Impact of environmental tobacco smoke exposure on anaesthetic and surgical outcomes in children: a systematic review and meta-analysis

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ABSTRACT

Background Tobacco smoke exposure in adults is linked to adverse anaesthetic and surgical outcomes. Environmental tobacco smoke (ETS) exposure, including passive smoking, causes a number of known harms in children, but there is no established evidence review on its impact on intraoperative and postoperative outcomes. 

Objectives To undertake a systematic review of the impact of ETS on the paediatric surgical pathway and to establish if there is evidence of anaesthetic, intraoperative and postoperative harm.

Eligibility criteria participants Children aged 0–18 years undergoing anaesthetic or surgical procedures, any country, English language papers.

Exposure ETS exposure assessed via questioning, observation or biological marker.

Outcome measures Frequency of respiratory and other adverse events during anaesthesia, surgery and recovery, and longer term surgical outcomes.

Results 28 relevant studies were identified; 15 considered anaesthetic outcomes, 12 surgical outcomes, and 1 a secondary outcome. There was sufficient evidence to demonstrate that environmental smoke exposure significantly increased risk of perianesthetic respiratory adverse events (Pooled risk ratio 2.52 CI 95% 1.68 to 3.77), and some evidence that ear and sinus surgery outcomes were poorer for children exposed to ETS.

Conclusions ETS exposure increases the risk of anaesthetic complications and some negative surgical outcomes in children, and this should be considered when planning surgery. Research is required to demonstrate whether changes in household smoking behaviour prior to surgery reduces risk of adverse outcomes, and to close the evidence gap around other outcomes such as wound healing and respiratory infections.

Trial registration number Review registration number 42014014557.

INTRODUCTION

Environmental tobacco smoke (ETS) exposure, also referred to as ‘secondhand smoke’ or ‘passive smoking’, is exposure to smoke from the burning of a tobacco product and smoke that is exhaled by smokers. ETS exposure has been demonstrated to have a significant impact on the health of children and young people. This includes increased incidence of respiratory infection,1 asthma,2 ear infection3 and meningitis. Children are more vulnerable than adults to ETS,4 and there is consensus on the importance of protecting children from the harms of ETS exposure.5

Rationale

In adults, there is evidence that tobacco smoking has a negative impact on surgical outcomes, including anaesthetic complications, reduced wound and bone healing,6,7 and increased morbidity and delayed discharge from hospital.8 Appropriate cessation of smoking before an operative episode reduces the likelihood of these events and improves patient outcomes.9 Economic benefits of effective preoperative smoking cessation have been modelled in adults, where cessation was conservatively estimated to save between one-half and three-quarters of a million pounds in London alone, with a potential to extend this to 5–13 million pounds with a more engaged programme.10

There is no similar evidence base around the impact of ETS exposure levels on surgery in children, and a review of PROSPERO abstracts suggests no similar systematic reviews (SRs) are in preparation.
Objectives
The objective of this SR was to answer the structured question ‘What is the evidence from observational studies that environmental tobacco smoke (ETS) exposure in children aged under 18 affects anaesthetic and surgical outcomes compared with those with lower or no ETS exposure?’

METHODS
This SR was conducted in line with current PRISMA guidance. Review coauthors agreed the review protocol, which was submitted to the University of York PROSPERO International Prospective Register of Systematic Reviews (ID 42014014557).

Eligibility criteria
Studies were eligible if they met the following four criteria:

(A) An observational study (as defined by the Cochrane Collaboration), including case–control, cohort, case-cohort, nested case–control and cross-sectional studies. Case studies, letters, editorials and reviews were excluded. Where relevant cohorts could be identified as nested within an interventional study (eg, a randomised controlled trial collecting ETS exposure as confounding), it was included.

(B) A population of children aged 18 or under undergoing any operative procedures, including studies of children, or containing a subgroup of children aged 18 or under.

(C) Study or subgroup analysis contained within it uses reported or observed ETS (eg, by parental questionnaire), or biological markers thereof, as an independent variable on outcome.

(D) Study included either any anaesthetic, recovery and surgical outcomes, for our protocol’s primary outcomes, or secondary outcomes including length of stay, cost of care, patient experience or change in close contact smoking behaviours or ETS exposure. Any length of follow-up was accepted.

Information sources
A standardised search protocol was developed and performed across all databases on 30 October 2014. We searched only English language publications.

MEDLINE (1946–2014), Embase (1974–2014) and PsycINFO (1967–2014) were searched via OVID, as well as IBSS (1951–2014) via ProQuest, CPCI (1990–2013) via Web of Science, CINAHL Plus (1964–2014) via EBSCO Health and OpenGray (inception–2014). The sample search strategy for MEDLINE is available in the online supplementary file S1. Reference lists of studies selected for inclusion were reviewed, but no further papers were identified. No contacts were made with authors to identify or obtain papers. Search results were imported into Mendeley (v1.12.3) and de-duplicated algorithmically, followed by manual inspection. A check was performed on final papers to confirm no duplicated publications.

Study selection
Two reviewers (CC and YA) independently screened titles and abstracts against the eligibility criteria. Where there was no consensus, the reviewers engaged in dialogue, with unresolved papers taken forward to full review. Full papers were obtained for all abstracts taken forward, and reviewed independently by the two reviewers against a pre-established checklist. Again, consensus on inclusion was reached through dialogue. A third reviewer was available for resolution of disagreements, but was not required.

Data extraction
A data extraction template was created to capture participant numbers, specialty, inclusion and exclusion criteria, measurement of ETS exposure, whether ETS was a primary or secondary measure and how ETS exposure was categorised. Outcomes were captured, including type of outcome, length of study, statistical method, results and adjustments for bias and confounding. Where only rates or percentages were reported, these were used to calculate raw numbers for inclusion.

Wherever possible, total and included study participants, raw event numbers and summary statistics were extracted. Other specific outcomes, such as ‘time to event’ were captured narratively. Primary outcomes were classified into three categories: anaesthetic (eg, laryngospasm), immediate postsurgical (eg, bleeding) and long-term surgical (eg, disease resolution or improvement).

The extraction tool was piloted on a scoping study, and then applied consistently to all papers by a study reviewer (YA). Results were independently cross-checked by the second reviewer (CC).

Quality scoring
Studies that met the inclusion criteria were independently scored for methodological quality by the two reviewers using a modified eight-point version of the Newcastle–Ottawa quality assessment scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) recognised by the Cochrane Collaboration Non-Randomised Studies Working Group. The content validity and inter-rater reliability of the tool are already established. The study reviewers selected a score of 7 or more as an indicator of high methodological quality.

Statistical methods
The protocol described that quantitative data synthesis would be undertaken where there were sufficient data. Surgical outcomes were too diverse, and are reported narratively. Anaesthetic respiratory adverse events (RAEs) were reported more consistently. A pooled, weighted risk ratio was estimated using random effects meta-analysis performed in RevMan V5.3.5,13 using the Mantel-Haenszel implementation of the DerSimonian Laird model, accompanied by tests for heterogeneity ($I^2$ statistic). A random effects model was chosen to reflect the range of variation in participants and specialties, and to support the understanding of impacts of ETS exposure on wider surgical populations.

The analysis used available data from all papers which measured ETS exposure as a primary variable of interest, and reported RAE outcomes. Where RAEs were reported in a way that could not be combined, laryngospasm was chosen as the dominant proxy to take into the meta-analysis. Where several time points were reported, the first time point after administration of anaesthetic was selected for inclusion, as it represented the theoretical point of maximum impact of ETS on RAEs.

The impact of missing data was not examined due to limitations in the available datasets and the heterogeneous nature of the studies. Sensitivity was tested by removing individual studies, and then the two most heavily weighted studies, from our analyses.

RESULTS
Study selection
Of the 6875 titles assessed for eligibility, 48 proceeded to full text review, with 28 studies fitting the full eligibility criteria. Figure 1 summarises the selection process. Twenty-four studies14–37 used cohorts to examine ETS exposure, and four38–41 used case-control methodologies.
Fifteen studies considered anaesthetic outcomes, and twelve studies considered surgical outcomes. One further study considered behaviour change, a secondary outcome. No studies identified immediate surgical outcomes and, unlike the adult evidence base, no studies considered long-term outcomes of wound or bone healing.

Studies covered ages from birth upwards. One study had a protocol that focused on children, but which reported an age range of 0–22 years in its data. The mean age was 5.8, and the reviewers agreed the study should be included as the majority of patients were within the protocol.

The anaesthetic outcome studies used a wide range of surgical groups, including general or mixed surgery, dental, ophthalmology and urology patients. All 12 studies considering surgical outcomes focused on ear, nose and throat (ENT) patients. The impact of ETS on this patient group was complicated by the confounding associated with ETS being a cause of delayed surgical recovery and a cause of primary disease or recurrence. In five studies, ETS exposure was treated as a confounding variable, rather than the primary focus of the study.

ETS exposure was usually measured as a binary exposed/unexposed variable, although additional measures such as identifying which family members smoked, levels of smoking and biological markers were also used. One study showed good correlation between parental questioning and urinary cotinine levels.

Studies reported a range of biological and clinical outcomes; the majority of anaesthetic outcomes reported were RAEs, particularly laryngospasm. Oxygen desaturations and muscle relaxant dosages were used as biological measures. Long-term surgical outcome markers included ciliary regeneration, as well as clinical measures such as change in symptoms and signs, complications or repeat procedures.

Studies from Australia, Canada, Finland, Ireland, South Korea, Switzerland, Turkey, UK and USA were included.

Of the 15 studies considering anaesthetic outcomes, 10 were assessed as high quality; for the 12 considering ENT surgical outcomes, 2 were assessed as high quality. The majority of surgical studies considered ETS exposure as a confounding factor in a wider intervention study, and the ETS impact related only to specific subcohorts which had been given less methodological consideration. Online supplementary file S2 contains a summary of the assessment.

Table 1 summarises the characteristics of the studies examining anaesthetic and recovery outcomes, including methodology, age groups and sample sizes and measurement technique for ETS. It also summarises relevant outcome measures. A similar table describing the surgical papers is available in the online supplementary file S3.

**Individual study outcomes**

### Anaesthetic outcomes

Table 2 describes the key findings of studies related to anaesthetic outcomes. Three of fifteen studies considering anaesthetic outcomes did not show that ETS had significant impact on anaesthetic outcomes, with a further study showing a higher rate of RAE but not undertaking a statistical analysis. The remaining 11 studies showed significant effects. The most common adverse outcomes were increased rates of laryngospasm, bronchospasm and coughing. Both studies considering biological markers demonstrated some impact of ETS exposure.

**Pooled estimate of respiratory adverse event (RAE) risk**

Eleven studies were eligible for dichotomous meta-analysis with a random effects model to create a pooled
Table 1  Characteristics of 15 studies focusing on anaesthetic and recovery outcomes

<table>
<thead>
<tr>
<th>Study author</th>
<th>Year</th>
<th>Outcome methodology</th>
<th>Age group (defined/ included)</th>
<th>Surgical group</th>
<th>Location</th>
<th>ETS measure (number exposed)</th>
<th>ETS priority</th>
<th>Outcomes</th>
<th>Quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drongowski et al.</td>
<td>2003</td>
<td>Prospective cohort</td>
<td>3 months–13 years (n=146/146)</td>
<td>Inguinal hernia repair</td>
<td>USA</td>
<td>Parent questionnaire on smoking history/ exposure and urinary cotinine (57 ETS+)</td>
<td>1°</td>
<td>Observed respiratory events in induction, emergence and recovery</td>
<td>8</td>
</tr>
<tr>
<td>Jones et al.</td>
<td>2006</td>
<td>Prospective cohort</td>
<td>1–18 years (n=428/405)</td>
<td>Elective day case: mixed specialties</td>
<td>USA</td>
<td>Parent completed risk factor questionnaire, included smoking history (168 ETS+)</td>
<td>1°</td>
<td>Airway complications observed against graded scale intraoperatively and post anaesthesia</td>
<td>7</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>2013</td>
<td>Retrospective cohort</td>
<td>Child: not defined (n=159/159)</td>
<td>Had URI symptom; ENT and ophthalmology</td>
<td>South Korea</td>
<td>Passive smoking documented in anaesthetic record (28 ETS+)</td>
<td>1°</td>
<td>Respiratory adverse events documented in notes at intubation, intra-extubation and post-extubation, and in recovery</td>
<td>7</td>
</tr>
<tr>
<td>Laikshmipathy et al.</td>
<td>1996</td>
<td>Retrospective cohort</td>
<td>Child: not defined (n=322/310)</td>
<td>Elective day case: ENT and urology</td>
<td>USA</td>
<td>Parent reported regular smoker at home (96 ETS+)</td>
<td>1°</td>
<td>Laryngospasm documented in records</td>
<td>7</td>
</tr>
<tr>
<td>Lyons et al.</td>
<td>1996</td>
<td>Prospective cohort</td>
<td>1–12 years (n=7/125)</td>
<td>Elective day case: not ENT</td>
<td>Ireland</td>
<td>Parental questionnaire of home and other smoker contacts (63 ETS+)</td>
<td>1°</td>
<td>Respiratory adverse events observed by blinded anaesthetist at preoperative, intraoperative and postoperative points</td>
<td>6</td>
</tr>
<tr>
<td>Mamie et al.</td>
<td>2004</td>
<td>Prospective cohort</td>
<td>1–14 years (n=800/743)</td>
<td>Mixed specialties</td>
<td>Switzerland</td>
<td>Parent completed allergy/ asthma questionnaire, including smoking (429 ETS+)</td>
<td>2°</td>
<td>Intraoperative, postoperative and perioperative respiratory adverse events</td>
<td>7</td>
</tr>
<tr>
<td>O’Rourke et al.</td>
<td>2006</td>
<td>Prospective matched cohort</td>
<td>5–15 years (n=93 at recovery; 96 at discharge)</td>
<td>Convenience sample; non-cavity surgery</td>
<td>USA</td>
<td>Direct parental questioning (46 ETS+ at recovery, 49 ETS+ at discharge)</td>
<td>1°</td>
<td>Pulmonary function as percentage predicted; respiratory events secondary outcome 'Good' vs 'bad' anaesthetic outcome, including adverse respiratory, gastrointestinal and circulatory events</td>
<td>7</td>
</tr>
<tr>
<td>Parnis et al.</td>
<td>2011</td>
<td>Prospective case–control</td>
<td>Child: not defined (n=2/205)</td>
<td>Mixed specialties</td>
<td>Australia</td>
<td>Parental smoking status as part of wider research questionnaire (926 ETS+)</td>
<td>2°</td>
<td>'Good' vs 'bad' anaesthetic outcome, including adverse respiratory, gastrointestinal and circulatory events</td>
<td>6</td>
</tr>
<tr>
<td>Reiski et al.</td>
<td>2004</td>
<td>Prospective cohort</td>
<td>4–10 years (n=40/40)</td>
<td>ENT surgery; convenience sample</td>
<td>Turkey</td>
<td>Parental questioning of child's overall ETS exposure (20 ETS+)</td>
<td>1°</td>
<td>Rocuronium dose observed for neuromuscular blockade</td>
<td>6</td>
</tr>
<tr>
<td>Seyidov et al.</td>
<td>2011</td>
<td>Prospective cohort</td>
<td>3 months–12 years (n=402/385)</td>
<td>Elective surgery</td>
<td>Turkey</td>
<td>Parental questioning of quantity of smoke exposure (234 ETS+)</td>
<td>1°</td>
<td>Respiratory adverse events observed by blinded team</td>
<td>7</td>
</tr>
<tr>
<td>Skolnick et al.</td>
<td>1998</td>
<td>Prospective cohort</td>
<td>1 month–12 years (n=602/499)</td>
<td>Elective surgery</td>
<td>USA</td>
<td>Urinary cotinine and parental enquiry (262 ETS+)</td>
<td>1°</td>
<td>Respiratory adverse events</td>
<td>8</td>
</tr>
<tr>
<td>Tait et al.</td>
<td>2001</td>
<td>Prospective cohort</td>
<td>1 month–18 years (n=1078/407)</td>
<td>Elective surgery with active URI</td>
<td>USA</td>
<td>Questionnaire including parental smoking habits</td>
<td>2°</td>
<td>Contribution of factor to overall predictive multiple regression model</td>
<td>6</td>
</tr>
<tr>
<td>Thikkurissy et al.</td>
<td>2012</td>
<td>Prospective cohort</td>
<td>19 months–12 years (n=7/99)</td>
<td>Dental</td>
<td>USA</td>
<td>Parental interview on smoking status and quantity (51 ETS+)</td>
<td>1°</td>
<td>Respiratory adverse events observed by blinded anaesthetist and recovery nurse</td>
<td>7</td>
</tr>
<tr>
<td>Tütüncü et al.</td>
<td>2011</td>
<td>Prospective cohort</td>
<td>1–15 years (n=7/150)</td>
<td>Convenience sample; lower abdominal/ urology</td>
<td>Turkey</td>
<td>Parental questionnaire including parent smoking status (100 ETS+)</td>
<td>1°</td>
<td>Secondary outcome of postoperative respiratory complications</td>
<td>5</td>
</tr>
<tr>
<td>von Ungern-Sternberg et al.</td>
<td>2010</td>
<td>Prospective cohort</td>
<td>Child: not defined (n=10496/9038)</td>
<td>Anaesthesia for elective and urgent</td>
<td>Australia</td>
<td>Parent smoking report at preoperation check (2929 ETS+)</td>
<td>1°</td>
<td>Perioperative adverse events</td>
<td>8</td>
</tr>
</tbody>
</table>

*Study age range from 0 to 22 years. Mean age 5.8. Reviewers made decision to include in study.
†There is an apparent numerical error in the original paper where the identified total appears not to include exclusions.
ENT, ear, nose and throat; ETS, environmental tobacco smoke; URI, upper respiratory infection.
estimate of the risk ratio of a RAE with ETS exposure. Data were not available for one study, and attempts to contact the author were unsuccessful.

Figure 2 shows the outcome of the analysis, demonstrating that ETS exposure showed an increased risk ratio for a RAE in the perianaesthetic period of 2.52 (95% CI 1.68 to 3.77, \( p<0.0001 \)) compared with not being exposed. There was moderate statistical heterogeneity (I\(^2\)=62%). Subgroup analysis of studies focusing only on laryngospasm was undertaken, recognising the variety of outcomes that grouped RAEs would assess. This retained significance with a risk ratio of 3.54 (95% CI 2.37 to 5.28, \( p<0.001 \)) and reduced heterogeneity (I\(^2\)=23%).
The subgroup of grouped RAE studies only was marginally non-significant with a risk ratio of 1.75 (95% CI 0.95 to 3.21, p=0.07). The subgroup of only the studies that achieved a high-quality score on the Newcastle–Ottawa scale retained a significant risk ratio of 2.38 (95% CI 1.45 to 3.90, p<0.0001).

No evidence of publication bias was identified when examined through a funnel plot (figure 3). Sensitivity analysis showed that significance was retained if any individual study was removed, and also if the two most heavily weighted studies were removed.

Surgical outcomes
Table 3 shows that there was inconsistency between studies on the impact of ETS exposure on prognosis after ENT surgical procedures. Three studies\textsuperscript{12,38,39} showed no significant effects on outcomes, although two studies suggested some evidence that ETS exposure decreased the effectiveness or duration of tympanostomy (ventilation) tubes.\textsuperscript{28,35} Other studies showed ETS exposure caused a potential deterioration of either subjective\textsuperscript{39,34,36} or objective\textsuperscript{31,33,40} outcomes.

Secondary outcomes
One paper\textsuperscript{37} considered the impact of surgery on smoking behaviours for relatives of patients, a secondary outcome. Their analysis of survey data showed that parents who smoked were more likely to make a cessation attempt if their child had had recent surgery (OR 2.61 CI 95% 1.56 to 4.35, p<0.001), but that they were not more likely to maintain abstinence (OR 0.51 CI 95% 0.20 to 1.28, p=0.150).

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**Figure 2** Meta-analysis of environmental tobacco smoke (ETS) exposure and its association with likelihood of respiratory adverse events (RAEs) in the perianaesthetic period, including subgroups.

**Figure 3** Funnel plot assessing potential for publication bias within anaesthetic outcome studies included in meta-analysis.
Chiswell C, Akram Y. Arch Dis Child 2016;0:1–8. doi:10.1136/archdischild-2016-310687

DISCUSSION
Summary of evidence
The range of papers, generally assessed as high quality, show that ETS exposure increases the risk of anaesthetic complications for children undergoing surgery. The pooled estimate suggests that children are two and a half times more likely to experience a respiratory adverse event. Subgroup analysis suggests laryngospasm is a particular risk for exposed children.

No evidence was identified considering whether there were delayed harms such as infection or delayed wound and bone healing. The only evidence of the impact on surgical outcomes relates to ENT surgery, with a mixed picture of impact on surgical success. The quality of studies is mixed, and complex interactions make establishing causal linkages difficult.

Only one observational study looked at the impact of surgery on parental behaviour. It showed parents were more likely to make a quit attempt if their child had surgery in the preceding year, but that this attempt was no more likely to be successful.

The review is important to clinical teams in anticipating the increased risks of complications and discussing anaesthesia risks for ETS-exposed children. This information may create a 'teachable moment' for parents and carers to consider smoking cessation, giving our findings public health implications as well.

Strengths and limitations
This review is the first to bring together evidence of the impact of ETS exposure on outcomes of paediatric surgery. The search strategy was comprehensive and applied across the appropriate range of sources. It is disappointing that it did not identify papers covering outcomes such as infection and wound healing, but this is judged to be due to an absence of evidence.

Papers relating to anaesthetic outcomes were of good quality, reflecting the short-term outcomes being observed, and opportunities to blind observers to exposure status. A variety of methods were used for assessing ETS levels, but biological markers offered more robust techniques for stratifying cohorts. Where less reliable methods were used alongside biological markers, it was reassuring to note reasonable segregation of the cohorts.

The surgical outcomes evidence is limited. ETS exposure was often considered as a coincidental variable or subgroup. This was accommodated by evaluating paper quality solely on the interaction within the ETS study element, but it meant papers scored poorly on quality assessment because they had never been-conceived to address our research question.

Also, ETS exposure increases the incidence and prevalence of ENT conditions, and while we were clear that an appropriate temporal relationship was required; the detail available in some studies meant a reverse relationship could not be excluded. This is illustrated by Chen's conclusion that tonsillitis increased the influence of ETS on cough, as opposed to ETS increasing the persistence of cough after tonsillectomy. Both are feasible interpretations which cannot be separated by this review. Well-conceived methodologies that can demonstrate temporality do exist that can address this.

Conclusions
Exposure to ETS increases the risk of respiratory adverse events during anaesthesia for children undergoing surgery. It may also impact on the success of surgical procedures, particularly in ENT surgery. Exploration is now needed of whether information on increased risk provides an opportunity to promote smoking cessation, and whether even temporary cessation can be effective in reducing risk.

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Acknowledgements The authors thank Carole Cummins and Kate Jolly for their advice on the protocol, Carole Cummins for review of the manuscript prior to submission and David Moore for his advice on application of the study quality appraisal tool. Christopher Chiswell is supported by the NIHR CLAHRC West Midlands initiative. This paper presents independent research and the views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Collaborators Dr Carole Cummins.

Contributors The manuscript has been read and approved by all authors. CC instigated the review. CC and YA drafted the protocol. YA performed the searches. CC and YA screened the results, quality-assessed the papers and extracted data. CC drafted the manuscript for publication and responded to reviewer comments in communication with YA.

Competing interests None declared.
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