Effect of tobacco control policies on perinatal and child health

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Effect of tobacco control policies on perinatal and child health: a systematic review and meta-analysis

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Summary

Background Tobacco smoking and smoke exposure during pregnancy and childhood cause considerable childhood morbidity and mortality. We did a systematic review and meta-analysis to investigate whether implementation of WHO’s recommended tobacco control policies (MPOWER) was of benefit to perinatal and child health.

Methods We searched 19 electronic databases, hand-searched references and citations, and consulted experts to identify studies assessing the association between implementation of MPOWER policies and child health. We did not apply any language restrictions, and searched the full time period available for each database, up to June 22, 2017. Our primary outcomes of interest were perinatal mortality, preterm birth, hospital attendance for asthma exacerbations, and hospital attendance for respiratory tract infections. Where possible and appropriate, we combined data from different studies in random-effects meta-analyses. This study is registered with PROSPERO, number CRD42015023448.

Findings We identified 41 eligible studies (24 from North America, 16 from Europe, and one from China) that assessed combinations of the following MPOWER policies: smoke-free legislation (n=35), tobacco taxation (n=11), and smoking cessation services (n=3). Risk of bias was low in 23 studies, moderate in 16, and high in two. Implementation of smoke-free legislation was associated with reductions in rates of preterm birth (−3·77% [95% CI −6·37 to −1·16]; ten studies, 27 530 183 individuals), rates of hospital attendance for asthma exacerbations (−9·83% [−16·62 to −3·04]; five studies, 684 826 events), and rates of hospital attendance for all respiratory tract infections (−3·45% [−4·45 to −2·45]; two studies, 1 681 020 events) and for lower respiratory tract infections (−18·48% [−32·79 to −4·17]; three studies, 887 414 events). Associations appeared to be stronger when comprehensive smoke-free laws were implemented than when partial smoke-free laws were implemented. Among two studies assessing the association between smoke-free legislation and perinatal mortality, one showed significant reductions in stillbirth and neonatal mortality but did not report the overall effect on perinatal mortality, while the other showed no change in perinatal mortality. Meta-analysis of studies on other MPOWER policies was not possible; all four studies on increasing tobacco taxation and one of two on offering disadvantaged pregnant women help to quit smoking that reported on our primary outcomes had positive findings. Assessment of publication bias was only possible for studies assessing the association between smoke-free legislation and preterm birth, showing some degree of bias.

Interpretation Smoke-free legislation is associated with substantial benefits to child health. The majority of studies on other MPOWER policies also indicated a positive effect. These findings provide strong support for implementation of such policies comprehensively across the world.

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Introduction

Almost half of children worldwide are regularly exposed to second-hand smoke, and 28% of the 600 000 deaths each year related to second-hand smoke occur in children. Maternal smoking and second-hand smoke exposure during pregnancy are detrimental to fetal growth and development, leading to adverse birth outcomes such as preterm birth, low birthweight, being small for gestational age, and perinatal and infant mortality. Additionally, second-hand smoke exposure presents substantial health risks postnatally by increasing the risk of asthma and respiratory tract infections. Protection of children from the adverse health implications of second-hand smoke during important phases of development and the subsequent disease burden carried on into adulthood is crucial. The WHO Framework Convention on Tobacco Control (FCTC) aims to reduce tobacco consumption and second-hand smoke exposure through national tobacco control programmes. In 2008, six MPOWER measures were introduced to guide FCTC implementation (panel). With tobacco use increasingly becoming a problem of developing countries already experiencing the largest burden of early-life morbidity and mortality, the absence of tobacco regulation is set to be a big driver of between-country inequality in child health outcomes. However, evaluations of the effectiveness of tobacco control interventions have generally excluded children, focusing instead on smoking rates and adult health outcomes.
In a previous systematic review, we partly addressed this gap in the literature by synthesising available evidence on the effect of smoke-free legislation (ie, “P” in MPOWER, for “Protect people from tobacco smoke”) on perinatal and child health. By combining data from 11 studies, we found smoke-free legislation to be associated with substantial reductions in preterm birth and hospital admissions for asthma among children. Studies have since addressed various knowledge gaps identified in our previous review, including assessments of the effect of smoke-free legislation on respiratory tract infections, the most important contributor to the global burden of paediatric morbidity and mortality associated with tobacco smoke exposure. The increased number of studies now available was also anticipated to allow investigation of another knowledge gap: exploration of a potential dose–response association between the comprehensiveness of smoke-free laws and their effect on child health. Furthermore, we sought to substantially broaden the focus of our study by evaluating the early-life health effect of the entire range of WHO-recommended tobacco control policies (ie, MPOWER). Following a prespecified and peer-reviewed protocol, we did a comprehensive literature search for experimental and quasi-experimental studies assessing associations between implementation of MPOWER policies and key perinatal and childhood outcomes associated with tobacco smoke exposure.

### Evidence before this study

Tobacco smoke exposure is the world’s leading cause of preventable morbidity and premature mortality. Children cannot control their tobacco smoke exposure and therefore need protection through tobacco control measures. In a previous systematic review, we investigated the associations between smoke-free legislation and perinatal and child health outcomes. We searched 14 online medical research databases, the WHO International Clinical Trials Registry Platform, hand-searched references and citations, and consulted a panel of experts in the field to identify published and unpublished literature in any language from January, 1975, to May, 2013, on the associations between smoke-free legislation and our outcomes of interest. The primary outcomes were preterm birth, low birthweight, and hospital attendance for asthma. We identified 11 studies showing that smoke-free legislation was associated with significant reductions in preterm birth and severe asthma exacerbations. Studies have since addressed various knowledge gaps identified in our previous review, including assessments of the effect of smoke-free legislation on respiratory tract infections, the most important contributor to the global burden of paediatric morbidity and mortality associated with tobacco smoke exposure. The increased number of studies now available was also anticipated to allow investigation of another knowledge gap: exploration of a potential dose–response association between the comprehensiveness of smoke-free laws and their effect on child health. Furthermore, we sought to substantially broaden the focus of our study by evaluating the early-life health effect of the entire range of WHO-recommended tobacco control policies (ie, MPOWER). Following a prespecified and peer-reviewed protocol, we did a comprehensive literature search for experimental and quasi-experimental studies assessing associations between implementation of MPOWER policies and key perinatal and childhood outcomes associated with tobacco smoke exposure.

### Added value of this study

To our knowledge, this is the first systematic review examining the association between the full spectrum of MPOWER policies and perinatal and child health. Our findings add value to the existing evidence base by identifying a link between smoke-free legislation and a substantial reduction in severe paediatric respiratory tract infections, providing consistent evidence that comprehensive smoke-free laws are associated with broad health effects, and collating evidence supporting the potential for other MPOWER measures to benefit child health. We also identified several key knowledge gaps, including a shortage of studies in low-income and middle-income countries, and of studies assessing MPOWER measures other than smoke-free legislation, tobacco tax increases, and smoking cessation services.

### Implications of all the available evidence

With most of the world’s population currently not covered by comprehensive tobacco control policies, there is great potential for global public health gains by protecting unborn babies and children from tobacco smoke exposure. Future efforts should focus on increasing the uptake of comprehensive MPOWER policies worldwide to protect the health of children, while developing and evaluating new and ongoing tobacco control policy initiatives around the world.

### Methods

#### Search strategy and selection criteria

This systematic review and meta-analysis was done according to a peer-reviewed protocol that is published and registered with PROSPERO (CRD42015023448). We followed the PRISMA checklist when reporting our findings. Ethical approval was not required for this study. Studies were eligible for inclusion if they investigated the association between one or more MPOWER tobacco control policies and health outcomes among fetuses, neonates, or children (ie, the majority of the study population aged <12 years).

We searched for published studies in the following databases: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, PsycINFO,
Our primary outcomes of interest were stillbirth, early neonatal mortality, perinatal mortality, preterm birth, very preterm birth, gestational age (continuous scale), congenital anomalies, asthma, wheezing, respiratory tract infections, upper respiratory tract infections, lower respiratory tract infections, otitis media with effusion, and chronic cough. Studies were excluded if they only measured smoking prevalence, smoking behaviour, second-hand smoke exposure, surrogate outcomes, or economic outcomes. Studies that reported outcomes for both adults and children were included if paediatric subgroup data were available.

**Data analysis**

Two reviewers (TF and AK) independently assessed all search results by title and abstract, and by full text for potential eligible studies identified. Any disagreements were resolved through joint discussion or via an adjudicator (JVB).

Relevant data were extracted with a customised data extraction form (appendix, pp 3–5). Study authors were contacted for clarification where necessary and to obtain relevant data that were missing from the reports. A risk-of-bias assessment form was created on the basis of EPOC criteria for interrupted time series and controlled before-and-after studies. Two reviewers (TF and AK) independently extracted data and assessed risk of bias, with disagreements resolved through discussion or arbitration (JVB).

Point estimates and corresponding 95% CIs for effect sizes or association measures were extracted. For dichotomous outcomes, risk ratios (RRs) were extracted. Where RRs were not available, we calculated RRs from odds ratios (ORs) using the following formula, where PEER is the patient-expected event rate in the control group:

\[
RR = \frac{OR}{(1 – PEER) + (PEER \times OR)}
\]

When PEER was not available in interrupted time series studies we used the overall event rate across the study population as an approximation. For outcomes that could occur more than once (eg, hospital attendances for asthma and respiratory tract infections), we used incidence rate ratios (IRR).

Aggregated effect estimates were calculated to assess the association between each tobacco control policy and individual health outcomes, where feasible. Relative risk differences were extracted or calculated from absolute risk differences and were pooled in random-effects meta-analyses given anticipated heterogeneity. Step changes (ie, immediate risk changes) following introduction of an intervention were pooled in separate analyses from slope changes (ie, gradual risk changes). Heterogeneity was assessed by the \( I^2 \) statistic. For the meta-analyses, we selected the effect estimate of the most comprehensive intervention within each MPOWER category from each
Articles

Figure 1: PRISMA flow diagram
EPOC= Effective Practice and Organization of Care (a Cochrane Review Group). MPOWER=WHO’s recommended tobacco control policies (see panel).

Panel: MPOWER policies
Monitor tobacco use
Eligible policies include those that enforce accurate measurement of the extent of the tobacco epidemic and of the interventions to control it.

Protect people from smoke
Eligible policies include legislation to create smoke-free public environments (both indoors and outdoors).

Offer help to quit tobacco use
Eligible policies include tobacco cessation advice or interventions offered through health-care services, free telephone quit lines, and providing access to free or low-cost cessation medicines.

Warn about the dangers of tobacco
Eligible policies include health warnings on tobacco products, plain packaging of tobacco products, and mass media campaigns to educate the public about the dangers of tobacco.

Enforce bans on tobacco advertising, promotion and sponsorship
See WHO Framework Convention on Tobacco Control (FCTC) guidelines for implementation of Article 13, which provides a non-exhaustive list of advertising, promotion, and sponsorship within the terms of the FCTC.

Raise taxes on tobacco
Eligible policies include increasing percentage excise tax share in final tobacco.

Results
We identified 25 478 citations from bibliographic databases and an additional 20 from other sources. After removal of duplicates, 12 392 unique citations were screened by title and abstract, and 65 full texts were sourced. Of these, 41 EPOC studies and three non-EPOC studies fit the inclusion criteria (figure 1; appendix, pp 6, 7). The EPOC studies included data from more than 57 million births, and from 4·6 million GP diagnoses and 2·7 million hospital admissions for respiratory conditions.

We assessed risk of bias across studies using funnel plots when ten or more studies were included in a meta-analysis.

Role of the funding source
The funders 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.

Study. In case of overlapping populations between studies, we selected one study according to the following hierarchy: the lowest risk of bias, the most comprehensive intervention, or the largest study population. We also extracted data on changes in smoking behaviour and second-hand smoke exposure if reported. The comprehensiveness of smoke-free legislation was assessed by counting the number of locations that were made completely smoke-free, out of eight prespecified options as suggested by WHO. Policies that were completely smoke-free in all eight locations were considered to be comprehensive.

We did sensitivity analyses to explore the robustness of our findings by reanalysing the data for the primary outcomes with the addition of non-EPOC studies, and by restricting analyses to studies with low risk of bias and moderate risk of bias. Where possible, we did subgroup analyses according to the comprehensiveness of each intervention. Where possible, the effect of each intervention was reported according to socioeconomic status, alongside its overall effect.

We assessed risk of bias across studies using funnel plots when ten or more studies were included in a meta-analysis.

References

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The appendix (pp 8–20) details the main characteristics of the EPOC studies. Among these, 26 were interrupted time series studies, 14 were controlled interrupted time series studies, and one had a regression discontinuity design, a quasi-experimental design bearing close resemblance to interrupted time series methodology. The three non-EPOC studies were uncontrolled before-and-after studies (appendix, p 21). Model characteristics of individual studies can be found in the appendix (pp 22–31). The EPOC studies were done in 14 countries across North America (24 studies) and Europe (16 studies), with one study from Hong Kong, China. Several US studies
| Details of intervention | Population at risk (n) | Events (n) | Slope before intervention (% change in events per year) | Direct change in events (step change, %; 95% CI) | Sustained change in events per year (slope change, %; 95% CI) | Summary of findings |
|------------------------|------------------------|------------|--------------------------------------------------------|-------------------------------------------------|----------------------------------------------------------|-------------------|
| **Perinatal mortality** |                        |            |                                                        |                                                 |                                                          |                   |
| Peelen (2016)† ‡        | First smoke-free law: workplaces and public transport except for restaurants and bars* (allowing designated smoking areas) | 1980727    | 13027                                                  | NA because of non-linear time trend              | First smoke-free law: −1·99% (−8·95 to 5·96)              | National smoke-free workplaces and public transport, and smoke-free restaurants and bars, were not associated with significant changes in perinatal mortality |
|                        | Second smoke-free law: expansion of first smoke-free law to include restaurants and bars (allowing designated smoking areas) |            |                                                        |                                                 | First smoke-free law: −5·96% (−12·93 to 1·99)              |                   |
|                        |                        |            |                                                        |                                                 |                                                          |                   |
| **Preterm birth**       |                        |            |                                                        |                                                 |                                                          |                   |
| Bakolis (2016)          | Public places and workplaces (including restaurants and bars) | 1800906    | 126527                                                | NR                                              | Analysis of a 1, 2, 3, or 5 month time window around the intervention cutoff date (July 1, 2007): ±1 month, −4·67% (−16·00 to −0·93); ±2 months, −8·42% (−15·05 to −1·86); ±3 months, −5·60% (−10·31 to −0·93); ±5 months, −3·73% (−7·48 to −0·93) | National comprehensive smoke-free legislation was associated with a 4–9% decrease in preterm births |
| Bartholomew (2016)       | Comprehensive (workplaces, restaurants, and bars) Restrictive (workplaces and restaurants, no restriction in bars) Moderate (workplaces, partial restriction in restaurants, and no restriction in bars) Limited (partial restriction in workplaces, any restriction in restaurants, and no restriction in bars) | 293715     | 32250                                                 | NR                                              | Comprehensive: −0·015%§ (−0·022 to −0·008) Restrictive: 0·003%§ (−0·005 to 0·011) Moderate: 0·004%§ (−0·002 to 0·010) Limited: 0·001%§ (−0·006 to 0·007) | County-wide, comprehensive smoke-free legislation was associated with a 0·015 percentage point decrease in preterm births |
|                        |                        |            |                                                        |                                                 |                                                          |                   |
| Bhasidwaj (2014)        | Restaurants and bars (in addition to existing smoke-free laws in public places and workplaces) | 822 (intervention group), 3185 (control group) | 46 (intervention group), 183 (control group) | NR                                              | −2·55%§ (−5·52 to 0·42) | National smoke-free restaurants and bars were not associated with significant changes in preterm births among women working in restaurants and bars |
| Cox (2013)              | Public places and workplaces (excluding catering industry) restaurants (in addition to existing smoke-free laws in public places and workplaces); and bars serving food (in addition to existing smoke-free laws in public places and workplaces, including restaurants) | 606877     | 36663                                                 | NR                                              | Public places and workplaces: single smoke-free law, −0·59% (−2·63 to 1·49); final model, no significant changes Restaurants (in addition to public places and workplaces): single smoke-free law, −2·28% (−4·73 to −0·59); final model, −3·18% (−5·38 to −0·94) Bars serving food (in addition to restaurants and public places and workplaces): single smoke-free law, −1·24% (−3·05 to 0·60); final model, no significant changes | Public places and workplaces single smoke-free law, −1·95% (−3·50 to −0·37); final model, no significant changes Restaurants (in addition to public places and workplaces): single smoke-free law, −1·42% (−2·87 to 0·05); final model, no significant changes Bars serving food (in addition to restaurants and public places and workplaces): single smoke-free law, −2·30% (−4·82 to 0·69); final model, −3·30% (−6·35 to −0·57) | National smoke-free public places and workplaces were not associated with significant changes in preterm births; expansion of national smoke-free legislation to include bars was associated with a gradual 4% per year decrease in preterm births |

(Table 1 continues on next page)
| Details of intervention | Population at risk (n) | Events (n) | Slope before intervention (% change in events per year) | Direct change in events (step change, %; 95% CI) | Sustained change in events per year (slope change, %; 95% CI) | Summary of findings |
|-------------------------|------------------------|-----------|--------------------------------------------------------|-----------------------------------------------|-------------------------------------------------------------|-------------------|
| Hade (2011)** | Public places and workplaces (including restaurants and bars) | 583 | 530 | NR | NR | No significant changes** | No significant changes** | State-wide, smoke-free public places and workplaces were not associated with significant changes in preterm birth |
| Haydu (2017)** | Public places and workplaces (including restaurants and bars) | 18755 | NR | NR | NR | -1.9% (-4.3 to 0.5) | NA | National smoke-free legislation was not associated with significant changes in preterm birth among female restaurant and bar workers compared with women working in places other than restaurants and bars |
| Hankins (2016)** | Workplaces, restaurants, and bars | NR | NR | NR | Workplaces: 0.07% (-0.11 to 0.25) Restaurants: 0.09% (-0.13 to 0.31) Bars: -0.29% (-0.49 to -0.09) | NA | State-wide or county smoke-free workplaces and restaurants were not associated with significant changes in preterm births; state-wide or county smoke-free bars were associated with an immediate 0.3 percentage point decrease in preterm births |
| Hawkins (2014)** | 100% smoke-free workplaces and restaurants | 16198654 | 1555071 | NR | 0.72% (-0.11 to 1.55) | NA | State-wide smoke-free workplaces and restaurants were not associated with significant changes in preterm births |
| Mackay (2012)** | Public places and workplaces (including restaurants and bars) | 709756 | 41998 | NR | Casual: -11.0% (-15.15 to -6.79) Adjusted: -11.72% (-15.87 to -7.35) | NA | National smoke-free public places and workplaces were associated with an immediate 12% decrease in preterm births, and a subsequent gradual 4% increase per year |
| Markowitz (2013)** | Workplaces with complete smoke-free law Workplaces with smoking restrictions (requiring designated smoking areas) Restaurants with complete smoke-free laws Restaurants with smoking restrictions (requiring designated smoking areas) | Maternal age <20 years: 343 Maternal age 20-24 years: 7120 Maternal age 25-34 years: 11026 Maternal age >34 years: 3718 | Maternal age <20 years: 543 Maternal age 20-24 years: 7120 Maternal age 25-34 years: 11026 Maternal age >34 years: 3718 | NR | Workplaces with complete smoke-free laws: NR Workplaces with smoking restrictions: NR Restaurants with complete smoke-free laws: maternal age <20 years, 0.7% (-3.5 to 4.9); 20-24 years, -0.2% (-1.5 to 1.3); 25-34 years, -0.3% (-0.8 to 0.2); >34 years, -0.6% (-1.9 to 0.7) Restaurants with smoking restrictions: maternal age <20 years, -0.6% (-3.3 to 2.6); 20-24 years, -0.1% (-1.1 to 0.9); 25-34 years, -0.8% (-1.2 to 0.4); >34 years, -0.3% (-1.7 to 1.1) | NA | State-wide complete smoke-free laws were not associated with significant changes in preterm births, but state-wide restaurant smoking restrictions were associated with a 0.8 percentage point decrease in preterm births among women aged 25-34 years |
| McKinnon (2015)** | Public places and workplaces (including restaurants and bars) | 470199 | 19321 | NR | Casual: -6% (-10 to -3) Adjusted: -5% (-9 to 0) | NA | State-wide smoke-free legislation was associated with a 5% decrease in preterm births 9 months after its implementation |
| Page (2012)** | Public places and workplaces (including restaurants and bars) | 6712 (intervention group), 32293 (control group) | 515 (intervention group), 2767 (control group) | NR | Casual: -20.6% (-34.7 to -3.4) Adjusted: -23.1% (-40.11 to 1.3) | NA | City-wide smoke-free public places and workplaces were associated with a 23% decrease in preterm births |

(Continued from previous page)
### Details of intervention Population at risk Events (n) Slope before intervention (% change in events per year) Direct change in events (step change, %; 95% CI) Sustained change in events per year (slope change, %; 95% CI) Summary of findings

**Peelen (2016)**
- First smoke-free law: workplaces and public transport except for restaurants and bars (allowing designated smoking areas)
- Second smoke-free law: expansion of first smoke-free law to include restaurants and bars (allowing designated smoking areas)
- First smoke-free law: 0·94% (−1·89 to 3·77)
- Second smoke-free law: −0·94% (−3·78 to 2·83)
- National smoke-free workplaces and public transport, and smoke-free restaurants and bars, were not associated with significant changes in preterm births

**Simón (2017)**
- First smoke-free law: complete smoke-free workplaces and partial smoke-free restaurants and bars
- Second smoke-free law: public places and workplaces (including restaurants and bars)
- First smoke-free law: 4·6% (2·9 to 6·2)
- Second smoke-free law: −4·5% (−6·1 to −2·9)
- National partial smoke-free legislation was associated with a 5% increase in preterm births; the subsequent national comprehensive smoke-free legislation was associated with a 5% decrease in preterm births

**Vicedo-Cabrera (2016)**
- Public places and workplaces (including restaurants and bars), with several exceptions in the hospitality sector††
- First smoke-free law: 25·0% (−2·6 to 60·4)
- Second smoke-free law: −11·0% (−28·6 to 11·1)
- Partial and comprehensive national smoke-free legislation were not associated with significant immediate changes in asthma-related hospital admissions via emergency departments

**Asthma exacerbations requiring hospital attendance**

| Study | Details of intervention | Population at risk (n) | Events (n) | Slope before intervention (% change in events per year) | Direct change in events (step change, %; 95% CI) | Sustained change in events per year (slope change, %; 95% CI) | Summary of findings |
|-------|-------------------------|------------------------|------------|------------------------------------------------------|-------------------------------------------------|---------------------------------------------------------------|-------------------|
| Gaccio (2016)** | Public places and workplaces (including restaurants and bars) | 13 246 809 | 335 88 | NR | −17% (−18 to −15) | NA | State or local smoke-free legislation was associated with an immediate 17% decrease in emergency department visits for asthma |
| Croghan (2015)** | Public places and workplaces (including restaurants and bars) | NR | 1531 | 1·1% (0·2 to 2·0) | −24·9% (−40·5 to −5·3) | −1·5% (−2·9 to −0·1) | National smoke-free legislation was associated with an immediate 25% decrease in emergency department visits for children with asthma, and a subsequent gradual 1·5% decrease per year |
| Galán (2017)** | First smoke-free law: complete smoke-free workplaces and partial smoke-free restaurants and bars
Second smoke-free law: public places and workplaces (including restaurants and bars) | NR | NR | NR | First smoke-free law: 25·0% (−2·6 to 60·4)
Second smoke-free law: −11·0% (−28·6 to 11·1) | NA | Partial and comprehensive national smoke-free legislation were not associated with significant immediate changes in asthma-related hospital admissions via emergency departments |
| Gaudreau (2013)** | Public places and workplaces (including restaurants and bars), allowing designated smoking areas | NR | 3050 | NR | 11% (−37 to 95) | 0% (−2 to 2) | Provincial smoke-free public places and workplaces were not associated with significant changes in hospital admissions for paediatric asthma |
| Hawkins (2016)** | State or local 100% smoke-free workplaces or restaurants, or both | NR | 128 807 | NR | State: −3% (−8 to 2)
Local: 2% (−6 to 11) | NA | State or local smoke-free workplaces or restaurants were not associated with significant changes in emergency department visits for paediatric asthma |
| Landers (2014)** | 100% smoke-free workplaces, restaurants, and bars‡‡ | NR | NR | Mean rate across all states and years: 9·02 per 10 000 per quarter (SD 9·66; range 0·00–144·47) | Any state law: 0·12% (−0·38 to 0·62)
Any county law: −1·32% (−2·34 to 0·00)
Interaction term of state law and county law: 0·51% (−1·04 to 2·06) | NA | County-level smoke-free laws were associated with a one percentage point decrease in discharge rates among children admitted for asthma; state smoke-free laws were not associated with significant changes in discharge rates among children admitted for asthma, besides the effect of county laws |

(Table 1 continues on next page)
| Details of intervention | Population at risk (n) | Events (n) | Slope before intervention (% change in events per year) | Direct change in events (step change, %; 95% CI) | Sustained change in events per year (slope change, %; 95% CI) | Summary of findings |
|------------------------|------------------------|------------|------------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------|-------------------|
| (Continued from previous page) | | | | | | |
| **Mackay (2010)** | | | | | | National smoke-free public places and workplaces were associated with a gradual 20% decrease per year in paediatric emergency asthma admissions. |
| | Public places and workplaces (including restaurants and bars) | NR | 21415 | 4.4% (3.3 to 5.5) | NA | −19.5% (−22.4 to −16.5) | National smoke-free public places and workplaces were associated with a gradual 20% decrease per year in paediatric emergency asthma admissions. |
| **Millett (2013)** | | | | | | National smoke-free public places and workplaces were associated with an immediate 9% decrease in emergency admissions to hospital for paediatric asthma, and a subsequent gradual 3% decrease per year. |
| | Public places and workplaces (including restaurants and bars) | NR | 217381 | 2.2% (2 to 3) | −8.9% (−11 to −7) | −3.4% (−4 to −2) | National smoke-free public places and workplaces were associated with a gradual 3% decrease per year. |
| **Rajens (2008)** | Most businesses open to the public (including restaurants and bars)$§§$ | 395 116 | 5322 | 12.7% | −18.0% (−29.0 to −4.0) | NA | National smoke-free public places and workplaces were associated with a gradual 20% decrease per year. |
| **Shetty (2011)** | All workplaces except restaurants and bars: 100% smoke-free | NR | NR | NR | 100% smoke-free workplaces: 14.6% (3.7 to 25.5) Any smoke-free law: 9.0% (1.1 to 19.3) | NA | National smoke-free public places and workplaces were associated with a gradual 20% decrease per year. |
| **RTI admissions (upper and lower)** | | | | | | |
| **Been, Millett (2015)** | Public places and workplace (including restaurants and bars) | NR | 1651675 | NR | −35% (−47 to −23) | −0.5% (−0.9 to −0.1) | State or local smoke-free workplaces or restaurants were not associated with significant changes in emergency department visits for paediatric asthma. |
| **Vicedo-Cabrera (2017)** | Public places and workplaces (including restaurants and bars), with several exceptions in the hospitality sector†† | NR | 29 345 | NR | 2.7% (−0.7 to 16.7) | NA | Federal smoke-free legislation was not associated with a significant change in RTI hospital admissions. |
| **Upper RTI admissions** | | | | | | |
| **Been, Millett (2015)** | Public places and workplaces (including restaurants and bars) | NR | 979 370 | NR | 19% (0.5 to 3.2) | −1.9 (−2.3 to −1.5) | State or local smoke-free workplaces or restaurants were not associated with significant changes in emergency department visits for upper RTIs. |
| **Hawkins (2016)** | State or local 100% smoke-free workplaces or restaurants, or both | NR | 410 686 | NR | State: −2% (−6 to 2) Local: 6% (−2 to 14) | NA | State or local smoke-free workplaces or restaurants were not associated with significant changes in emergency department visits for upper RTIs. |
| **Lower RTI admissions** | | | | | | |
| **Been, Millett (2015)** | Public places and workplaces (including restaurants and bars) | NR | 672 305 | NR | −13.8% (−15.6 to −12.0) | 0.2% (−0.6 to 0.9) | State or local smoke-free workplaces or restaurants were not associated with significant changes in emergency department visits for lower RTIs. |

(Table 1 continues on next page)
assessed the same outcomes in partially overlapping study populations.36-38,41,43-45,48-49,51-53,56,62

Risk of bias of individual studies is reported in detail in the appendix (pp 32, 33). For the EPOC studies, risk of bias was low in 23 studies,16–18,28,30–33,36,37,39,40,44–48,51–53,58,63,64 moderate in 16, 19,34,35,41–43,49,50,54–57,59–62 and high in two.7,38 For the non-EPOC studies, risk of bias was high for two studies66,67 and unclear for one.65

28 studies assessed the association between smoke-free legislation and one or more primary outcomes (ie, perinatal mortality, preterm birth, asthma exacerbations requiring hospital attendance, and respiratory tract infections requiring hospital attendance), five assessed the association between tobacco taxation and primary outcomes, and two assessed the association between policies providing smoking cessation services and our primary outcomes (tables 1, 2, and 3); four studies assessed a combination of these interventions, and ten studies only assessed secondary outcomes. A meta-analysis was only possible for studies on smoke-free legislation because studies on tax increases and smoking cessation services had variable outcome reporting and overlapping study populations.

A national study from the Netherlands, comprising 1980727 births, found no change in perinatal mortality following a law to prohibit smoking in workplaces and on public transport, or following expansion of the law to include restaurants and bars.58 In a study from England, comprising 1029113 births, comprehensive smoke-free legislation in public places and workplaces (including restaurants and bars) was associated with a reduction in stillbirths (−7·8%; 95% CI −18·0 to −3·5) and neonatal deaths (−7·6%; −11·7 to −3·4).32 The overall effect on perinatal mortality (ie, stillbirths and early neonatal deaths combined) was not reported in this study. Therefore, no meta-analysis was possible with these two studies.

15 studies investigated the association between smoke-free legislation and preterm births.30,31,34,37,43–46,52–54,56,58,62

In the meta-analysis, smoke-free legislation was associated with a significant immediate reduction in preterm births (ten studies, 27530183 individuals; −3·77% [95% CI −6·37 to −1·16]; figure 2A). Two studies caused some funnel plot asymmetry suggestive of publication bias, but this asymmetry was unlikely to have affected our findings (appendix p 34). No additional gradual change in preterm births was evident (two studies, 1316633 individuals; −0·01% per year [95% CI −6·76 to 6·73]; figure 3A). One study examined the association between provision of smoking cessation services and preterm births. Medicaid enrolment policies permitting low-income pregnant women to receive smoking cessation services were not associated with a change in preterm births (table 2).55 Reductions in preterm birth were observed after tobacco tax increases among women in specific population subgroups in two studies. No study reported tobacco taxation to be associated with reduced rates of preterm deaths.

### Table 1: Association between implementation of smoke-free legislation and primary outcomes

| Details of intervention | Population at risk (n) | Events (n) | Slope before intervention (% change in events per year) | Direct change in events (step change, %; 95% CI) | Sustained change in events per year (slope change, %; 95% CI) | Summary of findings |
|-------------------------|------------------------|------------|------------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------|---------------------|
| Hawkins (2016)57        | State or local 100% smoke-free workplaces or restaurants or both | NR         | 1392 39                                             | −11·9% (−15·0 to −8·7)               | NA                                                            | State: −8·1% (−13·0 to −3·0) Local: 3·3% (−6·0 to 12·0) |
| Lee (2016)58            | Public places and workplaces (including restaurants) | NR         | 175 70                                              | −33·5% (−36·4 to −30·3)              | NA                                                            | State-wide smoke-free workplaces or restaurants were associated with an immediate 34% reduction in hospital admissions for childhood lower RTIs, and a subsequent gradual decrease of 14% per year |

*Both smoke-free laws were accompanied by a tobacco-free zone and mass media campaign. Long-term data for this smoke-free law were obtained from local government and Mass Media Campaign.‡Less than one per year. **All 100% smoke-free legislation in large establishments. Including but not limited to restaurants, bars, hotels, convention centers, and others. RTI = respiratory tract infection. 11 State-wide smoke-free legislation was associated with a subsequent reduction in annual hospital admissions for childhood lower RTIs. **Both smoke-free laws were accompanied by a tobacco-free zone and mass media campaign. †Exceptions to this smoke-free law were: hotels, bars and restaurants, sports, arts and culture venues, amusement arcades, and tobacconist shops. §Mass media campaign. §§Including, but not limited to restaurants, bars, bowling alleys, bingo halls, convenience stores, laundromats, and other businesses open to the public.
### Table 2: Association between implementation of smoking cessation services and primary outcomes

| Details of intervention | Population at risk (n) | Events (n) | Slope before intervention (% change in events per year) | Direct change in events (step change, %; 95% CI) | Sustained change in events per year (slope change, %; 95% CI) | Summary of findings |
|-------------------------|------------------------|------------|--------------------------------------------------------|---------------------------------------------|--------------------------------------------------|-------------------|
| **Preterm birth**       |                        |            |                                                        |                                             |                                                  |                   |
| Jarlenski (2014)         | 24544                  | NR NR      | Overall: −1.4% (−4.7 to 2.0) Non-comprehensive: −2.2% (−5.9 to 1.5) Non-comprehensive: 1.3% (−2.4 to 5.1) | NA                                          | Neither optional Medicaid enrolment policy was associated with significant changes in preterm birth |
| **Asthma exacerbations requiring hospital attendance** |                        |            |                                                        |                                             |                                                  |                   |
| Hawkins (2016)           | NR 112 808             | NR         | 2% (−4 to 8)                                           | NA                                          | The state-wide health reform legislation in MA, USA, was not associated with significant changes in emergency department visits for asthma |
| **Upper RTI admissions** |                        |            |                                                        |                                             |                                                  |                   |
| Hawkins (2016)           | NR 337 628             | NR         | −6% (−10 to −1)                                        | NA                                          | The state-wide health reform legislation in MA, USA, was associated with a 6% decrease in emergency department visits for upper RTIs |
| **Lower RTI admissions** |                        |            |                                                        |                                             |                                                  |                   |
| Hawkins (2016)           | NR 113 137             | NR         | 0% (−6 to 6)                                           | NA                                          | The state-wide health reform legislation in MA, USA, was not associated with significant changes in emergency department visits for lower RTIs |

NR=not reported. NA=not applicable. RTI=respiratory tract infection. *Presumptive eligibility: low-income pregnant women are presumed to be eligible for Medicaid, so they can receive care (including smoking cessation services) while their Medicaid applications are still pending. The unborn-child option: the state can consider a fetus a "targeted low-income child", allowing coverage of prenatal care (including smoking cessation services) and delivery to low-income pregnant women, even if they cannot provide documentation of citizenship or residency.

birth among white mothers with low levels of education and among black mothers irrespective of level of education (table 3). The other study reported a 0.7 percentage point decrease in preterm births per USD increase in tax among women aged 20–24 years, and a 1.0 percentage point decrease per USD increase in tax among women older than 34 years (table 3).

Associations between smoke-free legislation and the incidence of hospital attendances for childhood asthma were reported in ten studies (table 1). In the meta-analysis, both an immediate reduction in asthma exacerbations requiring hospital attendance (five studies, 684 826 events; −9.83% [95% CI −16.62 to −3.04]; figure 2B) and an additional gradual reduction were seen (four studies, 243 377 events; −5.94% per year [95% CI −11.48 to −0.41]; figure 3B). No change in asthma admissions was seen following a health reform legislation that provided smoking cessation services for Medicaid recipients in one study. Among three US studies, with overlapping populations evaluating tobacco taxation and asthma exacerbations requiring hospital attendance, the study with the lowest risk of bias found no significant reductions following state-wide increases in cigarette excise tax (table 3).

The association between smoke-free legislation and the incidence of hospital admissions for acute respiratory tract infections was reported in four studies (table 1). In the meta-analysis, an immediate reduction was seen in respiratory tract infections (upper and lower respiratory tract infections combined) requiring hospital attendance (two studies, 1681 020 events; −3.45% [95% CI −4.64 to −2.25]; figure 2C). For the studies that reported specifically on lower respiratory tract infections, the meta-analysis showed an immediate reduction in admissions for lower respiratory tract infections following smoke-free legislation (three studies, 887 414 events; −18.48% [95% CI −32.79 to −4.17]; figure 2D). No additional gradual reduction in lower respiratory tract infections was observed (two studies; 748 175 events; −6.81% per year [95% CI −20.63 to 7.01]; figure 3C). No significant association between smoke-free legislation and admissions for upper respiratory tract infections was seen in the meta-analysis (two studies; 1390 056 events; 0.42% [95% CI −3.28 to 4.13]; figure 2E). One study reported that a health reform legislation that provided smoking cessation services for Medicaid recipients was associated with an immediate −6% (95% CI −10 to −1) decrease in hospital admissions for childhood upper respiratory tract infection, but not in admissions for lower respiratory tract infection (table 2). The same study evaluated the effect of tobacco taxation, showing a −9% decrease (95% CI −16 to −2) in lower respiratory tract infections requiring admission to hospital per USD increase in cigarette excise tax at the state level (table 3).
We did not identify any studies assessing the effect of other MPOWER policies on child health.

In sensitivity analyses, inclusion of non-EPOC studies in the meta-analyses or restriction of the primary analyses to studies with low to moderate risk of bias did not materially change the effect estimates for smoke-free legislation and our primary outcomes (appendix pp 35–39).

| Details of intervention | Population at risk (n) | Events (n) | Slope before intervention (% change in events per year) | Direct change in events (step change, %; 95% CI) | Sustained change in events per year (slope change, %; 95% CI) | Summary of findings |
|------------------------|------------------------|------------|-------------------------------------------------------|--------------------------------------------------|--------------------------------------------------------|------------------|
| **Preterm birth**      |                        |            |                                                      |                                                  |                                                        |                  |
| Hawkins (2014)          | Effect of cigarette excise tax increase (in USD$; December 2010 rates) on mothers, by years of maternal education | 9 881 855 | NR                                                    | NR                                               | White mothers: 0–11 years, −0·07%§ (−0·11 to −0·02); 12 years, −0·02%§ (−0·05 to 0·01); 13–15 years, −0·01%§ (−0·03 to 0·00); ≥16 years, −0·00%§ (−0·01 to 0·01) per USD$ increase in tax | NA                |
| Hawkins (2014)          | Effect of cigarette excise tax increase (in USD$; December 2010 rates) on mothers, by years of maternal education | 2 722 846 | NR                                                    | NR                                               | Black mothers: 0–11 years, −0·08%§ (−0·14 to −0·03); 12 years, −0·04%§ (−0·07 to −0·01); 13–15 years, −0·03%§ (−0·05 to −0·04); ≥16 years, −0·01%§ (−0·01 to −0·00) per USD$ increase in tax | NA                |
| Hawkins (2014)          | Effect of cigarette excise tax increase (in USD$; December 2010 rates) on mothers, by years of maternal education | 2 444 673 | NR                                                    | NR                                               | Hispanic mothers: 0–11 years, 0·01%§ (−0·00 to 0·02); 12 years, −0·00%§ (−0·01 to 0·00); 13–15 years, −0·01%§ (−0·02 to 0·00); ≥16 years, −0·00%§ (−0·00 to 0·00) per USD$ increase in tax | NA                |
| Hawkins (2014)          | Effect of cigarette excise tax increase (in USD$; December 2010 rates) on mothers, by years of maternal education | 804 447  | NR                                                    | NR                                               | Asian/Pacific Islander mothers: 0–11 years, 0·01%§ (−0·01 to 0·04); 12 years, −0·02%§ (−0·03 to 0·00); 13–15 years, −0·00%§ (−0·01 to 0·01); ≥16 years, 0·00%§ (−0·00 to 0·00) per USD$ increase in tax | NA                |
| Hawkins (2014)          | Effect of cigarette excise tax increase (in USD$; December, 2010, rates) on mothers, by years of maternal education | 244 823  | NR                                                    | NR                                               | Native American/Alaska Native mothers: 0–11 years, −0·02%§ (−0·08 to 0·12); 12 years, 0·01%§ (−0·02 to 0·03); 13–15 years, 0·00%§ (−0·03 to 0·03); ≥16 years, −0·01%§ (−0·02 to 0·00) per USD$ increase in tax | NA                |
| Markowitz (2013)        | Cigarette excise tax increase (in 2008 USD$) | Maternal age <20 years: 54132 | Maternal age 20–24 years: 101 723 | Maternal age 25–34 years: 183 763 | Maternal age >34 years: 52 109 | Maternal age <20 years: 5413 | Maternal age 20–24 years: 7120 | Maternal age 25–34 years: 11 026 | Maternal age >34 years: 3 718 | Cigarette excise tax: maternal age <20 years, −2·0%§ (−4·0 to 0·0) per USD$ increase in tax; maternal age 20–24 years, −0·7%§ (−1·4 to −0·0) per USD$ increase in tax; maternal age 25–34 years, −0·2%§ (−1·0 to 0·0) per USD$ increase in tax; maternal age >34 years, −1·0%§ (−1·9 to −0·1) per USD$ increase in tax | Cigarette price: NR | State-wide increases in cigarette excise tax were associated with a 0·7 percentage point decrease in preterm births among women aged 20–24 years, and a 1·0 percentage point decrease among women aged >34 years | (Table 3 continues on next page)
Point estimates for the association between smoke-free legislation and our primary outcomes were generally much larger when subgroup analyses were restricted to studies assessing comprehensive smoke-free laws than when studies assessing partial smoke-free laws were analysed (preterm birth: seven studies, 9355 339 individuals, −5.12% [95% CI −7.24 to −2.99]; hospital attendances for asthma: four studies, 556019 events, −12.49% [−19.78 to −5.20]; appendices, pp 40–44).

11 studies assessed whether the association between implementation of tobacco control policies and child health varied according to indicators of socioeconomic status (appendix, pp 45, 46). One study69 showed that the most deprived children experienced the largest gradual reduction in hospital admissions for respiratory tract infection following smoke-free legislation (−1.5% per year [95% CI −2.1 to −1.0]). In two studies,44,46 improvements in perinatal outcomes were greater among babies born to parents with low levels of education following smoke-free legislation than among those born to parents with high levels of education,44 and among babies born to black mothers with any level of education and to white mothers with low levels of education following tobacco tax increases.46 Other studies did not identify a clear socioeconomic gradient in the association between tobacco control policies and child health.

27 studies assessed the association between tobacco control policies and secondary outcomes (appendix, including Table 3: Association between implementation of tobacco taxation and primary outcomes).

### Table 3: Association between implementation of tobacco taxation and primary outcomes

| Details of intervention | Population at risk (n) | Events (n) | Slope before intervention (% change in events per year) | Direct change in events (step change, %; 95% CI) | Sustained change in events per year (slope change, %; 95% CI) | Summary of findings |
|--------------------------|------------------------|------------|----------------------------------------------------------|--------------------------------------------------|------------------------------------------------------------|---------------------|
| **Asthma exacerbations requiring hospital attendance** | | | | | | |
| Hawkins (2016)28 | Cigarette excise tax increase in USD$ | NR | 128 807 | NR | −5% (−11 to 1) per USD$ increase in tax | NA | State-wide increase in cigarette excise tax was not associated with significant changes in emergency department visits for paediatric asthma |
| Landers (2014)29 | Cigarette excise tax increase in USD$ | NR | NR | Mean rate across all states and years: 9.02 per 10 000 (SD 9.66; range 0.00–144.47) | −0.53% (−0.99 to −0.06) per USD$ increase in tax | NA | State-wide increase in cigarette excise tax was associated with a 0.5 percentage point decrease in asthma discharge rates |
| Ma (2013)30 | USD$0.69 cigarette excise tax increase; USD$0.35 cigarette excise tax increase | 28 498 070 | 702 771 | 0.04 | USD$0.69 cigarette excise tax increase: −11.01% (−24.71 to 2.77); USD$0.35 cigarette excise tax increase: −22.02% (−33.46 to −9.95) | USD$0.69 cigarette excise tax increase: 4.88% (1.29 to 8.59); USD$0.35 cigarette excise tax increase: −4.72% (−8.01 to −1.44) | The first cigarette excise tax increase (USD$0.69) was not associated with significant immediate changes, but was associated with a significant, gradual increase in asthma-related hospital admissions of 0.5% per year; the second cigarette excise tax increase (USD$0.35) was associated with both a 22% immediate decrease as well as a gradual 5% decrease in asthma-related hospital admissions per year |
| **Upper RTI admissions** | | | | | | |
| Hawkins (2016)28 | Cigarette excise tax increase in USD$ | NR | 410 686 | NR | −2% (−6% to 2%) per USD$ increase in tax | NA | State-wide increase in cigarette excise tax was not associated with significant changes in emergency department visits for upper RTIs |
| **Lower RTI admissions** | | | | | | |
| Hawkins (2016)28 | Cigarette excise tax increase in USD$ | NR | 139 239 | NR | −9% (−16 to −2) per USD$ increase in tax | NA | State-wide increase in cigarette excise tax was associated with a 9% decrease in emergency department visits for lower RTIs |

NA=not applicable. NR=not reported. RTI=respiratory tract infection.
In the meta-analyses (appendix pp 77–85), smoke-free legislation was associated with immediate reductions in very preterm birth (five studies; 3354636 individuals; –9.99% [95% CI –15.74 to –4.24]), low birthweight (nine studies; 35206918 individuals, –2.77% [–4.36 to –1.19]), and small for gestational age births (eight studies; 27649380 individuals; –1.84% [–3.21 to –0.47]), a gradual reduction in very small for gestational age births (two studies; 1298276 individuals; –0.60% per year [–0.60 to –0.60]), and a small increase in birthweight (seven studies; 3238575 individuals; 12.45 g [95% CI 2.09–22.81]). No significant changes in other secondary outcomes were seen following smoke-free legislation. Legislation to promote prenatal care, including smoking cessation services for low-income pregnant women, was not associated with a change in small for gestational age births in one US study. In another US study, although such legislation was associated with increased duration of gestation, depending on time of enrolment (308521 participants; 0.063 weeks [95% CI 0.008–0.118] among women who enrolled in the Medicaid insurance programme before or during pregnancy and 0.086 weeks [0.004–0.168] among women who enrolled during pregnancy), it was not associated with a change in birthweight (appendix pp 66, 67). One study showed reductions in extremely and very preterm births following tobacco tax increases, with two others also showing an increase in gestation. Among five studies assessing the link between tobacco tax and birthweight, two showed a positive effect, albeit of very small magnitude. Accordingly, only one of these five studies showed a reduction in low birthweight following tobacco tax increases. This study also found reductions in small for gestational age births; both associations were confined to low socioeconomic groups. In two studies assessing very low birthweight, no changes were seen following tobacco tax increases. Tobacco taxes were associated with a decreased risk of infant mortality in two studies assessing this association. In one of these studies, however, an increase in fetal deaths was also observed. One study showed significant reductions in paediatric asthma prevalence following tobacco tax increases.

Discussion

This systematic review and meta-analysis provides considerable evidence indicating child health benefits associated with implementation of MPOWER policies. By pooling data of 27.5 million births, 685000 hospital admissions for asthma, and 2.3 million hospital admissions for respiratory tract infections, we found a 3.7% reduction in preterm births, a 9.8% reduction in childhood hospital admissions for asthma, and an 18.5% reduction in hospital admissions for lower respiratory tract infections following implementation of smoke-free legislation. Subgroup analyses suggested that health benefits were increased when the most comprehensive laws were applied. We also identified several studies indicating that tobacco tax increases and governmental support for smoking cessation services could benefit child health. Taken together with substantial existing evidence on the effectiveness of tobacco control policies in improving adult health, these findings provide strong support for implementation of such policies comprehensively across the world.

This study is, to our knowledge, the most comprehensive assessment done to date of the effect of tobacco control policies on perinatal and child health outcomes. On the basis of our previous work and the challenges of evaluating governmental policies through randomised trials, we anticipated that most eligible studies would be of quasi-experimental design. We therefore followed EPOC guidelines to restrict our primary analyses to study types that were considered to be at lowest risk of bias. We confirmed the robustness of our findings via a number of prespecified sensitivity analyses, which indicated that our findings were not sensitive to exclusion of studies with a high risk of bias or inclusion of purely observational studies. Our work builds on existing evidence since it focuses on all available evidence on the effect of tobacco control policies on perinatal and child health. The consistency of this evidence, in our view, supports the validity of our findings.

However, our study has some limitations. The risks of residual confounding and bias in quasi-experimental studies—due to non-random allocation of the intervention and the absence of a control group—need to be considered when interpreting the results. Additional limitations include between-study heterogeneity in methodology, differences in follow-up duration and diagnosis ascertainment, the absence of assessment of the likely causal pathways between the policies and their health effects in several studies, and the low number of studies in each meta-analysis, which precluded assessment of publication bias for most outcomes and the use of meta-regression.

This study adds to our previous work. We identified an additional 24 studies on the effect of smoke-free legislation on child health, comprising additional data from more than 10 million births, 4.6 million GP diagnoses, and 2.2 million hospital admissions. These additional studies allowed us, for the first time, to identify the association between smoke-free legislation and reductions in severe respiratory tract infections, which is particularly relevant since respiratory tract infections account for the vast majority of the global burden of disease resulting from second-hand smoke exposure in children. We also broadened the scope of this study to include all MPOWER policies, identifying several studies on the effect of tobacco tax increases and smoking cessation services on child health. We also identified one study evaluating a tobacco control policy that could not be classified according to WHO’s MPOWER Framework. Following an increase in the
minimum legal age to purchase cigarettes from 18 years to 21 years in the US state of Pennsylvania, a 1.4 (95% CI –2.6 to –0.2) percentage point reduction in low birthweight was observed, which was largest among smoking mothers and associated with a significant reduction in prenatal cigarette consumption.72

Socioeconomic disparities in smoking and related morbidity are widely documented and affect both adults and children. For example, such disparities were estimated to account for 38% of the inequality in stillbirths and 31% of the inequality in infant deaths in Scotland.71 Previous systematic reviews74–75 showed that, among MPOWER measures, tobacco taxation has the greatest potential to reduce socioeconomic disparities associated with smoking in both young people and adults. We identified some evidence suggesting a pro-equity effect of both tobacco taxation and smoke-free legislation on early-life health. Since smokers are over-represented among deprived communities, such relative benefits of tobacco control policies translate into larger absolute effects in children from low socioeconomic groups than in children from high socioeconomic groups.
Given the inherent restrictions in attributing causality from quasi-experimental studies, it is important to interpret the findings in light of circumstantial evidence supporting the link between tobacco control policies and child health benefits. We have previously described the main likely causal pathways.\textsuperscript{21} Tobacco smoke exposure during fetal stages and childhood is associated with various adverse perinatal and child health outcomes.\textsuperscript{1,4,7,71,72} Several studies have shown substantial reductions in maternal smoking\textsuperscript{103,12,13,86–89} and in second-hand smoke exposure among adults (including pregnant women) and children after implementation of tobacco control policies (appendix pp 86–89, 12,13,86–89). Whereas smoke-free laws specifically target public spaces, various studies have shown subsequent increases in smoking cessation and reduced initiation,\textsuperscript{21,46,52} as well as changes in social norms leading to decreased smoking in the home environment\textsuperscript{95–97} which is probably the primary source of second-hand smoke exposure among children. Our study provides further support for a causal association, since we found the largest decreases in our outcomes of interest when comprehensive smoke-free legislation was considered. This observation is suggestive of a dose–response association, which has previously also been identified for adult studies.\textsuperscript{78} Because of the low number of studies in individual meta-analyses we did not formally test for this interaction, and future efforts to do so might strengthen our findings as more evidence becomes available.

The global health burden of tobacco use is tremendous and its total global economic cost is estimated to be around USD$1.4 trillion.\textsuperscript{96} Despite global progress in tobacco control, over a third of the world’s population remains unprotected by any MPOWER policy at the recommended level.\textsuperscript{2,11} This issue is important because 40–50% of children worldwide are regularly exposed to tobacco smoke, and tobacco control policies have substantial potential to reduce the associated burden of death and disease.\textsuperscript{7} This global burden is acknowledged by the prioritisation within SDG 3 of more effective FCTC implementation and its aim to reduce early-life mortality; our data now show that these initiatives can act synergistically. Because our effect estimates are expressed as relative changes, background prevalence of smoking and second-hand smoke exposure, and of the health outcomes evaluated, should be considered when extrapolating our findings to local contexts. We did not formally assess the comparative effectiveness or cost-effectiveness of different MPOWER policies. Tax increases are considered to be the most effective measure to reduce smoking prevalence,\textsuperscript{2} and although our review indicates that tobacco taxation is likely to be associated with child health benefits, the evidence was particularly strong for smoke-free legislation. Smoke-free laws are the tobacco control policy most strongly supported by the public and appear to be the most straightforward measure to protect child health, particularly when implemented comprehensively.\textsuperscript{12} The synergistic effect of various policies implemented at the highest recommended levels in reducing smoking prevalence should be considered when planning policy changes,\textsuperscript{12} which, when implemented as part of a strong tobacco control programme, can be highly cost-effective.\textsuperscript{90,91} Ongoing monitoring is needed to continue to evaluate the effectiveness of policies aimed at reducing the impact of tobacco, in particular the effectiveness of novel endgame strategies targeted at ending rather than controlling the global tobacco epidemic.\textsuperscript{92}

Reports indicate that at least two of five people living in low-income and middle-income countries remain unprotected by any MPOWER policy measure,\textsuperscript{2} and that wide variations in implementation and compliance are present across these countries.\textsuperscript{93} This finding is of concern, since these countries have the largest burden of tobacco-related illness and death, and harbour nearly 80% of the world’s smokers.\textsuperscript{2} We highlight an important gap in
the literature as more research is required in low-income and middle-income countries to understand the effect of tobacco control policies in these regions. Modelling approaches are increasingly being used to estimate the effect of tobacco control policies in low-income and middle-income countries, and original studies are now becoming available. Efforts are underway to address the current absence of a child health focus in this area, which will be essential to inform the global policy agenda. Furthermore, we found no studies specifically evaluating early-life health outcomes in relation to legislation to prohibit tobacco advertising and sponsorship, or warnings against the dangers of tobacco. Priority should be given to establishing a core set of outcomes related to perinatal and child health, alongside adult health, for all future studies examining the effect of tobacco control policies.

In conclusion, given the positive findings of this systematic review it is crucial that the uptake of comprehensive tobacco control policies is accelerated worldwide to further protect children from the health hazards of tobacco smoke exposure, in parallel with efforts to evaluate the effectiveness of novel policy initiatives.

Contributors
JVB and AS secured funding for this work, JVB, JPM, CM, SB, and AS designed the study and wrote the protocol. TF and AK did the study search, study selection, data extraction, and risk of bias assessment. JVB supervised all the steps in the review process. TF did the data analysis and created the figures. All authors interpreted the findings. TF, AK, and JVB drafted the manuscript and appendix. AS supervised the writing, and JPM, CM, and SB provided feedback.

Declaration of interests
We declare no competing interests.

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