Measuring the Impact of Smoke-free Legislation on Population Health in Two Cities of China

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Abstract

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on Population Health in Two Cities of China

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Exposure to secondhand smoke (SHS) increases the risk of morbidity and premature mortality. Smoke-free legislation is an effective way to protect the population from the harms of SHS and has been implemented nation wide in at least 62 countries. The central government of China has not passed a national smoke-free law, but an increasing number of local governments (direct-controlled municipalities and provincial capitals) have enacted city level smoke-free laws that prohibit smoking in public places over the last decade. The primary objective was to estimate the impact of the smoke-free legislation on cardiovascular and cerebrovascular diseases in two smoke-free cities (Tianjin and Qingdao) and explore underlying reasons for the disparity in the magnitude of the effect of city level smoke-free legislations. As reliable population-level incidence data is crucial for assessing the effectiveness of preventive measures and the evaluation of the burden of disease, the second objective was to assess the completeness of case ascertainment for the surveillance of acute myocardial infarction (AMI) and stroke incident cases and to estimate the incidence of AMI and stroke in Tianjin.

The first paper, *Impact of smoke-free legislation on acute myocardial infarction and stroke mortality in Tianjin, China (2007-2015)*, was developed to estimate the change of AMI and stroke mortality rate associated with the implementation of the smoke-free legislation in Tianjin. The study utilized incidence and mortality data routinely collected in the chronic incidence

surveillance system and all-cause mortality surveillance system respectively. An interrupted time series design adjusting for underlying secular trends, seasonal patterns, population size changes, and meteorological factors, was conducted to analyze the immediate and gradual effect of implementing the law on AMI and stroke events. There was an incremental 16% (RR: 0.84; 95% CI: 0.83–0.85) decrease per year in AMI mortality trend and a 2% (RR: 0.98; 95% CI: 0.97–0.99) annual decrease in stroke mortality trend among the population aged ≥ 35 years in Tianjin following the implementation of the smoke-free law. Immediate post-legislation reductions in mortality were not statistically significant due to the progressive enforcement of the law. An estimated 10,000 (22%) AMI deaths were prevented within 3.5 years of the implementation of the law.

The second paper, *Implementation matters: Assessment of Qingdao's smoke-free legislation on hospitalizations and mortality of cardiovascular diseases using interrupted time series design*, quantified the impact of the smoke-free legislation on cardiovascular and cerebrovascular diseases in Qingdao and explored the factors associated with the disparity in the magnitude of the effect. The study utilized data from electronic medical records, all-cause mortality surveillance system, existing program file, annual reports, governments' work report, published and unpublished literature. The theory of change was used to map backwards and identify preconditions and contextual factors of success. The smoke-free legislation in Qingdao was associated with gradual reductions in AMI and stroke incidence. Demonstrable but modest effects on stroke admissions and AMI/stroke mortality rate were observed among the older age group after the law had been implemented for about one year. The impact of the smoke-free law on population health in Qingdao is lower than that in Tianjin mainly because Qingdao was outperformed by Tianjin and some other smoke-free cities in China in the implementation and enforcement of the smoke-free law, and in achieving most of the expected interim outcomes. Understaffing, the initial lack of designated funding for law enforcement and the absence of effective monitoring and evaluation scheme lead to insufficient enforcement of the law and consequent limited compliance, awareness and health impact in Qingdao. Therefore, active steps including capacity building for enforcement agency staff, routine monitoring, rigorous implementation of penalties should be taken to enhance coordinated enforcement compliance and achieve expected health impact in the population.

The third paper, *Assessing the completeness of incident AMI and stroke reporting in Tianjin, China*, dealt with the issue arising in the evaluation of Tianjin's smoke-free law on AMI and stroke incidence wherein the changes in the extent of missing reports biased the results. The DisMod II program was applied to model the incidence of AMI and stroke from other epidemiological indicators. The completeness of AMI and stroke incidence reporting was assessed by comparing the sex and age-specific incidence rates derived from the incidence surveillance system in 2007, 2010 and 2015 with the modeled incidence rates. The overall completeness of incidence report was 36% (95% CI: 35%-38%) for AMI and 54% (95% CI: 53%-55%) for stroke. Completeness of AMI and stroke incidence surveillance was low in Tianjin but has improved in recent years primarily owing to the incorporation of automatic reporting component into the information systems of health facilities, the increase in the utilization of healthcare service and campaigns promoting access to prevention services and timely emergency treatment for AMI and stroke.

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Chapter 1. INTRODUCTION

Secondhand smoke (SHS) is a serious health hazard that can cause or worsen a wide range of health effects, including cardiovascular and respiratory diseases[1]. The dangers of SHS exposure have prompted large-scale efforts to protect public health through the adoption of smoking bans. An increasing number of countries have enacted partial or comprehensive national smoke-free laws that usually prohibit smoking in indoor workplaces, indoor public places, public transportation and, as appropriate, other public places as required by the World Health Organization Framework Convention on Tobacco Control [2]. The prevalence of smoking and exposure to second hand smoking (SHS) among non-smokers in China is still one of the highest in the world [3-5]. Nevertheless, China lags behind other countries to revise tobacco control legislations at the national level. In the past decade, tobacco control efforts have accelerated beyond expectations and subnational smoke-free laws have become increasingly widespread in China, particularly in its direct-controlled municipalities and provincial capitals [6, 7].

As two of the pioneer cities in implementing smoke-free legislation, Tianjin (the third largest city in China) and Qingdao (the largest city in Shandong province) enacted and implemented its first comprehensive smoke-free law in 2012 and 2013 respectively, banning smoking in indoor public and working places, schools, restaurants and hospitals. Deterrent fines will be given to any person who violates the no-smoking provisions of the law, regardless of being individual smokers, managers or owners of premises.

Studies showed that 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 following the implementation of the smoke-free law in major cities of China [6, 8, 9]. However, the evidence generated in these studies is insufficient for understanding the health effects of implementing the smoking ban in those cities. Understanding the health impact of smoke-free legislation of these pioneer cities is critical to informing effective development, implementation of national laws going forward. The current study contributes to this knowledge base through three papers exploring the impact of the municipal level smoke-free legislation on Acute Myocardial Infarction (AMI) and stroke events, the major causes of hospitalization and the leading causes of premature mortality in China [10, 11], and the factors associated with the magnitude of the health impact in the post-legislation period.

1.1 Statement of the Problem

1.1.1 *Smoking and secondhand smoke exposure in China*

China is world's largest producer and consumer of tobacco, with over 300 millions smokers, nearly one third of the world's total [3]. About one in every three cigarettes smoked in the world is smoked in China, more than in the other top four tobacco-consuming countries (Russia, USA, Indonesia and Japan) or all low- and middle-income countries combined [12]. According to 2015 China adult tobacco survey, 27.7% of the adult (aged $\geq$ 15) smokes, including 52.1% of men and 2.7% of women [3]. China's annual death toll from tobacco related diseases was 1.7 million in 2015, and is estimated to reach 2 million by 2030 and 3 million by 2050 if current trends continue [13, 14]. In addition to the direct health hazard to smokers themselves, a considerable number of non-smokers in China suffer health risks related to their secondhand smoke (SHS) exposure. About 740 million non-smokers, including about 180 million children under 15 in China are routinely exposed to secondhand smoke (SHS), which caused approximately 100, 000 deaths every year [15]. According to a nationally representative household survey, 72.4% of adults in China were exposed to SHS, with 52.5% exposed to SHS daily [16]. Results from China Global Youth Tobacco Survey in 2013 shows that 57.2% of youth (aged 13-15) are exposed to SHS inside enclosed public spaces, and 44.4% are exposed at home [5].

1.1.2 *Smoke-free legislation*

Article eight of World Health Organization Framework Convention on Tobacco Control (WHO FCTC) requires each party to adopt and implement effective legislative measures to protect people from exposure to tobacco smoke in indoor workplaces, indoor public places, public transport and, as appropriate, other public places [17]. The number of countries that have adopted a comprehensive smoke-free law covering all public places and working places in increased from 49 in 2015 to 55 in 2017 and 62 in 2019 [2, 18, 19]. Despite of the high prevalence of smoking and SHS exposure, China lags behind other countries to revise tobacco control legislation at the national level as required by WHO FCTC, and is still the only country from the BRICS (Brazil, Russia, India, China, South Africa) group that does not have a comprehensive national smoke-free law [6, 20]. However, one positive step that has been taken by the Chinese government on the lead up to the draft of the national prohibition of smoking in all public places is the enactment and implementation of smoke-free legislation in major cities.

Since 2008, more than 20 cities in China have taken encouraging steps to enact or amend laws or regulations promoting smoke-free work sites and public places. Shanghai initiated its first smoke controlling law in 2010, prohibiting smoking in selected places including schools, hospitals and libraries. In 2015, Shanghai People’s Congress amended the existing law and extended its smoking ban to all indoor public venues and workplaces and many outdoor public places. Tianjin and Qingdao are two of the first cities in China that implement a comprehensive smoke-free law. Tianjin passed the smoke free law in 2012 that prohibits smoking in selected places, including indoor government offices, schools, healthcare facilities, supermarkets and all public transportation. Other indoor public places including bars, restaurants and hotels are covered by a partial smoking ban which allows for designated smoking rooms. Qingdao's smoke-free law passed in September 2013 also bans smoking at indoor public area of restaurants, hotels and entertainment venues, and does not allowed for DSRs or smoking area. Beijing passed its new smoke-free law by requiring 100% smoke-free indoor public places, workplaces, public transportation and some outdoor areas as of June 2015, and including stringent fines for non-compliance, which fully aligns with Article 8 of the WHO FCTC.

Evidence from assessment of the implementation of city-level smoking free demonstrates that partial or comprehensive bans on smoking in public places are effective in reducing SHS, but compliance differ across cities and districts due to variation of degree of law enforcement. A study comparing SHS exposure pre and post the smoke-free law in Guangzhou suggested a significant reduction in SHS exposure in public places where smoking was fully banned [21]. A report released by Shanghai government shows that the smoking prevalence declined by 4% in entertainment venues and 6.4% in restaurants from 2013 to 2014, and declined by 11.5% in internet bars from 2012 to 2014 [6]. Evaluations of the smoke-free law conducted one year after the ban among 1860 venues in Harbin and 1852 venues in Tianjin found that the overall compliance was 88% and 73% respectively, and compliance was lower in internet bars, restaurants of both cities [9]. 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 [6, 8, 9].

1.1.3 *Measuring health impact of smoke-free law*

Numerous studies have been conducted to find out if public smoke-free legislation could reduce cardiovascular and cerebrovascular events, respiratory symptoms, preterm birth and asthma [22]. However, there have been no studies, to my knowledge, done on the specific health impact of smoke free law in mainland China excluding Hong Kong and Macau. The most frequently used indicators in those impact evaluation studies were the hospital admissions, incidence or mortality rates of AMI/stroke as they are short-term health outcomes with rapid onset. A grow body of evidence from past study has suggested that the acute effects of either active or passive smoking on AMI/stroke disappear quickly after the exposure is removed [1, 23]. Several national and regional-scale studies conducted in Italy, US, England, Switzerland, Spain and Argentina found a reduction in the rates of hospital admissions for AMI in the general population or indoor workers after the enforcement of smoke-free law in indoor public places [24-28]. Some studies suggested that smoking bans are associated with significant reduction in AMI mortality in the general population [29-32]. The magnitude of the reduction, which ranged from approximately 5% up to 70%, is uncertain due to sampling variations, difference in the prevalence of active and passive smoking and different lengths of following up [33, 34]. Among these studies, three used simple before and after comparisons of the rate or number of events [25, 29, 35], other studies applied interrupted time series design with or without the control group, adjusting for time-varying risk factors including long term trend, seasonal pattern, day of the week, air pollutants such as PM 2.5, temperature and influenza [23-28, 31, 32, 36-40].

1.1.4 *Assessment of Epidemiology consistency using DisMod II*

AMI and stroke have become the major causes of hospitalization and the leading causes of premature mortality [10, 11, 41] in China. Given the increasing burden of AMI and stroke, it is essential to monitor the incidence in China. However, empirical data on the incidence of the two diseases at either national or sub-national level is limited.. Estimates of incidence of cardiovascular and cerebrovascular diseases in China are rare and often incomplete. Major studies addressing incidence of cardiovascular disease in China include the Sino-Monica project (1987-1993), the PRC-USA Collaborative Study (1981-2000), the China Multicenter Collaborative Study of Cardiovascular Epidemiology Cohort (enrolled during 1991-1995 and followed up for 11 years) and Chinese Multi-provincial Cohort Study (1992-2002) [42-44]. China Chronic Disease and Risk Factor Surveillance survey, which encompassed 162 counties and all 31 provinces in mainland China, is the main national representative data source for CVDs prevalence but does not capture incidence information [45]. Tianjin CDC established the first routine population wide Non-Communicable Incidence Surveillance System in China in 1984. In 2007, Tianjin started to incorporate the NCDs incidence surveillance component into the Hospital Information System (HIS), reporting new cases directly via HIS rather than exclusively relying on manually reporting cards. Observed incidence data of CVDs from this system has been utilized in several studies, but the quality of the data was not investigated in any of these published studies [46-48].

Measuring incidence is often much more difficult than measuring mortality, thus more incident cases than deaths are likely to be missed in many cases [49]. DisMod II is a multistate life table that has been widely used to assess consistency on data that were available and supplement missing epidemiological data from observational set, including age-specific incidence, prevalence, remission, case fatality and mortality [50-53]. Compared with the original DisMod that requires three transition hazards - incidence, remission and case fatality as inputs, DisMod II allows for a wider range of input variables including incidence as a population rate, prevalence, duration, and mortality. When the input variables do not consist of the three transition hazards, the "downhill simplex" optimization procedure in the model will adjust the values of the input variables so that they are internally consistent while remain as close as possible to the original values. The input variable with a higher weight applied by user will remain closer to the original value [51].

1.2 AIMS AND OVERVIEW OF STUDIES

The study has two overall goals: a) To offer a robust and comprehensive assessment of the health impact of the smoke-free legislation by applying rigorous analytical techniques on time-series data collated from different routine surveillance systems; b) To evaluate the completeness of the reported AMI and stroke incidence rate that was initially used as one of the indicators for the impact evaluation.

To achieve these general goals, the following specific aims are accomplished in the three papers:

1. The first and second paper aims to determine the impact of the smoke-free legislation on the incidence and mortality of AMI and stroke in Tianjin and Qingdao. This aim is to answer the question of whether the smoke-free law lead to statistically significant reduction in cardiovascular and cerebrovascular disease events, what is the magnitude of reduced cases compared to pre-legislation forecasted trend, and how these reductions differ by outcome indicators, districts/cities and subpopulation groups (smokers vs. nonsmokers, male vs. female, younger vs. older). The first and second paper entail

comprehensive collation of multi-source data including available morbidity, mortality and hospital admission time series data of passive smoking related diseases from routine health information system in the two cities. The two papers utilize the comprehensive quantitative dataset assembled to examine the impact of the law on health level of local residents.

2. The second paper also seeks to identify the factors associated with smoke-free legislation success. Successful smoke-free legislation is dependent on political will, enforcement and societal support [54]. One specific hypothesis that I test in the second paper is that the magnitude of the impact is positively associated with the compliance rate and strength of law enforcement, the city or district with lower compliance rate and weaker enforcement of the law having less reduction in fatal and nonfatal AMI/stroke events. This paper draws on a systematic search and collation of existing data on the implementation of the law, secondhand smoking exposure, intermediate indicators and health outcomes.
3. The third paper intends to investigate the consistency of estimates of incidence and mortality of AMI and stroke from the surveillance data in Tianjin. This paper utilizes mortality data obtained from the surveillance system, and the prevalence, case fatality, remission data from literatures including IHME's GBD publications to calculate with DisMod II the predicted incidence, and compare the predicted with the observed. The results of this paper suggest the possible measurement errors of the two diseases, and prompt underlying causes and feasible remedies.

1.3 SIGNIFICANCE

This is the first study that measures the specific health impact of smoke-free law in mainland China. Although several studies have been conducted that seek to evaluate the implementation of the policies and interventions for reducing secondhand smoking exposure in China, most focused on intermediate indicators such secondhand smoke exposure in public areas and indoor air quality, none assess their long-term or short-term quantitative health impact. The evidence they provide is insufficient for understanding the effect of implementing comprehensive smoking ban in public places. Doing so will fill the research gap and generate solid evidence to better inform decision making and policy action. The study will also help pave the way for creating feasible framework of impact evaluation to be adopted in other cities that have enacted or are in the process of enacting the smoke-free law in China.

This will also be the first study to analyze the completeness and consistency of the routine incidence surveillance system for non-communicable disease in Tianjin. Reliable and representative population incidence data is crucial for decision making in health service planning and delivery, and is also an important indicator of the effectiveness of preventive measures and management of risk factors. Although many researchers have utilized the data from this system for the studies on burden of disease (BoD) or determinants of health, none (to my knowledge) investigated the quality of incidence surveillance data. Doing so will suggest the causes of and remedies for measure errors, therefore contribute to the reliability improvement for the surveillance of non-communicable disease in China.

REFERENCE

1. U.S. Department of Health and Human Services, *The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General*. 2014, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta (GA).
2. WHO, *WHO report on the global tobacco epidemic, 2017: Monitoring tobacco use and prevention policies*. 2017, World Health Organization: Geneva: Switzerland. p. 20.
3. Centers for Disease Control and Prevention, *2015 China Adult Tobacco Survey*. 2015, China Center for Disease Control and Prevention: Beijing, China.
4. Nan, Y., et al., *The 2015 China Adult Tobacco Survey: exposure to second-hand smoke among adults aged 15 and above and their support to policy on banning smoking in public places.* Zhonghua Liu Xing Bing Xue Za Zhi, 2016. **37**(6).
5. WHO, *China Global Youth Tobacco Survey (GYTS): Fact Sheet*. 2014, World Health Organization.
6. World Health Organization Western Pacific Region and University of Waterloo and ITC Project, *Smoke-free Policies in China: Evidence of Effectiveness and Implications for Action*. 2015, World Health Organization Regional Office for the Western Pacific: Manila.
7. Mackay, J., *China: the tipping point in tobacco control.* Br Med Bull, 2016. **120**(1): p. 15-25.
8. Jiang, G., et al., *Comprehensive assessment on the outcome of Tianjin Act of Tobacco Control.* Zhonghua Liu Xing Bing Xue Za Zhi, 2015. **36**(6): p. 561-4.
9. International Union Against Tuberculosis and Lung Disease. *Smoke-free compliance in ten cities: Tianjin, China.* 2014 [cited 2018 May 1, 2018]; Available from: http://www.tobaccofreeunion.org/images/stories/factsheet/Tianjin_1_year_compliance_evaluation_factsheet1.pdf.

10. Xu, H., et al., *The China Acute Myocardial Infarction (CAMI) Registry: A national long-term registry-research-education integrated platform for exploring acute myocardial infarction in China.* American Heart Journal, 2016. **175**: p. 193-201.e3.

11. Zhou, M., et al., *Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017.* The Lancet, 2019.

12. Eriksen, M., J. Mackay, and N. Schluger, *The tobacco atlas*. 5th ed. 2015, Atlanta, Georgia USA: American Cancer Society, Inc. 30.

13. Global Burden of Disease Study 2015, *Global Burden of Didsease Study 2015 (GBD 2015) Results*. 2017, Institute for Health Metrcs and Evaluation (IHME): Seattle, United States.

14. Chen, Z., et al., *Contrasting male and female trends in tobacco-attributed mortality in China: evidence from successive nationwide prospective cohort studies.* Lancet, 2015. **386**(10002): p. 1447-56.

15. Chinese Center for Disease Control and Prevention, *Global Adult Tobacco Survey China 2010 Country Reporot*. 2011.

16. Xiao, L., et al., *Population-based survey of secondhand smoke exposure in China.* Biomed Environ Sci, 2010. **23**(6): p. 430-6.

17. WHO. *Resolution WHA 56.1. WHO Framework Convention on Tobacco Control*. in *56th World Health Assembly*. 2003. Geneva: Switzerland.

18. WHO, *WHO report on the global tobacco epidemic, 2015: Raising taxes on tobacco*. 2015, World Health Organization: Geneva: Switzerland. p. 57-58.

19. WHO, *WHO report on the global tobacco epidemic, 2019: Offer help to quit tobacco use*. 2019, World Health Organization: Geneva: Switzerland. p. 24.

20. Yang, G., et al., *The road to effective tobacco control in China.* Lancet, 2015. **385**(9972): p. 1019-28.

21. Ye, X., et al., *Second-hand smoke exposure in different types of venues: before and after the implementation of smoke-free legislation in Guangzhou, China.* BMJ Open, 2014. **4**(2): p. e004273.

22. WHO, *Literature Review on the Health Effects of Smoke-free Policies in Light of the WHO FCTC*. 2014.

23. Barone-Adesi, F., et al., *Effects of Italian smoking regulation on rates of hospital admission for acute coronary events: a country-wide study.* PLoS One, 2011. **6**(3): p. e17419.

24. Barr, C.D., et al., *Comprehensive smoking bans and acute myocardial infarction among Medicare enrollees in 387 US counties: 1999-2008.* Am J Epidemiol, 2012. **176**(7): p. 642-8.

25. Vander Weg, M.W., G.E. Rosenthal, and M. Vaughan Sarrazin, *Smoking bans linked to lower hospitalizations for heart attacks and lung disease among medicare beneficiaries.* Health Aff (Millwood), 2012. **31**(12): p. 2699-707.

26. Schoj, V., et al., *The impact of a 100% smoke-free law on the health of hospitality workers from the city of Neuquen, Argentina.* Tob Control, 2010. **19**(2): p. 134-7.

27. Trachsel, L.D., et al., *Reduced incidence of acute myocardial infarction in the first year after implementation of a public smoking ban in Graubuenden, Switzerland.* Swiss Med Wkly, 2010. **140**(9-10): p. 133-8.

28. Galan, I., et al., *Assessing the effects of the Spanish partial smoking ban on cardiovascular and respiratory diseases: methodological issues.* BMJ Open, 2015. **5**(12): p. e008892.

29. Rodu, B., N. Peiper, and P. Cole, *Acute myocardial infarction mortality before and after state-wide smoking bans.* J Community Health, 2012. **37**(2): p. 468-72.

30. Dove, M.S., et al., *The impact of Massachusetts' smoke-free workplace laws on acute myocardial infarction deaths.* Am J Public Health, 2010. **100**(11): p. 2206-12.

31. McAlister, A.L., et al., *Reductions in cigarette smoking and acute myocardial infarction mortality in Jefferson County, Texas.* Am J Public Health, 2010. **100**(12): p. 2391-2.

32. Thach, T.Q., et al., *The smoke-free legislation in Hong Kong: its impact on mortality.* Tob Control, 2015.

33. Lin, H., et al., *The effects of smoke-free legislation on acute myocardial infarction: a systematic review and meta-analysis.* BMC Public Health, 2013. **13**: p. 529.

34. Tan, C.E. and S.A. Glantz, *Association between smoke-free legislation and hospitalizations for cardiac, cerebrovascular, and respiratory diseases: a meta-analysis.* Circulation, 2012. **126**(18): p. 2177-83.

35. Sargent, R.P., R.M. Shepard, and S.A. Glantz, *Reduced incidence of admissions for myocardial infarction associated with public smoking ban: before and after study.* BMJ, 2004. **328**(7446): p. 977-80.

36. Mead, E.L., et al., *Association between Florida's smoke-free policy and acute myocardial infarction by race: A time series analysis, 2000-2013.* Prev Med, 2016. **92**: p. 169-175.

37. Stallings-Smith, S., et al., *Reductions in cardiovascular, cerebrovascular, and respiratory mortality following the national irish smoking ban: interrupted time-series analysis.* PLoS One, 2013. **8**(4): p. e62063.

38. Barone-Adesi, F., et al., *Short-term effects of Italian smoking regulation on rates of hospital admission for acute myocardial infarction.* Eur Heart J, 2006. **27**(20): p. 2468-72.

39. Ferrante, D., et al., *Reduction in hospital admissions for acute coronary syndrome after the successful implementation of 100% smoke-free legislation in Argentina: a comparison with partial smoking restrictions.* Tob Control, 2012. **21**(4): p. 402-6.

40. Sims, M., et al., *Short term impact of smoke-free legislation in England: retrospective analysis of hospital admissions for myocardial infarction.* BMJ, 2010. **340**: p. c2161.

41. Zhou, M., et al., *Cause-specific mortality for 240 causes in China during 1990-2013: a systematic subnational analysis for the Global Burden of Disease Study 2013.* Lancet, 2016. **387**(10015): p. 251-72.

42. Wu, Z., et al., *Sino-MONICA project: a collaborative study on trends and determinants in cardiovascular diseases in China, Part i: morbidity and mortality monitoring.* Circulation, 2001. **103**(3): p. 462-8.

43. *People's Republic of China--United States Cardiovascular and Cardiopulmonary Epidemiology Research Group. An epidemiological study of cardiovascular and cardiopulmonary disease risk factors in four populations in the People's Republic of China. Baseline report from the P.R.C.-U.S.A. Collaborative Study.* Circulation, 1992. **85**(3): p. 1083-96.

44. Liu, J., et al., *Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study.* JAMA, 2004. **291**(21): p. 2591-9.

45. Li, Y., et al., *Risk factors for noncommunicable chronic diseases in women in China: surveillance efforts.* Bull World Health Organ, 2013. **91**(9): p. 650-60.

46. Wang, D.Z., et al., *Fifteen-year trend in incidence of acute myocardial infarction in Tianjin of China.* Zhonghua Xin Xue Guan Bing Za Zhi, 2017. **45**(2): p. 154-159.

47. Li, W., et al., *[Incidence trends of cervical cancer in Tianjin, 2007-2013].* Zhonghua Liu Xing Bing Xue Za Zhi, 2016. **37**(5): p. 699-701.

48. Jiang, G., et al., *Epidemiological transition and distribution of stroke incidence in Tianjin, China, 1988-2010.* Public Health, 2016. **131**: p. 11-9.

49. Kruijshaar, M.E., J.J. Barendregt, and N. Hoeymans, *The use of models in the estimation of disease epidemiology.* Bull World Health Organ, 2002. **80**(8): p. 622-8.

50. Barendregt, J.J. and A. Ott, *Consistency of epidemiologic estimates.* Eur J Epidemiol, 2005. **20**(10): p. 827-32.

51. Barendregt, J.J., et al., *A generic model for the assessment of disease epidemiology: the computational basis of DisMod II.* Popul Health Metr, 2003. **1**(1): p. 4.

52. Scarborough, P., et al., *Assessing the external validity of model-based estimates of the incidence of heart attack in England: a modelling study.* BMC Public Health, 2016. **16**(1): p. 1135.

53. Chen, C.Y., Y.B. Huang, and C. Tzu-Chi Lee, *Epidemiology and disease burden of ischemic stroke in Taiwan.* Int J Neurosci, 2013. **123**(10): p. 724-31.

54. Vardavas, C.I., et al., *Ashtrays and Signage as Determinants of a Smoke-Free Legislation's Success.* PLOS ONE, 2013. **8**(9): p. e72945.

Chapter 2. IMPACAT OF SMOKE-FREE LEGISLATION ON ACUTE MYOCARDIAL INFARCTION AND STROKE MORTALITY IN 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 (SHS) and has been implemented in many countries. On May 31, 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 analyze the impact of the smoke-free law on the weekly mortality due to AMI and stroke. The study period was from January 1, 2007, to December 31, 2015, with a 3.5-year post-legislation 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% (RR: 0.84; 95% CI: 0.83–0.85) decrease per year in AMI mortality and a 2% (RR: 0.98; 95% CI: 0.97–0.99) annual decrease in stroke mortality among the population aged ≥ 35 years in Tianjin was observed. Immediate post-legislation 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.

2.1 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 World Health Organization 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 nonsmokers, 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 24 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 square km, population 15.6 million) of China, first implemented the smoke-free law on May 31, 2012. The law prohibits smoking in select places, including indoor government offices, schools, health care 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.

2.2 METHODS

2.2.1 *Study setting and 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 (ICD-10). 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 practicing 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.

2.2.2 *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 post-legislation period compared with that in the pre-legislation period. The age- and sex-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 modeled by annual sine and cosine terms. The study period was from January 1, 2007, to December 31, 2015, including a post-ban 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:

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

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 pre-legislation trend), β_2 is the coefficient of the indicator variable Ban (coded 0 for pre-ban period and 1 for post-ban 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 pre-legislation to post-legislation periods was quantified as 100(exp (β_2)-1). The annual relative change was quantified as 100(exp (52*β_3)-1). Each sex and age group (≥35, 35-64, 65-84, ≥85) was analyzed 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 six months and one year pre-legislation. 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 January 1, 2007, to December 31, 2015, subtracted from the predicted number of deaths without the influence of the law.

Sensitivity analyses were conducted to investigate the impact of varying a range of model assumptions. Given the potential problem of overdispersion, we ran negative binomial models and compared them to Poisson equivalents using likelihood ratio test. We refitted additional models with false law implementation dates at six months or one year pre-legislation to provide further validation that the final models detecting the true effect. All analyses were conducted using R version 3.5.3, and statistical modeling was conducted with the glm function.

2.3 RESULTS

There were approximately 86,300 AMI deaths and 99,900 stroke deaths among permanent residents aged 35 years and older in Tianjin (from January 1, 2007, through December

31, 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 (See Supplementary Table S2.3). 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 post-legislation period (See Figure 2.1). 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 ($p<0.001$).

Table 2.1 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)

The distribution of death locations stratified by sex and age group is shown in Table 2.1. 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 and sex- and age group-specific post-ban results of Poisson regressions for mortality in Tianjin are reported in Table 2.2. Following the implementation of smoke-free legislation, a 16% decrease in mortality per year was observed in AMI (RR: 0.84; 95% CI: 0.83–0.85). Likewise, a gradual 2% reduction per year was observed in stroke mortality (RR: 0.98; 95% CI: 0.97–0.99). Annual trend effects in AMI mortality were observed in both men (RR: 0.85; 95% CI: 0.83–0.86) and women (RR: 0.84; 95% CI: 0.82–0.85), 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: 0.90–1.02). For the age group 35-64, the 4% immediate post-legislation decrease in AMI mortality was followed by a gradual 13% decrease each post-legislation year. This resulted in a net post-legislation 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: 1.06–1.14), followed by a 17% decrease per year, resulting in a net post-legislation decrease of 25%. Similarly, a net post-legislation 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 post-legislation increase. There was no significant negative association between stroke mortality and smoke-free legislation.

Table 2.2 Multivariate analysis* of overall and age group- and sex-specific post-ban 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, 1.08)	0.84 (0.83, 0.85)	1.06 (1.02, 1.10)	0.85 (0.83, 0.86)	1.05 (1.01, 1.08)	0.84 (0.82, 0.85)
35-64	0.96 (0.90, 1.02)	0.87 (0.85, 0.89)	0.96 (0.90, 1.03)	0.87 (0.84, 0.90)	0.96 (0.85, 1.07)	0.84 (0.82, 0.86)
65-84	1.10 (1.06, 1.14)	0.83 (0.82, 0.85)	1.13 (1.07, 1.18)	0.84 (0.82, 0.86)	1.08 (1.02, 1.14)	0.83 (0.81, 0.85)
≥85	1.16 (1.09, 1.22)	0.81 (0.79, 0.83)	1.18 (1.08, 1.29)	0.8 (0.77, 0.83)	1.15 (1.06, 1.24)	0.82 (0.79, 0.85)
Stroke mortality						
All-age	1.05 (1.02, 1.08)	0.98 (0.97, 0.99)	1.05 (1.02, 1.09)	0.98 (0.96, 0.99)	1.04 (0.99, 1.08)	0.99 (0.97, 1.01)
35-64	1.05 (0.99, 1.11)	0.98 (0.95, 1.00)	1.06 (0.99, 1.14)	0.97 (0.94, 1.00)	1.02 (0.92, 1.13)	0.99 (0.94, 1.03)
65-84	1.09 (1.05, 1.12)	0.96 (0.95, 0.98)	1.07 (1.02, 1.12)	0.95 (0.93, 0.97)	1.11 (1.05, 1.17)	0.97 (0.95, 0.99)
≥85	1.06 (0.99, 1.13)	0.99 (0.96, 1.02)	1.13 (1.02, 1.25)	0.98 (0.94, 1.02)	1.00 (0.91, 1.09)	1.00 (0.96, 1.04)

* Adjusted for time trend, population, seasonality, temperature, and relative humidity.

For illustration, Figure 2.1 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 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 nonproblematic because seasonality that largely explains autocorrelation was controlled using circular distributions (See Supplementary Table S2.4).

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 (See Supplementary Table S2.5).

In the absence of municipal-level smoke-free legislation, an estimated 10,000 (95% CI: 9,312–10,688) additional AMI deaths would have occurred from May 31, 2012, to December 31, 2015. No deaths were prevented in association with stroke mortality.

2.4 DISCUSSION

In an analysis based on cause-specific mortality data for a permanent population of approximately 10 million people over nine 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.

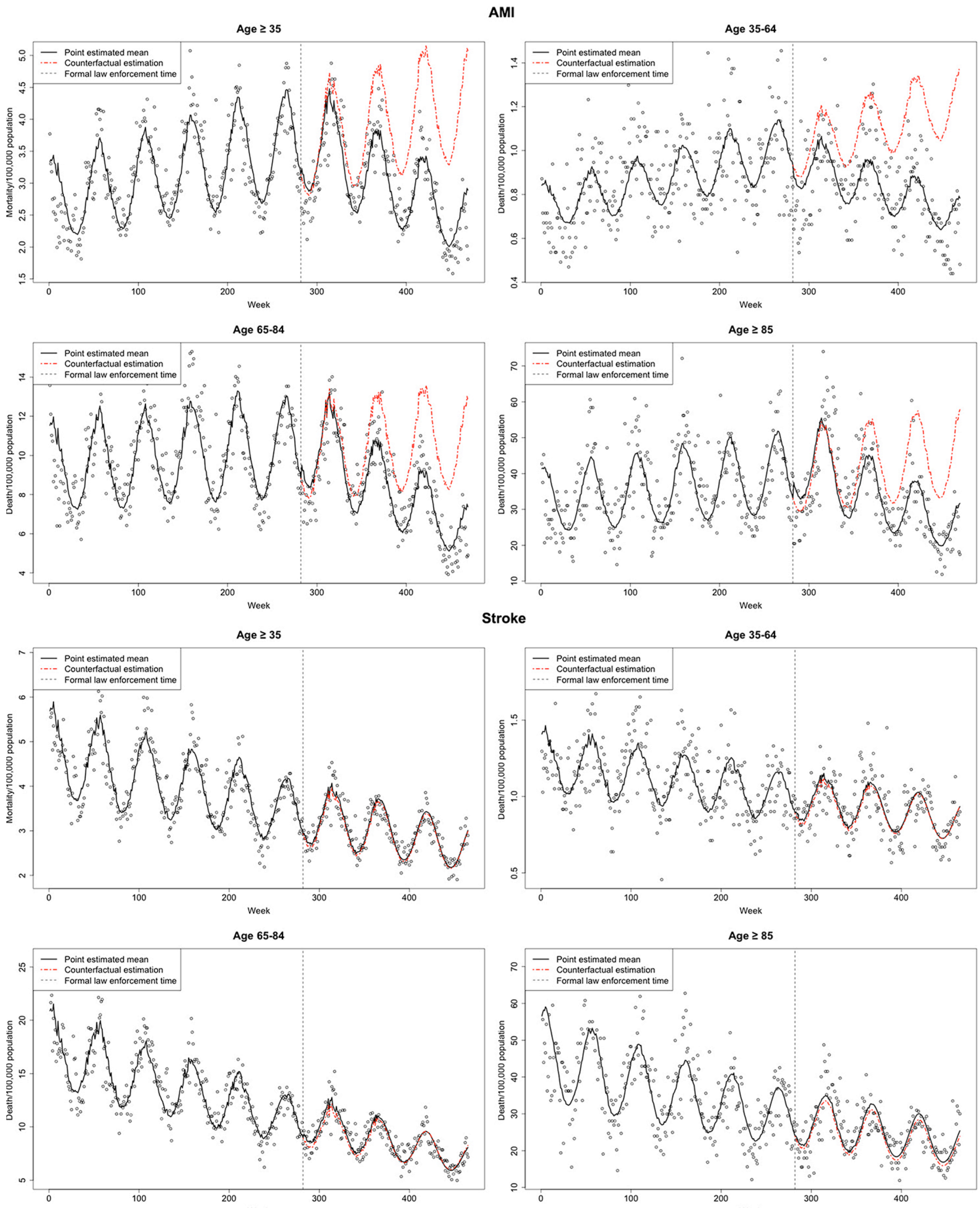


Figure 2.1 Observed and predicted weekly AMI and stroke mortality rate in Tianjin (2007-2015). Observed (circles) and predicted (solid and dotdashed lines) mortality rate. Black solid line, pre- and post-egislation trend; red dotdashed line, counterfactual scenario; dash line, law enforcement date.

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[20]. Decreases in AMI mortality are usually triggered by reductions in preventable behavioral, biological, and environmental risk factors as well as improvements in medical care[20-24]. 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 [25], and gradual establishment of Chest Pain Centers in 2014[25]. However, these prevention and control interventions were not implemented extensively[19, 25], 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 post-legislation period[15, 26] (See Supplementary Figure S2.2, Table S2.6); 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 to that on admissions[27]. The progressive enforcement of the smoke-free law in Tianjin since the implementation in May 2012 might have further delayed the effects[28]. 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[29-31]. 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 six 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[29]. 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[32-34] but contrary to those of studies conducted in Ireland, Scotland, and Arizona and a meta-analysis[17, 35-38]. 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[39], so the implementation of such laws may less-directly affect stroke. In addition, compared with AMI, a higher proportion of stroke incidence is nonfatal[40]. Therefore, the effect of smoke-free law on stroke may be restricted to nonfatal 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, 34]. 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 [27, 35, 38, 41].

We detected similar reductions in AMI mortality among men and women. Although many studies have not examined impacts stratified by sex[27, 32, 34, 42-45], the absence of an impact on women has been found in England and Italy[46-48]. This was mainly attributed to lower pre-legislative levels of and reductions in exposure to SHS among women[46]. Another potential reason is that higher prevalence of smoking among men allows for a larger percentage to quit. In contrast, studies conducted in Scotland[35] and the Piedmont region of Italy[49] 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[50], the prevalence of SHS exposure pre-legislation in public places or worksites among female nonsmokers was as high as that among male nonsmokers (72% versus 74%)[51], 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 [52, 53]. On the other hand, the extent of overrepresentation or underrepresentation 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 nonsmokers.

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 pre-legislation period). Using this population-based dataset, we were able to offer greater statistical power to detect secular trends and assess the health impact.

2.5 CONCLUSION

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.

REFERENCES

1. U.S. Department of Health and Human Services, *The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General*. 2014, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta (GA).
2. WHO. *Resolution WHA 56.1. WHO Framework Convention on Tobacco Control*. in *56th World Health Assembly*. 2003. Geneva: Switzerland.
3. WHO, *WHO report on the global tobacco epidemic, 2015: Raising taxes on tobaccl*. 2015, World Health Organization: Geneva: Switzerland. p. 57-58.
4. WHO, *WHO report on the global tobacco epidemic, 2017: Monitoring tobacco use and prevention policies*. 2017, World Health Organization: Geneva: Switzerland. p. 20.
5. Centers for Disease Control and Prevention, *2015 China Adult Tobacco Survey*. 2015, China Center for Disease Control and Prevention: Beijing, China.
6. Eriksen, M., J. Mackay, and N. Schluger, *The tobacco atlas*. 5th ed. 2015, Atlanta, Georgia USA: American Cancer Society, Inc. 30.
7. Chinese Center for Disease Control and Prevention, *Global Adult Tobacco Survey China 2010 Country Report*. 2011.
8. Liu, Y. and L. Chen, *New medical data and leadership on tobacco control in China.* Lancet, 2011. **377**(9773): p. 1218-20.
9. Global Burden of Disease Study 2016, *Global Burden of Didsease Study 2016 (GBD 2016) Results*. 2018

, Institute for Health Metrcs and Evaluation (IHME): Seattle, United States.

10. Nan, Y., et al., *The 2015 China Adult Tobacco Survey: exposure to second-hand smoke among adults aged 15 and above and their support to policy on banning smoking in public places.* Zhonghua Liu Xing Bing Xue Za Zhi, 2016. **37**(6).

11. WHO, *China Global Youth Tobacco Survey (GYTS): Fact Sheet*. 2014, World Health Organization.

12. Yang, G., et al., *The road to effective tobacco control in China.* Lancet, 2015. **385**(9972): p. 1019-28.

13. World Health Organization Western Pacific Region and University of Waterloo and ITC Project, *Smoke-free Policies in China: Evidence of Effectiveness and Implications for Action*. 2015, World Health Organization Regional Office for the Western Pacific: Manila.

14. Jie, Y., *The survey report on enfcorement of smoke free law in cities of China*. 2015, Beijing, China: China Democracy and Law Press. 162.

15. Jiang, G., et al., *Comprehensive assessment on the outcome of Tianjin Act of Tobacco Control.* Zhonghua Liu Xing Bing Xue Za Zhi, 2015. **36**(6): p. 561-4.

16. International Union Against Tuberculosis and Lung Disease. *Smoke-free compliance in ten cities: Tianjin, China.* 2014 [cited 2018 May 1, 2018]; Available from: http://www.tobaccofreeunion.org/images/stories/factsheet/Tianjin_1_year_compliance_evaluation_factsheet1.pdf.

17. Stallings-Smith, S., et al., *Reductions in cardiovascular, cerebrovascular, and respiratory mortality following the national irish smoking ban: interrupted time-series analysis.* PLoS One, 2013. **8**(4): p. e62063.

18. Wang, X., et al., *All-cause mortality in Tianjin, China, 1999-2004.* Prev Chronic Dis, 2009. **6**(4): p. A132.

19. Wang, X., et al., *Surveillance of trend and distribution of stroke mortality by subtype, age, gender, and geographic areas in Tianjin, China, 1999-2006.* Int J Stroke, 2009. **4**(3): p. 169-74.

20. Chang, J., X. Liu, and Y. Sun, *Mortality due to acute myocardial infarction in China from 1987 to 2014: Secular trends and age-period-cohort effects.* International Journal of Cardiology. **227**: p. 229-238.

21. Torpy, J.M., A.E. Burke, and R.M. Glass, *JAMA patient page. Coronary heart disease risk factors.* JAMA, 2009. **302**(21): p. 2388.

22. Wang, X., W. Kindzierski, and P. Kaul, *Air Pollution and Acute Myocardial Infarction Hospital Admission in Alberta, Canada: A Three-Step Procedure Case-Crossover Study.* PLoS One, 2015. **10**(7): p. e0132769.

23. Takii, T., et al., *Trends in acute myocardial infarction incidence and mortality over 30 years in Japan: report from the MIYAGI-AMI Registry Study.* Circ J, 2010. **74**(1): p. 93-100.

24. Gillum, R.F., *Trends in acute myocardial infarction and coronary heart disease death in the United States.* J Am Coll Cardiol, 1994. **23**(6): p. 1273-7.

25. Wang, D.Z., et al., *Analysis on the trends in mortality following acute myocardial infarction from 1999 to 2015 in Tianjin of China.* Zhonghua Xin Xue Guan Bing Za Zhi, 2017. **45**(11): p. 985-991.

26. Wang, D.Z., et al., *Fifteen-year trend in incidence of acute myocardial infarction in Tianjin of China.* Zhonghua Xin Xue Guan Bing Za Zhi, 2017. **45**(2): p. 154-159.

27. Dove, M.S., et al., *The impact of Massachusetts' smoke-free workplace laws on acute myocardial infarction deaths.* Am J Public Health, 2010. **100**(11): p. 2206-12.

28. Bernal, J.L., S. Cummins, and A. Gasparrini, *Interrupted time series regression for the evaluation of public health interventions: a tutorial.* Int J Epidemiol, 2017. **46**(1): p. 348-355.

29. Tianjin Commission for Health Improvement, *2012 Annual Report on Tobacco Control in Tianjin*. 2013: Tianjin.

30. Tianjin Commission for Health Improvement, *2013 Annual Report on Tobacco Control in Tianjin*. 2014: Tianjin.

31. Tianjin Commission for Health Improvement, *2014 Annual Report on Tobacco Control in Tianjin*. 2015: Tianjin.

32. Juster, H.R., et al., *Declines in hospital admissions for acute myocardial infarction in New York state after implementation of a comprehensive smoking ban.* Am J Public Health, 2007. **97**(11): p. 2035-9.

33. Edwards, R., et al., *After the smoke has cleared: evaluation of the impact of a new national smoke-free law in New Zealand.* Tob Control, 2008. **17**(1): p. e2.

34. Thach, T.Q., et al., *The smoke-free legislation in Hong Kong: its impact on mortality.* Tob Control, 2015.

35. Mackay, D.F., et al., *Impact of Scotland's Comprehensive, Smoke-Free Legislation on Stroke.* PLoS One, 2013. **8**(5).

36. Herman, P.M. and M.E. Walsh, *Hospital admissions for acute myocardial infarction, angina, stroke, and asthma after implementation of Arizona's comprehensive statewide smoking ban.* Am J Public Health, 2011. **101**(3): p. 491-6.

37. Li, J., et al., *Maternal mortality in Yunnan, China: recent trends and associated factors.* BJOG, 2007. **114**(7): p. 865-74.

38. Tan, C.E. and S.A. Glantz, *Association between smoke-free legislation and hospitalizations for cardiac, cerebrovascular, and respiratory diseases: a meta-analysis.* Circulation, 2012. **126**(18): p. 2177-83.

39. U.S. Department of Health and Human Services, *The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General*. 2006, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta (GA).

40. Benjamin, E.J., et al., *Heart Disease and Stroke Statistics—2017 Update: A Report From the American Heart Association.* Circulation, 2017.

41. Barone-Adesi, F., et al., *Effects of Italian smoking regulation on rates of hospital admission for acute coronary events: a country-wide study.* PLoS One, 2011. **6**(3): p. e17419.

42. Khuder, S.A., et al., *The impact of a smoking ban on hospital admissions for coronary heart disease.* Prev Med, 2007. **45**(1): p. 3-8.

43. Ferrante, D., et al., *Reduction in hospital admissions for acute coronary syndrome after the successful implementation of 100% smoke-free legislation in Argentina: a comparison with partial smoking restrictions.* Tob Control, 2012. **21**(4): p. 402-6.

44. Sargent, R.P., R.M. Shepard, and S.A. Glantz, *Reduced incidence of admissions for myocardial infarction associated with public smoking ban: before and after study.* BMJ, 2004. **328**(7446): p. 977-80.

45. Bartecchi, C., et al., *Reduction in the incidence of acute myocardial infarction associated with a citywide smoking ordinance.* Circulation, 2006. **114**(14): p. 1490-6.

46. Sims, M., et al., *Short term impact of smoke-free legislation in England: retrospective analysis of hospital admissions for myocardial infarction.* BMJ, 2010. **340**: p. c2161.

47. Vasselli, S., et al., *Reduction incidence of myocardial infarction associated with a national legislative ban on smoking.* Minerva Cardioangiol, 2008. **56**(2): p. 197-203.

48. Cesaroni, G., et al., *Effect of the Italian smoking ban on population rates of acute coronary events.* Circulation, 2008. **117**(9): p. 1183-8.

49. Barone-Adesi, F., et al., *Short-term effects of Italian smoking regulation on rates of hospital admission for acute myocardial infarction.* Eur Heart J, 2006. **27**(20): p. 2468-72.

50. Mackay, J., *China: the tipping point in tobacco control.* Br Med Bull, 2016. **120**(1): p. 15-25.

51. Xiao, L., et al., *Population-based survey of secondhand smoke exposure in China.* Biomed Environ Sci, 2010. **23**(6): p. 430-6.

52. Yang, G., et al., *Validation of verbal autopsy procedures for adult deaths in China.* Int J Epidemiol, 2006. **35**(3): p. 741-8.

53. Wang, L., et al., *Evaluation of the quality of cause of death statistics in rural China using verbal autopsies.* J Epidemiol Community Health, 2007. **61**(6): p. 519-26.

SUPPLEMENTARY

Table S2.3 AMI and stroke mortality rate for permanent residents aged 35 years and older

	Person year				AMI mortality Rate (per 100 000 person years)				Stroke mortality Rate (per 100 000 person years)			
	Age≥ 35	35-64	65-84	≥85	Age≥ 35	35-64	65-84	≥85	Age≥ 35	35-64	65-84	≥85
Total	53116290	41862361	10263097	990832	162.4	44.8	481.7	1826.5	188.1	53.9	598.8	1603.8
Gender												
Men	26215238	20847342	4828698	439198	182.8	65.5	542.2	1843.8	217.6	75.0	705.7	1669.2
Women	26901052	20105019	5334399	551634	142.6	25.4	435.9	1812.8	159.3	34.4	513.2	1551.8
Year												
2007	5568735	4475347	1016077	77311	133.7	36.4	456.4	1528.9	233.4	60.2	844.6	2222.2
2008	5677320	4544687	1043569	89064	161.1	45.8	518.1	1857.1	227.8	62.8	788.3	2082.8
2009	5771943	4603155	1068641	100147	169.3	46.6	537.8	1876.2	219.9	60.2	746.4	1939.1
2010	5834128	4636260	1091095	106773	179.5	48.1	550.5	2095.1	207.2	57.4	682.1	1857.2
2011	5901051	4658993	1126740	115318	173.0	50.4	505.9	1875.7	181.0	52.4	574.7	1526.2
2012	5948505	4673496	1152744	122265	175.3	46.5	510.7	1934.3	174.1	50.8	542.6	1414.1
2013	6026688	4731431	1184462	110795	181.5	47.3	517.3	2323.2	169.4	51.2	512.4	1549.7
2014	6138812	4759163	1253745	125904	162.2	46.0	445.5	1734.7	151.1	47.2	436.9	1234.3
2015	6249108	4779829	1326024	143255	126.7	36.0	327.0	1298.4	138.6	43.5	373.1	1139.9

Table S2.4 Multivariate analysis* of overall and age group- and sex-specific post-ban effects on mortality rates using negative binomial models, Tianjin, 2007–2015

	Overall		Male		Female	
	Immediate Effect	Graduate Effect per Annum	Immediate Effect	Graduate Effect per Annum	Immediate Effect	Graduate Effect per Annum
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
AMI Mortality						
All Age	1.05 (0.98, 1.14)	0.84 (0.81, 0.87)	1.06 (0.98, 1.15)	0.84 (0.82, 0.87)	1.05 (0.97, 1.13)	0.84 (0.81, 0.87)
35-64	0.96 (0.88, 1.05)	0.87 (0.83, 0.90)	0.96 (0.88, 1.05)	0.87 (0.83, 0.90)	0.96 (0.84, 1.10)	0.86 (0.81, 0.91)
65-84	1.11 (1.03, 1.20)	0.83 (0.80, 0.86)	1.13 (1.03, 1.23)	0.84 (0.80, 0.87)	1.08 (1.00, 1.18)	0.83 (0.80, 0.86)
>=85	1.16 (1.02, 1.32)	0.81 (0.77, 0.85)	1.18 (1.02, 1.37)	0.80 (0.76, 0.84)	1.15 (0.99, 1.32)	0.82 (0.77, 0.86)
Stroke Mortality						
All Age	1.03 (0.99, 1.06)	0.99 (0.97, 1.01)	1.04 (0.99, 1.08)	0.99 (0.97, 1.00)	1.02 (0.97, 1.06)	1.00 (0.98, 1.03)
35-64	1.03 (0.98, 1.09)	0.99 (0.97, 1..02)	1.05 (0.98, 1.12)	0.98 (0.96, 1.01)	0.99 (0.90, 1.09)	1.01 (0.97, 1.05)
65-84	1.07 (1.02, 1.11)	0.98 (0.96, 0.99)	1.05 (1.00, 1.11)	0.97 (0.94, 0.99)	1.09 (1.03, 1.14)	0.98 (0.96, 1.01)
>=85	1.04 (0.95, 1.14)	1.01 (0.97, 1.04)	1.11 (0.99, 1.22)	0.99 (0.95, 1.04)	0.99 (0.87, 1.12)	1.01 (0.97, 1.06)

* **Negative binomial models** adjusted for time trend, population, seasonality, temperature, and relative humidity; Newey-West heteroskedasticity and autocorrelation consistent (HAC) standard errors were used to accommodate for serial autocorrelation.

Table S2.5 Results from multivariate Poisson models* with false law implementation dates at six months or one year pre-legislation, Tianjin, 2007–2015

		Overall Immediate Effect	Overall Graduate Effect per Annum	Male Immediate Effect	Male Graduate Effect per Annum	Female Immediate Effect	Female Graduate Effect per Annum
		RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Six month	**AMI Mortality**						
	All Age	1.14 (1.11, 1.18)	0.84 (0.83, 0.85)	1.15 (1.11, 1.20)	0.85 (0.83, 0.86)	1.15 (1.09, 1.19)	0.84 (0.82, 0.85)
	35-64	1.03 (0.97, 1.10)	0.87 (0.84, 0.89)	1.03 (0.96, 1.11)	0.87 (0.84, 0.90)	1.03 (0.91, 1.17)	0.86 (0.82, 0.90)
	65-84	1.2 (1.16, 1.26)	0.83 (0.82, 0.85)	1.23 (1.16, 1.30)	0.84 (0.82, 0.86)	1.18 (1.12, 1.26)	0.83 (0.81, 0.85)
	>=85	1.29 (1.21, 1.37)	0.81 (0.79, 0.83)	1.32 (1.20, 1.45)	0.8 (0.77, 0.83)	1.27 (1.16, 1.38)	0.82 (0.79, 0.85)
	Stroke Mortality						
	All Age	1.04 (1.01, 1.07)	0.99 (0.98, 1.00)	1.06 (1.02, 1.10)	0.98 (0.97, 0.99)	1.03 (0.98, 1.08)	1.00 (0.98, 1.01)
	35-64	1.05 (0.99, 1.17)	0.98 (0.96, 1.01)	1.06 (0.99, 1.15)	0.98 (0.95, 1.01)	1.02 (0.91, 1.14)	0.99 (0.99, 1.04)
	65-84	1.09 (1.05, 1.14)	0.97 (0.95, 0.98)	1.08 (1.03, 1.14)	0.96 (0.94, 0.98)	1.11 (1.05, 1.18)	0.98 (0.96, 1.00)
	>=85	1.04 (0.97, 1.12)	1.00 (0.97, 1.03)	1.13 (1.01, 1.25)	0.99 (0.95, 1.03)	0.98 (0.88, 1.08)	1.01 (0.97, 1.05)
One year	**AMI Mortality**						
	All Age	1.24 (1.21, 1.29)	0.84 (0.83, 0.85)	1.25 (1.20, 1.31)	0.85 (0.84, 0.86)	1.25 (1.19, 1.31)	0.84 (0.82, 0.85)
	35-64	1.11 (1.03, 1.19)	0.87 (0.85, 0.89)	1.11 (1.02, 1.21)	0.87 (0.84, 0.90)	1.11 (0.97, 1.28)	0.86 (0.82, 0.90)
	65-84	1.32 (1.26, 1.38)	0.83 (0.82, 0.85)	1.34 (1.26, 1.43)	0.84 (0.82, 0.86)	1.30 (1.22, 1.39)	0.83 (0.81, 0.85)
	>=85	1.43 (1.33, 1.53)	0.81 (0.79, 0.83)	1.47 (1.32, 1.63)	0.80 (0.77, 0.83)	1.39 (1.27, 1.53)	0.82 (0.79, 0.85)
	Stroke Mortality						
	All Age	1.05 (1.02, 1.09)	0.99 (0.98, 1.00)	1.07 (1.02, 1.11)	0.98 (0.96, 0.99)	1.03 (0.98, 1.09)	1.00 (0.98, 1.01)
	35-64	1.06 (0.99, 1.13)	0.98 (0.96, 1.01)	1.08 (0.99, 1.17)	0.98 (0.95, 1.01)	1.02 (0.90, 1.15)	0.99 (0.95, 1.04)
	65-84	1.11 (1.07, 1.16)	0.97 (0.95, 0.98)	1.10 (1.04, 1.07)	0.96 (0.94, 0.98)	1.12 (1.05, 1.20)	0.98 (0.96, 1.00)
	>=85	1.04 (0.96, 1.13)	1.00 (0.98, 1.03)	1.14 (1.01, 1.28)	0.99 (0.95, 1.03)	0.97 (0.87, 1.09)	1.01 (0.97, 1.05)

* Poisson models adjusted for time trend, population, seasonality, temperature, and relative humidity

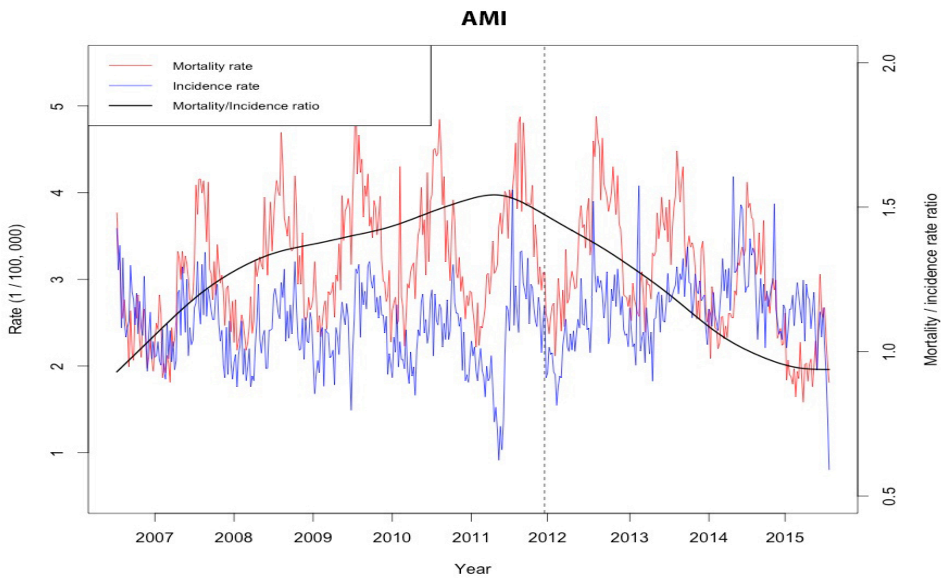
Table S2.6 Multivariate analysis* of overall and age group- and sex-specific post-ban effects on incidence rates, Tianjin, 2007–2015

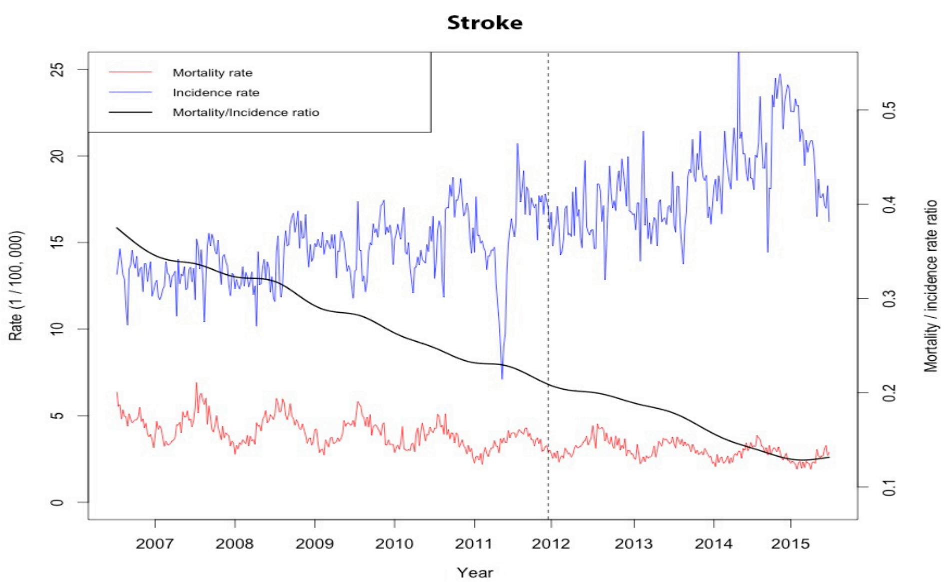
	Overall		Male		Female	
	Immediate Effect	Graduate Effect per Annum	Immediate Effect	Graduate Effect per Annum	Immediate Effect	Graduate Effect per Annum
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
AMI Incidence						
All Age	1.04 (1.01, 1.07)	1.06 (1.05, 1.07)	1.09 (1.05, 1.13)	1.06 (1.04, 1.07)	0.97 (0.93, 1.02)	1.07 (1.05, 1.09)
35-64	0.94 (0.90, 0.98)	1.07 (1.05, 1.09)	1.03 (0.98, 1.09)	1.06 (1.04, 1.09)	0.71 (0.65, 0.78)	1.11 (1.07, 1.16)
65-84	1.14 (1.08, 1.19)	1.04 (1.02, 1.06)	1.16 (1.09, 1.23)	1.03 (1.01, 1.06)	1.11 (1.04, 1.18)	1.04 (1.02, 1.07)
>=85	1.16 (1.03, 1.31)	0.98 (0.94, 0.98)	1.14 (0.96, 1.35)	0.97 (0.91, 1.04)	1.18 (1.01, 1.40)	0.99 (0.93, 1.06)
Stroke Incidence						
All Age	0.98 (0.97, 0.99)	1.05 (1.04, 1.06)	0.99 (0.97, 1.01)	1.05 (1.04, 1.06)	0.97 (0.95, 0.99)	1.05 (1.04, 1.06)
35-64	0.96 (0.95, 0.98)	1.07 (1.06, 1.08)	0.97 (0.95, 0.99)	1.06 (1.05, 1.07)	0.95 (0.92, 0.98)	1.08 (1.07, 1.10)
65-84	1.00 (0.98, 1.02)	1.02 (1.01, 1.03)	1.01 (0.98, 1.03)	1.03 (1.02, 1.04)	0.99 (0.97, 1.02)	1.01 (1.00, 1.02)
>=85	1.06 (1.00, 1.12)	1.00 (0.98, 1.02)	1.15 (1.06, 1.24)	1.04 (1.01, 1.08)	1.09 (1.01, 1.19)	1.03 (0.99, 1.06)

* Poisson models adjusted for time trend, population, seasonality, temperature, and relative humidity.

Figure S2.2 Trend of AMI and stroke mortality/incidence rate ratio in Tianjin, Age≥35

Red line, mortality rate; Blue line, incidence rate; Black solid line, morality/incidence rate ratio (smoothed); dash line, law enforcement date.





Chapter 3. IMPLEMENTATION MATTERS: ASSESSMENT OF QINGDAO'S SMOKE-FREE LEGISLATION ON HOSPITALIZATIONS AND MORTALITY OF CARDIOVASCULAR DISEASES USING INTERRUPTED TIME SERIES DESIGN

Status: submitted on 07/11/2019 (Reference ADD-19-0194.R2)

Abstract

Background and aims: Over 20 cities in China have enacted local smoke-free laws or regulations that prohibit smoking in public places. However, only two of these smoke-free cities have examined the health impact of the law. Enacted in August 2013, Qingdao's smoke free-law was stricter than most other municipal smoke-free laws because it closed the legal loophole allowing designated smoking rooms. Our objective was to estimate the impact of the smoke-free legislation on cardiovascular and cerebrovascular diseases in Qingdao and to explore underlying reasons for the disparity in the magnitude of the effect of city level smoke-free legislations in China. ***Design, setting and participants***: We used an interrupted time series design with adjustment for underlying secular trend, seasonal pattern, meteorology factors to determine the impact of the smoke-free law on acute myocardial infarction (AMI) and stroke events among permanent residents aged 35 years or older in Qingdao, China. Outcome measures were weekly numbers of hospitalizations and deaths, derived from electronic medical records and all cause mortality surveillance system respectively, due to AMI/stroke. The study period was from 1 January 2010 to 31 December 2015, with a post-legislation follow-up of about two and a half years. ***Findings:*** Following the smoke-free legislation, an incremental 20% (95% CI: 14%-26%) decrease per year was observed in AMI admissions. Gradual reductions in AMI admissions were found in both younger and older age groups. A 6% (95% CI: 1%-12%) and 13% (95% CI: 8%-18%) annual decrease in AMI mortality rate and stroke admissions among those aged between 65 and 84 years was observed respectively. ***Conclusions:*** The smoke-free legislation in Qingdao was associated with gradual reductions in fatal and nonfatal AMI and stroke events. Demonstrable but modest effects on stroke admissions and AMI/stroke mortality rate were observed among the older age group after the law had been implemented for about one year. The study indicates the urgent to strengthen the monitoring and enforcement of the current smoke-free legislation in Qingdao.

3.1 INTRODUCTION

Secondhand smoke (SHS) is a serious health hazard that can cause or worsen a wide range of health effects, including cardiovascular and respiratory diseases[1]. The dangers of SHS exposure have prompted large-scale efforts to protect public health through the adoption of smoking bans. An increasing number of countries have enacted partial or comprehensive national smoke-free laws that usually prohibit smoking in indoor workplaces, indoor public places, public transportation and, as appropriate, other public places as required by the World Health Organization Framework Convention on Tobacco Control [2-4]. Comprehensive smoke-free law is in place in at least 62 countries, protecting over 1.6 billion people, or 22% of the population worldwide [4].

China is home to the largest number of smokers in the world. In 2014, over 40% of the world's cigarettes were consumed in China, more than the next top 29 cigarette consuming countries combined[5]. The high smoking prevalence among Chinese men and the absence of the national comprehensive smoke-free law lead to high levels of non-smokers' exposure to SHS in public places, workplaces and homes. While 2.7% of adult women in China smoke, 71.6% of non-smoking women are exposed to SHS in a typical week, which is among the highest in the world [6, 7]. Moreover, 72.9% of youth in China are routinely exposed to SHS at home, public places or public transportation, and 57.2% are exposed inside enclosed public spaces [8].

While China lags behind other countries to revise tobacco control legislations at the national level, local smoke-free laws have become increasingly widespread, particularly in its direct-controlled municipalities and provincial capitals [9]. Qingdao, the largest city (area 11, 067 square km, population about 9 million) in Shandong Province of China, enacted the smoke-free law on 31 Aug 2013 that prohibits smoking in selected public places, including indoor government offices, health facilities, shopping malls, restaurants, hotels, indoor workplaces, arenas, all public transport and wait areas of public transport. The law also bans smoking in indoor and outdoor public areas of kindergartens, primary and middle schools, maternal and child health care facilities, children's hospitals and other designated space for juvenile activities. The smoke-free law does not allow for designated smoking rooms in smoke-free venues and specifies strong deterrent penalties for violations and a clear set of responsibilities for enforcement agencies. The penalty includes a fine of up to 30, 000 CNY for managers or owners for serious, repeated violations, and 200 CNY for individuals.

Since 2008, over 20 cities (megacities of provincial capitals) have enacted local smoke-free laws or regulations that ban smoking in public places. Several of these cities have conducted process evaluations of the smoke-free law, which focused primarily on measuring and assessing the implementation activities and/or associated interim outcomes [9-11]. Nearly all previous national and regional-scale studies in North America and Europe have reported statistically significant reductions, ranging from 5% to 70%, in rates of hospital admissions or mortality due to acute myocardial infarction (AMI) following smoke-free laws[12-19]. Studies have shown evidence of decreases in admissions or mortality of stroke and its sub-types [20-24]. However, only two cities in mainland China, Hong Kong and Tianjin, have investigated the health impact of smoke-free legislation and reported a 12.9% and 16% trend reduction per year post in the crude AMI mortality rate respectively after the implementation of the law [25, 26].

Before Qingdao enacted its smoke-free law, almost all smoke-free policies and laws adopted by other cities in China had been subject to the loophole that allowed designated smoking rooms [9, 27]. Quality of the implementation and enforcement of the smoke-free laws varies across cities, with compliance continuing to be a challenge [27]. The primary aim of this study was to estimate the overall effect size of the smoke-free legislation on the risk of cardiovascular diseases among the general population of Qingdao. We also intended to explore underlying factors influencing the likelihood and magnitude of health impact and therefore to provide implications for further actions in Qingdao and other cities in China that have implemented or are in the process of enacting the smoke-free law.

3.2 METHOD

3.2.1 *Study setting and data*

Impact indicators

Mortality data were obtained from the all-cause mortality surveillance system of Qingdao Center for Disease Control and Prevention for the period from 1 January 2010 to 31 December 2015. Deaths were ascertained through the procedures that have been proposed to use in the Disease Surveillance Points of China. The reporting procedures have been described elsewhere [28]. In brief, practicing clinicians from hospitals filled out deaths certificates for the hospital deaths and reported them to the surveillance system. Trained community clinicians or village doctors investigated the underlying causes of non-hospital deaths through the verbal autopsy approach on a door to door basis. The classification of the cause of death for the study period was based on International Classification of Disease, 10th Revision. The sample was restricted to AMI (I21) and stroke (I60-I64) deaths among Qingdao permanent residents aged≥35 years to reflect a relative closed population at risk for smoking-related mortality.

Data on hospital inpatient admissions were obtained from five tertiary hospitals (three in the urban area, two in the suburban area) that handle the majority of AMI and stroke inpatients in Qingdao. The database is in the form of de-identified individual records that include age, sex, dates of admission and principal diagnosis at discharge. We identified admissions selecting all records with principal discharge diagnosis of AMI (I21) or stroke (I60-I64). Readmission to hospital for the same condition within 28 days was not included in admission calculations, and recurrence after 28 days was considered as a new case. Data on admissions due to the other two diseases not related to smoking or SHS exposure, cholecystitis (K81) and appendicitis (K35-K38) were also extracted as nonequivalent dependent variables to minimize internal validity threats in our design[21, 25, 29, 30]. The sample was restricted to patients aged ≥ 35 years with admission dates between 1 January 2010 and 31 August 2015.

Data related to meteorology, including the average daily temperature and relative humidity (time-varying risk factors for cardiovascular and cerebrovascular disease)[31, 32], were obtained from the local Meteorological Bureau. Single-year population estimates by sex and age were taken from the Bureau of Statistics. As the data were de-identified and results were presented at group level, ethical approval was not required.

Input, policy performance and outcome indicators

Input indicators (smoke-free law and terms, smoke-free law enforcement funding, existence of violation reporting hotline, tobacco control staff), performance indicator (coverage of smoke-free signage in indoor work places and public areas, ashtray, indoor nicotine concentrations, numbers of violation report, number and total amount of fines for violation) and outcome indicators (SHS exposure, defined as noticing someone smoking in the past 30 days in the specific venues, the percentage of indoor workplaces/public areas with no smoking in the past 30 days, awareness of existing indoor smoking ban) of Qingdao and Tianjin were collected through reviewing both published and unpublished data, articles, reports and government's work report and program files.

3.2.2 *Analysis*

Impact evaluation

We adopted segmented negative binomial models (NB2 form) using interrupted time-series design to examine the immediate and gradual health effects of the smoke-free legislation. The responsible variable was the weekly number of events (hospital admissions or deaths) for the selected diseases. An indicator variable was used in the model to define the smoke-free legislation, with a value of zero given to the weeks before the law implementation and a value of one given to the weeks after. An interaction term between the smoke-free legislation and time elapsed since the implementation of the law was included in the regressions to estimate the change of the slope of the secular trend in the post-legislation period, compared with the pre-legislation period. The age group and sex-specific population was included as an offset in the models. Given the initial exploration of long-term trend suggesting the appropriateness of the linear assumption, we used a linear predictor to adjust the long-term time trend, which quantified changes in population risk factors, treatment and other secular trends. We added annual sine and cosine functions in the regressions to capture the seasonal pattern of events. Other time-varying risk factors for cardiovascular and cerebrovascular disease adjusted in the models are the weekly mean temperature and relative humidity[31, 32]. Extreme outliers were identified and were excluded from analysis by visually inspecting the data and the three standard deviations rule (log transformed outcome). For hospital admissions models, data of Jan 2012 (week 104-109) were excluded from the analysis given the overwhelming underreporting because of the maintenance and update of hospital information system. The Cook's distance statistics was used to detect influential observations.

The negative binomial model equation estimating weekly events was expressed as follows:

$$\ln(E(Y)) = \beta_0 + \beta_1 \mathrm{T} + \beta_2 \mathrm{I} + \beta_3 (\mathrm{I} * \mathrm{T}') + \beta_4 \sin(\frac{2T\pi}{52}) + \beta_5 \cos(\frac{2T\pi}{52}) + \beta_k (\mathrm{Tem, Hum}) + offset(P)$$

where Y denotes the response variable (weekly case counts), T and T' is the time (week) since the start of the study and the time since the implementation of the law respectively. β_0 represents the baseline level at T=0, β_1 is the coefficient for the underlying pre-legislation secular trend, β_2 is the coefficient of the indicator variable Intervention (I: indexed 0 for pre-legislation period and 1 for post-legislation period) denoting the step/immediate change following the intervention, β_3 indicates the slope/gradual change following the smoke-free law and β_k denotes t model coefficients for a set of covariates. The estimated immediate relative change (in percentage) in the hospitalization/mortality rate from the pre-legislation to post-legislation periods was quantified as $100(\exp(\beta_2)-1)$. The annual relative change was quantified as $100(\exp(52*\beta_3)-1)$. The number of averted events associated with the smoke-free law was calculated as the regression-based prediction of the account of events subtracted from the predicted number of events in the absence of the law (counterfactual scenario) within the study period.

We compared the negative binomial models to Poisson equivalents using likelihood ratio based Vuong test, which confirmed that negative binomial was more appropriate than Poisson for our data. Newey-West heteroskedasticity and autocorrelation consistent (HAC) standard errors were used to accommodate for serial autocorrelation. Autocorrelation of up to three lags was accommodated within our models, per the results of the PACF and Cumby-Huizinga general test for time series autocorrelation. Given initial analysis suggesting insignificant step changes for some indicators, we compared the saturated models with the reduced models without the step change terms (See Table S3.5) using the Akaike information criterion (AIC) and Bayesian information criterion (BIC) statistics. These provided evidence against the reduced models in favor of the current models.

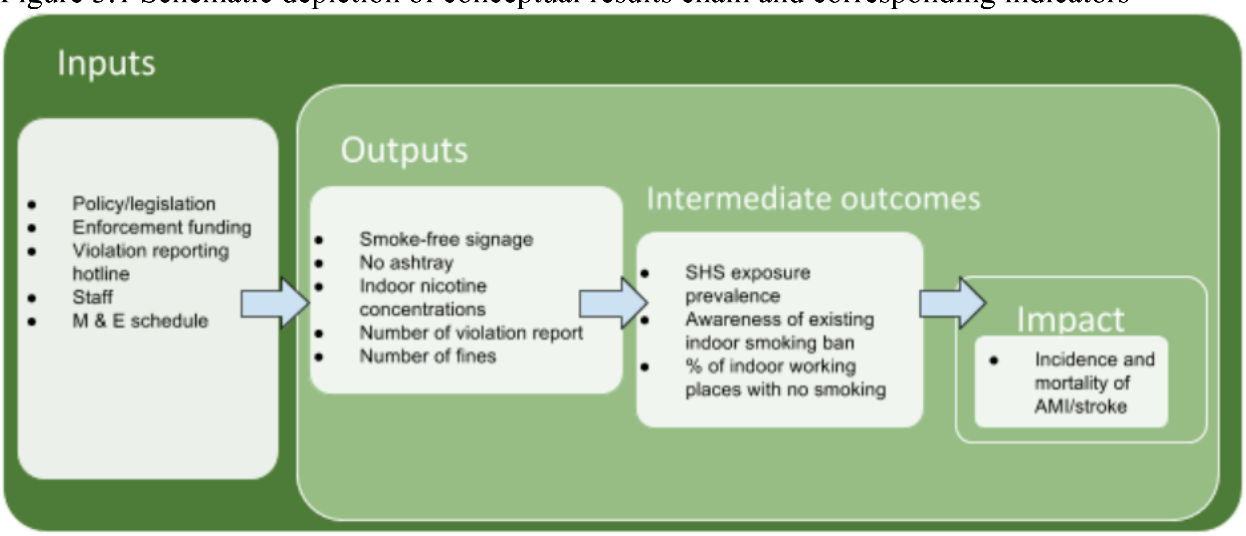
Given the potential issue of residual autocorrelation, our initial a priori analysis plan was to use Seasonal Autoregressive Integrated Moving Average (SARIMA) models. However, the final model we employed was segmented regression model with negative binomial distribution. We did not use ARIMA model for two reasons. First, factors including seasonality that largely explains residual autocorrelation in our data are controlled in segmented regression models. Second, the assumption of normality in ARIMA model is not likely to be valid because the outcome is count data with overdispersion. However, we still used Gaussian seasonal autoregressive integrated moving average (SARIMA $(1,0,1) \times (1,0,1)_{12}$) models fitted to logarithmically transformed case count plus one to examine the robustness of the estimates.

In order to assess the differences in the impact among population subgroups, we stratified the data by sex and age (35~64, 65~84, ≥85) and conducted analysis on each subgroup. To provide further validation that the final models detecting the true effect, we refitted additional models with false law implementation dates at six months or one year pre-legislation. Additional sensitivity analyses were conducted to investigate the robustness of the results against the inclusion of the lagged (by one week) effect of mean temperature and humidity[32, 33] on the outcomes in the models. All analyses were conducted using R version 3.5.3.

Implementation evaluation

We applied the theory of change, a comprehensive diagnostic tool that is used to explain how activities undertaken by an intervention produce a chain of results that contribute to achieving the final intended or observed impacts [34], to map backwards and identify preconditions and contextual factors of success. We first mapped out a framework for the theory of change presented in results chain by reviewing documented activities and objectives, previous evaluations and research on similar health policies, consultations with key stakeholders, including experts, policy makers and implementers. The results chain framework (See Figure 3.1) represents the theory of change in terms of a series of boxes, which start with long-term impact, work backward toward interim outcomes and activities, and then map required resources for the implementation. The framework was then used to guide the collection of qualitative and quantitative data of the indicators, and to explain impact heterogeneity. By measuring and inspecting these indicators, and comparing the degree to which the inputs, activities and outcomes have been accomplished in the two cities, we identified key barriers and facilitators to achieving the success of the smoke-free legislation.

Figure 3.1 Schematic depiction of conceptual results chain and corresponding indicators



3.3 RESULTS

For the five hospitals included in the study, 10, 371, 56,101 and 10,900 inpatients were admitted for AMI, stroke and control conditions respectively from 1 January 2010 to 31 August 31 2015. During the study period, 32, 196 AMI deaths and 49, 711 stroke deaths occurred among Qingdao permanent residents aged ≥ 35 years, which constituted a crude mortality rate of 115 (male 125.2, female 105.1) and 177.5 (male 192.6, female 162.9) deaths per 100, 000 population per year for AMI and stroke respectively. The population at mortality risk was 4.7 million, mean figures from 2010 through 2015 mid-year population estimates. For visual inspection, an overall increase was observed in hospital admissions for AMI, stroke and non-smoking related control conditions (See Figure 3.2). Monthly AMI and stroke mortality showed an overall upward trend and a strong seasonal pattern, with the highest mortality rate occurring in winter.

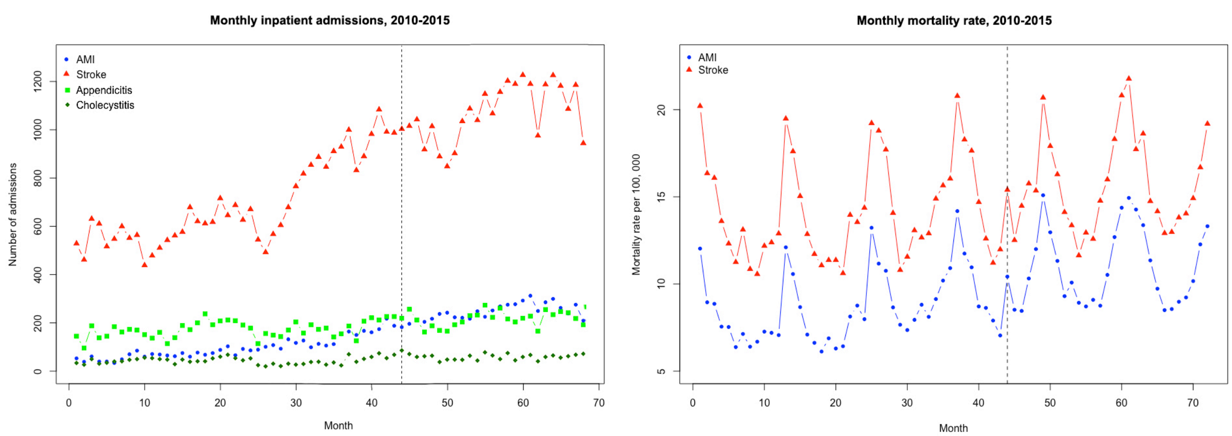


Figure 3.2 Observed monthly inpatient admissions by diagnosis and mortality rate by cause in Qingdao (2010-2015). The dash line refers to the month of smoke-free legislation enforcement. Monthly admissions/mortality rates are displayed rather weekly for a clearer visual representation of trend

Table 3.1 Multivariate analysis† of overall and age group and sex-specific post-ban effects on the hospital admissions rate, Qingdao, Jan 2010- Aug 2015††

	Overall		Male		Female	
	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
AMI admissions						
All Age	1.13 *	0.80 ***	1.05	0.79 ***	1.30	0.81
	(1.02, 1.25)	(0.74, 0.86)	(0.95, 1.18)	(0.73, 0.86)	(1.13, 1.51)	(0.73, 0.88)
35-64	1.01	0.82 ***	1.00	0.80	1.06	0.81 *
	(0.88, 1.16)	(0.73, 0.88)	(0.86, 0.17)	(0.72, 0.89)	(0.83, 1.36)	(0.66, 0.99)
65-84	1.17 *	0.8 ***	1.09	0.79	1.31	0.82 ***
	(1.04, 1.31)	(0.73, 0.88)	(0.93, 1.27)	(0.69, 0.90)	(1.10, 1.55)	(0.73, 0.91)
>=85	1.41*	0.86	1.19	0.93	1.12	1.00
	(1.11, 1.83)	(0.73, 1.01)	(0.90, 1.58)	(0.77, 1.13)	(0.84, 1.50)	(0.82, 1.22)
Stroke admissions						
All Age	0.96	0.92 **	0.97	0.93 *	0.96	0.9 **
	(0.87, 1.07)	(0.87, 0.97)	(0.88, 1.07)	(0.87, 0.99)	(0.84, 1.09)	(0.83, 0.97)
35-64	0.95	0.98	0.97	0.95	0.91	1.02
	(0.85, 0.97)	(0.91, 1.05)	(0.87, 1.08)	(0.88, 1.03)	(0.77, 1.08)	(0.92, 1.13)
65-84	0.98	0.87 ***	0.96	0.90 **	0.99	0.83 ***
	(0.91, 1.05)	(0.82, 0.92)	(0.86, 1.08)	(0.84, 0.97)	(0.86, 1.13)	(0.77, 0.89)
>=85	1.13	0.79 **	1.22	0.84	1.05	0.73 ***
	(0.90, 1.41)	(0.68, 0.91)	(0.93, 1.62)	(0.70, 1.01)	(0.79, 1.40)	(0.62, 0.87)
Non-smoking related diseases (cholecystitis and appendicitis) admissions						
All Age	0.99	1.02	1.02	1.02	0.96	1.02
	(0.89, 1.11)	(0.94, 1.10)	(0.90, 1.17)	(0.92, 1.13)	(0.83, 1.11)	(0.93, 1.13)
35-64	0.96	1.02	0.95	1.05	0.98	1.00
	(0.86, 1.08)	(0.95, 1.11)	(0.82, 1.09)	(0.94, 1.17)	(0.82, 1.16)	(0.90, 1.11)
65-84	1.09	0.97	1.25	0.91	0.95	1.04
	(0.91, 1.30)	(0.84, 1.12)	(0.97, 1.61)	(0.74, 1.12)	(0.77, 1.16)	(0.89, 1.21)
>=85	0.96	1.27	1.24	1.28	0.80	1.27
	(0.60, 1.51)	(0.90, 1.80)	(0.57, 2.72)	(0.75, 2.18)	(0.47, 1.36)	(0.83, 1.95)

† Adjusted for time trend, population, seasonality, temperature and relative humidity.
†† Qingdao's smoke-free law took effect on 31 Aug 31 2013.
*** p<0.001 ** p<0.01 *p<0.05

Overall and age group and sex-specific results of the regression analysis on hospital admissions are reported in Table 3.1. Following the implementation of the smoke-free legislation, a 20% (RR: 0.80; 95% CI: 0.74-0.86) decrease in the trend per year was observed in

AMI admissions, which resulted in a net decrease of 11% (791) within two years after the smoke-free law was implemented. The effect on AMI admissions was observed in both genders and all of the age groups below 85 years. For stroke admissions, a gradual 10% (RR: 0.90; 95% CI: 0.84-0.97) and 17% (RR: 0.83; 95% CI: 0.77-0.89) reduction per year was observed in stroke admissions for males aged 65-84 years and females aged 65-84 years respectively. In contrast to AMI and stroke admissions, no immediate effects (Bayes factor, $BF_{+0} = 0.13$) or annual trend effects ($BF_{+0} < 0.01$) on post-legislation hospital admissions were detected for diseases not related to smoking exposure.

Table 3.2 Multivariate analysis† of overall and age group and sex-specific post-ban effects on mortality rates, Qingdao, Jan 2010- Dec 2015††

	Overall		Male		Female	
	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
AMI mortality						
All Age	1.02 (0.93, 1.12)	0.96 (0.92, 1.01)	1.03 (0.94, 1.13)	0.96 (0.91, 1.01)	1.02 (0.91, 1.14)	0.97 (0.91, 1..03)
35-64	0.97 (0.87, 1.07)	0.95 (0.90, 1.01)	0.93 (0.82, 1.06)	0.96 (0.90, 1.04)	1.08 (0.88, 1.32)	0.91 (0.81, 1.03)
65-84	1.04 (0.94, 1.15)	0.94 * (0.88, 0.99)	1.06 (0.94, 1.19)	0.94 * (0.89, 0.99)	1.01 (0.90, 1.14)	0.94 * (0.88, 0.99)
>=85	1.14 (0.98, 1.33)	0.99 (0.92, 1.08)	1.19 (0.99, 1.42)	0.98 (0.89, 1.08)	1.11 (0.94, 1.31)	1.00 (0.91, 1.10)
Stroke mortality						
All Age	0.98 (0.92, 1.07)	1.01 (0.96, 1.05)	1.00 (0.92, 1.10)	0.98 (0.93, 1.03)	0.96 (0.87, 1.06)	1.04 (0.98, 1.10)
35-64	0.94 (0.83, 1.05)	0.98 (0.92, 1.04)	0.92 (0.81, 1.04)	0.98 (0.91, 1.06)	0.98 (0.84, 1.15)	0.97 (0.89, 1.04)
65-84	1.02 (0.94, 1.10)	0.98 (0.93, 1.02)	1.06 (0.97, 1.15)	0.94 ** (0.90, 0.98)	0.97 (0.88, 1.07)	1.02 (0,97, 1.09)
>=85	1.04 (0.90, 1.20)	1.07 (0.98, 1.16)	1.09 (0.90, 1.31)	1.08 (0.97, 1.22)	1.02 (0.88, 1.18)	1.05 (0.97, 1.14)

† Adjusted for time trend, population, seasonality, temperature and relative humidity.
†† Qingdao's smoke-free law took effect on 31 Aug 2013.
*** p<0.001 ** p<0.01 *p<0.05

The results of the regression analysis on mortality rate are reported in Table 3.2. For AMI, no immediate effects (BF_{+0} = 0.11) in AMI mortality rate were detected among any age group. A gradual 6% (RR: 0.94; 95% CI: 0.84-0.99) decrease in mortality rate each post-legislation year was observed among both men and women aged 65-84 years, resulting in a net post-legislation decrease of about 2% (340) in 28 months. For stroke mortality rate, a gradual 6% decrease each post-legislation year was detected among men aged 65-84 and no immediate effects (BF_{+0} = 0.10) were found.

For illustration, Figure 3.2 displays the predicted pre-legislation trend, the post-legislation trend, and the predicted counterfactual line (represented by the ongoing trend if the law had not been implemented) for those aged ≥ 35 years. The estimated health effect, under the interrupted time series Negative Binomial regression, is visible in the discontinuity of the pre-intervention line and post-intervention line at the beginning of the implementation, and the change of secular trend after the implementation of the law. Given that most of the points for AMI and stroke admissions lie below the counterfactual line, there is a visual suggestion of decreases in the AMI and stroke admissions in the post-legislation period. After the smoke-free legislation, the crude AMI mortality rates were slightly lower than expected, starting approximately one year after implementation of the law. There was no notable net decrease in stroke mortality rate or admissions for the controlled conditions.

Additional sensitivity analyses were conducted to investigate the impact of varying a range of model assumptions. The testing of false law implementation dates showed that gradual effects were generally smaller in magnitude (Table S3.6) compared to actual effects but did not lead to systematic changes in the results reported above. Results remained substantively unchanged with the lagged effect of the mean temperature and relative humidity incorporated in the model.

SARIMA models yielded very close point estimates and standard errors (Table S3.7) that did not alter our inference from the main analysis.

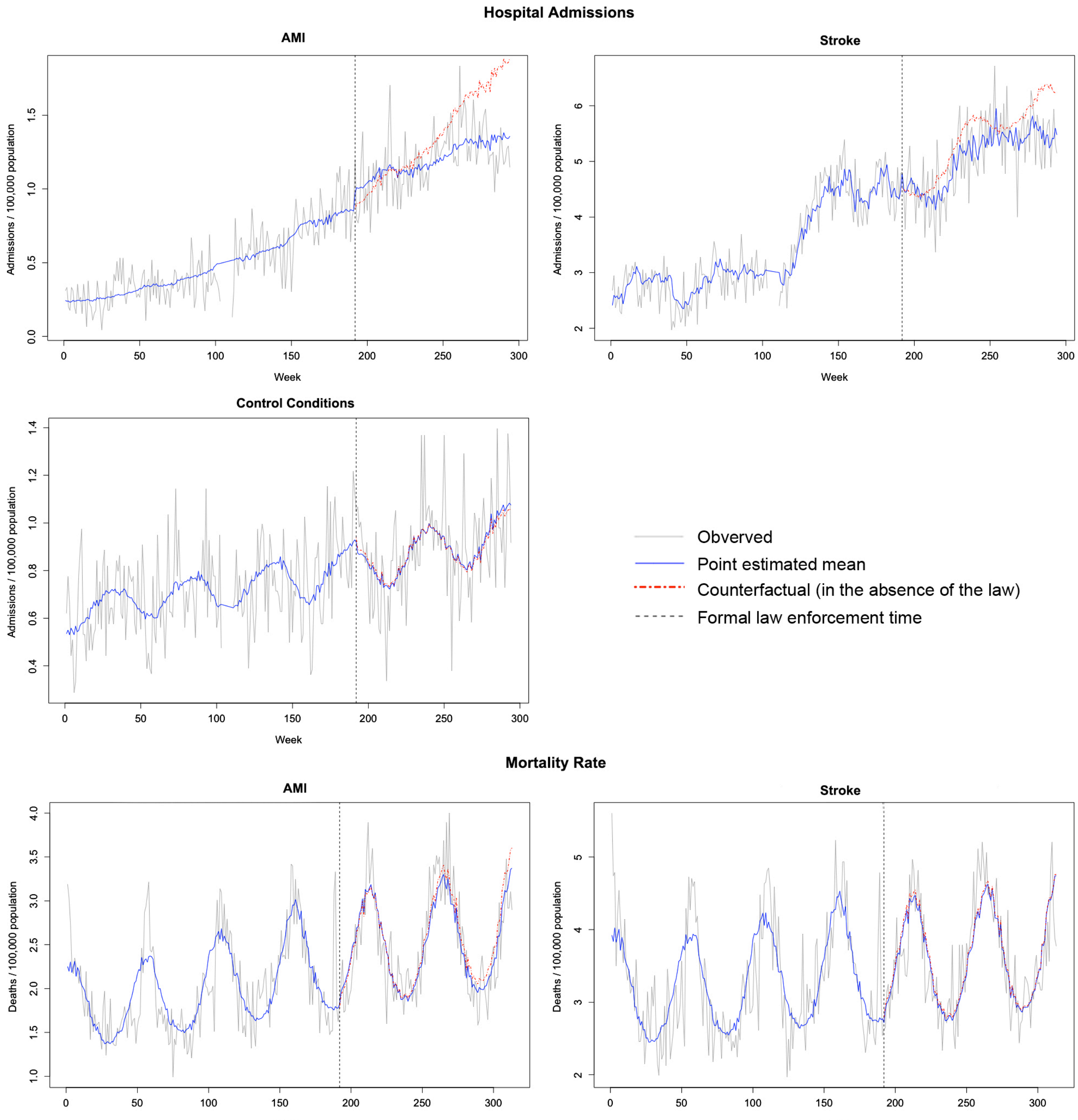


Figure 3.3 Observed and predicted weekly hospital admission/mortality rate trends in Qingdao (2010-2015). Observed (grey lines) and predicted (blue and red lines) hospital admissions/mortality rate. Blue solid line, estimated pre and post- legislation mean; red dash-dotted line, counterfactual trend if the law had not been implemented; dashed line, law enforcement date

Table 3.3 Comparison of the indicators of input and performance between Qingdao and Tianjin

Indicators		Qingdao	Tianjin
Inputs	Legislation	More comprehensive smoke-free legislation; Multi-agency enforcement approach	Partial smoke-free legislation allowing for designated smoking areas; Multi-agency enforcement approach
	Designated enforcement funding	No [1]	Yes, 1.3 million RMB in the first year [1]
	Violation reporting hotline	Yes, multiple hotlines[1]	Yes, single hotline[1]
	Internal M & E scheme	No	Yes [2]
Activities and outputs	Smoke-free signage	50% (95% CI: 45%-56%) in 2014 [3]	39% (95% CI: 29%-50%) in 2012[4], 75% (95% CI: 71%-79%) in 2014 [5]
	No ashtray	No data available	97% (95% CI: 90%-99%) [4]
	Public education campaigns	Yes (83 from 2013 to 2015) [13]	Yes [2]
	Number of violations reported via phone	211 in the first year [1]	117 in the first year, 92 in the second year.[2]
	Number of ticket fines	0 in the first year [1], 3 in 2014-2015[13], 0 in 2018 [12]	67 (2012), 44 (2013), 82 (2014) [2]
	Routine Inspections & Rectification notice	First 2 years: 29, 739[13] 326 rectification notices	First 2 years: 84, 999, including 1, 319 Written notices and 14, 787 verbal notices [2]
Interim Outcomes	Smoking prevalence	No significant change [6]	No significant change [2, 7, 8]
	Active smoking intensity	The highest number of cigarettes per day [9]	Number of cigarettes per day drop [7, 9]
	Awareness of existing law	52% (95% CI: 50%-54%) overall 35% (95% CI: 25%-48%) restaurant 64% (95% CI: 54%-74%) taxi 55% (95% CI: 42%-67%) in university [3, 9]	56% (95% CI: 54%-58%) overall 73% (95% CI: 68%-85%) in taxi 63% (95% CI: 54%-71%) in university [5, 9]
	Indoor nicotine	No significant decrease [10,11]	No data available
	Indoor PM 2.5	No significant decrease [10,11]	25%-73% decrease in smoke-free venue [2]
	SHS exposure prevalence in public areas	75% (95% CI: 73%-77%) overall and 65% (95% CI: 63%-67%) in public areas in 2014 [9]	62% (95% CI: 65%-67%) in 2012 43% (95% CI: 42%-44%) in 2014 15% (95% CI: 14 %-16%) in 2016 [2,9]
	SHS exposure at indoor working places	30% (95% CI: 28%-32%) in 2014 [3]	35% (95% CI: 35%-47%) in 2010 20% (95% CI: 19%-21%) in 2014 [4, 5]

Data sources:

1. Yang, J., *The survey report on enforcement of smoke free law in cities of China*. 2015, Beijing, China: China Democracy and Law Press. 162.
2. Tianjin Commission for Health Improvement, *Annual Report on Tobacco Control in Tianjin*. 2013-2017: Tianjin.
3. Yang, G. and Wang, K., *Assessment of the implementation of the smoke-free law in Qingdao*. 2015, Institute of Basic Medical Sciences Chinese Academy of Medical Sciences: Beijing.
4. Wan, X., et al., *Development of policy performance indicators to assess the implementation of protection from exposure to secondhand smoke in China.* Tob Control, 2013. **22 Suppl 2**: p. ii9-15.
5. Yang, G. and Wang, K., *Assessment of the implementation of the smoke-free law in Tianjin*. 2015, Institute of Basic Medical Sciences Chinese Academy of Medical Sciences: Beijing.
6. Qi, F., et al., *Smoking and passive smoking status and awareness of tobacco hazard among adults in Qingdao.* Chinese Journal of Disease Control and Prevention, 2017. **21**(5).
7. Chen, J., et al., *Tobacco smoking and nitocine dependence among Tianjin city dweller: a population-based cross-sectional study.* Chinese Journal of Public Health, 2013. **29**(7).
8. Xue, X., et al., *Analysis of smoking status and its influencing factors among urban residents in Tianjin*. Chinese Journal of Chronic Disease Prevention and Control, 2016. **24**(6).
9. Liang X(editor), *Report of China City Adult Tobacco Survey 2013–14*. 2015, CDC Foundation: Atlanta, Georgia, USA.
10. Li, S., H. liu, and F. Qi, *Indoor PM2.5 concentration in public places in Qingdao city, 2012.* China Journal of Public Health, 2016. **32**(5).
11. Liu, H., et al., *Monitoring and analysis of indoor environmental tobacco smoke pollution in some public places in Qingdao in 2013*, in *The Fourth Session of the First Annual Conference of the Public Health Management Branch of Chinese Preventive Medicine Association.* 2017, Chinese Preventive Medicine Association: Yanbian, China.
12. "No fine issued in 11 smoke-free cities(无烟城市控烟效果报告发布 11 个无烟城市未开罚单_执法)", August 16, 2019. http://www.sohu.com/a/334137384_99996846.
13. Qingdao CDC, 2015

The comparisons of the indicators between Tianjin and Qingdao are presented in Table 3.3. In terms of the characteristics and strength of the smoke-free legislation, both cities ban smoking in almost all indoor public places, workplaces and public transport, as well as some outdoor areas such as schools and kindergartens, and child and maternal hospital campuses. Deterrent fines are supposed to be given to any person (individual smokers, owners or manager of premises) who violates the no-smoking provisions of the law. Nevertheless, the ban in Qingdao is more comprehensive because designated smoking rooms are not permitted there but are allowed in Tianjin as long as the designated smoking rooms in non-smoking venues are separately ventilated according to the no-smoking provisions of the law. Tianjin had designated funding for law enforcement and internal monitoring and evaluation (M&E) scheme while Qingdao had no enforcement funding or M&E scheme for the enforcement. Tianjin integrated the violation reporting hotlines from each enforcement agency into one memorable line (88908890) that covers the whole city, while Qingdao had multiple complaint hotlines corresponding to different types of venues, administrative divisions and enforcement agents and some of these numbers are not easily memorable.

Qingdao was outperformed by Tianjin in the implementation and enforcement of the smoke-free law, and in achieving most of the expected interim outcomes where we have comparable data on corresponding indicators for both cities. Smoke-free environment signages were seen in a higher proportion of smoke-free areas in Tianjin as compared to Qingdao (75% verse 50%; RR= 1.5; $p<0.05$). Tianjin had more public education campaigns to raise the awareness and knowledge of the smoke-free law and health consequence of SHS, and promote quit attempts than Qingdao. Compared with Tianjin that issued 67, 44 and 82 fines for violations of the smoke-free law in

2012, 2013 and 2014 respectively, Qingdao did not issue any ticket for violation in the first (Sep 1, 2013-Sep 31, 2014) and most recent (2018-2019) law enforcement year.

The smoking prevalence did not drop ($p>0.05$) after the implementation of the law in either Qingdao or Tianjin. However, the average number of cigarettes consumed per day among smokers in Qingdao is the highest among smoke-free cities in China, and has dropped ($p<0.05$) among smokers in Tianjin since the implementation of the smoke free law. In Qingdao, 52% (95% CI: 50%-54%) of the respondents were aware that the government had enacted the smoke-free law, 64% (95% CI: 53%- 74%) and 35% (95% CI: 25%-48%) of the respondents were aware that smoking is prohibited in taxi and restaurants respectively. The prevalence of exposure to SHS and the prevalence of exposure to SHS in public areas during the previous week among respondents in Qingdao was 75% (95% CI: 73%-77%) and 65% (95% CI: 63%-67%) in 2014, about one year since the law had been enacted. The prevalence of exposure to SHS in public areas in Tianjin dropped from 62% (95% CI: 65%-67%) in 2012 to 43% (95% CI: 42% -44%) in 2014 and 15% (95% CI: 14%-16%) in 2016. Indoor nicotine and PM 2.5 concentration of smoke free venues did not significantly decrease ($p>0.05$) in Qingdao. The indoor PM 2.5 concentration in Tianjin decreased by 25% to 73% ($p<0.05$).

3.4 Discussion

In an analysis based on hospital admissions and cause-specific mortality data of a population about 4.7 million over 6 years, we found the smoke-free law was associated with reductions in hospitalizations for AMI and stroke, and mortality due to AMI in the population aged 35 years and above. The decrease of AMI admissions was detected in both sexes, and among both young and old age categories. The decrease in stroke admissions and AMI mortality rate associated with the smoke-free law was only confined to people aged ≥ 65.

No immediate post-legislation effects were seen in admissions or mortality rates. These findings that reductions of AMI or stroke events were seen gradually rather than immediately are compatible with results of similarly-designed studies conducted in New York and Pueblo[35, 36] and recent studies conducted in the other two cities of Mainland China [25, 26]. As the implementation of the smoke-free law in Qingdao had a gradual rollout [37], our findings add to evidence that the progressive enforcement of the smoke-free law is associated with additive health effect.

The decreases in AMI admissions were evident in both young and old groups, while decreases in AMI mortality and decreases in stroke admissions were observed only among those aged $\geq$ 65. Our findings are contrary to those of the US Surgeon General's report which concluded that effective smoke-free laws had an impact on coronary events in younger people only[1]. The report also indicated that evidence for the causal relationship between effective smoke-free law and reduction in stroke events is insufficient. In our analysis, we were able to supplement Surgeon General's analysis with our data discerning between hospital admissions and mortality, or between nonfatal and fatal events. Reductions found in AMI admissions rather than AMI mortality rate among the younger group could be explained in that mortality is a less sensitive indicator than morbidity for the younger group. It could also be potentially explained by the partial enforcement of the law given the dose-response relationship between the comprehensiveness or enforcement strength of the smoke-free law and health benefits[24, 38].

Our findings that the effect was evident in the older age group are consistent with studies conducted in Tianjin and Hong Kong [25, 26]. While these findings are contrary studies conducted in North American and European countries, which indicated that declines in cardiovascular events associated with smoke-free policies were mainly contributed by younger people due to weaker relative risk of smoke-free policies with lower rates of cardiovascular event rate among older people[19, 20, 24]. In urban China, many elderly use public transportations, favor exercise in parks, go to grocery stores, and eat out with family at restaurants. These places tended to have high levels of SHS exposure before the smoke-free law. The relatively higher exposure of the elderly in Qingdao could possibly explain the impact of the law on those aged ≥ 65. Although the decrease among the senior may be triggered by reductions in other preventable risk factors and the improvement in the access to primary health care[39], there has been no evidence that any extensive intervention targeting older people in Qingdao was initiated during the study period.

The reduction in AMI mortality we found was substantially smaller than that in other areas of China[25, 26]. The smaller size in the effect is probably due to several reasons. First, the reduction in AMI risk could be smaller in areas with lower decrease in smoke prevalence and/or the amount of cigarette consumption as the protective effect of smoke-free law can be directly attributed to reducing active smoking[40-42]. Although there has been no statistically significant change in smoking prevalence among adults in either Qingdao[43, 44] or Tianjin[45, 46] since the smoke-free law was introduced, the average number of cigarettes smoked per day among smokers, especially nondaily smokers, in Tianjin has decreased[47]. Whereas the average consumption of cigarettes per day and the proportion of heavy smokers among current daily smokers in Qingdao remained the highest among the 14 cities that had local tobacco control legislations[44].

Second, the decrease in the exposure to SHS exposure level in Qingdao may not be as significant as in other cities that have passed the law. Routine monitoring data showed that the prevalence of SHS exposure among non-smokers in Tianjin dropped from 64.5% in 2010 to

61.5% in 2012 (post-legislation period), 43% in 2014 and 15.3% in 2016. Due to the lack of comparable data, it is uncertain what the magnitude of the decrease in SHS exposure level in Qingdao has been. However, the overall SHS exposure prevalence (defining as being exposed to SHS in the past month), the SHS exposure at public areas and worksites was still as high as 75%, 65% and 30% respectively after the smoke-free law had been implemented for about one year [48]. Compared with the pre-legislation period, the concentrations of indoor particulate matter 2.5 (PM 2.5) and airborne nicotine in many public venues of Qingdao did not drop [49, 50].

The considerably modest effect on AMI and stroke events in Qingdao probably reflects the weak law enforcement. Qingdao closed the loophole in the law that allows for designated smoking rooms in smoke-free places, making its smoke-free law more comprehensive than the laws implemented in other cities at that time [9, 44]. However, there has been very limited designated funding allocated from the municipal government to support the implementation of the law in Qingdao compared to other cities including Tianjin, Shanghai and Beijing [37]. Although the compliance rate was modest and the smoke-free law in Qingdao had specified strong penalties for violations and a clear set of responsibilities for enforcement agencies, no ticket for violation had been issued within the first year of law implementation[37]. This could be due to the fact that there is more than one compliant hotline in Qingdao as the smoke-free law is enforced by multiple agencies, and some of these hotlines are not easily memorable. Besides, Qingdao used existing enforcement staff that are overloaded with various duties and are often not motivated to take additional task of smoke-free enforcement. Moreover, Qingdao's law requires that a penalty can only be issued if the violation is repeated and not corrected, which considerably reduced the deterrent effect of the law [27, 37].

Strengths of this study include using mortality surveillance data that covered a considerably large and relatively closed population and spanned a long period of follow up, which enabled us to offer great statistical power to detect secular trends. In addition, we were able to distinguish the effect on nonfatal events and that on fatal events by using both hospital admissions and mortality. Several limitations of this study should be noted. First, we only extracted admissions from major tertiary hospitals with complete electronic health records, which account for the majority of total admissions in Qingdao but are subject to exogenous factors at hospital level. However, the inclusion of nonequivalent dependent variables would control for potential common shocks and reduce threats to internal validity of the ITS design for our admission data. Second, we were unable to measure the misclassification of causes of death with existing data and resources. While previous studies have shown that estimates of mortality from AMI and stroke are only mildly affected by ill-defined causes of deaths due to the compensatory patterns of misclassification [51], and that the extent of the potential misclassification of causes of death was most likely not associated with smoke-free law, thus may not bias the results. Third, although we controlled for some covariates and adjusted for seasonality, we were unable to control other population-level variables that are associated with the onset of cardiovascular diseases, such as air pollutants, smoking prevalence and population cholesterol levels. Finally, due to the lack of comparable monitoring data, we were not able to test the difference in all the indicators identified between the two cities.

3.5 Conclusion

The results of this study suggest that the smoke-free legislation in Qingdao is associated with gradual reductions in the trend of cardiac and cerebrovascular events. The findings extend the impact of effective smoke-free legislation to those aged 65 years or older. They also indicate a dose-response effect, with stronger laws being associated with bigger effect, which has critical implication for strengthening the monitoring and implementation of current smoke-free laws in Qingdao and other cities of China.

Evidence before this study

- Environmental tobacco smoke exposure increases the risk of premature mortality and the onset of a wide range of diseases among non-smoking children and adults. Smoke-free legislation proves to be an effective way to protect the population from the detrimental effects of SHS and has been adopted by an increasing number of countries. Lines of evidence have shown that smoke-free legislation was associated with the reduction in AMI and stroke events, the two most frequently used indicators measuring the health impact of the smoke-free law. Following the implementation of the smoke-free law in over 20 major cites of China, reductions in SHS exposure and increases in public awareness of the health hazards of passive smoking has been reported, but whether the law had a positive impact on the health of local residents has rarely been investigated.

Added value of this study

- In this quasi-experimental study, we used segmented regression to detect the change in AMI and stroke events associated with the implementation of the smoke-free law among permanent residents aged 35 years or above in Qingdao. The study filled the evaluation gap in Qingdao and paved the way for similar studies assessing the health impact of smoke-free legislation in other cities of China. With repeated cross-sectional data from routine health information system that covered a large and relatively closed population, the results of the study corroborated the health impact of effective implemented smoke-free legislation and extended the evidence of reductions in AMI and stroke risk following smoke-free legislation to women and older people. This study also indicated the dose-response relationship between the enforcement strength of the smoke-free law and health benefits, reinforcing the necessity for strengthening the implementation of the smoke-free law in Qingdao.

Implications of all the available evidence

- This study added further support to existing evidence that smoke-free law is an effective public health intervention to reduce smoking and SHS related morbidity and mortality due to cardiovascular diseases. Whereas previous impact evaluations have shown smoke-free laws at local of national level to be associated with subsequent reductions in AMI mortality rate, the effect we observed on mortality rate was modest. Substantial challenges including insufficient resource investment and accordingly weak enforcement remained and hindered the full effect of the smoke-free law, indicating the urgent need for policy maker and implementers to take additional strategic actions.

REFERENCES

1. U.S. Department of Health and Human Services, *The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General*. 2014, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta (GA).
2. WHO, *WHO report on the global tobacco epidemic, 2015: Raising taxes on tobaccl*. 2015, World Health Organization: Geneva: Switzerland. p. 57-58.
3. WHO, *WHO report on the global tobacco epidemic, 2017: Monitoring tobacco use and prevention policies*. 2017, World Health Organization: Geneva: Switzerland. p. 20.
4. WHO, *WHO report on the global tobacco epidemic, 2019: Offer help to quit tobacco use*. 2019, World Health Organization: Geneva: Switzerland. p. 77.
5. Yang, G., et al., *The road to effective tobacco control in China.* Lancet, 2015. **385**(9972): p. 1019-28.
6. Nan, Y., et al., *The 2015 China Adult Tobacco Survey: exposure to second-hand smoke among adults aged 15 and above and their support to policy on banning smoking in public places.* Zhonghua Liu Xing Bing Xue Za Zhi, 2016. **37**(6).
7. Nazar, G.P., et al., *Socioeconomic Inequalities in Secondhand Smoke Exposure at Home and at Work in 15 Low- and Middle-Income Countries.* Nicotine & Tobacco Research, 2016. **18**(5): p. 1230-1239.
8. WHO, *China Global Youth Tobacco Survey (GYTS): Fact Sheet*. 2014, World Health Organization.
9. World Health Organization Western Pacific Region and University of Waterloo and ITC Project, *Smoke-free Policies in China: Evidence of Effectiveness and Implications for Action*. 2015, World Health Organization Regional Office for the Western Pacific: Manila.
10. Jiang, G., et al., *Comprehensive assessment on the outcome of Tianjin Act of Tobacco Control.* Zhonghua Liu Xing Bing Xue Za Zhi, 2015. **36**(6): p. 561-4.

11. Xiao, L., et al., *Smoking reduced in urban restaurants: the effect of Beijing Smoking Control Regulation.* Tob Control, 2017. **26**(e1): p. e75-e78.

12. Barr, C.D., et al., *Comprehensive smoking bans and acute myocardial infarction among Medicare enrollees in 387 US counties: 1999-2008.* Am J Epidemiol, 2012. **176**(7): p. 642-8.

13. Vander Weg, M.W., G.E. Rosenthal, and M. Vaughan Sarrazin, *Smoking bans linked to lower hospitalizations for heart attacks and lung disease among medicare beneficiaries.* Health Aff (Millwood), 2012. **31**(12): p. 2699-707.

14. Ferrante, D., et al., *Reduction in hospital admissions for acute coronary syndrome after the successful implementation of 100% smoke-free legislation in Argentina: a comparison with partial smoking restrictions.* Tob Control, 2012. **21**(4): p. 402-6.

15. Schoj, V., et al., *The impact of a 100% smoke-free law on the health of hospitality workers from the city of Neuquen, Argentina.* Tob Control, 2010. **19**(2): p. 134-7.

16. Sims, M., et al., *Short term impact of smoke-free legislation in England: retrospective analysis of hospital admissions for myocardial infarction.* BMJ, 2010. **340**: p. c2161.

17. Trachsel, L.D., et al., *Reduced incidence of acute myocardial infarction in the first year after implementation of a public smoking ban in Graubuenden, Switzerland.* Swiss Med Wkly, 2010. **140**(9-10): p. 133-8.

18. Galan, I., et al., *Assessing the effects of the Spanish partial smoking ban on cardiovascular and respiratory diseases: methodological issues.* BMJ Open, 2015. **5**(12): p. e008892.

19. Mayne, S.L., et al., *Longitudinal Associations of Smoke-Free Policies and Incident Cardiovascular Disease: CARDIA Study.* Circulation, 2018.

20. Mackay, D.F., et al., *Impact of Scotland's Comprehensive, Smoke-Free Legislation on Stroke.* PLoS One, 2013. **8**(5).

21. Stallings-Smith, S., et al., *Reductions in cardiovascular, cerebrovascular, and respiratory mortality following the national irish smoking ban: interrupted time-series analysis.* PLoS One, 2013. **8**(4): p. e62063.

22. Herman, P.M. and M.E. Walsh, *Hospital admissions for acute myocardial infarction, angina, stroke, and asthma after implementation of Arizona's comprehensive statewide smoking ban.* Am J Public Health, 2011. **101**(3): p. 491-6.

23. Li, J., et al., *Maternal mortality in Yunnan, China: recent trends and associated factors.* BJOG, 2007. **114**(7): p. 865-74.

24. Tan, C.E. and S.A. Glantz, *Association between smoke-free legislation and hospitalizations for cardiac, cerebrovascular, and respiratory diseases: a meta-analysis.* Circulation, 2012. **126**(18): p. 2177-83.

25. Thach, T.Q., et al., *The smoke-free legislation in Hong Kong: its impact on mortality.* Tob Control, 2015.

26. Xiao, H., et al., *Impact of the smoke-free legislation on the incidence and mortality of AMI and stroke in Tianjin China: analysis of routinely collected data.* Tobacco Induced Diseases, 2018. **16**(1).

27. Gan, Q., *Tobacco control in China*. 2018, Singapore: Springer Singapore. 323.

28. Wan, X., et al., *Mortality trends for ischemic heart disease in China: an analysis of 102 continuous disease surveillance points from 1991 to 2009.* BMC Public Health, 2017. **18**(1): p. 52.

29. Coryn, C.L.S. and K.A. Hobson, *Using nonequivalent dependent variables to reduce internal validity threats in quasi-experiments: Rationale, history, and examples from practice.* New Directions for Evaluation, 2011. **2011**(131): p. 31-39.

30. Wagenaar, B.H., et al., *Using routine health information systems for well-designed health evaluations in low- and middle-income countries.* Health Policy and Planning, 2015. **31**(1): p. 129-135.

31. Dilaveris, P., et al., *Climate Impacts on Myocardial infarction deaths in the Athens TErritory: the CLIMATE study.* Heart, 2006. **92**(12): p. 1747-51.

32. Madrigano, J., et al., *Temperature, myocardial infarction, and mortality: effect modification by individual- and area-level characteristics.* Epidemiology, 2013. **24**(3): p. 439-46.

33. Zeng, Q., et al., *Estimating Temperature-Mortality Exposure-Response Relationships and Optimum Ambient Temperature at the Multi-City Level of China.* International journal of environmental research and public health, 2016. **13**(3): p. 279.

34. Rogers, P., *Methodological Briefs Impact Evaluation No. 2-Theory of Change*. 2014, UNICEF Office of Research: Florence, Italy.

35. Juster, H.R., et al., *Declines in hospital admissions for acute myocardial infarction in New York state after implementation of a comprehensive smoking ban.* Am J Public Health, 2007. **97**(11): p. 2035-9.

36. Bartecchi, C., et al., *Reduction in the incidence of acute myocardial infarction associated with a citywide smoking ordinance.* Circulation, 2006. **114**(14): p. 1490-6.

37. Yang, J., *The survey report on enfcorement of smoke free law in cities of China*. 2015, Beijing, China: China Democracy and Law Press. 162.

38. Vicedo-Cabrera, A.M., et al., *Benefits of smoking bans on preterm and early-term births: a natural experimental design in Switzerland.* Tob Control, 2016. **25**(e2): p. e135-e141.

39. Torpy, J.M., A.E. Burke, and R.M. Glass, *JAMA patient page. Coronary heart disease risk factors.* JAMA, 2009. **302**(21): p. 2388.

40. Lin, H., et al., *The effects of smoke-free legislation on acute myocardial infarction: a systematic review and meta-analysis.* BMC Public Health, 2013. **13**: p. 529.

41. Bajoga, U., et al., *Does the introduction of comprehensive smoke-free legislation lead to a decrease in population smoking prevalence?* Addiction, 2011. **106**(7): p. 1346-1354.

42. Nagelhout, G.E., et al., *The effect of tobacco control policies on smoking prevalence and smoking-attributable deaths. Findings from the Netherlands SimSmoke Tobacco Control Policy Simulation Model.* Addiction, 2012. **107**(2): p. 407-16.

43. Qi, F., et al., *Smoking and passive smoking status and awareness of tobacco hazard among adults in Qingdao.* Chinese Journal of Disease Control and Prevention, 2017. **21**(5).

44. Liang X(editor), *Report of China City Adult Tobacco Survey 2013–14*. 2015, CDC Foundation: Atlanta, Georgia, USA.

45. Chen, J., et al., *Tobacco smoking and nitocine dependence among Tianjin city dweller: a population-based cross-sectional study.* Chinese Journal of Public Health, 2013. **29**(7).

46. Xue, X., et al., *Analysis of smoking status and its influencing factors among urban residents in Tianjin.* Chinese Journal of Chronic Disease Prevention and Control, 2016. **24**(6).

47. Tianjin Commission for Health Improvement, *2012 Annual Report on Tobacco Control in Tianjin*. 2013: Tianjin.

48. Yang, G. and K. Wang, *Assessment of the implementation of the smoke-free law in Qingdao*. 2015, Institute of Basic Medical Sciences Chinese Academy of Medical Sciences: Beijing.

49. Li, S., H. liu, and F. Qi, *Indoor PM2.5 concentration in public places in Qingdao city, 2012.* China Journal of Public Health, 2016. **32**(5).

50. Liu, H., et al., *Monitoring and analysis of indoor environmental tobacco smoke pollution in some public places in Qingdao in 2013*, in *The Fourth Session of the First Annual Conference of the Public Health Management Branch of Chinese Preventive Medicine Association*. 2017, Chinese Preventive Medicine Association: Yanbian, China.

51. Yang, G., et al., *Validation of verbal autopsy procedures for adult deaths in China.* Int J Epidemiol, 2006. **35**(3): p. 741-8.

SUPPLEMENTARY

Table S3.4 Multivariate analysis† of overall and age group and sex-specific post-ban effects on hospital admissions /mortality rates, Qingdao, Jan 2010- Dec 2015††

	Overall		Male		Female	
	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
AMI admissions						
	1.15 **	0.79 ***	1.07	0.78 ***	1.30 ***	0.8 ***
All Age	(1.06, 1.25)	(0.75, 0.83)	(0.97, 1.18)	(0.73, 0.84)	(1.16, 1.54)	(0.73, 0.88)
	1.03	0.79 ***	1.02	0.79 ***	1.11	0.80 *
35-64	(0.92, 1.17)	(0.73, 0.86)	(0.89, 1.17)	(0.72, 0.87)	(0.82, 1.49)	(0.65, 0.99)
	1.19 **	0.81 ***	1.10	0.79 ***	1.29 **	0.81**
65-84	(1.06, 1.33)	(0.75, 0.87)	(0.95, 1.27)	(0.72, 0.88)	(1.08, 1.55)	(0.71, 0.92)
	1383 **	0.80 **	1.13	0.84	1.1	0. 97
>=85	(1.02,1.88)	(0.65, 0.98)	(0.72, 1.79)	(0.60, 1.16)	(0.72, 1.68)	(0.72, 1.28)
Stroke admissions						
	0.95 **	0.94 ***	0.93 **	0.96 **	0.97	0.91 ***
All Age	(0.91, 0.98)	(0.92, 0.96)	(0.89, 0.97)	(0.93, 0.99)	(0.92, 1.02)	(0.87, 0.95)
	0.97	0.98	0.97	0.97	0.98	1.00
35-64	(0.92, 1.03)	(0.94, 1.02)	(0.90, 1.03)	(0.92, 1.01)	(0.89, 1.07)	(0.94, 1.07)
	0.94 **	0.91 ***	0.90 **	0.96	0.98	0.86 ***
65-84	(0.89, 0.98)	(0.88, 0.95)	(0.84, 0.96)	(0.91, 1.01)	(0.91, 1.06)	(0.82, 0.91)
	0.86 **	0.88 ***	0.92	0.95	0.81 **	0.82 **
>=85	(0.76, 0.98)	(0.80, 0.96)	(0.76, 1.11)	(0.83, 1.08)	(0.67, 0.97)	(0.72, 0.93)
Non-smoking related diseases (cholecystitis and appendiictis) admissions						
	0.99	1.02	1.02	1.01	0.96	1.02
All Age	(0.92, 1.08)	(0.96, 1.08)	(0.91, 1.15)	(0.93, 1.10)	(0.86, 1.08)	(0.94, 1.11)
	0.97	1.02	0.95	1.04	0.99	0.99
35-64	(0.88, 1.07)	(0.95, 1.09)	(0.83, 1.09)	(0.95, 1.15)	(0.86, 1.14)	(0.90, 1.09)
	1.08	0.99	1.25	0.92	0.95	1.05
65-84	(0.92, 1.27)	(0.88, 1.10)	(0.99, 1.56)	(0.78, 1.07)	(0.76, 1.18)	(0.90, 1.23)
	0.87	1.27 *	1.08	1.27	0.74	1.27
>=85	(0.58, 1.30)	(0.96, 1.69)	(0.56, 2.04)	(0.81, 1.99)	(0.44, 1.24)	(0.88, 1.83)
AMI mortality						

	1.02	0.96 **	1.02	0.96 **	1.02	0.97 *
All Age	(0.98, 1.07)	(0.94, 0.99)	(0.96, 1.09)	(0.92, 0.99)	(0.96, 1.09)	(0.93, 1.01)
	0.97	0.95	0.93	0.96	1.08	0.91
35-64	(0.87,1.08)	(0.89, 1.02)	(0.82, 1.06)	(0.89, 1.04)	(0.86, 1.33)	(0.80, 1.04)
	1.04	0.94 **	1.06	0.94	1.01	0.94 **
65-84	(0.97, 1.11)	(0.90, 0.98)	(0.97, 1.15)	(0.89, 0.99)	(0.92, 1.11)	(0.88, 0.99)
	1.14 ***	0.99	1.19 **	0.98	1.11 **	0.99
>=85	(1.06, 1.24)	(0.94, 1.04)	(1.05, 1.35)	(0.91, 1.06)	(1.01, 1.24)	(0.94, 1.06)
Stroke mortality						
	0.98	1.01	1.01	0.98	0.96	1.04 **
All Age	(0.95, 1.02)	(0.98, 1.03)	(0.96, 1.06)	(0.95, 1.01)	(0.91, 1.01)	(1.01, 1.07)
	0.94	0.98	0.92	0.98	0.98	0.97
35-64	(0.85, 1.03)	(0.92, 1.03)	(0.82, 1.02)	(0.91, 1.05)	(0.84, 1.15)	(0.87, 1.07)
	1.02	0.98	1.06 *	0.94 **	0.97	1.03
65-84	(0.97, 1.07)	(0.95, 1.01)	(0.99, 1.13)	(0.90, 0.98)	(0.90, 1.04)	(0.98, 1.08)
	1.05	1.06 **	1.1 *	1.08 **	1.02	1.05 *
>=85	(0.98, 1.13)	(1.02, 1.11)	(0.99, 1.23)	(1.01, 1.15)	(0.93, 1.11)	(0.99, 1.11)

† Poisson models adjusted for time trend, population, seasonality, temperature and relative humidity.
† †Qingdao's smoke-free law took effect on 31 Aug 2013.
*** p<0.001 ** p<0.01 *p<0.05

Table S3.5 Multivariate analysis† of overall and age group and sex-Specific post-legislation effects on hospital admissions and mortality rate, Qingdao, 2010-2015

		Gradual effect per annum on hospital admissions rate, RR (95% CI)			Gradual effect per annum on mortality rate, RR (95% CI)		
		Overall	Male	Female	Overall	Male	Female
AMI							
	All Age	0.82 *** (0.76, 0.88)	0.8 *** (0.74, 0.87)	0.84 *** (0.76, 0.93)	0.97 (0.92, 1.02)	0.96 (0.91, 1.02)	0.97 (0.91, 1.04)
	35-64	0.8 *** (0.73, 0.89)	0.8 *** (0.82, 0.89)	0.83 (0.67, 1.01)	0.95 (0.89, 1.01)	0.95 (0.88, 1.03)	0.93 (0.82, 1.04)
	65-84	0.83 *** (0.76, 0.91)	0.81 *** (0.71, 0.92)	0.85 (0.76, 0.96)	0.94 * (0.89, 0.99)	0.95 (0.89, 1.02)	0.94 * (0.87, 1.01)
	>=85	0.73 * (0.57, 0.93)	0.94 (0.78, 1.13)	1.02 (0.88, 1.23)	1.02 (0.93, 1.12)	1.01 (0.90, 1.13)	1.02 (0.92, 1.13)
Stroke							
	All Age	0.91 *** (0.86, 0.95)	0.92 ** (0.87, 0.97)	0.88 *** (0.83, 0.95)	1.00 (0.95, 1.05)	0.98 (0.93, 1.03)	1.03 (0.98, 1.09)
	35-64	0.96 (0.90, 1.02)	0.94 (0.88, 0.99)	0.99 (0,90, 1.08)	0.96 (0.90, 1.03)	0.96 (0.89, 1.04)	0.96 (0.88, 1.06)
	65-84	0.86 *** (0.82, 0.91)	0.89 *** (0.84, 0.95)	0.82 *** (0.77, 0.88)	0.98 (0.93, 1.03)	0.95 ** (0.90, 0.99)	1.02 (0.96, 1.08)
	>=85	0.83 ** (0.73, 0.93)	0.91 (0.78, 1.06)	0.75 *** (0.66, 0.86)	1.08 (1.00, 1.17)	1.10 (0.98, 1.24)	1.06 (0.98, 1.14)
Non-smoking related diseases (cholecystitis and appendicitis)							
	All Age	1.01 (0.95, 1.10)	1.03 (0.94, 1.12)	1.01 (0.93, 1.10)			
	35-64	1.01 (0.94, 1.10)	1.03 (0.93, 1.13)	0.99 (0.89, 1.10)			
	65-84	1.00 (0.88, 1.13)	0.98 (0.81, 1.18)	1.02 (0.90, 1.16)			
	>=85	1.26 (0.91, 1.73)	1.37 (0.81, 2.32)	1.19 (0.93, 1.54)			

† The reduced models (negative binomial models) do not include the step change terms and are adjusted for time trend, population, seasonality, temperature and relative humidity.
*** p<0.001 ** p<0.01 *p<0.05

Table S3.6 Estimates of the effect from sensitivity analysis.

	Sensitivity analysis 1 †		Sensitivity analysis 2 ††		Sensitivity analysis 3 †††	
	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
AMI admissions						
All Age	1.13 (1.02, 1.25)	0.80 *** (0.74, 0.86)	1.23 *** (1.11, 1.37)	0.86 *** (0.80, 0.92)	1.13 (0.98, 1.32)	0.91 * (0.83, 0.99)
35-64	1.02 (0.88, 1.17)	0.80 *** (0.72, 0.89)	1.15 (1.00, 1.33)	0.83 *** (0.76, 0.92)	1.10 (0.92, 1.31)	0.86 ** (0.77, 0.96)
65-84	1.15 (1.02, 1.30)	0.80 *** 0.73, 0.88)	1.27 *** (1.12, 1.43)	0.88 ** (0.81, 0.95)	1.15 (0.96, 1.38)	0.93 (0.83, 1.03)
>=85	1.42 *** (1.10, 1.83)	0.80 *** (0.68, 0.95)	1.48 * (1.07, 2.04)	0.95 (0.80, 1.14)	1.65 ** (1.18, 2.32)	1.16 (0.96, 1.41)
Stroke admissions						
All Age	0.98 (0.89, 1.10)	0.91 ** (0.86, 0.97)	1.03 (0.96, 1.12)	0.92 ** (0.88, 0.96)	1.21 *** (1.12, 1.30)	0.95 (0.90, 1.00)
35-64	0.95 (0.85, 1.06)	0.97 (0.91, 1.05)	1.01 (0.93, 1.10)	0.96 (0.90, 1.01)	1.18 *** (1.10, 1.27)	0.99 (0.93, 1.04)
65-84	1.00 (0.90, 1.12)	0.86 *** (0.81, 0.92)	1.05 (0.97, 1.14)	0.87 *** (0.84, 0.92)	1.2 *** (1.13, 1.33)	0.92 (0.87, 0.97)
>=85	1.21 (0.97, 1.51)	0.77 *** (0.67, 0.89)	1.19 (0.99, 1.42)	0.85 ** (0.77, 0.95)	1.43 (1.17, 1.76)	0.96 (0.84, 1.10)
Non-smoking related diseases (cholecystitis and appendicitis) admissions						
All Age	0.98 (0.87, 1.09)	1.02 (0.95, 1.11)	1.05 (0.94, 1.17)	1.01 (0.95, 1.08)	0.99 (0.89, 1.10)	1.02 (0.95, 1.10)
35-64	0.95 (0.84, 1.07)	1.02 (0.94, 1.11)	0.99 (0.88, 1.12)	1.00 (0.93, 1.08)	0.93 (0.82, 1.06)	0.99 (0.92, 1.08)
65-84	1.07 (0.89, 1.29)	0.97 (0.84, 1.11)	1.20 * (1.02, 1.41)	1.01 (0.91, 1.12)	1.19 (1.01, 1.40)	1.07 (0.97, 1.18)
>=85	0.92 (0.58, 1.46)	1.28 (0.91, 1.81)	1.28 (0.92, 1.78)	1.14 (0.93, 1.41)	1.05 (0.68, 1.61)	1.31 (1.00, 1.71)
AMI mortality						
All Age	1.04 (0.95, 1.14)	0.96 (0.91, 1.01)	1.03 (0.94, 1.12)	0.98 (0.93, 1.03)	1.06 (0.97, 1.16)	0.99 (0.94, 1.05)
35-64	0.98 (0.89, 1.08)	0.95 (0.90, 1.01)	1.03 (0.92, 1.16)	0.95 (0.89, 1.01)	1.17 ** (1.04, 1.32)	0.99 (0.93, 1.07)
65-84	1.04 (0.95, 1.16)	0.94 * (0.88, 0.99)	1.03 (0.93, 1.13)	0.95 (0.90, 1.01)	1.04 (0.94, 1.16)	0.96 (0.90, 1.03)
>=85	1.18 * (1.02, 1.37)	0.99 (0.92, 1.07)	1.20 * (1.04, 1.39)	1.04 (0.96, 1.13)	1.21 ** (1.06, 1.38)	1.12 ** (1.03, 1.21)
Stroke mortality						
All Age	0.99 (0.92, 1.08)	1.00 (0.96, 1.05)	1.02 (0.93, 1.11)	1.00 (0.96, 1.05)	1.05 (0.97, 1.15)	1.02 (0.97, 1.07)
35-64	0.94 (0.83, 1.05)	0.98 (0.91, 1.04)	1.06 (0.93, 1.20)	0.96 (0.90, 1.02)	1.21 ** (1.06, 1.37)	1.00 (0.94, 1.07)
65-84	1.03 (0.95, 1.11)	0.97 (0.93, 1.02)	1.08 (1.00, 1.18)	0.99 (0.94, 1.03)	1.11 * (1.02, 1.21)	1.02 (0.97, 1.07)
>=85	1.07 (0.94, 1.21)	1.06 (0.99, 1.14)	1.05 (0.92, 1.19)	1.08 (1.00, 1.16)	1.01 (0.89, 1.15)	1.10 (1.00, 1.19)

† Models with lagged effect of meteorological factor
†† Models with false law implementation dates at six months pre-legislation
††† Models with false law implementation dates at one year pre-legislation
*** $p<0.001$ ** $p<0.01$ *$p<0.05$

Table S3.7 Estimates of the effect from ARIMA (1,0,1) × (1,0,1) $_{12}$ models†

	Overall		Male		Female	
	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum	Immediate effect	Graduate effect per annum
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
AMI admissions						
	1.16 *	0.81 ***	1.10	0.81 **	1.35 **	0.84 *
All Age	(1.01, 1.34)	(0.73, 0.90)	(0.92, 1.30)	(0.71, 0.92)	(1.10, 1.68)	(0.71, 0.98)
	1.03	0.83 **	1.04	0.82 *	1.15	0.89
35-64	(0.86, 1.23)	(0.72, 0.95)	(0.85, 1.23)	(0.70, 0.95)	(0.90, 1.47)	(0.75, 1.06)
	1.20 *	0.87	1.22	0.81 *	1.38 ***	0.90 **
65-84	(1.00, 1.44)	(0.71, 1.01)	(0.98, 1.52)	(0.68, 0.97)	(1.26, 1.51)	(0.84, 0.96)
	1.59 **	0.81 *	1.38 **	0.9	1.27	0.92
>=85	(1.21, 2.09)	(0.68, 0.98)	(1.12, 1.75)	(0.77, 1.05)	(0.99, 1.64)	(0.78, 1.09)
Stroke admissions						
	1.02	0.93	1.00	0.96	1.05	0.88
All Age	(0.90, 1.18)	(0.78, 1.11)	(0.87, 1.15)	(0.83, 1.12)	(0.85, 1.29)	(0.73, 1.06)
	1.01	0.97	1.02	0.93	1.04	0.99
35-64	(0.86, 1.20)	(0.85, 1.10)	(0.88, 1.18)	(0.84, 1.03)	(0.80, 1.37)	(0.81, 1.21)
	1.02	0.86	0.98	0.92	1.02	0.82 *
65-84	(0.84, 1.26)	(0.74, 1.00)	(0.83, 1.17)	(0.79, 1.06)	(0.83, 1.26)	(0.69, 0.96)
	1.11	0.84	1.02	0.93	1.07	0.78*
>=85	(0.79, 1.55)	(0.68, 1.00)	(0.73, 1.37)	(0.78, 1.12)	(0.78, 1.46)	(0.64, 0.94)
Non-smoking related diseases (cholecystitis and appendiictis) admissions						
	0.98	1.02	1.01	1.02	0.94	1.04
All Age	(0.86, 1.11)	(0.93, 1.12)	(0.87, 1.17)	(0.91, 1.13)	(0.80, 1.11)	(0.92, 1.18)
	0.95	1.03	0.93	1.05	0.98	1.03
35-64	(0.82, 1.09)	(0.93, 1.15)	(0.79, 1.11)	(0.93, 1.20)	(0.80, 1.20)	(0.89, 1.18)
	1.04	1.02	1.17	0.97	0.91	1.10
65-84	(0.87, 1.25)	(0.88, 1.18)	(0.89, 1.54)	(0.78, 1.21)	(0.77, 1.08)	(0.95, 1.26)
	0.75	1.19	0.94	1.12	0.78	1.14
>=85	(0.56, 1.01)	(0.98, 1.45)	(0.73, 1.21)	(0.94, 1.33)	(0.58, 1.02)	(0.95, 1.38)
AMI mortality						
	1.01	0.97	1.03	0.96	1.01	0.98
All Age	(0.89, 1.15)	(0.89, 1.05)	(0.92, 1.16)	(0.89, 1.04)	(0.90, 1.15)	(0.91, 1.06)
	1.04	0.93	0.98	0.95	1.22	0.90
35-64	(0.91, 1.17)	(0.86, 1.01)	(0.85, 1.13)	(0.86, 1.04)	(0.98, 1.54)	(0.78, 1.03)
	1.04	0.93	1.09	0.91	1.01	0.95
65-84	(0.93, 1.17)	(0.85, 1.01)	(0.94, 1.27)	(0.82, 1.01)	(0.90, 1.13)	(0.87, 1.03)
>=85	1.08	0.99	1.10	0.97	1.06	1.03

	(0.95, 1.22)	(0.92, 1.07)	(0.95, 1.29)	(0.88, 1.06)	(0.86, 1.30)	(0.91, 1.17)
Stroke mortality						
	0.96	1.00	0.99	0.99	0.96	1.03
All Age	(0.85, 1.10)	(0.93, 1.09)	(0.89, 1.10)	(0.92, 1.06)	(0.85, 1.08)	(0.95, 1.12)
	0.96	0.99	0.91	0.99	1.04	0.98
35-64	(0.83, 1.11)	(0.90, 1.08)	(0.78, 1.06)	(0.90, 1.09)	(0.86, 1.26)	(0.88, 1.10)
	1.00	0.96	1.04	0.93	0.97	1.03
65-84	(0.89, 1.13)	(0.89, 1.05)	(0.92, 1.18)	(0.86, 1.02)	(0.88, 106)	(0.96, 1.11)
	1.03	1.07	1.03	1.08	1.06	1.07
>=85	(0.91, 1.17)	(0.99, 1.16)	(0.89, 1.20)	(0.99, 1.20)	(0.88, 1.27)	(0.95, 1.21)

† Adjusted for time trend, population, seasonality, temperature and relative humidity. Weekly case counts were logarithmically transformed after adding one.
*** p<0.001 ** p<0.01 *p<0.05

Chapter 4. ASSESSING THE COMPLETENESS OF INCIDENT AMI AND STROKE REPORTING IN TIANJIN, CHINA.

Abstract

Objectives: The objectives of this study were to assess the completeness of case ascertainment for the surveillance of myocardial infarction (AMI) and stroke incident cases and to estimate the incidence of AMI and stroke in Tianjin, China. **Methods:** We applied the DisMod II software program to model the incidence of AMI and stroke from other epidemiological indicators. Inputs for DisMoD II include mortality rates from Tianjin's all-cause mortality surveillance system, the point prevalence, remission rate and relative risk for AMI and stroke taken from IHME's Global and Local Burden of Disease (LBD) studies, and We assessed the completeness of AMI and stroke incidence reporting by comparing the sex and age-specific incidence rates derived from the incidence surveillance system in 2007, 2010 and 2015 with the modeled incidence rates. 95% confidence intervals were derived around reported incidence rates and DisMod II estimates based on sampling variance. **Results**: The age and sex standardized modeled incidence rate (1/100, 000 person year) decreased ($p<0.05$) from 138 (95% CI: 125-145) in 2007 to 119 (95% CI: 113-125) in 2015 for AMI, and increased ($p<0.05$) from 520 (95% CI: 450-582) in 2007 to 534 (95% CI: 534-618) in 2015 for stroke. The overall completeness of incidence report was 36% (95% CI: 35%-38%) for AMI and 54% (95% CI: 53%-55%) for stroke. The completeness was higher in men than in women for both AMI (42% vs 30%, $p<0.05$) and stroke (55% vs 53%, $p<0.05$), and was higher in residents aged 30-59 than those aged 60 or older for AMI (57% vs 38%, $p<0.05$). The completeness of reporting increased by 7.2 (95% CI: 4.6-9.7) and 15.7 (95% CI: 14.4-16.9) percentage points for AMI and stroke respectively from 2007 to 2015 among those aged 30 or above. The increases were observed in both men and women ($p<0.05$), were more profound ($p<0.05$) among those aged between 30-59 (AMI 12.6, 95% CI: 6.7-18.6; Stroke 25.9, 95% CI: 23.8-28.2) and occurred primarily during the 2010 and 2015 period. **Conclusions**: Completeness of AMI and stroke incidence surveillance was low in Tianjin but has improved in recent years primarily owing to the incorporation of automatic reporting component into the information systems of health facilities, the increase in the utilization of healthcare service and campaigns promoting access to prevention services and timely emergency treatment for AMI and stroke.

4.1 INTRODUCTION

Reliable and representative population-level disease incidence is crucial for the prioritization of health service planning and policy making, and an important indicator for assessing the effectiveness of preventive measures and management of risk factors. Furthermore, incidence estimates are essential inputs for the calculation of the Disability-Adjusted Life Year (DALY), a metric increasingly relied on for the evaluation of burden of diseases [1]. Estimates of epidemiological data come from different sources: mortality typically from civil registration and vital statistics; incidence from disease registry or population-level cohort studies [2]. For many diseases, incidence is often more difficult to measure than mortality, resulting in severer incompleteness and significant internal inconsistency [3]. Lack of consistency in epidemiology estimates, an indicator for potential measurement error, exists even within a well-defined population [2].

AMI and stroke have become the major causes of hospitalization and the leading causes of premature mortality [4, 5] in China. Given the increasing burden of AMI and stroke, it is essential to monitor the incidence in China. However, empirical data on the incidence of the two diseases at either national or sub-national level is limited. Major sources of the incidence of cardiovascular and cerebrovascular diseases in China include Sino-Monica project (1987-1993), the PRC-USA Collaborative Study (1981-2000), the China Multicenter Collaborative Study of Cardiovascular Epidemiology Cohort (participants enrolled between 1991-1995 and followed up for 11 years) and Chinese Multi-provincial Cohort Study (1992-2002) [6-9]. These data sources have not yielded sufficient and long-term continuous AMI incidence information. Although the China Acute Myocardial Infarction (CAMI) Registry launched in 2013 included over 100 hospitals from all provinces and municipalities throughout Mainland China except Hong Kong and Macau. The registry, which obtains clinical characteristics, risk factors, diagnosis, treatment and outcomes of Chinese AMI patients, does not provide AMI incidence estimates at the population level [4].

Tianjin, the third largest city (area 11, 860 square km, population 15.6 million) in China, has been routinely collecting incidence data of major non-communicable diseases (NCDs) including AMI and stroke through the Incidence Surveillance System established in 1984. In 2007, Tianjin started to incorporate the NCDs Incidence Surveillance component into the Hospital Information System (HIS) of some pilot hospitals, reporting new cases directly via HIS rather than exclusively relying on the conventional manually reporting cards. The reported incidence has been utilized in several burden of disease studies, whereas the quality of the data on the dimensions of completeness of incident case ascertainment and consistency with external datasets or other epidemiological indicators has not be investigated [10-12].

Originally developed for the Global Burden of Disease studies, DisMod II has been extensively used to supplement observational data and assess internal consistency [2]. DisMod II is a multistate life table that describes the transitions between the disease states “health”, “diseased” and “dead” by using the transition rates incidence, remission and case fatality (Figure S 4.4) [13]. By solving a set of linear differential equations, DisMod II can estimate age-specific incidence, prevalence of a disease given sufficient data on other disease variables. Compared with the original DidMod, an IPM (Incidence–Prevalence–Mortality) model that requires three transition hazards incidence, remission and case fatality as inputs, DisMod II allows for a wider range of input variables including incidence as a population rate, prevalence, duration, and mortality. In comparison with the capture-recapture analysis, an alternative method that has been advocated in estimating the completeness of a dataset, the application of DisMod II in estimating the incidence of a disease does not require multiple independent incidence data sources as prerequisites.

In this study, we intended to estimate the model (DisMod II) based incidence rates of AMI and stroke, examine the completeness and consistency of the reported AMI and stroke incidence rate by comparing the observed rates with predicted ones, and assess if the completeness of the reported data has been improved since the introduction of the direct reporting through HIS.

4.2 METHODS

4.2.1 *Data*

<u>*Incidence rate*</u>

Incidence cases were extracted from the Incidence Surveillance System of Tianjin CDC, which was initially launched in 1984 for a community-based program on the prevention and control of four major NCDs (malignant tumor, heart disease, stroke and hypertension) and was extended to include another four conditions (injury, diabetes, mental illness and cirrhosis) in 2005 [12]. The study subjects are residential registered cases who have experienced AMI or stroke, diagnosed by a hospital or clinic in 2007, 2010 or 2015. Cases were included in the dataset if they met all the following inclusion criteria:

1. Strike detected and diagnosed by a medical practitioner within 28 days of onset;

2. AMI/stroke onset within the study period. Recurrence within 28 days was not included in incidence calculations, and recurrence after 28 days was considered as a new case;

3. Registered permanent (with Hukou) resident of Tianjin at the time of AMI/stroke onset

The recording process and quality control of the data have been described elsewhere [12]. New case reporting cards were required to be completed or entered into the Non-Communicable

Disease Incidence Surveillance System by clinicians in the hospitals or community clinics in Tianjin. The records include gender, date of birth, the diagnosis and diagnostic basis, date of events, job, insurance status, smoking status, district of residence. In 2007, Tianjin CDC incorporated the NCDs incidence surveillance component into the Hospital Information System (HIS) of some pilot hospitals. By 2015, over 70% of the new cases from the chronic non-communicable incidence surveillance system were reported directly via HIS[14]. New cases in the surveillance system, either reported by cards or via HIS, were verified through various methods including regular training for doctors, checking daily report for recurrence, logical errors and codes on a case-by-case basis at three levels (hospital, district/county CDC and Tianjin CDC).

Incidence classification was coded in accordance with the International Classification of Disease, 10th Revision (ICD-10). The diseases used as incidence outcome measures in this study are AMI (ICD-10, I21) and stroke (ICD-10, I60-I64). Definitions included patients with symptoms, and imaging, laboratory and clinical examinations. Hemorrhagic stroke was defined as a stroke event with the diagnosis of subarachnoid hemorrhage or intracerebral hemorrhage, and ischemic stroke was defined as a stroke event with the diagnosis of thrombosis or embolism (hemorrhagic stroke ICD-10: I60, I61, I62; ischemic stroke: I63).

Cause-specific mortality rate

The age- and sex specific mortality rate of AMI and stroke for the year 2007, 2010 and 2015 were obtained from the all-cause mortality surveillance system, which monitors the entire residential population of the city. Deaths were ascertained through the procedures that have been proposed to use in the Disease Surveillance Points (DSP) in China. The recording process and quality control of the data have been described elsewhere [15, 16]. In brief, practicing clinicians from hospitals or community clinical centers filled out deaths certificates and reported them to the mortality surveillance system. Trained community clinicians investigated the underlying causes of non-hospital deaths through interviewing the deceased's relatives and reviewing available medical records 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[16]. Cause of death classification for the study period was based on ICD-10.

Prevalence, remission rate and relative risk

Data on the prevalence, remission rate and relative risk of AMI and stroke in Tianjin were taken from the Global Burden of Disease (GBD) and Local Burden of Disease (LBD) studies conducted by the Institute for Health Metric and Evaluation (IHME). These epidemiological estimates were modeled using the DisMod-MR 2.0, a Bayesian mixed-effects meta-regression modeling developed for IHME's GBD/LBD studies. The estimates are initially made at the global level then sequentially revised down to the national and subnational levels using progressively more detailed data.

The prevalence, expressed as a proportion, is the number of cases in a population at a moment in time. The remission rate is the number of cases that resolve or are cured per person-year. Incidence rate is the number of new cases per person-year. Stroke events are categorized into four groups in IHME's dataset: acute/chronic ischemic stroke, and acute/chronic hemorrhage stroke. We used the sum of the prevalence of each stroke subtype as the prevalence of all stroke, and the weighted mean of the remission rates/relative risks as the remission rate/relative risk of all stroke. The percent weight given to each subtype was calculated as its fraction of all stroke prevalence. As the estimates from GBD studies were not produced on a yearly basis, we utilized the 2016 estimates and the mean of the estimates for the year 2005 and 2010 as the approximation for inputs of DisMod II for the year 2015 and 2007 respectively.

Population structure

Single-year permanent population estimates by sex and five-year age group for the year 2007, 2010 and 2015 were taken from the Residence Registry Section of the Municipal Bureau of Public Security. We used WHO World Standard Population based on world average population between 2000 and 2025 for the purpose of calculating age standardized rates. Ethical approval for this study is not required because data sources are existing population data or de-identified datasets.

4.2.2 *Model setting and analysis*

The raw input data and population data were recorded by sex and 5 year age groups. In order to have smooth rates for all the consistent modeled outputs, the first step of the modeling process for DisMod II is to interpolate the input data into single age estimates. For the four types of the input data, mortality rate, prevalence, remission rate and relative risk, this step was achieved using a cubic spline interpolation on the raw data. Figure 4.1 shows the model input data (both original and smoothed) by age for AMI of men in 2007.

Analyses were conducted with and without accounting for trends in incidence rates. When trends were accounted for, an annual change in the AMI incidence rate of -2% for both male and female, and an annual change in the stroke incidence rate of 3% and 2% for male and female respectively since the year 2000 were incorporated into the models. These trends were based on studies of AMI and stroke trends in Tianjin [10, 12, 17, 18]. We conducted DisMod II uncertainty analysis to assess the 95% confidence interval of the modeled incidence estimates. In the uncertainty analysis, DisMod II conducts a bootstrapping exercise where the input variables are assumed to follow a specific distribution. We allowed the estimates of AMI and stroke prevalence to vary with a normal distribution and set the number of bootstrap iterations to 100. Due to the lack of computing power, we were not able to assess the uncertainty around the modeled estimates for the models where trends were incorporated.

We calculated the proportion of incidence cases ascertained by the incidence surveillance system (completeness of reporting) as the observed incidence rate divided by the modeled incidence rate accounting for trends (the incidence rate ratio, IRR). We tested if the IRR increased from 2007 to 2010 and 2015 using one-sided Z-test. All the statistical tests were performed with R Version 3.5.3 using a 0.05 significance level. The DisMod II analytical software tool is freely available for use and can be downloaded from http://www.epigear.com/index_files/dismod_ii.html.

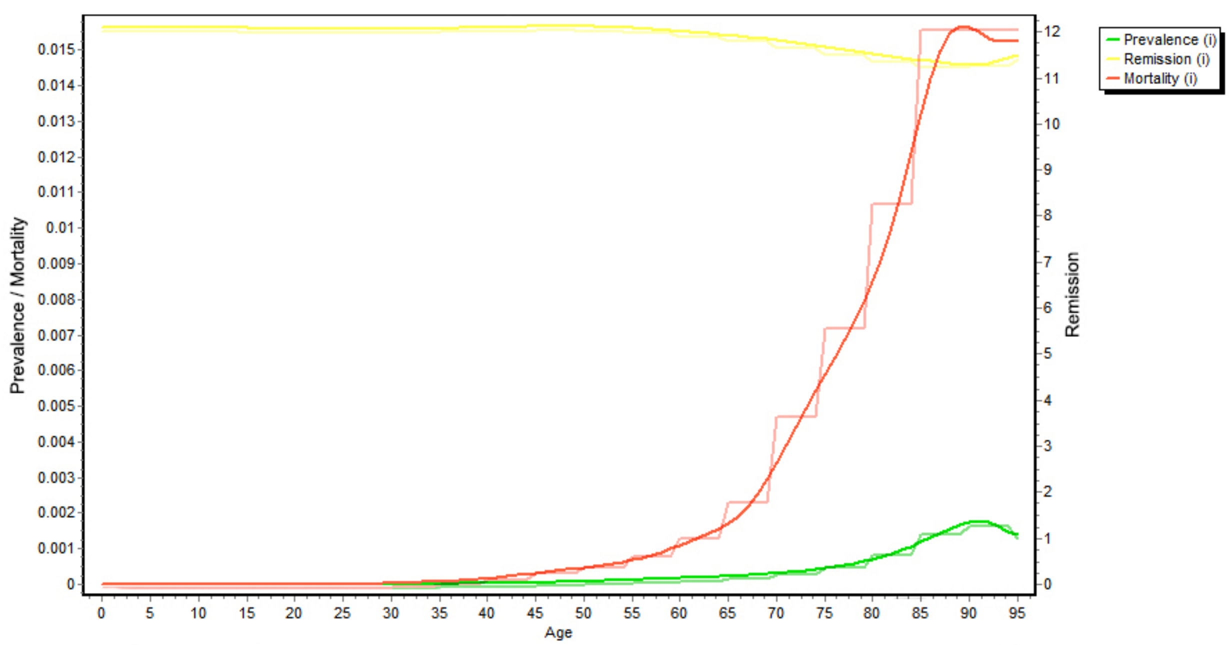


Figure 4.1. The data inputs for the DisMod II: actual and smoothed AMI prevalence, remission and mortality rate for male in 2007. Relative risk is not presented in the graph given the scale of y-axis.

4.3 RESULTS

23, 371 AMI incident cases and 152, 394 stroke incident cases were ascertained by Tianjin's incidence surveillance system for the three years, which constituted an age-standardized incidence rate of 51 (male 65, female 36) and 316 (male 389, female 242) per 100 000 population per year for AMI and stroke respectively. 92.4% of the AMI incident cases were diagnosed based on electrocardiography (ECG) and or imaging examination including ultrasound test and coronary angiography (CAG), 93.7% of the stroke incident cases were diagnosed based on CT or MRI scanning. Observed AMI incidence to mortality rate ratio was below one from 2007 to 2015, and observed stroke incidence to mortality rate ratio increased significantly from 2.90 (95% CI: 2.84-2.96) in 2007 to 7.71 (95% CI: 7.54- 7.90) in 2015 (Figure S4.5).

Table 4.1 shows that AMI and stroke incidence rates, both reported and modeled, are higher ($p<0.05$) in men than in women, and are higher ($p<0.05$) in older age groups than in younger age groups. Observed AMI incidence rate showed a monotonic downward trend from 2007 to 2015 for both men and women, and for the majority of age groups. Observed stroke incidence rate showed a monotonic upward trend for both men and women, and for all the age groups, with the upward trend becoming more pronounced after 2010. An overall decrease in modeled AMI incidence and increase in modeled stroke incidence rates, both trended and non-trended estimates, were found among men and women for the majority of age groups. The age and sex standardized modeled incidence rate (1/100, 000 person year) decreased ($p<0.05$) from 138 (95% CI: 125-145) in 2007 to 119 (95% CI: 113-125) in 2015 for AMI, and increased ($p<0.05$) from 520 (95% CI: 450-582) in 2007 to 534 (95% CI: 534-618) in 2015 for stroke.

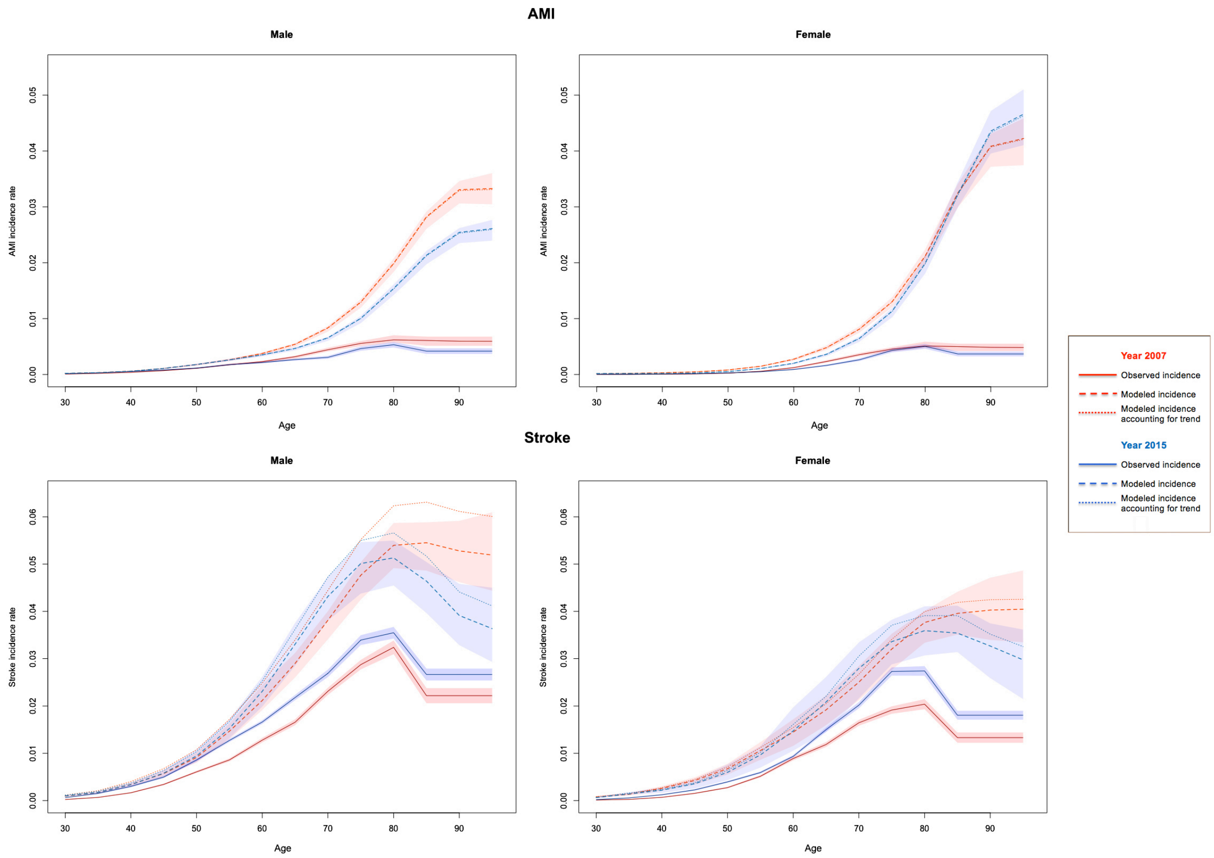


Figure 4.2. Age specific incidence rates of AMI and stroke in Tianjin, 2007 and 2015

For illustration, Figure 4.2 presents the age-specific observed and modeled incidence rates for AMI and stroke in 2007 and 2015. The solid lines show the observed incidence rates with accompanying 95% confidence intervals (the shades). The dashed lines show the trended estimates from DisMod II with accompanying 95% confidence intervals. The dotted lines show the non-trended estimates from DisMod II. The red lines and shades are estimates for 2007 and the blue ones are estimates for 2015. The figures show that, for both men and women, the reported incidence rates are significantly lower than the modeled estimates. The trended estimates from DisMod II for stroke incidence is higher than the non-trended estimates.

Table 4.2 presents the sex and age-group specific ratio of observed to modeled incidence rate, both trended and non-trended estimates, for AMI and stroke. For AMI, there is no significant difference between trended and non-trended ratios, for either men or women, and either younger or older groups. While for stroke, the trended ratio is lower (p<0.05) than non-trended one for both men and women, and both younger and older groups. The trended ratio for AMI increased significantly from 2007 to 2015 in the 30-59 age group for both men (0.64 vs 0.73, p<0.05) and women (0.29 vs 0.44, p<0.05). The trended ratio for stroke increased in both the younger (30-59) age group (0.48 verse 0.78 for men, and 0.36 verse 0.55 for women, p<0.05), and the older (≥ 60) age group (0.50 verse 0.61 for men, and 0.55 verse 0.65 for women, p<0.05).

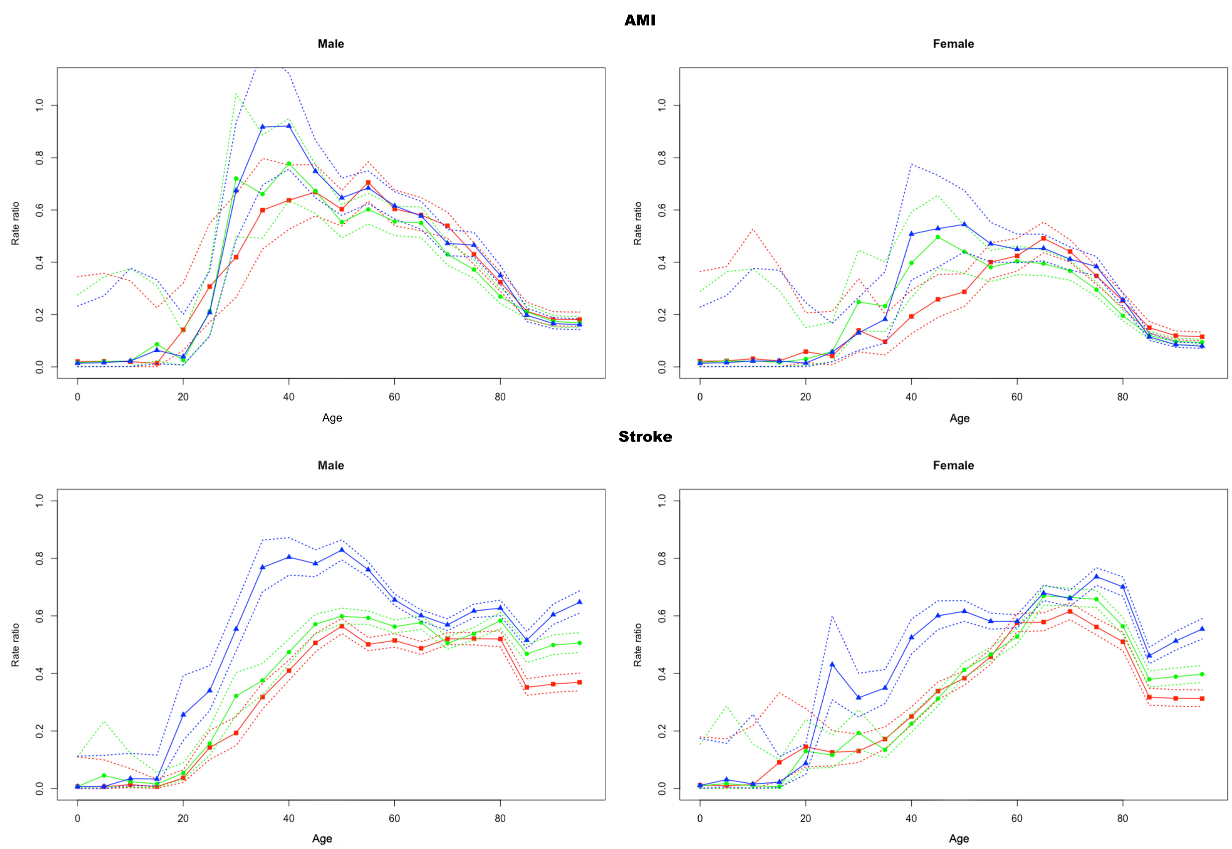


Figure 4.3. Age-specific ratio of reported to modeled incidence rate (trended) of AMI and stroke by sex and year. Red lines are estimates for 2007; Green lines are estimates for 2010; Blue lines are estimates for 2015. Dashed lines are upper and lower boundaries of the 95% confidence intervals.

For those aged 30 years or above, the ratio was higher in men than in women, for both AMI and stroke incidence, and for both younger subgroup (age 30 - 59) and older subgroup (age ≥ 60), except for stroke incidence among the older age group (age ≥ 60). For the 60-plus age group, the ratio for stroke was consistently higher ($p<0.05$) than that for AMI for both men and women. For the 30-59 age group, the ratio for stroke was lower ($p<0.05$) in 2007 and 2010, but higher ($p<0.05$) in 2015 than that for AMI. Figure 4.3 illustrates the age-specific ratio of reported to modeled incidence rate for AMI and stroke by sex and year. It shows that the increases in the ratio for both AMI and stroke occurred primarily during the 2010 and 2015 period.

4.4 Discussion

This is the first published study that aims to estimate the completeness of routine surveillance data for cardiac and cerebrovascular diseases incidence using external data in Tianjin. Our quantitative methods indicate that the overall case ascertainment in Tianjin's was approximately 39% and 58% for AMI and stroke respectively. Eliminating trends in the incidence rate of stroke in the DisMod II settings resulted in observed and estimated stroke incidence being less divergent at both younger and older ages than without trends. From 2007 to 2015, an overall increase in the estimated completeness for both AMI and stroke was observed, predominantly attributed to the improvement in the case reporting among the population aged 60 years or younger after the year 2010.

Completeness of reporting for incident cardiovascular and cerebrovascular diseases depends primarily on access to and utilization of healthcare services, and conscientious notification in an accurate timely manner [19]. The relatively low overall completeness of routine incidence reporting under passive surveillance in Tianjin could be attributed to several major reasons. First, neither cause-specific mortality data nor healthcare claim data has been linked to the incidence surveillance of the two diseases. Passive incidence registry is often unlikely to capture incident cases that lead to sudden deaths before patients reach health facilities. The average time from AMI symptoms onset to hospital arrival is 4 hours in China[20]. In Tianjin, over 70% of AMI and stroke deaths occur at home [21], indicating that successfully identifying and deriving death certificates cases is important to supplement incidence surveillance data. In addition, the incidence registry in Tianjin fails to record incidence cases for whom healthcare is not sought for or is sought for in health facilities out of Tianjin. Access to healthcare claim data, collected and compiled by the Municipal Bureau of Human Resources and Social Security, is important to AMI and stroke incidence surveillance as a means of finding cases not captured by local health facilities. Second, patients with minor events may be less likely to seek medical care urgently and are more often coded as other in the administrative database of health facilities. It has been reported previously that the proportion of patients with minor stroke is higher than reported in even high-quality stroke incidence studies and the underestimation is likely to be much greater in incidence surveillance from low-to-middle income countries, where healthcare utilization is often relatively low [22]. However, it’s impossible to estimate the number of minor cases in Tianjin as stratifications of incidence rates by disease severity were not presented in our dataset. Third, unlike death certificates that are required by law to be filled out and reported by practicing clinicians from health facilities, AMI and stroke incidence reporting is not mandatory in Tianjin [12]. Although there have been training programs designed for focal health workers that are expected to fill the reporting cards, and routine procedures for accuracy and recurrence checking, the reporting frequency by an individual health worker and/or facility has not been continuously monitored. The passive surveillance in Tianjin relies heavily on an extensive network and cooperation of health workers of multilevel health facilities, from tertiary hospitals to community health centers. Therefore, it's difficult to assure the completeness and timeliness of data without providing stimulus to health workers and health facilities in the form of monitoring-based individualized feedback or other incentives. Visual inspections of the distribution of monthly incident cases reported by each health facility (a representative sample from 331 health facilities including secondary and tertiary hospitals) demonstrate spurious fluctuations and zero reporting in specific months and/or years (Figure S4.6,

Figure S4.7).

Our results suggest that the estimated completeness of reporting of AMI and stroke incidence was lower in female and older population, which could be in part explained by behavioral, diagnostic and pathological factors. Age of patient in China negatively influences the decision to seek health care [23, 24] owing primarily to limited access to healthcare services and health insurance availability. Women in China are less likely to seek health care due to higher sensitivity to cost, social power relations and inherently inequality [23, 25]. It has been reported that un-witnessed sudden cardiac death is more likely to occur among women and older people [26] due to unusual pathophysiological mechanism [27, 28], their lower awareness of the warning signs and symptoms [29](chow, 2008) and a higher chance of being unemployed/living alone. This hypothesis is supported by the evidence that a higher proportion of AMI and stroke deaths for women and older people in Tianjin occur at home [21]. In addition, women have less typical symptoms than men and women with minor stroke or transient ischemic attack are less likely to be diagnosed with a stroke compared to men despite having similar symptoms at presentation [30].

We believe that the improvement in the estimated completeness during the period from 2007 to 2015 could be attributed to several factors. First, Tianjin started to incorporate the NCDs

Incidence Surveillance component into the Hospital Information System (HIS) of a few pilot hospitals in 2007, before which new incident cases were exclusively reported through the manually filled paper cards. By 2015, over 70% of the new cases from the chronic non-communicable incidence surveillance system were reported directly via HIS. The automatic reporting component embedded in HIS significantly reduced the workload of health workers, improving the timeliness and continuity of routine case reporting. Second, the out-of-pocket financial concern is associated with (adjusted for other factors including distance to care) prolonged time in care-seeking and hospital arrival after the onset of cardiovascular disease in China[20]. China's health care system reform beginning in 2009 has rapidly expanded health insurance coverage, significantly reduced the share of out-of-pocket expenditure and therefore increased the accessibility and timely utilization of health service [31-33]. Increased access and utilization of health service of the general public allows the primary care computer systems to systematically identify patients with cardiovascular and cerebrovascular disease.

Third, the extensively implemented secondary and tertiary prevention programs and campaigns in recent years may have further increased the likelihood of AMI and stroke patients being captured by the routine incidence surveillance system. Tianjin initiated the Stroke Screening and Prevention Project (SSPP) in 2011, targeted residents aged 40 years or older as the screening population. The SSPP assessed eight major risk factors for stroke and recommends labs and imaging tests to be performed on the basis of personal risk estimation (i.e., 3 or more risk factors or past stroke)[34, 35]. The proactive free screening at the community level in Tianjin enhanced the public's health literacy to recognize warning signs, symptoms of stroke and to make appropriate health-seeking decisions. The screening project also increased the chance of being diagnosed and coded as having stroke for patients at high risk and patients with minor stroke events [36]. Since 2014, Tianjin has gradually established chest pain centers (CPC) and the chest pain rescue network that aims to optimize the diagnosis and treatment processes for patients with acute chest pain, especially AMI [37, 38]. Increased access to urgent treatment and reduced hospital arrival time would lower the proportion of uncaptured incident patients that die at home or on the way to health facilities.

This study is beset with several limitations. First, we have assumed that the estimate from DisMod II reflect the true incidence rate and is the "gold standard" for measuring the completeness of reported incident events. Results from some previous studies have shown that the DisMod II estimates for both men and women were very similar to estimates derived from the routine health information system or population health survey [3, 39]. Scarborough et al. compared DisMod II estimates of age-specific incidence rates for AMI with those observed in the external dataset from England [40]. The DisMod II model estimates did not replicate age-specific incidence rates of AMI derived from population-based study although they were of similar magnitude. Our estimate of the completeness of case reporting is likely to be biased when the "gold standard" is not the true "gold standard". Second, the lack of any other rigorous research on the prevalence of AMI/stroke, the relative risk of mortality and remission of patients with AMI/stroke in Tianjin had led us to accept the epidemiological estimates provided by IHME's mixed-effects meta regression modeling using the DisMod-MR 2.0. The accuracy of these local estimates has not been investigated before. Nevertheless, they are internally consistent with the observed mortality rate derived from local all-cause mortality surveillance. Third, The ideal input data for the DisMod II would be estimates of the increased all-cause mortality for people who have had AMI or stroke. Given the lack of direct measure, we used mortality data where AMI or stroke was indicated as the underlying primary cause of death. This metrics does not account for increased mortality risk for other conditions (e.g. increased risk of respiratory disease and peripheral vascular disease) [40, 41].

Our model is open to further research and validity investigation. Reliable incidence data from extensive prospective follow-up study and other independent incidence data sources with information at individual level that could be linked to elements of CDC's incidence surveillance data can be used to supplement the assessment of completeness of routine reporting. More over, alternative prevalence and remission rate data will help to further confirm the validity of our findings.

4.5 CONCLUSION

Reporting of AMI and stroke incidence was incomplete in Tianjin. However, the completeness of the surveillance has been improving since 2010 primarily owing to the incorporation of automatic reporting component into the information systems of health facilities, the increase in the utilization of healthcare service and campaigns promoting access to prevention services and timely emergency treatment.

Table

REFERENCES

1. Saha, S., et al., *Modelling disease frequency measures in schizophrenia epidemiology.* Schizophr Res, 2008. **104**(1-3): p. 246-54.

2. Barendregt, J.J. and A. Ott, *Consistency of epidemiologic estimates.* Eur J Epidemiol, 2005. **20**(10): p. 827-32.

3. Kruijshaar, M.E., J.J. Barendregt, and N. Hoeymans, *The use of models in the estimation of disease epidemiology.* Bull World Health Organ, 2002. **80**(8): p. 622-8.

4. Xu, H., et al., *The China Acute Myocardial Infarction (CAMI) Registry: A national long-term registry-research-education integrated platform for exploring acute myocardial infarction in China.* American Heart Journal, 2016. **175**: p. 193-201.e3.

5. Zhou, M., et al., *Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017.* The Lancet, 2019.

6. *People's Republic of China--United States Cardiovascular and Cardiopulmonary Epidemiology Research Group. An epidemiological study of cardiovascular and cardiopulmonary disease risk factors in four populations in the People's Republic of China. Baseline report from the P.R.C.-U.S.A. Collaborative Study.* Circulation, 1992. **85**(3): p. 1083-96.

7. Wu, Z.S., et al., *The Sino-MONICA-Beijing Study: report on results between 1984 and 1986.* Acta Med Scand Suppl, 1988. **728**: p. 60-6.

8. Wu, Y., et al., *Estimation of 10-year risk of fatal and nonfatal ischemic cardiovascular diseases in Chinese adults.* Circulation, 2006. **114**(21): p. 2217-25.

9. Liu, J., et al., *Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study.* JAMA, 2004. **291**(21): p. 2591-9.

10. Wang, D.Z., et al., *Fifteen-year trend in incidence of acute myocardial infarction in Tianjin of China.* Zhonghua Xin Xue Guan Bing Za Zhi, 2017. **45**(2): p. 154-159.

11. Li, W., et al., *[Incidence trends of cervical cancer in Tianjin, 2007-2013].* Zhonghua Liu Xing Bing Xue Za Zhi, 2016. **37**(5): p. 699-701.

12. Jiang, G., et al., *Epidemiological transition and distribution of stroke incidence in Tianjin, China, 1988-2010.* Public Health, 2016. **131**: p. 11-9.

13. Barendregt, J.J., et al., *A generic model for the assessment of disease epidemiology: the computational basis of DisMod II.* Popul Health Metr, 2003. **1**(1): p. 4.

14. Wang, D., *Leveraging the surveillance system for NCDs to develop health policy*. 2016: Tianjin, China.

15. Wang, X., et al., *All-cause mortality in Tianjin, China, 1999-2004.* Prev Chronic Dis, 2009. **6**(4): p. A132.

16. Wang, X., et al., *Surveillance of trend and distribution of stroke mortality by subtype, age, gender, and geographic areas in Tianjin, China, 1999-2006.* Int J Stroke, 2009. **4**(3): p. 169-74.

17. Lu, H., et al., *Trends in stroke incidence among elderly low-income residents of rural China: a population-based study from 1992 to 2016.* Aging, 2018. **10**(11): p. 3438-3449.

18. Institute for Health Metrics and Evaluation (IHME). *Epi Visualization*. 2018 [cited 2018 May 21]; Available from: http://vizhub.healthdata.org/epi

19. Lambo, J.A., et al., *Completeness of reporting and case ascertainment for neonatal tetanus in rural Pakistan.* Int J Infect Dis, 2011. **15**(8): p. e564-8.

20. Guan, W., et al., *Time to hospital arrival among patients with acute myocardial infarction in China: a report from China PEACE prospective study.* European heart journal. Quality of care & clinical outcomes, 2019. **5**(1): p. 63-71.

21. Xiao, H., et al., *Impact of the smoke-free legislation on the incidence and mortality of AMI and stroke in Tianjin China: analysis of routinely collected data.* Tobacco Induced Diseases, 2018. **16**(1).

22. Bejot, Y., et al., *Impact of completeness of ascertainment of minor stroke on stroke incidence: implications for ideal study methods.* Stroke, 2013. **44**(7): p. 1796-802.

23. Brown, P.H. and C. Theoharides, *Health-seeking behavior and hospital choice in China's New Cooperative Medical System.* Health Economics, 2009. **18**(S2): p. S47-S64.

24. Lu, H., et al., *Healthcare seeking behaviour among Chinese elderly.* International Journal of Health Care Quality Assurance, 2017. **30**(3): p. 248-259.

25. Song, Y. and Y. Bian, *Gender differences in the use of health care in China: cross-sectional analysis.* International journal for equity in health, 2014. **13**: p. 8-8.

26. Lewis, M.E., et al., *Estimated incidence and risk factors of sudden unexpected death.* Open Heart, 2016. **3**(1): p. e000321.

27. Mehta, L.S., et al., *Acute Myocardial Infarction in Women.* Circulation, 2016. **133**(9): p. 916-947.

28. Stecker, E.C., et al., *Population-Based Analysis of Sudden Cardiac Death With and Without Left Ventricular Systolic Dysfunction: Two-Year Findings from the Oregon Sudden Unexpected Death Study.* Journal of the American College of Cardiology, 2006. **47**(6): p. 1161-1166.

29. Chow, C.-M., et al., *Lack of awareness of heart disease and stroke among Chinese Canadians: results of a pilot study of the Chinese Canadian Cardiovascular Health Project.* The Canadian journal of cardiology, 2008. **24**(8): p. 623-628.

30. Yu, A.Y.X., et al., *Sex Differences in Presentation and Outcome After an Acute Transient or Minor Neurologic Event.* JAMA Neurol, 2019.

31. Li, L. and H. Fu, *China's health care system reform: Progress and prospects.* The International Journal of Health Planning and Management, 2017. **32**(3): p. 240-253.

32. Cheng, L., et al., *The Impact of Health Insurance on Health Outcomes and Spending of the Elderly: Evidence from China's New Cooperative Medical Scheme.* Health Economics, 2015. **24**(6): p. 672-691.

33. Lei, X. and W. Lin, *The New Cooperative Medical Scheme in rural China: does more coverage mean more service and better health?* Health Economics, 2009. **18**(S2): p. S25-S46.

34. Wang, J., et al., *Risk Factors for Stroke in the Chinese Population: A Systematic Review and Meta-Analysis.* Journal of Stroke and Cerebrovascular Diseases, 2017. **26**(3): p. 509-517.

35. Stroke Prevention Project Committee, National Health and Family Planning Commission, and P.R.China, *Technical guideline for stroke screening and prevention.* Chinese Journal of the Frontiers of Medical Science (Electronic Version), 2013(9): p. 44-50.

36. Wang, Y., et al., *Is the Population Detected by Screening in China Truly at High Risk of Stroke?* Journal of Stroke and Cerebrovascular Diseases, 2018. **27**(8): p. 2118-2123.

37. Wang, D.Z., et al., *Analysis on the trends in mortality following acute myocardial infarction from 1999 to 2015 in Tianjin of China.* Zhonghua Xin Xue Guan Bing Za Zhi, 2017. **45**(11): p. 985-991.

38. Dingcheng, X. and Y. Shaodong, *Chest pain centers in China: Current status and prospects.* Cardiology Plus, 2017. **2**(2): p. 18-21.

39. Manuel, D.G., et al., *How many people have had a myocardial infarction? Prevalence estimated using historical hospital data.* BMC Public Health, 2007. **7**: p. 174.

40. Scarborough, P., et al., *Assessing the external validity of model-based estimates of the incidence of heart attack in England: a modelling study.* BMC Public Health, 2016. **16**(1): p. 1135.

41. Smolina, K., et al., *Long-Term Survival and Recurrence After Acute Myocardial Infarction in England, 2004 to 2010.* Circulation: Cardiovascular Quality and Outcomes, 2012. **5**(4): p. 532-540.

Table 4.1 Number and rate of AMI/stroke incidence in Tianjin, 2007, 2010 and 2015

		Number									Incidence rate** per 100, 000 (95% confidence interval)								
		2007			2010			2015			2007			2010			2015		
		Observed	DisMod II	DisMod II*	Observed	DisMod II	DisMod II*	Observed	DisMod II	DisMod II*	Observed	DisMod II	DisMod II*	Observed	DisMod II	DisMod II*	Observed	DisMod II	DisMod II*
AMI																			
Men	0-29	21	203	200	16	229	226	16	218	215	1 (0, 1)	12 (11, 13)	12	1 (0,1)	13 (11, 14)	13	1 (0, 1)	13 (11, 14)	13
	30-64	1634	2560	2527	1738	2846	2806	1950	2787	2751	61 (58, 65)	96 (87, 105)	95	61 (57, 64)	98 (87, 106)	97	69 (65, 72)	96 (87, 102)	95
	65+	2870	6548	6487	2956	7954	7800	3391	7722	7649	380 (364, 396)	880 (808, 917)	872	344 (322, 347)	917 (840, 976)	901	311 (292, 316)	712 (655, 741)	705
	Total	4525	9311	9215	4710	11029	10832	5357	10727	10615	69 (66, 71)	147 (134, 155)	146	64 (62, 66)	153 (139, 163)	150	63 (61, 65)	127 (116, 134)	126
Women	0-29	3	160	158	4	212	210	3	204	202	1 (0,1)	10 (9, 12)	10	1 (0, 1)	13 (12, 14)	13	1 (0, 1)	13 (12, 14)	13
	30-64	380	1298	1283	484	1243	1225	452	1001	987	14 (12, 16)	50 (44, 53)	49	16 (15, 18)	43 (38, 47)	43	15 (13, 17)	34 (30, 37)	34
	65+	2365	7220	7171	2405	9366	9289	2683	9104	9010	283 (269, 297)	869 (798, 922)	863	252 (239, 265)	952 (875, 1002)	944	236 (224, 249)	759 (689, 805)	751
	Total	2748	8678	8612	2893	10821	10724	3138	10309	10199	39 (37, 41)	128 (116, 136)	127	36 (35, 38)	137 (125, 145)	135	34 (32, 35)	110 (100, 117)	109
Stroke																			
Men	0-29	50	866	1086	65	787	908	129	600	682	2 (1, 3)	47 (40, 52)	57	3 (2, 3)	40 (33, 48)	45	5 (4, 6)	34 (29, 38)	38
	30-64	7978	13660	16114	9488	15276	16729	13210	15388	16928	294 (286, 302)	514 (453, 576)	608	320 (311, 328)	526 (470, 585)	577	453 (444, 463)	528 (460, 595)	582
	65+	14863	25470	29665	17399	29442	31992	25944	38899	42717	1965 (1929, 2001)	3384 (3038, 3674)	3943	2040 (2004, 2076)	3444 (3066, 3796)	3743	2396 (2358, 2435)	3597 (3218, 3993)	3950
	Total	22891	39995	46865	29364	45505	49629	39283	54888	60327	345 (340, 351)	620 (552, 680)	727	364 (359, 370)	628 (558, 696)	685	458 (452, 464)	644 (560, 718)	708
Women	0-29	31	358	381	30	432	467	63	421	450	1 (1, 2)	23 (16, 30)	24	1 (1, 2)	26 (17, 32)	28	3 (2, 3)	27 (23, 30)	29
	30-64	3948	10106	10713	4505	11130	11884	6015	9847	10548	145 (140, 151)	381 (308, 447)	404	148 (142, 153)	386 (311, 464)	412	202 (195, 208)	338 (250, 420)	367
	65+	10990	18782	20002	13803	21719	23323	19575	27975	30392	1343 (1313, 1373)	2227 (1881, 2526)	2442	1492 (1461, 1524)	2321 (1934, 2682)	2493	1686 (1653, 1720)	2376 (1843, 2889)	2581
	Total	14969	29246	31096	20234	33281	35674	25653	38244	41389	215 (211, 220)	420 (348, 483)	455	234 (230, 238)	434 (356, 510)	466	278 (273, 283)	424 (325, 517)	458

* With trend ** Standardized incidence rate

Table 4.2. Ratio of reported to modeled* incidence rate of AMI and stroke in Tianjin, 2007, 2010 and 2015

		2007		2010		2015	
		Male	Female	Male	Female	Male	Female
AMI	0-29	0.07 (0.05, 0.11)	0.01 (0.00, 0.04)	0.05 (0.03, 0.09)	0.01 (0.01, 0.03)	0.05 (0.03, 0.08)	0.01 (0.00, 0.03)
	30-59	0.64 (0.59, 0.69)	0.29 (0.25, 0.33)	0.62 (0.57, 0.67)	0.38 (0.33, 0.43)	0.72 (0.67, 0.77)	0.43 (0.37, 0.50)
	60+	0.43 (0.42, 0.45)	0.33 (0.31, 0.35)	0.38 (0.36, 0.40)	0.26 (0.25, 0.28)	0.44 (0.41, 0.46)	0.31 (0.29, 0.33)
	Total	0.47 (0.45, 0.49)	0.31 (0.29, 0.33)	0.42 (0.40, 0.44)	0.27 (0.25, 0.28)	0.50 (0.48, 0.52)	0.31 (0.29, 0.32)
AMI*	0-29	0.07 (0.05, 0.12)	0.01 (01, 0.04)	0.05 (0.03, 0.09)	0.01 (0.01, 0.03)	0.05 (0.03, 0.08)	0.01 (0.00, 0.03)
	30-59	0.64 (0.60, 0.69)	0.29 (0.25, 0.33)	0.63 (0.58, 0.68)	0.38 (0.34, 0.44)	0.73 (0.68, 0.78)	0.44 (0.38, 0.51)
	60+	0.44 (0.41, 0.46)	0.33 (0.31, 0.35)	0.38 (0.36, 0.40)	0.27 (0.25, 0.28)	0.44 (0.42, 0.47)	0.31 (0.30, 0.33)
	Total	0.47 (0.45, 0.49)	0.31 (0.29, 0.33)	0.43 (0.41, 0.45)	0.27 (0.25, 0.28)	0.5 (0.48, 0.52)	0.31 (0.29, 0.33)
Stroke	0-29	0.05 (0.04, 0.06)	0.06 (0.04, 0.09)	0.06 (0.05, 0.08)	0.04 (0.03, 0.06)	0.15 (0.13, 0.18)	0.10 (0.08, 0.13)
	30-59	0.57 (0.55, 0.59)	0.38 (0.36, 0.40)	0.61 (0.59, 0.63)	0.38 (0.37, 0.40)	0.86 (0.83, 0.88)	0.60 (057, 0.62)
	60+	0.58 (0.57, 0.59)	0.59 (0.57, 0.60)	0.59 (0.58, 0.61)	0.64 (0.63, 0.66)	0.67 (0.65, 0.68)	0.71 (0.69, 0.73)
	Total	0.56 (0.55, 0.57)	0.5 (0.49, 0.52)	0.58 (0.57, 0.59)	0.54 (0.53, 0.55)	0.71 (0.70, 0.72)	0.66 (0.64, 0.67)
Stroke*	0-29	0.04 (0.03, 0.05)	0.06 (0.04, 0.08)	0.06 (0.04, 0.07)	0.04 (0.03, 0.06)	0.14 (0.11, 0.16)	0.09 (0.07, 0.13)
	30-59	0.48 (0.47, 0.50)	0.36 (0.34, 0.38)	0.55 (0.54, 0.57)	0.36 (0.34, 0.37)	0.78 (0.76, 0.80)	0.55 (0.53, 0.57)
	60+	0.50 (0.49, 0.51)	0.55 (0.53, 0.57)	0.55 (0.53, 0.56)	0.6 (0.58, 0.61)	0.61 (0.59, 0.62)	0.65 (0.64, 0.67)
	Total	0.48 (0.47, 0.48)	0.47 (0.46, 0.48)	0.53 (0.52, 0.54)	0.50 (0.49, 0.51)	0.65 (0.64, 0.66)	0.61 (0.59, 0.62)

* With trend

SUPPLEMENTARY

Table S4.3. Input data for AMI DisMod II

Year	Age groups	Prevalence 1/100, 000		Mortality rate 1/100, 000		Remission rate		Relative risk	
		Female	Male	Female	Male	Female	Male	Female	Male
2007	0-4	1.2293	1.1588	0.0000	0.0000	12.1121	12.1027	812.6021	807.5271
	5-9	1.0833	1.0101	0.0000	0.0000	12.1131	12.1051	2,210.0864	1,846.5094
	10-14	0.9563	0.8778	0.4847	0.0000	12.1029	12.0949	2,885.7782	2,412.6441
	15-19	0.8770	0.7892	0.0000	0.5599	12.0817	12.0720	2,801.2208	2,324.6645
	20-24	0.8852	0.7884	0.0000	1.5948	12.0682	12.0582	2,334.2846	1,850.3003
	25-29	1.0112	0.9043	0.5846	1.3941	12.0622	12.0534	2,101.4431	1,665.0841
	30-34	1.1095	1.2336	0.9957	5.1755	12.0630	12.0619	1,700.8999	1,336.5763
	35-39	1.1664	1.8709	3.6602	10.7443	12.0704	12.0836	1,194.0887	956.8506
	40-44	1.4209	3.5160	6.6943	23.4308	12.0911	12.1042	843.0859	689.5936
	45-49	1.9435	6.4878	14.3086	40.0583	12.1249	12.1237	631.2714	534.9905
	50-54	3.7899	10.2375	23.0582	55.5937	12.1382	12.1070	478.3652	414.9399
	55-59	7.3877	14.9688	33.9042	86.3837	12.1311	12.0541	373.8574	323.2864
	60-64	13.7322	20.4901	82.8982	135.6744	12.1071	11.9777	301.7061	268.0642
	65-69	23.2575	26.6180	164.7428	233.9031	12.0663	11.8780	253.4794	237.1858
	70-74	40.6931	37.8526	326.0513	467.9765	12.0238	11.7482	200.5722	181.0481
	75-79	67.2701	56.2252	538.7795	710.0354	11.9796	11.5882	160.8919	132.7770
	80-84	118.0356	90.5835	944.7685	1,050.2939	11.9110	11.4471	108.8007	89.9142

	85-90	205.3242	149.1386	1,529.4091	1,528.2155	11.8180	11.3249	67.8474	58.4953
	90-95	315.1579	170.2190	1,529.4091	1,528.2155	11.7997	11.3424	43.0845	38.8312
	95+	460.9287	137.4736	1,529.4091	1,528.2155	11.8563	11.4995	27.1009	25.9152
2010	0-4	1.2800	1.1900	0.0000	0.0000	12.1163	12.1034	810.3057	807.0533
	5-9	1.1300	1.0500	0.0000	0.0000	12.1170	12.1069	2,201.5403	1,850.9758
	10-14	0.9920	0.9090	0.0000	0.5124	12.1062	12.0983	2,868.1747	2,408.8217
	15-19	0.9020	0.8110	0.0000	1.1029	12.0839	12.0772	2,777.9146	2,303.6875
	20-24	0.9140	0.8080	0.9010	2.3738	12.0702	12.0633	2,321.0504	1,831.2699
	25-29	1.0600	0.9320	1.4981	2.6101	12.0651	12.0564	2,103.8425	1,652.7522
	30-34	1.1300	1.2500	2.2843	6.6491	12.0619	12.0642	1,704.2970	1,328.0340
	35-39	1.0800	1.8400	3.7430	14.9468	12.0606	12.0865	1,189.9034	950.1067
	40-44	1.2400	3.5100	8.3939	30.5391	12.0786	12.1089	837.2971	684.2247
	45-49	1.6700	6.6100	15.0540	51.9220	12.1157	12.1313	626.8930	530.5071
	50-54	3.6000	10.4011	19.8843	72.0634	12.1360	12.1174	475.5715	412.3730
	55-59	7.4800	15.0700	39.8615	104.5043	12.1395	12.0673	372.3315	322.5279
	60-64	13.9572	20.3282	91.3074	169.9647	12.1252	11.9956	299.3041	265.0586
	65-69	23.4280	26.0120	196.2021	279.2452	12.0933	11.9026	249.9631	231.5259
	70-74	40.9830	36.7915	372.0690	484.1771	12.0481	11.7681	198.2545	177.3535
	75-79	67.8366	54.5063	666.4624	803.3331	11.9896	11.5923	160.0180	131.8288
	80-84	118.6309	86.8525	1,125.8744	1,281.0312	11.9117	11.4429	108.5442	89.8249
	85-90	205.6428	141.5436	2,127.1614	2,054.2842	11.8144	11.3201	67.8044	58.4834
	90-95	318.3286	158.8108	2,127.1614	2,054.2842	11.7973	11.3371	43.0637	38.8180
	95+	471.6020	122.3725	2,127.1614	2,054.2842	11.8605	11.4941	27.0460	25.8759

2015	0-4	1.3183	1.1849	0.0000	0.0000	12.1187	12.1013	804.5514	790.3335
	5-9	1.1610	1.0384	0.0000	0.0000	12.1201	12.1024	2,177.7785	1,805.9021
	10-14	1.0234	0.9025	0.0000	0.0000	12.1090	12.0924	2,854.0131	2,376.9289
	15-19	0.9361	0.8023	0.0000	0.9574	12.0855	12.0714	2,793.5975	2,313.4436
	20-24	0.9482	0.7946	0.7095	2.3523	12.0716	12.0582	2,328.4709	1,835.9452
	25-29	1.0947	0.9100	1.1292	2.8580	12.0673	12.0526	2,084.5054	1,631.2680
	30-34	1.1572	1.2316	2.1461	5.2671	12.0639	12.0629	1,679.0227	1,302.3023
	35-39	1.0973	1.8498	3.0634	11.5129	12.0614	12.0889	1,172.7018	932.9930
	40-44	1.2394	3.5304	5.5439	17.8232	12.0787	12.1144	825.1596	672.1129
	45-49	1.6613	6.6142	7.3194	35.8816	12.1156	12.1393	617.5167	520.6561
	50-54	3.5698	10.4701	13.3280	52.7915	12.1399	12.1285	468.2070	405.1384
	55-59	7.4426	15.2914	25.4222	82.7336	12.1515	12.0819	366.3768	317.5741
	60-64	13.6544	19.9649	43.9669	112.6891	12.1604	12.0424	286.6918	249.9776
	65-69	22.6612	24.3150	103.0056	176.2876	12.1667	12.0100	230.9657	206.1308
	70-74	39.0038	32.5781	201.3167	276.2213	12.1480	11.8963	181.5168	160.4519
	75-79	63.7695	45.7318	444.0738	531.5885	12.1042	11.7012	147.2160	126.4677
	80-84	109.3637	70.2775	750.6058	859.4930	12.0241	11.5291	101.7913	88.5683
	85-90	185.3225	112.4937	1,320.5405	1,271.6175	11.9075	11.3799	65.8151	58.0803
	90-95	297.2282	127.2160	1,320.5405	1,271.6175	11.8621	11.3835	42.5906	38.6983
	95+	465.8731	102.6315	1,320.5405	1,271.6175	11.8879	11.5400	26.8737	25.8021

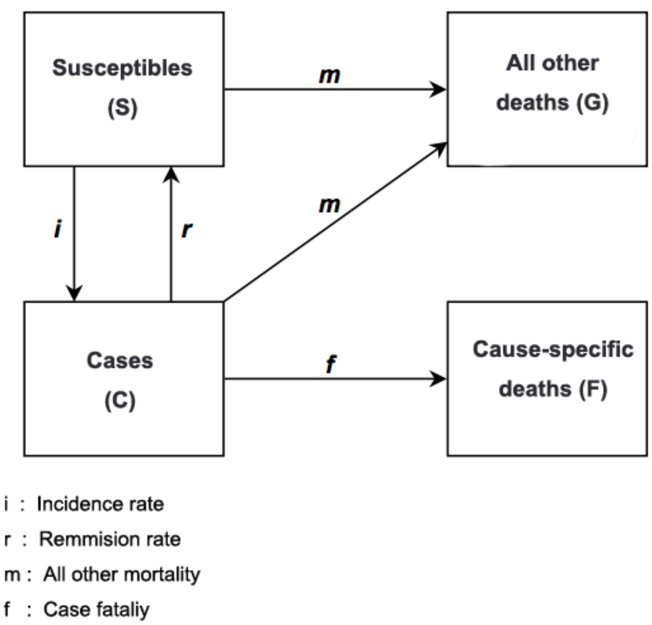
Table S4.4 Input data for stroke DisMod II

Year	Age groups	Prevalence 1/100, 000		Mortality rate 1/100, 000		Remission rate		Relative risk	
		Female	Male	Female	Male	Female	Male	Female	Male
2007	0-4	58.6673	67.2299	0.0000	0.0000	0.4581	0.5853	340.0002	332.8040
	5-9	82.9380	101.2343	0.0000	0.0000	0.1606	0.2604	370.0103	284.9970
	10-14	118.6350	159.7144	0.4847	0.0000	0.1103	0.1667	149.7652	87.6585
	15-19	165.0075	242.3417	0.2956	0.0000	0.0711	0.1049	55.5100	32.9437
	20-24	220.0179	346.2145	0.2406	1.3670	0.0519	0.0734	22.9570	12.6071
	25-29	281.9181	464.2887	1.1691	2.5093	0.0448	0.0584	19.7761	10.3089
	30-34	367.6382	621.0858	1.3276	4.5286	0.0641	0.0720	19.2644	10.7746
	35-39	541.3294	912.4085	4.7060	13.1028	0.0898	0.0933	17.3987	11.4992
	40-44	867.4984	1,429.9726	9.5952	29.4558	0.1279	0.1414	14.6469	10.7749
	45-49	1,533.2987	2,441.0086	21.8266	60.5643	0.1465	0.1746	11.8011	9.1149
	50-54	2,563.6657	3,955.1420	37.8503	80.9830	0.1394	0.1809	8.6634	6.7874
	55-59	3,992.5403	5,973.5653	79.4236	142.3906	0.1291	0.1830	6.3640	4.9564
	60-64	5,708.3823	8,399.9333	158.9264	250.2959	0.1143	0.1785	4.9527	3.9879
	65-69	7,433.8614	11,074.3917	292.8760	437.8813	0.1021	0.1751	4.1160	3.5012
	70-74	9,104.8025	13,766.5667	576.2061	829.5947	0.1089	0.1847	3.5588	3.0754
	75-79	10,870.4243	16,374.3872	1,037.9924	1,389.0410	0.1277	0.2054	3.2364	2.7987
	80-84	12,203.6631	18,244.1300	1,664.8664	2,013.7590	0.1410	0.2071	2.9286	2.5562
	85-90	12,081.7796	18,364.1995	2,065.1602	2,426.1164	0.1631	0.2001	2.7157	2.3698
	90-95	11,006.2418	17,342.5715	2,065.1602	2,426.1164	0.1995	0.2065	2.4694	2.1619
	95+	9,821.3627	16,020.1948	2,065.1602	2,426.1164	0.2449	0.2186	2.2179	1.9574

2010	0-4	58.9875	67.5969	0.0000	0.0000	0.4563	0.5452	330.3833	327.6580
	5-9	82.9363	101.2322	0.0000	1.0991	0.1467	0.2157	356.4415	277.3020
	10-14	116.5811	156.9494	0.0000	0.0000	0.0948	0.1372	137.6078	81.3017
	15-19	160.8639	236.2562	0.3947	0.3676	0.0612	0.0862	51.0796	30.4024
	20-24	213.9157	336.6122	0.2253	1.2948	0.0448	0.0600	20.6903	11.3591
	25-29	274.1579	451.5086	0.2497	3.7965	0.0386	0.0474	17.4119	9.2463
	30-34	358.7061	605.9960	1.6317	7.5989	0.0613	0.0635	17.5795	10.0614
	35-39	532.1153	896.8783	2.0155	12.6473	0.0915	0.0875	16.5242	11.0526
	40-44	861.9078	1,420.7573	9.7055	33.7537	0.1374	0.1456	14.1637	10.5664
	45-49	1,544.4452	2,458.7537	17.4539	57.5469	0.1613	0.1869	11.4587	8.9764
	50-54	2,606.3133	4,020.9373	34.0243	85.2861	0.1551	0.1942	8.4126	6.6469
	55-59	4,080.2212	6,104.7518	57.4972	124.9615	0.1446	0.1954	6.1948	4.8311
	60-64	5,859.2282	8,621.9043	104.1935	198.6649	0.1260	0.1944	4.8226	3.8709
	65-69	7,677.0175	11,436.6269	247.8342	380.1155	0.1086	0.1968	4.0028	3.3909
	70-74	9,452.1610	14,291.7769	396.6280	625.0042	0.1126	0.2018	3.4712	2.9807
	75-79	11,310.9166	17,037.9116	765.0869	1,073.5377	0.1302	0.2104	3.1678	2.7118
	80-84	12,697.7946	18,982.8426	1,301.0360	1,672.2364	0.1413	0.2042	2.8675	2.4843
	85-90	12,490.1304	18,984.8891	1,799.3913	1,930.8143	0.1594	0.1924	2.6532	2.3106
	90-95	11,241.2516	17,712.8772	1,799.3913	1,930.8143	0.1915	0.1951	2.4094	2.1133
	95+	9,880.1761	16,116.1287	1,799.3913	1,930.8143	0.2321	0.2040	2.1636	1.9183
2015	0-4	39.8504	45.6667	0.0000	0.0000	0.4316	0.5833	285.2972	283.7948

5-9	64.4269	78.6396	0.0000	0.0000	0.1731	0.2706	319.7667	251.1039
10-14	94.2080	126.8291	0.0000	0.0000	0.1072	0.1670	129.0885	79.6902
15-19	128.8924	189.3006	0.0000	0.9574	0.0678	0.1056	47.9795	30.1644
20-24	168.8272	265.6621	1.0643	1.0081	0.0503	0.0748	19.5049	11.5062
25-29	215.1717	354.3646	0.4517	1.5389	0.0448	0.0600	16.6372	9.4745
30-34	285.3953	482.1451	0.9538	6.4121	0.0731	0.0805	17.4974	9.9669
35-39	444.2605	748.7993	2.7570	13.9366	0.1069	0.1066	16.5329	10.0590
40-44	775.7984	1,278.8156	8.8702	23.1985	0.1521	0.1671	13.4302	9.4868
45-49	1,534.6294	2,443.1270	11.1053	42.5933	0.1700	0.1951	10.1288	8.1506
50-54	2,777.6507	4,285.2712	20.1013	63.0869	0.1551	0.1934	7.1656	5.9406
55-59	4,590.4276	6,868.1133	35.1826	94.8801	0.1385	0.1896	5.1976	4.2062
60-64	6,854.4087	10,086.3210	58.7793	125.1558	0.1167	0.1845	4.0870	3.4248
65-69	9,189.0715	13,689.1679	122.5030	218.9317	0.0970	0.1849	3.4879	3.0979
70-74	11,412.4805	17,255.8027	232.1591	376.1699	0.0993	0.1885	3.1411	2.7618
75-79	13,559.3914	20,424.8445	494.5533	640.2282	0.1176	0.1977	2.9367	2.5190
80-84	14,994.6725	22,416.6100	773.2619	898.6626	0.1307	0.1901	2.6206	2.3138
85-90	14,337.9186	21,793.5111	1,141.9166	1,145.2264	0.1456	0.1735	2.3690	2.1522
90-95	12,351.9342	19,462.9835	1,141.9166	1,145.2264	0.1686	0.1724	2.1317	1.9737
95+	10,255.1130	16,727.7101	1,141.9166	1,145.2264	0.1974	0.1783	1.9134	1.8014

Figure S 4.4 State transition model of the disease used by DisMod II



Source: Barendregt, 2003

Figure S4.5 Trend of AMI and stroke incidence to mortality rate ratio in Tianjin, Age≥35 Red line, mortality rate; Blue line, incidence rate; Black solid line, incidence to mortality rate ratio (smoothed); dash line, law enforcement date.

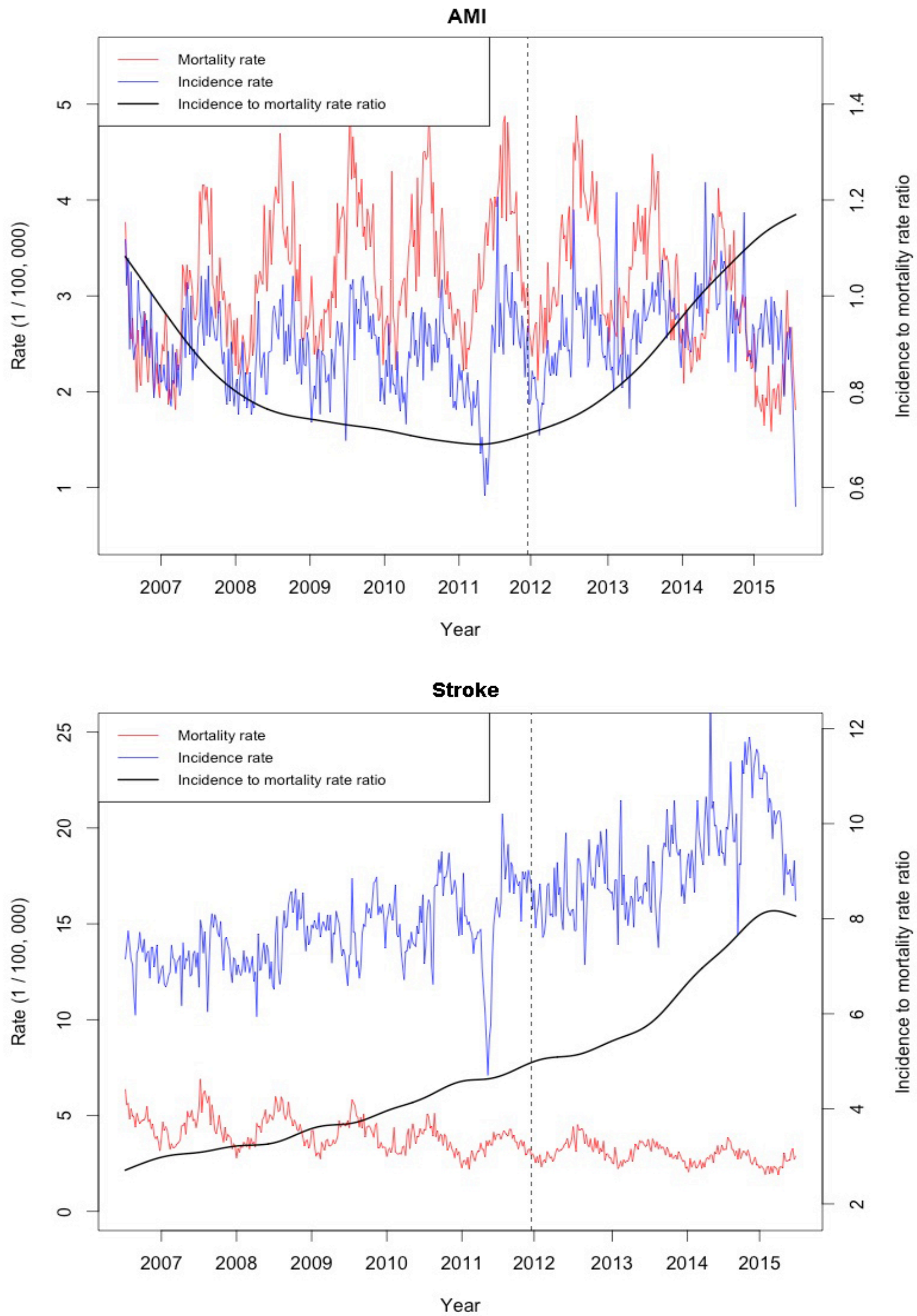
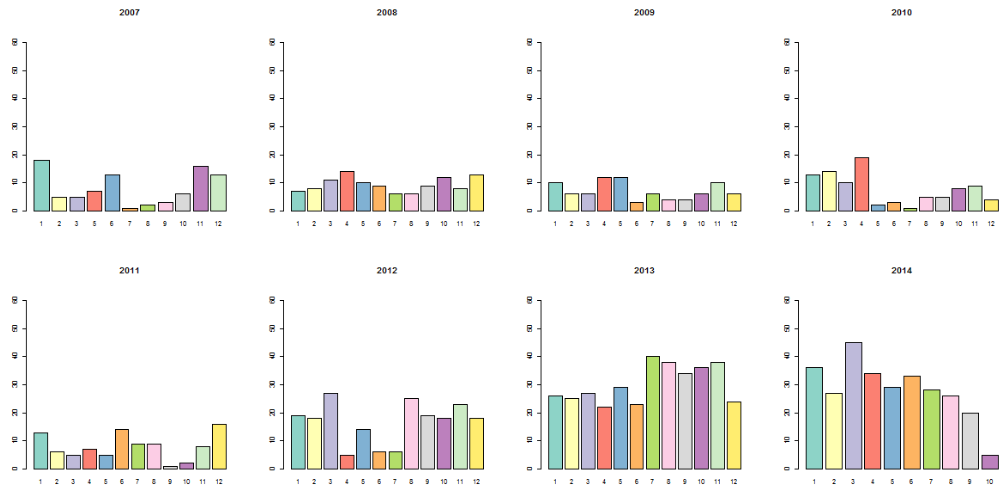
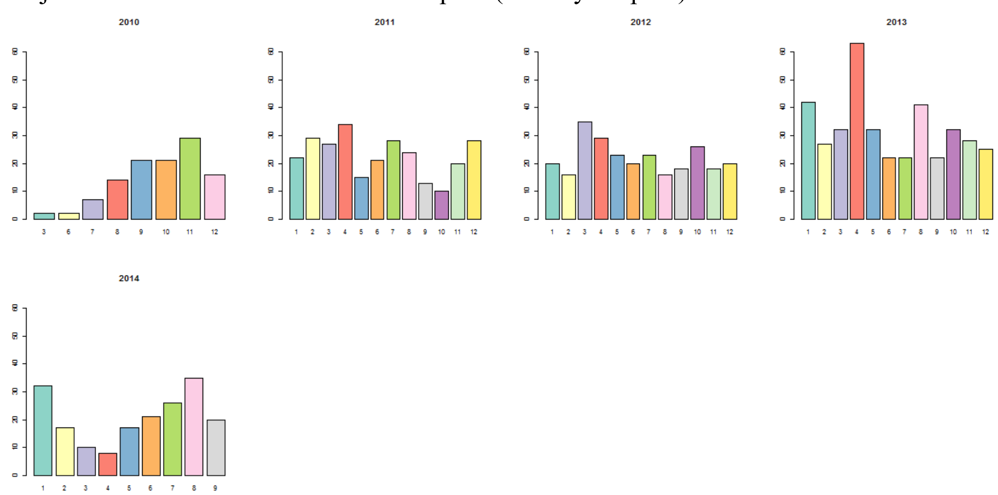


Figure S4.6 Monthly AMI incidence reported by selected hospitals, 2007-2014

Tianjin TEDA International Cardiovascular Hospital (Tertiary hospital)



Tianjin Chinese & Western Medicine Hospital (Tertiary hospital)



Tianjin Hongqiao Hospital (Secondary hospital)

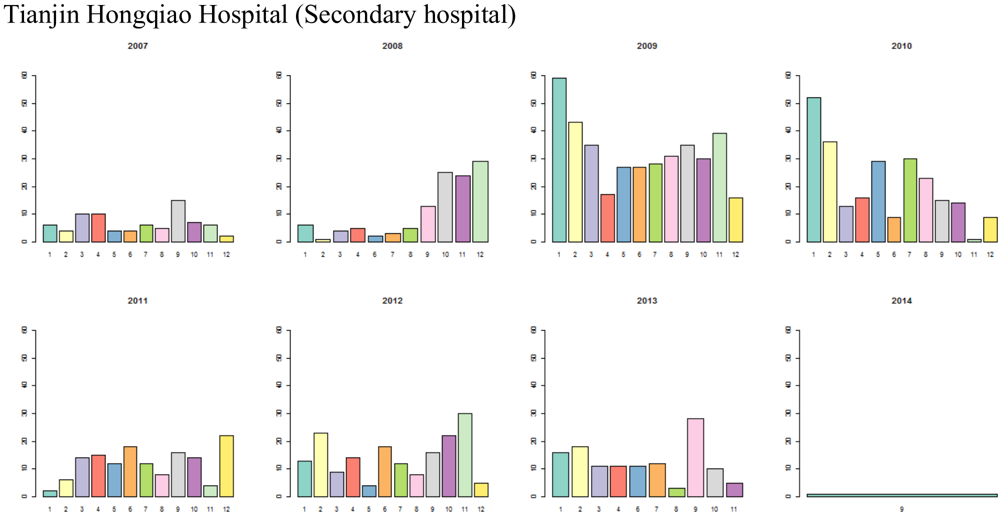
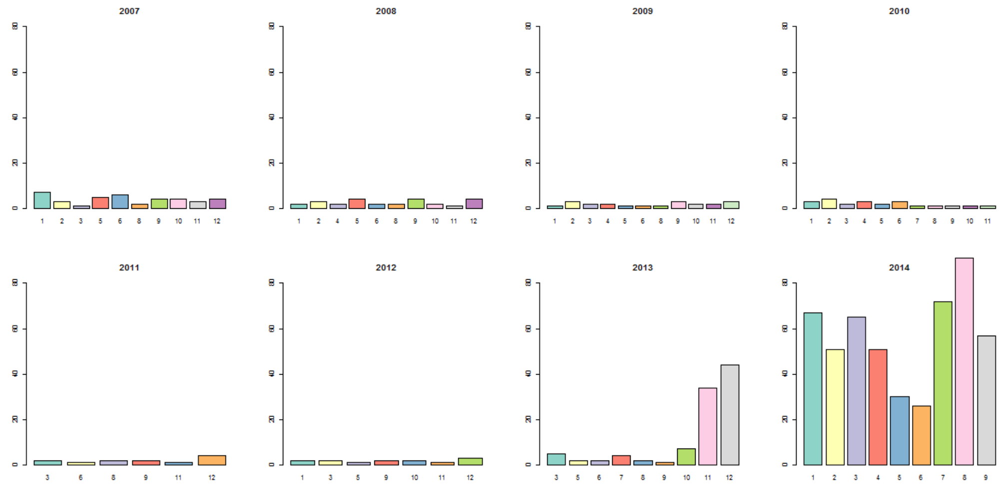
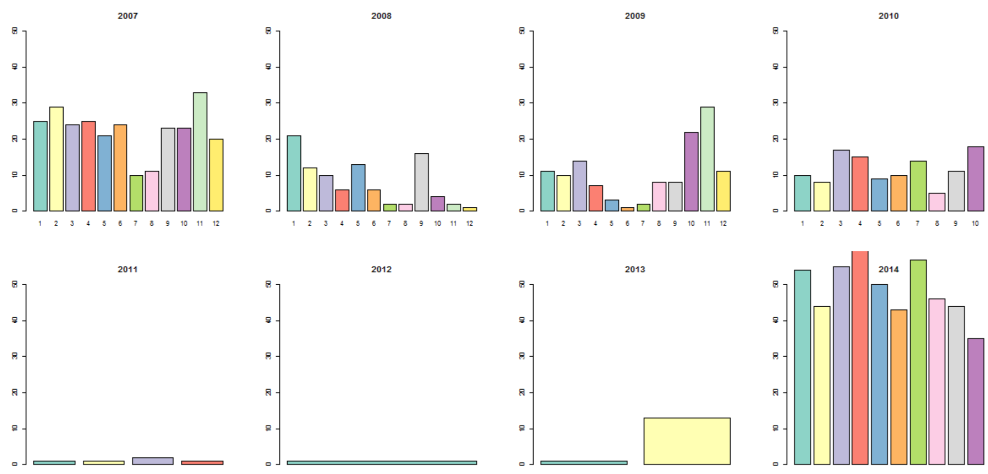


Figure S4.7 Monthly stroke incidence reported by selected hospitals, 2007-2014

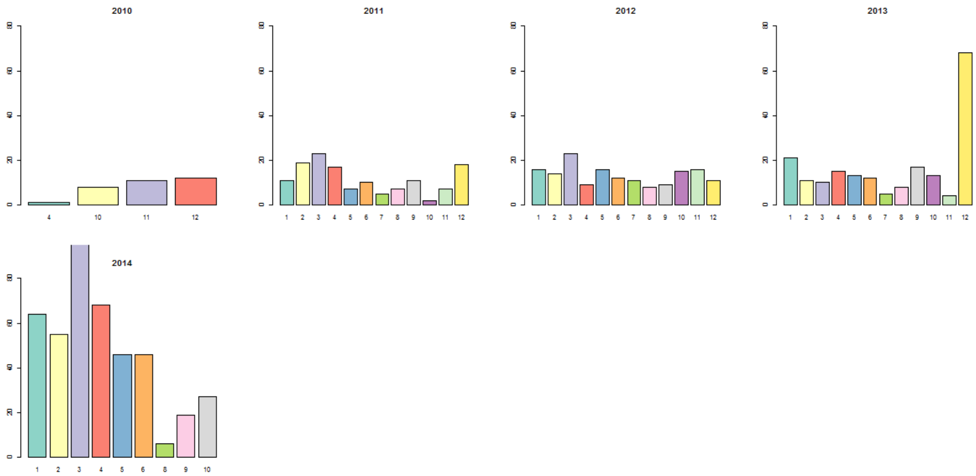
Tianjin Third Hospital (Tertiary hospital)



Tianjin People's Hospital of Ji County (Tertiary hospital)



Tianjin Xianshuigu Township Hospital (Secondary hospital)


2010
2011
2012
2013
2014

Chapter 5. CONCLUDING REMARKS AND FUTURE WORK

5.1 CONCLUSION

Smoke-free legislation is an effective way to protect the population from the harms of secondhand smoke (SHS) and has been implemented in many countries. In the part decade, 24 cities in mainland China (excluding Hong Kong and Macau) have passed the laws or regulations that prohibit smoking in worksites and public areas. However, none of theses cities have assessed the health of implanting the local smoking-free law. This study filled the evaluation gap in Tianjin and Qingdao and paved the way for similar studies assessing smoke-free legislation using the interrupted time series design in other cities or regions of China. With repeated cross-sectional surveillance data spanning a considerably 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 the onset of fatal and non-fatal myocardial infarction/stroke events.

This study added further support to existing evidence that smoke-free law is an effective public health intervention to reduce smoking and SHS related morbidity and mortality due to cardiovascular diseases, and extended the evidence of reductions in AMI and stroke risk following smoke-free legislation to women and older people. In Tianjin, the implementation of the smoke-free law is associated with the decline in the annual trends of AMI and stroke mortality. Immediate post-legislation reductions in mortality were not statistically significant mainly due to the gradual rollout of the law. An incremental 16% (RR: 0.84; 95% CI: 0.83–0.85) decrease per year in AMI mortality and a 2% (RR: 0.98; 95% CI: 0.97–0.99) annual decrease in stroke mortality among the population aged $\geq$ 35 years in Tianjin was observed, preventing an estimated 10, 000 (22%) averted AMI deaths within 3.5 years of implementing the law. The reduction in AMI mortality associated with the implementation of the smoke-free law was observed in both men and women, and both younger (aged 35-64) and older (aged ≥ 65) age groups.

No immediate reduction in AMI/stroke admissions and mortality associated with the smoke-free law was detected in Qingdao. However, an incremental 20% (95% CI: 14%-26%) decrease in the trend per year was observed in AMI admissions following the smoke-free legislation. Gradual reductions in AMI admissions were found in both younger and older age groups. Decrease (13%, 95% CI: 8%-18%) in the trend of stroke admissions was only observed among those aged between 65 and 84 years. The effect on mortality of AIM/stroke was modest and was observed among the older age group (aged ≥ 65) about one year after the law had been enacted.

The magnitude of the effect of the smoke-free law on reducing AMI and stroke mortality in Qingdao was smaller than that in Tianjin although Qingdao's smoke free-law was stricter in the way that it closed the loophole in the existing law of other cities including Tianjin that allowed designated smoking rooms. Qingdao was outperformed by Tianjin and other smoke-free cities in China in the implementation and enforcement of the smoke-free law, and in achieving most of the expected interim outcomes. Understaffing, the initial lack of designated funding for law enforcement and the absence of effective monitoring and evaluation scheme lead to insufficient enforcement of the law and consequent limited compliance, awareness and health impact. Therefore, active steps including capacity building for enforcement agency staff, routine monitoring, rigorous implementation of penalties should be taken to enhance coordinated enforcement compliance and achieve expected health impact in the population.

The completeness of incidence reporting in Tianjin, calculated as the ratio of observed incidence rate to the incidence rate estimated from the DisMod II, was 36% (95% CI: 35%-38%) for AMI and 54% (95% CI: 53%-55%) for stroke. Disparities in the completeness of AMI/stroke incidence reporting between men and women and between younger and older age groups were observed, the completeness of reporting being lower among women and older category (aged ≥ 60). Completeness of AMI and stroke incidence surveillance has improved in recent years primarily owing to the incorporation of automatic reporting component into the information systems of health facilities, the increase in the utilization of healthcare service and campaigns promoting access to prevention services and timely emergency treatment for AMI and stroke.

5.2 FUTURE WORK

This dissertation aims to offer a robust and comprehensive assessment of the health impact of the smoke-free legislation in two megacities of China by applying rigorous analytical techniques on time-series data collated from heterogeneous sources, and to evaluate the completeness of the reported AMI and stroke incidence rate that was initially used as one of the indicators for the impact evaluation. Although the key assumptions have been assessed and sensitivity analysis have been conducted to examine the validity of the methods, some improvements and future extensions to our work could be made.

One future direction is to extend the scope of the evaluation. As all of the evaluation framework and statistical methodology in this study is extendable to the other geographical areas, we could consider to include the other 22 cities in China that have passed the smoke-free laws in future evaluation study. In addition to mortality data, other indicators and data sources such as cigarette consumptions, hospital discharge data and claim data (stored in the Bureau of Labour and Social Security) could be utilized for outcome measurement.

Moreover, given that the interrupted time series design in this study can not exclude all possible history bias due to some con-interventions or simultaneous events, one approach to minimize the potential confounding is to add a comparable and appropriate control group that has not implemented smoke-free in the interrupted time series design. In the controlled interrupted time series (CITS) design, it's important for researchers to carefully and systematically consider a priori what confounding events and factors may exist, what control series are available and whether introducing the controls can exclude these bias or if they may bring new sources of bias to the study. If the results of the CITS and the ITS analysis are aligned, CITS studies can provide strong evidence on the effectiveness of smoke-free law [1]. In addition to considering multivariable regression and propensity score matching for the CITS design, a robust evaluation framework that combines the synthetic controls approach and ITS design where multiple potential controls exist can be applied to generate a comparable control and strengthen internal validity [1-3].

Including more smoke-free cities in the evaluation study will make it possible to quantify the dose-response relationship between factors along the causal pathway within the evaluation framework. This will require a systematic review and collation of data on indicators of inputs, activities, outputs, outcomes and impacts. The evidence generated can be utilized in a mathematical health policy model to quantify the likely effects of changes in implementation/enforcement and their varying impact.

Lastly, we used the estimate from the DisMod II as the benchmark for measuring the completeness of reported incident events, assuming both the external validity of DisMod II program for modeling AMI/stroke epidemiological indicators in China and reliability of the input data for the models, including sex and age-specific cause mortality rate, prevalence, remission rate, relative risk. Therefore, it is critical to carefully interpret the results. Further research and validity investigation using alternative data sources such as extensive prospective follow-up study and independent incidence data sources with information at individual level linked to elements of incidence surveillance data from CDC would help to establish confidence in the results.

References

1. Lopez Bernal, J., S. Cummins, and A. Gasparrini, *The use of controls in interrupted time series studies of public health interventions.* International Journal of Epidemiology, 2018. **47**(6): p. 2082-2093.
2. Linden, A., *Combining synthetic controls and interrupted time series analysis to improve causal inference in program evaluation.* Journal of Evaluation in Clinical Practice, 2018. **24**(2): p. 447-453.
3. Abadie, A., A. Diamond, and J. Hainmueller, *Synthetic Control Methods for Comparative Case Studies: Estimating the Effect of California's Tobacco Control Program.* Journal of the American Statistical Association, 2010. **105**(490): p. 493-505.