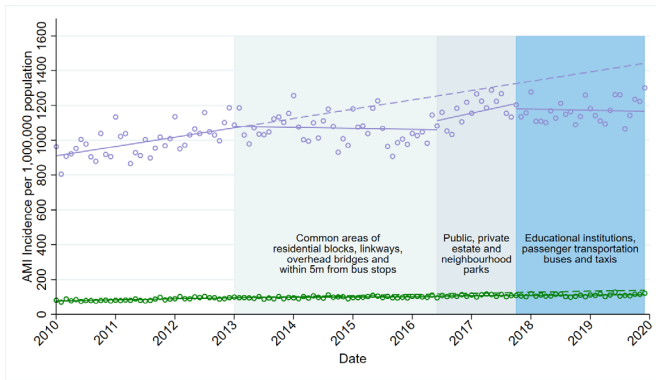


Figure 2 Monthly incidence of acute myocardial infarction in Singapore by age group, January 2010 to December 2019. The hollow purple circles represent the observed AMI incidence among individuals aged 65 years or above while the solid purple line represents the de-seasoned trend of AMI incidence among these individuals. The solid purple circles represent the counterfactual trend of AMI cases among older adults aged 65 years or above in the absence of the smoke-free legislation introduced in 2013. The hollow green circles represent the observed AMI incidence among individuals under the age of 65 while the solid green line represents the de-seasoned trend of AMI incidence among these individuals. The solid green circles represent the counterfactual trend of AMI incidence among those under the age of 65 years in the absence of the smoke-free legislation introduced in 2013. The different coloured sections depict the respective extensions of the smoke-free legislation in January 2013, June 2016 and October 2017. AMI, acute myocardial infarction.

in Ohio³² and 27% AMI hospitalisation in Colorado.³⁴ In addition, a meta-analysis of 18 studies showed an overall relative risk reduction of 0.87 associated with indoor smoking bans in workplaces and public spaces.⁵ This suggests that smoke-free environments may be beneficial for cardiovascular health around the world, thus understanding the impact of expanding smoke-free areas is of significant global health importance.

In this study, the extension of the smoke-free law to outdoor areas frequently accessed by the public such as the common areas of residential blocks, linkways, overhead bridges and the vicinity of bus stops was associated with a protective effect on AMIs, with an estimated 2097 cases from 2013 to 2020, which may have been avoided and leading to a tangible and measurable health and economic impact. Each AMI hospitalisation is estimated to cost US\$11 686, with additional US\$13 501 for percutaneous coronary intervention and US\$37 611 for coronary artery bypass graft.⁴⁵ More than 80% of the population in Singapore reside in high-rise apartment blocks. Common areas of their residential building and residential estate are spaces that they would likely frequent as part of their routine of getting from one place to another or even when they consider relaxation or physical activities. Frequenting such areas may increase their cumulative dose exposure to any present tobacco smoke. We hypothesise that the smoke-free laws in these areas contributed

to a reduction in the cumulative exposure of tobacco smoke and, thus a reduction in AMI risk.

Smoking has a dose-dependent impact on AMI, where the risk of the latter increases by 2%–3% per gram of tobacco smoked daily.⁴⁶ Biologically, proposed mechanisms include an acute increase in platelet aggregation, endothelial dysfunction, proinflammatory effects with increase in adhesion molecules, interleukin-6 and procoagulant effects of smoking due to increased tissue factor microparticles and fibrinogen.⁴⁷ The overall prothrombotic effect from passive cigarette exposure increases the risk of coronary thrombosis and AMI to a degree comparable to active smoking,⁴⁸ hence a further reduction in secondhand smoke may reduce AMI cases.

In stratified analysis, we detected evidence of effect modification by age: the effect of the 2013 smoke-free law expansion in reducing AMI incidence was much greater in individuals aged 65 years and above than those below that. Our results were consistent with those reported elsewhere. In a study conducted in Hong Kong by Thach *et al*, where there was a 13.6% decrease in AMI mortality in those ≥65 years, but the effect was not obvious in those <65 years.⁴³ In Hong Kong, AMI was only reduced in older individuals, which may be due to cultural differences where the older population frequently eat out with friends and family in restaurants and visit local tea houses or mahjong parlours.⁴³

When we stratified our analysis by sex, we found a significant step-reduction in male AMI incidence associated with the 2013 smoke-free law and a non-significant step-increase in female AMI incidence. This finding was consistent with a previous study, which reported a reduction in male AMI but not female AMI, following the introduction of national smoke-free legislation²⁷ and a previous study in the United Kingdom, where the reduction in AMI admissions in men was significant in men aged 60 and below but not in women of the same age category.⁴⁹ A potential reason might have been that the smoke-free law contributed to a greater motivation to reduce or quit smoking as some studies have reported,^{50 51} thus reducing the number of male individuals with smoking as a risk factor as well as the overall amount of environmental tobacco smoke. Male smoking prevalence declined from 24% at the start of the study duration to about 18% at the end, while female smoking prevalence only declined from 4% to 3% over the same period.²³

Older adults may be more susceptible to the procoagulant and proinflammatory effects of tobacco smoke and air pollutants such as PM_{2.5}.⁵² Our study found that extending the smoking ban to outdoor walkways, link bridges, residential blocks and proximity to bus stops where older people frequently visit was associated with a reduced risk of AMI by 5.9 cases per 1 000 000 population per month. This translates to 19 591 more cases of AMI, which may have occurred from July 2013 to December 2019 had the 2013 extension not taken place. The increasing incidence rate of AMI in Singapore during

the study period has been previously reported. This is possibly a result of population ageing and the increase in prevalence of cardiovascular risk factors.⁵³ Considering the rapidly ageing population in Singapore and many other developed nations, smoke-free law extension to outdoors public areas may have increasing associated health and economic benefits.

The post-2016 step-rise in AMI incidence was an unexpected study finding given that public smoke-free laws should reduce environmental smoke exposure in public places and this should theoretically reduce the risk of smoke-induced AMI cases. From 2010 to 2015, the average annual proportion of individuals aged 65 and above in the study area was 10.4% but rose to an average of 13.4% from 2016 to 2019. From 2010 to 2015, those aged 75 years and above formed 2.1% of the study population, whereas from 2016 to 2019, this group of individuals formed 2.7% of the population.⁵⁴ Furthermore, the incidence of AMI rose from 324.0 per 100 000 population in 2016 to 354.4 per 10 000 population in 2017, a substantial rise compared those in the years proximate to that.¹⁹ A new blood biomarker, high sensitivity troponin, was rolled out to hospitals for AMI detection from 2014. However, there is no public information on the rate of hospital uptake over time. We hypothesise that the improvement in this diagnostic could have contributed in part to the rise in AMI cases from 2016. Age has previously been reported in previous studies as an important risk factor for AMI.⁵⁵ Future studies analysing age-standardised AMI incidence rates may provide deeper insights into this observation.

The extension of the smoke-free law to the indoor and outdoor spaces in all educational institutions, passenger transportation buses and taxis in 2017 did not show evidence of an association with the number of AMI cases in our study. However, the direction of effect for the 2017 smoke-free legislation on AMI incidence was downwards and this was consistent even in age-stratified and sex-stratified subgroup analysis. The decline (though non-significant) was the greatest in those under 65 years of age, which would be consistent with the target population in the areas the law was extended to. This effect is biologically plausible, but insufficient study power may have limited the statistical significance of this finding. When more data points are available with longer follow-up, another study may be conducted to better interrogate the effect of the 2017 smoking law extension more closely.

Strengths and limitations

Our study had a number of strengths. We used all nationally reported cases of AMIs over a 10-year period, therefore reducing selection bias and resulting in strong internal validity. All AMIs were identified based on ECG assessment and the clinician's diagnosis documented in case notes and medical records, with all diagnoses centrally adjudicated at the NRDO. This greatly reduced the potential for outcome misclassification. We adjusted for time-varying confounders such as monthly seasonal patterns and autocorrelation using SARIMA models to

improve the accuracy of our estimates. Finally, there were no other national-level policy implementations that we were aware of that could have influenced the trend of AMIs.

Our study had a number of limitations. Being an observational study, the associations that we found do not provide evidence for causation. The findings from our study setting in a city-state may only be generalisable to other similar urban cities. We were not able to adjust for individual-level confounders as this was an ecological study. We did not have access to disposable income trends to normalise the effect of changing income levels on tobacco retail prices; this may have influenced the estimation of the association between tobacco prices and the risk of AMI. We did not have access to meteorological and air quality data and could not make adjustments for their effects. Finally, the inclusion of an additional disease outcome that is unlikely to be affected by tobacco smoke could have strengthened the study findings.

CONCLUSION

We found that the smoke-free law extension in 2013 to the outdoors was associated with a reduction in the monthly incidence trend of AMIs in Singapore. The reduction was particularly evident in those who were 65 years old and above. The 2016 smoke-free law extension was not associated with a reduction in AMI incidence. The 2017 smoke-free law extension suggested a potential step-reduction in AMI incidence—although further studies are required to understand the health impacts of both these extensions. Our study findings suggest that existing smoking laws should be evaluated for their health impacts before further extensions are considered. Health authorities in other similar urban cities seeking to review their smoke-free laws should consider the specific areas where intended beneficiary groups are at greater risk of tobacco smoke exposure in assessing the population health merits of further law extensions.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Ethics approval was not required and the researchers were neither able nor required to obtain individual participant consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. This study used pre-existing routinely collected data from a national registry. We are not the data controllers for the data used and, under the terms of our data sharing agreement with the data controller, we are not permitted to pass the data onto a third party. Anyone wishing to obtain these, or similar, data should apply directly to the National Registry of Diseases Office via HBP_SERVICENRDO@hpb.gov.sg.

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