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Association between Smokefree Legislation and Hospitalizations for Cardiac, Cerebrovascular and Respiratory Diseases: A Meta-Analysis

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Abstract

Background—Secondhand smoke causes cardiovascular and respiratory disease. Smokefree legislation is associated with a lower risk of hospitalization and death from these diseases.

Methods and Results—Random effects meta-analysis was conducted by law comprehensiveness to determine the relationship between smokefree legislation and hospital admission or death from cardiac, cerebrovascular, and respiratory diseases. Studies were identified using a systematic search for studies published before November 30, 2011 using Science Citation Index, Google Scholar, PubMed, and Embase and references in identified papers. Change in hospital admissions (or deaths) in the presence of a smokefree law, duration of follow-up, and law comprehensiveness (workplaces only; workplaces and restaurants; or workplaces, restaurants, and bars) were recorded. Forty-five studies of 33 smokefree laws with median follow-up of 24 months (range 2–57 months) were included. Comprehensive smokefree legislation was associated with significantly lower rates of hospital admissions (or deaths) for all 4 diagnostic groups: coronary events (RR .848, 95% CI .816–.881), other heart disease (RR .610, 95% CI .440–.847), cerebrovascular accidents (RR .840, 95% CI .753–.936), and respiratory disease (RR .760, 95% CI .682–.846). The difference in risk following comprehensive smokefree laws does not change with longer follow-up. More comprehensive laws were associated with larger changes in risk.

Conclusions—Smokefree legislation was associated with a lower risk of smoking-related cardiac, cerebrovascular, and respiratory diseases, with more comprehensive laws associated with greater changes in risk.

Keywords

myocardial infarction; stroke; lung; health care policy; tobacco

Secondhand smoke causes cardiovascular, respiratory, and neoplastic disease in adults, adverse reproductive outcomes in women, and delayed growth and respiratory and infectious disease in children.[1–3] Smokefree legislation, which prohibits smoking in certain

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AUTHOR CONTRIBUTIONS

Both authors had full access to all the data in the study, worked together on the analysis, and take responsibility for the integrity of the data and the accuracy of the data analysis.

CONFLICT OF INTEREST

Neither author has any conflict of interest.

settings, reduces exposure of nonsmokers to secondhand smoke and creates an environment that helps smokers cut down or quit smoking.[4, 5] Because of the large and rapid effects of secondhand smoke on the cardiovascular system,[3, 6] these laws would be expected to lead to reductions in acute myocardial infarctions (AMI) and other cardiac events. Because it is impossible to do a randomized controlled trial of a large scale public policy interventions such as a smokefree law, these laws are studied using interrupted time series analysis, in which one estimates changes following the law, typically after accounting for pre-existing time trends (often including seasonal variation) and other factors.[7] Three prior meta-analyses of the literature confirmed that smokefree laws were followed by immediate reductions in AMI[8, 9] and other cardiac [10] hospitalizations and that effects grew over time. The number of studies on the effect of smokefree laws has rapidly grown since these earlier meta-analyses to include not only AMI but also non-AMI cardiac disease, cerebrovascular accidents, and respiratory disease. These new reports add extended follow-up periods, new study populations and locations, and smokefree laws with varying degrees of comprehensiveness (i.e., workplaces only; workplaces and restaurants only; or workplaces, restaurants, and bars). This paper presents a meta-analysis of these new outcomes, including assessment of a dose-response effect of the comprehensiveness of the laws.

METHODS

Study Identification

Study identification occurred from October 1, 2011 through November 30, 2011. Because there was already an identified literature in this area, we began our search for new studies by using Science Citation Index, Google Scholar and PubMed to identify publications that cited the paper that first reported a drop in AMI after implementation of a smokefree law in Helena, Montana,[11] three recent meta-analyses of AMI or other cardiac outcomes,[8–10] and the first paper identifying a reduction in respiratory (asthma) emergency admissions after a smokefree law.[12] We also searched PubMed and Embase using search terms “smoking ban,” or “smoke-free” or “smokefree” with “legislation” or “law” or “ordinance” with “acute myocardial infarction,” “heart attack,” “asthma,” “respiratory,” “pulmonary,” and “stroke.” Reference lists were reviewed for all papers located as well as for the Institute of Medicine report *Secondhand Smoke Exposure and Cardiovascular Effects*,[3] and the Cochrane review, “Legislative smoking bans for reducing secondhand smoke exposure, smoking prevalence and tobacco consumption.”[4] Finally, we identified relevant reports written by state public health departments and independent researchers through contacts in the tobacco control network. One non-English study[13] was translated from French using Google Translate.

We identified 47 studies: 36 peer-reviewed publications,[11, 12, 14–47] 7 abstracts,[48–54] 1 presentation,[13] and 3 reports by state health departments.[55–57] These studies cover 37 different smokefree laws (10 national, 12 state, and 15 local).

We included studies examining the association between smokefree laws and cardiovascular or respiratory hospitalizations or deaths with sufficient data to calculate the relative risk and confidence interval before and after or, in two studies,[27, 34] localities with and without a law. Two of the 47 studies were excluded because they did not meet these inclusion criteria. One tobacco industry-supported paper[41] comparing trends in AMI death rates in six US states that passed state laws was conducted using nonstandard methodology that did not report or present data that permitted estimating relative risk and confidence intervals. In addition, the analysis was based on a very small number of data points, had very low power to detect changes, and did not account for the presence of a large number of comprehensive local laws in two states (California and New York), all of which bias the results to the null. An abstract[53] based a Malta study was excluded because of discrepancies between the results

reported in text and the figure that could not be resolved; we contacted the authors who reported they had not completed a manuscript based on the abstract.

Three studies performed separate analyses of reductions in hospitalizations following state laws on localities with no prior law versus localities with existing laws.[18, 32, 35] In this situation, we only used the estimates from localities without prior laws only to capture the full effect of the state law. One result for stroke from the New York State study[18] was excluded because no information was available from localities without prior laws; other results from this study were included in our analysis.

Because the risk of coronary heart disease due to smoking decreases with age,[58] in the seven studies that stratified results on age,[14, 20, 21, 26, 32, 36, 50] we used the results for 65 years and younger (or the nearest alternative) for the primary meta-analysis.

For studies that presented estimates for diseases nested within diagnostic categories (e.g. AMI and unstable angina classified under acute coronary syndrome),[14, 44, 47] we used the most disaggregated level of data.

For studies that provide multiple estimates of the change in hospitalization rates for different time periods after law implementation,[15, 17, 23, 28, 38, 42] we used the estimate from the longest follow-up period to prevent double-counting in the meta-analysis. Separately, we performed a metaregression to test whether hospitalization rates changed over time following implementation of the law; in this case, we included all available estimates from various time points. For this regression, when a law was phased in[13, 29, 54] (with restaurant or bar provisions typically taking effect after workplace restrictions), we used only the first implementation phase so that the post-implementation period and risk change associated with the law was measured consistently from the “no law” condition.

After screening all studies and excluding those with missing or incomplete data and those that did not meet inclusion criteria, 43 papers [11–40, 42–52, 54–57] were selected for meta-analysis (Supplementary Tables 1–5, Supplementary Figure 1). The outcomes are AMI, acute coronary syndrome (ACS), acute coronary events (ACE), ischemic heart disease (IHD), angina, coronary heart disease (CHD), sudden cardiac death (SCD), stroke, transient ischemic attack (TIA), chronic obstructive pulmonary disease (COPD), asthma, lung infections, and spontaneous pneumothorax.

Median pre-legislation time was 29.5 months (range 3–99 months); median follow-up time was 24 months (range 2–57 months) (Supplementary Table 6). Laws were categorized based on comprehensiveness: 1) laws applying only to workplaces, 2) workplaces and restaurants, and 3) workplaces, restaurants, and bars. Since many studies looked at more than one law or one disease outcome or stratified results by age or gender, our review collectively yielded 86 risk estimates for the meta-analysis.

Estimates of Risk Reductions Following Laws

Relative risks are estimated taking “no law” as the reference condition. Thirteen studies[11, 13, 16, 29, 35, 37, 38, 44, 49, 51, 52, 55, 56] reported changes in absolute number or rates of disease events rather than the relative risk following implementation of a smokefree law. For these, we used the frequency data published in the paper or obtained by contacting the authors to estimate incidence rate reduction (as an estimate of relative risk) using negative binomial regressions. Models included the effect of the law and, when applicable, seasonality, or they were structured to mirror the analysis in the published study (as detailed in Supplementary Tables 1–4). Thirty-one of the 43 papers accounted for long-term secular trends, 26 by including time as a variable in the analysis and 5 by doing time-matched

comparisons with control communities. Nineteen of the papers included seasonality in their models.

Analysis

All analyses were conducted using two-sided tests with a significance level of $\alpha = 0.05$.

Q tests revealed statistically significant heterogeneity ($p<0.001$) between studies for all outcomes except for acute coronary events (2 studies[20, 50] with borderline heterogeneity, p=.067). To account for this heterogeneity and to employ a more conservative approach, we performed a random effects meta-analysis for each outcome, stratified by comprehensiveness of laws using Stata 10.1 or 9.2 metan.

We performed a random effects metaregression (Stata metareg) with dummy variables for the 13 disease outcomes to determine whether they were similar enough to be grouped into diagnostic categories for further analysis. The regressions (Supplementary Table 7) showed no significant differences between hospital admissions or deaths for:

- Coronary events: AMI, ACS, ACE, IHD
- Other heart disease: Angina, CHD, and out-of-hospital SCD
- Cerebrovascular accident: Stroke and TIA
- Respiratory disease: COPD, asthma, lung infection, and spontaneous pneumothorax

We performed analyses for these 4 diagnostic groups as well as the 13 individual outcomes.

We conducted a random effects metaregression to test whether the risk reduction following smokefree laws increased over time, as previously reported,[8–10] for each outcome and each diagnostic group. For each study, the duration of follow-up post-legislation was used as the time measure.

To test whether the comprehensiveness of a law was associated with greater reductions in hospital admissions (or deaths in 6 cases[14, 20, 24, 32, 50, 54]), we performed a random effects metaregression with comprehensiveness of law as an ordinal variable (0 for workplaces only; 1 for workplaces and restaurants; 2 for workplaces, restaurants and bars) including dummy variables for different outcomes.

We conducted a separate random effects meta-analysis for older people that were excluded from the primary meta-analysis, using results from six studies[14, 20, 26, 32, 36, 50] that reported the risk of coronary events in older populations (median cutoff age 70, range 60–75, Supplementary Tables 1–4).

For 10 studies[21, 23–26, 30, 32, 36, 42, 43] that presented results from gender-stratified analyses, we also conducted meta-analyses for females and males.

Finally, to test for the possibility of publication bias in the meta-analysis, we performed Egger's test, examined a funnel plot (using Stata metafunnel), and conducted a Duval and Tweedie[59] nonparametric trim and fill to estimate the effects of any publication bias (using Stata metatrim for a random effects meta-analysis).

RESULTS

Comprehensive smokefree laws were followed by significant reductions in hospital admissions for AMI, ACS, ACE, IHD, angina, CHD, SCD, stroke, asthma, and lung infection but not TIA, COPD, or spontaneous pneumothorax (Figure 1). Because there were

only a few studies for some of these specific outcomes, we also pooled specific outcomes into 4 diagnostic groups as described in Methods in order to increase the number of studies in each group; comprehensive smokefree laws were followed by significant reductions in hospital admissions for all four diagnostic groups (Figure 2 and Supplementary Figures 2–5).

There was an overall pattern of more comprehensive laws being associated with greater reductions in hospital admissions (p=.001 for individual outcomes, Figure 1, and p=.002 for disease groups, Figure 2).

Contrary to previous findings,[8–10] we did not find that the AMI risk reduction associated with smokefree laws increased with time (p=.537, Supplementary Figure 6) or other disease outcomes and diagnostic groups for which there was sufficient data to conduct this analysis (p>.318 for all of them).

Consistent with the fact that the relative risk of coronary heart disease due to smoking declines with age, [58] there was no significant change in risk of AMI or coronary events among older patients[14, 20, 26, 32, 36, 50] following a comprehensive smokefree law (RR .973, 95% CI .918–1.032 and RR .980, 95% CI .953–1.008, respectively).

Reductions in AMI hospitalizations were similar for females (RR .897; 95% CI .847–.950) and males (RR .912, 95% CI .872–.955) following smokefree laws of all degrees of comprehensiveness).

While Egger's test was statistically significant for publication bias (p=.007) and the funnel plot suggested possible publication bias among the papers selected for the meta-analysis (Supplementary Figure 7), the nonparametric trim and fill estimate of the effects of publication bias[59] produced essentially the same results as the meta-analysis of the published studies: RR .839 (95% CI .818–.861) for actual studies vs. RR .829 (95% CI . 808–.851) from the fill and trim analysis for all outcomes and RR .846 (95% CI .803–.890) vs. RR .803 (95% CI .764–.84.) for studies of AMI following comprehensive laws, suggesting that publication bias is not likely to explain our findings.

DISCUSSION

Given that secondhand smoke has been established to cause cardiovascular and respiratory disease,[1–3] one would expect that hospitalization for these disease would drop when exposure to secondhand smoke is substantially reduced or eliminated. Consistent with three prior meta-analyses[8–10] that concluded that smokefree laws are associated with significant decreases in AMI and other cardiac hospital admissions, we found that comprehensive smokefree laws (covering workplaces, restaurants, and bars) were associated with a 15% decrease in AMI hospitalizations. In addition, we found that the laws were followed by decreases in hospitalizations for ACS, ACE, IHD, angina, CHD, SCD, stroke, asthma, and lung infection (Figure 1), as well as decreased risk of hospitalizations for coronary events, other heart disease, cerebrovascular accident, and respiratory disease (Figure 2). For TIA, COPD, and spontaneous pneumothorax, which demonstrated no statistically significant association, negative findings should be interpreted cautiously because of the small numbers of studies that examined these outcomes.

Based on a much larger evidence base than prior meta-analyses,[8–10] we did not find that the reduction in risk associated with these laws increased with longer follow-up.

We also found evidence of a dose-response, with more comprehensive laws being associated with larger effects (Figures 1 and 2).

Our results are consistent with an earlier meta-analysis of stroke associated with secondhand smoke exposure quantified in individuals, which showed an overall risk of 1.25 (95% CI 1.12–1.38) and a nonlinear dose response.[60] This overall risk is consistent with the reductions in hospital admissions for stroke that we observed following smokefree laws (RR .795; 95% CI .680, .930 [Figure 1], corresponding to risk increases associated with secondhand smoke of RR 1.26; 95% CI 1.08–1.47).

Several studies included in the meta-analysis documented reductions in health care costs associated with fewer hospitalizations for cardiovascular or respiratory diseases. Health care savings were reported at the city, state, and national levels, ranging from $302,000 in AMI expenses after 35 months in Starkville, Mississippi[55] to €2.6 million ($3.3 million, 9.6% decrease from baseline) in angina-related hospitalization costs and €5.3 million ($6.9 million, 20.1% decrease from baseline) AMI-related hospitalization costs during the first year after smokefree law implementation in Germany.[46] (See Supplementary Tables 1–4 for more details.)

Evidence on the association between smokefree legislation and other health effects is emerging. A study in Ireland[61] found a drop in pre-term births (OR 0.75; 95% CI .59–.96) but an increase in low birthweight (OR 1.43; 1.10, 1.85) one year after the smokefree law. Another study from Scotland[62] found a significant decreases in babies small for gestational age (by 4.5%), preterm delivery (11.7%), and spontaneous preterm labor (11.4%).

Smokefree legislation *per se* does not produce the effects that we observed, which are due to the associated reductions in secondhand smoke exposure and increases in smoking cessation that accompany these laws. As more places adopt smokefree policies (whether by law in subordinate jurisdictions or voluntarily), the marginal effects of subsequent laws will be smaller, as was observed in New York and Massachusetts when those states passed comprehensives law after many localities had.[18, 32] The passage of these laws reflects changes in social norms that also affect smoking behavior; the laws both formalize and accelerate this social change and the associated health benefits.

Limitations

The interrupted time series observational studies that form the foundation for this meta-analysis alone do not establish causation. At the same time, a randomized controlled trial of the effects of enacting legislation is impractical or impossible. The studies included in our meta-analysis consistently meet standards for high quality interrupted time series studies;[7] in particular, all used objective measures of outcomes, and most considered secular trends and seasonality. The observed reductions in hospitalizations are, however, consistent with the known biological pathways by which tobacco smoke exposure causes disease and triggers acute events. The observation that AMI admissions in Helena, Montana[11] rebounded after enforcement of its smokefree law was suspended due to a lawsuit also supports a causal link.

While compliance with smokefree laws is generally high and many studies have documented drops in secondhand smoke exposure after law implementation (Supplementary Tables 1–4), we could not assume any one individual's level of exposure has decreased and subsequently reduced their risk of hospitalization. Few studies included in the meta-analysis measured tobacco smoke exposure or smoking status in individual cases.[16, 22, 38, 39] Because a randomized control trial is impossible, an analysis measuring individual smoking and secondhand smoke exposure would offer the most valid evidence regarding the effectiveness of smokefree laws.

We entered the ordinal variable for comprehensiveness of a law (0 for workplaces only; 1 for workplaces and restaurants; 2 for workplaces, restaurants and bars) in the metaregression

to test whether more comprehensive laws were followed by greater reductions in hospital admissions (or deaths). We treated comprehensiveness of law as an ordinal, not an interval (continuous) variable, which is why we only reported the P value for law comprehensiveness and not an effect size. While this is a standard approach for integrating ordinal variables into regression analyses, we investigated use of this procedure to ensure that our conclusions were not sensitive to this technique by treating law comprehensiveness as a categorical variable (together with dummy variables for the different outcome groups, as we do in the analysis in the paper that treats law comprehensiveness as an interval variable) and tried recoding the law comprehensiveness using alternative codings (0, 1, 3) and (0, 1, 4). As described in detail in the Supplemental Text, these analyses gave essentially the same results as the main analysis, indicating that the approach we use in the paper produces robust evidence for a dose-response effect of the law, treating law comprehensiveness as an ordinal variable.

Although it is not usual in epidemiological studies, we did not consider multiple testing. Readers should take into account potential inflation from multiple testing when interpreting significance levels (alpha) and confidence intervals.

In one study,[47] authors expressed concern about misclassification between different outcomes.

Publication bias is always a concern in meta-analysis (Supplementary Figure 7). The nonparametric trim and fill analysis, however, indicated that adjusting for publication bias had little effect on the results.

Conclusion

This study provides evidence that smokefree laws are followed by fewer hospitalizations and lower health care expenditures for a wide range of diseases and that comprehensive laws ending smoking in workplaces, restaurants, and bars are associated with greater effects. The general public, public health professionals, and policy makers should consider these positive associations as they develop smokefree legislation and decide whether or not to include exceptions to these laws.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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CLINICAL COMMENTARY

Secondhand smoke causes cardiovascular and respiratory disease, and implementation of smokefree legislation is followed by drops hospitalizations and deaths from these diseases. This meta-analysis of 45 studies of 33 smokefree laws found that smokefree legislation was associated with significantly lower rates of hospital admissions (or deaths) for coronary events, other heart disease, cerebrovascular accidents, and respiratory disease. There was a dose-response relationship between the strength of the law, with more comprehensive laws (including workplaces, restaurants, and bars) having the largest health benefits. This study provides strong evidence not only of the health benefits of smokefree laws but also of the need to enact comprehensive laws without exceptions.

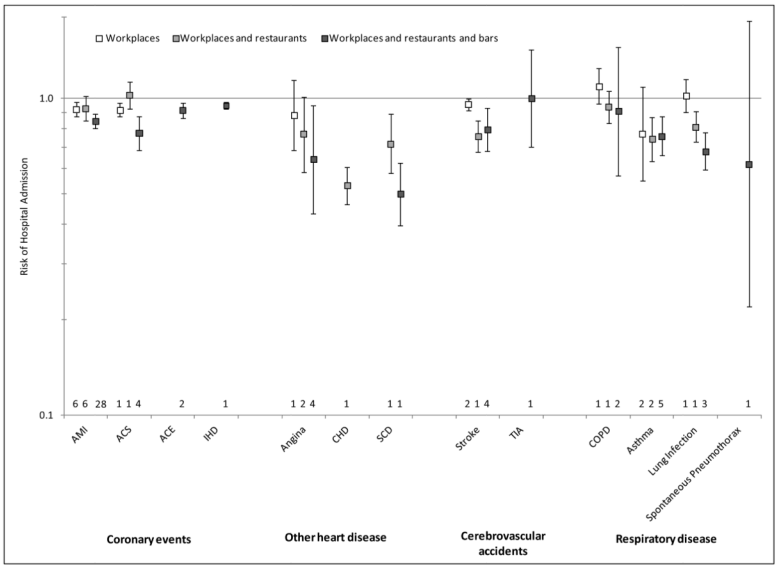

Figure 1.

Relative risk of hospital admissions for various conditions (except sudden cardiac death [SCD], which is defined as out-of-hospital deaths) after implementation of a smokefree law compared to before the law was implemented. Error bars indicate 95% confidence intervals, and numbers above the horizontal axis indicate number of studies used to compute the estimate.

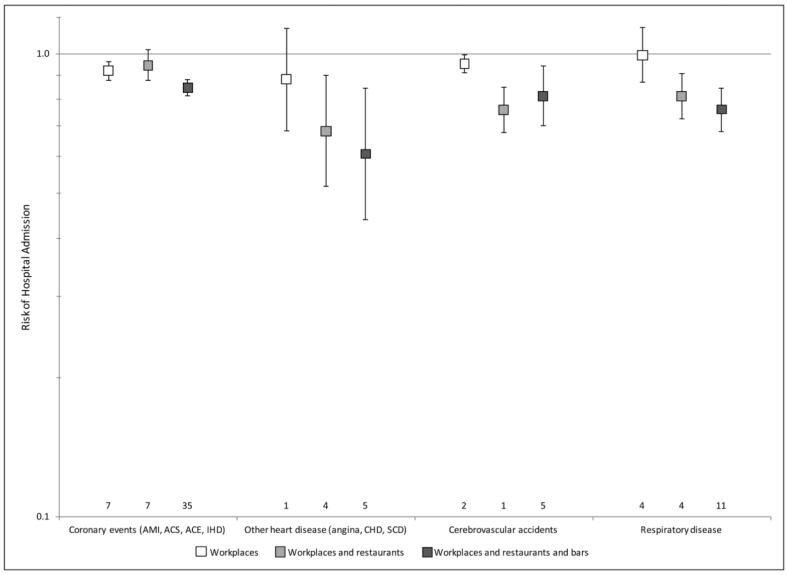

Figure 2.

Relative risk of hospital admissions for various disease categories after implementation of a smokefree law compared to before the law was implemented. Error bars indicate 95% confidence intervals, and numbers above the horizontal axis indicate number of studies used to compute the estimates.

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