

QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES

Cardiovascular Effect of Bans on Smoking in Public Places

A Systematic Review and Meta-Analysis

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Objectives	A systematic review and a meta-analysis were performed to determine the association between public smoking bans and risk for hospital admission for acute myocardial infarction (AMI).
Background	Secondhand smoke (SHS) is associated with a 30% increase in risk of AMI, which might be reduced by prohibiting smoking in work and public places.
Methods	PubMed, EMBASE, and Google Scholar databases plus bibliographies of relevant studies and reviews were searched for peer-reviewed original articles published from January 1, 2004, through April 30, 2009, using the search terms “smoking ban” and “heart” or “myocardial infarct.” Investigators supplied additional data. All published peer-reviewed original studies identified were included. Incidence rates of AMI per 100,000 person-years before and after implementation of the smoking bans and incidence rate ratios (IRRs) with 95% confidence intervals (CIs) were calculated. Random effects meta-analyses estimated the overall effect of the smoking bans. Funnel plot and meta-regression assessed heterogeneity among studies.
Results	Using 11 reports from 10 study locations, AMI risk decreased by 17% overall (IRR: 0.83, 95% CI: 0.75 to 0.92), with the greatest effect among younger individuals and nonsmokers. The IRR incrementally decreased 26% for each year of observation after ban implementation.
Conclusions	Smoking bans in public places and workplaces are significantly associated with a reduction in AMI incidence, particularly if enforced over several years. (J Am Coll Cardiol 2009;54:1249–55) © 2009 by the American College of Cardiology Foundation

Secondhand smoke (SHS) increases the risk of acute myocardial infarction (AMI) by 25% to 31% (1–5). In countries where smoking prevalence is high, for example, Britain 50% (6), Europe 62% (7), and Greece 156% (8), versus 22% in the U.S. (2,9), AMI in nonsmokers is particularly increased. The dose-response relationship between SHS and AMI is nonlinear, increasing rapidly even at low concentrations (10–12). Bans on smoking in public places and workplaces have been instituted in several countries, 32 U.S. states, and many cities and counties in the U.S. We performed a systematic literature review and meta-analysis to estimate the overall effect of public (workplace and public place) smoking bans on the risk of AMI in the general population.

Methods

We searched PubMed, EMBASE, and Google Scholar from January 1, 2004, through April 30, 2009, using the

search terms “smoking ban” and “heart” or “myocardial infarct” and reviewed pertinent bibliographies. One unpublished abstract and 1 nonpeer-reviewed report were excluded, leaving 11 peer-reviewed published studies concerning 10 geographic locations. Duplicate data abstracting was performed by 2 authors (D.G.M. and J.S.N.). Only AMI cases were included (some investigators supplied additional data), except where the case definition was acute coronary syndrome (ACS), which required an elevated serum troponin.

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To avoid duplicate cases (Piedmont and Latium [Rome] were separately reported), only the regions of Friuli Venezia Giulia (Trieste) and Campania (Naples) were analyzed from the Italian study of 4 regions. Results were converted to incidence rates (new cases/100,000 person-years) using the most recent official census and including all age groups.

Meta-analysis used the random-effects model in the *metan* statistical package in STATA version 10 (Stata Corp., College Station, Texas) (13) because heterogeneity was significant in the fixed effects model ($p < 0.001$). Unlike previously pub-

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Abbreviations and Acronyms

- ACS** = acute coronary syndrome
- AMI** = acute myocardial infarction
- CI** = confidence interval
- ICD** = International Classification of Diseases
- IRR** = incidence rate ratio
- SHS** = secondhand smoke

lished meta-analyses, which used average yearly incidence rates (14,15), we weighted studies by person-years, thus considering both population size and duration of observation, and assumed that the incidence of AMI satisfied a Poisson process (16). Because the funnel plot showed systematic heterogeneity among the study results, we performed a meta-regression analysis using the *metareg* package of STATA 10

to examine whether the estimate of incidence rate ratio (IRR) depends on such factors as post-ban duration, population size, or region (U.S. or non-U.S.).

Results of the Systematic Review

Abstractor agreement was 100%. Results are summarized in Table 1. All studies reported decreases in incidence (at least in a subgroup), with the largest decreases observed in the U.S. Table 2 lists important study parameters based on the Newcastle-Ottawa scale (17). No study had all parameters, although the Scotland study had nearly all. All studies excluded transients and matched observation periods by season.

Helena, Montana. This community of 47,154 persons passed a ban on public smoking (all but 2 businesses complied) in June 2002, which was judicially suspended in December 2002 (18). Investigators screened cases of AMI by International Classification of Diseases (ICD) 9th Edition codes (410xx) and confirmed cases by chart review (criteria not published). Incidence decreased from 170 to 102 cases/100,000 person-years, then returned to baseline, a 40% temporary decline. In the surrounding area, incidence increased from 118 to 172 cases/100,000 person-years, an increase of 46%. This was the first study of a public smoking ban and the only study to include data from after a ban was suspended.

Pueblo, Colorado. Pueblo (population 103,648) banned smoking in bars, restaurants, bowling alleys, and business establishments, whereas Colorado Springs (population 370,448), 45 miles distant in El Paso County, did not (19). Cases included a primary diagnosis of AMI by ICD-9 code 410xx (with no confirmation by biomarkers) for 18 months before and the initial 18 months during ban enforcement. During the ban, AMI incidence in the city of Pueblo decreased by 27% (257 to 187 cases/100,000 person-years, IRR: 0.73, 95% confidence interval [CI]: 0.64 to 0.82). The surrounding Pueblo County (noncity population 44,103) decreased 15% (135 to 115 cases/100,000 person-years, IRR: 0.85, 95% CI: 0.56 to 1.14). Adjacent El Paso County (population 550,478) experienced a 4% decrease (157 to 150 cases/100,000 person-years, IRR: 0.96, 95% CI: 0.87 to 1.04). An additional 18 months of observation noted a further 19% reduction in Pueblo City (152 cases/100,000 person-years) for an overall 3-year reduction of 41% (IRR: 0.59, 95% CI: 0.49 to 0.70) with no reduction in either Pueblo County (IRR: 1.03, 95% CI: 0.68 to 1.39) or adjacent El Paso County (IRR: 0.95, 95% CI: 0.87 to 1.03) (20). This study used well-separated communities and shared the longest observation period.

New York State. Many communities in New York State (population 18,976,457) had banned public smoking, and the state had increased taxation on tobacco before the July 2003 implementation of a statewide ban on work and public smoking (bars, restaurants, and hospitality venues) (21). A statewide database (252 hospitals) was searched for the primary diagnosis of AMI cases (ICD-9 codes 410.0 to 410.99 with no biomarker confirmation) for 1995 through 2004. The AMI incidence decreased 8%, from 483 (46,332 cases) to 445 cases/100,000 person-years (45,412 cases). Compliance with the ban was 93%. Had there been no local laws, the comprehensive state law would have been associated with a 19% decline in admissions. From 2002 to 2004, New York City smoking prevalence decreased from 21.5%

Table 1 Summary Results of Smoking Bans

Ban Location	Population Exposed to Ban	Post-Ban Observation Period (Yrs)	Pre-Ban Rate*	Post-Ban Rate*	Incidence Rate Change in Ban Area	Incidence Rate Change in Non-Ban Area
U.S.						
Helena	68,140	0.5	170	102	-40%	+46%
Pueblo	698,229	3.0	257	152	-41%	-5%
New York	18,976,457	1.0	483	445	-8%	None
Indiana	239,332	1.5	14	7	-50%	-20%
Ohio	29,636	3.0	277	223	-20%	-5%
Canada						
Saskatoon	202,340	1.0	176	152	-13%	None
Europe						
Piedmont	~4,300,000	0.5	200	204	+2%†	None
Rome	2,663,182	1.0	252	253	0%‡	None
Italy	7,033,451	0.2	159	149	-6%	None
Scotland§	~3,000,000	0.8	129	107	-17%	-4%

*Cases per 100,000 person-years. †The acute myocardial infarction incidence decreased 9.8% in those age <65 years and increased 6.2% in those age >65 years. ‡The acute myocardial infarction incidence decreased 11% in those age <65 years and decreased 8% in those age 75 to 84 years, particularly among men. §The end point was acute coronary syndrome.

Table 2 Important Study Parameters

Location	Prospective Design	Population >1 Million	Follow-Up >1 Yr	AMI Primary Diagnosis	Case Smoking Status Ascertained	SHS Measured	Compliance With the Ban	Smoking Prevalence	Contemporaneous Controls
U.S.									
Helena							×		×
Pueblo			×	×					×
New York		×	×	×		×	×	×	
Indiana			×		×				×
Ohio			×	×					×
Canada									
Saskatoon			×	×			×	×	
Europe									
Piedmont		×		×		×	×	×	
Rome		×	×			×		×	
Italy		×		×					
Scotland	×	×		×	×	×	×		×

AMI = acute myocardial infarction; SHS = secondhand smoke.

to 18.5% (22). Exposure, as measured by salivary cotinine, decreased 47% (23). This is the largest population studied. **Monroe County, Indiana.** Monroe County (population 120,563) banned smoking in all restaurants, retail outlets, and workplaces in 2003, but excluded bars until 2005 (24). Delaware County (population 118,769), 90 miles distant, did not restrict smoking. Cases during 18 months before and during the ban were ascertained by ICD-9 codes for primary and secondary diagnosis of AMI (410.0x to 410.9x) and confirmed with biomarkers. Patients with a “. . .past cardiac procedure. . .” or who had “. . .comorbidity such as hypertension and high cholesterol that could have precipitated acute myocardial infarction. . .” were excluded (24). Case smoking status was ascertained. The AMI incidence decreased 50%, from 14 to 7 cases/100,000 person-years. The Delaware County rate of 15 cases/100,000 person-years declined by 20% to 12 cases/100,000 person-years. The reduction was primarily among nonsmokers, whose admissions decreased 70% (–12 cases, 95% CI: –21.2 to –2.8). The exclusion of subjects with prior cardiac procedures or risk factors likely reduced AMI incidence.

Bowling Green, Ohio. Investigators compared admissions for coronary heart disease (ICD-9 codes 410 to 414 and 428 including angina, heart failure, atherosclerosis, and AMI with no biomarker confirmation) in Bowling Green, Ohio (population 29,636), which banned smoking in workplaces and public places except bars, to admissions in Kent, Ohio (population 27,906), 150 miles distant with no ban (25). Hospital discharge data for 3 years before and after the ban (6 months immediately after ban implementation were excluded) for cases in the 2 cities were obtained from a state database. The AMI incidence in Bowling Green decreased by 19%, from 277 to 223 cases/100,000 person-years ($p = 0.015$). Incidence in Kent did not significantly change (440 cases/100,000 person-years in 1999 to 2002 and 417 cases/100,000 person-years in 2003 to 2005, $p = 0.22$). This

study shared the longest observation period. Only AMI data supplied by the investigators were used.

Saskatoon, Canada. Saskatoon (population 202,340) implemented a smoking ban in all enclosed public places and outdoor seating areas in July 2004. The AMI cases (ICD-9 410.00 to 410.92 and ICD-10 121.1 to 121.9) in the database of the Strategic Health Information Planning Service were identified (no biomarker confirmation) for 1 year during the ban and for the previous 4 years (26). Compliance was 99%. Incidence of AMI decreased 14%, from 176 (95% CI: 165 to 187 cases/100,000 person-years) to 152 cases/100,000 person-years (95% CI: 135 to 169 cases/100,000 person-years). Smoking prevalence was 24% in 2003 and 18% in 2005.

Piedmont, Italy. Italy banned smoking in cafes, restaurants, bars, and discos in 2005. Investigators used ICD-9 codes (410.xx) in the Hospital Discharge Registry of the Piedmont region (population 4,300,000) to identify AMI cases (no confirmation) before and during 5 months after ban initiation (27). Before the ban, an average of 3,581 AMIs were reported between February and June (200 cases/100,000 person-years). During the comparable 5 months of ban enforcement, 3,655 cases were reported (204 cases/100,000 person-years). A decrease was observed only among women <60 years of age (women IRR: 0.75, 95% CI: 0.58 to 0.96; men IRR: 0.91, 95% CI: 0.83 to 1.01). Cases in persons >60 years of age were unchanged (IRR: 1.05, 95% CI: 1.00 to 1.11). The ban was almost universally observed (28), nicotine vapor in public places decreased 90% to 95% (29), cigarette sales declined 8.9% (28), and cigarette consumption decreased 7.6% (28). The investigators suggested a greater effect of the ban on younger people and a lower attributable risk of AMI from smoking among older people (27). This study provided age- and sex-specific data.

Rome, Italy. Investigators in Rome (population 2,663,182), using 2 databases, identified all hospital admissions with a primary or secondary diagnosis of ACS, including AMI (ICD-9-CM code 410.xx without biomarker confirmation)

or other forms of ischemic heart disease (ICD-9-CM code 411) and all out-of-hospital deaths caused by ischemic heart disease, among persons >34 years of age before and after enactment of the smoking ban (30). Pre-ban incidence was 252 cases/100,000 person-years. During the ban, incidence was 253 cases/100,000 person-years. Incidence decreased significantly in 35- to 64-year-old men (IRR: 0.89, 95% CI: 0.85 to 0.93) and in 65- to 74-year-old men (IRR: 0.92, 95% CI: 0.88 to 0.97), but not in 75- to 84-year-old men (IRR: 1.02, 95% CI: 0.98 to 1.07). Among women (30% of AMI cases), the decrease was confined to the young (IRR: 0.90, 95% CI: 0.81 to 1.00 in 35- to 64-year-old women and IRR: 0.95, 95% CI: 0.88 to 1.04 in 65- to 74-year-old women). Decreases occurred in indoor particle and urinary cotinine concentrations and per capita cigarette sales, whereas nicotine replacement product sales increased (31,32). This study adjusted for several confounders, including weather and temporal trends. The meta-analysis used AMI data supplied by the investigators.

Four regions, Italy. The Italian Health Ministry used regional databases to identify cases (age 40 to 64 years) discharged with AMI (ICD-9 code 410.xx, no biomarker confirmation) in 4 regions of Italy with 16,995,734 people (Piedmont, Friuli Venezia Giulia, Latium, and Campania), representing 28% of the Italian population, during corresponding 2-month periods before and during the national ban (33). The AMI incidence decreased 6%, from 159 to 149 cases/100,000 person-years. The preceding years had increasing rates. Reduction in incidence was limited to 45- to 54-year-old men, an 8% decrease. No sex or age group experienced an increase in AMIs. This study had the shortest observation period. The meta-analysis excluded the regions of Piedmont and Latium (Rome), reported separately (27,30).

Scotland. Since March 2006, smoking has been prohibited in all enclosed public places in Scotland (population 5.1 million). Investigators identified all patients admitted to 9 hospitals (catchment area included approximately 3 million persons, accounting for 64% of the country's hospital admissions) for a diagnosis of ACS from June 2005 through March 2006 and for the corresponding 10 months after ban institution (34). An ACS was defined as chest pain with "a detectable level of cardiac troponin," routinely measured in all cases of chest pain. Case smoking status was ascertained by self-report and serum cotinine levels, which allowed estimation of passive exposure to SHS. Results were compared with admissions in England, which did not have a ban. In the 10 months before the ban, 3,235 patients were admitted. After the ban, 2,684 patients were admitted, a 17% decrease (95% CI: 16% to 18%). England experienced a 4% decrease. In Scotland, admissions decreased by 14% in smokers, 19% in former smokers, and 21% in never smokers. The investigators estimated that 67% of the admissions prevented involved nonsmokers. Nonsmokers reporting exposure to SHS decreased from 43% to 22%. Serum cotinine levels decreased by 18%. Compliance was 98%: SHS in bars decreased by 86% within 2 weeks of ban implementation (35). This is the only prospective study and used both direct and indirect measurement of exposure.

Results of the Meta-Analysis

As shown in Figure 1, the overall IRR comparing AMI before and after smoking bans is 0.83 (95% CI: 0.75 to 0.92), indicating that smoking bans on average reduced AMI incidence by 17%.

To further examine the adequacy of a random-effect meta-analysis, a funnel plot of the estimated IRR versus the standard error of natural log of IRR was obtained (Fig. 2).

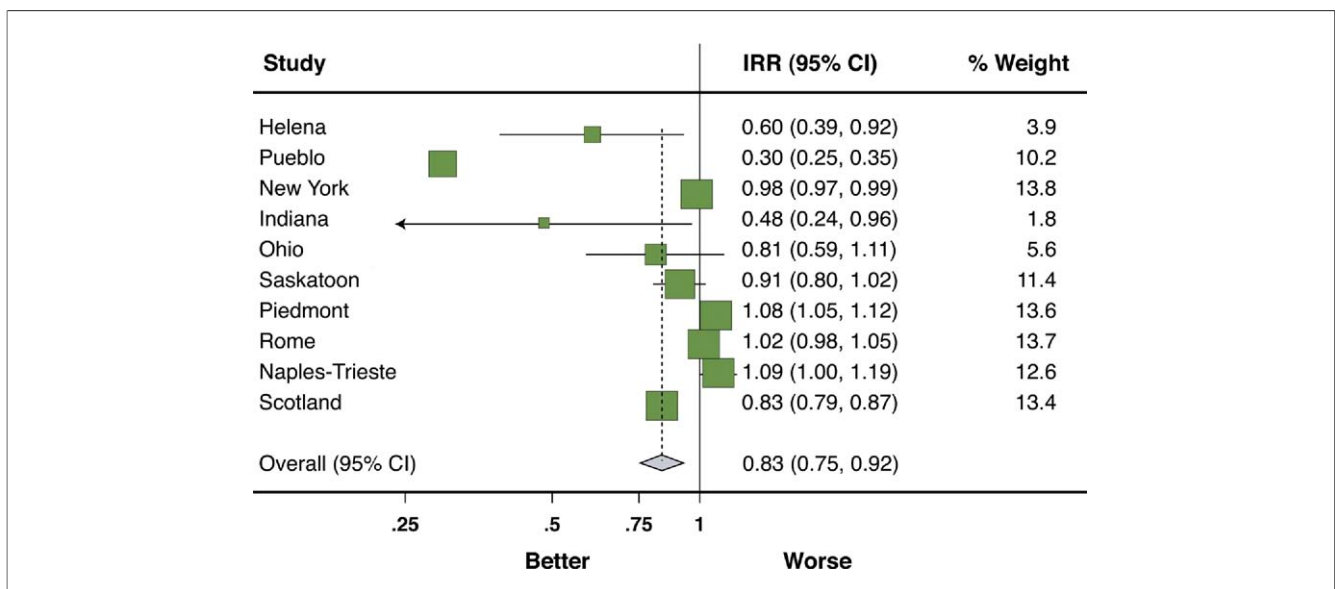


Figure 1 Effects of Community Smoking Bans on Incident Acute Myocardial Infarction (Person-Year Approach)

Meta-analysis results for 11 studies in 10 geographic locations. CI = confidence interval; IRR = incidence rate ratio.

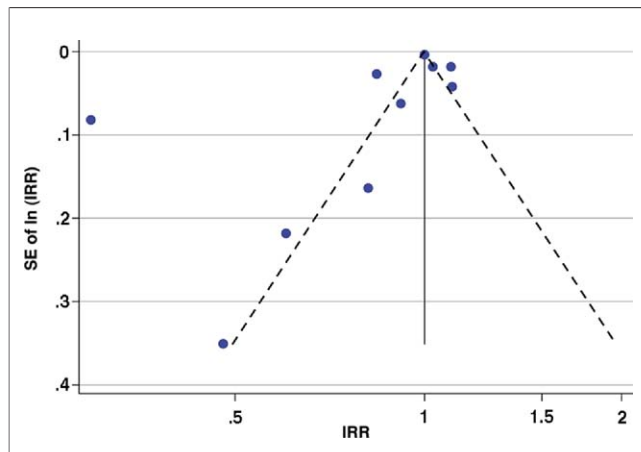


Figure 2 Funnel Plot of Estimated IRRs

A funnel plot with all points evenly distributed on both sides of the **solid vertical line** indicates no publication bias. In this plot there are more points to the **left of the vertical line**, suggesting heterogeneity caused by either variation in length of observation or publication bias. IRR = incidence rate ratio.

The funnel plot shows asymmetry, indicating either publication bias or heterogeneity that cannot be explained by a random-effect meta-analysis. Contact with other investigators has not indicated the presence of unpublished peer-reviewed studies. Meta-regression modeling showed that heterogeneity is at least partially explained by variation in population size and observation duration.

We notice that studies with smaller effect sizes (IRR close to 1.0) include all non-U.S. studies and the New York State study, all of which have large populations and short post-ban durations (≤ 1 year). Meta-regression analysis was used to examine whether region (U.S. or non-U.S.), population size, and post-ban duration affect IRR. When tested separately the effect of population size is not significant ($p = 0.19$), whereas both post-ban duration ($p = 0.002$) and region (U.S. vs. non-U.S., $p = 0.03$) are significant. Post-ban duration becomes borderline significant ($p = 0.096$) and region becomes not significant ($p = 0.399$) when they are included in the same model. Because the effect of bans may not be maximal in ≤ 1 year, it is likely that post-ban observation time is inversely related to IRR (effect size). This relationship is shown in **Figure 3**, in which the trend line illustrates the overall relationship between the estimated IRR and post-ban duration estimated by meta-regression analysis. The size of each bubble is proportional to the weight of the study (the inverse of the standard deviation of the natural log of IRR). The coefficient of post-ban duration in the meta-regression model is -0.30 (95% CI: -0.49 to 0.11), meaning that the IRR decreases by 26% (95% CI: 10% to 39%) for each year of post-ban observation (e.g., IRR: 0.74 after 1 year, then 0.55, then 0.41 compared with pre-ban).

Discussion

This meta-analysis of 11 studies in 10 locations suggests that community smoking bans are associated with an overall

17% reduction in risk of AMI. This is consistent with reductions of 5% to 19% predicted by modeling (36,37). A meta-analysis of the 4 earliest studies reported a relative risk (RR) of 0.73 (14). Subsequent meta-analysis by the same author (15) included 8 studies (including an unpublished report noting an 11% decrease in ACS (38), which was not used in the current analysis) and yielded a pooled risk reduction estimate of 19% (95% CI: 14% to 24%). The large studies from the Italian Piedmont (27), 4 regions (33), and Scotland (34), which observed smaller effects than the earlier American studies, had not yet been published.

In New York, local laws were enacted beginning in 1995, before the implementation of a statewide law on July 24, 2003. Our analysis may capture only the additive effect of this state law, in addition to local laws, rather than the cumulative effect of local and state laws together. Because 1995 is the year within 1995 to 2004 that is affected the least by local laws, we reanalyzed the data using only 1995 as the pre-ban period, versus 2004 as the post-ban period. The estimated IRR for New York State is only slightly smaller than the original estimate based on all data within 1995 to 2004 (0.97 vs. 0.98).

The evidence for an association between smoking bans and reduced AMI incidence is strengthened by beneficial changes in several intermediate factors: high levels of compliance with bans (28,35,39), decreased smoking prevalence and sales of tobacco (20,28,32), improved air quality (29,31,35), and reduced environmental exposure to tobacco smoke (28–30,35,40). Noteworthy is the Helena study (18), which documented a return to the pre-ban AMI incidence rate in the 6 months after suspension of the ban.

Two studies determined the smoking status of AMI cases (24,34). The Indiana study (24) observed a 70% decline in nonsmokers compared with no change among smokers,

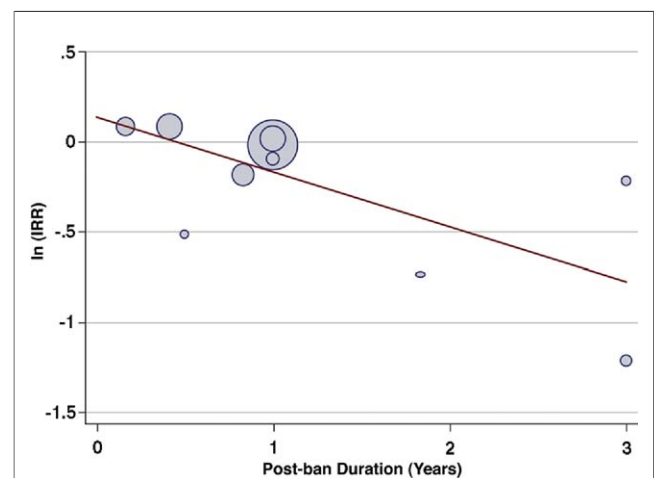


Figure 3 Bubble Plot of Estimated Effects of Smoking Bans (Log of IRR) and the Post-Ban Duration (Years)

The **size of the bubbles** indicates the weight of each study in the meta-analysis. The **trend line** indicates the degree to which the incidence rate ratio (IRR) decreases as the duration of the post-ban period increases.

whereas the Scottish study (34) noted a 19% to 21% decrease in admissions among nonsmokers and a 14% decrease among smokers.

The Italian 4 regions study (33) observed a reduced risk in men only, whereas the Piedmont region (27) and Scotland (34) studies experienced a larger decrease in women. A greater benefit in men might be attributed to their higher prevalence of smoking, allowing for a larger percentage to quit. In Italy, men were more likely than women to quit smoking after the ban (41). Because the workforce has proportionately more men, workplace bans might have a greater effect on SHS exposure among men. Yet, a greater post-ban reduction in serum cotinine levels in nonsmoking women (47%) compared with men (37%) in Scotland (34) suggests that exposure decreased more among women. The relative risk associated with smoking is greater in women than men and has a steeper dose response (42).

A greater effect in younger individuals was noted in the studies that evaluated age-specific incidence (27,30,33,34). Smoking bans encourage cessation particularly among young smokers (43–45). Older individuals might benefit less from smoking restrictions in the workplace, bars, and discos. As risk of AMI associated with smoking decreases with age, the largest effect of eliminating SHS would occur in younger persons.

The smaller effect size in the 5 non-U.S. studies (RR: 0.95 vs. 0.75) may be partially explained by their shorter post-ban observation time. Additional causes might include differences in AMI case definition (although a uniform definition has been suggested [46]), lifestyle and diet, smoking prevalence (U.S. 22.1%, Canada 21.3%, Europe 30.0%), and compliance. Yet, studies from Italy (47) and Ireland (48) indicate substantial reductions in SHS exposure.

The beneficial effect of smoking bans seems to be rapid, with declines in AMI incidence within 3 months (33). Among smokers, incident ACS is reduced within days after smoking cessation (11,41). In nonsmokers, even brief exposure to SHS has been associated with changes in platelet activation (49–51), vascular elasticity (52), endothelial function (53), heart rate variability (54), and lipid metabolism (55,56), supporting the biological plausibility of smoking bans' effect on AMI.

The 11 studies are all ecological in design. Such a design is primarily hypothesis generating. Many of these studies differ in case definition, SHS exposure information, smoking prevalence data, and case confirmation. Many were of short-term duration.

The advantage of person-year analysis in the current study is that analysis is based on the actual total counts of AMI events rather than the estimated average rate. Thus, the total variation of incidence over time is considered. One population estimate for each region was used regardless of the pre- and post-ban observation times. This may explain why our estimates of IRR are sometimes different from the RR based on average age-adjusted rate as published in the original reports. With the limited number and durations of

studies, we are unable to ascertain whether the IRR changes associated with post-ban observation time follow a nonlinear pattern, as suggested by the dose-response relationship of SHS to AMI (10–12).

A non-peer-reviewed working paper (57) used U.S. databases and smoking ban implementation dates to model the effect of workplace and public place smoking bans on mortality and AMI admissions. The investigators found no significant effect of these bans in any outcome for any age group. The investigators suggest that the observed benefits in other studies are attributable to the wide variation in incidence related to small samples.

Although additional reports can be expected (e.g., Ireland and France), the 11 reports included represent the current findings. These studies include nearly 24 million people, observed 215,524 cardiac events, and suggest that community smoking bans are associated with a 17% reduction in AMI incidence. If this association represents a cause-and-effect relationship, and assuming approximately 920,000 incident AMIs each year in the U.S., a nationwide ban on public smoking might ultimately prevent as many as 156,400 new AMIs yearly.

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