

# BMJ Open The design of a multicentre Canadian surveillance study of sedation safety in the paediatric emergency department

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## ABSTRACT

**Introduction:** Procedural sedation and analgesia have become standard practice in paediatric emergency departments worldwide. Although generally regarded as safe, serious adverse events such as bradycardia, asystole, pulmonary aspiration, permanent neurological injury and death have been reported, but their incidence is unknown due to the infrequency of their occurrence and lack of surveillance of sedation safety. To improve our understanding of the safety, comparative effectiveness and variation in care in paediatric procedural sedation, we are establishing a multicentre patient registry with the goal of conducting regular and ongoing surveillance for adverse events in procedural sedation.

**Methods:** This multicentre, prospective cohort study is enrolling patients under 18 years of age from six paediatric emergency departments across Canada. Data collection is fully integrated into clinical care and is performed electronically in real time by the healthcare professionals caring for the patient. The primary outcome is the proportion of patients who experience a serious adverse event as a result of their sedation. Secondary outcomes include the proportion of patients who experience an adverse event that could lead to a serious adverse event, proportion of patients who receive a significant intervention in response to an adverse event, proportion of patients who experience a successful sedation, and proportion of patients who experience a paradoxical reaction to sedation. There is no predetermined end date for data collection.

**Ethics and dissemination:** Ethics approval has been obtained from participating sites. Results will be disseminated using a multifaceted knowledge translation strategy by presenting at international conferences, publication in peer-reviewed journals, and through established networks.

## INTRODUCTION

Procedural sedation and analgesia have become standard practice in paediatric

## Strengths and limitations of this study

- This will be the first multicentre study to estimate the risk of serious adverse events in paediatric emergency department procedural sedation.
- This study uses a novel data collection method that is integrated into clinical care, eliminating duplicate documentation, and increasing efficiency and data quality by utilising built-in error checking and other smart functions.
- All participating sites are tertiary care paediatric emergency departments, thus, findings may not be directly generalisable to general emergency department (ED) settings or other procedural sedation settings outside of the operating room.

emergency departments worldwide. Each year, thousands of North American children receive emergency department (ED) procedural sedation, and the number is rapidly increasing as emergency department (ED) experience and expertise has grown.<sup>1 2</sup>

Although procedural sedation performed outside the operating room is generally regarded as safe, serious adverse events have been known to occur.<sup>3–8</sup> Bradycardia, asystole, pulmonary aspiration, permanent neurological impairment, and death have been reported, but their incidence is unknown due to the infrequency of their occurrence and lack of consistent surveillance of safety of sedation.<sup>4 5 7 8</sup> These serious adverse outcomes have not been reported in paediatric ED procedural sedation, though they are understood to be preceded by more commonly occurring events, such as oxygen desaturation, vomiting, apnoea and laryngospasm. The occurrence rates for these events have been reported to be between 2% and 26% based on small, single centre ED cohorts.<sup>9–19</sup> Unfortunately,

these studies have sample sizes that are too small to reliably determine the comparative safety of different sedation modalities for both minor and major adverse events. Moreover, aggregation of results from these studies has been difficult as they have used varied terminology and definitions to describe the same adverse events and outcomes.

To improve our understanding of the safety, comparative effectiveness and variation in care of paediatric ED procedural sedation, we have established a multicentre patient registry that is fully integrated with clinical documentation of patients undergoing procedural sedation in participating Canadian paediatric EDs. This sustainable design uses methodology that results in prospectively collected, consistently complete data, without the use of research personnel for patient recruitment or data collection. As such, this system allows for ongoing data collection and surveillance of adverse events and rescue interventions.

## OBJECTIVES

The objective of our multicentre prospective cohort study is to establish a surveillance system for adverse events in procedural sedation in six paediatric EDs across Canada by implementing a standardised electronic data collection system that is fully integrated within clinical care.

## METHODS

### Study design

This is an ongoing multicentre prospective cohort study. We are enrolling all consenting patients undergoing procedural sedation in six Canadian paediatric EDs. Data collection began in July 2010 in a staged rollout across sites with the most recent site being added in June 2013. There is no predetermined end date for data collection. The parents of patients who experience an adverse event, and 15% of enrolled patients at each site who do not experience an adverse event, will be contacted by telephone 1–2 weeks following ED discharge to determine their child's state of physical and psychological health after receiving procedural sedation in the ED.

### Study setting

The study is taking place in the EDs of 6 of the 12 tertiary care children's hospitals in Canada. Participating sites are: IWK Health Centre (Halifax, Nova Scotia), Montreal Children's Hospital (Montreal, Quebec), Children's Hospital of Eastern Ontario (Ottawa, Ontario), The Hospital for Sick Children (Toronto, Ontario), Stollery Children's Hospital (Edmonton, Alberta) and Alberta Children's Hospital (Calgary, Alberta). All sites are members of Pediatric Emergency Research Canada (PERC), a national collaborative research network of 15 Canadian paediatric EDs.<sup>20–22</sup> The sites have a combined annual ED census of approximately 350 000 patient visits and cumulatively perform parenteral sedation for an estimated 3500 children each year.

## Inclusion criteria

1. Age less than 18 years.
2. Patients undergoing ED procedural sedation for painful procedures.

## Exclusion criteria

1. Patients receiving only anxiolytic medications.
2. Patients receiving only analgesic medications.
3. Patients receiving a combination of oral, inhaled and/or intranasal medications *without* any intravenous medications for procedural sedation and analgesia.
4. Insurmountable language barrier that prevents informed consent and follow-up by telephone

## Outcome measures

### Primary outcome measure

The primary outcome is the proportion of patients who experience a serious adverse event as a result of their sedation. Serious adverse events are apnoea, laryngospasm, hypotension, bradycardia, complete airway obstruction, clinically apparent pulmonary aspiration, permanent neurological injury and death, as defined by the Quebec Guidelines.<sup>23 24</sup>

### Secondary outcome measures

1. Proportion of patients who experience an adverse event that could lead to a serious adverse event. These events are: oxygen desaturation, partial airway obstruction and vomiting, as defined by the Quebec Guidelines.<sup>23 24</sup>
2. Proportion of patients who receive a significant intervention in response to an adverse event. Significant interventions are: bag-mask ventilation, tracheal intubation, administration of vasoactive medications, administration of neuromuscular blockade agents and chest compressions.
3. Proportion of patients who experience any adverse event as a result of their sedation. Adverse events are defined by the Quebec Guidelines.<sup>23 24</sup>
4. Proportion of patients who experience a successful sedation, as defined by the Quebec Guidelines.<sup>23 24</sup>
5. Proportion of patients who experience a paradoxical reaction to sedation, as defined by the Quebec Guidelines.<sup>23 24</sup>
6. Duration of the sedation, defined as the time from the administration of the first sedation medication to the end of physiologic recovery.
7. Proportion of patients undergoing ketamine sedation who have preprocedural agitation (agitated and responds to comforting, or, agitated and does not respond to comforting).
8. Proportion of patients who experience age-inappropriate recovery reactions (crying, agitation, delirium, dysphoria, nightmares or hallucinations) as specified by the Quebec Guidelines.<sup>23 24</sup>
9. Patient characteristics that may be associated with respiratory adverse events and vomiting and system-level characteristics that may be associated with any

adverse event. These characteristics are further defined and described in the online supplementary appendix 1A–C.

10. The proportion of children experiencing maladaptive behaviours following their ED discharge, as reported by a summary score on the modified Post-hospital Behaviour Questionnaire (PHBQ).<sup>25–27</sup> On the PHBQ, behaviours that increase after a procedure are scored positively, behaviours that decrease are scored negatively, and behaviours that do not change are given a score of 0. Summary scores can range from –54 to +54. A positive score indicates a maladaptive behaviour change.
11. The proportion of children who experience vomiting in the first 48 h following ED discharge.

## Overview of data collection

### Electronic data collection tool

A unique electronic procedural sedation form (Microsoft InfoPath) has been created for each site that aesthetically resembles their paper sedation record (Red Engine, Edmonton, Alberta, Canada). The unique form contains all data elements required for the study as well as information that is captured on their paper sedation record. This eliminates the need for duplicate documentation. Radio buttons, check boxes and dropdown menus have been employed, and functions are automated, where possible, to increase efficiency and data quality. Free text is only permitted for details of medications administered and descriptions of procedures performed if not found in the dropdown menus. Built-in data validation will ensure complete datasets for each patient. Errors in data input and blank fields (including consent questions) are flagged by the programme and corrected by the user at the time of documentation. The electronic sedation forms reside on tablet computers housed on mobile carts which are securely stored in a convenient, accessible area in each ED. The tablet computers are used exclusively for this purpose.

### Definitions

Standardised definitions for sedation terminology (pre-sedation state, efficacy of sedation), time intervals and adverse events have been used according to the Quebec Guidelines.<sup>23 24</sup>

### Study documentation

Study documentation includes patient demographic characteristics, preprocedure assessment and interventions, medication choice, behaviour information, adverse event review and recovery information. Where applicable, free text variables can be inputted by the user in imperial or metric units, but are automatically converted and stored in metric units by the programme. All times are stored in relation to the start of the sedation (time of first sedation medication) which is stored as ‘time zero’. Events prior to the sedation are stored as negative minutes, and events following the sedation are stored as

positive minutes. Details about each data field to be collected and the electronic format for each variable can be found in the online supplementary appendix 2.

## Study procedures

### Training and introduction to electronic documentation

Prior to study initiation, all sites used paper sedation records. The PI (MB) and/or the project technology coordinator (Gabino Travassos) conducted formal small group and one-on-one training sessions for site champions and end users at each site. The site champions completed training of all end users before the site-specific ‘go-live’ date. *Phase I* of training consisted of (1) demonstration of the electronic form by the trainer to the end user either one-on-one or in a small group, (2) end user completion of three sample cases using the electronic documentation form while being directly observed by the trainer. Completion of this step was required by 80% of end users prior to the go-live date. During *Phase II* (2 weeks duration, following the go-live date), site champions and/or research assistants were called in for all sedations taking place in the ED (24 h a day, 7 days a week) to support the team with the electronic documentation for all sedations (‘at elbow’ training). During *Phase III* (6 weeks duration following the end of Phase II), the site champions/research assistants were available on an on-call basis to help the ED team with any problems or questions encountered during the electronic documentation (by telephone and in person on a case-by-case basis). Buy-in was elicited from nursing and medical leadership prior to initiation of the study. Sites have been encouraged to remove all paper sedation records from the ED to maximise the use of the electronic sedation documentation form.

### Procedure for data collection in the ED

When a decision is made that a patient requires ED procedural sedation, the healthcare team member caring for the patient opens the electronic sedation record on the tablet computer and begins documentation. The tablet computer remains with the patient for the duration of their ED stay, as the electronic form is used to document all sedation care, from the preprocedural assessment to recovery and discharge. All documentation is completed by the health professional caring for the patient (physician, nurse, respiratory therapist), minimising the need for research personnel to sustain the study. Informed written consent and/or assent for collection of study information and transmission of de-identified records to a central database is also obtained by the healthcare professional in accordance with the specific requirements dictated by each site’s Research Ethics Board (details below). If a patient/parent does not consent to participation, the sedation is still documented electronically, but the programme logic prevents study information from being saved to the tablet database. At ED discharge, a site-specific sedation paper record is printed from the electronic form which

becomes the official record of care provided to the patient. The printed document is identical to the site-specific sedation record and does not contain any of the extra information collected for study purposes. After printing, the user is asked to submit the form to an encrypted database residing on the tablet computer, saving only information collected for study purposes and discarding all site-specific clinical information. All data fields must be complete and correctly formatted in order for the form to be submitted to the database.

### Data transmission

Research personnel at each site complete a data transfer process, at minimum, on a weekly basis. This manually initiated but automated process transfers records from the tablet computers to a private local network drive and will simultaneously transfer these records in de-identified form to a central database (Clinical Research Informatics Core (CRIC), University of Alberta, Edmonton, Canada). Once the transfer of data to the central database is successful, the records are automatically deleted from the tablet database.

### Patient follow-up

The parents of all patients who experience an adverse event as well as a random sample of 15% of patients who were sedated at each site and who did not experience an adverse event are contacted by telephone within 1 week of their ED discharge. The weekly list of telephone follow-ups for each site is automatically generated by the central database (CRIC) and sent by email to the site coordinator and physician site lead. Parents are asked about their child's occurrence of maladaptive behaviours following the ED sedation using the PHBQ (modified), as well as additional questions about the occurrence of vomiting. These questions can be found in online supplementary appendix 3. Phone calls are conducted by trained, experienced research assistants and coordinators. Three attempts are made to contact the family at varied times of the day. Data is recorded on a standardised paper data collection form.

### Estimation of missed, eligible patients

To estimate the proportion of procedural sedation cases not captured at each site, surveillance for missed cases is performed during the 3rd week of each month. We will extrapolate these numbers to generate overall compliance/consent rates. Since this study will enrol patients for a period of years, daily surveillance for missed patients was thought too onerous for the sites to maintain over the long term. To minimise sampling bias, we monitor all shift times during the 7 days of surveillance. The site coordinator performs a review to identify children who were sedated during this 7-day period but are not registered in the database. Methods to identify missed patients vary by site. Daily hand searching of ED charts, pharmacy record queries and electronic medication dispensing system queries are used depending on

site opinion of the most reliable method at their institution. A medical record review is performed on all missed patients, and an electronic data collection form is used to document the following patient information (1) age, (2) sex, (3) sedation medication received and (4) adverse events experienced.

### Data analysis

Patient, sedation and system-level characteristics, overall and by site, will be summarised using descriptive statistics. Discrete variables will be summarised using frequency and percentage. Continuous variables will be summarised using mean, SD, median, IQR and range, as appropriate.

The primary analysis will use logistic regression to compute OR, by medication, of a serious adverse event, adjusting for key potential confounders: age, body mass index (<25, ≥25), use of preprocedural opioids, nil per os (NPO) ≥6 h for solids, NPO ≥2 h for liquids, presence of an underlying health risk, personnel present (represented as a fraction of 4 possible personnel) and site. ORs will be reported together with 95% CIs. Two-sided p values less than 0.05 will be considered statistically significant.

### Secondary analyses

For the outcomes of (1) an adverse event that could lead to a serious adverse event, (2) a significant intervention being performed in response to an adverse event, (3) any adverse event, (4) successful sedation and (5) paradoxical reaction to sedation, similar analyses to the primary analysis will be performed. The same variables as for the primary analysis will be adjusted for in each of these analyses.

The distribution of duration of sedation will be examined, and if necessary, transformed to achieve approximate normality. Linear regression will be used to examine the relationship between the duration of sedation, procedure type, patient characteristics and occurrence of an adverse event. Length of stay in the ED will be analysed similarly. Residuals will be examined to ensure goodness of fit.

Sedation practices and outcomes in children under 2 years of age will be compared with children aged 2 years and older. For discrete variables, comparisons will be made using Pearson's  $\chi^2$  test or Fisher's exact test, as appropriate. For continuous variables, comparisons will be made using a Student t test or the Wilcoxon test, as appropriate.

The association between preprocedural agitation and adverse events, interventions and outcomes for patients undergoing ketamine sedation will be examined using logistic regression or linear regression as appropriate. Patient characteristics (age, weight, sex), patient state on recovery (age appropriate/age inappropriate), occurrence of adverse events, length of procedure (measured from start of sedation until start of physiological recovery in minutes), total dose of sedation medication administered

(in mg/kg), route of administration (intravenous/intramuscular), and length of stay will be examined in children with and without preprocedural agitation.

The proportion of children experiencing vomiting and maladaptive behaviours, as reported by a summary score on the modified PHBQ<sup>25–27</sup> will be explored overall and by medication administered. Analysis will be conducted separately for the four most common medication combinations, and will be adjusted for important covariates (age, sex, type of procedure, length of procedure (minutes), occurrence of an emergence reaction).

## ETHICS AND DISSEMINATION

### Ethical considerations

There is minimal risk to patients involved in this study, as it is purely observational and will not interfere with patient care. Risks exist in the realm of privacy of data. Identifying patient information (name, medical record number) will be stored in study records in the tablet database. The following steps have been taken to ensure maximal privacy for all records stored on these computers: (1) the tablet database is encrypted making it difficult to easily access information (2) there is restricted access to these computers with a user authentication process (3) all files are deleted from the tablet database once the central data transfer process is complete (performed at minimum, once per week). We estimate that a maximum of five records will be contained in a tablet database at anytime. No further identifying information will be contained in the database. Date of birth is stored as age and all times and dates are recorded as minutes prior to or following the sedation. These study processes have been approved by the privacy commissioner at all participating sites.

Research Ethics Board approval has been obtained from all participating sites. The informed consent process varies by site as approved by each individual Research Ethics Board. The Montreal Children's Hospital, The Hospital for Sick Children, Children's Hospital of Eastern Ontario and the IWK Health Centre only enrol patients after written informed consent has been obtained from parents or legal guardians. Assent is also obtained at these sites from participants over 7 years old. Stollery Children's Hospital and Alberta Children's Hospital enrol patients if verbal consent is given by the parent or legal guardian. Consent is obtained for the possibility of receiving a follow-up telephone call within 1 week of ED discharge.

### Knowledge translation

A multifaceted knowledge translation strategy will be used. We will disseminate the results of this study at international conferences, in manuscripts in peer-reviewed journals, and to a broad range of stakeholders using the PERC and TREKK (TRanslating Emergency Knowledge for Kids) networks. TREKK is a unique partnership, and knowledge exchange between 36 general EDs across

Canada and 12 PERC sites. The annual PERC and TREKK meetings and internal communication structures of these organisations will allow knowledge gained in this study to be widely and rapidly disseminated.

This cohort will represent the largest known ED procedural sedation cohort allowing us to explore predictors (patient, sedation and system factors) leading to the safest sedations for children. To further ensure distribution of study results and best sedation practices, the principal investigator will work with PERC and TREKK sites to create multidisciplinary improvement teams within each institution in order to develop systematic improvements in sedation care and patient outcomes.

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**Contributors** MB, GJ and DWJ created the study concept. MB, MGR and DWJ led the design and selected outcome measures. MB wrote the first draft of the manuscript with contributions from DWJ, MGR, KJF, SA, ASD, AD, CMMcT, SB and NB. MB, DWJ, MGR, KJF, SA, ASD, AD, CMMcT, SB and NB provided critical review and have given final approval of the submitted manuscript.

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**Competing interests** None declared.

**Ethics approval** Ethics approval has been obtained from the institutional research ethics boards at all six participating sites. Specifically, the IWK Health Center, Halifax (1003634), Montreal Children's Hospital, Montreal (PED-07-027), Children's Hospital of Eastern Ontario, Ottawa (#09/15X), The Hospital for Sick Children (1000024842), Stollery Children's Hospital, Edmonton (Pro00003165), Alberta Children's Hospital, Calgary (E-21351).

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