Supplementary File 2: Assessment of quality and bias

In preparing the tool, it was not possible to identify a dominant factor for which studies should be controlled for, instead recognising several key variables. Comparability was therefore scored against a single criterion of 'effectively controlling for relevant factors', meaning a maximum of eight points, rather than nine, were available. Where a nested cohort or matched case group was identified within an interventional study, it was agreed that the quality of the study as applied to impact of ETS would be appraised, and not the main interventional study outcomes. This acknowledged that high quality trials not relevant to the impact of ETS exposure could contain poor quality cohorts that were appropriate for inclusion, or vice versa.

A point was awarded for satisfactory response on each question, indicated by a tick in the relevant table.

Cohort Outcome Measures

Domain and outcomes		Point
Representativeness of the exposed cohort		
A	Truly representative of the paediatric population undergoing surgery	✓
B	Somewhat representative of the paediatric population undergoing surgery	✓
C	Selected subgroup of the population undergoing surgery	
D	No description of the cohort selection process	
Selection of the non-exposed cohort		
A	Drawn from the same community as the exposed cohort	✓
B	Drawn from a different source	
C	No description of the derivation of the non-exposed cohort	
Ascertainment of exposure		
A	Secure record (e.g. surgical record, biological test)	✓
B	Structured interview	✓
C	Written self-report of self-completed questionnaire	
D	No description	
Demonstration that outcome of interest was not present at start of the study		
A	Yes	✓
B	No	
Comparability of cohorts on the basis of the design or analysis		
A	Study controls for reasonable factors (e.g. age, premorbid disease state, gender, type of anaesthesia, length of surgery, socioeconomic status)	✓
B	Study does not control for reasonable co-variates	
Assessment of outcome		
A	Independent or blind assessment	✓
B	Record linkage or objective measure	✓
C	Self-reported outcome	
D	No description	
Was follow-up long enough for outcomes to occur?		
A	Yes	✓
B	No	
Adequacy of follow up of cohorts		
A	Complete follow up – all subjects accounted for	✓
B	Subjects lost to follow up unlikely to introduce bias (>90% follow up, or description provided of those lost)	✓
C	Follow up rate <90%, or no description of the lost	
D	No statement	

Case Control Outcome Measures

Domain and outcomes		Point
Is the case definition adequate?		
A	Yes, with independent validation	✓
B	Yes, based on self-reports or record linkage	
C	No description	
Representativeness of the cases		
A	Consecutive or obviously representative sample of cases	✓
B	Potential for selection biases or not stated	
Selection of controls		
A	Community controls (defined as those undergoing similar procedures)	✓
B	Hospital controls (defined as those not undergoing similar procedures)	
C	No description	
Definition of controls		
A	No history of endpoint	✓
B	No description of source of controls	
Comparability of cases and controls on the basis of the design or analysis		
A	Study controls for reasonable factors (e.g. age, premorbid disease state, gender, type of anaesthesia, length of surgery, socioeconomic status)	✓
B	Study does not control for reasonable co-variates	
Ascertainment of exposure		
A	Secure record (e.g. surgical records)	✓
B	Structured interview where blind to case/control status	✓
C	Interview not blinded to case/control status	
D	Written self-report or general medical record (not linked to procedure)	
E	No description	
Same method of ascertainment for cases and controls		
A	Yes	✓
B	No	
Non-response rate		
A	Same rate for both groups	✓
B	Non-respondents described	
C	Rate different and no designation	

The following pages describe the outcome of scoring and brief narrative on all selected papers. The letter shows the answer selected. Boxes shaded grey show those areas where the quality was insufficient to be awarded a point.

Anaesthetic Outcome Studies

Cohort Outcome Methods	Cohort choice	Non-exposed cohort	Exposure measures	Absent baseline	Other factors controlled	Outcome measures	Sufficient follow-up time	Adequacy of follow up	Quality Score	Notes and Commentary
Drongowski 2003	B	A	A	A	A	A	A	A	8	Only considers children undergoing inguinal hernia repair. Validates parental reported smoking with urinary cotinine as biological measure. Standardised anaesthetic protocol. Observers blinded to smoking status.
Jones 2006	A	A	C	A	A	A	A	B	7	Consecutive patient series undergoing elective procedures. Questionnaire used to capture ETS exposure. Observers blinded to questionnaire responses. Clearly described grading scale. Comprehensive co-variates considered.
Kim 2013	B	A	B	A	A	B	A	C	7	Retrospective review of patient records. Primary focus on predicting events in children with active upper respiratory tract infection, therefore not widely applicable to broader patient groups easily. Exposure obtained through interview. Any missing data exclusions not described.
Lakshmipathy 1996	B	A	B	A	B	A	A	B	7	Semi-retrospective analysis for laryngospasm only. Clear description of exclusions. Outcome only determined from written anaesthetic record with agreed criteria. Smoking exposure determined by telephone contact after surgical outcome known.

Cohort Outcome Methods	Cohort choice	Non-exposed cohort	Exposure measures	Absent baseline	Other factors controlled	Outcome measures	Sufficient follow-up time	Adequacy of follow up	Quality Score	Notes and Commentary
Lyons 1996	B	A	C	A	B	A	A	A	6	Patient selection process not fully described. ETS exposure measured via self-report questionnaire. Assessment of respiratory complications undertaken by anaesthetist unaware of parental smoking behaviours. Quantitative outcome metric of oxygen saturation also included.
Mamie 2004	B	A	B	A	A	A	A	C	7	45 children refused participation, without clear reason identified. Outcomes for specific ETS exposed cohort not reported as secondary variable in study; only presented as part of multiple logistic regression. Effective control of other factors due to wide scope of study.
O'Rourke 2006	B	A	D	A	A	A	A	A	7	Methodology describes selection of matched controls, but actually selects a cohort of non-ETS exposed patients. Appears to be convenience sample. No description of ascertainment of ETS status methodology. Objective measure of impact used with pulmonary function metrics. Variable time to performing final readings driven by discharge appropriateness.
Reisli 2004	B	A	C	A	B	A	A	A	6	Unclear selection process for inclusion within the cohorts, particularly as groups are equal size within study. No description of ETS ascertainment methodology. Outcome measurement using a semi-objective measure of neuromuscular blockade

Cohort Outcome Methods	Cohort choice	Non-exposed cohort	Exposure measures	Absent baseline	Other factors controlled	Outcome measures	Sufficient follow-up time	Adequacy of follow up	Quality Score	Notes and Commentary
Seyidov	B	A	B	A	B	A	A	B	7	Elective surgical group with description of exclusions and reasons. Assessment of outcomes by individuals unaware of group allocation. ETS exposure assessment by blinded recovery nurse. RAE outcome not controlled for other factors.
Skolnick	B	A	A	A	A	A	A	B	8	Good description of inclusion criteria, and of subject disposal throughout study. Description of co-variates included within analysis. Assessment of outcome by blinded clinician. Objective measure of urinary cotinine used to cross-reference parental reported ETS exposure.
Tait 2001	C	A	C	A	A	B	A	B	6	Focus on children with upper respiratory tract infections only. Exclusions described. Exposure determined by self-report questionnaire only. No stated blinding of outcome assessment, but clear scoring framework described.
Thikkurissy 2012	B	A	B	A	B	A	A	B	7	Dental anaesthesia papers only. Exposure ascertained through interview with parents using calibrated assessors and specific questions. Assessment of outcomes undertaken by blinded anaesthetist. Co-variates not described or considered in relevant analysis.
Tütüncü 2012	B	A	C	A	B	B	A	D	5	Primary analysis focuses on biological variables, but within SR scope, only post op respiratory complications relevant. Appears to be convenience sample. Unclear if final cohort relevant to ETS exposure includes all enrolled from presented information.

Ungern-Sternberg 2010	A	A	B	A	A	B	A	B	8	Substantial cohorts. Identification of exposure by modified version of validated questionnaire undertaken before outcome known. Anaesthetic events documented using structured record, and evaluation of co-variates included within analysis.
Case-Control Outcome Methods	**Case Definition**	**Case Selection**	**Control Selection**	**Control Definition**	**Other factors controlled**	**Exposure Measures**	**Equal treatment of groups**	**Adequacy of Responses**	**Quality Score**	**Notes and Commentary**
Parnis 2011	A	B	A	A	A	B	A	C	6	Recording of information in structured interview with dedicated research nurse using tool. Data sheet of events used to capture cases so clear separation of case/control. Group refusing surgery not fully described. ETS exposure included as part of multiple logistic regression model, but separate data not available.

Surgical (ENT) Outcome Studies

Cohort Outcome Methods	Cohort choice	Non-exposed cohort	Exposure measures	Absent baseline	Other factors controlled	Outcome measures	Sufficient follow-up time	Adequacy of follow up	Quality Score	Notes and Commentary
Hammaren-Malmi 2007	B	B	B	A	A	C	A	B	7	Some concern over initial selection criteria and loss of eligible patients. Tobacco habits documented via questioning of family. Some inconsistencies in tabulated reporting of results. Outcomes captured via self-reported patient diary. Confounding risk if ETS causes outcome directly.
Chen 1998	B	A	C	A	A	C	B	C	4	Extracting ETS relevant data from a nested cohort within a much larger study. Cohort relied on self-reporting, and response rates are not well described. Follow up was for unknown periods as timing of the surgical procedure is not captured.
Atef 2009	C	A	A	A	B	A	A	A	6	Very selected group of patients within cohort. However, objective assessment of smoking exposure used alongside questionnaire, and outcome evaluation uses pathology sample. No major consideration of impact of confounding.
Maw 1993	C	A	D	A	A	A	A	C	5	Tenuous for inclusion within SR as only very small data subgroup within study relevant to this PICO question. However, study quality is good.
Ilicali 2001	B	A	A	A	B	B	A	A	7	Only subgroup follow up of patients in case group for post-operative complications is relevant. Cotinine assessment used alongside questionnaire. No detail on independence of assessor for outcomes.

Cohort Outcome Methods	Cohort choice	Non-exposed cohort	Exposure measures	Absent baseline	Other factors controlled	Outcome measures	Sufficient follow-up time	Adequacy of follow up	Quality Score	Notes and Commentary
Ramadan 2001	B	A	D	A	B	A	A	A	6	Only looking at subgroup analysis table 6. No description of how smoke exposure identified, and no correction for potential confounding factors between the two groups. Steroid/Placebo groups adequately controlled through prior randomisation.
Ramadan 2004	B	A	D	A	A	B	A	A	6	Relies on self-assessment of outcomes and no clear detail on establishing ETS exposure status. Univariate analysis only corrects for surgical group, although randomisation between treatment arms of main study should reduce bias.
Praveen 2005	B	A	D	A	B	A	A	A	6	No description of methodology of obtaining smoking status. No correction for additional confounding factors within analysis relevant to the PICO question. Objective endpoint and measurement techniques described.
Ramadan 2002	B	A	C	A	A	C	A	D	5	Study relies on self-report of exposure and symptom changes with no biological validation. Follow up loss not clearly stated in study, and high exclusions described.

Case-Control Outcome Methods	Case Definition	Case Selection	Control Selection	Control Definition	Other factors controlled	Exposure Measures	Equal treatment of groups	Adequacy of Responses	Quality Score	Notes and Commentary
Gov-Ari 2012	B	A	A	B	A	D	A	B	4	Nested case-control study. Methodology not ideal to examine ETS impact, as looking at requirement for additional surgical procedure. Case definition therefore restricted, and controls poorly defined. Exposure is coded by self-report, and response rates not fully considered in context of ETS. Appropriate for inclusion as exposure precedes outcome.
Ilicali 1999	A	B	A	A	B	C	C	A	4	Unclear narrative on decision to report maternal outcomes only within paper. No description of sequence of case selection, nor exclusions or withdrawal. Loss to follow up not described. Some differences in control group vs. case group with confounding not considered on recurrence
Kim 2005	A	B	A	A	A	E	A	A	6	No description of selection of case series, and decision to undertake investigation made retrospectively. Potential for selection bias not described. Formal scoring criteria used for grading outcomes.