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Association of restaurant smoking ban and the incidence of acute myocardial infarction in Finland.

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Abstract

Objective

To describe the changes in nationwide AMI incidence following the implementation of a law banning smoking indoors in restaurants on June 1st 2007.

Methods

Retrospective registry study of all hospitalizations for acute myocardial infarctions (AMI) in Finland. All 34887 hospitalizations for AMI between June 1st 2005 and May 31st 2009 were identified from the Care Register for Health Care (CRHC) and statistics for tobacco consumption were obtained from the National Institute for Health and Welfare. Comorbidities for individual hospitalizations were searched from the CRHC.

Results

The incidence rate of AMI was reduced by 6.3% (95%CI 4.1-8.6%; $p<0.0001$) in the latter half of the study period following the smoking ban when adjusted for age, gender and overall population prevalence of smoking. There was no effect on in-hospital mortality for AMI (6.8%). Short term incidence of AMI (6 month prior vs. 6 months after the smoking ban) was also reduced (4.5%, 95% CI 0.2-9.0%; $p=0.0399$). The incidence rates declined similarly for both men and women.

Conclusion

Banning indoors tobacco smoking in restaurants was associated with a mild additional reduction in AMI incidence on a nationwide level in Finland.

What this paper adds

-Previous results on the effectiveness of smoking bans and coronary event incidence have been mixed.

-This study describes the additional effects of a restaurant smoking ban in a country with already implemented otherwise comprehensive workplace restrictions on indoors smoking.

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-It appears that focused additional legislative measures aimed at reducing tobacco smoke exposure result in measurable reductions in myocardial infarction incidence.

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Introduction

Tobacco smoke exposure, both first hand and environmentally, has been unequivocally linked to an increased risk of ischemic heart disease and acute myocardial infarction (AMI).[1] Tobacco smoke increases the risk of acute cardiac events by multiple mechanisms including prothrombotic effects, low-density lipoprotein oxidation, activation of inflammatory pathways and impaired vascular repair.[2-4] A previous Cochrane review suggested that indoor smoking bans have decreased the incidence of AMI on a population level via a decrease in second hand smoking (SHS).[5] Since the implementation of new anti-tobacco legislation in Finland from June 1st 2007 smoking has been prohibited indoors in public places such as restaurants. The aim of this study is to retrospectively assess the effects of the new legislation on the incidence of myocardial infarctions in Finland.

Materials and methods

We searched the Care Register for Health Care (CRHC)a nationwide obligatory and automated database maintained by Finnish National Institute for Health and Welfare that contains hospital discharge diagnosis codes of all medical admissions in Finland, for patients hospitalized with a primary diagnosis of acute myocardial infarction (ICD-10 codes I21.0-49).

The study period was from June 1st 2005 up to May 31st 2009 and the search covered all University Hospitals (n=5) and Central Hospitals (n=17) in Finland (2007 population 5,300,484) along with eight of the largest district hospitals. Secondary diagnoses of the admission were used to identify comorbidities.

The data was divided into two main time periods: pre-legislation (from July 1st 2005 to May 31st 2007) and post-legislation (June 1st 2007 to May 31st 2009). For evaluation of the immediate implications of the legislation the period was divided into 6 month periods. Data on smoking

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prevalence in the general population by gender, age and year were obtained from Statistics Finland (www.tilastokeskus.fi).

Statistical methods

The continuous variables were described in terms of mean and standard deviation. Categorical variables were presented as frequencies and proportions (percentages). Generalized linear model was fitted using Poisson distribution to describe the count of infarctions in terms of incidence rate ratios (IRR). Logarithmically transformed population size was used as an offset parameter. The results were adjusted for gender, age and smoking habits. All analyses were conducted using SAS System for Windows, version 9.4TS1M1 (SAS Institute Inc., Cary, NC, USA). P-values less than .05 were considered as statistically significant.

Results

There were 656044 hospitalizations during the study period of which 34887 were for myocardial infarctions.

The incidence rate of AMI was reduced by 6.3% (95%CI 4.1-8.6%; p<0.0001) following the smoking ban when adjusted for age, gender and overall population prevalence of smoking. Reduction in short term incidence of AMI (6 month prior vs. 6 months after the smoking ban) was similar (4.5%, 95% CI 0.2-9.0%; p=0.0399) to that in the whole study period and was prominent in the working middle aged group (25-44 years old); RR between the latter and first halves of 2007 0.83 (95%CI 0.65-1.08, p=0.16) (figure 1.). Incidence rate ratios for AMI in 6 month intervals are shown in figure 2, with a dotted line representing the implementation of the law.

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Patient features and comorbidities prior to and after June 1st 2007 are presented in table 1. A slightly larger proportion of infarction patients were female in the latter half of the study period, but declines in infarction rates were similar for males and females over the period. Increasing age and male gender were associated with increased risk for AMI (Table 2). Furthermore, age- and gender specific smoking prevalence in the general population was also associated with occurrence of AMI (Table 2).

Table 1. Comorbidities and characteristics of patients hospitalized between June 2005 and May 2009 for myocardial infarctions in Finland before and after the law banning indoor smoking in restaurants since June 2007.

Variable	Before June 2007 (n=18487)	After June 2007 (n=16400)	p-value
Age	68.5±11.4	68.3±11.3	0.187
Female gender	6491 (35.1%)	5453 (33.3%)	<0.001
Hypertension	2869 (15.5%)	2615 (15.9%)	0.275
Diabetes	1630 (8.8%)	1464 (8.9%)	0.719
Hypercholesterolemia	1435 (7.8%)	1364 (8.3%)	0.057
Congestive heart failure	1985 (10.7%)	1770 (10.8%)	0.868
Atrial fibrillation	1085 (5.9%)	969 (5.9%)	0.876
Peripheral arterial disease	145 (0.8%)	150 (0.9%)	0.185
Chronic lung disease	447 (2.4%)	357 (2.2%)	0.134
Chronic kidney disease	157 (0.8%)	154 (0.9%)	0.373
Malignancy	191 (1.0%)	169 (1.0%)	0.980

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Prior revascularization	666 (3.6%)	553 (3.4%)	0.242
Rheumatoid arthritis	102 (0.6%)	80 (0.5%)	0.408
Thyroid disease	46 (0.2%)	52 (0.3%)	0.229

Table 2. Factors associated with AMI incidence in Finland between between before and after a June 1st 2007 legislation banning indoor restaurant smoking .

Variable	IRR	95% confidence interval	p
Age (per year)	1.050	1.048-1.051	<0.0001
Male gender	1.578	1.536-1.621	<0.0001
Prelegislation period	1.063	1.041-1.086	<0.0001
Higher smoking prevalence	1.031	1.028-1.034	<0.0001

IRR=incidence rate ratio.

Myocardial infarction presented with ST-segment elevation (STEMI) in 37% (n=12923) of patients. The ratio between STEMI and non-STEMI did not change over the study period. Inhospital mortality for AMI was 6.8% both before and after the smoking ban.

Discussion

This nationwide study associates a nationwide ban on indoors tobacco smoking in public places with a slightly reduced incidence rate of myocardial infarctions on a population level in Finland. The reduction of AMI rate was most notable in patients aged 40-50 years. No difference in rate reduction between genders was found.

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A previous meta-analysis of studies on the effect of indoors smoking bans showed an average reduction of 17% in AMI incidence with individual studies ranging between 8% and 50%.[5,6] The current study demonstrated only a 4.5% reduction in AMI incidence when comparing the first and latter halves of the year 2007 and a 6.3% reduction in longer time scale. The most obvious reason for the modest reduction in our study is that there are differences in the smoking bans: for example in Italy the ban was implemented in all working places whereas smoking in other work places than restaurants had been banned since 1995 in Finland making the target population in this study considerably smaller. Moreover, the declining smoking prevalence in Finland was associated with reductions in AMI incidence in the present study (Table 2.), although the countries represented in the meta-analysis by Meyers and colleagues had similar and declining smoking prevalences of 24-29% before implementation of bans. It should be noted that, despite significant improvement attributable to nationwide public health measures in the last decades, Finland has an almost twofold AMI incidence compared to the countries describing reductions with indoor smoking bans.[7] Thus the absence of a more pronounced effect cannot bet attributed to low rate of vascular events in the population.

Typically the occurrence of AMI increases exponentially with aging as seen in the present study as well (figure 1.).[8] There was a slightly more pronounced decrease in IRR specifically in patients aged 25-44 years old when comparing pre- and postlegislative periods. This population cohort includes both restaurant patrons and most of the approximately 43,000 persons who were classified as restaurant staff in 2008 (data obtained from the Finnish Ministry of Education). It is conceivable that the new legislation could have deterred smoking in a number of active smokers among this populace and thus further reduced both first hand and environmental exposure to tobacco smoke both in- and outside restaurants. The fact that tobacco smoking prevalence decreased markedly in persons aged 15-44 between 2007 and 2008 (Finnish National Institute for Health and Welfare

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Tobacco Statistics 2014) lends support to the aforementioned hypothesis.[9] Non-smoking rapidly halves the risk of myocardial infarction.[10] In 2007 out of restaurant waiters and bartenders, 37% and 67% respectively would have been exposed for over 4 hours per shift to environmental tobacco smoke and about 28% were active smokers.[11] Previous studies have already showed that the 2007 ban was effective in reducing environmental exposure and consequently symptoms in restaurant workers.[12] This reduction in occupational exposure alone should translate into some hundreds of myocardial infarctions less per year such as shown in the results of this study.

Limitations of this study are those inherent to a retrospective registry study; i.e. all confounders cannot be accounted for particularly as the study group had no access to individual patient records but only the information contained in the CRHC, which, however has been validated for AMI patients.[13] As our data consisted only of those AMI patients who were admitted, those who died prior to hospitalization were not included.

Whereas other studies that have shown a negligible effect of indoor smoking bans on AMI incidence have speculated that the modest effect might have been due to short follow up periods,[14,15] the present study had an extensive observation period and our results are comparable both in the short and long term adding to the strength of our study. However, even as the association of the smoking ban with reduction in AMI rate is evident in this study the prolonged effects are harder to discern especially as there was a nationwide public health project from 2000 to 2010 aimed at improving outcomes of diabetes; this project has no doubt affected AMI rates in addition to other outcomes .[16] Lastly, the effect of environmental tobacco smoke exposure on the risk of cardiovascular disease is dependent both on the dose and duration of exposure.[4] Our ecological study design does not allow accounting for these factors so our interpretation focuses on the population level.

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Conclusions

Legislative measures stopping indoor smoking in restaurants and other public spaces were associated with an incremental reduction in the incidence of acute myocardial infarctions on a national level in Finland. The reduction was most pronounced in those of working age which represent the demographics most likely to frequent and work in restaurants. The results suggest that in a country with an already implemented prohibitive legislation on workplace smoking the incidence of AMI can still be, albeit modestly, reduced with a ban on restaurant smoking.

Funding

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Competing Interests

The authors declare no competing interests relevant to the study.

Contributor

JG prepared and submitted the manuscript. JS, PR and VK planned the study. TK and JG analyzed the data. TK prepared the figures.

Ethics approval

Approved by the Finnish National Institute for Health and Welfare.

What this paper adds

- Previous studies have shown that legislative measures to prohibit indoors smoking result in a decrease in population level myocardial infarction incidence.

- Results have, however, been heterogeneous.

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- This study shows that in a country with previous extensive bans on public and workplace smoking the addition of a restaurant ban results in a measurable reduction in myocardial infarction incidence on a nationwide level.

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Figure 1. Incidence of hospitalization for acute myocardial infarction in Finland. June 1st 2007 was the implementation of a nationwide restaurant smoking ban.

Figure 2. Incidence rate ratios of acute myocardial infarction for 6 month intervals in Finland. Dotted line indicates implementation of a new law banning smoking in restaurants. 1 indicates first half of year and 2 the latter half (e.g. 2009/1 and 2009/2).

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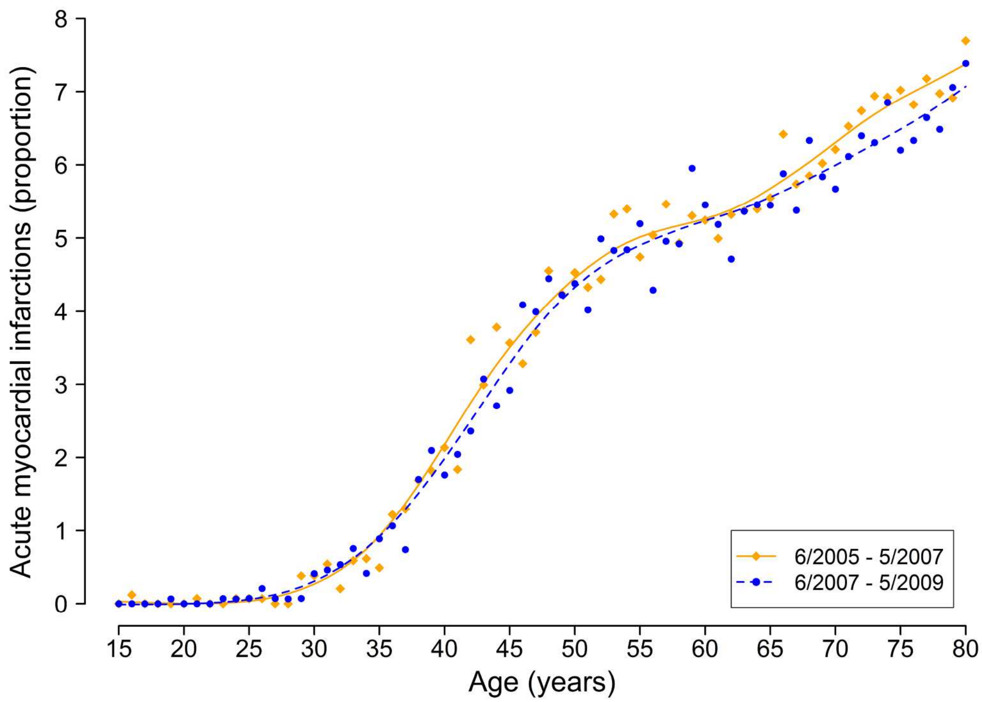

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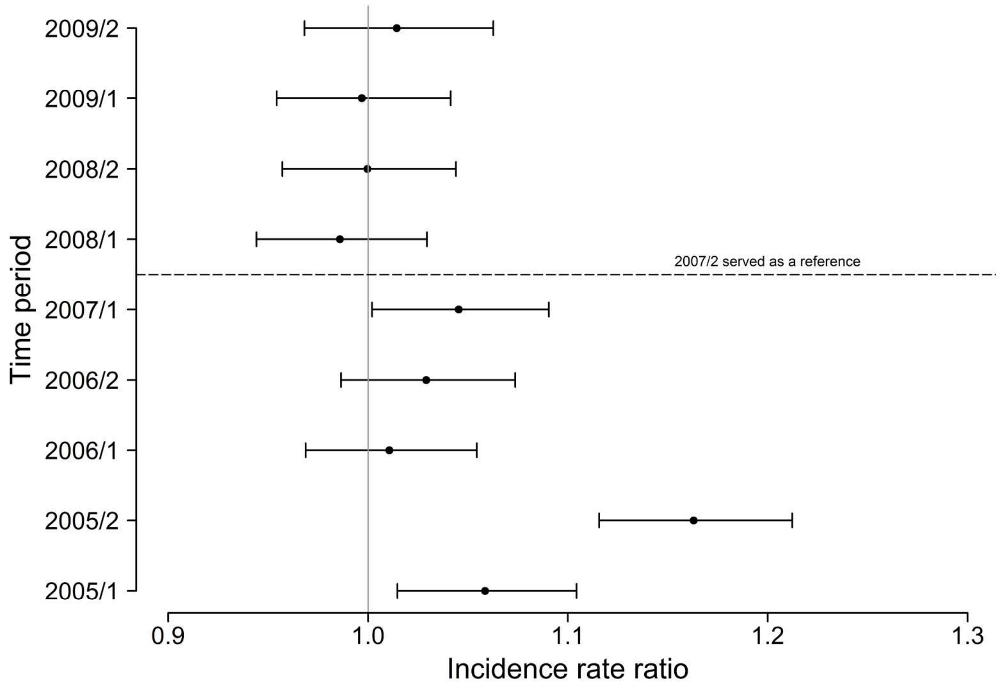

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Abstract

Objective

To describe the changes in nationwide AMI incidence following the implementation of a law banning smoking indoors in restaurants on June 1st 2007.

Methods

Retrospective registry study of all hospitalizations for acute myocardial infarctions (AMI) in Finland. All 34887 hospitalizations for AMI between June 1st 2005 and May 31st 2009 were identified from the Care Register for Health Care (CRHC) and statistics for tobacco consumption were obtained from the National Institute for Health and Welfare. Comorbidities for individual hospitalizations were searched from the CRHC.

Results

The incidence rate of AMI was reduced by 6.3% (95%CI 4.1-8.6%; p<0.0001) in the latter half of the study period following the smoking ban when adjusted for age, gender and overall population prevalence of smoking. There was no effect on in-hospital mortality for AMI (6.8%). Short term incidence of AMI (6 month prior vs. 6 months after the smoking ban) was also reduced (4.5%, 95% CI 0.2-9.0%; p=0.0399) and was largest in the oldest ages but observed also in the working middle aged group (40-50 years old); RR between the latter and first halves of 2007 0.83 (95%CI 0.65-1.08, p=0.16). The incidence rates declined similarly for both men and women.

Conclusion

Banning indoors tobacco smoking in restaurants was associated with a mild additional reduction in AMI incidence on a nationwide level in Finland.

Strengths and limitations of this study

- This is a study into the effects of a restaurant smoking ban on incidence of myocardial infarction (MI) in a situation where workingplace smoking is already prohibited. Validated, obligatory national registry was used to provide reliable nationwide coverage.

- Limitations of this study include the unavailability of data on tobacco smoke exposure, medication or therapies implemented. In addition, our data do not cover patients who died of a MI prior to reaching hospital.

- The decline in MI incidence in the oldest age groups after the implementation of the ban may be confounded by the general decline in these age groups reported previously.

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Introduction

Tobacco smoke exposure, both first hand and environmentally, has been unequivocally linked to an increased risk of ischemic heart disease and acute myocardial infarction (AMI).[1] and the effect is seen already at low exposure levels [2, 3] Tobacco smoke increases the risk of acute cardiac events by multiple mechanisms including prothrombotic effects, low-density lipoprotein oxidation, activation of inflammatory pathways and impaired vascular repair.[4-6] A previous Cochrane review suggested that indoor smoking bans have decreased the incidence of AMI on a population level via a decrease in second hand smoking (SHS).[7]

Smoking on workplaces has been prohibited in Finland since 1995. This was followed by a 2-3 % reduction in smoking prevalence. The ban did not initially include restaurant workers but was extended to cover them in 2000. However, as restaurant customers were still allowed to smoke indoors uninhibited the extension was deemed insufficient to protect restaurant workers and since June 1st 2007 smoking has been prohibited indoors in all public places. Large restaurants were allowed to request for transition time until June 2009 but only 5% of restaurants used this opportunity. Restaurants and other workplaces are allowed to build isolated, air-conditioned smoking cubicles The aim of this study is to retrospectively assess the effects of the new legislation on the incidence of myocardial infarctions in Finland.

Materials and methods

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We searched the Care Register for Health Care (CRHC)a nationwide obligatory and automated database maintained by Finnish National Institute for Health and Welfare that contains hospital discharge diagnosis codes of all medical admissions in Finland, for patients hospitalized with a primary diagnosis of acute myocardial infarction (ICD-10 codes I21.0-49).

The study period was from June 1st 2005 up to May 31st 2009 and the search covered all University Hospitals (n=5) and Central Hospitals (n=17) in Finland (2007 population 5,300,484) along with eight of the largest district hospitals. Secondary diagnoses of the admission were used to identify comorbidities.

The data was divided into two main time periods: pre-legislation (from July 1st 2005 to May 31st 2007) and post-legislation (June 1st 2007 to May 31st 2009). For evaluation of the immediate implications of the legislation the period was divided into 6 month periods. Data on smoking prevalence in the general population by gender, age and year were obtained from Statistics Finland (www.tilastokeskus.fi), the national authority conducting continuous smoking surveillance in Finland. The smoking data are nationwide and include all age groups.

Statistical methods

The continuous variables were described in terms of mean and standard deviation. Categorical variables were presented as frequencies and proportions (percentages). Generalized linear model was fitted using Poisson distribution to describe the count of infarctions in terms of incidence rate ratios (IRR). Logarithmically transformed population size was used as an offset parameter. The results were adjusted for gender, age and smoking habits. All analyses were conducted using SAS System for Windows, version 9.4TS1M1 (SAS Institute Inc., Cary, NC, USA). P-values less than .05 were considered as statistically significant.

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Results

There were 656044 hospitalizations on internal medicine wards during the study period of which 34887 were for a primary diagnosis of myocardial infarction.

The incidence rate of AMI was reduced by 6.3% (95%CI 4.1-8.6%; p<0.0001) following the smoking ban when adjusted for age, gender and overall population prevalence of smoking. Reduction in short term incidence of AMI (6 month prior vs. 6 months after the smoking ban) was similar (4.5%, 95% CI 0.2-9.0%; p=0.0399) to that in the whole study period and was most prominent in the oldest age groups but observed also in the working middle aged group (40-50 years old); RR between the latter and first halves of 2007 0.83 (95%CI 0.65-1.08, p=0.16) (figure 1.). Incidence rate ratios for AMI in 6 month intervals are shown in figure 2, with a dotted line representing the implementation of the law.

Patient features and comorbidities prior to and after June 1st 2007 are presented in table 1. A slightly larger proportion of infarction patients were female in the first half of the study period, but declines in infarction rates were similar for males and females over the period. Increasing age and male gender were associated with increased risk for AMI (Table 2). Furthermore, age- and gender specific smoking prevalence in the general population was also associated with occurrence of AMI (Table 2).

Table 1. Comorbidities and characteristics of patients hospitalized between June 2005 and May 2009 for myocardial infarctions in Finland before and after the law banning indoor smoking in restaurants since June 2007.

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Variable	Before June 2007 (n=18487)	After June 2007 (n=16400)	p-value
Age	68.5±11.4	68.3±11.3	0.187
Female gender	6491 (35.1%)	5453 (33.3%)	<0.001
Hypertension	2869 (15.5%)	2615 (15.9%)	0.275
Diabetes	1630 (8.8%)	1464 (8.9%)	0.719
Hypercholesterolemia	1435 (7.8%)	1364 (8.3%)	0.057
Congestive heart failure	1985 (10.7%)	1770 (10.8%)	0.868
Atrial fibrillation	1085 (5.9%)	969 (5.9%)	0.876
Peripheral arterial disease	145 (0.8%)	150 (0.9%)	0.185
Chronic lung disease	447 (2.4%)	357 (2.2%)	0.134
Chronic kidney disease	157 (0.8%)	154 (0.9%)	0.373
Malignancy	191 (1.0%)	169 (1.0%)	0.980
Prior revascularization	666 (3.6%)	553 (3.4%)	0.242
Rheumatoid arthritis	102 (0.6%)	80 (0.5%)	0.408
Thyroid disease	46 (0.2%)	52 (0.3%)	0.229

Table 2. Factors associated with AMI incidence on Poisson regression in Finland between June 2005 and May 2009.

Variable	IRR	95% confidence interval	p
Age (per year)	1.050	1.048-1.051	<0.0001
Male gender	1.578	1.536-1.621	<0.0001

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Period before June 1st 2007 *	1.063	1.041-1.086	<0.0001
Higher smoking prevalence per %	1.031	1.028-1.034	<0.0001

IRR=incidence rate ratio. *: a nationwide legislation banning indoors smoking in restaurants was implemented on June 1st 2007. §: age and gender –adjusted yearly nationwide smoking prevalence in the population aged 15 years and older.

Myocardial infarction presented with ST-segment elevation (STEMI) in 37% (n=12923) of patients. The ratio between STEMI and non-STEMI did not change over the study period.

Discussion

This nationwide study associates a nationwide ban on indoors tobacco smoking in public places with an immediate 4.5% reduction and a longer-term 6.3% reduction in the incidence rate of myocardial infarctions on a population level in Finland. The reduction of AMI rate was most notable in the oldest age-groups but also noted in the working-aged population 40-50 years of age. No difference in rate reduction between genders was found nor did the ratio of STEMI to NSTEMI change.

A previous meta-analysis of studies on the effect of indoors smoking bans showed an average reduction of 17% in AMI incidence with individual studies ranging between a non-significant increase and a 50% reduction.[7-13] The current study demonstrated only a 4.5% reduction in AMI incidence when comparing the first and latter halves of the year 2007 and a 6.3% reduction in longer time scale. The most obvious reason for the modest reduction in our study is that there are differences in the smoking bans: for example in Italy the ban was implemented in all working

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places whereas smoking in other work places than restaurants had been banned since 1995 in Finland making the target population in this study considerably smaller. Moreover, the declining smoking prevalence in Finland was associated with reductions in AMI incidence in the present study, although the countries represented in the meta-analysis by Meyers and colleagues had similar and declining smoking prevalences of 24-29% before implementation of bans. It should be noted that, despite significant improvement attributable to nationwide public health measures in the last decades, Finland has an almost twofold AMI incidence compared to the countries describing reductions with indoor smoking bans.[14] Thus the absence of a more pronounced effect cannot bet attributed to low rate of vascular events in the population. On the other hand, contrary to many other countries, the proportion of STEMI as the form of AMI has steadily increased in Finland.[15-18] The reason for this is unknown, but considering the pathophysiologic differences of STEMI and NSTEMI [19] one could suppose that population-specific factors might result in differences between clinical outcomes of smoking bans in different countries. However, we did not find support for proposition as our results show no change in the ratio of STEMI vs. NSTEMI over the study period.

The reduction in AMI incidence following the ban was greatest in the age group 40-50 years which includes both restaurant patrons and a large proportion of the approximately 43,000 persons who were classified as restaurant staff in 2008 (data obtained from the Finnish Ministry of Education). It is conceivable that the new legislation could have deterred smoking in a number of active smokers among this populace and thus further reduced both first hand and environmental exposure to tobacco smoke both in- and outside restaurants. The fact that tobacco smoking prevalence decreased markedly in persons aged 25-60 between 2007 and 2008 (Finnish National Institute for Health and Welfare Tobacco Statistics 2014) lends support to the aforementioned hypothesis.[20] This could also explain why there was no reduction in age groups 60-70 years of age as no decline

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but rather an increase in smoking prevalence was observed for them. Furthermore, the decline in smoking prevalence was greater in those 40-50 years of age compared to those 50-60 years of age. Additionally, we do not have data as to when exactly during the study period the decline has taken place and possible differences in the temporal pattern of quitting smoking could explain the differences. Even greater declines were observed in the population below 40 years of age, but the marginal incidence of AMI in these age groups probably explains the lack of effect on AMI incidence. Non-smoking rapidly halves the risk of myocardial infarction.[21] In 2007 out of restaurant waiters and bartenders, 37% and 67% respectively would have been exposed for over 4 hours per shift to environmental tobacco smoke and about 28% were active smokers.[22] Previous studies have already showed that the 2007 ban was effective in reducing environmental exposure and consequently symptoms in restaurant workers.[23] This reduction in occupational exposure alone should translate into some hundreds of myocardial infarctions less per year such as shown in the results of this study.

Interestingly, also the oldest age groups from 70 years up showed reduced rates of AMI following the ban in our study. As people of this age do not frequent restaurants and bars and showed no decline in smoking prevalence following the ban it seems there must be some other explanation for their reduced risk. Indeed, earlier studies have shown that up to 67% of the reduction in AMI incidence after smoking bans may be accounted for by non-smokers [13] and these effects may be conveyed by the decreased smoking of carers and relatives in the case of the elderly. Considering that the risk of AMI rises with age [24] it seems probable that elderly people are also more sensitive to external AMI triggers than younger ones. Nevertheless, the decline in AMI incidence in European populations over the last decades has been shown to be more pronounced in the age group of 65-74 years compared to those 35-64 years of age [25] and this may confound the results of the

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elderly. The fact that we found no change in the AMI risk of those 60-70 years of age nonetheless limits the propability of this confounding.

Limitations of this study are those inherent to a retrospective registry study; i.e. all confounders cannot be accounted for particularly as the study group had no access to individual patient records but only the information contained in the CRHC, which, however has been validated for AMI patients.[26] As our data consisted only of those AMI patients who were admitted, those who died prior to hospitalization were not included. Whereas other studies that have shown a negligible effect of indoor smoking bans on AMI incidence have speculated that the modest effect might have been due to short follow up periods,[8, 27, 28] the present study had an extensive observation period and our results are comparable both in the short and long term adding to the strength of our study. However, even as the association of the smoking ban with reduction in AMI rate is evident in this study the prolonged effects are harder to discern especially as there was a nationwide public health project from 2000 to 2010 aimed at improving outcomes of diabetes; this project has no doubt affected AMI rates in addition to other outcomes.[29] Lastly, the effect of environmental tobacco smoke exposure on the risk of cardiovascular disease is dependent both on the dose and duration of exposure.[4] Our ecological study design does not allow accounting for these factors so our interpretation focuses on the population level. We found incidence of MI diagnoses to decrease in the first half of 2006 compared to 2005. Although reason for this remains speculative, it may be related to transition phase in more widespread use of non-high sensitivity troponin assays in MI diagnosis.

Conclusions

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Legislative measures stopping indoor smoking in restaurants and other public spaces coincided with an incremental reduction in the incidence of acute myocardial infarctions on a national level in Finland. Although these results suggest that in a country with an already implemented prohibitive legislation on workplace smoking the incidence of AMI can still be, albeit modestly, reduced with a ban on restaurant smoking factors associated with the continual decline of AMI incidence may also explain this.

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Competing Interests

The authors declare no competing interests relevant to the study.

Contributor

JG prepared and submitted the manuscript which all other authors had commented and helped revise. JS, PR and VK planned the study. TK and JG analyzed the data. TK prepared the figures. JS prepared the revision which all other authors commented.

Data sharing

No additional data available.

Ethics approval

Approved by the Finnish National Institute for Health and Welfare.

What this paper adds

- This study suggests that in a country with previous extensive bans on public and workplace smoking the addition of a restaurant ban may further reduce myocardial infarction incidence on a nationwide level.

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- The reduction in myocardial infarction incidence rate is sustained over a 2.5-year observation period following the ban but this may be confounded by the continual decline of AMI incidence.
- The reduction in AMI incidence can be observed both in elderly and working-age populations.

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LEGENDS FOR FIGURES

Figure 1. Incidence of hospitalization for acute myocardial infarction in Finland. June 1st 2007 was the implementation of a nationwide restaurant smoking ban.

Figure 2. Incidence rate ratios of acute myocardial infarction for 6 month intervals in Finland. Dotted line indicates implementation of a new law banning smoking in restaurants. 1 indicates first half of year and 2 the latter half (e.g. 2009/1 and 2009/2).

Figure 3. The proportion of smokers according to age group in the Finnish population in the pre-ban (from July 1st 2005 to May 31st 2007) and post-ban (June 1st 2007 to May 31st 2009) study periods.

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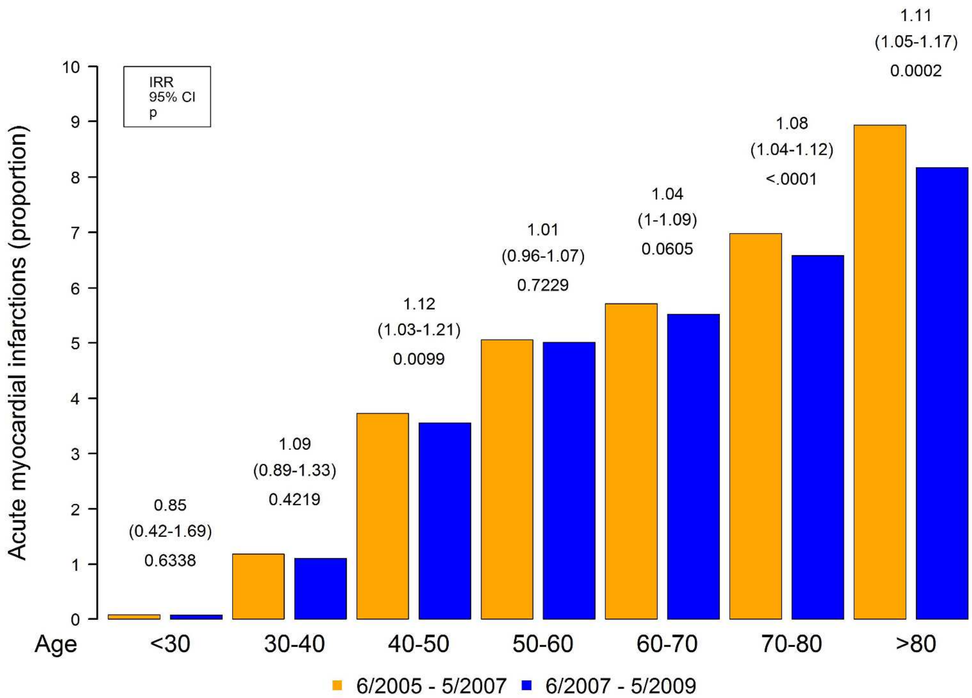

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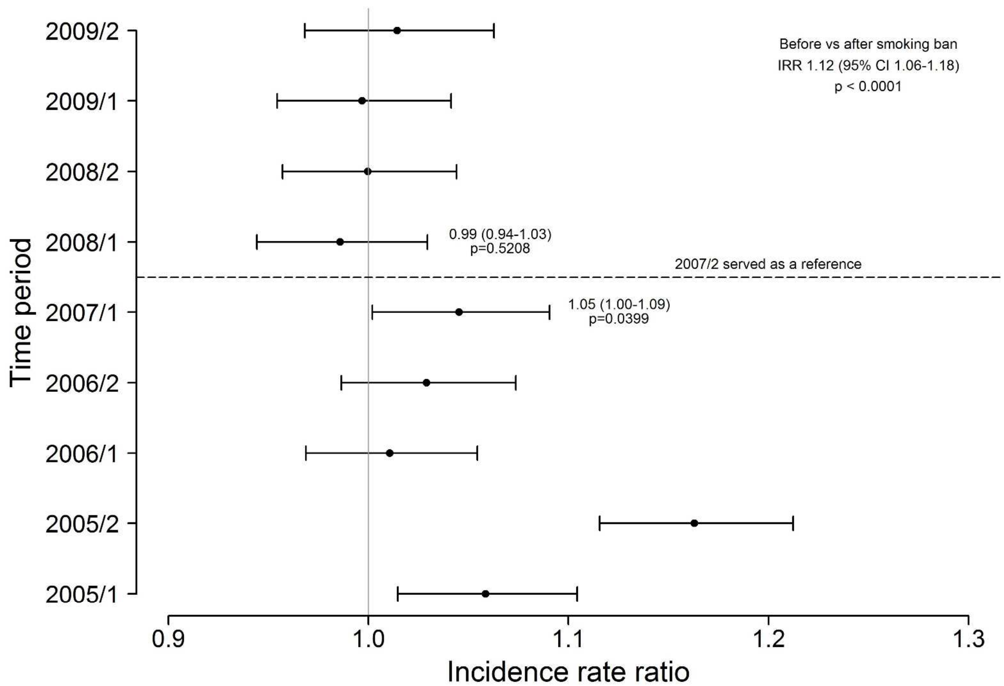

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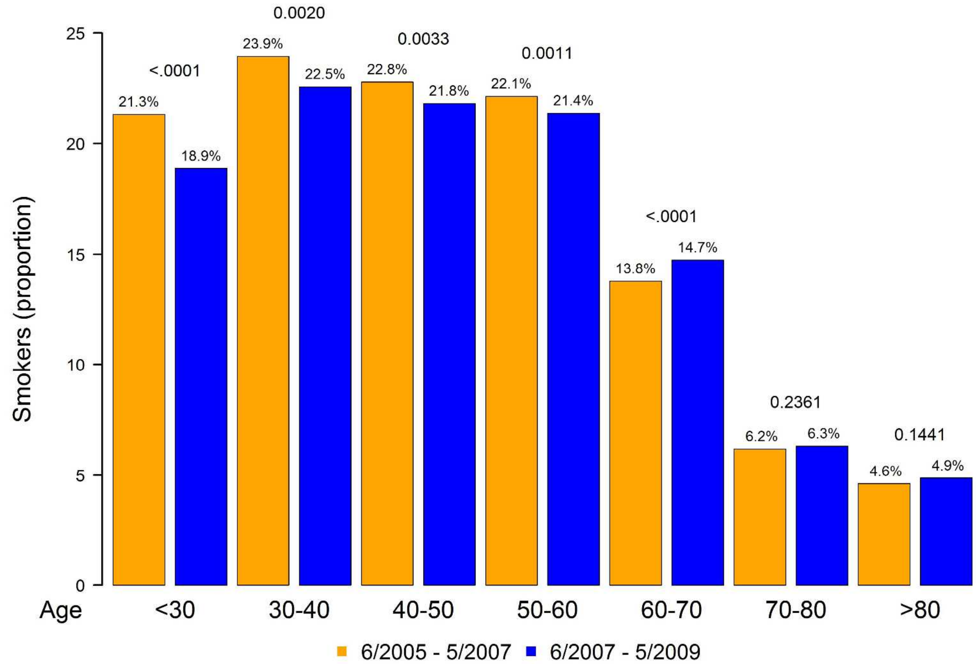

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The following checklist has been completed to the extent necessary for the current study.

Jarmo Gunn, MD

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

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Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Secondary Subject Heading:	Cardiovascular medicine, Epidemiology
Keywords:	PUBLIC HEALTH, Cardiac Epidemiology < CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Ischaemic heart disease < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

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Association of restaurant smoking ban and the incidence of acute myocardial infarction in Finland.

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Word count: 3732

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Key words: tobacco, second hand smoke, acute myocardial infarction

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Abstract

Objective

To describe the changes in nationwide acute myocardial infarction (AMI) incidence following the implementation of a law banning smoking indoors in restaurants on June 1st 2007.

Methods

Retrospective registry study of all hospitalizations for AMI in Finland. All 34887 hospitalizations for AMI between June 1st 2005 and May 31st 2009 were identified from the Care Register for Health Care (CRHC) and statistics for tobacco consumption were obtained from the National Institute for Health and Welfare. Comorbidities for individual hospitalizations were searched from the CRHC.

Results

The incidence rate of AMI was reduced by 6.3% (95% CI 4.1-8.6%; p<0.0001) in the latter half of the study period following the smoking ban when adjusted for age, gender and overall population prevalence of smoking. Short term incidence of AMI (6 month prior vs. 6 months after the smoking ban) was also reduced (4.5%, 95% CI 0.2-9.0%; p=0.0399) and was largest in the working middle aged group (40-50 years old) but observed also in the oldest ages (>70 years) . The incidence rates declined similarly for both men and women.

Conclusion

Banning indoors tobacco smoking in restaurants was associated with a mild additional reduction in AMI incidence on a nationwide level in Finland.

Strengths and limitations of this study

- This is a study into the effects of a restaurant smoking ban on incidence of acute myocardial infarction (AMI) in a situation where working place smoking is already prohibited. A validated,

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obligatory national registry was used to provide reliable nationwide coverage.

- Limitations of this study include the unavailability of detailed data on tobacco smoke exposure, medication or therapies implemented. In addition, our data do not cover patients who died of an AMI prior to reaching hospital.

- The decline in AMI incidence in the oldest age groups after the implementation of the ban may be confounded by the previously reported general decline of incidence in these age groups.

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Introduction

Tobacco smoke exposure, both first hand and environmentally, has been unequivocally linked to an increased risk of ischemic heart disease and acute myocardial infarction (AMI)[1] and the effect is

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seen already at low exposure levels [2, 3] Tobacco smoke increases the risk of acute cardiac events by multiple mechanisms including prothrombotic effects, low-density lipoprotein oxidation, activation of inflammatory pathways and impaired vascular repair.[4-6] A previous Cochrane review suggested that indoor smoking bans have decreased the incidence of AMI on a population level via a decrease in second hand smoking (SHS).[7]

Smoking on workplaces has been prohibited in Finland since 1995. This was followed by a 2-3 % reduction in smoking prevalence in the following year. The ban did not initially include restaurant workers but was extended to cover them in 2000. However, as restaurant customers were still allowed to smoke indoors uninhibited the extension was deemed insufficient to protect restaurant workers and since June 1st 2007 smoking has been prohibited indoors in all public places. Large restaurants were allowed to request for transition time until June 2009 but only 5% of restaurants used this opportunity. Restaurants and other workplaces are allowed to build isolated, air-conditioned smoking cubicles. The aim of this study is to retrospectively assess the effects of the new legislation on the incidence of acute myocardial infarctions in Finland.

Materials and methods

We searched the Care Register for Health Care (CRHC), a nationwide obligatory and automated database maintained by Finnish National Institute for Health and Welfare that contains hospital discharge diagnosis codes of all medical admissions in Finland, for patients discharged from hospital with a primary diagnosis of acute myocardial infarction (ICD-10 codes I21.0-49).

The study period was from June 1st 2005 up to May 31st 2009 and the search covered all University Hospitals (n=5) and Central Hospitals (n=17) in Finland (2007 population 5,300,484) along with eight of the largest district hospitals. This sample includes all Finnish hospitals that have

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a coronary catheterization laboratory and a cardiac care unit (CCU) and to which all acute coronary patients in scope of active treatment are transferred. Secondary diagnoses of the admission were used to identify comorbidities. Patients who had been transferred from one hospital to another were identified and are presented only once in the results.

The data was divided into two main time periods: pre-legislation (from July 1st 2005 to May 31st 2007) and post-legislation (June 1st 2007 to May 31st 2009). For evaluation of the immediate implications of the legislation the period was divided into 6 month periods. Data on smoking prevalence in the general population by gender, age and year were obtained from Statistics Finland (www.tilastokeskus.fi), the national authority conducting continuous smoking surveillance in Finland. The smoking data are nationwide and include all age groups.

Statistical methods

The continuous variables were described in terms of mean and standard deviation. Categorical variables were presented as frequencies and proportions (percentages). Generalized linear model was fitted using Poisson distribution to describe the count of infarctions in terms of incidence rate ratios (IRR). Logarithmically transformed population size was used as an offset parameter. The results were adjusted for gender, age and smoking habits. All analyses were conducted using SAS System for Windows, version 9.4TS1M1 (SAS Institute Inc., Cary, NC, USA). P-values less than .05 were considered as statistically significant.

Results

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There were 656044 hospitalizations on internal medicine wards during the study period of which 34887 were for a primary diagnosis of acute myocardial infarction. The mean age of AMI patients was 68±11 years and majority were male (66 %). Patient features and comorbidities prior to and after June 1st 2007 are presented in Table 1. A slightly larger proportion of AMI patients were female in the first half of the study period.

The incidence rate of AMI was reduced by 6.3% (95% CI 4.1-8.6%; p<0.0001, table 2) in the two years following the smoking ban when compared to the pre-legislation period and adjusted for age, gender and overall population prevalence of smoking (figure 1). Short-term reduction in incidence of AMI was observed already in the six months following the ban (4.5% compared to the preceding six months, 95% CI 0.2-9.0%; p=0.0399, figure 2) , andwas most prominent in the working middle aged group (40-50 years old) but observed also in the oldest age groups of over 70 years of age

. Increasing age and male gender were associated with increased risk for AMI (Table 2). Furthermore, age- and gender specific smoking prevalence in the general population (Figure 3) was also associated with occurrence of AMI (Table 2). Acute myocardial infarction presented with ST-segment elevation (STEMI) in 37% (n=12923) of patients. The ratio between STEMI and non-STEMI did not change over the study period.

Table 1. Comorbidities and characteristics of patients hospitalized between June 2005 and May 2009 for acute myocardial infarctions in Finland before and after the law banning indoor smoking in restaurants since June 2007.

Variable	Before June 2007 (n=18487)	After June 2007 (n=16400)	p-value
Age	68.5±11.4	68.3±11.3	0.187

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Female gender	6491 (35.1%)	5453 (33.3%)	<0.001
Hypertension	2869 (15.5%)	2615 (15.9%)	0.275
Diabetes	1630 (8.8%)	1464 (8.9%)	0.719
Hypercholesterolemia	1435 (7.8%)	1364 (8.3%)	0.057
Congestive heart failure	1985 (10.7%)	1770 (10.8%)	0.868
Atrial fibrillation	1085 (5.9%)	969 (5.9%)	0.876
Peripheral arterial disease	145 (0.8%)	150 (0.9%)	0.185
Chronic lung disease	447 (2.4%)	357 (2.2%)	0.134
Chronic kidney disease	157 (0.8%)	154 (0.9%)	0.373
Malignancy	191 (1.0%)	169 (1.0%)	0.980
Prior revascularization	666 (3.6%)	553 (3.4%)	0.242
Rheumatoid arthritis	102 (0.6%)	80 (0.5%)	0.408
Thyroid disease	46 (0.2%)	52 (0.3%)	0.229

Table 2. Factors associated with AMI incidence in Finland between June 2005 and May 2009.

Variable	IRR	95% confidence interval	p
Age (per year)	1.050	1.048-1.051	<0.0001
Male gender	1.578	1.536-1.621	<0.0001
Period before June 1st 2007 *	1.063	1.041-1.086	<0.0001
Higher smoking prevalence per % §	1.031	1.028-1.034	<0.0001

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IRR=incidence rate ratio. *: a nationwide legislation banning indoors smoking in restaurants was implemented on June 1st 2007. §: age and gender –adjusted yearly nationwide smoking prevalence in the population aged 15 years and older.

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Discussion

This study associates a nationwide ban on indoors tobacco smoking in public places with an immediate 4.5% reduction and a longer-term 6.3% reduction in the incidence rate of acute myocardial infarctions on a population level in Finland. The reduction of AMI rate was most notable in the working-age population 40-50 years of age but observed also in people >70 years of age. . No difference in rate reduction between genders was found nor did the ratio of STEMI to NSTEMI change.

A previous meta-analysis of studies on the effect of indoors smoking bans showed an average reduction of 17% in AMI incidence with individual studies ranging between a non-significant increase and a 50% reduction.[7-13] The current study demonstrated only a 4.5% reduction in AMI incidence when comparing the first and latter halves of the year 2007 and a 6.3% reduction in longer time scale. The most obvious reason for the modest reduction in our study is that there are differences in te smoking bans: for example in Italy the ban was implemented in all working places whereas in Finland smoking in other work places than restaurants had been banned since 1995 making the target population in the present study considerably smaller. Moreover, the declining smoking prevalence in Finland was associated with reductions in AMI incidence in the present study, although the countries represented in the meta-analysis by Meyers and colleagues had similar and declining smoking prevalences of 24-29% before implementation of bans. It should be noted that, despite significant improvement attributable to nationwide public health measures in the last decades, Finland has an almost twofold AMI incidence compared to the countries describing reduced AMI incidence following indoor smoking bans.[14] Thus the absence of a more pronounced effect cannot bet attributed to low rate of vascular events in the population. On the other hand, contrary to many other countries, the proportion of STEMI as the form of AMI has

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steadily increased in Finland.[15-18] The reason for this is unknown, but considering the pathophysiologic differences of STEMI and NSTEMI [19] one could suppose that population-specific factors might result in differences between clinical outcomes of smoking bans in different countries. However, our results showed no change in the ratio of STEMI vs. NSTEMI over the study period.

The reduction in AMI incidence following the ban was greatest in the age group 40-50 years which includes both restaurant patrons and a large proportion of the approximately 43,000 persons who were classified as restaurant staff in 2008 (data obtained from the Finnish Ministry of Education). It is conceivable that the new legislation could have deterred smoking in a number of active smokers among this populace and thus further reduced both first hand and environmental exposure to tobacco smoke both in- and outside restaurants. The fact that tobacco smoking prevalence decreased markedly in persons aged 25-60 between 2007 and 2008 (Finnish National Institute for Health and Welfare Tobacco Statistics 2014) lends support to the aforementioned hypothesis.[20] This could also explain why there was no reduction of AMI incidence in age groups 60-70 years of age as their smoking prevalence rather showed an increase . Furthermore, the decline in smoking prevalence was greater in those 40-50 years of age compared to those 50-60 years of age. Additionally, we do not have data as to when exactly during the study period the decline has taken place and possible differences in the temporal pattern of quitting smoking could explain the differences. Even greater declines of smoking prevalence were observed in the population below 40 years of age, but the marginal incidence of AMI in these age groups probably explains the lack of effect on AMI incidence. Non-smoking rapidly halves the risk of myocardial infarction.[21] In 2007, an environmental tobacco smoke exposure of over four hours per shift occurred for 37% of restaurant waiters and 67% of bartenders and about 28% of restaurant workers were active smokers.[22] Previous studies have already showed that the 2007 ban was effective in reducing

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environmental exposure and consequently symptoms in restaurant workers.[23] This reduction in occupational exposure alone should translate into some hundreds of acute myocardial infarctions less per year such as shown in the results of this study.

Interestingly, also the oldest age groups from 70 years up showed reduced rates of AMI following the ban in our study. As people of this age do not frequent restaurants and bars and showed no decline in smoking prevalence following the ban it seems there must be some other explanation for their reduced risk. Indeed, earlier studies have shown that up to 67% of the reduction in AMI incidence after smoking bans may be accounted for by non-smokers [13] and these effects may be conveyed by the decreased smoking of carers and relatives in the case of the elderly. Considering that the risk of AMI rises with age [24] it seems probable that elderly people are also more sensitive to external AMI triggers than younger ones. Nevertheless, the decline in AMI incidence in European populations over the last decades has been shown to be more pronounced in the age group of 65-74 years compared to those 35-64 years of age [25] and this may confound the results of the elderly. The fact that we found no change in the AMI risk of those 60-70 years of age nonetheless limits the propability of this confounding.

Limitations of this study are those inherent to a retrospective registry study; i.e. all confounders cannot be accounted for particularly as the study group had no access to individual patient records but only the information contained in the CRHC, which, however has been validated for AMI patients.[26] As our data consisted only of those AMI patients who were admitted, those who died prior to hospitalization were not included. Whereas other studies that have shown a negligible effect of indoor smoking bans on AMI incidence have speculated that the modest effect might have been due to short follow up periods,[8, 27, 28] the present study had an extensive observation period and our results are comparable both in the short and long term adding to the strength of our study.

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However, even as the association of the smoking ban with reduction in AMI rate is evident in this study the prolonged effects are harder to discern especially as there was a nationwide public health project from 2000 to 2010 aimed at improving outcomes of diabetes; this project has no doubt affected AMI rates in addition to other outcomes.[29] Lastly, the effect of environmental tobacco smoke exposure on the risk of cardiovascular disease is dependent both on the dose and duration of exposure.[4] Our ecological study design does not allow accounting for these factors so our interpretation focuses on the population level. We found incidence of AMI diagnoses to decrease in the first half of 2006 compared to 2005. Although reasons for this remain speculative, it may be related to transition phase in more widespread use of non-high sensitivity troponin assays in AMI diagnosis.

Conclusions

Legislative measures stopping indoor smoking in restaurants and other public spaces coincided with an incremental reduction in the incidence of acute myocardial infarctions on a national level in Finland. These results suggest that in a country with an already implemented prohibitive legislation on workplace smoking the incidence of AMI can still be, modestly reduced with a ban on restaurant smoking. However, factors associated with the continual decline of AMI incidence may also explain this finding to some extent.

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Competing Interests

The authors declare no competing interests relevant to the study.

Contributor

JG prepared and submitted the manuscript which all other authors had commented and helped revise. JS, PR and VK planned the study. TK and JG analyzed the data. TK prepared the figures. JS prepared the revisions which all other authors commented.

Data sharing

No additional data available.

Ethics approval

Approved by the Finnish National Institute for Health and Welfare.

What this paper adds

- This study suggests that in a country with previous extensive bans on public and workplace smoking the addition of a restaurant ban may further reduce acute myocardial infarction incidence on a nationwide level.

- The reduction in acute myocardial infarction incidence rate is sustained over a 2.5-year observation period following the ban but this may be confounded by the continual decline of AMI incidence.

- The reduction in AMI incidence can be observed both in elderly and working-age populations.

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LEGENDS FOR FIGURES

Figure 1. Incidence of hospitalization for acute myocardial infarction in Finland. June 1st 2007 was the implementation of a nationwide restaurant smoking ban.

Figure 2. Incidence rate ratios of acute myocardial infarction for 6 month intervals in Finland. Dotted line indicates implementation of a new law banning smoking in restaurants. 1 indicates first half of year and 2 the latter half (e.g. 2009/1 and 2009/2).

Figure 3. The proportion of smokers according to age group in the Finnish population in the pre-ban (from June 1st 2005 to May 31st 2007) and post-ban (June 1st 2007 to May 31st 2009) study periods.

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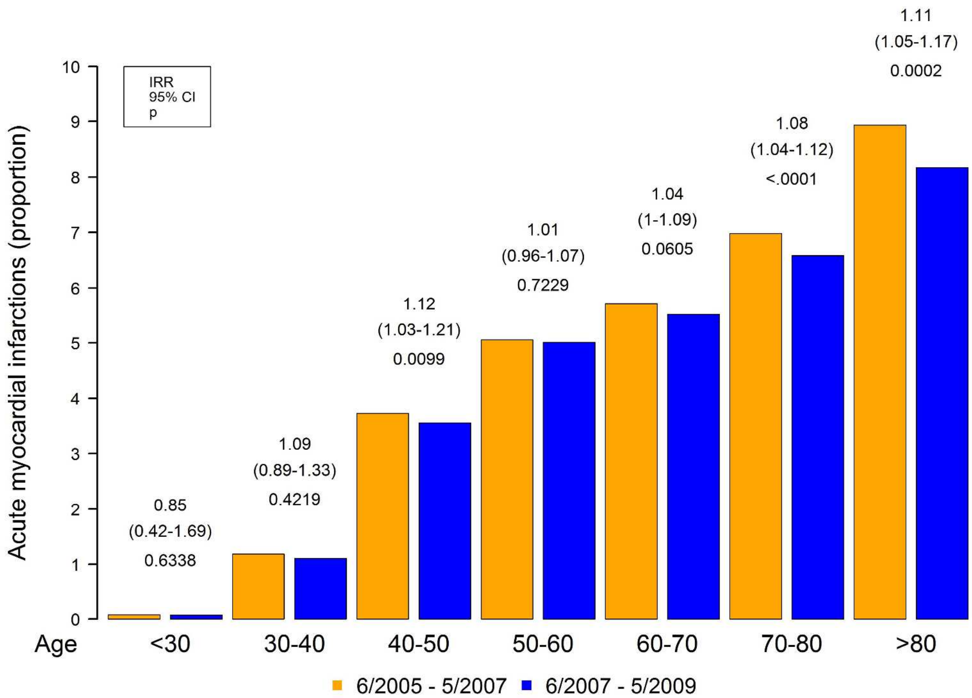

Figure 1. Incidence of hospitalization for acute myocardial infarction in Finland. June 1st 2007 was the implementation of a nationwide restaurant smoking ban.
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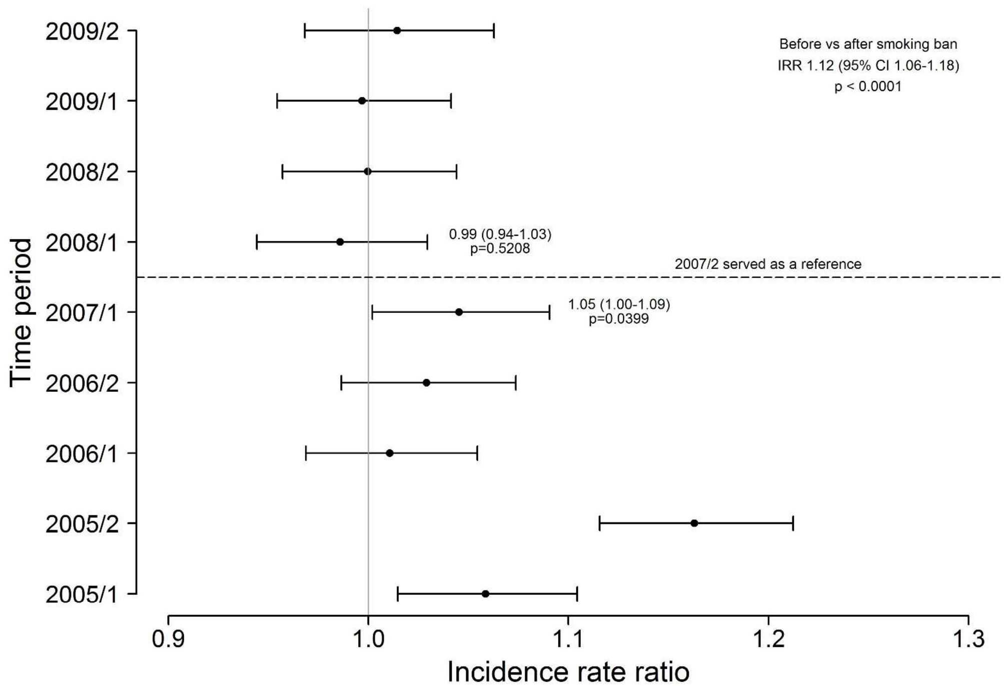

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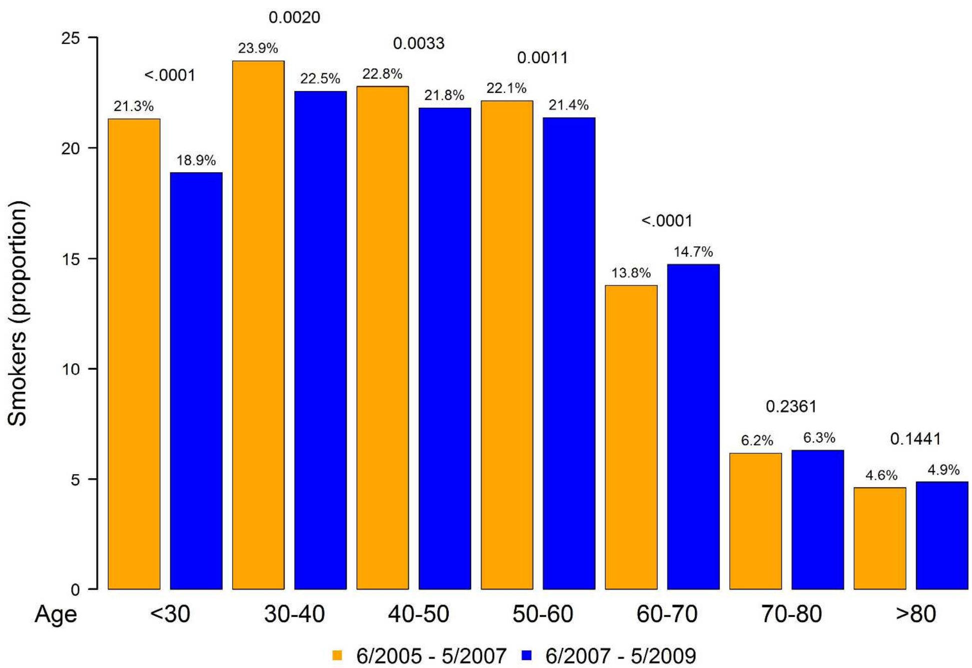

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The following checklist has been completed to the extent necessary for the current study.

Jarmo Gunn, MD

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

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Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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