Risk assessment for respiratory complications in paediatric anaesthesia: a prospective cohort study

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Summary

Background **Perioperative respiratory adverse events in children are one of the major causes of morbidity and mortality during paediatric anaesthesia. We aimed to identify associations between family history, anaesthesia management, and occurrence of perioperative respiratory adverse events.**

Methods **We prospectively included all children who had general anaesthesia for surgical or medical interventions, elective or urgent procedures at Princess Margaret Hospital for Children, Perth, Australia, from Feb 1, 2007, to Jan 31, 2008. On the day of surgery, anaesthetists in charge of paediatric patients completed an adapted version of the International Study Group for Asthma and Allergies in Childhood questionnaire. We collected data on family medical history of asthma, atopy, allergy, upper respiratory tract infection, and passive smoking. Anaesthesia management and all perioperative respiratory adverse events were recorded.**

Findings **9297 questionnaires were available for analysis. A positive respiratory history (nocturnal dry cough, wheezing during exercise, wheezing more than three times in the past 12 months, or a history of present or past eczema) was associated with an increased risk for bronchospasm (relative risk [RR] 8·46, 95% CI 6·18–11·59; p<0·0001), laryngospasm (4·13, 3·37–5·08; p<0·0001), and perioperative cough, desaturation, or airway obstruction (3·05, 2·76–3·37; p<0·0001). Upper respiratory tract infection was associated with an increased risk for perioperative respiratory adverse events only when symptoms were present (RR 2·05, 95% CI 1·82–2·31; p<0·0001) or less than 2 weeks before the procedure (2·34, 2·07–2·66; p<0·0001), whereas symptoms of upper respiratory tract infection 2–4 weeks before the procedure significantly lowered the incidence of perioperative respiratory adverse events (0·66, 0·53–0·81; p<0·0001). A history of at least two family members having asthma, atopy, or smoking increased the risk for perioperative respiratory adverse events (all p<0·0001). Risk was lower with intravenous induction compared with inhalational induction (all p<0·0001), inhalational compared with intravenous maintenance of anaesthesia (all p<0·0001), airway management by a specialist paediatric anaesthetist compared with a registrar (all p<0·0001), and use of face mask compared with tracheal intubation (all p<0·0001).**

Interpretation **Children at high risk for perioperative respiratory adverse events could be systematically identified at the preanaesthetic assessment and thus can benefit from a specifically targeted anaesthesia management.**

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Introduction

Despite the development of guidelines for anaesthesia management, perioperative respiratory adverse events remain one of the major causes of morbidity and mortality during paediatric anaesthesia.[1–4] Many factors related to a child's medical history, anaesthesia management, and surgery contribute to their occurrence. Although previous studies have reported some risk factors for perioperative respiratory adverse events,[2,4–7] whether children at high risk are being identified in clinical practice is uncertain.

Increased airway sensitivity, which can be associated with current asthma, recent upper respiratory tract infection, or passive smoking, probably increases the risk of perioperative respiratory adverse events.[2,5–7] The incidence of upper respiratory tract infection in children presenting for anaesthesia is high[8] and the prevalence of asthma is increasing in the paediatric population,[9] thus anaesthetists have to manage increasing numbers of children at high risk of perioperative respiratory adverse events in everyday clinical practice. However, most paediatric studies have focused on a specific population,[10] a specific condition (eg, upper respiratory tract infection),[5,7] or the incidence of specific complications, particularly laryngospasm.[5,11]

Accurate assessment of the risk of perioperative respiratory adverse events during the preanaesthetic assessment would enable anaesthetic management to be tailored to reduce the likelihood of those complications. A suitable risk assessment questionnaire that could be used in the preoperative setting would be useful, especially because perioperative consultations are changing from being medically-based to nurse-based.[12]

We aimed to identify any associations between family history, anaesthesia management, and occurrence of perioperative respiratory adverse events by assessing children preoperatively with an adapted version of the International Study Group for Asthma and Allergies in Childhood (ISAAC) questionnaire.[13]

Methods

Study design

We prospectively included all children who had general anaesthesia for surgical or medical interventions, elective or urgent procedures at Princess Margaret Hospital for Children, Perth, Australia, from Feb 1, 2007, to Jan 31, 2008. On the day of surgery, the anaesthetist in charge of the patient used the modified ISAAC questionnaire[13] to record upper respiratory tract infection, including time of the infection (present, <2 weeks earlier, or 2–4 weeks earlier) and the symptoms involved (clear or green runny nose, fever [body temperature >38°C], and dry or moist cough); asthma and wheezing in the past 12 months (including the number of wheezing attacks) or wheezing with exercise; nocturnal dry cough persisting for more than 2 weeks in the past year; present or past hayfever, eczema, or allergy; passive smoke exposure; and the occurrence of asthma, eczema, or hayfever in first-degree relatives. Full details of the type of procedure, the level of experience of the anaesthetist in charge of airway management, anaesthetic management, and postoperative care were also recorded. The webappendix shows the modified questionnaire and the data collection sheet.

See Online for webappendix

Questionnaires were attached to the anaesthesia record and were completed by the anaesthetist in charge of the patient. An interpreter was available if needed to overcome language difficulties in families whose first language was not English. The anaesthetists were not masked to patient information when completing the questionnaire because it formed part of the preoperative assessment and we cannot ethically exclude such information. However, anaesthetists were not aware of the study hypotheses until the data collection was completed. Anaesthesia management was left to the discretion of the anaesthetist in charge with no restrictions or guidelines imposed by the study. We used the ISAAC questionnaire[13] for all the items related to bronchial hyper-reactivity, asthma, and allergy and added information about passive or active smoking.

We documented all perioperative respiratory adverse events and their time of occurrence (during anaesthesia induction, during maintenance of anaesthesia, at emergence from anaesthesia, or in the postanaesthetic care unit). All episodes of laryngospasm, bronchospasm, airway obstruction, oxygen desaturation (<95%), and severe or sustained cough were reported as perioperative respiratory adverse events. Children were also assessed in the postanaesthetic care unit for the occurrence of stridor. Laryngospasm was defined as complete airway obstruction associated with muscle rigidity of the abdominal and chest walls. Bronchospasm was defined as increased respiratory effort, especially during expiration, and wheeze on auscultation. Airway obstruction was defined as the presence of partial airway obstruction in combination with a snoring noise and respiratory efforts. We recorded any treatment that was needed in response to perioperative respiratory adverse events.

After approval by the institutional ethics committee, this study was done as a quality of care audit and parental consent was waived because no change to standard management was involved.

Statistical analysis

Statistical analysis was done with SPSS (version 15.0). We did univariate statistics with the Mann-Whitney *U* test for continuous variables and the χ^2 test for categorical variables. For all analyses, we used two-sided tests, with p values less than 0·05 denoting statistical significance. We adjusted p values by the step-down Bonferroni method with SAS (version 9.1.3).

We developed multivariate models for perioperative bronchospasm, laryngospasm, and all other complications as dependent variables. There were many possible independent candidate variables, and therefore development of the multivariate models needed variable selection to avoid problems of redundancy and over-specification. We chose the independent variables in the multivariate models on the basis of uncorrected p values of the univariate tests ($p<0·05$) and on medical considerations; some variables with a p value less than 0·05 were not included into the set of candidate-independent variables. Categorical variables with several categories were transformed to binary variables along the highest relative risk (RR) following the univariate testing.

When independent variables are correlated, there are difficulties in estimation of model coefficients; the greater the multicollinearity, the greater the standard errors. To avoid multicollinearity, the structure of the correlation of the candidate variables used in the multivariate model was examined first by factor analysis and resulted in five factors: variables associated with heightened airway sensitivity (present or recent [<2 weeks] cold, wheezing with exercise, wheezing more than three times in the past 12 months, and nocturnal dry cough); present or past eczema; family history (asthma, rhinitis, or eczema in at least two family members, or both parents smokers); anaesthesia (management by registrar, inhalational induction, or change of anaesthetist during airway management); and otolaryngology procedures. Instead of producing new artificial variables by factor analysis, we collapsed original variables belonging to the factors using the OR logical operator. These collapsed variables were used in the multivariate analyses together with age and airway management. Multivariate analysis was done by RR regression because this method is appropriate for modelling the risk factors of prospective studies. Multivariate analysis uses a generalised linear model with log-link function and binomial-dependent variable. Model fit was assessed by a likelihood ratio test with stepwise elimination process variables and possible interactions with age, and some medically plausible interactions were also examined. Variables and their interactions remained in the model if they improved the model fit with the likelihood ratio test.

Multiple occurrences of risk factors were handled in two ways; highly correlated variables expressing similar clinical meanings were collapsed into one variable and a multivariate analysis was done on these and other less correlated variables. By contrast, multiple occurrences of respiratory complications were considered as separate events in the same patient unless otherwise stated. Any associations that lost significance after correction are reported as such in the text.

	Number (%)
Age (n=9297)	
≤1 year	1890 (20%)
2–6 years	3622 (39%)
7–12 years	2448 (26%)
≥13 years	1337 (14%)
Female (n=9297)	3743 (40%)
ASA physical status score (n=9284)	
1	4565 (49%)
2	3394 (37%)
3	1202 (13%)
4	123 (1%)
Upper respiratory tract infection (n=9289)	
None	6142 (66%)
Present	1238 (13%)
Within past 2 weeks	869 (9%)
Within past 2–4 weeks	1040 (11%)
Wheezing in the past 12 months (n=9297)	1387 (15%)
Number of attacks of wheezing in the past 12 months (n=9297)	
0	7910 (85%)
1–3	909 (10%)
4–12	332 (4%)
>12	146 (2%)
Wheezing at exercise (n=9258)	872 (9%)
Nocturnal dry cough (n=9261)	1161 (13%)
Hayfever (n=9251)	1163 (13%)
Eczema in past 12 months (n=9249)	1307 (14%)
Family history of asthma (n=8611)	
None	5925 (69%)
Mother	1610 (19%)
Father	505 (6%)
≥2 family members	571 (7%)
Family history of rhinitis (n=8685)	
None	6639 (76%)
Mother	1204 (14%)
Father	493 (6%)
≥2 family members	349 (4%)
Family history of eczema (n=8717)	
None	7048 (81%)
Mother	1281 (15%)
Father	178 (2%)
≥2 family members	210 (2%)
Family history of smoking (n=9038)	
None	6109 (68%)
Mother	815 (9%)
Father	1039 (11%)
Both parents	1075 (12%)

n values are the number of patients from whom the information was available. Percentages do not add up to 100% in some cases because of rounding. ASA=American Society of Anesthesiologists.

Table 1: **Demographics and baseline characteristics**

	Number (%)
Procedure (n=9297)	
Elective	6006 (65%)
Urgent	3291 (35%)
Otolaryngology surgery (n=9297)	1189 (13%)
Premedication (n=9292)	
Midazolam	635 (7%)
Other	179 (2%)
None	8478 (91%)
Induction of anaesthesia (n=9283)	
Inhaled sevoflurane	3597 (39%)
Intravenous propofol	5686 (61%)
Anaesthesia maintenance (n=9297)	
Propofol	1289 (14%)
Inhaled drug	8008 (86%)
Sevoflurane	6221 (78%)
Isoflurane	1469 (18%)
Desflurane	318 (4%)
Myorelaxants (n=9297)	1449 (16%)
Person responsible for airway management (n=9297)	
Registrar	6219 (67%)
Consultant	3078 (33%)
Device used for airway management (n=9297)	
Face mask	820 (9%)
Laryngeal mask airway	5586 (60%)
Endotracheal tube	2891 (31%)
Insertion of laryngeal mask airway (n=5558)	
Inserted turning	1819 (33%)
Inserted straight	3739 (67%)
Endotracheal tube (n=2884)	
Uncuffed	1268 (44%)
Cuffed	1616 (56%)
Endotracheal tube (n=2882)	
Nasal	494 (17%)
Oral	2388 (83%)
Endotracheal tube vocal cords sprayed (n=2891)	558 (19%)
Airway device inserted successfully (n=8102)	
At the first attempt	7006 (86%)
At second attempt	898 (11%)
After three or more attempts	198 (2%)
Devices removed (n=8415)	
Awake	4433 (53%)
Under deep anaesthesia	3982 (47%)

n values are the number of patients from whom the information was available. Percentages do not add up to 100% in some cases because of rounding.

Table 2: **Management of anaesthesia**

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

Results
After the 12 months, 9297 questionnaires (from 10 496 children) were available for analysis. The mean age of the children was 6·21 years (SD 4·8). Tables 1 and 2 show demographic data and details of anaesthetic management.

1392 (15%) of 9297 children had perioperative respiratory adverse events: 193 (2%) had bronchospasm, 351 (4%) laryngospasm, 332 (4%) airway obstruction, 919 (10%) oxygen desaturation, 687 (7%) coughing, and 58 stridor (1%; table 3). Urgent procedures had a higher risk for perioperative respiratory adverse events than did elective procedures (17% [546 of 3291] *vs* 14% [846 of 6006]; RR 1·2, 95% CI 1·1–1·3; p=0·001).

The American Society of Anesthesiologists (ASA) physical status classification system is used in clinical practice to assess the risk for morbidity in paediatric anaesthesia. We used this system to assess risk in 9284 children. 201 (27%) of 750 children with a positive respiratory history versus 288 (8%) of 3815 of those with no infection in the past 4 weeks in ASA 1 had perioperative respiratory adverse events; 389 (33%) of 1167 versus 279 (12·5%) of 2227 in ASA 2; and 104 (33·2%) of 313 versus 98 (11%) of 889 in ASA 3 (all p<0·0001). However, for children with ASA 4, five of 25 with a positive respiratory history had perioperative respiratory adverse events compared with 27 of 98 children without (p=0·61).

Table 4 shows the effect of different aspects of anaesthetic management on the risk for perioperative respiratory adverse events. The risk of perioperative respiratory adverse events was higher in children premedicated with midazolam than in those not premedicated; if anaesthesia was maintained with desflurane rather than sevoflurane; or if the cords were sprayed with lignocaine than if not (table 4). Maintenance with sevoflurane was not associated with an increased incidence of perioperative bronchospasm compared with propofol (RR adjusted for age 1·21, 95% CI 0·76–1·90; p=0·50) but was associated with a higher incidence of laryngospasm (2·37, 1·49–3·76; p<0·0001) independent of age (p for interaction=0·139). The risk for laryngospasm was higher when three or more attempts were required to secure the airway than when the airway was

	History of respiratory problems*		RR (95% CI)	p value†	Absolute risk reduction (95% CI)
	No (n=7041)	Yes (n=2256)			
During surgery					
Bronchospasm	30 (0%)	133 (6%)	13·84 (9·34 to 20·50)	<0·0001	5·47% (4·49 to 6·45)
Laryngospasm	142 (2%)	180 (8%)	3·96 (3·19 to 4·90)	<0·0001	5·96% (4·80 to 7·13)
Cough	267 (4%)	286 (13%)	3·34 (2·85 to 3·92)	<0·0001	8·88% (7·44 to 10·33)
Desaturation <95%	373 (5%)	389 (17%)	3·25 (2·85 to 3·72)	<0·0001	11·94% (10·30 to 13·59)
Airway obstruction	130 (2%)	136 (6%)	3·27 (2·58 to 4·13)	<0·0001	4·18% (3·15 to 5·21)
Any‡	584 (8%)	595 (26%)	3·18 (2·87 to 3·53)	<0·0001	18·08% (16·15 to 20·01)
In the PACU§					
Bronchospasm	23 (0%)	10 (0%)	1·36 (0·65 to 2·86)	1·0	0·12% (–0·17 to 0·42)
Laryngospasm	11 (0%)	28 (1%)	7·98 (3·97 to 16·0)	<0·0001	1·15% (0·83 to 1·47)
Cough	72 (1%)	115 (5%)	5·01 (3·74 to 6·69)	<0·0001	4·32% (3·62 to 5·01)
Desaturation <95%	105 (2%)	109 (5%)	3·25 (2·45 to 4·23)	<0·0001	3·54% (2·79 to 4·29)
Airway obstruction	49 (1%)	20 (1%)	1·28 (0·76 to 2·15)	1·0	0·20% (–0·22 to 0·63)
Stridor	28 (0%)	30 (1%)	3·36 (2·01 to 5·61)	<0·0001	0·99% (0·59 to 1·38)
Any‡	198 (3%)	216 (10%)	3·42 (2·84 to 4·12)	<0·0001	7·17% (6·15 to 8·19)
During surgery or in the PACU					
Bronchospasm	52 (1%)	141 (6%)	8·46 (6·18 to 11·59)	<0·0001	5·51% (4·49 to 6·53)
Laryngospasm	151 (2%)	200 (9%)	4·13 (3·37 to 5·08)	<0·0001	6·72% (5·50 to 7·94)
Cough	319 (5%)	368 (16%)	3·60 (3·12 to 4·15)	<0·0001	11·78% (10·18 to 13·38)
Desaturation <95%	455 (6%)	464 (21%)	3·18 (2·82 to 3·59)	<0·0001	14·11% (12·34 to 15·87)
Airway obstruction	178 (3%)	154 (7%)	2·70 (2·19 to 3·33)	<0·0001	4·30% (3·19 to 5·40)
Any‡	693 (10%)	699 (31%)	3·15 (2·87 to 3·46)	<0·0001	21·14% (19·11 to 23·17)

RR=relative risk. PACU=post-anaesthesia care unit. *Upper respiratory tract infection within the past 2 weeks or wheezing at exercise or wheezing more than three times during past 12 months or nocturnal dry cough. †After correction by the step-down Bonferroni method. ‡Bronchospasm, laryngospasm, cough, desaturation less than 95%, or airway obstruction. §6682 patients in the no group and 2132 in the yes group.

Table 3: **Incidence of respiratory adverse events**

secured on the first attempt (table 4). However, the risk for stridor was not higher when three or more attempts were required (table 4).

When investigating the incidence of each individual respiratory complication, we could not detect any significant difference between the incidence of complications after removal of the tracheal tube or the laryngeal mask airway in awake or deeply anaesthetised children (data not shown). By contrast, the overall incidence of perioperative respiratory adverse events was higher in children who were awake when their laryngeal mask airway was removed and lower in those who were awake when their tracheal tube was removed (table 4); however, these differences were no longer detected with either device in the recovery room (table 4).

We noted a higher rate of perioperative laryngospasm in children who had an uncuffed tracheal tube than in those who had a cuffed tracheal tube (10% [122 of 1268] *vs* 3% [42 of 1616], RR adjusted for age 3·18, 95% CI 2·14–4·73; p<0·0001). The rate of perioperative bronchospasm did not differ by use of uncuffed tracheal tubes compared with cuffed tracheal tubes (5% [63 of 1268] *vs* 3% [45 of 1616]; RR adjusted for age 1·08; 0·57–2·05; p=0·811), but in case of uncuffed tracheal tube, the incidence of bronchospasm increased with age (RR adjusted for endotracheal tube by age interaction 1·10, 1·04–1·15; p=0·001). The incidence of stridor was lower when cuffed tracheal tubes were used (0% [six of 1400]) than when uncuffed tracheal tubes were used (4% [38 of 1039]; RR adjusted for age 0·22, 0·09–0·56; p=0·001), independent of age (p for interaction=0·50).

In multivariate analyses, the major risk factors for perioperative respiratory adverse events were the collapsed variables positive respiratory history, eczema, family history (atopy and smoking), and anaesthetic management (tables 5–7). The risk for perioperative respiratory adverse events was higher when children were exposed to maternal smoking (RR 1·87, 95% CI 1·72–2·04; p<0·0001) or both parents smoking (2·09, 1·85–2·36; p<0·0001), it was lower when only the father smoked (1·19, 1·08–1·31; p=0·001) The risk factors for bronchospasm (table 5), laryngospasm (table 6), and other perioperative respiratory adverse events (table 7) were similar except that older children were less likely to have laryngospasm and other perioperative respiratory adverse events (cough, desaturation, or airway obstruction) than were younger children. We noted no interactions between age, type of anaesthetic management, or positive respiratory history on the risk for perioperative respiratory adverse events (data not shown).

The risk for perioperative respiratory adverse events was higher for children with present or recent upper respiratory tract infection than for those who had not had a respiratory infection in the past 4 weeks (table 8). Parental reports of present fever were associated with increased risk of perioperative bronchospasm and other perioperative respiratory adverse events and recent fever (<2 weeks) was associated with risk of laryngospasm compared with patients with no symptoms (table 9).

Discussion

Findings from this large prospective cohort study show that factors easily obtained at a preanaesthetic assessment, including respiratory symptoms, eczema, or a family history of asthma, rhinitis, eczema, or exposure to tobacco smoke, were associated with an increased risk for the occurrence of perioperative respiratory adverse events. Additionally, an upper

	Total*	Number (%)	RR (95% CI)	p value
Premediaction with midazolam				
Laryngospasm				
Not premedicated	8657	177 (2%)	1·00	0·39
Premedicated	635	16 (3%)	1·23 (0·74–2·04)	..
Bronchospasm				
Not premedicated	8657	330 (4%)	1·15 (0·75–1·8)	0·59
Premedicated	635	21 (3%)	1·00	..
Perioperative respiratory adverse events				
Not premedicated	8657	1123 (13%)	1·00	..
Premedicated	635	151 (24%)	1·83 (1·58–2·13)	<0·0001†
Inhaled anaesthesia maintenance				
Bronchospasm				
Sevoflurane	6221	124 (2%)	1·00	..
Isoflurane	1469	11 (1%)	0·38 (0·20–0·69)	0·0018‡
Desflurane	318	39 (12%)	6·153 (4·37–8·70)	<0·0001†
Laryngospasm				
Sevoflurane	6221	252 (4%)	1·00	..
Isoflurane	1469	51 (3%)	0·85 (0·64–1·15)	0·31
Desflurane	318	28 (9%)	2·17 (1·50–3·15)	<0·0001†
Desflurane				
Perioperative respiratory adverse events				
Laryngeal mask airway				
Desflurane	45	25 (56%)	1·00	..
No desflurane	5541	567 (10%)	5·43 (4·13–7·14)	<0·0001†
Tracheal tube				
Desflurane	273	88 (32%)	1·28 (1·06–1·53)	0·013§
No desflurane	2618	659 (25%)	1·00	..
Anaesthesia maintenance: sevoflurane *vs* propofol				
Bronchospasm				
Sevoflurane	6221	123 (2%)	1·34 (0·83–2·16)	0·26
Propofol	1289	19 (1%)	1·00	..
Laryngospasm				
Sevoflurane	6221	251 (4%)	2·60 (1·66–4·08)§	..
Propofol	1289	20 (2%)	1·00	<0·0001¶
Intubated with myorelaxants				
Laryngospasm				
Myorelaxants used	1449	75 (5%)	1·47 (1·15–1·88)	0·003‖
Myorelaxants not used	7848	276 (4%)	1·00	..

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	Total*	Number (%)	RR (95% CI)	p value
(Continued from previous page)				
Vocal cords sprayed with lignocaine				
Bronchospasm				
Sprayed	558	38 (7%)	2·17 (1·48–3·19)	<0·0001†
Not sprayed	2234	70 (3%)	1·00	..
Laryngospasm				
Sprayed	558	62 (11%)	2·89 (2·10–3·95)	<0·0001†
Not sprayed	2234	86 (4%)	1·00	..
Airway management				
Stridor				
Registrar	6012	45 (1%)	1·61 (0·87–2·99)	0·156
Consultant	2802	13 (0%)	1·00	..
Airway device inserted successfully				
Perioperative laryngospasm				
After 3 or more attempts	198	28 (14%)	4·25 (2·95–6·14)	<0·0001†
At first attempt	7006	233 (3%)	1·00	..
Stridor				
After 3 or more attempts	183	2 (1%)	2·00 (0·49–8·25)	0·27
At first attempt	6596	36 (1%)	1·00	..
Removing device				
Perioperative respiratory adverse events				
Removing laryngeal mask airway				
Awake	2855	333 (12%)	1·28 (1·10–1·50)	0·001**
Under deep anaesthesia	2705	246 (9%)	1·00	..
Removing tracheal tube				
Awake	1578	352 (22%)	0·75 (0·66–0·85)	<0·0001††
Under deep anaesthesia	1277	381 (30%)	1·00	..
Removing laryngeal mask airway or tracheal tube in the recovery room				
Awake	4433	214 (5%)	1·12 (0·91–1·36)	0·27
Under deep anaesthesia	3982	172 (4%)	1·00	..

RR=relative risk. *Number of patients from whom this information was available. †p<0·0001 after correction by the step-down Bonferroni method. ‡p=0·083 after correction. §p=0·50 after correction. ¶p=0·0002 after correction. ||p=0·13 after correction. **p=0·09 after correction. ††p=0·0004 after correction.

Table 4: **Anaesthetic drugs, airway management, and respiratory complications**

respiratory tract infection was associated with an increased risk for perioperative respiratory adverse events only when the symptoms were present or had occurred within the 2 weeks before the procedure. These risk factors could form a risk assessment for perioperative respiratory adverse events that would allow anaesthetic management to be tailored to a child's risk profile. This study also emphasised the importance of the effect of skilled anaesthesia management by consultant paediatric anaesthetists on the prevention of perioperative respiratory adverse events, particularly when intravenous anaesthesia and non-invasive airway devices were used.

Our goal was to identify risk factors that are easily detectable during the preanaesthetic assessment by use of a validated questionnaire adapted to the anaesthetic environment. The anaesthetists were not masked to patient information when completing the questionnaire; thus, we cannot exclude the possibility that asking the relevant questions might have potentially affected the subsequent anaesthetic management. We attempted to keep to a minimum the effect of potential confounding results from highly associated risk factors by using combined variables in the multivariate analyses.

This study shows that a positive respiratory history is a better predictor for the occurrence of perioperative respiratory adverse events in paediatric anaesthesia than the ASA physical status. Additionally, the risk within each ASA category was higher in children with a positive respiratory history than in those without. Age also influenced the risk for perioperative respiratory adverse events,[7] particularly laryngospasm, with the relative risk decreasing by 11% for each yearly increase in age (data not shown).

A positive respiratory history was more predictive for bronchospasm and, to a lesser extent, for laryngospasm than for other perioperative respiratory adverse events. The risk for bronchospasm was ten times higher in patients with nocturnal dry cough than in patients without. Similarly, a personal history of eczema increased the relative risk for bronchospasm, which might be explained by the fact that eczema, especially in older children, is frequently associated with atopy, present wheeze, and asthma.[14] A personal history of hayfever was also associated with an increased risk for bronchospasm, which underlies the potential association between atopy and perioperative bronchospasm.

In agreement with previous studies, a present or recent upper respiratory tract infection increased the risk for perioperative respiratory adverse events, particularly for laryngospasm.[5,7,15] Additionally, symptoms of upper respiratory tract infection—including moist cough, green runny nose, and fever—were associated with increased rates of perioperative respiratory adverse events. This significantly higher incidence of such adverse events in children with a present or recent upper respiratory tract infection might be attributed to airway inflammation, interaction with the autonomic nervous system, and consecutively to airway sensitivity induced by the upper respiratory tract infection, which lasts for several weeks in some patients.[16,17] Although the timing for the peak occurrence of perioperative respiratory adverse events and the decision of how long to postpone surgery is still debated,[5,8,18] this study provides evidence that the high risk for perioperative respiratory adverse events is limited to the first 2 weeks after an upper respiratory tract infection and thus rescheduling a patient 2–3 weeks after upper respiratory tract infection would be a safe approach. This recommendation is in line with previous studies[7,19] suggesting that there is no increase in the incidence of perioperative respiratory adverse events in children with an upper respiratory tract infection more than 2 weeks before the procedure.

Lower respiratory tract signs, comorbidities, and the type of procedure need to be considered when scheduling

	Univariate						Multivariate (n=9256)	
	Yes		No		RR (95% CI)	p value	RR (95% CI)	p value
	Total	Value	Total	Value				
Age (years)	5·88 (5·01)		6·22 (4·81)		0·99 (0·96–1·02)	0·33	..	..
Male	5554	96 (2%)	3743	97 (3%)	0·67 (0·51–0·88)	0·004	..	..
Hayfever	1163	57 (5%)	8088	136 (2%)	2·92 (2·15–3·95)	<0·0001	..	..
Positive respiratory history								
Upper respiratory tract infection <2 weeks	869	35 (4%)	8420	158 (2%)	2·15 (1·50–3·08)	<0·0001	..	..
Wheezing at exercise	872	86 (10%)	8386	107 (1%)	7·73 (5·87–10·18)	<0·0001	..	..
Wheezing >3 times in past 12 months	478	54 (11%)	8819	139 (2%)	7·17 (5·31–9·68)	<0·0001	..	..
Nocturnal dry cough	1161	116 (10%)	8100	77 (1%)	10·51 (7·93–13·93)	<0·0001	..	..
Any of the above	2256	141 (6%)	7041	52 (1%)	8·46 (6·18–11·59)	<0·0001	5·65 (4·09–7·82)	<0·0001*
Eczema								
In the past 12 months	1307	66 (5%)	7942	127 (2%)	3·16 (2·36–4·23)	<0·0001	..	..
Ever (excluding past 12 months)	2181	112 (5%)	7038	79 (1%)	4·58 (3·44–6·08)	<0·0001	..	..
Any of the above	2235	114 (5%)	7021	79 (1%)	4·53 (3·42–6·02)	<0·0001	2·60 (1·95–3·47)	<0·0001*
Family history								
Asthma in ≥2 family members	571	37 (6%)	8040	118 (1%)	4·42 (3·08–6·33)	<0·0001	..	..
Rhinitis in ≥2 family members	349	22 (6%)	8336	140 (2%)	3·75 (2·43–5·81)	<0·0001	..	..
Eczema in ≥2 family members	210	8 (4%)	8507	148 (2%)	2·19 (1·09–4·40)	0·025	..	..
Both parents smokers	1075	49 (5%)	8222	144 (2%)	2·60 (1·89–3·58)	<0·0001	..	..
Any of the above	1808	80 (4%)	7489	113 (2%)	2·93 (2·21–3·89)	<0·0001	1·86 (1·41–2·46)	<0·0001†
Anaesthesia								
Airway managed by registrar	6219	171 (3%)	3078	22 (1%)	3·85 (2·47–5·98)	<0·0001	..	..
Inhalational induction of anaesthesia	3597	116 (3%)	5686	77 (1%)	2·38 (1·79–3·17)	<0·0001	..	..
Change of anaesthesiologist during airway management	269	21 (8%)	9021	172 (2%)	4·09 (2·65–6·34)	<0·0001	..	..
Any of the above	7398	181 (2%)	1899	12 (1%)	3·87 (2·16–6·93)	<0·0001	3·08 (1·73–5·48)	0·0001‡
Type of surgery								
Otolaryngology	1189	34 (3%)	8108	159 (2%)	1·46 (1·01–2·10)	0·043	..	..
Airway management device used								
Laryngeal mask *vs* face mask	5586	79 (1%)	820	6 (1%)	1·93 (0·85–4·42)	0·12	1·54 (0·68–3·49)	0·30
Tracheal tube *vs* face mask	2891	108 (4%)	820	6 (1%)	5·11 (2·25–11·57)	<0·0001	3·52 (1·56–7·94)	0·002§

Data are mean (SD) or number (%). RR=relative risk. *p<0·0001 after correction by the step-down Bonferroni method. †p=0·0007 after correction. ‡p=0·008 after correction. §p=0·10 after correction.

Table 5: **Risk factors associated with perioperative bronchospasm**

surgery for a child with a recent upper respiratory tract infection.[8] A history of wheezing with exercise or more than three episodes in the past 12 months was associated with a greater risk of perioperative bronchospasm compared with the presence of a recent upper respiratory tract infection. These findings might be related to the presence of increased airway sensitivity, possibly caused by underlying chronic airway inflammation.

Although a family history of asthma and allergy has been suggested to increase the prevalence of these diseases in children,[20,21] its effect on perioperative respiratory adverse events is unknown. In this study, the presence of asthma in at least two family members was associated with a significantly increased relative risk of bronchospasm. Moreover, eczema, rhinitis, or asthma in at least two family members increased the risk of potentially life threatening complications (laryngospasm and bronchospasm) by nearly three times. This study shows that a family history of allergy or asthma is an independent risk factor for perioperative respiratory adverse events. Previous studies identified exposure to tobacco smoke as a risk factor for perioperative respiratory adverse events.[6,11,22] Data from this study provide further insight into the effect of the smoking habits of different family members; the risk for perioperative respiratory adverse events was higher when children were exposed to maternal smoking or both parents smoking than when only the father smoked. These findings might be related to the difference in exposure to tobacco smoke from the primary caregiver. Previous reports have suggested that the risk of heightened bronchial responsiveness is highest if both parents smoke.[23]

The importance of management of anaesthesia by specialist paediatric anaesthetists to decrease perioperative respiratory adverse events has been

	Univariate						Multivariate	
	Yes		No		RR (95% CI)	p value	RR (95% CI)	p value
	Total	Value	Total	Value				
Age	4·06 (4·227)		6·30 (4·82)		0·89 (0·87–0·92)	<0·0001	0·90 (0·88–0·93)	<0·0001*
Male	5554	191 (3%)	3743	160 (4%)	0·81 (0·66–0·99)	0·038	..	..
Hayfever	1163	45 (4%)	8088	302 (3%)	1·04 (0·76–1·41)	0·82	..	..
Positive respiratory history								
Upper respiratory tract infection <2 weeks	869	90 (10%)	8420	261 (3%)	3·34 (2·66–4·20)	<0·0001	..	..
Wheezing at exercise	872	89 (10%)	8386	261 (3%)	3·28 (2·61–4·13)	<0·0001	..	..
Wheezing >3 times in past 12 months	478	44 (9%)	8819	307 (3%)	2·64 (1·96–3·58)	<0·0001	..	..
Nocturnal dry cough	1161	127 (11%)	8100	223 (3%)	3·97 (3·22–4·90)	<0·0001	..	..
Any of the above	2256	200 (9%)	7041	151 (2%)	4·13 (3·37–5·08)	<0·0001	3·26 (2·65–4·01)	<0·0001*
Eczema								
In the past 12 months	1307	84 (6%)	7942	267 (3%)	1·91 (1·51–2·43)	<0·0001	..	..
Ever (excluding past 12 months)	2181	126 (6%)	7038	220 (3%)	1·85 (1·49–2·29)	<0·0001	..	..
Any of the above	2235	133 (6%)	7021	218 (3%)	1·92 (1·55–2·37)	<0·0001	..	..
Family history								
Asthma in ≥2 family members	571	61 (11%)	8040	228 (3%)	3·77 (2·88–4·93)	<0·0001	..	..
Rhinitis in ≥2 family members	349	35 (10%)	8336	269 (3%)	3·12 (2·22–4·35)	<0·0001	..	..
Eczema in ≥2 family members	210	23 (11%)	8507	298 (4%)	3·13 (2·09–4·67)	<0·0001	..	..
Both parents smokers	1075	99 (9%)	8222	252 (3%)	3·01 (2·40–3·76)	<0·0001	..	..
Any of the above	1808	158 (9%)	7489	193 (3%)	3·39 (2·77–4·16)	<0·0001	2·57 (2·10–3·15)	<0·0001*
Anaesthesia								
Airway managed by registrar	6219	290 (5%)	3078	61 (2%)	2·35 (1·79–3·09)	<0·0001	..	..
Inhalational induction of anaesthesia	3597	235 (7%)	5686	116 (2%)	3·20 (2·57–3·98)	<0·0001	..	..
Change of anaesthesiologist during airway management	269	41 (15%)	9021	307 (3%)	4·48 (3·31–6·06)	<0·0001	..	..
Any of the above	7398	331 (4%)	1899	20 (1%)	4·25 (2·71–6·65)	<0·0001	3·10 (1·99–4·84)	<0·0001*
Type of surgery								
Otolaryngology	1189	75 (6%)	8108	276 (3%)	1·85 (1·45–2·37)	<0·0001	1·29 (1·01–1·66)	0·042†
Airway management device used								
Laryngeal mask *vs* face mask	5586	183 (3%)	820	4 (0%)	6·72 (2·50–18·04)	<0·0001	5·23 (1·95–13·99)	0·001‡
Tracheal tube *vs* face mask	2891	164 (6%)	820	4 (0%)	11·63 (4·33–31·26)	<0·0001	7·57 (2·83–20·30)	<0·0001§

Data are mean (SD) or number (%). RR=relative risk. *p<0·0001 after correction by the step-down Bonferroni method. †p=1·0 after correction. ‡p=0·052 after correction. §p=0·004 after correction.

Table 6: **Risk factors associated with perioperative laryngospasm**

debated.[2,3,24] This study confirms the increased risk for perioperative respiratory adverse events when a patient has been cared for by a registrar, and underlines the further increased risk when the registrar failed to secure the airways. We reported an increased risk of perioperative respiratory adverse events associated with otolaryngology surgery,[2,4] and with urgent procedures. The type of anaesthesia induction seemed to greatly affect the risk for perioperative respiratory adverse events; intravenous induction (propofol) was associated with a significantly lower incidence of perioperative respiratory adverse events than was inhalational induction (sevoflurane), particularly with regard to the occurrence of laryngospasm. Although extrapolation of the results to one intervention is difficult because most children might be taking a combination of drugs between induction and maintenance and might be given different airway devices, our results suggest that intravenous anaesthesia might be associated with lower incidence of perioperative respiratory adverse events.

Additionally, propofol used as a maintenance drug was better at prevention of perioperative respiratory adverse events than sevoflurane,[25] whereas the use of desflurane was associated with a significant increase in perioperative respiratory adverse events. This finding is not surprising because we recently showed that the use of desflurane in children was associated with an increase in airway resistance in children, particularly in those with heightened airway sensitivity.[26] In agreement with the strong bronchodilating effects of isoflurane,[27,28] the incidence of bronchospasm was significantly lower when this drug was used to maintain anaesthesia. The incidence of all perioperative respiratory adverse events, particularly laryngospasm, is increased after direct

	Univariate						Multivariate (n=9256)	
	Yes		No		RR (95% CI)	p value	RR (95% CI)	p value
	Total	Value	Total	Value				
Age	4·95 (4·67)		6·41 (4·81)		0·94 (0·93–0·95)	<0·0001	0·95 (0·94–0·96)	<0·0001*
Male	5554	767 (14%)	3743	508 (14%)	1·02 (0·92–1·13)	0·74	..	..
Hayfever	1163	209 (18%)	8088	1052 (13%)	1·38 (1·21–1·58)	<0·0001	..	..
Positive respiratory history								
Upper respiratory tract infection <2 weeks	869	215 (25%)	8420	1056 (13%)	1·97 (1·73–2·24)	<0·0001	..	..
Wheezing at exercise	872	306 (35%)	8386	967 (12%)	3·04 (2·73–3·39)	<0·0001	..	..
Wheezing >3 times in past 12 months	478	156 (33%)	8819	1119 (13%)	2·57 (2·24–2·96)	<0·0001	..	..
Nocturnal dry cough	1161	421 (36%)	8100	853 (11%)	3·44 (3·12–3·80)	<0·0001	..	..
Any of the above	2256	630 (28%)	7041	645 (9%)	3·05 (2·76–3·37)	<0·0001	2·37 (2·14–2·62)	<0·0001*
Eczema								
In the past 12 months	1307	300 (23%)	7942	966 (12%)	1·89 (1·68–2·12)	<0·0001	..	..
Ever (excluding past 12 months)	2181	442 (20%)	7038	806 (11%)	1·77 (1·59–1·97)	<0·0001	..	..
Any of the above	2235	465 (21%)	7021	801 (11%)	1·82 (1·64–2·02)	<0·0001	1·25 (1·14–1·38)	<0·0001†
Family history								
Asthma in ≥2 family members	571	160 (28%)	8040	883 (11%)	2·55 (2·21–2·95)	<0·0001	..	..
Rhinitis in ≥2 family members	349	96 (28%)	8336	998 (12%)	2·30 (1·92–2·75)	<0·0001	..	..
Eczema in ≥2 family members	210	75 (36%)	8507	1005 (12%)	3·02 (2·50–3·66)	<0·0001	..	..
Both parents smokers	1075	259 (24%)	8222	1016 (12%)	1·95 (1·73–2·20)	<0·0001	..	..
Any of the above	1808	427 (24%)	7489	848 (11%)	2·09 (1·88–2·32)	<0·0001	1·55 (1·40–1·70)	<0·0001*
Anaesthesia								
Airway managed by registrar	6219	1015 (16%)	3078	260 (8%)	1·93 (1·70–2·20)	<0·0001	..	..
Inhalational induction of anaesthesia	3597	707 (20%)	5686	567 (10%)	1·97 (1·78–2·18)	<0·0001	..	..
Change of anaesthesiologist during airway management	269	150 (56%)	9021	1122 (12%)	4·48 (3·98–5·05)	<0·0001	..	..
Any of the above	7398	1140 (15%)	1899	135 (7%)	2·17 (1·83–2·57)	<0·0001	1·80 (1·52–2·12)	<0·0001*
Type of surgery								
Otolaryngology	1189	276 (23%)	8108	999 (12%)	1·88 (1·67–2·12)	<0·0001	1·10 (0·99–1·22)	0·080
Airway management device used								
Laryngeal mask *vs* face mask	5586	520 (9%)	820	53 (6%)	1·44 (1·10–1·89)	0·009	1·21 (0·92–1·58)	0·17
Tracheal tube *vs* face mask	2891	702 (24%)	820	53 (6%)	3·76 (2·87–4·91)	<0·0001	2·70 (2·07–3·53)	<0·0001*

Data are mean (SD) or number (%). RR=relative risk. *p<0·0001 after correction by the step-down Bonferroni method. †p=0·0003 after correction.

Table 7: **Risk factors associated with perioperative cough, desaturation, or airway obstruction**

	No infection in past 4 weeks (n=6142)	Present infection (n=1238)	RR (95% CI)	p value	Infection <2 weeks earlier (n=869)	RR (95% CI)	p value	Infection 2–4 weeks earlier (n=1040)	RR (95% CI)	p value
Bronchospasm	97 (2%)	45 (4%)	2·30 (1·63–3·26)	<0·0001	35 (4%)	2·55 (1·74–3·73)	<0·0001	16 (2%)	0·97 (0·58–1·65)	0·922
Laryngospasm	158 (3%)	89 (7%)	2·80 (2·17–3·60)	<0·0001	90 (10%)	4·03 (3·14–5·16)	<0·0001	14 (1%)	0·52 (0·30–0·90)	0·019*
Cough	363 (6%)	166 (13%)	2·27 (1·91– 2·70)	<0·0001	120 (14%)	2·34 (1·93–2·84)	<0·0001	34 (3%)	0·55 (0·39–0·78)	0·001
Desaturation <95%	490 (8%)	207 (17%)	2·10 (1·80–2·44)	<0·0001	162 (19%)	2·34 (1·99–2·75)	<0·0001	57 (5%)	0·69 (0·53–0·90)	0·006†
Airway obstruction	174 (3%)	96 (8%)	2·74 (2·15–3·49)	<0·0001	46 (5%)	1·87 (1·36–2·57)	<0·0001	15 (1%)	0·51 (0·30–0·86)	0·011‡
Any of the above	748 (12%)	309 (25%)	2·05 (1·82–2·31)	<0·0001	248 (29%)	2·34 (2·07–2·66)	<0·0001	83 (8%)	0·66 (0·53–0·81)	<0·0001

Data are number (%). RR=relative risk. p values that are no longer significant after correction by the step-down Bonferroni method are indicated. For all other p values after correction, see webappendix p 7. *p=0·65 after correction. †p=0·22 after correction. ‡p=0·46 after correction.

Table 8: **Risk of perioperative respiratory adverse events according to timing of upper respiratory tract infection**

stimulation of the upper airways by laryngeal mask airway or tracheal tube. Use of airway management as an independent factor in the multivariate analysis drew attention to the increased risk for the occurrence of all perioperative respiratory adverse events, particularly laryngospasm. However, although there was no

	Bronchospasm			Laryngospasm			All complications		
	Present	<2 weeks	2–4 weeks	Present	<2 weeks	2–4 weeks	Present	<2 weeks	2–4 weeks
Clear runny nose	1·98 (1·32–2·98; 0·001*)	1·10 (0·60–2·03; 0·74)	1·05 (0·50–2·22; 0·90)	1·98 (1·48–2·69; <0·0001)	2·04 (1·45–2·87; <0·0001)	1·16 (0·65–1·94; 0·67)	1·49 (1·26–1·75; <0·0001)	1·37 (1·13–1·66; 0·001†)	0·95 (0·72–1·27; 0·74)
Green runny nose	1·93 (0·87–4·28; 0·107)	2·36 (1·12–4·93; 0·023‡)	0·75 (0·31–1·80; 0·51)	4·40 (2·97–6·52; <0·0001)	6·62 (4·80–9·12; <0·0001)	0·09 (0·01–0·63; 0·015§)	3·12 (2·56–3·80; <0·0001)	3·37 (2·79–4·07; <0·0001)	0·23 (0·12–0·42; <0·0001)
Dry cough	1·67 (0·96–2·91; 0·071)	2·09 (1·15–3·81; 0·015§)	0·57 (0·18–1·76; 0·33)	2·16 (1·50–3·10; <0·0001)	2·14 (1·38–3·30; 0·001)	0·53 (0·22–1·27; 0·16)	1·71 (1·41–2·07; <0·0001)	1·88 (1·51–2·31; <0·0001)	0·31 (0·17–0·56; 0·0001)
Moist cough	3·27 (2·13–5·01; <0·0001)	4·00 (2·55–6·28; <0·0001)	0·27 (0·07–1·10; 0·069)	3·89 (2·89–5·23; <0·0001)	6·53 (5·01–8·53; <0·0001)	0·08 (0·01–0·58; 0·012)¶	3·05 (2·64–3·51; <0·0001)	3·42 (2·94–3·98; <0·0001)	0·45 (0·30–0·68; 0·0001)
Fever	4·20 (2·04–8·66; <0·0001)	1·99 (0·76–5·27; 0·16)	0·77 (0·25–2·38; 0·65)	2·34 (1·14–4·80; 0·020‖)	5·28 (3·47–8·02; <0·0001)	0·57 (0·22–1·51; 0·26)	2·89 (2·19–3·81; <0·0001)	2·92 (2·28–3·81; <0·0001)	0·54 (0·32–0·89; 0·017**)

Data are relative risk compared with no symptoms (95% CI; p value). p values that are no longer significant after correction by the step-down Bonferroni method are indicated. For all other p values after correction, see webappendix p 8. *p=0·052 after correction. †p=0·067 after correction. ‡p=0·73 after correction. §p=0·57 after correction. ¶p=0·48 after correction. ‖p=0·66 after correction. **p=0·58 after correction.

Table 9: **Risk factors for perioperative bronchospasm, laryngospasm, or all complications according to timing of symptoms and respiratory adverse events**

difference between the laryngeal mask airway and the face mask with regard to the occurrence of perioperative bronchospasm, the use of laryngeal mask airway was associated with a significantly higher risk for laryngospasm, but to a lesser extent than with the use of tracheal tube. This finding is in line with previous reports[29,30] and can be attributed to the fact that both the laryngeal mask airway and the face mask do not stimulate the trachea.[19] Taken together with the increased risk of perioperative respiratory adverse events in children with a positive respiratory history or recent upper respiratory tract infection, the data from the present study suggest that children at increased risk of perioperative respiratory adverse events should be managed by an experienced paediatric anaesthetist with induction and maintenance of anaesthesia done with intravenous propofol and the airway maintained with a laryngeal mask airway.

The incidence of perioperative laryngospasm and bronchospasm was significantly higher when the vocal cords were sprayed with lignocaine before tracheal intubation. Although some investigators have reported that lidocaine can attenuate the neutrally-mediated reflexes that provoke bronchoconstriction,[31–33] others have reported a potential increase in airway tone after aerosol[34] and intravenous[35] administration of lignocaine. Thus, despite the results of our study, further systematic investigations are needed to confirm the effect of lignocaine in the presence of bronchial hyper-reactivity.

Although there was a potential reporting bias in this large prospective cohort study, we were able to identify risk factors in children's medical history that were associated with an increased risk for perioperative respiratory adverse events (history of a recent cold, wheezing during exercise, wheezing more than three times in the past 12 months, nocturnal dry cough, eczema, or a family history of asthma, rhinitis, eczema, or exposure to tobacco smoke). These risk factors should be explored during the preoperative assessment in all children to establish the best anaesthesia care. Children at high risk of perioperative respiratory adverse events might benefit from anaesthesia management including a specialist paediatric anaesthetist, intravenous induction and maintenance with propofol, and avoidance of tracheal tube for airway management when possible.

Contributors

BSvU-S was the principal investigator, designed the study, did the literature search, collected, analysed, and interpreted the data, coordinated the team, and wrote the report. KB was the statistician, analysed and interpreted the data, and wrote the report. NAC designed the study, collected and interpreted data, and wrote the report. CR did the literature search, collected data, and wrote the report. CJ collected data and wrote the report. PDS designed the study, interpreted the data, and wrote the report. WH designed the study, analysed and interpreted the data, did the literature search, and wrote the report.

Conflicts of interest

We declare that we have no conflicts of interest.

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