

Original Article

Incidence of severe critical events in paediatric anaesthesia in the United Kingdom: secondary analysis of the anaesthesia practice in children observational trial (APRICOT study)

T. Engelhardt,^{1,2} D. Ayansina,³ G. T. Bell,⁴ V. Oshan,⁵ J. S. Rutherford,⁶ and N. S. Morton⁷ for the APRICOT Group of the European Society of Anaesthesiology Clinical Trial Network

1 Consultant, Department of Anaesthesia, Royal Aberdeen Children's Hospital, Aberdeen 2 Honorary Professor, Institute of Education for Medical and Dental Sciences, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Aberdeen

3 Research Fellow, Medical Statistics Team, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, Scotland, UK

4 Consultant, Department of Anaesthesia, Royal Hospital for Children, Glasgow, Scotland, UK

5 Consultant, Department of Anaesthesia, Royal Manchester Children's Hospital, Manchester University NHS Foundation Trust, Manchester, UK

6 Designated Paediatric Anaesthetist, Dumfries and Galloway Royal Infirmary, Dumfries, Scotland, UK

7 Retired Reader, Department of Paediatric Anaesthesia and Pain Management, University of Glasgow, Glasgow, Scotland, UK.

Summary

The anaesthesia practice in children observational trial of 31,127 patients in 261 European hospitals revealed a high (5.2%) incidence of severe critical events in the peri-operative period and wide variability in practice. A sub-analysis of the UK data was undertaken to investigate differences compared with the non-UK cohort in the incidence and nature of peri-operative severe critical events and to attempt to identify areas for quality improvement. In the UK cohort of 7040 paediatric patients from 43 hospitals, the overall incidence of peri-operative severe critical events was lower than in the non-UK cohort (3.3%, 95%CI: 2.9–3.8 vs. 5.8%, 95%CI: 5.5–6.1, RR 0.57, $p < 0.001$). There was a lower rate of bronchospasm (RR 0.22, 95%CI: 0.14–0.33; $p < 0.001$), stridor (RR 0.42, 95%CI: 0.28–0.65; $p < 0.001$) and cardiovascular instability (RR 0.69, 95%CI: 0.55–0.86; $p = 0.001$) than in the non-UK cohort. The proportion of sicker patients where less experienced teams were managing care was lower in the UK than in the non-UK cohort (10.4% vs. 20.4% of the ASA physical status 3 and 9% vs. 12.9% of the ASA physical status 4 patients). Differences in work-load between centres did not affect the incidence and outcomes of severe critical events when stratified for age and ASA physical status. The lower incidence of cardiovascular and respiratory complications could be partly attributed to more experienced dedicated paediatric anaesthesia providers managing the higher risk patients in the UK. Areas for quality improvement include: standardisation of serious critical event definitions; increased reporting; development of evidence-based protocols for management of serious critical events; development and rational use of paediatric peri-operative risk assessment scores; implementation of current best practice in provision of competent paediatric anaesthesia services in Europe; development of specific training in the management of severe peri-operative critical events; and implementation of systems for ensuring maintenance of skills.

Correspondence to: N. S. Morton

Email: neilmorton@mac.com

Accepted: 30 October 2018

Keywords: critical incident reporting; paediatric anaesthesia; quality improvement

Introduction

The anaesthesia practice in children observational trial (APRICOT) was a prospective multi-centre observational study of severe critical events during paediatric anaesthesia from 261 hospitals in 33 European countries [1]. In 31,127 anaesthetic procedures in 30,874 children, the overall incidence of peri-operative severe critical events was reported as 5.2% (95%CI: 5.0–5.5) with respiratory and cardiovascular critical events predominating. The main risk factors identified for a severe critical event were young age, a previous medical history and the physical condition of the patient. Considerable variation in the incidence and management of severe peri-operative critical events between European countries was reported and has raised concerns regarding current paediatric anaesthesia training, the experience of the teams managing sick children, work-load, resources and infrastructure [1, 2].

The UK was the largest single regional contributor to the APRICOT study, with more than 25% of the total patients enrolled, and the APRICOT Trial Steering Committee agreed to conduct a sub-analysis in order to test the hypothesis that primary outcome measures were not different between the UK and non-UK participating centres. The primary aim of this secondary analysis was to detail the incidence of severe critical peri-operative events in children undergoing anaesthesia in the UK centres participating in APRICOT compared with the rest of Europe. Secondary aims were to compare the time of occurrence, type, treatment and outcome of peri-operative severe critical events between the UK and non-UK centres and to explore the influence of hospital type, work-load and experience of the anaesthetic team.

Methods

Detailed methods for APRICOT have previously been published [1]. Peri-operative data that described the anaesthesia management, serious critical events and outcomes of children aged from birth to 15 years of age were prospectively collected during a consecutive two-week period determined in advance by each centre between 1 April 2014 and 31 January 2015. Of 261 participating centres across 33 European countries, 43 were from the UK. (Appendix A1). Before data collection, a local investigator provided details of their hospital's paediatric anaesthesia activity, peri-operative care facilities, estimated annual number of procedures and the number of certified or dedicated paediatric anaesthetists.

All patients undergoing an inpatient or outpatient diagnostic or surgical procedure, whether elective, urgent or

emergency, in-hours or out-of-hours, under sedation or general anaesthesia, with or without regional analgesia or under regional anaesthesia alone, were eligible for inclusion. Children were followed up for up to 60 min after anaesthesia or sedation in the post-anaesthesia recovery unit, and the child's status at discharge, or at 30 days if still in hospital, was recorded. Children were not included if they were admitted directly to the operating room with their tracheas already intubated, or if the procedure was performed in the neonatal or paediatric intensive care unit.

All pre-defined severe critical events (bronchospasm, laryngospasm, pulmonary aspiration, drug error, anaphylaxis, cardiovascular instability, neurological damage, peri-anaesthetic cardiac arrest, postoperative stridor) [1] as well as their time of occurrence (during anaesthesia induction, maintenance, emergence or in the post-anaesthesia recovery unit), the treatment required and the immediate outcome were documented. Severe critical events were defined as those that led, or might have led, to major disability or death and required immediate intervention. A detailed patient history, type of procedure, anaesthetic and airway management details, the experience of the anaesthetic team and postoperative care (for up to 60 min) were available for further analysis. Outcome at hospital discharge, or at 30 days if still in hospital, was documented.

Anonymised data were uploaded onto a secure Internet-based electronic database (OpenClinica, Boston, MA, USA) and held by the European Society of Anaesthesiology (ESA). The data subset from participating UK centres was transferred securely from the ESA to the University of Aberdeen and analysed by a professional statistician. An a priori statistical analysis plan for the UK data was approved by the APRICOT Steering Committee in 2017 after publication of the primary analysis of APRICOT. In APRICOT, a minimum of 25,000 patients were required to provide an acceptable 95%CI for the overall incidence of severe critical events, assuming that the lowest incidence of severe critical events was 0.1% (95%CI [0.065–0.147]). For this UK study, no a priori power analysis was performed. However, the pre-study survey of UK participating centres estimated an annual paediatric anaesthesia case-load in 2012 of over 212,000 patients. In a secondary analysis of the 2013 UK National Health Service (NHS) Anaesthesia Activity Survey of the Fifth National Audit Project (of the Royal College of Anaesthetists), the annual paediatric case-load was estimated to be 486,900 children [3]. The APRICOT UK cohort of 7040 patients, if annualised to 183,040, represents 38% of this estimated annual caseload. A post-hoc power

analysis performed on the incidence of serious critical events in the UK cohort (3.3%) vs. the non-UK cohort (5.8%) with 7040 UK patients and an α of 0.01 gave a power of 100%. From these data, for a future study, a sample size of 1284 patients would be needed with $\alpha = 0.01$ to give 95% power.

Statistical analysis was performed using SPSS (version 24) statistical software. The 95%CI was computed for small proportions using the Wilson method [4]. Risk ratios (RR) were calculated for serious critical events in the UK vs. non-UK cohorts with appropriate confidence intervals. Multiple logistic regression models were constructed to compute odds ratios and 95%CI for the effects of the type of hospital, experience of the anaesthesia team and the hospital case-load (calculated per annum) on the occurrence of critical events (respiratory, cardiovascular and others). The models were adjusted for age of the patient and the ASA physical status (recategorised as ASA physical status 1 and 2, and ASA physical status 3–5). A p value of < 0.05 was considered statistically significant.

Results

The UK dataset contained details of 7092 anaesthetic procedures in 7040 children in 43 participating centres (Table 1). For the UK cohort, the mean (SD) age was 6.2 (4.5) years with 594 (8.4%) neonates and infants (< 1 -year-old), 3005 (42.7%) pre-school children (1–5 years), 2505 (35.6%) schoolchildren (6–12 years) and 936 (13.3%) adolescents (13–15 years). There were 233 severe critical events reported by UK centres, hence the incidence of severe critical events in the UK was 3.3% (95%CI: 2.9–3.8), which was lower (RR 0.57, 95%CI: 0.49–0.65; $p < 0.001$) than the overall incidence of severe critical events in the non-UK cohort, which was 5.8% (95%CI: 5.5–6.1) (Table 2). The UK reported a lower rate of bronchospasm (RR 0.22, 95%CI: 0.14–0.33; $p < 0.001$); stridor (RR 0.42, 95%CI: 0.28–0.65; $p < 0.001$); and cardiovascular instability (RR 0.69, 95%CI: 0.55–0.86; $p = 0.001$) compared with the non-UK cohort. Although there was a higher proportion of ASA physical status 3 and 4 patients in the UK subset (15%) compared with the non-UK cohort (10%), the incidence of cardiovascular and respiratory serious critical events was lower.

The distribution among anaesthesia teams according to ASA physical status is shown in Table 3. In 83.8% of ASA physical status 3 and 83.1% of ASA physical status 4 cases, the patients were managed by dedicated paediatric anaesthesia providers in the UK compared with 67% of ASA physical status 3 and 76.5% of ASA physical status 4 patients in the non-UK cohort. Sicker patients (ASA physical status > 2), in which less experienced teams were managing care,

Table 1 Types of UK participating centres and number of patients recruited to APRICOT within the 2-week study period. Values are median (IQR [range]).

Hospital type	n	Number of consultants	Patients recruited	Estimated annualised cases per consultant
Paediatric hospital	10	25 (16–33 [7–37])	308 (205–488 [124–614])	348 (270–583 [172–939])
Mixed adult–paediatric hospital	17	30 (14–40 [3–20])	107 (48–248 [8–400])	93 (58–216 [32–362])
District general hospital	16	16 (9–31 [4–36])	63 (32–93 [19–136])	73 (51–180 [27–302])

Table 2 Incidence of severe critical events for UK and non-UK participating centres. Values are proportion (95%CI).

	n	UK	n	Non-UK
Laryngospasm	78	1.1% (0.9–1.4)	290	1.2% (1.1–1.4)
Bronchospasm ^a	22	0.3% (0.2–0.5)	349	1.4% (1.3–1.6)
Aspiration	9	0.13% (0.10–0.20)	20	0.08% (0.05–0.13)
Stridor ^a	23	0.3% (0.2–0.5)	185	0.8% (0.7–0.9)
Cardiovascular instability ^a	92	1.3% (1.1–1.6)	457	1.9% (1.7–2.1)
Anaphylaxis	0	0%	3	0.012% (0.01–0.04)
Neurological damage	2	0.03% (0.01–0.10)	3	0.012% (0.01–0.04)
Drug error	4	0.06% (0.20–0.15)	45	0.2% (0.10–0.30)
Total ^a	233	3.3% (2.9–3.8)	1404	5.8% (5.5–6.1)

^a95%CI for the UK data does not overlap with that of the non-UK data.

Table 3 Distribution of cases among anaesthesia teams according to ASA physical status for UK and non-UK patients. Specialists are anaesthetists with mainly (> 80%) paediatric cases, Frequent are specialist anaesthetists with frequent (50–80%) paediatric anaesthesia cases, Occasional are specialist anaesthetists with occasional (< 50%) paediatric anaesthesia cases and Training are anaesthetists in training, anaesthetic nurses or technicians. Values are number (proportion).

	Total ^a	Specialist	Frequent	Occasional	Training
ASA 1 UK	4343 (61.7%)	2089 (48.1%)	589 (13.6%)	1126 (25.9%)	539 (12.4%)
Non-UK	14540 (60.4%)	8093 (55.7%)	2274 (15.6%)	3108 (21.4%)	1062 (7.3%)
ASA 2 UK	1624 (23.1%)	1107 (68.2%)	178 (11%)	196 (12.1%)	143 (8.8%)
Non-UK	7115 (29.5%)	4522 (63.6%)	950 (13.4%)	1178 (16.6%)	465 (6.5%)
ASA 3 UK	889 (12.6%)	745 (83.8%)	52 (5.8%)	39 (4.4%)	53 (6%)
Non-UK	2098 (8.7%)	1404 (67.0%)	266 (12.7%)	276 (13.2%)	151 (7.2%)
ASA 4 UK	178 (2.5%)	148 (83.1%)	14 (7.9%)	8 (4.5%)	8 (4.5%)
Non-UK	320 (1.4%)	245 (76.6%)	34 (10.6%)	36 (11.3%)	5 (1.6%)
ASA 5 UK	5 (0.1%)	5 (100%)	0 (0%)	0 (0%)	0 (0%)
Non-UK	7 (<0.1%)	6 (85.7%)	1 (14.3%)	0 (0%)	0 (0%)
Total UK	7039 (100%)	4094 (58.2%)	833 (11.8%)	1369 (19.4%)	743 (10.6%)
Total Non-UK	24080 (100%)	14270 (59.3%)	3525 (14.6%)	4598 (19.1%)	1683 (7.0%)

ASA, ASA physical status.

^arefers to the number (proportion) of UK or non-UK patients in each ASA physical status group.

comprised 10.4% of the ASA physical status 3 and 9% of the ASA physical status 4 patients in the UK, whereas in the non-UK cohort, these proportions were higher at 20.4% and 12.9%, respectively.

The time of occurrence, type, treatment and outcome of peri-operative severe critical events are shown in Table 4 (respiratory) and Table 5 (cardiovascular).

Severe respiratory and cardiovascular critical events in the UK (as in the non-UK cohort) were more common in younger patients (Fig. 1). Of 130 respiratory severe critical events, laryngospasm was the most frequent, followed by post-anaesthetic stridor, bronchospasm and aspiration (Fig. 2, Table 4). Cardiovascular instability (n = 91) was the second largest category of serious critical events in the UK, comprising hypotension, arrhythmias and bleeding (Table 5). The incidence of drug errors was low in the UK

compared with the non-UK cohort with only four incidents reported (0.06% vs. 0.20%; RR 0.30, 95%CI: 0.11–0.84; p = 0.001) with two wrong drug doses and two wrong site drug administrations each. These occurred at induction (n = 1) and maintenance (n = 3) of anaesthesia and required no further treatment.

The effect of hospital type, experience of the team and annual case-load per anaesthetist on the occurrence of severe respiratory and cardiovascular critical events is shown in Table 6. No effect of hospital type, team experience or case-load was observed when adjusted for age and ASA physical status, with the exception of trainees having fewer critical cardiovascular events and mixed adult-paediatric hospitals having slightly fewer severe critical cardiovascular events. Younger age was associated with an increase in severe respiratory critical events. An ASA physical status of

Table 4 Severe respiratory critical events, their time of occurrence, type, treatment and outcome. Patients may have suffered more than one severe respiratory critical event at any one time and received more than one treatment. Values are number (proportion).

	Laryngospasm		Bronchospasm		Aspiration		Stridor	
	UK n = 76	Non-UK n = 292	UK n = 21	Non-UK n = 350	UK n = 9	Non-UK n = 20	UK n = 24	Non-UK n = 184
Time of occurrence								
Induction	30 (39.5%)	102 (34.9%)	2 (9.5%)	116 (33.1%)	3 (33.3%)	10 (50%)		
Maintenance	21 (27.6%)	48 (16.4%)	10 (47.6%)	89 (25.4%)	4 (44.4%)	4 (20%)		
Awakening	22 (28.9%)	143 (49.0%)	8 (38.1%)	159 (45.4%)	2 (22.2%)	6 (30%)	16 (66.6%)	141 (76.6%)
Recovery area	3 (3.9%)	9 (3.1%)	1 (4.8%)	15 (4.3%)		2 (10%)	12 (50.0%)	55 (29.9%)
Treatment								
Propofol	60 (78.9%)	195 (66.8%)						
Succinylcholine	23 (30.3%)	46 (15.8%)						
Intubation/prolonged intubation	16 (21.1%)	57 (19.5%)	3 (14.2%)	53 (15.1%)	4 (44.4%)			
Bronchodilators			9 (42.6%)	215 (61.4%)		13 (65%)		
Adrenaline			3 (14.2%)	16 (4.6%)			5 (20.9%)	49 (27.2%)
Deepening anaesthesia			3 (14.2%)	82 (23.4%)				
Tracheobronchial suction					8 (88.8%)	15 (75%)		
Antibiotics						2 (10%)		
CPAP					1 (11.1%)		13 (54.1%)	71 (38.6%)
Intravenous steroids							4 (16.6%)	27 (14.7%)
Other treatments	10 (13.2%)	78 (26.7%)	7 (33.3%)	73 (20.9%)			8 (33.3%)	55 (29.9%)
Outcome								
Uneventful	75 (98.7%)	283 (96.9%)	14 (66.6%)	202 (57.7%)	7 (77.8%)	11 (55%)	20 (83.3%)	178 (96.7%)
Intubation/prolonged intubation	1 (1.3%)	8 (2.7%)		11 (3.1%)		4 (20%)	2 (8.3%)	7 (3.8%)
Pulmonary oedema		1 (0.3%)						
Hypoxaemia			6 (28.5%)	139 (39.7%)	2 (22.2%)	8 (40%)		
Admission intensive care			1 (4.8%)	1 (0.3%)				
Pneumonia						1 (5%)		
Tracheostomy							1 (4.2%)	
Other				5 (1.4%)				

Table 5 Severe cardiovascular critical events, their time of occurrence, type, treatment and outcome. Patients may have suffered more than one severe cardiovascular critical event at any one time and received more than one treatment. Values are number (proportion).

	Severe cardiovascular events	
	UK n = 91	Non-UK n = 458
Time of occurrence		
Induction	27 (27.6%)	116 (20.9%)
Maintenance	66 (67.3%)	388 (69.8%)
Awakening	2 (2.0%)	30 (5.3%)
Recovery area	3 (3.1%)	22 (4.0%)
Type of event		
Bleeding	14 (15.4%)	98 (21.4%)
Arrhythmia (all)	32 (35.2%)	104 (22.7%)
Arrhythmia (bradycardia)	15 (16.5%)	71 (15.5%)
Arrhythmia (ventricular tachycardia)	1 (1.1%)	1 (< 0.1%)
Arrhythmia (ventricular fibrillation)	1 (1.1%)	
Hypotension	50 (54.9%)	334 (72.9%)
Vasodilation	6 (6.6%)	31 (6.8%)
Hypertension	2 (2.2%)	5 (1.1%)
Cardiac dysfunction	1 (1.1%)	3 (0.1%)
Myocardial ischaemia		2 (< 0.1%)
Miscellaneous	2 (2.2%)	12 (2.6%)
Treatment		
Fluid resuscitation	50 (54.9%)	266 (58.1%)
Blood products	12 (13.2%)	112 (24.5%)
Fluids and blood products ^a	11 (12.1%)	18 (3.9%)
Vasopressors	36 (39.6%)	265 (57.9%)
Fluids/blood products and vasopressors ^a	26 (28.6%)	159 (34.7%)
Atropine	20 (22.0%)	118 (25.8%)
Defibrillation	4 (4.4%)	4 (0.9%)
Other treatments	14 (15.4%)	37 (8.1%)
Outcome		
Uneventful	85 (93.4%)	391 (85.4%)
Cardiac arrest	3 (3.3%)	5 (1.1%)
Coagulopathy	2 (2.2%)	17 (3.7%)
Extracorporeal membrane oxygenation	1 (1.1%)	1 (< 0.1%)
Myocardial ischaemia		1 (< 0.1%)
Admission intensive care	1 (1.1%)	4 (0.9%)
Re-operation for haemostasis		2 (< 0.4%)

^aSub-group of children who received both interventions for cardiovascular critical events.

3 or greater was associated with an increase in severe cardiovascular critical events.

Discussion

The main strength of APRICOT is the detailed prospective capture of paediatric peri-operative care and outcome data, including severe critical events and their treatment, in a

large number of European centres [1, 2]. This revealed a high incidence of severe critical events and substantial variability (Appendix A2) but similar ultimate outcomes compared with previous reports [1, 2, 5–10]. The greater use of intravenous anaesthesia in the UK may explain the lower incidence of severe respiratory critical events at induction of anaesthesia because inhalational induction was shown to

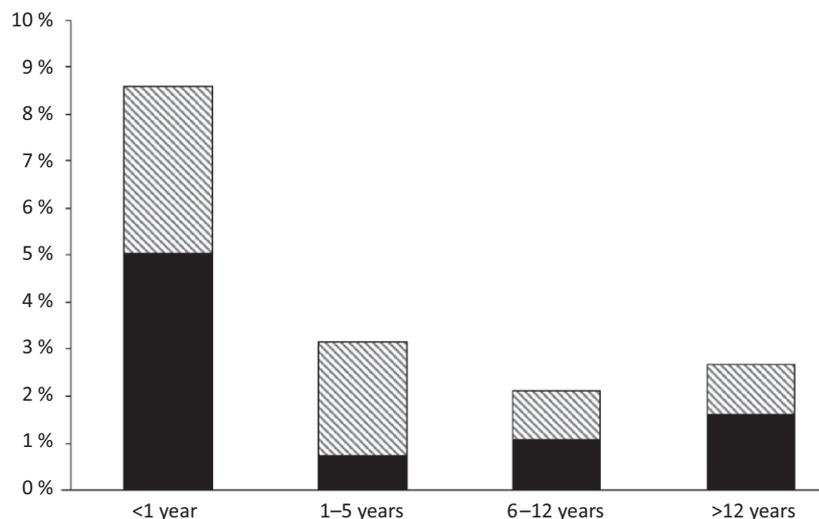


Figure 1 The incidence of severe respiratory (striped) and cardiovascular (solid) critical events according to age of the patient.

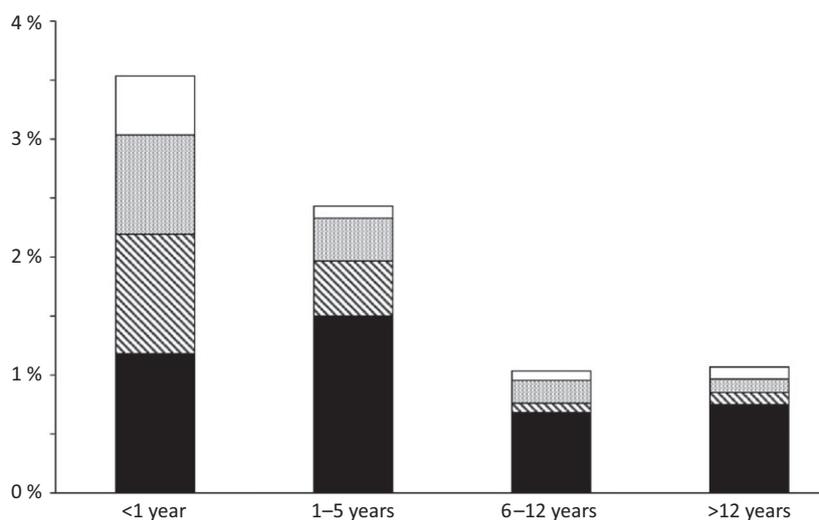


Figure 2 The incidence of severe respiratory critical events (solid – laryngospasm, striped – stridor, dotted – bronchospasm, no fill – aspiration) according to age of the patient.

be associated with a higher risk in APRICOT [1, 2]. Although numbers in each category were small, the pattern of use of bronchodilators and adrenaline for bronchospasm, the use of succinylcholine for laryngospasm and blood product use varied between the UK and non-UK cohorts and could reflect differences in training or lack of an evidence base for the initial management of such events. The low incidence of drug errors reported in the UK and Europe is encouraging but may be due to under-reporting, as a recent review highlighted that drug errors in paediatric anaesthesia are more frequent than in adult practice [11].

The nature of voluntary participation and the snapshot method of recruitment may miss unusual and

potentially dangerous practices and introduce reporting bias and it is also possible that the recruitment period of April until December may have resulted in a seasonal bias. However, annualised Scottish data suggest that the samples captured in the APRICOT recruitment period were representative of the annual paediatric case-load in Scotland. In APRICOT, the dataset represented 88% of all procedures in the participating centres during the 2-week inclusion period [1]. However, there may have been bias in patient inclusion into APRICOT because more than two-thirds of cases came from just a quarter of the countries and a follow-up analysis of the remainder has been suggested [2]. In a recent large UK survey, 90% of

Table 6 Influence of hospital type, experience of team and annual case-load per anaesthetist on the occurrence of critical respiratory and cardiovascular events when adjusted for ASA physical status and age. Values are OR (95%CI).

	Critical respiratory event	Critical cardiovascular event	Total critical events
Hospital type			
Paediatric hospital	1	1	1
Mixed adult–paediatric hospital	0.92 (0.54–1.53)	0.46 (0.22–0.99)*	0.67 (0.44–1.01)
District general	1.04 (0.47–2.26)	1.59 (0.48–5.26)	1.05 (0.55–2)
Experience			
Specialist	1	1	1
Frequent	1.09 (0.57–2.07)	0.56 (0.21–1.47)	0.83 (0.49–1.41)
Occasional	1.43 (0.75–2.71)	0.38 (0.12–1.16)	0.86 (0.49–1.5)
Training	1.08 (0.55–2.08)	0.21 (0.05–0.89)*	0.72 (0.41–1.25)
Case-load			
< 100 pa	1	1	1
100–200 pa	1.37 (0.66–2.84)	0.98 (0.34–2.81)	1.11 (0.6–2.03)
> 200 pa	1.27 (0.68–2.38)	0.75 (0.29–1.87)	1.02 (0.61–1.7)
ASA			
ASA 1 and 2	1	1	1
ASA 3–5	1.12 (0.67–1.86)	4.54 (2.83–7.28)**	2.0 (1.43–2.8)**
Age; months	0.99 (0.986–0.994)**	1 (0.998–1.006)	0.995 (0.992–0.998)**

Specialist, anaesthetist with mainly (> 80%) paediatric cases; frequent, specialist anaesthetist with frequent (50–80%) paediatric anaesthesia cases; occasional, specialist anaesthetist with occasional (< 50%) paediatric anaesthesia cases; training, anaesthetist in training, anaesthetic nurse, or technician; ASA, ASA physical status.

* $p < 0.05$, ** $p < 0.001$.

children (1–15 years old) were ASA physical status 1 or 2 and 41% were managed in district general hospitals. Almost all (89%) were ASA physical status 4 and 5 children, and 92% of infants were managed in specialist hospitals [3]. The majority (84.8%) of the APRICOT UK cohort were ASA physical status 1 or 2 and 18.3% were managed in district general hospitals [1]. For the sicker patients, we found that a higher proportion were managed by experienced teams in the UK compared with the non-UK cohort, and only a few ASA physical status 4 and 5 cases were managed by less experienced teams. However, when adjusted for age and ASA physical status, no increase in critical events was observed. It is possible that some of the staff were post-accreditation paediatric anaesthesia fellows or other experienced senior trainees acting under consultant supervision. Current advice from professional bodies is that all high-risk paediatric cases should have direct consultant-level care by an experienced specialist wherever possible. The APRICOT trial found that senior anaesthetists had 1% fewer critical respiratory events per year of experience and those centres with a higher case-load had a lower rate of serious critical events, an inverse case-load–outcome

effect which has previously been demonstrated [1, 2, 12]. This effect was not observed in the UK patient cohort.

Triage of the sickest children to the most experienced teams is a challenge in all countries and relies on accurate assessment. The ASA physical status does not capture paediatric illness severity or anaesthetic risk very well, prompting attempts to identify high-risk paediatric cases more accurately [8, 10, 13–15], and these tools need to be used more widely.

The UK NHS provides children's services in major specialist paediatric hospitals, large mixed adult and paediatric centres and smaller district general hospitals. Operational standards and training are highly regulated in the UK by government, professional bodies and the Royal Colleges. All healthcare professionals caring for children are mandated to update and maintain their paediatric knowledge and skills in order to maintain their licence to practice. This may have affected the pattern of severe critical peri-operative events and the identification of relevant organisational effects. Currently, in Europe, paediatric anaesthesia is not recognised as a subspecialty and training programmes often do not allow acquisition of sufficient paediatric skills and experience to support independent

practice [2]. Most trainees who wish to become specialists in paediatric anaesthesia undertake extra training of 1–2 years in the form of fellowships, often including a component of paediatric critical care medicine training and experience. In the UK, such fellowships are usually locally funded and are often undertaken after training accreditation has been completed. In Scandinavia, a modular 2-year paediatric anaesthesia fellowship programme has been established very successfully. Further experience and mentoring may be needed in 'super-specialties' such as paediatric neuroanaesthesia or paediatric cardiac anaesthesia, and for managing complex neonates. Assessments of competence vary widely in Europe and there have been calls for a standardised approach to training and credentialing of paediatric anaesthetists in the future [2]. Having acquired the knowledge, skills and experience to manage children safely in the peri-operative period, maintenance of these competencies and recertification processes are also needed. The UK Royal College of Anaesthetists has been a leader in developing a continuing education matrix which informs annual appraisals for all anaesthetists and is now accrediting departments of anaesthesia against a detailed set of standards, with paediatrics featuring throughout [16, 17]. The European Society for Paediatric Anaesthesiology (ESPA) and ESA are collaborating to produce a similar process in Europe.

A strength of APRICOT was the use of detailed, standardised definitions of serious critical events in paediatric anaesthesia and this could form the basis of a reporting and quality improvement system in Europe similar to that developed in the USA [1, 2, 8–10, 13, 15, 18, 19]. Recently, a tool for reporting adverse events associated with paediatric sedation was developed [20] and this could be a good model to follow for peri-operative serious critical event reporting and quality improvement [21].

The management of severe critical events varied in the UK and Europe and we suggest that evidence-based protocols for the management of peri-operative severe critical events should be implemented more widely to guide future practice. For more than 10 years, a simulation-based educational initiative 'managing emergencies in paediatric anaesthesia' (MEPA, www.mepa.org.uk) has been carefully validated and the curriculum for this course covers several of the severe critical event scenarios described in APRICOT [22]. Versions of the MEPA course are aimed at core basic knowledge and skill acquisition and may also be adapted for more advanced practice and skill

maintenance. These have proved highly successful and have been accredited by national professional bodies in several countries [22]. The MEPA scenarios have been run regularly as workshops during congresses of the ESPA and the Association of Paediatric Anaesthetists of Great Britain and Ireland (APAGBI). There is also a version of the course aimed at those with more occasional paediatric anaesthetic practice [22]. We suggest that the MEPA curriculum should in future cover all the serious critical events defined in APRICOT.

Human factors play a key role in all serious critical events [11, 23, 24] and anaesthetic training in the UK now incorporates learning points from human factor analysis into the core curriculum and continued professional development for all anaesthetists.

Ideally, preventive strategies to reduce severe critical events should be used and an important project is the 'safe anaesthesia for every child' (Safetots) initiative (www.safetots.org) which promotes safe peri-operative practice by adhering to clear principles of 'homeostasis' ('10-Ns' are suggested as norms for the peri-operative period) and ensuring care is in an appropriate setting with adequate support and infrastructure ('5-Ws') [25, 26].

In conclusion, this study has shown that the UK compares favourably with a non-UK cohort in terms of the incidence of peri-operative severe critical events. This may be due to differences in organisation of paediatric services, training, clinical practices, preventative strategies and team culture. The engaged, enthusiastic network of paediatric anaesthetists who contributed to APRICOT are already active in another detailed study of neonatal anaesthesia and are keen to learn from these studies and to disseminate best-practice guidance to improve the care of children throughout Europe.

Acknowledgements

APRICOT was registered with ClinicalTrials.gov (NCT01878760). The funding source (ESA) provided the infrastructure for the trial. The UK national study coordinating investigator (NM), liaised with the local investigators regarding their ethics submission process and the inclusion period, and monitored the data entry and cleaning. A UK-wide waiver for individual patient/family consent was granted and Caldicott guardian approval was given for data management, anonymisation procedures and data security. Authors NM, TE and DA had full access to all UK data in the study and had the final responsibility for the decision to submit the manuscript. The ESA principal investigators approved the manuscript content before submission.

- APRICOT Principal Investigators W. Habre and F. Veyckemans approved this manuscript
- APRICOT Trial Steering Committee: W. Habre, K. Becke, K. Boda, N. Disma, T. Hansen, M. Johr, F. Veyckemans, E. Schindler, E. Vermeulen, M. Zielinska, N. Morton
- ESA staff who extracted UK data: B. Leva, S. Damster, P. Harlet
- UK APRICOT centre leads: D. Love, J. Rutherford, C. Bradbury, S. Courtman, G. Bell, S. Bew, V. Oshan, S. Roberts, R. Thomas, P. Martin, R. Marcus, M. Taylor, M. Browning, L. Flewin, E. Dekker, M. Dickinson, K. Melarkode, A. Smith, P. Dix, T. Engelhardt, P. Baraggia, A.-H. Abdel-Hafiz, P. Paranthaman, S. King, K. Bartholomew, S. Ahmed, W. Rutherford, N. Barber, C. Barr, D. Rogerson, T. Geary, M. Crawford, C. Cumming, S. Winship, F. Sage, J. Whiteside, H. Wellesley, B. Foster, A. Makin, C. Smith, V. Muir, L. Chee, A. Kotecha, P. Singh, J. Gaynor, A. Thomas, K. Watson, C. Hunter, M. Mifsud, A. Ferguson, C. Lang
- Scottish Paediatric Anaesthesia Network
- All staff who helped with UK data collection.
- TE and NM are part of the Safetots initiative
- NM is on the Trial Steering Committee of APRICOT and is the UK APRICOT Lead
- TE, GB, JR and VO were UK APRICOT centre leads.

References

1. Habre W, Disma N, Virag K, et al. Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe. *Lancet Respiratory Medicine* 2017; **5**: 412–25.
2. Lerman J. Time for a paradigm shift in paediatric anaesthesia in Europe. *Lancet Respiratory Medicine* 2017; **5**: 365–7.
3. Sury MR, Arumainathan R, Belhaj AM, Mac GPJH, Cook TM, Pandit JJ. The state of UK paediatric anaesthesia: a survey of National Health Service activity. *Paediatric Anaesthesia* 2015; **25**: 1085–92.
4. Wilson EB. Probable inference, the law of succession, and statistical inference. *Journal of the American Statistical Association* 1927; **22**: 209–12.
5. Murat I, Constant I, Maud'huy H. Perioperative anaesthetic morbidity in children: a database of 24,165 anaesthetics over a 30-month period. *Pediatric Anesthesia* 2004; **14**: 158–66.
6. van der Griend BF, Lister NA, McKenzie IM, et al. Postoperative mortality in children after 101,885 anaesthetics at a tertiary paediatric hospital. *Anesthesia and Analgesia* 2011; **112**: 1440–7.
7. Walker RW. Pulmonary aspiration in pediatric anesthetic practice in the UK: a prospective survey of specialist pediatric centers over a one-year period. *Pediatric Anesthesia* 2013; **23**: 702–11.
8. Kurth CD, Tyler D, Heitmiller E, Tosone SR, Martin L, Deshpande JK. National pediatric anaesthesia safety quality improvement program in the United States. *Anesthesia and Analgesia* 2014; **119**: 112–21.
9. Lee JH, Kim EK, Song IK, et al. Critical incidents, including cardiac arrest, associated with pediatric anaesthesia at a tertiary teaching children's hospital. *Pediatric Anesthesia* 2016; **26**: 409–17.
10. Zgleszewski SE, Graham DA, Hickey PR, et al. Anesthesiologist- and system-related risk factors for risk-adjusted pediatric anaesthesia-related cardiac arrest. *Anesthesia and Analgesia* 2016; **122**: 482–9.
11. Kaufmann J, Wolf AR, Becke K, Laschat M, Wappler F, Engelhardt T. Drug safety in paediatric anaesthesia. *British Journal of Anaesthesia* 2017; **118**: 670–9.
12. Auroy Y, Ecoffey C, Messiah A, Rouvier B. Relationship between complications of pediatric anaesthesia and volume of pediatric anaesthetics. *Anesthesia and Analgesia* 1997; **84**: 234–5.
13. von Ungern-Sternberg BS, Boda K, Chambers NA, et al. Risk assessment for respiratory complications in paediatric anaesthesia: a prospective cohort study. *Lancet* 2010; **376**: 773–83.
14. Malviya S, Voepel-Lewis T, Chiravuri SD, et al. Does an objective system-based approach improve assessment of perioperative risk in children? A preliminary evaluation of the 'NARCO'. *British Journal of Anaesthesia* 2011; **106**: 352–8.
15. Williams GD, Muffly MK, Mendoza JM, Wixson N, Leong K, Claire RE. Reporting of perioperative adverse events by pediatric anesthesiologists at a tertiary children's hospital: targeted interventions to increase the rate of reporting. *Anesthesia and Analgesia* 2017; **125**: 1515–23.
16. RCOA. *Guidelines for the provision of Paediatric Anaesthetic services 2017*. London, UK: RCOA, 2017.
17. RCOA. *Anaesthesia clinical services accreditation standards*. London, UK: RCOA, 2018.
18. Munting KE, van Zaane B, Schouten AN, van Wolfswinkel L, de Graaff JC. Reporting critical incidents in a tertiary hospital: a historical cohort study of 110,310 procedures. *Canadian Journal of Anesthesia* 2015; **62**: 1248–58.
19. de Graaff JC, Sarfo MC, van Wolfswinkel L, van der Werff DB, Schouten AN. Anaesthesia-related critical incidents in the perioperative period in children; a proposal for an anaesthesia-related reporting system for critical incidents in children. *Pediatric Anesthesia* 2015; **25**: 621–9.
20. Roback MG, Green SM, Andolfatto G, Leroy PL, Mason KP. Tracking and reporting outcomes of procedural sedation (TROOPS): standardized quality improvement and research tools from the international committee for the advancement of procedural sedation. *British Journal of Anaesthesia* 2018; **120**: 164–72.
21. RCOA. *Raising the Standards: a compendium of audit recipes for continuous quality improvement in anaesthesia*. London, UK: Royal College of Anaesthetists, 2012.
22. Everett TC, MacKinnon R, de Beer D, Taylor MTaylor M, Bould MD. Ten years of simulation-based training in pediatric anaesthesia: the inception, evolution, and dissemination of the Managing Emergencies in Pediatric Anaesthesia (MEPA) course. *Paediatric Anaesthesia* 2017; **27**: 984–90.
23. Gariel C, Cogniat B, Desgranges F-P, Chassard D, Bouvet L. Incidence, characteristics, and predictive factors of medication errors in paediatric anaesthesia. A prospective incident monitoring study. *British Journal of Anaesthesia* 2018; **120**: 563–70.
24. Litman RS. How to prevent medication errors in the operating room? Take away the human factor *British Journal of Anaesthesia* 2018; **120**: 438–40.
25. Weiss M, Vutskits L, Hansen TG, Engelhardt T. Safe Anaesthesia for every tot – the SAFETOTS initiative. *Current Opinion in Anaesthesiology* 2015; **28**: 302–7.
26. Weiss M, Hansen TG, Engelhardt T. Ensuring safe anaesthesia for neonates, infants and young children: what really matters. *Archives of Disease in Childhood* 2016; **101**: 650–2.

Appendix A1

Number of patients recruited from each UK centre during a 2-week period.

City	Hospital	n
Glasgow	RHSC Yorkhill	614
Leicester	Leicester Royal Infirmary	291
Guildford	Royal Surrey County Hospital NHS Foundation Trust	62
Hull	Hull and East Yorkshire Hospitals NHS Trust	122
Chelmsford	Broomfield Hospital	93
Aberdeen	Royal Aberdeen Children's Hospital	177
Plymouth	Derriford Hospital	168
Manchester	Royal Manchester Children's Hospital	451
Birmingham ^a	Birmingham Children's Hospital	199
Exeter	Royal Devon & Exeter NHSFT	82
Newcastle-upon-Tyne	Great North Children's Hospital/Royal Victoria Infirmary	400
Swansea	Morrison Hospital, ABMU Health Board	107
Truro	Royal Cornwall Hospital	50
Coventry	University Hospital	136
Carmarthen	West Wales General Hospital	27
Kilmarnock	University Hospital Crosshouse	94
Derby	Royal Derby Hospital (Derbyshire Children's Hospital)	93
Edinburgh	Royal Hospital for Sick Children Edinburgh	248
London	Evelina London Children's Hospital	367
Leeds	Leeds Children's Hospital	391
Sheffield	Sheffield Children's Hospital	500
Liverpool	Alder Hey Children's NHS Foundation Trust	511
Halifax	Calderdale & Huddersfield NHS Foundation Trust	115
Southampton	University Hospital Southampton	313
Maidstone & Tunbridge Wells	Maidstone & Tunbridge Wells NHS Trust	71
East Kilbride	Hairmyres Hospital	40
London	Chelsea & Westminster NHS Trust	195
Salisbury	Salisbury District Hospital	68
Greenock	Inverclyde Royal Hospital	8
Paisley	Royal Alexandra Hospital	33
Belfast	The Royal Belfast Hospital for Sick Children	124
London ^a	Great Ormond Street Hospital	224
Dundee	Ninewells	96
Cambridge	Addenbrooke's Hospital	248
Inverness	Raigmore Hospital	47
Kirkcaldy	Victoria Hospital	43
Dumfries	Dumfries and Galloway Royal Infirmary	28
Redhill	East Surrey Hospital	64
Airdrie	Monklands	19
Larbert	Forth Valley Royal Hospital	48
Wishaw	Wishaw General	31
Melrose	Borders General Hospital	10
Livingston	St John's Hospital	37

^aThese centres recruited during a shorter period than 2 weeks and their data were not included in those analyses requiring annualisation estimates.

Appendix A2

Variation in severe critical events across Europe. The boxes are incidence and the whiskers are 95%CI. The UK has been identified as number 7.

