UK PROTOCOL – CRICKET

TITLE

CRICKET : Critical Events in anaesthetised kids undergoing tracheal intubation – a prospective multi-centre observational study

SHORT STUDY TITLE

- CRICKET

PROTOCOL VERSION NUMBER AND DATE

- **V1.3 23 / 4 / 2024**

RESEARCH REFERENCE NUMBERS

IRAS Number:	342202
SPONSORS Number:	RHM CRI0441
FUNDERS Number:	NA

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: ....

Date: 23 April 2024

Name (please print): Sharon Davies-Dear

Position: Deputy Research & Development Quality Assurance Manager

Chief Investigator:

Signature: ....

Date: 23/04/2024

Name: (please print): .....Tom Bennett.....

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KEY STUDY CONTACTS

Chief Investigator	Dr Tom Bennett tom.bennett@uhs.nhs.uk University Hospital Southampton Tremona Road Southampton SO16 6YD +44 07590062152
Study Co-ordinator	PD Dr. med Thomas Riva, Bern thomas.riva@insel.ch Department of anaesthesiology and pain medicine Inselspital Bern University Hospital Friburgstrasse 8 3010 Bern Switzerland +41 31 632 27 25.
Sponsor	Ms Sharon Davis-Dear R&D Department University Southampton NHS Foundation Trust Duthie Building Mailpoint 138 Tremona Road Southampton SO16 6YD 023 8210 5044
Funder(s)	This study is financed by the research fund of the Department of Anaesthesiology and Pain Medicine, Inselspital Bern and IRCCS Istituto Giannina Gaslini. There is no funding or financial influence through any other company. There is no conflict of interest by any of the investigators. No funding is available for the running of the study in individual sites

Key Protocol Contributors	Dr Tom Bennett
Committees	See attached PDF for full steering committee details

STUDY SUMMARY

Study Title	CRICKET: Critical events in anaesthetised kids undergoing tracheal intubation – a prospective, multi-centre observational study
Internal ref. no. (or short title)	CRICKET, RHM CRI0441
Study Design	Prospective, international multi-centre observational trial. Participating centres will collect data over a consecutive period of three months.
Study Participants	Inclusion All paediatric patients requiring tracheal intubation performed by the anaesthesia team for procedures or interventions requiring general anaesthethesia 0-16 years Exclusion Patients >16 years
Planned Size of Sample (if applicable)	This study expects to include 8000 cases across the UK. This estimate is based on previous similar studies such as PINEAPPLE and PEACHY which collected data over a 2 week period in around 100 centres achieving numbers between 5000-7000. Where only 30% of children are intubated for surgical procedures, a longer data collection period, 8000 cases would be a conservative estimate based on a similar number of participating centres. With a critical event rate of around 1% in paediatric intubations, as higher number as possible will be needed to draw conclusions.
Follow up duration (if applicable)	Children with critical events will be followed up until resolution of the event or for a maximum of 30 days whichever comes earlier.

Planned Study Period	Target a continuous 3 month data between June 2024-Dec 2024
End of Study Definition	The final day for patients to be included in the study is 31st December 2024. They will be followed up for a maximum of 30 days from this date should a critical event occur.
Research Question/Aim(s)	Assessment and analysis of the incidence of airway management related critical events during tracheal intubation in children.

FUNDING AND SUPPORT IN KIND

FUNDER(S)	FINANCIAL AND NON FINANCIALSUPPORT GIVEN
Department of Anaesthesiology and Pain Medicine, Inselspital Bern and IRCCS Istituto Giannina Gaslini	Funding the study set up and running from central site in Bern. There is no funding available internationally

ROLE OF STUDY SPONSOR AND FUNDER

The Sponsor is University Hospital Southampton NHS Foundation Trust (UHS), which is the organisation that is taking legal responsibility for the study.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Study Steering Groups

International steering committee with representation from other countries partaking in data collection to contribute to the combined data analysis.

Contribution to study design, conduct and implementation of study protocol and approved the final version of the protocol manuscript.

Steering Committee Chair

- Prof. Dr. Robert Greif, Department of Anesthesiology and Pain Medicine, Inselspital Bern University Hospital, Switzerland

Full list :

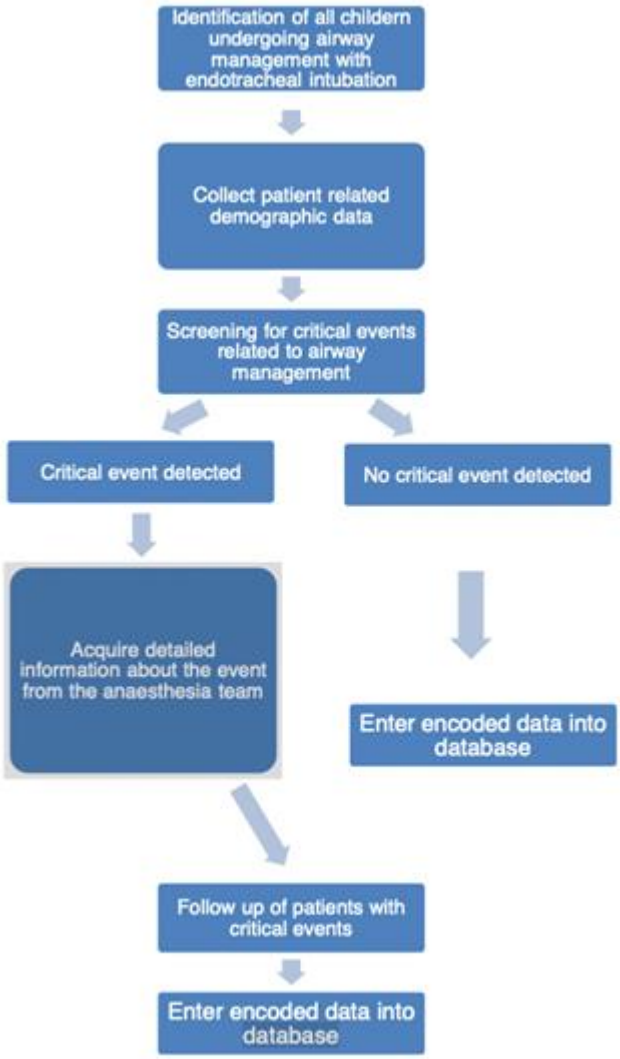
- Dr. Tom Bennett, Shackleton Department of Anaesthetics Southampton Children's Hospital, University Hospital Southampton, UK
- Prof. Dr. Nicola Disma, Dept Anesthesia, G. Gaslini Children's Hospital, Italy.
- Prof. Thomas Engelhardt, Dept. Anesthesia, Montreal Children's Hospital, McGill University Health Centre, Canada.
- Prof. John Fiadjoe, Department of Anesthesiology, Critical Care and Pain Medicine, USA.
- Dr. Alexander Fuchs, Dept. Anaesthesiology and Pain Medicine, Inselspital Bern, Switzerland.
- Prof. Annery Garcia-Marcinkiewicz, MD, Dept of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, USA.
- Prof. Dario Gregori, Head of the Unit of Biostatistics,Epidemiology and Public Health, Padova University, Italy.
- Prof. Dr. Robert Greif, Dept. Anaesthesiology and Pain Medicine, Inselspital Bern, Switzerland.
- Prof. Dr. Walid Habre, Unité d'anesthésie pédiatrique, Hôpital des Enfants / HUG, Switzerland.
- Prof. Dr. Maren Kleine-Brueggeney, Department of Cardiac Anesthesiology and Intensive Care Medicine, German Heart Center, Berlin, and Department of Cardiac Anesthesiology and Intensive Care Medicine, Charité Universitätsmedizin Berlin, Germany.
- Prof. Clyde Matava, Dept. Anesthesia, The Hospital for Sick Children, Canada M5G 1X8.
- Dr. Vinicius Quintao, Universidade de São Paulo, Hospital das Clínicas, Faculdade de Medicina, São Paulo, Brazil
- Thomas Riva, Dept. Anaesthesiology and Pain Medicine, Inselspital Bern, Switzerland
- Prof. Dr. Britta von Ungern-Sternberg, Department of Anaesthesia and Pain Management, Perth Children's Hospital, Australia.

PROTOCOL CONTRIBUTORS

- Protocol written by Thomas Riva as sponsor investigator
- Steering committee contribute, sign off and agree on final version of protocol
- Adapted for UK study Tom Bennett

KEY WORDS: Neonatal, Paediatric, Airway, Critical Events, Complications

STUDY FLOW CHART



1 BACKGROUND

The Pediatric Difficult Intubation (PeDi) Registry has taught us that the number of airway management attempts correlates with an increase in critical events in children with anticipated and unanticipated difficult airways (7). The new guidelines for difficult airway management from the American Society of Anesthesiologists (8) also emphasise limiting the number of intubation attempts as this can reduce complications. Major complications of airway management might lead to immediate life-threatening situations for the patient.

The NAP4 study (9) estimated that major complications during airway management occur with an incidence of up to 1 in 5500 anaesthesia cases in adults and children. The few reported cases with a "cannot intubate cannot ventilate" (CICV) situation had very severe consequences (death, brain damage, prolonged hospitalisation, unplanned ICU admission). The APRICOT study (10) showed that paediatric airway management nowadays is a very safe practice with an incidence of difficult airways of 0.28%. In new-borns, this incidence rises steeply to up to 6% with half of these patients suffering serious complications such as hypoxia or bradycardia. Fortunately, these situations have not resulted in increased mortality and emergency front of neck access (FONA) has not been reported in NECTARINE (11).

Desaturation to an SpO2 of 90% occurs within 2 minutes in 2-5 year-olds (12). During emergency intubation in paediatric intensive care units worldwide, desaturation to SpO2 values < 80% was reported in 27.7% to 44.2% (3), and tracheal intubation–associated cardiac arrest was reported in 1.7% (5). Furthermore, a recent study examining neonates undergoing nonemergency nasotracheal intubation showed a desaturation rate (SpO2 <80% exceeding 60 seconds) of 60 to 66% (13). Tracheal intubation has potential for injury of the airways, is painful and distressing (14). A small study including 162 neonates demonstrated an incidence of adverse events of 4 in 10 neonatal intubations 16 with non-severe and severe events in 35% and 8.8% of intubations, respectively (15). Non-severe events during intubation included oesophageal intubation with immediate recognition, main stem bronchial intubation, oral/airway injury with bleeding, difficult bag-mask ventilation or emesis while severe complications included hypotension necessitating treatment, hypoxia causing bradycardia requiring chest compressions, pneumothorax and the administration of resuscitation drugs.

The UK national quality safety project NAP4 (9), the PeDi Registry (7) and the APRICOT study (10) focused primarily on major complications, i.e. loss of airway or death. In this study, we aim to study a larger cohort of children and to record more detailed data on critical events associated with tracheal intubation in children up to 16 years of age. This may allow us to identify children at particularly high-risk for major complications which might consecutively help with the development of improved management strategies.

2 RATIONALE

While the children included in this observational study do not have an immediate benefit, the knowledge gain might lead to improved outcomes in future patients.

3 THEORETICAL FRAMEWORK

To gain high-quality data with minimal risk of bias, we will perform a prospective observational study including all consecutive children undergoing general anaesthesia with tracheal intubation during the three months study period at the participating sites.

4 RESEARCH QUESTION/AIM(S)

Define the incidence and nature of critical events related to tracheal intubation in children.

4.1 Objectives

Our overall objective is to assess the incidence of critical events related to tracheal intubation at all international study sites. Furthermore, the study will investigate the used intubation techniques and identify possible improvement measures to increase patient safety.

4.2 Outcome

Primary study outcome is the incidence of anaesthesia cases with critical events associated with endotracheal intubation requiring intervention from the start of anaesthesia until the discharge of the patient from the post-anaesthesia care unit or end of anaesthesia (defined as handover to the paediatric or neonatal intensive care unit, the ward or discharge home straight from anaesthesia care) in children aged 0 - 16 years. Facultatively for those who do not have capacity the acquisition of data stops at the end of anaesthesia (defined as handover to the post-anaesthesia care unit).

Secondary study outcome parameters are the incidences of the individual critical events as listed below. Also, we will assess the number of events per case as a secondary outcome parameter.

5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYSIS

CRICKET is a prospective observational multi-centre study collecting health related patient data over a period of three months. This serves best the study's purpose to detect the incidence and nature of problems related to tracheal intubation and how such problems are handled with the aim to further improve patient safety. During the observational period the anaesthesia staff in charge will complete a screening questionnaire for critical events associated with tracheal intubation for every patient undergoing general anaesthesia with tracheal intubation. If no critical events arise there are no further requirements. If a critical event occurs, the anaesthesia provider will complete a more detailed questionnaire which includes more questions about what exactly happened.

Patient characteristics will be extracted from the anaesthesia records. We will extract such data for all patients undergoing tracheal intubation and additional data for those with critical events. The research will not intervene with the clinical conduct of patient care.

The collected health related data will be transferred to an electronic research data base in REDCap (see section 8). In this data base data will be encoded Every patient with a critical event will be followed up until the end of the event or 30 days whichever is sooner.

Access to REDCap will be granted only to data collecting staff of participating centres, in accordance with the procedures outlined in the present protocol. Each participating centre is granted access only to the patient data it has generated and recorded on the REDCap platform. The data will be recorded using an encrypted data connection (HTTPS) in input masks via a web browser or mobile app.

In terms of descriptive statistics, categorical data will be summarised with count and percentages.

Continuous data will be summarized using median (interquartile range).

The incidence of critical events will be estimated and reported together with 95% Confidence Interval, Furthermore, critical events incidence will be provided for different age categories, operator's experience, operator's speciality, and centre volume (secondary and tertiary).

In terms of risk factor analysis, a univariable and multivariable mixed-effect logistic regression model will be computed based on possible predictors, which include e.g. age (< or equal to 12 months), weight (< or equal to 10 kg), number of attempts (>2), presence of co-morbidities (ASA score > or equal to 3), comorbidity related to airway management (e.g. relevant syndromes), expected difficult intubation, type of anaesthesia induction (IV or inhalational), no neuromuscular blocking agent given, airway surgery or ENT surgery and experience level of intubator. Goodness-of-fit, calibration, discriminatory capacity and predictive skill of the regression models will be assessed by means of Nagelkerke pseudo r-squared, calibration belts, Area Under the Receiver Operating Characteristics (AUROC) and Brier Score, respectively.

A p-value < 0.05 is considered statistically significant. All analyses will be performed with R

6 STUDY SETTING

- Data collected by participating centres in the UK by those with routine access to notes as part of their role i.e. Anaesthetists or members of the anaesthetic department.
- All paediatric patients requiring tracheal intubation by the anaesthesia team will be included. This is most likely to be in the theatre environment but may extend to neonatal ICU and Paediatric ICU in some centres. This will also include anaesthesia for imaging where tracheal intubation is required.
- Study participants will be identified by investigators who are part of the clinical care team at each study site. Participants will be identified prospectively for planned intubations or retrospectively for unplanned tracheal intubation.
- This setting meets the requirements to answer the question posed by the study as we are looking into the incidence of critical events while under the care of the anaesthetic team.
- UHS are sponsor for this study.
- We will involve the paediatric anaesthetic trainee research network (PATRN) in running the study. They have been approached and are happy to help with data collection.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

7.1.1 Inclusion criteria

- All paediatric patients requiring tracheal intubation, performed by the anaesthesia team for procedures or interventions requiring general anaesthesia
- Patients between 0-16

7.1.2 Exclusion criteria

- Patients > 16

7.2 Sampling

7.2.1 Size of sample

We anticipate a UK sample size of around 8000. This is assuming a similar number of participating centres to previous studies and a data collection period of 3 months.

7.2.2 Sampling technique

In order to avoid bias and achieve an accurate denominator, we aim to collect data on all intubations in children under 16 in participating theatres during a 3 month period. This can be reduced to a shorter time period as is feasible to each centre.

7.3 Recruitment

Due to the observational and non-interventional nature of this study, it will be non-consenting and data will only be collected by those who would have access to it in their usual roles. Eligible patients will be identified by the anaesthetic team and the anaesthetist will be asked to complete questionnaires for all eligible patients. To ensure high data quality and further prevent bias by underreporting, a dedicated study person not involved directly in clinical care, if available, will ensure completeness and clarity of the completed questionnaires. The data at this point will be non-identifiable.

7.3.1 Sample identification

The sample will be identified by the clinical team. This is all children who require tracheal intubation. Questionnaires can be filled in contemporaneously.

There is no change to routine care or any intervention.

7.3.2 Consent

Consent will not be required as this is an observational study only collecting non-identifiable data. There will be no change to clinical management and all data collected is routinely recorded as part of standard clinical care. The clinical information will only be accessed by those who have access to this data as part of their role in the clinical care team.

7.3.3 End of Study Definition

The final day for patients to be included in the study is 31st December 2024. They will be followed up for a maximum of 30 days from this date should a critical event occur.

Statistical analysis and draft manuscript preparation is scheduled to occur in April 2025. We aim to disseminate the findings by December 2025.

8 ETHICAL AND REGULATORY CONSIDERATIONS

The research methods answer the research question through observational data. The research will not intervene with the clinical conduct of patient care.

8.1 Assessment and management of risk

- The children in the study will not have an immediate benefit but the knowledge from the study may lead to improved outcomes for future patients. The only risk posed is the very small risk from data handling. Data will be collected during routine anaesthetic practice.

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

The sponsor will ensure that the trial protocol and submitted supporting documents have been approved by the appropriate regulatory body, Health Research Authority (HRA), main research ethics committee (REC) and that local permission has been obtained prior to any subject recruitment.

All substantial amendments and non-substantial amendments (as determined by the sponsor) will not be implemented until HRA/REC have provided the relevant authorisations. The NHS R&D departments will also be informed of any substantial amendments and non-substantial amendments.

Relevant approvals must be obtained before any substantial amendment and non-substantial amendments may be implemented at sites. All correspondence with the HRA and the REC will be retained in the Trial Master File and the Investigator Site File (maintained by the site).

An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended.

Within 90 days after the end of the trial (as defined in section 7.10), the CI/Sponsor will ensure that the HRA and the main REC are notified that the study has finished. If the study is terminated prematurely, those reports will be made within 15 days after the end of the trial.

The CI will supply the Sponsor with a summary report of the study, which will then be submitted to the main REC within 1 year after the end of the trial.

All results will be published on a publicly accessible database.

Regulatory Review & Compliance

The Investigator agrees to comply with the requirements of the Protocol and Good Clinical Practice. Prospective, planned deviations or waivers to the protocol are not allowed under the UK regulations on Clinical Trials and must not be used e.g. it is not acceptable to enrol a subject if they do not meet the eligibility criteria or restrictions specified in the trial protocol.

Accidental protocol deviations can happen at any time. They must be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.

Deviations from the protocol, which are found to frequently recur, are not acceptable and will require immediate action by the sponsor. Frequent non-compliances could potentially be classified as a serious breach.

8.3 Peer review

The current version of the protocol has been peer reviewed by 18 international experts in the field.

8.4 Patient & Public Involvement

PPI has been considered but has not been included in this study as it is not felt to be applicable. The study is investigating the anaesthetic management of paediatric airways. The information gathered from this study will be relevant to clinical practice and delivery of care by clinicians caring for children under anaesthesia. Given the specific nature of the observational study into clinical practice, PPI has not been included.

8.5 Protocol compliance

- Deviations from the protocol may result in poor data
- We aim to have at least 1 person in each centre ensuring that the questionnaire is filled in fully for all intubated children
- Each centre will choose to monitor this in a way which suits their current practice

Monitoring, Audits and Inspections

This study will be monitored and may be participant to monitoring and audit by University Hospital Southampton NHS Foundation Trust, under their remit as sponsor and other regulatory bodies to ensure adherence to ICH GCP, UK Policy Framework for Health and Social Care Research, applicable contracts/agreements and national regulations. All study related documents will be made available on request for monitoring and audit by UHS, the relevant REC or other licensing bodies.

8.6 Data protection and patient confidentiality

Demographic data (age, weight, height (if available), sex, type of surgery) will be obtained from the anaesthesia record. All study data will be directly recorded in the CRF (on paper or electronically), which are considered as source data. These data will be either directly entered (eCRF) or transferred into the study management software REDCap (Research Electronic Data Capture)

The investigators affirm and uphold the principle of the participant's right to privacy and that they shall comply with applicable privacy laws. Notably, the privacy of the participants will be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.

Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. No data will be transferred to third parties without prior ethics committee approval. Subject confidentiality will be further ensured by utilising subject identification code numbers to correspond to treatment data in the computer files.

The code will be stored in a lockable cupboard in a suitable, safe location according to institutional guidelines at the individual sites.

All investigators and study site staff will comply with the requirements of the Data Protection Regulation with regards to the collection, storage, processing and disclosure of personal information and will uphold the Regulation's core principles.

ARCHIVING

Archiving will be authorised by the Sponsor following submission of the end of study report.

Location and duration of record retention for:

- Essential documents: Patient case notes will be stored and maintained according to standard rules and procedures. Pathology results are stored and maintained according to standard procedures.
- Study data will be held for minimum of 10 years

Destruction of essential documents will require authorisation from the Sponsor.

8.7 Indemnity

The sponsor of the trial is University Hospital Southampton NHS Foundation Trust. For NHS sponsored research HSG (96) 48 reference no.2 refers. If there is negligent harm during the clinical trial when the NHS body owes a duty of care to the person harmed, NHS Indemnity covers NHS staff, medical academic staff with honorary contracts, and those conducting the trial. NHS Indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm. Ex-gratia payments may be considered in the case of a claim.

8.8 Access to the final study dataset

- The research team will have access to the non-identifiable data set
- Each centre will have access to their own data set only

9 DISSEMINIATION POLICY

9.1 Dissemination policy

The results will be published in a peer-reviewed journal. Final decision on publishing the results will be kept by the steering committee of the study. Authors of the publication will be team members of the steering committee who contributed to the design, conduct or analysis of the study and who approved of the final version of the manuscript. Local PIs agree not to individually publish or present the results they obtain from the participation in the multicentre study before the publication of the main result of the study. Local PIs may, however, upon written notice to Sponsor and Steering committee participate in a joint, multicentre publication of the study results with other third-party principal investigators and/or institutions, provided that the proposed publication is first reviewed by Sponsor and Steering committee.

The study will be registered on clinicaltrials.gov.

9.2 Authorship eligibility guidelines and any intended use of professional writers

- See above

10 REFERENCES

1. Patel R, Lenczyk M, Hannallah RS, McGill WA. Age and the onset of desaturation in apnoeic children. Can J Anaesth. 1994;41(9):771-4.
2. Hardman JG, Wills JS. The development of hypoxaemia during apnoea in children: a computational modelling investigation. Br J Anaesth. 2006;97(4):564-70.
3. Nishisaki A, Ferry S, Colborn S, DeFalco C, Dominguez T, Brown CA, 3rd, et al. Characterization of tracheal intubation process of care and safety outcomes in a tertiary pediatric intensive care unit. Pediatr Crit Care Med. 2012;13(1):e5-10.
4. Stinson HR, Srinivasan V, Topjian AA, Sutton RM, Nadkarni VM, Berg RA, et al. Failure of Invasive Airway Placement on the First Attempt Is Associated With Progression to Cardiac Arrest in Pediatric Acute Respiratory Compromise. Pediatr Crit Care Med. 2017.

5. Shiima Y, Berg RA, Bogner HR, Morales KH, Nadkarni VM, Nishisaki A, et al. Cardiac Arrests Associated With Tracheal Intubations in PICUs: A Multicenter Cohort Study. Crit Care Med. 2016;44(9):1675-82.
6. Schwartz DE, A. MM, Cohen NH. Death and other complications of emergency airway management in critically ill adults. A prospective investigation of 297 tracheal intubations. Anesthesiology. 1995;82(2):367-76.

7. Fiadjoe JE, Nishisaki A, Jagannathan N, Hunyady AI, Greenberg RS, Reynolds PI, et al. Airway management complications in children with difficult tracheal intubation from the Pediatric Difficult Intubation (PeDI) registry: a prospective cohort analysis. The Lancet Respiratory Medicine. 2016;4(1):37-48.

8. Apfelbaum JL, Hagberg CA, Connis RT, Abdelmalak BB, Agarkar M, Dutton RP, et al. 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway. Anesthesiology. 2021.
9. Cook TM, Woodall N, Harper J, Benger J, Fourth National Audit P. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 2: intensive care and emergency departments. Br J Anaesth. 2011;106(5):632-42.

10. Habre W, Disma N, Virag K, Becke K, Hansen TG, Jöhr M, et al. Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe. The Lancet Respiratory Medicine. 2017;5(5):412-25.

11. Disma N, Virag K, Riva T, Kaufmann J, Engelhardt T, Habre W, et al. Difficult tracheal intubation in neonates and infants. NEonate and Children audiT of Anaesthesia pRactice IN Europe (NECTARINE): a prospective European multicentre observational study. Br J Anaesth. 2021;126(6):1173-81.

12. Ramesh Patel MD MLM, Raafat S. Hannallah MD, Willis A. McGill MD. Age and the onset of desaturation in apnoeic children. Can J Anaesth. 1994;41(9):771-4.
13. Durrmeyer X, Breinig S, Claris O, Tourneux P, Alexandre C, Saliba E, et al. Effect of Atropine With Propofol vs Atropine With Atracurium and Sufentanil on Oxygen Desaturation in Neonates Requiring Nonemergency Intubation: A Randomized Clinical Trial. Jama. 2018;319(17):1790-801.

14. Carbajal R, Eble B, Anand KJ. Premedication for tracheal intubation in neonates: confusion or controversy? Semin Perinatol. 2007;31(5):309-17.
15. Hatch LD, Grubb PH, Lea AS, Walsh WF, Markham MH, Whitney GM, et al. Endotracheal Intubation in Neonates: A Prospective Study of Adverse Safety Events in 162 Infants. The Journal of pediatrics. 2016;168:62-6.
16. Wallenstein MB, Birnie KL, Arain YH, Yang W, Yamada NK, Huffman LC, et al. Failed endotracheal intubation and adverse outcomes among extremely low birth weight infants. J Perinatol. 2016;36(2):112-5.
17. Dreyer NA, Tunis SR, Berger M, Ollendorf D, Mattox P, Gliklich R. Why observational studies should be among the tools used in comparative effectiveness research. Health Aff (Millwood). 2010;29(1544-5208 (Electronic)):1818-25.

18. Garcia-Marcinkiewicz AG, Kovatsis PG, Hunyady AI, Olomu PN, Zhang B, Sathyamoorthy M, et al. First-attempt success rate of video laryngoscopy in small infants (VISI): a multicentre, randomised controlled trial. The Lancet. 2020;396(10266):1905-13.

19. R Core Team, R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria 2022.
20. Höhle M. binomSamSize: Confidence Intervals and Sample Size Determination for a Binomial Proportion under Simple Random Sampling and Pooled Sampling [Internet]. Available from: https://CRAN.R-project.org/package=binomSamSize. 201