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The impact of smoke-free legislation on fetal, infant, and child health: a systematic review and meta-analysis

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Keywords: tobacco smoke, legislation, meta-analysis, child, infant

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Abstract

Introduction

Second-hand smoke (SHS) exposure increases adverse health outcomes and is estimated to kill 600,000 people worldwide annually. The World Health Organization (WHO) now recommends that smoke-free indoor public environments are enforced through national legislation. Such regulations have been shown to reduce SHS exposure and consequently, respiratory and cardiovascular morbidity. Evidence of particular health benefit in children is now emerging, including reductions in low birth weight deliveries, preterm birth, and asthma exacerbations. We aim to obtain a comprehensive assessment of the impact of smoke-free legislation on fetal, infant and childhood outcomes, which can inform further development and implementation of global policy and strategies to reduce early life SHS exposure.

Methods

Two authors will search online databases (1975-present) of published and unpublished or in progress studies, and reference lists and citations to articles of interest. We will consult experts in the field to identify additional studies. No language restrictions apply. Studies should describe associations between comprehensive or partial smoking bans in public places and health outcomes among children (0-12 years): stillbirth, preterm birth, low birth weight, small for gestational age, perinatal mortality, congenital anomalies, bronchopulmonary dysplasia, upper and lower respiratory infections, and wheezing disorders including asthma. Cochrane Effectiveness Practice and Organisational Care (EPOC) defined study designs are eligible.

Study quality will be assessed using the Cochrane 7-domain based evaluation for randomised and clinical trials, and EPOC criteria for quasi-experimental studies. Data will be extracted by two reviewers and presented in tabular and narrative form. Meta-analysis will be undertaken using fixed-effect or random-effects models depending on the degree of heterogeneity. Adjusted effect estimates will be pooled using generic inverse variance analysis. We will report sensitivity analyses according to study quality and design characteristics, and subgroup analyses according to intervention type, age group, and parental/maternal smoking status. Publication bias will be formally assessed.

INTRODUCTION

Tobacco use kills more than five million people annually making it the leading global cause of preventable death.[1] It is estimated that second-hand smoke (SHS) exposure kills an additional 600,000 people worldwide each year, including 165.000 children under 15 years.[1, 2] Among non-smoking adults SHS exposure furthermore increases the incidence of asthma, lung cancer and ischaemic heart disease.[2] In an attempt to reduce this substantial burden on second-hand or passive smokers, the World Health Organization (WHO) has recommended that smoke-free indoor public environments are enforced through national legislation and that educational strategies are pursued in parallel to reduce SHS exposure in the home.[3] Studies have since shown that smoking bans effectively reduce SHS exposure, even in absence of an overall decline in smoking prevalence in the population.[4] More importantly, consistent health effects have been reported in a recent Cochrane review summarising 25 studies including reductions in respiratory symptoms, sensory symptoms, and admissions for acute myocardial infarction (AMI).[4] These effects have since been reproduced by others,[5-7] while additional studies also demonstrated reductions in sudden cardiac arrest and mortality from AMI in response to implementation of smoke-free legislation.[8, 9]

As developing individuals, children are particularly vulnerable to the negative effects of SHS, which may even ensue before birth. Furthermore, they are unable to influence their own degree of exposure. Antenatal SHS exposure puts unborn babies at risk for stillbirth,[10] preterm delivery,[11] growth retardation,[12, 13] congenital anomalies,[13, 14] bronchopulmonary dysplasia,[15] and respiratory infections and asthma in childhood.[16, 17] Worldwide at least 40% of children are regularly exposed to SHS after birth, additionally predisposing them to upper and lower respiratory infections as well as asthma.[2] Children thus bear an important part of the disease burden associated with SHS and are likely to particularly benefit from restrictive legislation. Indeed, several recent studies provide evidence for beneficial effects of smoke-free laws on infant and child health. Epidemiological evaluations of the 2006 Scottish smoking ban have demonstrated reductions in low birth weight, childhood asthma hospitalisations, and possibly also preterm birth following its introduction.[18, 19] These results have now been confirmed in several follow-on studies.[20, 21]

Despite this increasing evidence for particular health benefits of smoke-free legislation in children, the systematic reviews currently available assessing its health effects in general have not included any studies on perinatal or paediatric outcomes.[4, 22, 23] A comprehensive estimate of the benefits associated with smoke-free legislation in newborns

and children will inform the development and implementation of global policy and strategies to further reduce SHS exposure in this particularly vulnerable population. Therefore, we will undertake a systematic review and meta-analysis of studies on fetal, infant, and child health outcomes related to introduction of smoke-free legislation in order to obtain the most comprehensive assessment to date of its effectiveness in improving the health of babies and children worldwide.

METHODS AND ANALYSIS

Design

Systematic review and meta-analysis.

Eligibility criteria

Types of interventions

- Comprehensive (e.g. bars, restaurants and working space) or partial (e.g. working space only) smoking ban in public places at national, state, city, or community level

Types of studies

- In keeping with Cochrane Effective Practice and Organisation of Care (EPOC) guidelines only the following study designs will be considered for inclusion: (cluster) randomised controlled trials (RCTs), controlled clinical trials (CCTs), quasi-experimental studies, controlled before-and-after studies, interrupted time series (ITS) analysis.[24] For non-randomised studies, comparisons may include either a similarly aged population evaluated in the time frame preceding the introduction of the smoking ban in the same region, or a similar population evaluated during the same time frame in an adjacent geographical area where a smoking ban was not in place.
- Modelling, case-control, cohort, cross-sectional, and uncontrolled before-and-after studies are excluded

Types of participants

- Fetuses > 20 wks gestation
- Newborns > 20 wks gestation
- Children aged 0-12 years. In order to minimise the confounding effect of self-smoking, we will restrict our analyses to children aged 12 years and under.

Types of outcome measures

Outcome measures should preferably be reported or documented by a health worker; alternatively, parent-reported outcomes or parent-reported physician diagnoses are

acceptable. Outcomes may be defined as pure incidences, or by health facility use (e.g. doctor or emergency department visits, hospitalisation), or by medication use (e.g. inhaled corticosteroids in case of asthma/wheezing)).

- primary outcomes:
  - preterm birth (live birth between 20th and 37th week of gestation)
  - low birth weight (<2500 grams)
  - asthma (recurrent or persistent wheezing in children aged 5 years or older)
- secondary outcomes:
  - perinatal outcomes
    - stillbirth (intrauterine death of a fetus > 20 wks gestational age)
    - early neonatal death (<1 wk postnatally)
    - perinatal death (stillbirth + neonatal death)
    - late neonatal death (death 7-28 days postnatally)
    - neonatal death (death 0-28 days postnatally)
    - very preterm birth (<32 weeks gestational age)
    - very low birth weight (<1500 grams)
    - extremely low birth weight (<1000 grams)
    - small for gestational age (birth weight < 10th percentile for gravidity, ethnicity and sex)
    - congenital anomalies
    - bronchopulmonary dysplasia
  - childhood outcomes
    - upper respiratory, infectious (pooled)
      - coryza, pharyngitis, tonsillitis, laryngitis/tracheitis, sinusitis, acute otitis media, influenza
    - upper respiratory, non-infectious
      - otitis media with effusion
    - lower respiratory, infectious (pooled)
      - bronchitis/bronchiolitis, whooping cough, pneumonia
    - lower respiratory, non-infectious
      - wheezing (≥2 wheezing episodes in children aged 4 years or younger)
      - chronic cough (cough lasting >4 weeks)
  - outcomes not included in the review
    - surrogates and intermediates for adverse outcome (e.g. intima media thickness, blood pressure, anti-oxidant activity)

- smoke-related behaviours (e.g. teenage smoking, attitude towards smoking, stopping behaviour)
- measures of smoke exposure (e.g. smoke exposure in the home, environmental nicotine measures, cotinine levels)
- economic data (costs, cost-effectiveness)

Search methods

- Eligible study reports will be identified as follows:
  - Published work will be searched for in the following databases: Cochrane Library (CENTRAL), Medline, EMBASE, AMED, CAB, Global Health, CINAHL, WHO Global Health Library (in addition to Medline covering AIM (AFRO), LILACS (AMRO/PAHO), IMEMR (EMRO), IMSEAR (SEARO), WPRIM (WPRO), WHOLIS (KMS), SciELO), IndMED, TRIP, ISI Web of Science, KoreaMed, Google Scholar
  - In addition, reference lists of articles of interest and citations to included articles will be screened for additional eligible published studies
  - Unpublished and in progress studies will be identified from the following trial registries: ClinicalTrials.gov; ISRCTN Register; WHO International Clinical Trials Registry Platform; EU Clinical Trials Register; Current Controlled Trials; Australian New Zealand Clinical Trial Registry; Pan African Clinical Trials Registry; Chinese Clinical Trial Register; Clinical Trials Register India; Brazilian Clinical Trials Registry; Clinical Research Information Service, Republic of Korea; Cuban Public Registry of Clinical Trials; German Clinical Trials Register; Iranian Registry of Clinical Trials; The Netherlands' Trialregister; Sri Lanka Clinical Trials Registry; UMIN Clinical Trials Registry
  - Expert consultation
- search strategy: see appendix 1 and 2 (online supplements)
- restrictions:
  - time span: 1975-current. (Rationale: the first regional smoking ban was introduced in 1975 in the US state of Minnesota).[25]
  - language: none (for foreign language papers translations will be sought)

Study selection

Two authors (JVB, UN) will search databases and screen titles and abstracts for potentially eligible studies. Disagreement will be resolved by consensus, or arbitration involving a third author where necessary. Full text articles will be retrieved for selected studies, and two authors (JVB, UN) will assess whether these meet inclusion criteria. Disagreement will be

resolved by discussion amongst reviewers, with referral to a third author if necessary. Reasons for exclusion of studies will be noted.

Quality assessment and analysis

Study quality will be assessed using the Cochrane handbook 7-domain based evaluation for RCTs, quasi RCTs and CCTs (Cochrane handbook Table 8.5.a).[26] For controlled before-after studies and ITS analyses, EPOC guidelines will be used.[27] We will grade each parameter of trial quality: A - low risk of bias; B - moderate risk of bias; C - high risk of bias and an overall assessment for each controlled trial using the same three criteria will be made. Risk of bias will be assessed in part by recording design features (assessed by formal list in Cochrane handbook Table 13.2.a) as well as whether or not confounding is accounted for.[26] The primary confounder considered is maternal or parental smoking. Documentation of maternal/parental smoking according to smoke-free legislation status will be assessed, as well as adjustment of the final analyses for a potential confounding effect of this variable. All assessments of study quality will be performed by two authors (JVB, UN) with any disagreement resolved by consensus, or arbitration involving a third author where necessary.

Data extraction

Data will be extracted from selected papers by two reviewers (JVB, UN), with any disagreement resolved by consensus, or arbitration involving a third author where necessary. The following information will be extracted:

a. Geographical setting (e.g. country, city)
b. Reported study type (e.g. RCT, quasi-experimental study)
c. Design features (assessed by formal list in Cochrane handbook (Table 13.2.a)).[26]
d. Eligible population size
e. Included population size / number of clusters + cluster sizes
f. Relevant demographic characteristics (including age)
g. Description of intervention (including locations where ban was in effect (e.g. bars, workplace, government buildings) and level of enforcement)
h. In-/exclusion criteria
i. Outcomes
j. Effect sizes (univariate + multivariate)
k. Confounders adjusted for (e.g. parental smoking)
l. Bias assessment
m. Adverse effects
n. Follow-up rate and handling of drop-outs

o. Follow-up period

Data analysis

Data will be presented in tabular and narrative form. If possible, meta-analysis will be performed on similar studies reporting main, primary, and secondary outcomes, and be presented in forest plots. Choice of statistical tests used will depend on the nature of the outcome variable. Application of either a fixed effect or random effects model will be dependent on the degree of heterogeneity. Heterogeneity will be assessed both qualitatively and quantitatively using I^2 statistic. Where possible, adjusted effect estimates will be pooled in meta-analyses using generic inverse-variance analysis. Adjustment for maternal/parental smoking is mandatory in order for a study to be included in these analyses. Point estimates and 95% confidence intervals will be reported for all analyses.

Sensitivity analyses will be performed in subgroups of study quality and of design characteristics (randomised vs. non-randomised; prospective vs. retrospective). If possible, analyses will be performed in subgroups made according to the following defining parameters: setting of smoking restriction (comprehensive vs. location specific (e.g. working space, bars and restaurants)), age of study subjects (under five years vs. five years and older), smoking status in the home or maternal smoking for perinatal outcomes.

When the number of included studies per outcome is sufficient, publication bias will be assessed visually through Funnel plots and tested by Egger's regression test and Begg's rank correlation test.[28, 29]

ETHICS AND DISSEMINATION

Ethical issues

As no primary data collection will be undertaken, no additional formal ethical assessment and no informed consent is required.

Publication plan

The systematic review protocol will be registered with PROSPERO International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/prospero). Findings will be summarised in a single manuscript.

Timeline

Start date: December 1st, 2012

Finishing date: November 30th, 2013

Reporting date: November 30th, 2013

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AUTHORS' CONTRIBUTIONS

JVB developed the first protocol draft and designed the search strategies. UN was involved in protocol development and search strategy design. OCPvS was involved in protocol development. AS was involved in protocol development and supervised the writing process.

FUNDING

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COMPETING INTERESTS

The authors declare that they have no conflicts of interest with regard to this study.

Appendix 1:
Search strategy: Medline format

1. exp Tobacco Smoke Pollution/
2. smok*.mp.
3. cigar*.mp.
4. tobacco.mp.
5. or/1-4
6. exp Government Regulation/
7. exp Law Enforcement/
8. exp Legislation as Topic/
9. exp Policy Making/
10. exp Environmental Policy/
11. exp Health Policy/
12. free.mp.
13. regulat*.mp.
14. policy.mp.
15. policies.mp.
16. ban.mp.
17. bans.mp.
18. banned.mp.
19. restriction*.mp.
20. ordinance*.mp.
21. hospitality.mp.
22. prohibit*.mp.
23. law.mp.
24. laws.mp.
25. decree*.mp.
26. enactment.mp.
27. act.mp.
28. mandat*.mp.
29. injunct*.mp.
30. constitution*.mp.
31. or/6-30
32. exp Child/
33. exp Minors/
34. exp Infant/
35. exp Fetus/
36. exp Stillbirth/
37. exp Premature Birth/
38. child*.mp.
39. infant*.mp.
40. baby.mp.
41. babies.mp.
42. newborn*.mp.
43. neonat*.mp.
44. infant*.mp.
45. toddler*.mp.
46. preterm*.mp.
47. prematur*.mp.
48. fetus*.mp.
49. foetus*.mp.
50. fetal.mp.
51. foetal.mp.
52. stillbirth*.mp.

53. kids.mp.
54. minor.mp.
55. minors.mp.
56. or/32-55
57. exp Epidemiologic Studies/
58. exp Intervention Studies/
59. exp Evaluation Studies/
60. exp Comparative Studies/
61. exp Follow-up Studies/
62. exp Prospective Studies/
63. exp Retrospective Studies/
64. exp Clinical trial/
65. exp Controlled Clinical Trial/
66. exp Randomized Controlled Trial/
67. exp Quasi-randomized controlled trial/
68. exp Controlled before and after studies/
69. exp Interrupted time series/
70. exp Random Allocation/
71. exp Double-Blind Method/
72. exp Single-Blind Method/
73. exp Primary prevention/
74. exp Secondary prevention/
75. epidemiologic*.mp.
76. compar*.mp.
77. evaluat*.mp.
78. follow-up.mp.
79. followup.mp.
80. observation*.mp.
81. interrupted time series.mp.
82. intervention*.mp.
83. prospective.mp.
84. retrospective.mp.
85. analy*.mp.
86. control*.mp.
87. trial*.mp.
88. double-blind.mp.
89. single-blind.mp.
90. RCT
91. random*.mp.
92. prevention.mp.
93. or/57-92
94. 5 AND 31 AND 56 AND 93
95. advertisements/ or animation/ or architectural drawings/ or bibliography/ or biography/ or book illustrations/ or bookplates/ or charts/ or comment/ or letter/ or editorial/ or news/ or patient education handout/ or published erratum/ or “retraction of publication”/
96. 94 not 95
97. limit 96 to yr="1975 - current"

Appendix 2:
Search strategy: free-field format

(smok* OR cigar* OR tobacco)

AND

(free OR regulat* OR policy OR policies OR ban OR bans OR banned OR restriction* OR ordinance* OR hospitality OR prohibit* OR law OR laws OR decree* OR enactment OR act OR mandat* OR injunct* OR constitut*)

AND

(child* OR infant* OR baby OR babies OR newborn* OR infant* OR toddler* OR preterm* OR prematur* OR fetus* OR foetus* OR fetal* OR foetal* OR stillbirth* OR kids* OR minor OR minors)

AND

(analytical stud* OR epidemiologic* OR compar* OR evaluat* OR follow-up OR followup OR observation* OR interrupted time series OR intervention* OR prospective OR retrospective OR analy* OR control* OR trial* OR clinical trial* OR double-blind OR single-blind OR RCT OR random* OR prevention)

BMJ open

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Ethics and dissemination

Ethics assessment is not required. Results will be presented in one manuscript. The protocol is registered with PROSPERO

Registration number**:** CRD42013003522

INTRODUCTION

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As developing individuals, children are particularly vulnerable to the negative effects of SHS, which may even ensue before birth.[10-12] Furthermore, they are unable to influence their own degree of exposure. Antenatal SHS exposure puts unborn babies at risk for stillbirth,[13] preterm delivery,[14] growth retardation,[12, 15] congenital anomalies,[15, 16] bronchopulmonary dysplasia,[17] and respiratory infections and asthma in childhood.[11, 18] Worldwide at least 40% of children are regularly exposed to SHS after birth, additionally predisposing them to upper and lower respiratory infections as well as asthma.[2] Children thus bear an important part of the disease burden associated with SHS and are likely to particularly benefit from restrictive legislation. Indeed, several recent studies provide evidence for beneficial effects of smoke-free laws on infant and child health. Epidemiological evaluations of the 2006 Scottish smoking ban have demonstrated reductions in low birth weight, preterm birth, and childhood asthma hospitalisations following its introduction.[19, 20] These results have now been confirmed in several follow-on studies.[21, 22]

Despite this increasing evidence for particular health benefits of smoke-free legislation in children, the systematic reviews currently available assessing its health effects in general have not included any studies on perinatal or paediatric outcomes.[4, 23, 24] A comprehensive estimate of the benefits associated with smoke-free legislation in newborns and children will inform the development and implementation of global policy and strategies

to further reduce SHS exposure in this particularly vulnerable population. Therefore, we will undertake a systematic review and meta-analysis of studies on fetal, infant, and child health outcomes related to introduction of smoke-free legislation in order to obtain the most comprehensive assessment to date of its effectiveness in improving the health of babies and children worldwide.

METHODS AND ANALYSIS

Design

Systematic review and meta-analysis.

Eligibility criteria

Types of interventions

- Comprehensive (e.g. bars, restaurants and working space) or partial (e.g. working space only) smoking ban in public places at national, state, city, or community level

Types of studies

- In keeping with Cochrane Effective Practice and Organisation of Care (EPOC) guidelines that have set the standard for reviews of interventions designed to improve delivery of effective health services, only the following study designs will be considered for inclusion: (cluster) randomised controlled trials (RCTs), controlled clinical trials (CCTs), quasi-experimental studies, controlled before-and-after studies, interrupted time series (ITS) analysis.[25] For non-randomised studies, comparisons may include either a similarly aged population evaluated in the time frame preceding the introduction of the smoking ban in the same region, or a similar population evaluated during the same time frame in an adjacent geographical area where a smoking ban was not in place.
- Modelling, case-control, cohort, cross-sectional, and uncontrolled before-and-after studies are excluded given the difficulty to attribute causation from such studies.

Types of participants

- Fetuses > 20 wks gestation
- Newborns > 20 wks gestation
- Children aged 0-12 years. In order to minimise the confounding effect of self-smoking, we will restrict our analyses to children aged 12 years and under.

Types of outcome measures

Outcome measures should preferably be reported or documented by a health worker; alternatively, parent-reported outcomes, parent-reported physician diagnoses, or diagnoses based on medication use or prescriptions (e.g. inhaled corticosteroids as a surrogate for asthma diagnosis) are acceptable. Outcomes may be defined as absolute (e.g. incidence) or relative disease occurrence (e.g. relative risk, odds ratio), or by associated health facility use (e.g. doctor or emergency department visits, hospitalisation). Outcomes of interest are selected based on their relevance for fetal, infant, and/or paediatric health, and their recognised association between antenatal and/or postnatal SHS exposure. In addition selection of primary outcomes is based on the magnitude of their burden for paediatric health, as well as their recognised reduction after introduction of smoke-free legislation shown by at least one high quality study.

- primary outcomes:
    - preterm birth (live birth between 20th and 37th week of gestation)
    - low birth weight (<2500 grams)
    - asthma (recurrent or persistent wheezing in children aged 5 years or older)
- secondary outcomes:
    - perinatal outcomes
        - stillbirth (intrauterine death of a fetus > 20 wks gestational age)
        - early neonatal death (<1 wk postnatally)
        - perinatal death (stillbirth + neonatal death)
        - late neonatal death (death 7-28 days postnatally)
        - neonatal death (death 0-28 days postnatally)
        - very preterm birth (<32 weeks gestational age)
        - very low birth weight (<1500 grams)
        - extremely low birth weight (<1000 grams)
        - small for gestational age (birth weight < 10th percentile for gravidity, ethnicity and sex)
        - congenital anomalies
        - bronchopulmonary dysplasia
    - childhood outcomes
        - upper respiratory, infectious (pooled)
            - coryza, pharyngitis, tonsillitis, laryngitis/tracheitis, sinusitis, acute otitis media, influenza
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        - lower respiratory, non-infectious
            - wheezing (≥2 wheezing episodes in children aged 4 years or younger)
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    - outcomes not included in the review
        - surrogates and intermediates for adverse outcome (e.g. intima media thickness, blood pressure, anti-oxidant activity)
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- Expert consultation

- search strategy: see appendix 1 and 2 (online supplements)
- restrictions:
  - time span: 1975-current. (Rationale: the first regional smoking ban was introduced in 1975 in the US state of Minnesota).[26]
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a. Geographical setting (e.g. country, city)

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g. Description of intervention (including locations where ban was in effect (e.g. bars, workplace, government buildings) and level of enforcement)
h. In-/exclusion criteria
i. Outcomes
j. Effect sizes (univariate + multivariate)
k. Confounders adjusted for (e.g. parental smoking)
l. Bias assessment
m. Adverse effects
n. Follow-up rate and handling of drop-outs
o. Follow-up period

Data analysis

Data will be presented in tabular and narrative form. If possible, meta-analysis will be performed on similar studies reporting main, primary, and secondary outcomes, and be presented in forest plots. Choice of statistical tests used will depend on the nature of the outcome variable. We will apply a random effects model in all analyses given the expected degree of heterogeneity in population and design between studies. Heterogeneity will be assessed both qualitatively and quantitatively using I^2 statistic. Meta-analysis will not be undertaken when I^2 is equal to or greater than 75%. Where possible, adjusted effect estimates will be pooled in meta-analyses using generic inverse-variance analysis. Adjusted effect estimates derived from the most adjusted model in the original paper will be selected for these analyses. Point estimates and 95% confidence intervals will be reported for all analyses.

Sensitivity analyses will be performed in subgroups of study quality and of design characteristics (randomised vs. non-randomised; prospective vs. retrospective). If possible, analyses will be performed in subgroups made according to the following defining parameters: setting of smoking restriction (comprehensive vs. location specific (e.g. working space, bars and restaurants)), age of study subjects (under five years vs. five years and older), smoking status in the home or maternal smoking for perinatal outcomes. For meta-analyses of adjusted effect estimates, an additional sensitivity analysis will be performed

according to whether or not maternal or parental smoking was part of the adjusted model in the original study.

For any meta-analysis that includes ten or more studies, publication bias will be assessed visually through Funnel plots and tested by Egger's regression test and Begg's rank correlation test.[29, 30] All statistical analyses will be performed using Stata.

ETHICS AND DISSEMINATION

Ethical issues

As no primary data collection will be undertaken, no additional formal ethical assessment and no informed consent is required.

Publication plan

The systematic review protocol is registered with PROSPERO International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/prospero). Findings will be summarised in a single manuscript.

Timeline

Start date: January 1st, 2013
Finishing date: March 31th, 2014
Reporting date: March 31th, 2014

ACKNOWLEDGEMENTS

We thank Marshall Dozier for valuable feedback on our search strategy, and the Netherlands Asthma Foundation, the Maastricht University Medical Centre, the Thrasher Research Fund, and the International Pediatric Research Foundation for funding this work.

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AUTHORS' CONTRIBUTIONS

JVB developed the first protocol draft and designed the search strategies. UN was involved in protocol development and search strategy design. OCPvS was involved in protocol development. AS was involved in protocol development and supervised the writing process.

FUNDING

This work was supported by Thrasher Research Fund Early Career Award NR-0166, Netherlands Asthma Foundation Long Term Fellowship 3.4.12.128FE (JVB), a Maastricht University Medical Centre Kootstra Talent Fellowship (JVB), and the International Pediatric Research Foundation Young Investigator Exchange Programme (JVB).

COMPETING INTERESTS

The authors declare that they have no conflicts of interest with regard to this study.

The impact of smoke-free legislation on fetal, infant, and child health: a systematic review and meta-analysis protocol

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[2] Allergy & Respiratory Research Group, Centre for Population Health Sciences, The University of Edinburgh Medical School, Edinburgh, UK

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Keywords: tobacco smoke, legislation, meta-analysis, child, infant

Word count: 2088~~1837~~

Abstract

Introduction

Second-hand smoke (SHS) exposure ~~increases adverse health outcomes and~~ is estimated to kill 600,000 people worldwide annually. The World Health Organization (WHO) ~~now~~ recommends that smoke-free indoor public environments are enforced through national legislation. Such regulations have been shown to reduce SHS exposure and consequently, respiratory and cardiovascular morbidity. Evidence of particular health benefit in children is now emerging, including reductions in low birth weight deliveries, preterm birth, and asthma exacerbations. We aim to ~~obtain a~~ comprehensively assess~~ment of~~ the impact of smoke-free legislation on fetal, infant and childhood outcomes. This can~~,~~ ~~which can~~ inform further development and implementation of global policy and strategies to reduce early life SHS exposure.

Methods

Two authors will search online databases (1975-present; no language restricions) of published and unpublished ~~or~~ /in progress studies, and reference~~s lists~~ and citations to articles of interest. We will consult experts in the field to identify additional studies. ~~No language restrictions apply.~~ Studies should describe associations between comprehensive or partial smoking bans in public places and health outcomes among children (0-12 years): stillbirth, preterm birth, low birth weight, small for gestational age, perinatal mortality, congenital anomalies, bronchopulmonary dysplasia, upper and lower respiratory infections, and wheezing disorders including asthma. Cochrane Effectiveness Practice and Organisational Care (EPOC) defined study designs are eligible.

Study quality will be assessed using the Cochrane 7-domain based evaluation for randomised and clinical trials, and EPOC criteria for quasi-experimental studies. Data will be extracted by two reviewers and presented in tabular and narrative form. Meta-analysis will be undertaken using ~~fixed-effect or~~ random-effects models, and generic inverse variance analysis for ~~depending on the degree of heterogeneity.~~ A~~a~~djusted effect estimates ~~will be pooled using generic inverse variance analysis~~. We will report sensitivity analyses according to study quality and design characteristics, and subgroup analyses according to ~~intervention type~~coverage of ban, age group, and parental/maternal smoking status. Publication bias will be ~~formally~~ assessed.

Ethics and dissemination

Ethics assessment is not required. Results will be presented in one manuscript. The protocol is registered with PROSPERO (…).

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INTRODUCTION

Tobacco use kills more than five million people annually making it the leading global cause of preventable death.[1] It is estimated that second-hand smoke (SHS) exposure kills an additional 600,000 people worldwide each year, including 165,000 children under 15 years.[1, 2] Among non-smoking adults SHS exposure furthermore increases the incidence of asthma, lung cancer and ischaemic heart disease.[2] In an attempt to reduce this substantial burden on second-hand or passive smokers, the World Health Organization (WHO) has recommended that smoke-free indoor public environments are enforced through national legislation and that educational strategies are pursued in parallel to reduce SHS exposure in the home.[3] Studies have since shown that smoking bans effectively reduce SHS exposure, even in absence of an overall decline in smoking prevalence in the population.[4] More importantly, consistent health effects have been reported in a recent Cochrane review summarising 25 studies including reductions in respiratory symptoms, sensory symptoms, and admissions for acute myocardial infarction (AMI).[4] These effects have since been reproduced by others,[5-7] while additional studies also demonstrated reductions in sudden cardiac arrest and mortality from AMI in response to implementation of smoke-free legislation.[8, 9]

As developing individuals, children are particularly vulnerable to the negative effects of SHS, which may even ensue before birth.[10-12] Furthermore, they are unable to influence their own degree of exposure. Antenatal SHS exposure puts unborn babies at risk for stillbirth,[13~~0~~] preterm delivery,[1~~4~~4] growth retardation,[12, 1~~3~~5] congenital anomalies,[1~~3~~5, 1~~4~~6] bronchopulmonary dysplasia,[1~~5~~7] and respiratory infections and asthma in childhood.[11, 1~~6~~8, ~~17~~] Worldwide at least 40% of children are regularly exposed to SHS after birth, additionally predisposing them to upper and lower respiratory infections as well as asthma.[2] Children thus bear an important part of the disease burden associated with SHS and are likely to particularly benefit from restrictive legislation. Indeed, several recent studies provide evidence for beneficial effects of smoke-free laws on infant and child health. Epidemiological evaluations of the 2006 Scottish smoking ban have demonstrated reductions in low birth weight, preterm birth, and childhood asthma hospitalisations~~, and possibly also preterm birth~~ following its introduction.[1~~8~~9, ~~19~~20] These results have now been confirmed in several follow-on studies.[2~~1~~0, 2~~1~~2]

Despite this increasing evidence for particular health benefits of smoke-free legislation in children, the systematic reviews currently available assessing its health effects in general have not included any studies on perinatal or paediatric outcomes.[4, 2~~3~~2, 2~~4~~3] A comprehensive estimate of the benefits associated with smoke-free legislation in newborns

and children will inform the development and implementation of global policy and strategies to further reduce SHS exposure in this particularly vulnerable population. Therefore, we will undertake a systematic review and meta-analysis of studies on fetal, infant, and child health outcomes related to introduction of smoke-free legislation in order to obtain the most comprehensive assessment to date of its effectiveness in improving the health of babies and children worldwide.

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o. Follow-up period

Data analysis

Data will be presented in tabular and narrative form. If possible, meta-analysis will be performed on similar studies reporting main, primary, and secondary outcomes, and be presented in forest plots. Choice of statistical tests used will depend on the nature of the outcome variable. We will apply a ~~Application of either a fixed effect or~~ random effects model in all analyses given the expected degree of heterogeneity in population and design between studies. ~~will be dependent on the degree of heterogeneity.~~ Heterogeneity will be assessed both qualitatively and quantitatively using I^2 statistic. Meta-analysis will not be undertaken when I^2 is equal to or greater than 75%. Where possible, adjusted effect estimates will be pooled in meta-analyses using generic inverse-variance analysis. Adjusted effect estimates derived from the most adjusted model in the original paper will be selected for these analyses. ~~Adjustment for maternal/parental smoking is mandatory in order for a study to be included in these analyses.~~ Point estimates and 95% confidence intervals will be reported for all analyses.

Sensitivity analyses will be performed in subgroups of study quality and of design characteristics (randomised vs. non-randomised; prospective vs. retrospective). If possible, analyses will be performed in subgroups made according to the following defining parameters: setting of smoking restriction (comprehensive vs. location specific (e.g. working

space, bars and restaurants)), age of study subjects (under five years vs. five years and older), smoking status in the home or maternal smoking for perinatal outcomes. For meta-analyses of adjusted effect estimates, an additional sensitivity analysis will be performed according to whether or not maternal or parental smoking was part of the adjusted model in the original study.

For any meta-analysis that includes~~When the number of included studies per outcome is sufficient~~ ten or more studies, publication bias will be assessed visually through Funnel plots and tested by Egger's regression test and Begg's rank correlation test.[2~~8~~9, ~~29~~30] All statistical analyses will be performed using Stata.

ETHICS AND DISSEMINATION

Ethical issues

As no primary data collection will be undertaken, no additional formal ethical assessment and no informed consent is required.

Publication plan

The systematic review protocol ~~will be~~is registered with PROSPERO International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/prospero). Findings will be summarised in a single manuscript.

Timeline

Start date: ~~December~~ January 1st, 201~~2~~3

Finishing date: March~~November~~ 3~~0~~1th, 201~~3~~4

Reporting date: March~~November~~ 3~~0~~1th, 201~~3~~4

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AUTHORS' CONTRIBUTIONS

JVB developed the first protocol draft and designed the search strategies. UN was involved in protocol development and search strategy design. OCPvS was involved in protocol development. AS was involved in protocol development and supervised the writing process.

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COMPETING INTERESTS

The authors declare that they have no conflicts of interest with regard to this study.

Appendix 1:
Search strategy: Medline format

1. exp Tobacco Smoke Pollution/
2. smok*.mp.
3. cigar*.mp.
4. tobacco.mp.
5. or/1-4
6. exp Government Regulation/
7. exp Law Enforcement/
8. exp Legislation as Topic/
9. exp Policy Making/
10. exp Environmental Policy/
11. exp Health Policy/
12. free.mp.
13. regulat*.mp.
14. policy.mp.
15. policies.mp.
16. ban.mp.
17. bans.mp.
18. banned.mp.
19. restriction*.mp.
20. ordinance*.mp.
21. hospitality.mp.
22. prohibit*.mp.
23. law.mp.
24. laws.mp.
25. decree*.mp.
26. enactment.mp.
27. act.mp.
28. mandat*.mp.
29. injunct*.mp.
30. constitution*.mp.
31. or/6-30
32. exp Child/
33. exp Minors/
34. exp Infant/
35. exp Fetus/
36. exp Stillbirth/
37. exp Premature Birth/
38. child*.mp.
39. infant*.mp.
40. baby.mp.
41. babies.mp.
42. newborn*.mp.
43. neonat*.mp.
44. infant*.mp.
45. toddler*.mp.
46. preterm*.mp.
47. prematur*.mp.
48. fetus*.mp.
49. foetus*.mp.
50. fetal.mp.
51. foetal.mp.
52. stillbirth*.mp.

53. kids.mp.
54. minor.mp.
55. minors.mp.
56. or/32-55
57. exp Epidemiologic Studies/
58. exp Intervention Studies/
59. exp Evaluation Studies/
60. exp Comparative Studies/
61. exp Follow-up Studies/
62. exp Prospective Studies/
63. exp Retrospective Studies/
64. exp Clinical trial/
65. exp Controlled Clinical Trial/
66. exp Randomized Controlled Trial/
67. exp Quasi-randomized controlled trial/
68. exp Controlled before and after studies/
69. exp Interrupted time series/
70. exp Random Allocation/
71. exp Double-Blind Method/
72. exp Single-Blind Method/
73. exp Primary prevention/
74. exp Secondary prevention/
75. epidemiologic*.mp.
76. compar*.mp.
77. evaluat*.mp.
78. follow-up.mp.
79. followup.mp.
80. observation*.mp.
81. interrupted time series.mp.
82. intervention*.mp.
83. prospective.mp.
84. retrospective.mp.
85. analy*.mp.
86. control*.mp.
87. trial*.mp.
88. double-blind.mp.
89. single-blind.mp.
90. RCT
91. random*.mp.
92. prevention.mp.
93. or/57-92
94. 5 AND 31 AND 56 AND 93
95. advertisements/ or animation/ or architectural drawings/ or bibliography/ or biography/ or book illustrations/ or bookplates/ or charts/ or comment/ or letter/ or editorial/ or news/ or patient education handout/ or published erratum/ or “retraction of publication”/
96. 94 not 95
97. limit 96 to yr="1975 - current"

Appendix 2:
Search strategy: free-field format

(smok* OR cigar* OR tobacco)

AND

(free OR regulat* OR policy OR policies OR ban OR bans OR banned OR restriction* OR ordinance* OR hospitality OR prohibit* OR law OR laws OR decree* OR enactment OR act OR mandat* OR injunct* OR constitut*)

AND

(child* OR infant* OR baby OR babies OR newborn* OR infant* OR toddler* OR preterm* OR prematur* OR fetus* OR foetus* OR fetal* OR foetal* OR stillbirth* OR kids* OR minor OR minors)

AND

(analytical stud* OR epidemiologic* OR compar* OR evaluat* OR follow-up OR followup OR observation* OR interrupted time series OR intervention* OR prospective OR retrospective OR analy* OR control* OR trial* OR clinical trial* OR double-blind OR single-blind OR RCT OR random* OR prevention)