

# Smokefree legislation effects on respiratory and sensory disorders: A systematic review and meta-analysis

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# **Abstract**

#### Aims

The aim of this systematic review and meta-analysis is to synthesize the available evidence in scientific papers of smokefree legislation effects on respiratory diseases and sensory and respiratory symptoms (cough, phlegm, red eyes, runny nose) among all populations.

#### Materials and methods

Systematic review and meta-analysis were carried out. A search between January 1995 and February 2015 was performed in PubMed, EMBASE, Cochrane Library, Scopus, Web of Science, and Google Scholar databases. Inclusion criteria were: 1) original scientific studies about smokefree legislation, 2) Data before and after legislation were collected, and 3) Impact on respiratory and sensory outcomes were assessed. Paired reviewers independently carried out the screening of titles and abstracts, data extraction from full-text articles, and methodological quality assessment.

#### Results

A total number of 1606 papers were identified. 50 papers were selected, 26 were related to symptoms (23 concerned workers). Most outcomes presented significant decreases in the percentage of people suffering from them, especially in locations with comprehensive measures and during the immediate post-ban period (within the first six months). Four (50%) of the papers concerning pulmonary function reported some significant improvement in expiratory parameters. Significant decreases were described in 13 of the 17 papers evaluating asthma hospital admissions, and there were fewer significant reductions in chronic obstructive pulmonary disease admissions (range 1–36%) than for asthma (5–31%). Six studies regarding different respiratory diseases showed discrepant results, and four papers about mortality reported significant declines in subgroups. Low bias risk was present in 23 (46%) of the studies.

# Conclusions

Smokefree legislation appears to improve respiratory and sensory symptoms at short term in workers (the overall effect being greater in comprehensive smokefree legislation in sensory symptoms) and, to a lesser degree, rates of hospitalization for asthma.

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**Data Availability:** All relevant data are within the paper and its Supporting Information files.

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# Introduction

Passive exposure to tobacco smoke (also known as exposure to environmental tobacco smoke, second-hand smoke, and passive smoking) multiplies the risk of coronary disease and lung cancer in adults. It also exacerbates asthma and respiratory symptoms, and increases the risk of sudden infant death syndrome amongst other health effects[1]. All of the above has led to legislative measures being adopted in order to protect the population's health in public areas and workplaces[2]. In 1998, in the United States, California was the first to put into practice these measures[3,4], and from 2004 all the members of the European Union have

adopted some kind of regulation[5]. There are different types of smokefree legislation (SFL): comprehensive (smoking is prohibited in all closed public areas and workplaces including public transport, bars, and restaurants) and partial (smoking is allowed in some private workplaces, for instance in the hospitality and entertainment sectors)[6]. Numerous studies have been published evaluating the impact of SFL from different perspectives: reduction of exposure to second-hand smoke[7], prevalence of tobacco use (no consistent evidence of a reduction attributable to SFL)[8], cardiovascular mortality (studies related to cardiovascular mortality have conflicting results possibly due to the quality of some of these papers)[9–12], cardiovascular morbidity (consistent evidence of reductions in cardiac events and hospitalizations following implementation of SFL)[13–19], and economic impact (SFL does not adversely affect business revenues or operating costs)[20] amongst others. Most systematic reviews have evaluated cardiovascular effects[15–19], tobacco consumption[8], exposure to second-hand smoke[7], and, in a more heterogeneous manner, respiratory diseases at population levels[8,21]. This last issue is, to the best of our knowledge, the least studied field.

A meta-analysis concerning the impact of banning smoking in the workplace concluded that the measure protected non-smokers from passive exposure and encouraged smokers to reduce their consumption[22]. A Cochrane Review from 2010 with 12 studies found that in ten of them legislation decreased respiratory symptoms in workers, some of the studies only assessed non-smokers[8]. A review of the impact of SFL on health and economic outcomes[20] concluded that there is a need for further research on indicators such as asthma and chronic obstructive pulmonary disease (COPD) with special attention regarding low-income populations, women, racial/ethnic minorities, and older adults. Tan and Glantz observed in a meta-analysis (2012) a 24% decrease in hospital admissions due to respiratory disease[23]. However, an updated Cochrane Review (2016) with the same inclusion criteria as the first review determined that effects of SFL on respiratory health, including COPD, asthma, and lung function were inconsistent[21].

It is essential to evaluate the impact of SFL on health[24]. In addition, a systematic review of the influence of laws which ban smoking in certain places on respiratory problems (e.g. asthma, COPD, upper and lower respiratory tract infections, and even ear, nose, and throat diseases), and in populations of all ages, irrespective of presenting respiratory diseases, would add greater value to the evidence obtained in other fields. To the best of our knowledge there is no overall, systematic review concerning the effect of SFL on respiratory and sensory symptomatology and disease. For a first approach, gathering data from previous reviews would be of great interest even if the populations differed.

The aim of this study is to synthesize the available evidence published in scientific journals on the effects of SFL on respiratory and sensory symptoms and diseases among all populations. Specifically, the objective is to assess the effects of SFL on admissions and emergency visits at hospital/primary health care centers, treatment use, and mortality in individuals suffering from asthma, COPD, and other respiratory diseases.

# Materials and methods

#### Data sources

A systematic review and meta-analysis were carried out to select published papers that assessed respiratory and sensory effects of SFL according to the Preferred Reporting Items for Systematic Reviews and Meta Analysis (PRISMA) guidelines[25]. The study protocol (CRD42015019647) was published in the International Prospective Register of Systematic Reviews (PROSPERO) (http://www.crd.york.ac.uk/PROSPERO/display\_record.asp?ID=CRD42015019647).

Searches were conducted in: PubMed, EMBASE, Cochrane Library, Scopus, Web of Science, and Google Scholar. S1 Table illustrates the different strategies. Due to the fact that a preliminary Google Scholar search revealed a considerable number of hits, only the first 200 results were scanned as prior bibliography[26–28]. This figure ensures the most relevant articles were obtained[29] and increased the sensitivity of the search[30]. A manual search in the reference lists of systematic reviews was performed. In addition, a national expert in tobacco control and public health was contacted to identify additional studies that might not have been obtained in the process. These sources were combined in order to gather as many relevant data as possible.

Inclusion criteria were: 1) Information concerning SFL (comprehensive or partial) implemented at national, regional, local, and workplace level; 2) Evaluation of SFL with data before and after its implementation; 3) Assessment of the impact of SFL on respiratory diseases (e.g. asthma, COPD and other pulmonary diseases, upper and lower respiratory tract infections, and ear, nose, and throat diseases) and outcomes including hospitalization and mortality/morbidity rate, respiratory (any respiratory symptom, wheezing, phlegm, morning cough, cough during the rest of the day, breathlessness, tightness in chest and asthma symptoms) and sensory symptoms (any sensory symptom, red/irritated eyes, runny nose/sneezing and sore/scratchy throat); 4) All populations irrespective of age, health or smoking status; 5) Original papers in peer-reviewed journals published from January 1, 1995. This date was selected as it is considered to be the first year a more comprehensive legislation was established with respect to workplaces and restaurants[6]; and 6) Papers written in English, French, Portuguese, Italian, Catalan or Spanish. Exclusion criteria concerning type of study design were editorials, letters to the editor, systematic reviews, conference proceedings, cost studies, and theoretical papers.

# Study selection

Study selection was composed of various stages (Fig 1): First, in February, 2015, the searches were carried out by two authors who identified 2726 papers. Thirty-one additional records were found through non database sources (contact with experts and manual search in the reference lists of the reviews) and 28 from Google Scholar. After removing duplicates 1606 records remained. Second, 12 paired researchers independently screened the titles and abstracts to see whether the papers met the inclusion criteria. Motives for exclusion were recorded. There were two additional reviewers for discrepancies. 1540 records were excluded leaving 66 full-text papers to review. Third, the reviewers read the 66 full-text papers, 46 of which were included in the study and four additional ones were accepted after manual exploration of the bibliography. Finally, 50 papers were selected[31–80] for data extraction and quality assessment.

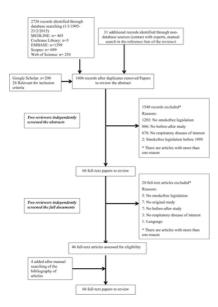


Fig 1. Flow diagram of literature search and study selection from papers evaluating smokefree legislation effects on respiratory and sensory disorders (1995–2015).

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## Data extraction and quality assessment

The following data were extracted from each full-text paper: Reference (author, year of publication), country, region, aims, type of legislation (i.e. comprehensive SFL banning smoking in virtually all indoor workplaces and public areas, including bars, restaurants and public transport with no designated smoking areas permitted, and partial which covers fewer locations[4,6,81]), study period, study design (following the classification of "Evaluative Designs in Public health: Methodological Considerations" [82] which groups the main evaluation designs in public health as non-experimental and quasi-experimental, and within each of these there are before-after studies and temporal series), study participants, sample size, respiratory and sensory outcomes, source of information, summary of findings, competing interest, and risk of bias (RoB). The latter was evaluated by a version we adapted of the Suggested Risk of Bias Criteria for the Cochrane Effective Practice and Organization of Care Group[83] (EPOC) reviews for uncontrolled before-and-after studies and interrupted time series. We included some domains/subdomains and some other were discarded others due to their unsuitability for evaluation studies and for the purpose of assessing non-randomized and non-comparative studies as in prior bibliography[84]. Overall methodological quality was rated as low, moderate, or high RoB (S2 Table). Revision of titles and abstracts, data extraction from full-text papers, and quality assessment were performed by two authors (six pairs of reviewers) independently and checked by a third in the case of discrepancies.

# Data analysis

Data were synthesized through a narrative review with summary and quantitative descriptive analysis. IBM SPSS Statistics V21.0 was employed for the descriptive analysis. A meta-analysis was performed using Review Manager (RevMan, version 5.3). The effect of SFL was estimated by mean differences (MD) in continuous outcomes and risk ratios (RR) and risk difference (RD) in dichotomous ones. Pooled effect measures were computed applying the inverse-variance method in a random-effect model. Heterogeneity was quantified with the I2 statistic, which describes the proportion of the total between-study variability due to heterogeneity[85]. If the P-value was less than 0.10 and I2 exceeded 50%, heterogeneity was considered to be substantial. Subgroup analysis was used to evaluate whether results differed according to the outcome (respiratory symptoms, sensory symptoms, spirometry parameters, and asthma, COPD and pneumonia/bronchitis admissions), type of SFL (comprehensive vs partial) and population (general population vs adult vs children). Within these subgroups, further subdivisions by study design (non experimental vs quasi-experimental), the quality of included studies (high vs moderate vs low RoB), and follow-up time (< or ≥12 months in the case of outcomes referred to symptomatology and < or ≥24 months in those referred to pathology) were carried out. When statistical heterogeneity was detected and there were more than three studies involved, several sensitivity analysis were performed assessing the relative influence of each study on pooled estimates by omitting one study at a time. Further reduced sets of analyzes were continued successively until I2 dropped below the intended threshold 50% (no more than two studies were drawn). Publication bias was assessed by using funnel plots if the meta-analysis included at least ten studies[86].

# Results

# Characteristics of studies

A total number of 1606 papers was identified. Information for each paper is presented in Tables 1, 2 and 3 and papers are classified by type of outcomes. S3 Table shows the characteristics of the 50 included studies[31–80]. The United States was the country with most publications (16 papers, 32.0%), and 24 (48.0%) collectively came from Europe. The hospitality sector represented 44.0% of the studies (22 papers, same percentage for city and regional locations), 33 (66.0%) evaluated comprehensive SFL, 27 (54.0%) presented a non-experimental before-after design (without control group), and 25 (50.0%) had a study population comprising of hospitality workers. The papers that assessed the effect of SFL on lung symptomatology and function had follow-up periods from one month to two years. In contrast, those evaluating diseases had longer periods: from eleven months to seven years. The most evaluated outcomes were respiratory (26 papers, 52.0%; symptoms were any respiratory symptom, wheezing, phlegm, morning cough, cough during the rest of the day, breathlessness, tightness in chest, and asthma symptoms) and sensory (19 papers, 38.0%; symptoms were any sensory symptom, red/irritated eyes, runny nose/sneezing and sore/scratchy throat) symptomatology followed by hospital admissions for asthma (17 papers, 34.0%) and COPD (nine papers, 18.0%).

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Table 1. Summary of studies on the impact of smoke-free legislation on symptomatology. https://doi.org/10.1371/journal.pone.0181035.t001

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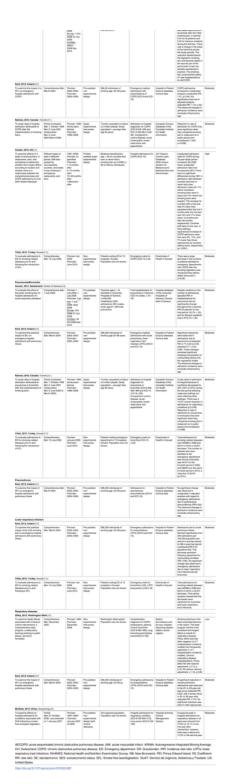


Table 2. Summary of studies on the impact of smoke-free legislation on admissions. https://doi.org/10.1371/journal.pone.0181035.t002

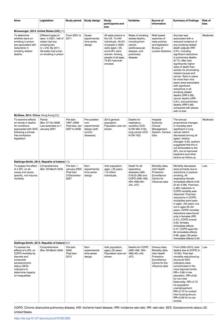


Table 3. Summary of studies on the impact of smoke-free legislation on mortality. https://doi.org/10.1371/journal.pone.0181035.t003

## SFL effect on respiratory symptoms

Of the 50 papers, 26 (52%) evaluated respiratory symptoms. Of these 26, 23 (88.5%) concerned workers, 22 (84.6%) were non-experimental, and 14 (53.8%) assessed comprehensive SFL. Evaluation periods were from one month to six years. The outcomes included: any respiratory symptom (17 studies, 65.4%), wheezing (16 studies, 61.5%), phlegm (14 studies, 53.8%), morning cough (ten, 38.5%), cough during the rest of the day (17 studies, 65.4%), breathlessness (seven, 26.9%), tightness in chest (four, 15.4%) and asthma symptoms (two, 7.7%)[37,58].

The majority of the outcomes presented a post-ban decrease period in the percentage of adults suffering from them. Those that decreased significantly in most of the studies were "any respiratory symptom" (range 7.7 to 42.0%), "morning cough" (4.4 to 30.0%), "coughing the rest of the day" (2.3 to 41.2%), and phlegm (3.5 to 42.0%). In comparison with partial SFL comprehensive SFL appears to produce the greater decline. Six studies reported post-ban decreases in comprehensive SFL for the outcomes breathlessness (range 6.2 to 25%) [32,40,67,76] and tightness in chest (10% of decrease)[67], however, along with wheezing (five papers with significant decreases[32,39,40,55,76] and five with non significant decreases[41,43,44,67,73]) and asthma[58], findings did not indicate a clear decline in these symptoms.

In addition, two studies focused on children in environments with non strictly comprehensive legislations (one with mixed types of SFL in the same paper[37] and one with partial SFL[47]). They showed discrepant results: an increase of 1.9%[47] in any respiratory symptom in the post-ban period and a decrease in asthmatic symptoms, persistent wheezing, and chronic night cough[37].

Effects regarding "any respiratory symptom" appeared to be more intense in the period immediately following implementation of the smoking law (maximum decrease of 42.0%[39]) than six months later (maximum 25.0%[43]), particularly in the studies that evaluated comprehensive SFL. In contrast, in partial SFL the declines in percentages of individuals with "any respiratory symptom" were similiar (around 15.0%[65,74]) irrespective of the moment of evaluation.

Ten studies were included in the meta-analysis for the outcome "any respiratory symptom" in comprehensive SFL setting (one study was stratified in two due to two regions being analyzed[55][56]). The pooled data (Fig 2) showed a decline of 19% in any respiratory symptom after comprehensive SFL (overall RD = -0.19, 95% confidence interval [95%CI]) = -0.26; -0.12) with substantial heterogeneity between studies (I2 = 70%, p = 0.0005). In the sensitivity analysis, the exclusion of individual studies did not substantially modify the estimates, with the pooled RDs of any respiratory symptom ranging from -0.18 to -0.21. One study[76] was the principal origin of heterogeneity and showed a minor magnitude of the effect. After excluding it from the analysis, heterogeneity decreased (I2 = 41%, p = 0.10) and the pooled data remained similar (overall RD = -0.21, 95%CI = -0.27; -0.15) (S4 Table). Subgroup analysis by study design did not significantly reduce heterogeneity. Minor heterogeneity was found in studies with a moderate or high RoB (although there were only two in each case) in contrast with those of low risk. With respect to subgroup analysis by follow-up time, studies with 12 or more months were less heterogeneous and the pool effect was smaller than those with a with shorter follow-up (S5 Table). Regarding to any respiratory symptom in a comprehensive SFL setting, the asymmetric funnel plot suggested publication bias (S1 Fig).

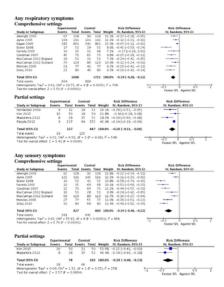


Fig 2. Risk difference between before and after the smokefree legislation (SFL) in any respiratory/sensory symptom. Abbreviations: CI, confidence interval; df, degrees of freedom; IV, Inverse Variance method. https://doi.org/10.1371/journal.pone.0181035.q002

Four studies were included in the meta-analysis for the outcome "any respiratory symptom" in a partial SFL setting. The pooled data (Fig 2) showed a decline of 20% in any respiratory symptom after the SFL (overall RD = -0.20, 95%Cl = -0.31; -0.08) with wide CI and considerable heterogeneity between studies (I2 = 54%, p = 0.09). In the sensitivity analysis, the exclusion of individual studies substantially modified the estimates, with the pooled RDs of any respiratory symptom ranging from -0.14 to -0.25. One study[56] was the principal origin of heterogeneity and had a greater magnitude of the effect in comparison with the rest of the studies. After excluding it from the analysis heterogeneity decreased (I2 = 0%, I3 = 0.45) and the pooled data was lower than in the previous analysis (overall RD = -0.14, I3 = 0.19; -0.10) (S4 Table). Subgroup analysis by study design did not significantly reduce heterogeneity. Minor heterogeneity was found in studies with moderate RoB, (a small number of studies involved only two) than those with low risk. With respect to subgroup analysis by follow-up time, there was only one study with a short follow-up. Studies with 12 or more months were heterogeneous although the pool effect was greater than the initial analysis (S5 Table).

# SFL effect on sensory symptoms

Of the 50 papers, 19 (38.0%) evaluated the presence of sensory symptoms. Of these 19, all solely focused on workers, 17 (89.5%) were non-experimental, and 11 (57.9%) evaluated a comprehensive SFL effect. Periods of evaluation ranged from one month to two years. Outcomes were: any sensory symptom (15 studies, 78.9%), red/irritated eyes (15 studies, 78.9%), runny nose/sneezing (14 studies, 73.7%), and sore/scratchy throat (13 studies, 68.4%).

All the 15 studies found significant decreases in the number of individuals who had "any sensory symptom" in the before-after comparision (range of decrease 11.0–100.0%) irrespective of the kind of legislation. Twelve studies showed statistically significant decreases for the outcomes "red/irritated eyes" (range 7.5 to 44.0%) and "runny nose /sneezing" (6.3 to 45.0%). The outcome "sore/scratchy throat" decreased non- significantly in four studies[55–57,72], and in the rest of the nine studies it declined in the post-ban period (range 12.0[32] to 48.7%[40]), particularly in those that evaluated comprehensive SFL.

The "any sensory symptom" outcome showed a greater decrease immediately following implementation of legislation (up to a maximum of 70.0–100.0%[62] at six months versus 50% at longer periods[41]), especially in the case of comprehensive SFL, with even higher percentages than respiratory symptoms in studies assessing both respiratory and sensory symptoms.

Nine studies were included in the meta-analysis for the outcome "any sensory symptom" in a comprehensive SFL setting (one study was stratified due to having two regions analyzed[55] [56]). The pooled data (Fig 2) showed a decline of 34% in any sensory symptom after the comprehensive SFL (overall RD = -0.34, 95%Cl = -0.26; -0.12) with substanial heterogeneity between studies (I2 = 86%, p < 0.001). In the sensitivity analysis, the exclusion of individual studies did not substantially modify the estimates, with the pooled RDs of any sensory symptom ranging from -0.31 to -0.37. No study was observed to be the main origin of heterogeneity between studies, I2 remained above 80% in the sensitivity analysis (S4 Table). Subgroup analysis by study design did not significantly reduce heterogeneity, although minor heterogeneity was found in studies with a moderate or high RoB (a small number of studies involved only two) than those with low. Regarding subgroup analysis by follow-up time, the studies with a short follow-up had a greater pool effect than those with 12 or more months, marked heterogeneity being maintained in both cases (S5 Table).

Two studies were included in the meta-analysis for the outcome "any sensory symptom" in a partial SFL setting. The pooled data (Fig 2) showed a decline of 30% in any sensory symptom after the SFL (overall RD = -0.30, 95%Cl = -0.46; -0.13) with wide Cl and low heterogeneity between the studies (I2 = 25%, p = 0.25).

# SFL effect on spirometry parameters

Out of the 50 papers, eight studies (16.0%)[39,43,52,58,67,68,71,78] assessed spirometric parameters in workers. Of these eight, all were non-experimental and five (62.5%) were performed in comprehensive SFL settings[39,43,58,67,68]. Evaluation periods ranged from one month to two years. Of the eight studies, four (50.0%) had an increase in forced expired volume in one second (FEV1)[39,58,68,71], although two of these were carried out with non-smokers[39,68] and asthmatic cohorts[68]. Six studies (75.0%) evaluated forced vital capacity (FVC) which increased significantly (range 3–4.2%) in five[39,43,68,71,78] although in one it was only augmented in an asthmatic cohort [68]. Discrepant results were obtained when the effect of comprehensive SFL on forced mid-expiratory flow rate  $(FEF_{25-75\%})[39,43,68,71]$  and peak expiratory flow rate (PEF)[43,68] was assessed.

Three studies were included in the meta-analysis for the outcome "FEV1" in a comprehensive SFL setting. Pooled results indicated a non significant net difference in FEV1 between before and after comprehensive SFL (overall MD = 0.10, 95%CI = -0.04; 0.24; I2 = 87%) (Fig 3). In the sensitivity analysis, the exclusion of individual studies did not substantially modify the estimates, with pooled

MDs of FEV1 ranging from non significant values of -0.04 to 0.13.

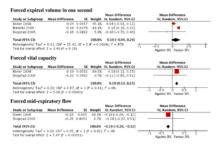


Fig 3. Mean difference between before and after comprehensive smokefree legislation (SFL) in spirometry parameters. Abbreviations: CI, confidence interval; df, degrees of freedom; IV, Inverse Variance method. https://doi.org/10.1371/journal.pone.0181035.g003

Only two studies could be included in the meta-analysis for the outcome "FVC" in a comprehensive SFL setting. Pooled results indicated a significant net difference in FVC between before and after comprehensive SFL (overall MD = 0.19, 95%CI = 0.13; 0.25) with homogeneity (I2 = 0%, p = 0.41) (Fig 3).

Only two studies could be included in the meta-analysis for the outcome "FEF<sub>25-75%</sub>" in a comprehensive SFL setting. Pooled results indicated a significant net difference in FEF<sub>25-75%</sub> between before and after comprehensive SFL (overall MD = -0.19, 95%CI = -0.26; -0.12) with homogeneity (I2 = 0%, p = 0.82) (Fig 3).

## SFL effect on asthma admissions

Out of the 50 papers, 17 (34%) concerned asthma admissions (all but two in hospital settings). Of these 17, nine (52.9%) were in the general population, five (29.4%) in adults, and three (17.6%) in children. Ten (58.8%) were non-experimental and 15 (88.2%) evaluated comprehensive SFL. One was conerned asthma treatment use (5.9%)[79]. Evaluation periods ranged from 11 months to seven years. Significant decreases were described in 13 of the 17 papers evaluating asthma hospital admissions.

With respect to the nine studies carried out in the general population[34,42,45,46,51,60,61,64,75], six of them (66.7%) were quasi-experimental[42,45,46,51,60,61], and, with the exception of one[61], all were performed in comprehensive SFL locations. In eight studies (88.9%), admission rates for asthma (both hospital and non-hospital admissions) significantly declined with a range of 5.0% [60] to 31.0% (the latter figure was for Caucasians in Texas[45]). In addition, a significant annual rate of reduction of -0.35 [95% confidence interval (CI) -0.53 to -0.018] in hospital asthma admissions was obtained in the sole study on partial SFL[61] when it compared SFL in restaurants versus public areas and workplaces over the ten-year study period. Four stratified studies (44.4%) [34,42,51,64] all reported significant reductions in asthma hospital admissions both in children (range 18.0[64]- 25.0%[34]) and adults (range 16.0[34]-24.0%[64]).

Six studies were included in a meta-analysis for the outcome "asthma admission" in a general population in a comprehensive SFL setting (Fig 4). According to the forest plot, there was a significant decrease of 13% after SFL (overall RR = 0.87; 95%CI = 0.81; 0.93). Heterogeneity was high (I2 = 78%, p <0.001). In the sensitivity analysis, the exclusion of individual studies did not substantially modify the estimates, with pooled RRs of asthma admissions ranging from 0.85 to 0.89. No study was found to be the main origin of heterogeneity between studies, I2 remained above 70% in the sensitivity analysis by omitting one at a time (S4 Table). Subgroup analysis by study design, risk of bias and follow-up time (less than 24 months vs 24 months or more) did not significantly reduce heterogeneity (S6 Table).

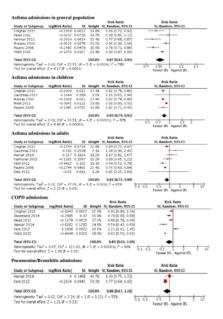


Fig 4. Risk ratio between before and after comprehensive smokefree legislation (SFL) in asthma, COPD and lung infection admissions. Abbreviations: CI, confidence interval; df, degrees of freedom; IV, Inverse Variance method. https://doi.org/10.1371/journal.pone.0181035.g004

Three studies were focused on children[35,37,59], in two (66.7%) there were significant reductions of hospital asthma admissions in comprehensive SFL locations (declines of 9.0%[59] and 18.2%[35]) whilst in the remaining paper on regions with different types of SFL there was no significant decrease[37].

Five studies were included in the meta-analysis for the outcome "asthma admission" in children in comprehensive SFL setting (three focused on children and two were stratified by age) (Fig 4). There was a significant decrease of 15% after SFL (overall RR = 0.85, 95%Cl = 0.79; 0.91). Heterogeneity was high (1.2 = 87%, 1.2 = 87%). In the sensitivity analysis, exclusion of individual studies did not substantially modify the estimates, with pooled RRs of asthma admissions ranging from 1.82 = 1.2

Five studies focused on adult populations[48,49,53,66,79], they all evaluated comprehensive SFL and had a non-experimental design. Three of them (60.0%) found significant reduction rates from 4.9%[53] to 36.0%[49] (all except one in hospital admissions[79]). One study reviewed the incidence rate ratio in non-hospital admissions [79] and reported a decrease of 15.0% in admissions after SFL. In the two remaining studies[48,66], results were discordant with no significant differences. With respect to asthma treatment in adults, the use of salbutamol and ipratropium descended in non-hospital emergency settings[79].

Seven studies were included in the meta-analysis for the outcome "asthma admission" in adults in comprehensive SFL setting (five focused on adults and two were stratified by age) (Fig 4). There was a significant decrease of 15% after SFL (overall RR = 0.85, 95%CI = 0.73; 0.99). Heterogeneity was considerable (12 = 65%, p = 0.009). In sensitivity analysis, exclusion of individual studies modified the estimates substantially, with pooled RRs of asthma admissions ranging from 0.80 to 0.90. Two studies were the main origin of heterogeneity between studies[42,48], they had no significant increases of asthma admissions. After excluding them from the analysis, the heterogeneity decreased (12 = 31%, p = 0.22) and the pooled data was more robust (overall RR = 0.77, 95%CI = 0.70; 0.85) (S4 Table). Subgroup analysis by study design and RoB did not significantly reduce heterogeneity. With respect to subgroup analysis by follow-up time, only one study had less than 24 months of follow-up, and those with longer periods had a greater pool effect than the initial analysis, maintaining high heterogeneity (S6 Table).

## SFL effect on COPD admissions

Nine (18.0%) of the 50 papers reported effects on COPD admissions[34,38,42,45,48,49,54,61,75](all except one in hospital settings): six (66.7%) in a general population and three (33.3%) in adults exclusively. Five (55.5%) were quasi-experimental and eight (88.9%) evaluated comprehensive SFL. Evaluation periods ranged from 11 months to 5.5 years. Significant decreases were described in 6 of the 9 papers evaluating asthma hospital admissions.

In four (66.7%)[38,42,45,61] of the six articles which focused on the general population and had a quasi-experimental design, significant decreases in COPD admissions, ranging from 1.0%[61] (a study that compared the different phases of SFL before becoming comprehensive) to 36.0%[45], were found. The other two studies (33.3%), with non-experimental design[34,75], presented non-significant declines.

There were three studies that evaluated comprehensive SFL in adults[48,49,54]. In two of them (66.7%), hospital admissions for COPD decreased significantly (from 15.0%[54] to 46.0%[48]) whilst in the other study (33.3%) they increased non significantly (adjusted relative risk 1.18; 95% CI 0.86–1.60[49]).

Six studies were included in the meta-analysis for the outcome "COPD admission" in a comprehensive SFL setting (Fig 4). There was a non significant decrease of 20% after SFL (overall RR = 0.80, 95%CI = 0.63; 1.00). Heterogeneity was high (I2 = 96%, p <0.001). In the sensitivity analysis, the exclusion of individual studies modified the estimates substantially, with pooled RRs of COPD admissions ranging from 0.73 to 0.85. No study was found to be the main origin of heterogeneity between studies, I2 remained above 80% in the sensitivity analysis (S4 Table). Analysis by subgroup showed significant values in the quasi-experimental studies (overall RR = 0.83, 95% CI = 0.74; 0.94, I2 = 40%, p = 0.20), in the low RoB ones (overall RR = 0.84, 95%CI = 0.73; 0.98, I2 = 61%) and in those with less than 24 months follow-up (overall RR = 0.61, 95%CI = 0.59; 0.63; I2 = 0%, p = 0.35) (S6 Table).

# SFL effect on other respiratory diseases admissions

Six papers evaluated: 1) Respiratory diseases taken together (three studies)[36,49,80] and 2) Other respiratory disease admisions (four studies)[48,49,61,75] such as pneumonia and pneumothorax. One paper fell into both categories[49]. Four (66.7%) of the six were in a general population and two exclusively in adults[48,49], five (83.3%) had a non-experimental design, three (50.0%) evaluated comprehensive SFL[48,49,75], and one (16.7%) different types of SFL[36]. The evaluation period ranged from 11 months to three years.

There were discrepant results in overall respiratory admissions (only one paper out of three reported a significant 15.0% decline in adults[49]) and in respiratory infection (two[49,75] of four papers found significant decreases up to 23.0%[49]).

Only two studies could be included in the meta-analysis for lung infections (pneumonia or bronchitis) in adults in a comprehensive SFL setting (Fig 4). There was a non significant decrease of 14% after SFL (overall RR = 0.86, 95% CI = 0.67; 1.10). The between-study heterogeneity was substantial (I2 = 55%, p = 0.13).

# SFL effect on respiratory mortality

Four (8.0%) of the 50 papers were based on mortality data[33,69,70,80]. These studies were heterogeneous with respect to type of population (one study [25.0%] in prisioners[33], two [50.0%] in adults[69,70], and one [25.0%] in a general population[80]), study design (three [75.0%] were non-experimental), type of SFL evaluated (two comprehensive [50.0%] [69,70], one [25.0%] partial[80], and one [25.0%] of different types) and range of post-ban evaluation (from one to seven years).

Two studies (50.0%) performed in Ireland analysed mortality data on respiratory diseases[69,70], and one focused on effects taking into account socioeconomic status[69]. Decreases in mortality rates were primarily due to reductions in passive smoking (these results were supported in that no observable change in smoking prevalence was seen as a result of the SFL), COPD mortality reduction rate was 0.62 (95% CI 0.46–0.83)[70], especially in women (reduction rate 0.47; 95%CI 0.32–0.70)[70] and in the most deprived areas[69]. In North American prisons[33], pulmonary death declined by 29.0% with men having significantly higher rates of death than women for all smoking-related causes. There was only one study about partial SFL which found no significant results[80].

#### Quality assessment of included studies

Methodological quality assessment was classified as summary RoB (S2 Table): low in 23 (46.0%) of the 50 papers, moderate in 19 (38.0%), and high in eight (16.0%). In general, the two main weaknesses were selection and attrition bias, and the highest rated domains were detection and reporting bias. The summary RoB was low in 18 (47.37%) of the 38 non-experimental studies and in five (41.67%) out of 12 of the quasi-experimental ones. The most highly rated domains (with a higher proportion of low RoB) in the non-experimental studies were reporting (92.1%) and detection bias 2 (Was the policy unlikely to affect data collection? [89.5%]). The lowest values (with a higher proportion of high RoB) were selection (28.9%), attrittion (18.4%) and other bias (18.4%). For the quasi-experimental studies the most highly rated domains were reporting (100%) and attrition (83.3%), and the worst other bias (16.7%) and confounding bias (16.7%). Papers that evaluated spirometric parameters, respiratory mortality, and sensory symptoms were those that presented the greatest percentages of low RoB (62.5, 50.0, and 47.7%, respectively).

# Discussion

SFL beneficial effects were observed in workers with respect to respiratory and sensory symptomatology. The majority of the studies reported a decrease in hospital admissions for asthma and COPD in all populations (overall population or population stratified by age). Regarding other lung diseases, respiratory mortality, and spirometric parameters, the results are heterogeneous and discrepant. Comprehensive SFL was more commonly evaluated than partial, and periods of assessment ranged from one month to seven years. SFL effect appeared to be greater when the legislation was comprehensive. Due to the reduced number of studies involved in the subgroup analysis, the conclusions of the meta-analysis should be considered with caution. We used a random effect model in order to be able to control heterogeneity. Sensitivity analysis of subgroups showed significant decreases in any respiratory symptoms (both in comprehensive and partial SFL settings) and asthma admissions in comprehensive settings (in adults and children). No significant results were found about the effect of SFL on FEV1, COPD and lung infection admissions. In the rest of the outcomes, either the number of studies involved was very low (FVC, FEF25-75% in comprehensive SFL setting and any sensory symptom in partial SFL setting) or heterogeneity was high despite sensitivity analysis (any sensory symptoms and asthma in a general population in comprehensive SLF settings). All of which hinders extrapolation of data to the whole population, and thus limits the strength of the conclusions drawn.

According to this review, SFL effects are more intense in a worker population with respect to sensory symptoms followed by respiratory ones. In contrast, effects on lung function were not so clear. Spirometry parameters could have been conditioned by other factors such as correct performance of the technique, whether the participant was a smoker or asthmatic and, in the case of the latter, whether asthma medication was being taken[87]. In fact, in one of the included studies the authors were unable to analyze the values due to the difficulties in gathering data (participants not fully co-operating in the test)[32]. Overall, asthma and COPD were the diseases most assessed. The majority of the studies reported favourable results for SFL with a maximum decrease in hospital admissions for adults of 46.0%[48] and 36.0%[49] for COPD and asthma, respectively. Few studies have evaluated SFL impact on other respiratory diseases and mortality, and their results have been heterogeneous. Nevertheless, an immediate 38.0% decrease in mortality due to COPD has been reported[70].

Most of the included studies analysed the impact of comprehensive SFL which can cause the greatest decrease in sensory and respiratory symptoms particularly in the immediate post-ban period. It is possible that, at long-term, these effects in worker population are not perceived due to the situation becoming normalized, that is to say, without exposure to second-hand smoke due to SFL. In the studies carried out in all populations, effects were evaluated at eleven months after SFL implementation and better results were observed with respect to decreased admissions due to respiratory diseases in locations with the strictest SFL. Nevertheless, data on respiratory mortality are scarce and from heterogeneous populations. In addition, the maximum time period for SFL implementation to be studied is 6.75 years[69] and differences have not yet been found between the time period immediately after SFL and long-term[70].

Some studies have performed analysis in subgroups and reported a greater decrease in the percentage of sensory and respiratory symptoms in a working, non-smoking population[43,52,76], greater decrease in COPD mortality in women[33,69,70] and in people older than 65 years[69,70], and fewer asthma admissions in a population aged over 20 years[64] and between 30–39 years[49]. Most studies detected a decrease of less intensity in children than in adults for asthma admissions after SFL implementation. However, the few studies that compared both populations reported heterogeneous findings. One explanation is that adults may be exposed to secondhand smoke at both home and work whilst children are only exposed at home[14,64].

In contrast with previous reviews that provided data on respiratory symptomatology and admissions, we identified a considerably larger number of studies (50 papers compared to 21 in the most extensive review by other authors)[21]. The review by Polanska et al[87] was limited to respiratory and sensory symptoms in a worker population. They found a reduction in respiratory symptoms in ten out of 12 studies, and in all except one of these ten studies a decline in sensory symptoms. Callinan et al[8] arrived at similar conclusions in their systematic review and mentioned, furthermore, a clear reduction in sensory symptoms in smokers and nonsmokers. In that review they analyzed spirometer parameters from five studies: in two there were significant increases in FEV1; in three significant increases in FVC; and in three significant reductions in FEF. With respect to symptomatology and lung function the results mentioned concur with those we obtained in our systematic review: 26 papers were identified related to respiratory symptoms, 19 to sensory symptoms, and eight to lung function. In contrast, the 2010 Cochrane[8] identified 12, ten, and six papers, respectively. Self-reported symptoms were excluded from the 2016 up-dated Cochrane Review[21] and symptomatology evidence was not updated with respect to the 2010 edition. In contrast, our review found 12 papers more in the period 2009-2015. The 2016 Cochrane Review selected papers that evaluated effects on health when follow-up was a minimum of six months post-ban (no restriction in our review) and institutional settings were not included. It was concluded that data regarding asthma and COPD admissions were inconsistent. Tan and Glantz[23], in their meta-analysis that included eight articles about respiratory disease admissions with a heterogeneity of 88%, obtained a relative risk of 0.760 (95% CI 0.682-0.846) for decreased asthma and lung infections without any statistically significant association for COPD and spontaneous pneumothorax (fewer studies), and without any follow-up time differences. According to our data, asthma in the general population decreased by 13% and asthma in adults by 23%, with no significant findings for COPD and lung infection. Been et al[88] in their meta-analysis based on three studies about asthma admission in children (with moderate bias risk) obtained an overall reduction of 10.10% (95% CI -15.2 to -5), and a nonsignificant trend towards an annual decrease rate (-7.5% per year, 95% CI -16 to 0.9). In this meta-analysis, a significant overall RR of 0.82 was found. According to the narrative synthesis, we observed that most articles reported a decrease in the number of hospital/non-hospital emergency admissions due to asthma (75.6% of papers) and/or COPD (66.7% of papers). However, as some of these papers only found evidence in population subgroups (children or adults), the results are inconclusive. With respect to the meta-analysis, it seems that SFL has a protective effect nevertheless due to the high heterogeneity between studies of the outcomes analysed the conclusions should be drawn with caution.

Most of the studies in this review had a non-experimental design. The lack of a control group only permits the evaluation of variations before and after SFL implementation; it does not allow the overall observed changes to be attributed to the legislation implemented. We have observed that in some studies significant results were only obtained when comparing locations with and without SFL or time periods with varying restrictions with respect to smoking bans[61].

The fact that the data source of the included studies with respect to symptomatology (self-administered International Union Against Tuberculosis and Lung Disease questionnaires) and hospital admissions (central registers) has been quite homogenous is a strength as it permits comparison with findings amongst different studies. However, self-reported data have limited validation compared to objective measures. There was a lack of simultaneous adjustment and stratification for confounders in some studies. A few of them stratified confounders such as sex[31,35], location[35,37,77], socioeconomic status[35,59,69], seasonality[64], smoking status[52], secondhand smoke[47,77], influenza/air polution[47], number of symptoms[31,63], comprehensiveness of SFL[54], population growth[60], different policies on tobacco[36], and being resident or not[48,60]. SFL is not the only measure that has had an impact on passive smoking and tobacco-related disease. Other actions that have influenced the consumption of tobacco are control of publicity, tax increases resulting in higher price[89,90], and restrictions on the sale of tobacco products[8]. Very often these steps are introduced at the same time as the new legislation comes into being. A policy may be considered ineffective when other components simultaneously occur which cause its impact to be under-rated. It might, therefore, be difficult to know how these different actions could influence the impact observed. As a result, it is important to perform sensitive analysis by subgroups[24].

In general, most articles were classified as low or moderate RoB with the non-experimental ones having a slightly higher percentage. Selection and attrition biases had the worst results, very probably due to convenience sampling (in the case of selection bias) in the studies on symptomatology. Moreover, losses of participants in the hospitality sector are habitual due to the temporal nature of this kind of employment[32,91]. In the twelve quasi-experimental studies (the majority about respiratory diseases in the general population) the confounding bias domain was the worst evaluated. This shows that in even the most robustly designed study it is necessary to analyze confounding factors that could over or underestimate SFL effect. In the systematic review of Frazer et al[21], a different assessment tool was used: "adequate sequence generation", "adequate allocation concealments", and "blinding of personnel/all outcomes" (more suitable for randomized clinical trials). These domains were adapted in this systematic review due to the type of studies (evaluating a policy). Papers were rated better in this systematic review than in the updated Cochrane Review. However, quality assessment of each paper were performed by two authors independently and checked by a third in the case of discrepancies.

## Strengths and limitations

To the best of our knowledge, this is the first scientific review performed with respiratory outcomes (symptoms, functionality, and hospital admissions) as an effect of SFL, measured in all groups (workers, adults, children, and general populations). The rigorous procedures employed (paired reviewers and a third one in the case of discrepancies) have ensured the validity of the data extraction. A detailed synthesis of sensory and respiratory symptomatology has been done (excluded from the up-dated Cochrane Review). Grey literature was not employed but the combination of heterogeneous sources of data adds value to the results. We tried to identify all the possible papers appearing in scientific journals from six different databases in addition to manually searching the references in the papers and consulting experts. One of the inclusion criteria was that papers were written in English, French, Portuguese, Italian, Catalan or Spanish. This did not have an effect on our results as only one document had to be excluded (Norway)[92].

Although identification and selection biases are common threats to validity in all systematic reviews, they are more likely in the case of non-randomized studies where registration is not standard practice[93]. Particular effort has been devoted to reducing identification bias, as shown by our search strategy which included several databases.

Variability in participants, type of SFL, outcome measures and definition, duration of follow-up and study design may affect the impact of SFL. In addition, the considerable heterogeneity observed hinders the drawing of conclusions about SFL from the meta-analysis. However, the narrative synthesis helps to investigate similarities and differences among studies as well to explore any patterns in the data to better understand the impact of SFL. A possible bias due to authors who may have had a financial conflict of interest arising from the tobacco industry is a complex issue. In fact, with respect to studies on passive smoking there are a number of such authors. Nevertheless, this type of article generally has low quality scores and was probably excluded from selection[94].

# Future lines of study

Building upon the present observations, we would like to underline the need to address several important issues for future research. None of the studies reported sensory/respiratory symptoms and lung function in the general population. Moreover, the effect of SFL with respect to respiratory symptomatology in children was only evaluated in two studies without conclusive results. It is notable that non-hospital setting was monitored in only two studies[34,79]. Neither are there data about respiratory mortality in worker and child populations. There are few, heterogeneous studies regarding lung function, medication use, respiratory infections (both upper and lower tracts), and mortality. In addition, it is essential to better study the mid- to long-term effects of SFL on mortality, COPD, and another chronic respiratory diseases. Finally, we believe there is a need for quasi-experimental design studies comparing locations with and without SFL, and partial versus comprehensive SFL, to better confirm its effects. Moreover, we consider that analysis by age, gender, and socio-economic factors are necessary given that tobacco consumption may vary.

# Conclusions

Results appear to indicate that comprehensive SFL decreases sensory symptomatology more than partial. Almost all the studies reported effectiveness of SFL in respiratory and sensory symptoms in workers and children with significance that decreased in the meta-analysis. There is a majority of studies denoting the effectiveness of SFL in admissions for asthma and COPD in all populations but without statistical significance for the latter in the meta-analysis. There are, however, few studies about respiratory mortality, respiratory infection, and lung function and they do not demonstrate strong effectiveness. It can be concluded, therefore, that it is important to continue conducting research into SFL effectiveness particularly in areas lacking results that can contribute to the available evidence.

# Supporting information

# S1 PRISMA checklist.

https://doi.org/10.1371/journal.pone.0181035.s001 (DOC)

S1 Table. Search strategy applied in the different databases: SFL effects on respiratory and sensory disorders.

https://doi.org/10.1371/journal.pone.0181035.s002 (PDF)

S2 Table. Quality assessment of the risk of bias of papers evaluating SFL effects on respiratory and sensory disorders (1995–2015).

https://doi.org/10.1371/journal.pone.0181035.s003 (PDF)

S3 Table. Descriptive characteristics of the 50 articles obtained for smokefree legislation effects on respiratory disorders (1995–2015).

https://doi.org/10.1371/journal.pone.0181035.s004 (PDF)

S4 Table. Sensitivity analysis by omitting one or two until I2 dropped below the intented threshold 50% and range.

https://doi.org/10.1371/journal.pone.0181035.s005 (PDF)

S5 Table. Subgroup analysis by study design and risk of bias among studies relating any respiratory and sensory symptoms.

https://doi.org/10.1371/journal.pone.0181035.s006 (PDF)

S6 Table. Subgroup analysis by study design and risk of bias among studies relating asthma and COPD admissions in comprehensive SFL setting.

https://doi.org/10.1371/journal.pone.0181035.s007 (PDF)

S1 Fig. Funnel plot of any respiratory symptom in comprehensive smokefree legislation setting.

Publication bias. https://doi.org/10.1371/journal.pone.0181035.s008 (PDF)

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