Effect of smoke-free legislation on perinatal and child health: a systematic review and meta-analysis

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Summary

Background Smoke-free legislation has the potential to reduce the substantive disease burden associated with second-hand smoke exposure, particularly in children. We investigated the effect of smoke-free legislation on perinatal and child health.

Methods We searched 14 online databases from January, 1975 to May, 2013, with no language restrictions, for published studies, and the WHO International Clinical Trials Registry Platform for unpublished studies. Citations and reference lists of articles of interest were screened and an international expert panel was contacted to identify additional studies. We included studies undertaken with designs approved by the Cochrane Effective Practice and Organisation of Care that reported associations between smoking bans in workplaces, public places, or both, and one or more predefined early-life health indicator. The primary outcomes were preterm birth, low birthweight, and hospital attendances for asthma. Effect estimates were pooled with random-effects meta-analysis. This study is registered with PROSPERO, number CRD42013003522.

Findings We identified 11 eligible studies (published 2008–13), involving more than 2·5 million births and 247 168 asthma exacerbations. All studies used interrupted time-series designs. Five North American studies described local bans and six European studies described national bans. Risk of bias was high for one study, moderate for six studies, and low for four studies. Smoke-free legislation was associated with reductions in preterm birth (four studies, 1 366 862 individuals; –10·4% [95% CI –18·8 to –2·0]; p=0·016) and hospital attendances for asthma (three studies, 225 753 events: –10·1% [95% CI –15·2 to –5·0]; p=0·0001). No significant effect on low birthweight was identified (six studies, >1·9 million individuals: –1·7% [95% CI –5·1 to 1·6]; p=0·31).

Interpretation Smoke-free legislation is associated with substantial reductions in preterm births and hospital attendance for asthma. Together with the health benefits in adults, this study provides strong support for WHO recommendations to create smoke-free environments.

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Introduction

Smoking is estimated to kill 5·7 million people each year, and effective tobacco control is a key instrument for reduction of global mortality and rates of non-communicable diseases.[1,2] The WHO Framework Convention for Tobacco Control provides a valuable means to implement and evaluate tobacco control measures.[3,4] As part of six key recommendations the implementation of smoke-free environments is advocated as an instrument to reduce the estimated 600 000 deaths and 10·9 million disability-adjusted life-years (DALYs) globally due to second-hand smoke exposure each year.[1,5] In support of this recommendation, there is now emerging evidence that smoke-free laws can effectively reduce second-hand smoke exposure and improve population health.[6] A 2012 meta-analysis showed a 15% reduction in cardiovascular events and a 24% reduction in admissions to hospital for respiratory diseases after introduction of smoke-free legislation.[7] However, although 177 nations have now ratified the Framework Convention for Tobacco Control, at present, only 16% of the world's population is covered by comprehensive smoke-free laws.[5]

A broad appreciation of the population health effects of smoke-free legislation might help to further strengthen its mandate. Most studies have focused on the evaluation of adult outcomes; however, children account for more than a quarter of all deaths and more than half of all DALYs due to second-hand smoke exposure.[1] The effect of in-utero and early-life exposures on health in childhood and later life is a growing specialty of research interest with major public health implications.[8] Children are particularly vulnerable to the adverse effects of second-hand smoke because their lungs and immune system are still undergoing development. The first reports of detrimental health effects of parental smoking on paediatric respiratory health date back to the early 1970s.[9] Second-hand smoke has since been linked to a range of adverse outcomes during early-life including stillbirth, preterm birth, low birthweight, congenital anomalies, neonatal and infant mortality, asthma, and respiratory infections.[10–12] Furthermore, recent studies implicate childhood second-hand smoke exposure in the development of non-communicable diseases in later life.[13,14] 40% of children worldwide are regularly exposed to second-hand smoke,[1] which is of great concern because they are generally unable to influence their own level of exposure. Smoke-free legislation has been shown to reduce second-hand smoke exposure in children and increase the proportion of smoke-free homes in several countries.[15–19]

Emerging evidence now shows particular benefits of smoke-free legislation on early-life health.[20–23] However, only a small minority of the world's population is covered by comprehensive smoke-free laws, and this proportion is increasing slowly.[5] This slow increase could at least partly be because of uncertainty about the potential health benefits, particularly concerning child health. A comprehensive assessment is therefore warranted to obtain a well informed appreciation of the effect of smoke-free public and work environments on early-life health and to inform national and international policy decisions on implementation of smoke-free legislation.

Methods

Search strategy and selection criteria

We followed the methods detailed in a peer-reviewed systematic review protocol that is registered with PROSPERO (CRD42013003522).[24] We searched online databases of medical literature (Medline, Embase, Google Scholar, ISI Web of Science, Cochrane Central Register of Controlled Trials, Trip, Cumulative Index to Nursing and Allied Health [CINAHL], Allied and Complementary Medicine Database [AMED], CAB International, Global Health, WHO Global Health Library [regional and global indexes], SciELO, IndMED, and KoreaMed) for published studies from January, 1975, to May, 2013, and the overarching WHO International Clinical Trials Registry Platform to identify unpublished work relevant to the research question. Appendix pp 1–3 shows an overview of the search terms used. The search was restricted to studies published from 1975 onwards, when, to the best of our knowledge, the first regional smoking ban was introduced in Minnesota, USA.[25] We did not apply any language restriction. Furthermore, we hand-searched reference lists, screened citations of articles of interest with ISI Web of Science and Google Scholar, and approached an international panel of experts in the field to identify additional published and unpublished studies.

See Online for appendix

Studies were eligible for inclusion if they investigated the association between introduction of a smoking ban in workplaces or public places, or both, and one or more prespecified health outcomes in children. We focused on children aged 12 years or younger to minimise potential confounding by self-smoking, but accepted ages up to 20 years as long as most of the population met the original age criterion. Corresponding authors of eligible studies that included children without reporting their outcomes separately from adults were approached to obtain paediatric subgroup analyses. Primary outcomes were stipulated a priori as preterm birth, low birthweight, and asthma. Secondary outcomes included various perinatal mortality indicators, very preterm birth, very low birthweight, small for gestational age, congenital anomalies, bronchopulmonary dysplasia, upper and lower respiratory infections, otitis media with effusion, wheezing, and chronic cough. Definitions and specifications and consideration of additional outcomes are described elsewhere.[24] Surrogate and intermediate outcomes, smoke-related behaviour, smoke-exposure, and economic data were not included. Following the Cochrane Effective Practice and Organisation of Care (EPOC) guidelines, we stipulated that only the following study designs were eligible: randomised controlled trials, controlled clinical trials, controlled before-and-after studies, and interrupted time series.[26] Searches were done independently by two reviewers, and final study selection was based on consensus between both reviewers and, if necessary, independent arbitration.

Data extraction and risk of bias assessment

Relevant data were extracted from each paper with customised data extraction forms. We contacted corresponding authors to obtain additional information when necessary. Risk of bias was assessed with EPOC quality criteria.[27] Two reviewers independently extracted data and assessed quality, and disagreement was resolved by consensus, or arbitration by a third author. Parental or maternal smoking was defined as the main confounder for which adjustment was recorded.

Statistical analysis

The main findings from the systematic review, including characteristics and key findings of individual studies are presented in tabular form. For the meta-analysis, relative risk differences were selected from the most adjusted model presented in each study and pooled with DerSimonian-Laird random-effects meta-analysis. Several papers evaluated both a step change (direct change in incidence) and a slope change (change in incidence with time) after introduction of a smoking ban (appendix p 4), which were pooled in separate analyses. For this purpose, effect estimates derived from difference-in-difference models were considered step changes (appendix p 5).[28] Appendix p 6 shows the formulas used to calculate relative risk differences from absolute estimates and 95% CIs from standard errors. Substantial between-study heterogeneity was anticipated and handled through random-effects models. Heterogeneity was assessed with the I^2 test. We assessed potential publication bias by visual interpretation of funnel plots for the primary analyses. In view of the small number of studies in each meta-analysis, no attempt was made to formally test for small-study effects.[29] For the same reason, we decided not to do the planned sensitivity and subgroup analyses.[24] All analyses were done with StatsDirect (version 8) and Stata (version 12.0).

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We screened 9228 titles from which we identified 20 potentially eligible studies (figure 1).[20–23,30–45] One study reporting a mixed paediatric and adult population was excluded because subgroup analyses for children could not be obtained.[45] Eight further studies were excluded because they did not meet EPOC design criteria.[37–44] Appendix p 7 shows the characteristics and findings of the eight excluded studies. We identified 11 eligible studies, reported between 2008 and 2013: eight published papers[20–23,32,34–36] and three online reports.[30,31,33] One study reported the effect of a state-wide smoking ban and the previous overall effect of a combination of local bans introduced at different timepoints.[30] Following EPOC guidelines,[26] only the evaluation of the state-wide ban was included. Corresponding authors of several reports provided supplementary unpublished data for this report.[20–23,30–34]

Table 1 and appendix p 8 show the detailed study characteristics of the 11 eligible studies. In summary, there were five North American studies describing effects of district-wide or state-wide bans, and six European studies investigating the effect of national bans. Smoke-free legislation was generally comprehensive and introduced at once, except in a Belgian study in which a step-wise approach was used.[22] Four studies described the effect on paediatric asthma,[20,23,32,36] whereas all other studies reported on perinatal outcomes.[21,22,30,31,33–35] All studies were classified as interrupted time series, although specific analytical strategies differed. Three studies used a difference-in-difference design, which can be deemed a form of interrupted time series with a control group (appendix p 5). Outcomes for all studies were based on retrospective interrogation of routinely collected health-care data. Definitions of outcomes were similar between studies with two exceptions: small for gestational age was defined as a birthweight below the 5th centile for gestational age by Kabir and colleagues,[34] and as a birthweight below the 10th centile by others;[21,22] and Rayens and colleagues[36] evaluated asthma-related emergency department visits, whereas other reports studied admissions to hospital.[20,23,32]

Four studies were deemed to have low risk of bias, six had moderate, and one had high (appendix p 9). Lower risk studies tended to be of European origin, have large study populations, and evaluate national-level bans.

Tables 2 and 3 show the findings from each individual study. Three of five studies reported a significant reduction in preterm births after introduction of smoke-free legislation (figure 2A). A non-significant trend was reported in the Norwegian study, which was likely to be underpowered.[31] Meta-analysis showed smoke-free legislation to be associated with a clinically important and statistically significant drop in preterm birth (four studies, 1 366 862 participants; –10·4% [95% CI –18·8 to –2·0], p=0·016; figure 2A) with no subsequent effect on preterm birth rate change over time (appendix p 10). Data from one study could not be obtained and this study was not included in the meta-analysis.[33]

One of six studies showed a reduction of low birthweight after smoke-free legislation (figure 2B). Meta-analysis identified an effect that was not statistically significant (six studies, >1·9 million participants; –1·7% [95% CI –5·1 to 1·6], p=0·31; figure 2B, appendix p 10).

Three of four studies reported a significant drop in hospital attendance because of asthma after introduction of smoke-free legislation. Meta-analysis showed both an immediate reduction (three studies, 225 753 events; –10·1% [95% CI –15·2 to –5·0], p=0·0001; figure 2C) and an additional non-significant trend towards an annual rate decrease (three studies, 241 846 events: –7·5% per year [95% CI –16·0 to 0·9], p=0·081; appendix p 11) after introduction of smoking bans.

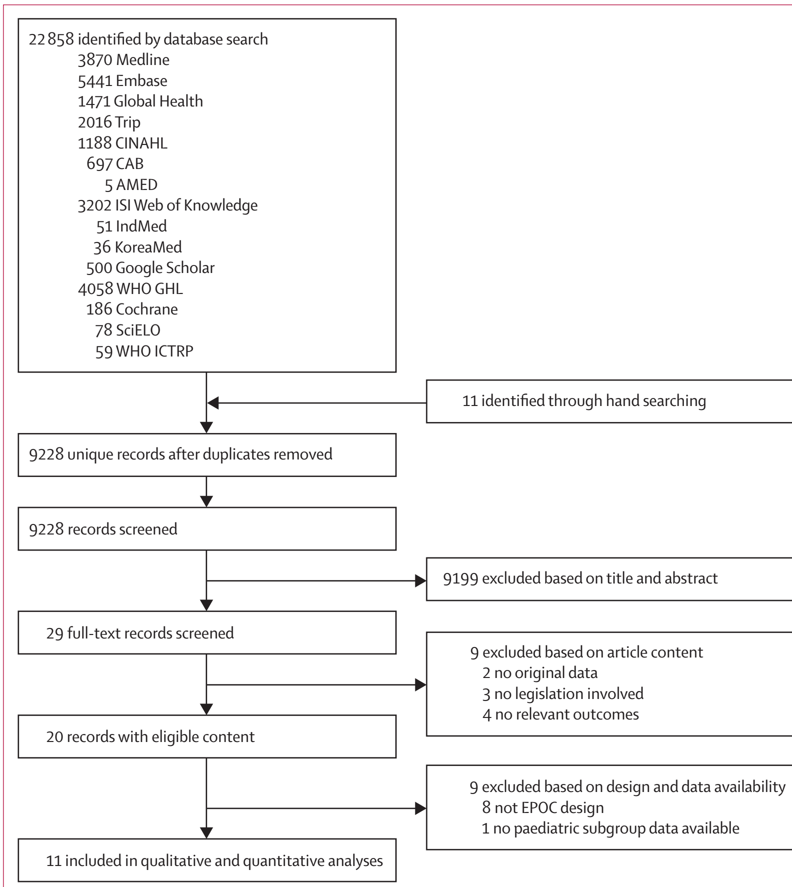

Figure 1: **Study selection**
EPOC=Cochrane Effective Practice and Organisation of Care.

In line with the overall effect of smoke-free legislation on preterm birth, one study[21] also reported a reduction in very preterm birth (table 3). One of two studies showed a significant effect on very low birthweight, with no significant effect observed after meta-analysis (figure 3A). Three studies investigated the effect of smoke-free

	Country (region)	Area pop ($\times10^6$)	Study design	Smoking ban			Age of partici-pants	Outcome				Summary risk of bias*
				Date	Location	Previous ban in place		Eligible outcomes	Definition	Data source	Exclusion criteria	
Amaral (2009)[30]	USA (California)	38·04	CITS	01/01/1995	Workplace (excluding hotels)	None (in intervention group)	Neonate	Low BW; very low BW	BW <2500 g; BW <1500 g	Birth certificates (California Dept for Health Services)	GA >4 SD	High
Bharadwaj (2012)[31]	Norway	4·95	CITS	01/06/2004	Bars and restaurants	Public places, workplace (excluding bars and restaurants)	Neonate	Preterm birth; low BW; very low BW; birth defects	GA <36 weeks; BW <2500 g; BW <1500 g; unclear	Medical Birth Registry of Norway	Babies whose mothers did not work in shop or hospitality industry	Moderate
Cox (2013)[22]	Belgium (Flanders)	6·25	ITS	01/01/2006 (ban 1), 01/01/2007 (ban 2), 01/01/2010 (ban 3)	Public places, workplace (excluding catering; ban 1), restaurants (ban 2), bars serving food (ban 3)	None (ban 1), public places, workplace (excluding catering; ban 2), public places, workplace (including restaurants not bars; ban 3)	Neonate	Preterm birth; low BW; small for GA	GA <37 weeks; GA <32 weeks; BW <2500 g; BW <p10 for GA	Study Centre for Perinatal Epidemiology	BW <500 g; GA <24 weeks; GA >44 weeks; multiple births; stillbirths	Low
Gaudreau (2013)[32]	Canada (Prince Edward Island)	0·14	ITS	01/06/2003	Public places, workplace (smoking areas allowed)	Unclear	0–14 years	Asthma admissions	ICD-9 493, ICD-10 J45/46	Discharge abstract database	None stated	Moderate
Hade (2011)[33]	USA (Ohio)	11·54	ITS	03/05/2007†	Public places, workplace	Variable (regional bans)	Neonate	Preterm birth Low BW	GA <37 weeks; BW <2500 g	Ohio certificates of livebirth	Multiple births	Moderate
Kabir (2013)[34]	Ireland	4·58	ITS	29/03/2004	Public places, workplace	None	Neonate	Small for GA; very small for GA	BW <p5 for GA; BW <p3 for GA	National Perinatal Reporting System	Multiple births; stillbirths	Low
Mackay (2010)[20]	UK (Scotland)	5·30	ITS	26/03/2006	Public places, workplace	None	0–14 years	Emergency asthma admissions	ICD-10 J45/46 (primary diagnosis)	Scottish Morbidity Record 01	None stated	Low
Mackay (2012)[21]	UK (Scotland)	5·30	ITS	26/03/2006	Public places, workplace	None	Neonate	Preterm birth; very preterm birth; low BW; small for GA; very small for GA	GA <37 weeks; GA <32 weeks; BW <2500 g; BW <p10 for GA; BW <p3 for GA	Scottish Morbidity Record 02	GA missing; GA <24 weeks; GA >44 weeks; multiple births; stillbirths	Low
Millett (2013)[23]	UK (England)	53·01	ITS	01/07/2007	Public places, workplace	None	0–14 years	Emergency asthma admissions to hospital	ICD-10 J45/46 (primary diagnosis)	Hospital Episode Statistics	None stated	Moderate
Page (2012)[35]	USA (Pueblo, El Paso, CO)	0·47	CITS	01/07/2003	Public places, workplace	None	Neonate	Preterm birth; low BW	GA <37 weeks; BW <2500 g	Colorado birth registry	Multiple births	Moderate
Rayens (2008)[36]	USA (Lexington-Fayette county, KY)	0·30	ITS	27/04/2004	Most public places	None	0–19 years	Asthma emergency department visit	ICD-9 493 (primary or secondary diagnosis)	Individual hospital (N=4) emergency department discharge records	None stated	Moderate

Pop=population. CITS=interrupted time series with control group. BW=birthweight. Dept=department. GA=gestational age. ITS=interrupted time series. p(n)=nth centile of birthweight for gestational age. ICD=International Classification of Diseases. *See appendix pp 9 for details. †Day enforcement began, ban implemented December, 2006.

Table 1: **Study characteristics—intervention and outcomes**

legislation on being small for gestational age, with two studies showing a significant step reduction. However, neither the step nor the slope reduction was significant after meta-analysis (figures 3B, appendix p 12). Important reductions were observed for very small for gestational age, although this was not a prespecified outcome. These reductions were statistically significant after pooling (two studies, 1 305 965 participants; step change: –5·3% [95% CI –5·4 to –5·2], p<0·0001, figure 3C; slope change: –0·6% per year [95% CI –0·604 to –0·596], p<0·0001; appendix p 12), but mainly driven by one study.[34] No effect was noted on birth defects in a small study, albeit with very wide CIs (table 3).[31] No studies were identified that investigated any of the other prespecified outcomes.[24]

Additional outcomes described in individual reports that are not reported here include preterm labour,[21] mild preterm birth,[21] moderate preterm birth,[21] extremely low birthweight,[31] birthweight less than 2000 g,[31] birthweight less than 3000 g,[35] sex,[31] Apgar score,[31] and birthweight and gestational age quantified on a continuous scale.[30]

	Population at risk (n)			Events (n)			Rate (%)		Slope before ban (% change in events per year)	Smoking ban effect estimates			Summary of findings
	Total	Before ban	After ban	Total	Before ban	After ban	Before ban	After ban		Model	Direct change in events (%): step change (95% CI)	Sustained change in events per year (%): slope change (95% CI)	
Preterm birth													
Bharadwaj (2012)[31]	822 (I), 3185 (C)	436 (I), 1659 (C)	386 (I), 1526 (C)	46 (I), 189 (C)	28 (I), 95 (C)	18 (I), 94 (C)	6·42 (I), 5·73 (C)	4·66 (I), 6·16 (C)	NR	Adjusted	–2·55%* (–5·52 to 0·42)	NA	Trend towards reduction in preterm birth in mothers newly exposed to work place smoking ban during pregnancy
Cox (2013)[22] (ban 1)	606 877	228 323	378 554	36 663	13 916	22 747	6·09	6·01	NR	Single ban, adjusted; final model, adjusted	–0·59% (–2·63 to 1·49); no effect	–1·95% (–3·50 to –0·37); no effect	Immediate 3% reduction in preterm births after smoking ban in restaurants and gradual 4% per year decrease in preterm birth rate after subsequent ban in bars serving food
Cox (2013)[22] (ban 2)	606 877	289 194	317 683	36 663	17 663	19 000	6·11	5·98	NR	Single ban, adjusted; final model, adjusted	–2·28% (–4·37 to –0·15); –3·18% (–5·38 to –0·94)	–1·42% (–2·87 to 0·05); no effect	Immediate 3% reduction in preterm births after smoking ban in restaurants and gradual 4% per year decrease in preterm birth rate after subsequent ban in bars serving food
Cox (2013)[22] (ban 3)	606 877	478 455	128 422	36 663	29 047	7616	6·07	5·93	NR	Single ban, adjusted; final model, adjusted	–1·24% (–3·05 to 0·60); no effect	–2·10% (–4·82 to 0·69); –3·50 (–6·35 to –0·57)	Immediate 3% reduction in preterm births after smoking ban in restaurants and gradual 4% per year decrease in preterm birth rate after subsequent ban in bars serving food
Hade (2011)[33]	583 530	NR	NR	NR	NR	NR	NR	NR	NR	Unclear	No effect	No effect	No significant change in preterm birth rate after smoking ban
Mackay (2012)[21]	709 756	541 031	168 725	41 998	32 137	9861	5·94	5·84	NR	Un-adjusted; adjusted	–11·07% (–15·15 to –6·79); –11·72% (–15·87 to–7·35)	2·28% (–0·03 to 4·66); 3·83% (1·42 to 6·30)	Immediate 12% reduction in preterm births after smoking ban, but gradual 4% per year increase subsequently
Page (2012)[35]	6717 (I), 32 293 (C)	3421 (I), 16 348 (C)	3296 (I), 15 945 (C)	515 (I), 2767 (C)	270 (I), 1296 (C)	245 (I), 1471 (C)	7·89 (I), 7·93 (C)	7·44 (I), 9·23 (C)	NR	Un-adjusted; adjusted	–20·6% (–34·7 to –3·4); –23·1% (–40·1 to –1·3)	NA; NA	Preterm births reduced by 23% after city-wide smoking ban compared with city where no ban was introduced

(Table 2 continues on next page)

	Population at risk (n)			Events (n)			Rate (%)		Slope before ban (% change in events per year)	Smoking ban effect estimates			Summary of findings
	Total	Before ban	After ban	Total	Before ban	After ban	Before ban	After ban		Model	Direct change in events (%): step change (95% CI)	Sustained change in events per year (%): slope change (95% CI)	
(Continued from previous page)													
LBW													
Amaral (2009)[30]	NR	NR	NR	NR	NR	NR	5·7†	5·7†	NR	Adjusted	−0·00%* (−0·14 to 0·14)	NA	No significant change in LBW rate after state-wide smoking ban
Bharadwaj (2012)[31]	822 (I); 3185 (C)	436 (I); 1659 (C)	386 (I); 1526 (C)	49 (I); 185(C)	26 (I); 98 (C)	23 (I); 87 (C)	5·96 (I); 5·91 (C)	5·96 (I); 5·70 (C)	NR	Adjusted	−0·06%* (−2·82 to 2·70)	NA	No significant change in LBW rate after smoking ban
Cox (2013)[22] (ban 1)	606 877	228 323	378 554	28 678	11 069	17 609	4·85	4·65	NR	Single ban, adjusted; final model, adjusted	−0·19% (−2·48 to 2·16); no effect	0·39% (−1·38 to 2·20); no effect	No significant change in LBW rate after smoking bans
Cox (2013)[22] (ban 2)	606 877	289 194	317 683	28 678	13 950	14 728	4·82	4·64	NR	Single ban, adjusted; final model, adjusted	0·06% (−2·33 to 2·52); no effect	0·21% (−1·44 to 1·89); no effect	No significant change in LBW rate after smoking bans
Cox (2013)[22] (ban 3)	606 877	478 455	128 422	28 678	22 831	5847	4·77	4·55	NR	Single ban, adjusted; final model, adjusted	−0·49% (−2·54 to 1·60); no effect	−1·26% (−4·35 to 1·92); no effect	No significant change in LBW rate after smoking bans
Hade (2011)[33]	583 530	NR	NR	50 185	NR	NR	NR	NR	NR	ARIMA; logistic regression	1% (−2 to 4); 2% (−1 to 6)	−1·4% (−1·5 to −1·3); NA	1% per year decrease in LBW rate after smoking ban
Mackay (2012)[21]	709 279	540 756	168 523	39 623	30 639	8984	5·67	5·33	NR	Unadjusted; adjusted	−9·53% (−13·82 to −5·04); −9·85% (−14·24 to −5·23)	−1·08% (−3·42 to 1·32); 0·89% (−1·56 to 3·41)	Immediate 10% reduction in low birthweight after smoking ban, with no subsequent annual rate change
Page (2012)[35]	6717 (I), 32 293 (C)	3421 (I), 16 348 (C)	3296 (I), 15 945 (C)	558 (I), 2612 (C)	291 (I), 1283 (C)	261 (I), 1329 (C)	8·51 (I), 7·85 (C)	7·92 (I), 8·34 (C)	NR	Unadjusted; adjusted	−13·3% (−28·4 to 5·0); 4·4% (−17·6 to 32·3)	NA; NA	No change in LBW after city-wide smoking ban compared with city without ban
Asthma													
Gaudreau (2013)[32]	NR	NR	NR	3050	2303	747	NR	NR	NR	Adjusted	11% (−37 to 95)	0% (−2 to 2)	No significant change in rate of paediatric asthma admission to hospital rate after smoking ban
Mackay (2010)[20]	NR	NR	NR	21 415	13 752	7663	0·253	0·222	4·4% (3·3 to 5·5)	Adjusted	NA	−19·5% (−22·4 to −16·5)	Paediatric asthma admissions decreased by 20% per year since smoking ban
Millett (2013)[23]	NR	NR	NR	217 381	NR	NR	NR	NR	2·2% (2 to 3)	Adjusted	−8·9% (−11 to −7)	−3·4% (−4 to −2)	Immediate 9% drop in paediatric asthma admissions to hospital after smoking ban with subsequent 3% per year decrease
Rayens (2008)[36]	395 116	NR	NR	5322	NR	NR	NR	NR	12·7%	Adjusted	−18% (−29 to −4)	NA	Immediate 18% drop in paediatric asthma emergency department visits after smoking ban

Effect size indicates relative change unless otherwise indicated. I=intervention group. C=control group. NR=not reported. NA=not analysed. LBW=low birthweight. ARIMA=autoregressive integrated moving average. GLM=generalised linear model. *Absolute change (percentage points). †Overall rate.

Table 2: **Primary outcomes per study**

	Population at risk			Events			Rate (%)		Slope (% change in events per year)	Smoking ban effect estimates			Summary of findings
	Total	Before ban	After ban	Total	Before ban	After ban	Before ban	After ban		Model	Direct change in events (%): step change (95% CI)	Sustained change in events per year (%): slope change (95% CI)	
Very preterm birth													
Mackay (2012)[21]	709 756	541 031	168 725	6265	4814	1451	0·89	0·86	NR	Unadjusted; adjusted	–16·60% (–25·92 to –6·11); –17·41% (–26·86 to –6·73)	2·40% (–3·37 to 8·52); 4·27% (–1·73 to 10·65)	Immediate 17% reduction in very preterm births after smoking ban, with trend towards subsequent increase in annual rate change
VLBW													
Amaral (2009)[30]	NR	NR	NR	NR	NR	NR	0·8†	0·8†	NR	Adjusted	–0·03%* (–0·09 to 0·03)	NA	No significant change in VLBW rate after state-wide smoking ban
Bharadwaj (2012)[31]	822 (I); 3185 (C)	436 (I); 1659 (C)	386 (I); 1526 (C)	14 (I); 43 (C)	10 (I); 18 (C)	4 (I); 25 (C)	2·29 (I); 1·08 (C)	1·04 (I); 1·64 (C)	NR	Adjusted	–1·89%* (–3·46 to –0·31)	NA	Absolute 2% decrease in VLBW in mothers newly exposed to working place smoking ban during pregnancy
SGA													
Cox (2013)[22] (ban 1)	606 877	228 323	378 554	59 799	23 423	36 376	10·26	9·61	NR	Single ban, adjusted; final model; adjusted	–0·25% (–2·07 to 1·60); no effect	–3·20% (–6·93 to 0·68); no effect	No significant change in SGA rate after smoking bans
Cox (2013)[22] (ban 2)	606 877	289 194	317 683	59 799	29 392	30 407	10·16	9·57	NR	Single ban, adjusted; final model; adjusted	–0·82% (–2·53 to 0·92); no effect	–3·44% (–7·96 to 1·31); no effect	No significant change in SGA rate after smoking bans
Cox (2013)[22] (ban 3)	606 877	478 455	128 422	59 799	47 543	12 256	9·94	9·54	NR	Single ban, adjusted; final model, adjusted	0·32% (–1·95 to 2·65); no effect	0·80% (–2·81 to 4·54); no effect	No significant change in SGA rate after smoking bans
Kabir (2013)[34]	588 997	283 628	305 369	39 773	19 725	20 048	6·95	6·57	NR	Adjusted	–0·45 % (–0·70 to –0·20)	–0·02% (–0·03 to 0·01)	Immediate 0·5% drop in SGA after smoking ban with subsequent 0·02% per year decrease
Mackay (2012)[21]	709 279	540 756	168 523	64 600	50 394	14 206	9·32	8·43	NR	Unadjusted; adjusted	–4·54% (–8·21 to –0·73); –4·52% (–8·28 to –0·60)	–2·68% (–4·54 to –0·77); –1·54 (–3·47 to 0·44)	Immediate 5% drop in SGA after smoking ban with trend towards subsequent decrease in yearly rate change
vSGA													
Kabir (2013)[34]	588 997	283 628	305 369	26 055	13 085	12 970	4·61	4·24	NR	Adjusted	–5·3% (–5·42 to –5·18)	–0·600% (–0·604 to –0·596)	Immediate 5% drop in vSGA after smoking ban with subsequent 0·6% per year decrease
Mackay (2012)[21]	709 279	540 756	168 523	14 460	11 373	3087	2·10	1·83	NR	Unadjusted; adjusted	–7·82% (–14·95 to –0·09); –7·95% (–15·19 to –0·08)	–3·03% (–6·85 to 0·94); –1·23% (–5·17 to 2·88)	Immediate 8% drop in vSGA after smoking ban with no subsequent difference in rate change
Birth defects													
Bharadwaj (2012)[31]	822 (I); 3185 (C)	436 I); 1659 (C)	386 I); 1526 (C)	45 (I); 203 (C)	26 (I); 115 (C)	19 (I); 88 (C)	5·96 (I); 6·93 (C)	4·92 (I); 5·77 (C)	NR	Adjusted	–0·03%* (–3·99 to 3·92)	NA	No change in birth defects among mothers newly exposed to working place smoking ban during pregnancy

Effect size indicates relative change unless otherwise indicated. NR=not reported. VLBW=very low birthweight. I=intervention group. C=control group. NA=not analysed. SGA=small for gestational age. vSGA=very small for gestational age.*Absolute change (percentage points). †Overall rate.

Table 3: **Secondary outcomes per study**

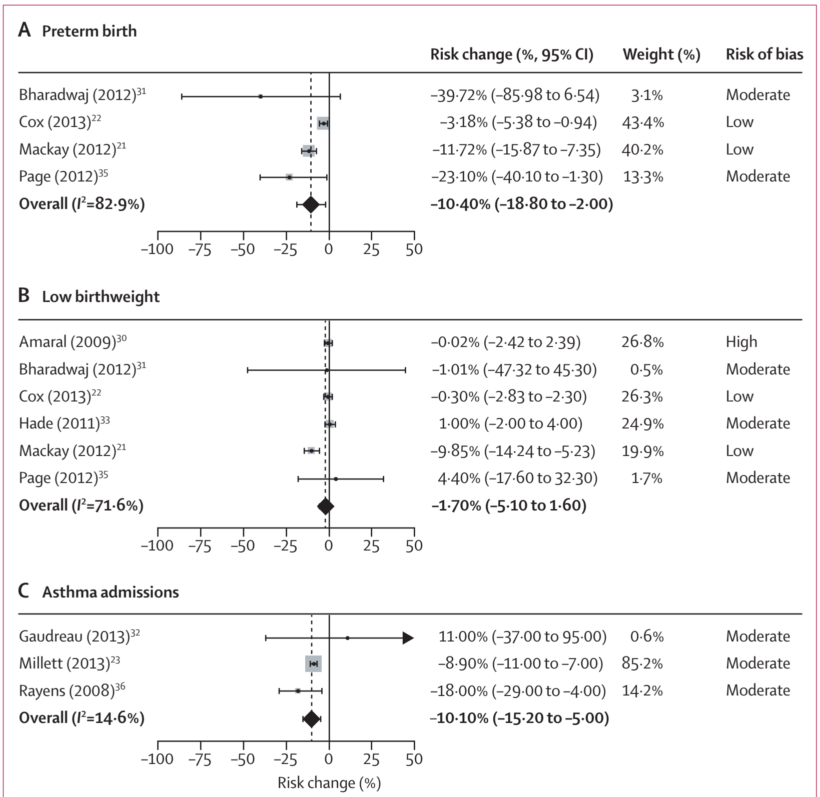

Figure 2: **Meta-analysis of step changes in primary outcomes after smoking ban**
(A) Preterm birth. (B) Low birthweight. (C) Asthma admissions to hospital. The low-birthweight point estimate for Cox and colleagues[22] was based on a backward selection model with a single step and single slope change, similar to the preterm birth model.

Visual interpretation of funnel plots showed potential publication bias for the studies on preterm birth, but not for those on low birthweight or asthma (appendix p 13).

Discussion

This systematic review and meta-analysis presents strong evidence supporting the effectiveness of smoke-free legislation to improve clinically important perinatal and child health outcomes. In particular, pooled estimates suggest that rates of both preterm birth and paediatric hospital admissions for asthma were reduced by 10% after its introduction. Additional reductions in the risk of being born very small for gestational age were identified. This Article adds important information from an early-life perspective to the growing evidence base supporting the mandate for worldwide implementation of smoke-free legislation as a means to improve population health.

As far as we are aware this is the first systematic review and meta-analysis of the effect of smoke-free legislation on child health. By use of a comprehensive search strategy, we were able to identify a substantial body of evidence, including an important share of unpublished reports.[30,31,33] Although unpublished reports might suggest that additional unidentified evaluations potentially exist, none were identified by our international panel of experts. The small number of studies hampered visual interpretation of funnel plots and precluded formal assessment of small study effects that might have indicated consequential publication bias.[24,29]

Substantial variation was present in sample size and the number of pre-ban and post-ban observations. As a result, precision of the reported point estimates varied greatly between studies and was very low in some, potentially suggesting that they were underpowered.[31,32] We therefore decided to address this issue by doing a meta-analysis to provide a better overall appreciation of the effect of smoke-free legislation on each outcome.[24] The inclusion of some very large studies,[46] and differences in study design, analysis strategy,[47] and smoking ban coverage and enforcement, are likely to contribute to the observed heterogeneity, which was handled through random-effects modelling.[48]

Intrinsic to community-based policy interventions, which rarely allow evaluation via randomised controlled trial designs,[47] the evidence presented here is derived from observational studies, which are inherently at risk of bias. All but one study had low to moderate risk of bias, and overall no clear association between risk of bias and effect size was apparent. To involve only the highest quality evidence available in our report, we followed EPOC guidelines and included only quasiexperimental studies.[26] On the suggestion of peer reviewers, we undertook a post-hoc sensitivity analysis that included studies that did not fit EPOC design criteria, but this analysis did not materially affect the results (data not shown). A limitation of this study is that we were unable to do the predefined subgroup and sensitivity analyses because of the low number of studies in each meta-analysis.[24]

Several within-study aspects that could have affected estimation of the effect of the smoking ban require consideration. Steep incidence changes in hospital attendance for asthma in the pre-ban period could have resulted in overestimation of the effect of the ban in one study,[36] and in underestimation in another.[32] Complicating interpretation of the difference-in-difference study by Page and colleagues[35] is the suggestion that the effect might be attributable to an increasing incidence in the control site rather than a decrease in the intervention site.[49] Although these issues underline some of the pitfalls in interpreting interrupted time series studies,[47] several studies also showed the robustness of the association with extensive sensitivity and subgroup analyses,[20–23,31,34] and by pinpointing the timing of public health benefit to that of introduction of the ban.[34] These issues are important in view of the criticism that interrupted time-series analyses might identify the intervention under study as being responsible for an effect that might in fact be due to other unmeasured factors.[47]

The positive effect of smoke-free legislation on selected indicators of child health adds an important dimension to the substantial body of evidence supporting its benefit to adult health. Reductions in cardiovascular and cerebrovascular events, hospital admissions for respiratory disease, and respiratory and sensory symptoms have been reported in several meta-analyses.[7,50–53] Causality is further supported by a dose-response effect for most outcomes, with comprehensive smoking laws having the largest health benefit.[7] Many studies have identified that smoking bans effectively reduce maternal smoking during pregnancy and second-hand smoke exposure during childhood.[23,31,35,43,54,55] The proportion of smoke-free homes increased in several countries after smoke-free laws, disproving initial fears that smoking would be displaced towards the home.[18,19,54–57] The health benefit in children is likely to be mediated through these reductions in antenatal and postnatal second-hand smoke exposure. Despite reports that smoke-free laws selectively reduce second-hand smoke exposure in less exposed and less deprived children,[15,18,54,55,58] its effect has been shown to be consistent across socioeconomic backgrounds.[20]

The association between smoke-free laws and reductions in preterm birth, birthweight for gestational age, and asthma events identified by our meta-analysis accord with recognised associations of these outcomes with second-hand smoke exposure and are biologically plausible.[10–12] Findings from meta-analyses have shown that second-hand smoke exposure is associated with an increased risk of low birthweight and intrauterine growth restriction.[59,60] Although observational evidence of the effect of second-hand smoke exposure on length of gestation is inconclusive,[59–61] a randomised controlled trial showed a significant reduction in very preterm birth after an intervention that decreased second-hand smoke exposure in the home.[62] A strong association between both antenatal and postnatal second-hand smoke exposure and childhood asthma furthermore exists,[1,63,64] supporting a positive effect of smoke-free legislation on asthma events.[20,23,36]

The public health effect of smoke-free legislation on perinatal and paediatric health is considerable. Worldwide, more than 11% of children are born preterm, amounting to 15 million babies each year.[65] Despite efforts to address this issue, preterm birth rates continue to rise in most regions.[65] In view of recent estimations that in high-income countries implementation of the five most effective preventive approaches (maternal smoking cessation, progesterone, cervical cerclage, decreasing non-medically indicated caesarean section, and labour induction, and limiting multiple embryo transfer in assisted reproductive technology) could maximally reduce preterm birth by 5%,[66] a possible 10% reduction by smoke-free legislation is promising. Although one negative study could not be included in the meta-analysis, potentially resulting in overestimation of the true effect, even a small reduction in preterm birth is relevant at the population level.[67] In view of the well recognised long-term adverse consequences of preterm birth, this health benefit holds potential to

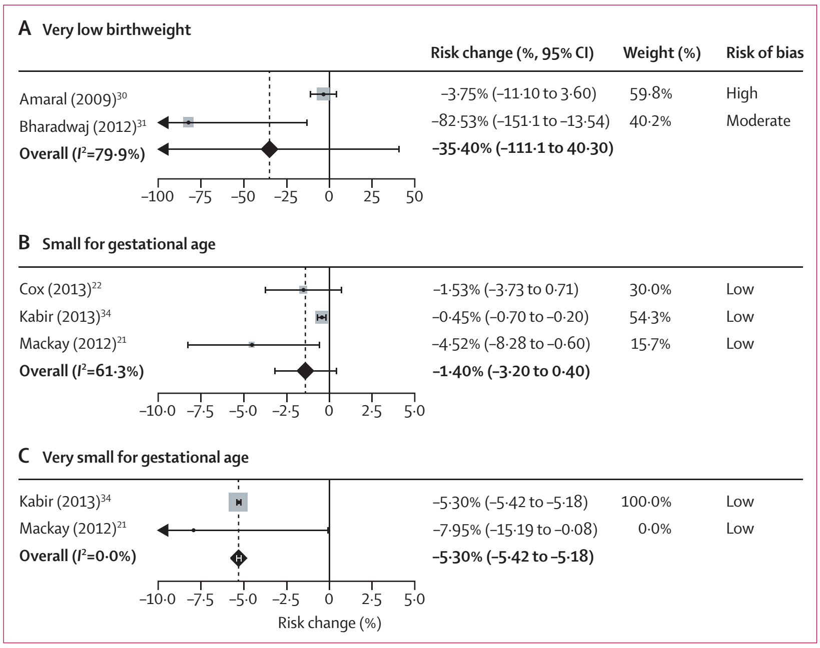

Figure 3: **Meta-analysis of step changes in secondary outcomes after smoking ban**
(A) Very low birthweight. (B) Small for gestational age. (C) Very small for gestational age. The small-for-gestational-age point estimate for Cox and colleagues[22] was based on a backward selection model with a single step and single slope change, similar to the preterm birth model.

extend throughout the entire lifecourse.[67] The adverse effect of intrauterine growth on adult health suggests that the same might be true for its effect on being very small for gestational age.[8] In view of its effect on preterm birth, it seems surprising that our meta-analysis did not identify an effect on low birthweight. Possibly, the risk reduction of preterm birth at the population level attributed to smoking bans is not large enough to translate into an effect on population birthweight. Furthermore, similar to myocardial infarction syndrome, second-hand smoke exposure could act as an onset factor or trigger for preterm birth, whereas birthweight is more importantly affected by its cumulative effect over time. The public health relevance of a reduction in asthma, which is now the most common chronic disease in childhood,[68] is unambiguous and might project into adulthood in view of evidence of long-term tracking of reduced lung function and a corresponding link with chronic obstructive pulmonary disease.[69]

Despite the emerging evidence for early-life health benefits associated with smoke-free legislation, several knowledge gaps remain. Although we searched relevant regional and global health databases, we were unable to identify any studies from low-income or middle-income countries, where the highest burden of early-life adverse outcomes lies.[70,71] Although this burden suggests great potential for smoke-free laws to benefit population health,[72] this promise might need to be tempered because of concerns about the challenges of enforcement and as yet contradictory effects on smoking patterns in the home.[18,73] Therefore, the possibility is raised that findings from high-income countries might not easily be globally generalisable, showing the pressing need for studies assessing the effect of tobacco control measures in countries with low and middle income. Additional studies would furthermore help to expand the present evidence base, which is now centred on a small number of studies, with pooled effect estimates consequentially less precise than in adult reports.[7,50–53] Most of the health burden of second-hand smoke exposure in childhood is related to respiratory tract infections, and studies are needed to estimate the effect of smoke-free legislation on this outcome.[1] In keeping with the recognised link between second-hand smoke and sudden infant death syndrome,[12] smoke-free public places have been associated with reductions in its incidence.[39] Further large studies are needed to assess their effect on early-life mortality. Finally, comprehensive assessment is needed of the early-life effect of additional tobacco control measures including taxation and advertisement bans, because these effects could be difficult to distinguish from those of smoke-free legislation and they might act synergistically to improve population health.[74]

Smoke-free legislation is a cost-effective population intervention in view of the magnitude of its public health benefits and the established absence of adverse economic effects that have long been claimed by the tobacco industry.[75–77] Formal cost-effectiveness studies are, however, needed to further substantiate this notion.

In conclusion, we provide clear evidence showing reductions in preterm birth, asthma events in childhood, and being born very small for gestational age after introduction of smoke-free legislation. Although the exact mechanisms by which smoke-free legislation exerts its effect are unknown, it is now evident that early-life protection from involuntary second-hand smoke exposure holds great potential to reduce the consequential disease burden and associated economic losses posed to society. This report thus provides support from an early-life perspective for present WHO recommendations to implement smoke-free public environments on a national level.[4,5] These findings should be regarded as an integral part of public health strategy to further reduce the worldwide burden of disease associated with smoking.[1,2,78]

Contributors

JVB coconceived and designed the study; secured funding; was involved in the search process, study selection, quality assessment, data extraction, and analysis; and wrote the manuscript. UBN was involved in the search process, study selection, quality assessment, and data extraction, and commented on the manuscript. BC and TSN were involved in data extraction and analysis, and figure preparation, and commented on drafts of the manuscript. CPvS advised in the study selection and data handling, and commented on drafts of the manuscript. AS coconceived this study, helped to develop the methods, supervised the work, and commented on drafts of the manuscript. JVB had full access to all the data presented and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare that we have no competing interests.

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