Practice Recommendations for Procedural Sedation in Paediatric Specialty Outside Operation Room

Version	Effective Date
3.0	01/05/2021

Document Number	HAHO-COC-GL-PAE-001-v03
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Custodian	Secretary, Coordinating Committee in Paediatrics
Approved/ Endorsed By	Coordinating Committee in Paediatrics
Approval Date	30 October 2020
Distribution List	Ha Staff working in paediatric specialty

Remarks: Paediatric Procedural Sedation Record on Page 75 has been further updated on 27 April 2021.

ACKNOWLEDGEMENT

This is a joint project of Coordinating Committee in Paediatrics, Hospital Authority and Hong Kong College of Paediatricans

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Working Group would also like to thank Dr Amy N M Chan, AC (Paed), QEH and Dr Grace Chiang, AC (Paed), AHNH in helping out the review and meta-analysis of intranasal dexmedetomidine.

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SECTION A: GENERAL PRINCIPLES

I. INTRODUCTION:

1. Advances in the treatment of paediatric diseases have led to an increase in the number of diagnostic or painful therapeutic procedures for which children will need effective sedation or anaesthesia. The choice between no sedation, sedation or anaesthesia will depend on the types of procedures, the characteristics of the patient, and possibly available manpower and resources of the individual hospital.

2. In adults, many procedures can be undertaken with local anaesthesia and reassurance. In children this is often not possible because of developmental immaturity or because the procedures are frightening and painful.

3. Sedation may not always be successful and occasionally the procedure has to be cancelled or re-scheduled. Sedation failure is not only distressing and inconvenient for both the children and their parents, it may hinder diagnostic and/or therapeutic plans as well as has major cost implications.

4. Sedation is not without risk. The risks of sedation include the following:
   - Sedation can cause unintended loss of consciousness.
   - Sedation can lead to depression of protective reflexes leading to airway obstruction.
   - Sedation can cause respiratory and cardiovascular depression.
   - It is possible that excessive amounts of sedatives may be used inadvertently to compensate for inadequate analgesia.
   - Sedation may outlast the procedure.
   - There are wide variations of patient's response to sedation, particularly in neonates, small infants or children with pre-existing medical conditions.

5. Many diagnostic and therapeutic procedures to be performed will require adequate sedation. Examples include CT scan, MRI scan, laceration repair, lumbar puncture and orthopaedic procedures, etc. In most cases, regardless of the types of procedures, young children often require at least moderate sedation for these procedures.

6. For these reasons, it is important for all medical practitioners to understand that safe sedation of children requires a systematic approach that includes the following:

   Medical practitioners:

   - Adequate medical supervision by experienced staff
   - Clear understanding of the pharmacokinetic and pharmacodynamic effects of the medications used for sedation
   - Appropriate training and skills in airway management
   - Sufficient number of healthcare workers to carry out or help out the procedure and monitor the patient

   Equipment, medication and venue:

   - Age and size appropriate equipment for airway management, venous access and resuscitation
   - Appropriate medications and reversal agents
   - Appropriate physiologic monitoring during and after the procedure
   - Properly equipped and staffed recovery area

Patient assessment:

- Careful pre-sedation evaluation (including physical examination) for underlying medical or surgical conditions that would place the child at increased risk from sedating medications
- Appropriate fasting for elective procedures and a balance between depth of sedation and risk for those who are unable to fast because of the urgent nature of the procedure
- Recovery to pre-sedation level of consciousness before discharge from recovery area
- Appropriate home discharge instructions

7. To enhance standards of patient care, the "Practice Recommendation for Sedation of Children in Diagnostic and Therapeutic Procedures" was published in 2013, based on references from literatures, local and international guidelines, and survey of existing practices within the Hospital Authority [1-57].

8. The present document makes reference to the previous practice recommendation in 2013. We have applied an updated methodology for evidence-based guideline production. We specifically identified several important clinical questions and addressed them in detail. We searched for the most updated evidence from multiple sources, evaluated the quality of evidence and produced recommendations according to the *Grading* of *Recommendations*, Assessment, Development and Evaluations (GRADE) methodology [58-61].

9. For general recommendations based on empirical evidence and good clinical practice where we thought it would not be fruitful to carry out in-depth appraisal of evidence, we provide general recommendations made in accordance with existing guidelines and consensus within the Working Group [62-64].

II. SCOPE OF THE RECOMMENDATION:

1. This Recommendation applies to all paediatric patients who receive sedation for any diagnostic, therapeutic, or interventional procedure under paediatric specialty in Hong Kong. Other specialties taking care of paediatric patients are welcome to make reference to this Recommendation where applicable and appropriate.

2. This Recommendation does not apply to:
   - Children receiving general anaesthesia (GA) and monitored anaesthesia care (MAC) by anaesthesiologists within or outside operating rooms
   - Sedation of children or neonates under intensive care management in Paediatric / Neonatal Intensive Care Unit (PICU / NICU)

III. DEFINITION OF SEDATION

1. Sedation is the depression of the central nervous system and/or reflexes by the administration of drugs by any route to decrease patient discomfort without producing unintended loss of consciousness.

   A. *Minimal Sedation (Anxiolysis):*
   A drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are unaffected.

B. *Moderate Sedation (Previously called Conscious Sedation)*:
A drug-induced depression of consciousness during which patients respond purposefully to verbal commands either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is maintained.

C. *Deep Sedation:*
A drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated or painful stimulation. Patients may require assistance in maintaining a patent airway and spontaneous ventilation may be inadequate.

D. *General Anaesthesia:*
A drug-induced loss of consciousness during which patients are not arousable, even to painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation. Cardiovascular function may be impaired.

SEDATION CONTINUUM				
	Minimal Sedation (Anxiolysis)	**Moderate Sedation (Conscious Sedation)**	**Deep Sedation**	**General Anaesthesia**
Responsiveness	Respond normally to verbal commands	Purposeful response to verbal or tactile stimulation	Purposeful response following repeated or painful stimulation	Unarousable even with painful stimulus
Airway	No intervention required	No intervention required	Intervention may be required	Intervention required
Spontaneous Ventilation	Adequate	Adequate	May be inadequate	Frequently inadequate
Cardiovascular Function	Maintained	Usually maintained	Usually maintained	May be impaired

Table 1: Definition of Sedation

2. The different stages of sedation represent a CONTINUUM and patients may quickly move from one level of sedation to another, resulting in the loss of the patient's protective reflexes. Therefore, medical practitioners who sedate children must be prepared to manage all levels of sedation, even if only moderate sedation is intended. There must be appropriate physiologic monitoring and continuous observation by personnel not directly involved with the procedure so that there can be accurate and rapid diagnosis of complications and initiation of appropriate rescue interventions.

IV. ASSESSMENT OF SEDATION

1. The assessment of sedation is difficult in children and depends on their verbal abilities, age, level of maturity, and current and underlying clinical conditions.

2. A common problem is the misinterpretation of any movement in response to touch or painful stimulus as "purposeful". Examples of purposeful movements include eyes opening, crying, saying "ouch," or pushing away the offending stimulus. Purely reflexive activities, such as the gag reflex, simple withdrawal from pain, or making inarticulate noises, do not constitute appropriate responses for the purpose of this definition. A sedated child who displays only reflex activities in response to tactile or verbal stimulation is in a state of deep sedation and should lead to an escalation of care because airway obstruction and respiratory depression may occur.

3. Accurate assessment of the depth of sedation is important as children may move rapidly into deep sedation, which will require an escalation of monitoring and a greater degree of vigilance. Because of their user friendliness, observational scoring systems are commonly used to assess sedation depth in clinical settings. The University of Michigan Sedation Score (UMSS) is a simple clinical observational scale to assess sedation depth over the entire continuum from the awake to unarousable state. It is reliable and valid in detecting changes in the level of sedation in children in clinical settings. (*Appendix A*)

SECTION B: GENERAL RECOMMENDATIONS

I. PRE-SEDATION ASSESSMENT

1. Before sedation, a pre-sedating evaluation will need to be performed by the medical doctor in-charge of the patient or by the doctor performing the sedation as appropriate. The purpose of this evaluation is not only to document baseline status but also to determine if the patient presents any specific risk factors that may warrant optimisation and consultation of appropriate specialist(s) before sedation. This evaluation will also screen out patients whose sedation will require more advanced airway or cardiovascular management skills and thus warrant the presence of an experienced medical practitioner or anaesthesiologist.

2. Pre-sedation assessment should include (more detailed information in Paediatric Procedural Sedation Record template):
   - Age of the child
   - Weight of the child in kilogram
   - Allergies and previous adverse drug reactions
   - History of sedation or general anaesthesia and any complications or unexpected responses
   - Current medical history and history of co-morbidities, disorders and hospitalisation
   - Medical diseases that might increase the potential for airway obstruction, such as a history of snoring or obstructive sleep apnoea
   - Current medications
   - Baseline vital signs, including heart rate, blood pressure, respiratory rate, and body temperature
   - Physical examination, including a focused evaluation of the airway, pulmonary and cardiac status
   - American Society of Anesthesiologists (ASA) physical status evaluation. (*Appendix B*)

II. PATIENT SELECTION FOR SEDATION

1. Children who are in ASA class I or II are frequently considered appropriate candidates for sedation.

2. Children with the following medical conditions are at increased risk of complications during sedation. Presence of experienced medical practitioners or anaesthesiologist is strongly recommended.

   ASA Physical Status III or IV
   Procedures requiring deep sedation
   History of airway obstruction (e.g., large tonsils), difficult tracheal intubation, loud snoring, obstructive sleep apnoea and central apnoea. (*Appendix C*)
   History of failed sedation, over-sedation or paradoxical response to sedation
   Prematurity or ex-premature infant, especially those with post conceptual age < 60 weeks. (*Appendix D)*
   Active pulmonary, cardiovascular, gastrointestinal, neurologic problems
   Poorly controlled asthma
   Obesity
   Poorly controlled seizures
   Uncontrolled gastro-oesophageal reflux
   Severe developmental delay
   Sedation in patients with a full stomach

III. FASTING (more detailed information in Appendix E)

1. Patients undergoing sedation for elective procedures should not have fluids or solid foods for a sufficient length of time to allow for gastric emptying and prevention of aspiration during sedation. However, unnecessarily long fasting may aggravate the feeling of hunger and stress, especially in small children, and result in reduction of sedation efficacy [65] and failure of procedural sedation [66, 67].

2. In general, risk of pulmonary aspiration in non-high risk procedural sedation is low. Studies revealed a very low incidence of aspiration of 2 and 2.2 per 10,000 cases respectively for both elective and emergency sedation without adequate fasting [68, 69].

3. Fasting does not guarantee that gastric emptying is complete [70].

4. For URGENT procedures in a child who has not been adequately fasted, the benefits of the procedures must be balanced against the possible risk of aspiration. URGENT procedural sedation should not be delayed based on fasting time alone [64, 71-73].

5. For children who are not at increased risk of delayed gastric emptying and thus not in the high risk group*, undergoing ELECTIVE procedures requiring / potentially requiring sedation other than oral chloral hydrate only, the new "1-4-6-8 rule" on fasting time as employed in general anaesthesia can be used [64, 74-77]:

   - Clear fluids** (up to 3ml/kg) is allowed up to 1 hour prior to sedation
   - Breast milk is allowed up to 4 hours prior to sedation
   - Formula milk and light meal are allowed up to 6 hours prior to sedation
   - Heavy meal or fatty food are allowed up to 8 hours prior to sedation

   *High risk groups refer to patients with delayed gastric emptying, include but not limited to: Gastro-esophageal reflux (GERD), renal failure, severe cerebral palsy, enteropathies, esophageal strictures, achalasia, diabetes mellitus with gastroparesis, and/or surgical abdominal conditions.

   **Examples of clear fluids include water, glucose water, infant electrolyte solutions, natural or artificial fruit juices without pulp, carbonated beverages, clear tea, and black coffee without any type of creamer or milk.

6. For non-high risk children undergoing oral chloral hydrate sedation only with sedation level UMSS ≤ 2 (*Appendix A*) [65, 66]:

   - Clear fluids (up to 3ml/kg) is allowed up to 1 hour prior to sedation [74, 75]
   - Milk is allowed up to 2 hours prior to sedation [78, 79]

7. Unless patient is on strict NPO order in the high risk aspiration group or for other reasons, essential oral medication can still be taken with a sip of water in the non-high aspiration risk children during the fasting period prior to sedation.

8. Recently, an international multidisciplinary consensus statement on fasting before procedural sedation in adults and children [80] was published which advocates less stringent fasting recommendations (the recommendations are based on extensive literature search and consensus developed using Delphi methodology). The consensus statement is undergoing peer review. Updated fasting recommendation for children under procedural sedation will be further reviewed in the future (Appendix E).

IV. TIME-OUT

Pre-procedural pause or "time-out" of the diagnostic or therapeutic procedure should be performed according to the hospital policy. It is performed immediately before the intended procedure. The "time out" includes a process of confirmation of the correct patient, verification of informed consent, confirmation of the correct procedure and site or side of the procedure. No intravenous sedation will be administered without completion of the "time out" procedure although oral sedation may be given in ward before the "time-out".

V. INTRAVENOUS ACCESS

1. Intravenous access when considered necessary should be established before sedation. It should be maintained throughout procedure until the child is safe from cardiopulmonary depression.

2. Intravenous access may not be necessary for patients undergoing light to moderate sedation with oral sedating agent alone for non-invasive procedures such as echocardiography, electrodiagnosis and neuroimaging.

VI. NON-PHARMACOLOGICAL METHODS (more detailed information in Appendix F)

Evidence-based recommendations for non-pharmacological method

- Non-pharmacological strategies can be considered as an adjunct or to replace pharmacological sedation in selected patients, taking into consideration of individual patient characteristics, technical availability and feasibility in different settings. These strategies may include a child-friendly environment, feed and wrap technique in infancy, distraction with audio-visual system and participation of trained child life specialists. (Weak recommendation, low quality of evidence)

- For painful procedures, techniques such as distraction, hypnosis, combined cognitive behaviour therapy, and breathing interventions may be helpful in older children, whereas sucking-related intervention and swaddling may benefit preterm babies and neonates. (Weak recommendation, low quality of evidence)

VII. USE OF IMMOBILISATION DEVICES

Immobilisation devices, if used, should be applied in such a way as to avoid airway obstruction or chest wall movement restriction. The child's head position and chest respiratory excursions should be checked frequently to ensure airway patency. The child should never be left unattended.

VIII. PERSONNEL AND TRAINING

1. For patient who just received minimal to moderate sedation with oral sedating agent alone or intranasal dexmedetomidine for a non-painful non-invasive procedure (e.g., transthoracic echocardiography, electrodiagnosis and neuro-imaging), monitoring and escort may be carried out by trained healthcare personnel, if considered appropriate after a pre-sedation assessment, and a post procedure sign-out assessment (see Paediatric Procedure & Sedation Record template).

2. The healthcare personnel escorting these low risk patients should be able to interpret the normal range of SPO2 and pulse rate displayed on the transport oximeter monitors. They also have ready access to a communication system, e.g. DECT phone, intercom system or cardiac arrest call bell, as appropriate so that they can contact trained healthcare professional whenever necessary and without delay. The proper functioning of the communication system should be regularly checked as DECT

phones or similar systems may fail in certain underground locations e.g., MRI, tomography centre. Trained healthcare professional should be readily available to supervise the healthcare personnel if the child develops any signs of sedation-related adverse effects (e.g. over-sedation, oxygen desaturation and airway obstruction, etc.).

3. If the child is assessed to have increased risk of sedation-related adverse events (e.g., ASA class III or IV, post conceptual age < 60 week old, see appendix D) increased vigilance and continuous monitoring by dedicated trained healthcare professional (e.g., nurse or doctor) should be arranged.

4. For procedures that require moderate sedation by the intravenous route, there should be a medical doctor responsible for administering sedation and monitoring the patient throughout the procedure. It is a good practice to have another healthcare professional (usually a nurse or another doctor) to assist the sedation and monitoring. This assisting healthcare professional may be allowed to participate in helping the procedure if the patient's level of sedation and vital signs are stable. In case the patient develops any significant changes in vital signs, all staff should give full attention to the patient.

5. In the clinical scenarios mentioned in 4 above that the medical doctor administering the sedation is also responsible for performing the procedure, then the second healthcare professional (usually a nurse or another doctor) must be available and fully dedicated to provide CONTINUOUS monitoring of the patient's conscious level and cardio-respiratory status. In this scenario, the assisting healthcare professional should not participate in the procedure and must pay full attention to the patient's sedation levels and vital signs.

6. Sedation is a continuum. Some patient may progress to a state of deep sedation (with risk of airway obstruction, respiratory and cardiovascular depression) despite the original intent of moderate sedation. Increased vigilance and extra trained healthcare professional should be readily available if this occurs. The trained healthcare professional providing sedation must be competent in rescuing the patient from deep sedation and its associated complications.

7. Deep Sedation:

   7.1 For procedures that require a deep level of sedation, e.g., bronchoscopy, there MUST be a dedicated medical doctor responsible for administering sedation and monitoring the patient throughout the procedure (*Appendix G*). It is also good to have another dedicated trained healthcare professional (usually a nurse or another doctor) to assist the sedation and monitoring. The trained healthcare professional should give full attention to the sedation process and monitoring of the patient. They should not engage in the procedure itself.

   7.2 Procedures requiring deep level of sedation are often prolonged, painful and / or invasive (e.g., paediatric flexible bronchoscopy, upper gastrointestinal endoscopy, etc.). Deliberate obtundation of airway reflexes by local anaesthetic sprays may be needed for the procedure. The risks of deep sedation during these procedures may be indistinguishable from those of general anaesthesia. The sedation should only be carried out by EXPERIENCED medical practitioners trained to perform these procedure-specific paediatric sedation techniques. Airway protection (by tracheal intubation) should be considered, if appropriate. If tracheal intubation is needed, this often means general anaesthesia (by anaesthesiologist) or intensive care management is required.

   7.3 Individual hospitals should identify the commonly performed diagnostic or therapeutic procedures in children that ROUTINELY require deep level of sedation. Only EXPERIENCED medical doctors trained can be considered as appropriate in performing sedation for these procedures. Alternatively, provision of regular general anaesthesia or monitored anaesthetic care (MAC) session or anaesthesiologist-led sedation service should be considered by the hospitals, if appropriate.

7.4 If the patient has any serious or unstable medical condition, the appropriate specialist should be consulted to optimise the patient's condition prior to any planned procedure under sedation. The involvement of an experienced medical doctor or anaesthesiologist should be considered to provide sedation or general anaesthesia as appropriate. Admission and monitoring in PICU should also be considered.

8 Healthcare professional responsible for pre-sedation assessment, provision of sedation, and monitoring of the children for sedation must be competent in the following areas:

- Good understanding of the basic physiology of the sedation process
- Knowledge and familiarity with the proper drug dosages for children and properties of the various sedative agents
- Ability to recognise and manage adverse reactions and overdose of sedative drugs.
- Proficiency of skills in airway management, provision of respiratory support, and cardiovascular resuscitation. At least one of healthcare professional is required to have attended the relevant training courses in paediatric sedation or life support. Medical staff providing paediatric sedation is encouraged to have continuous update with the prevailing guideline on paediatric sedation.

9 Healthcare personnel responsible for monitoring and escort of children under the influence of intravenous sedative medication should receive appropriate training in the following areas:

- Assessment of levels of sedation
- Observation of vital signs (including skin colour, respiratory rate, pulse rate, SpO_2 monitoring and blood pressure monitoring, as appropriate)
- Recognition and immediate care of the common sedation-related adverse effects, e.g. cyanosis, complete or partial airway obstruction, apnoea, hypoventilation, bradycardia, oxygen desaturation, nausea / vomiting and over sedation, etc.
- Transport monitors (e.g. portable pulse oximeter, ECG, BP, +/- capnography, as appropriate) should be used.

IX. FACILITIES AND MONITORING

1. The procedure should be performed in a location with adequate space, staff and equipment to deal with any possible cardiopulmonary emergency. All equipment and drugs must be checked and maintained on a scheduled basis. It is critical that a complete range of sizes of emergency and monitoring equipment be available for children of all ages and sizes.

2. The requirement list should include:
   - Adequate area and lighting for procedure and resuscitation
   - An operating table, bed or trolley, which can be tilted, should preferably be available
   - O_2 supply and suction and appropriate size suction catheters
   - A defibrillator should be available in close proximity. Defibrillation paddles for children should be available
   - Intravenous and airway management equipment (*Appendix H*)
   - Emergency medications (*Appendix I*)
   - Physiological Monitoring:
     - ✧ A stethoscope
     - ✧ Continuous pulse oximetry with appropriate probes for children
     - ✧ Blood pressure measuring device with appropriate paediatric cuffs
     - ✧ ECG as appropriate. Appropriate ECG electrode size for neonate, infants and children should be available
     - ✧ A means for the monitoring of respiration/ventilation, either visually or by continuous end tidal CO_2 (capnography) monitor***. The detail use of capnography and interpretation of its wave forms can be found from various references [81] and is beyond the scope of this recommendation.

   *** More detailed information on capnographic monitoring in *Appendix J*.

Evidence-based recommendations for Capnography

- We suggest that capnography is not routinely required for healthy children undergoing procedural sedation. (Weak recommendation, low to very low quality of evidence)
- As patients with conditions of ASA class III to V or with abnormal ETCO2 / pulse oximetry or requiring baseline O_2 were excluded in the design of reviewed studies, there is no evidence-based recommendation in these patient groups. The use of capnography in children with co-morbidities (e.g., those with syndromal diagnosis or congenital upper airway obstruction, e.g., Pierre Robin sequence or with abnormal ETCO2 or pulse oximetry) would need to be based on clinical judgment. (No recommendation)
- We suggest that capnography may be considered in the procedural sedation for GI endoscopy procedure. (Weak recommendation, low quality of evidence)

3. Continuous monitoring of oxygen saturation and heart rate, regular observation with time-based documentation of the vital signs, level of sedation and ventilatory function should be carried out until the patient meets discharge criteria.

4. For moderate sedation, patient parameters would be recorded every 10-15 minutes. If deep sedation is targeted or if a patient has significant underlying illnesses, vital signs should be measured at least every five minutes. As a practical consideration, unnecessary stimulation may hinder the sedation outcome and procedural success. Medical staff would need to exercise judgement with respect to the overall sedation risk, the type of procedure and the condition of the patient [62, 82, 83].

X. ADMINISTRATION OF MEDICATIONS

1. All medications should be checked according to hospital policy before being administered. (*Appendix I*)

2. Sufficient time must elapse between doses to allow the effect of each dose to be assessed before additional drug administration.

3. When drugs are administered by non-intravenous routes, allowance should be made for the time for drug absorption (expected drug effect onset time - e.g. 30 min for chloral hydrate and intranasal dexmedetomidine) before supplementation is considered.

4. Whether to give additional doses of a first-line agent (e.g. chloral hydrate) or second-line agent (e.g. rescue intranasal dexmedetomidine or IV midazolam) is subject to consideration of individual case nature, amount of the first dose given, perceived tolerance of side effect of different drugs and the prior fasting duration.

5. Concomitant uses of opioid analgesic will aggravate the sedative-induced respiratory depression of patient.

6. Appropriate dose reduction is necessary if both sedatives and analgesics are used and in certain at-risk patients.

Pharmacodynamics/kinetics of sedation drugs

Drug	**Onset time**	**Peak**	**Duration**	**Reference**
Chloral hydrate (PO)	15-30 mins	-	1-2 hrs	Lexi-comp
	10-15 mins	30-60 mins	1.29 hours (+/- 1.05 hours	Micromedex
Midazolam (IV)	3-5mins	3-5 mins	< 2 hrs [dose dependent]	Lexi-comp
	1-3 mins	-	20-30 mins	Micromedex
Dexmedetomidine (IN)	45-60 mins	90-105 mins	60-120 mins	Lexi-comp
	25 mins	30-60 mins	85 mins	Micromedex
	20-30 mins		45-60 mins [up to 120 mins possible]	Oxford paediatric procedural sedation handbook
Ketamine (IV)	30 sec	-	5-10 mins	Lexi-comp
	2 mins	-	-	Micromedex
	30-60 sec		10-15 mins	Oxford paediatric procedural sedation handbook

XI. DOCUMENTATION

1. Adequate documentation of all aspects of patient evaluation and monitoring is essential for high quality patient care. Using a standardized Sedation Form can facilitate the documentation. (See Paediatrics Procedural Sedation Record template for reference.)

2. This documentation shall include, but is not limited to:

A. *Pre-sedation Preparation:*
- Pre-sedation medical evaluation
- Fasting Status
- Consent

B. *Sedation Record –A Time-based Flow Sheet*
- Dosage, route, and time of administered drugs
- Patient's response to medication and the procedure
- Patient's vital signs, physiological data and level of sedation
- Any oxygen supplementation, its flow rate and duration, and method of administration
- Any interventions such as intravenous treatment or reversal therapy and the patient's response
- Any untoward reactions and their management

C. Post-sedation Monitoring and Discharge Criteria

- The criteria for discharge from the sedation area and disposition of the child are specified

XII. MANAGEMENT AFTER THE PROCEDURE

1. After the procedure, continuous monitoring of patient is mandatory until the following criteria are met:
   - Patient has a patent airway
   - Patient shows protective airway and breathing reflexes
   - Patient is haemodynamically stable
   - Patient is easily roused

2. Monitoring is preferably carried out in a recovery area near the procedure site.

3. If a recovery area is not available, the patient should be escorted back to the ward for continuous monitoring. During transport, the vital sign should also be monitored continuously by medical staff. Oxygen supplementation should be considered during transport. Suitable resuscitative equipment (e.g. manual resuscitative bag/valve/mask, airway devices etc.) and emergency medications should be prepared and carried. For the patient who has just received moderate sedation with an oral sedating agent (chloral hydrate) alone, the escort may be carried out by trained healthcare personnel if the patient is assessed to be stable by appropriate medical staff.

XIII. HOME DISCHARGE

Ensure that all of the following criteria are met before the child is discharged to home:

- Airway patency and cardiovascular function are satisfactory and stable
- The patient is alert, and protective reflexes are intact
- The patient can talk (if age-appropriate)
- The patient can sit up unaided (if age-appropriate)
- For a very young or handicapped child incapable of the usually expected responses, the pre-sedation level of responsiveness or a level as close as possible to the normal state of the child should be achieved
- The state of hydration is adequate
- The child should be accompanied by a parent or a responsible adult caretaker who should not be the driver
- The responsible adult should be provided with information on what to look out for after sedation and on how to obtain medical advice if problems arise

XIV. REPORTING AND AUDIT

1. It is important to have a mandatory reporting system for adverse events during procedural sedation to prospectively collect information for quality improvement. This will be very important when new procedural steps or medications are being introduced.

2. Tracking and Reporting Outcomes of Procedural Sedation (TROOPS) [84] is an international, multidisciplinary, consensus-based standardized tool applicable for all types of sedation practice. Modifications (with prior approval) are made and are incorporated into the Paediatrics Procedural Sedation Record template.

3. In-charge doctors are required to document shortly after the procedure finished on any adverse event has occurred during the procedure and to check the relevant boxes on the TROOPS table in the Paediatrics Procedural Sedation Record.

4. To facilitate prospective collection and future audit of patient outcomes, two new procedural codes (**oral sedation** and **administer intranasal sedation**) were created in the Hospital Authority Clinical Management System (CMS). A Generic Clinical Form in the CMS on the adverse event and outcome of sedation are now under preparation for easy reporting and future review.

5. For procedural sedation in long stay patients, in-charge doctors are advised to input the appropriate procedural and diagnostic codes after each procedure instead of coding upon discharge.

6. The following events, if occurred during the procedural sedation in Hospital Authority, will need to be reported to the Adverse Incident Reporting System (AIRS):

    - Tracheal intubation
    - Neuromuscular blockade
    - Pulmonary aspiration
    - Chest compressions
    - Vasoactive drug administration
    - Neurological deficit

7. Patient death if occurred during the procedural sedation in Hospital Authority will need to be reported as a Sentinel Event.

8. Future audit will be carried out to monitor the coding, adverse outcome reporting and the quality and safety of procedural sedation.

SECTION C: CHOICE OF DRUGS FOR DIFFERENT PROCEDURES AND DRUG INFORMATION

I. CHOICE OF DRUGS FOR DIFFERENT PROCEDURES

In relation to the choice of medications for sedation, we sought to enhance the evidence base for the recommendations. Therefore, we sought to make recommendation by GRADE methodology based on the questions:

- Is chloral hydrate effective and safe compared to other sedatives for paediatric patients undergoing procedural sedation? (Refer to *Appendix K*)
- Is intranasal dexmedetomidine effective and safe compared to other sedatives for paediatric patients undergoing procedural sedation? (Refer to *Appendix L*)

Detailed general recommendations are described below.

1. Painless procedures that require immobilization.

Examples: CT, MRI, DMSA scan, DTPA scan, bone scan and radiotherapy. Sedation is usually not required for co-operative children above 8 years of age. Extra care with reduction of the recommended dosage may be required in patients with pre-existing CNS depression.

A. First Line Drugs (see Chart 1)

Oral Chloral Hydrate	➢ **Usually for patients <3 years old (best for <2 years old or < 15kg)** ➢ **The drug is less effective in children above 3 years old. In children older than 5 years or in uncooperative children, consider using other medications.**
Neonate	➢ Inpatient: 30 to 50 mg/kg/dose to be given 45-60 minutes prior to procedure; doses up to 100 mg/kg may be used with respiratory monitoring. ➢ Outpatient: avoid sedation; can try feed and wrap +/- oral surcrose
Child ≥ 1 month	➢ 30 to 75 mg/kg/dose [max 1g per dose] to be given 45-60 minutes prior to procedure; may be increased up to 100 mg/kg or 2g per procedure if necessary.
Contraindication	➢ Liver failure, hepatic encephalopathy, severe cardiac disease, severe renal impairment

Intranasal Dexmedetomidine	➢ **Can be used as a first line agent in selected children 1 month to 9 years old, e.g. in children prone to vomiting or anticipated ease of administration with intranasal formulation.**
1 **month - 9 years**	➢ 2-3 microgram/kg/dose ➢ Max 200 mcg [100 mcg per nare] ➢ An additional dose may be administered in 30 minutes if necessary ➢ Max cumulative dose 4 microgram/kg
>9 years	➢ Insufficient data to demonstrate the efficacy in this population
Relative contraindication	➢ Heart block, severe hepatic impairment; ➢ Concomitant use of beta blockers

Intravenous Midazolam	➢ Intravenous Midazolam is often used instead of chloral hydrate for children 3 years of age or above.
1-5 months	➢ Limited data available in non-intubated infants; infants < 6 months are at higher risk for airway obstruction and hypoventilation; titrate dose with small increments to desired clinical effect; monitor carefully [Lexicomp] ➢ Initially 0.025-0.05 mg/kg, to be administered over 2-3 minutes, 5-10 minutes before procedure, dose can be increased if necessary in small steps to max total 0.2 mg/kg per course
Child ≥ 6 months	➢ 0.05-0.1 mg/kg, titrate and repeat doses if necessary after 2-3 minutes ➢ Max total dose = 0.6 mg/kg or 6 mg for 6 months to 5 years ➢ Max total dose = 0.4 mg/kg or 10 mg for 6 years or above

B. <u>Second Line Drugs:</u> *(If first line fails, see Chart 2)*

Intravenous Midazolam	Neonate: 0.05-0.15 mg/kg slow infusion over 5 min with cardiorespiratory monitoring [Neofax] Child ≥ 1 month: Refer to Midazolam under first line drug

Intranasal dexmedetomidine ***1month – 9 years***	Rescue (after chloral hydrate failure) 1-2 microgram/kg/dose

Intravenous Ketamine	
<3 months	➢ Contra-indicated [Lexi-comp as per American College of Emergency Physicians recommendation 2011]
≥ 3 months	➢ 1-2 mg/kg, if initial sedation inadequate or repeated doses are necessary to accomplish a longer procedure, may administer additional doses of 0.5-1 mg/kg every 5-15 minutes as needed [Lexicomp] ➢ Maximum up to a total dose of 4 mg/kg IV over 20 minutes for difficult patients. (See "Point 7. Precautions" under Ketamine)

Should the above measures fail, the procedure may have to be postponed and referral to an anaesthesiologist be considered.

Chart 1 Paediatric Sedation for Non-Painful Procedure (First Line Drugs)

First Line Drugs

Chloral Hydrate *(Preferred for children < 3 yrs)*	***OR***	***Intranasal Dexmedetomidine*** *(for 1mth – 9 yrs If chloral hydrate is contra-indicated / patient prone to vomiting or ease of administration)*	***OR***	***Intravenous Midazolam*** *(Preferred for children ≥ 3 yrs)*
Neonate: 30 to 50 mg/kg/dose; Up to 100 mg/kg with respiratory monitoring		**Child 1 month – 9 years:** 2-3 mcg/kg once; Max 200 mcg (100 mcg per nare); Max cumulative dose 4 mcg/kg		**Child 1 month – 5 months:** 0.025-0.05 mg/kg; Max total dose 0.2 mg/kg
Child ≥ 1 month: 30 to 75 mg/kg/dose (max 1g per dose); Maximum total dose 100 mg/kg or 2 g per procedure				**Child ≥ 6 months:** 0.05 – 0.1 mg/kg; Max total dose 0.6 mg/kg or 6 mg for 6 months to 5 years; 0.4 mg/kg or 10 mg for 6 years or above

Chart 2 Paediatric Sedation for Non-Painful Procedure (Second Line Drugs)

Second Line Drugs
(If first line drug fails)

Intranasal Dexmedetomidine *for chloral hydrate failure*	***OR***	***Intravenous Midazolam***	***OR***	***Intravenous Ketamine***
Child 1 month – 9 years: 1-2 microgram/kg once; Max 200 microgram (100 microgram per nare)		**Neonate:** 0.05-0.15 mg/kg slow infusion over 5 min with cardiorespiratory monitoring [Neofax] **Child ≥ 1 month:** Refer to Midazolam under first line drug		**Child ≥ 3 months:** 1-2 mg/kg; Up to maximum total dose of 4 mg/kg IV

2. Painful Short Procedures (refer to Chart 3)

Oral sucrose given pre-emptively to neonate or young infants before painful procedure has been shown to have mild analgesic effect in various studies. This can be considered to facilitate the procedure without altering patient's sedation level. Detail discussion of the evidence of analgesic effect of oral sucrose is beyond the scope of the present recommendation.

For other procedures like: biopsies with or without image guidance (CT, ultrasound or fluoroscopy), reduction of intussusception, bone marrow aspiration, lumbar puncture and pleurocentesis.

A. *Midazolam*
Midazolam 0.05 - 0.1 mg/kg IV initially, titrate and repeat if necessary after 2-3 minutes, up to a maximum dose of 0.4 mg/kg, together with local anaesthetic. It should be noted that the **midazolam dose may need to be reduced when combined with fentanyl or ketamine**.

OR

B. *Fentanyl*
1-2 microgram/kg IV (max: 50mcg/dose) [BNFc and Lexicomp]. If no respiratory depression is observed in 5 minutes, carefully titrate with ***midazolam*** IV boluses up to a maximum dose of 0.2 mg/kg (for midazolam).

OR

C. *Ketamine*
Refer to ketamine as second line drug for painless procedure above.

Chart 3 Paediatric Sedation for Painful Short Procedure

Option 1

Midazolam can be given together with local anaesthetic or fentanyl, or ketamine

It should be noted that the midazolam dose may need to be reduced when combined with fentanyl or ketamine.

Option 2

Fentanyl 1-2 microgram/kg IV. If no respiratory depression is observed in 5 minutes, carefully titrate with ***midazolam*** IV boluses up to a maximum dose of 0.2 mg/kg (for midazolam).

Option 3

***Ketamine* (for sedation and analgesic in patients ≥ 3 months)** 1-2 mg/kg IV with additional bolus doses of 0.5-1 mg/kg up to a maximum total dose of 4 mg/kg IV over 20 minutes for difficult patients. (See "Point 7. Precautions" under Ketamine)

or

Ketamine may also be given IM at 2-4 mg/kg.

+/-

Atropine 0.01- 0.02 mg/kg IV or IM may be given to reduce salivation.

+/-

Midazolam 0.025mg/kg may be added for prevention of hallucination.

Should the above measures fail, the procedure may have to be postponed and referral to an anaesthesiologist be considered.

Cost comparison of sedative drugs

Drug	Cost (as at May 2020)	10 kg child
Chloral hydrate	Syrup 1 gram/5ml $1.46 per ml	10x75mg=750mg $5.46
Dexmedetomidine	Injection 100mcg/ml, 2ml each $205.78 per ampoule	10x2mcg=20mcg =1 ampoule Plus cost of MAD*
Midazolam	Injection 1mg/ml, 5ml each $6.57 per ampoule Injection 5mg/ml, 3ml each $6.95 per ampoule	10x0.1mg=1mg =1 ampoule
Ketamine	Injection 50mg/ml,10 ml each $146 per ampoule	10x1mg=10mg = 1 ampoule

*mucosal atomization device (MAD) = $38 each (25 pieces / box)

II. COMMONLY USED DRUGS FOR SEDATION

- ***Chloral Hydrate (more detailed information in Appendix K)***

1. Chloral hydrate is one of the most widely used sedatives in neonates and children younger than 3 years of age. It is widely used to facilitate non-painful diagnostic procedures such as EEG and CT or MRI.

2. An oral dose of 50 mg/kg is used for brief procedures (15 minutes or less) while 75 mg/kg is required for sedation of children for MRI which is a noisy procedure lasting for more than 30 minutes.

3. The onset of action is 30 minutes and the duration of action is 4 to 8 hours.

4. Side effects occur in 5-10% of children including vomiting (the drug is irritating to mucous membrane) and paradoxical excitation.

5. The disadvantage is that sedation is not successful in 10% of the children and it is not as effective in older children. It is best for children below 2 years old and may be less satisfactory for those above 3 years of age.

6. Although it has a long safety record, it can cause respiratory depression due to airway obstruction, and deaths had been associated with its use alone and when combined with other sedating medications. One large series showed a 0.6% incidence of respiratory depression especially at larger doses (75-100 mg/kg).

7. Its effect is primarily mediated by the active metabolite trichloroethanol (TCE), which is formed by the liver and erythrocytes. TCE has a half-life of 10 hours in toddlers, 28 hours in term infants, and 40 hours in preterm infants.

Evidence-based recommendations for chloral hydrate

- We suggest chloral hydrate as the first-line agent in children who require sedation for non-painful procedures. (Weak recommendation, very low quality of evidence).
- This recommendation is based on overall assessment of evidence that:
  1. Chloral hydrate is a more effective or equally effective sedation agent compared with other alternatives in children.
  2. Chloral hydrate has a vast amount of information on safety. Chloral hydrate is a fairly safe drug for sedation in children. There is no evidence that serious adverse effects are excessive compared with alternative sedation agents.
  3. Chloral hydrate has a low cost compared with alternatives.

- ***Dexmedetomidine (more detailed information in Appendix L)***

1. Dexmedetomidine is an alpha-2 adrenergic receptor agonist with minimal respiratory depression. It has sedative, anxiolytic and analgesic properties. It can enhance endogenous sleep by decreasing noradrenergic output from locus ceruleus.

2. It has a shorter half-life (two hours) than chloral hydrate with the active metabolite trichloroethanol.

3. Major adverse effects include hypotension and bradycardia.

4. It is often used by the intranasal route for procedural sedation. Administration is preferably given via a special device, i.e., Mucosal Atomization Device (MAD) with special technique:

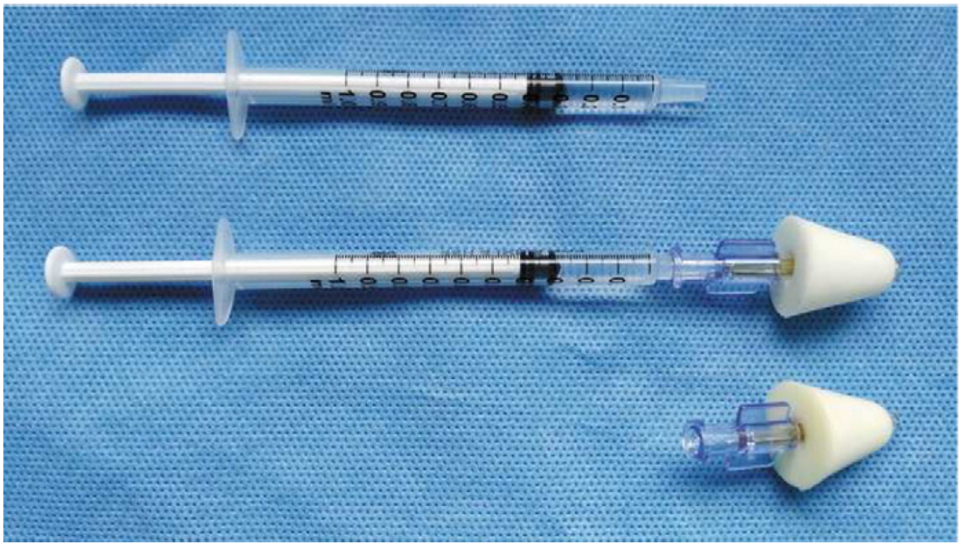
   - Use undiluted IV dexmedetomidine 100 mcg/ml solution
   - Draw up corresponding volume of dexmedetomidine ordered plus an additional 0.1 ml into a 1 ml or 3 ml syringe. [The extra 0.1 ml is to account for the dead space of MAD]
   - Attached the MAD to the syringe via the Luer-lock connector on the syringe
   - Briskly compressing the syringe plunger and deliver half of the medication dose into each nostril to maximize dispersion and absorption area

5. Intranasal dexmedetomidine can be considered as a rescue agent in patients failing chloral hydrate as the primary agent (see Section B. under X. Administration of medications) and in selected populations e.g., in children prone to vomiting or potential ease of administration with intranasal formulation.

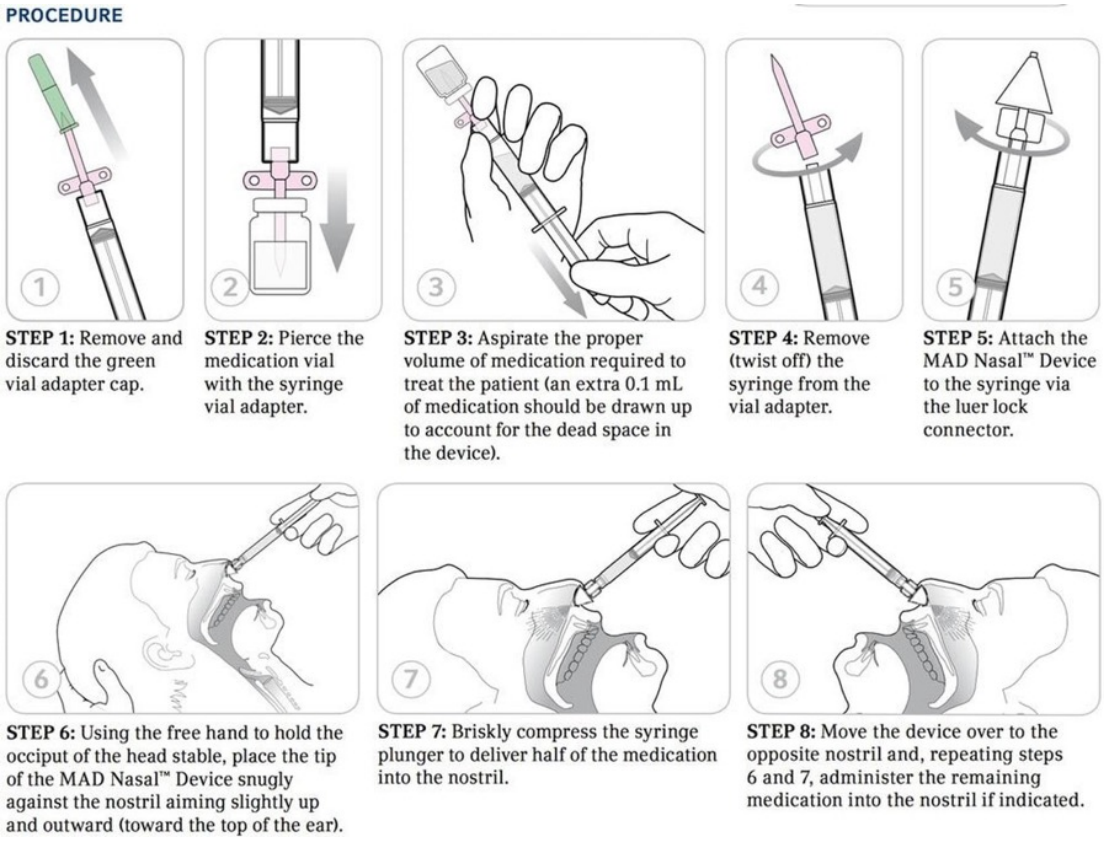
6. Though randomized controlled trials comparing IN dexmedetomidine with other sedative agents in children > 5 years old are not available, dosage recommendation of the drug is available up to 9 years old. The drug may be useful in older children who prefer non-parenteral route sedation.

Evidence-based recommendations for intranasal dexmedetomidine (IN DEX)

- Intranasal dexmedetomidine can be considered as a rescue agent in patients failing chloral hydrate as the primary agent. (Weak recommendation, low quality of evidence)
- We suggest the use of intranasal dexmedetomidine as a primary agent in selected children 1 month to 5 years old where IN DEX may show a more favourable side effect profile, e.g.in children prone to vomiting or potential ease of administration with intranasal formulation. (Weak recommendation, low to very low quality of evidence).



Photos of syringe and mucosal atomization device (MAD). (Adopted from Xie 2017 [85])



- ***Midazolam***

1. Midazolam is a short-acting, water-soluble benzodiazepine which should be administered intravenously. Nasal administration causes irritation and absorption after rectal administration is irregular. These routes of administration are less desirable for elective sedation procedures.

2. With intravenous use the onset of action is within minutes, duration of action is 1-2 hours which is the shortest among benzodiazepines.

3. Benzodiazepines produce mild respiratory depression and upper airway obstruction. Respiratory depression may become severe in compromised children or in children with tonsillar hypertrophy.

4. It can be used as a single agent in immobilising children for radiological examination.

5. It is often used alone or in combination with analgesics or local anaesthesia in painful or distressing procedures for sedation and amnesia. It should be noted that the midazolam dose may need to be reduced when combined with fentanyl or ketamine.

6. In neonate, it is recommended to infuse midazolam over 5 mins with close cardiorespiratory monitoring. Severe hypotension and seizures have been reported following rapid IV administration, particularly with concomitant fentanyl use. Neonates are also vulnerable to profound and/or prolonged respiratory effects of midazolam. Consultation of experienced doctor may be required for its use.

7. The effect of midazolam and other benzodiazepines can be reversed by flumazenil, a competitive antagonist, at doses from 0.01 mg/kg (up to max of 0.2 mg) every minute to a maximum cumulative dose of 0.05 mg/kg or max of 1 mg intravenously (max 2 mg in ICU setting). *(See also section III)*

- ***Ketamine***

1. Great precaution should be taken by non-anaesthesiologists using this drug for sedative/analgesic effects because of the associated potential risks which are often life threatening and critical.

2. Chemistry
   - Ketamine is a non-barbiturate anaesthetic agent and is a derivative of phencyclidine.

3. Clinical Uses
   - Ketamine can be used as an induction agent for general anaesthesia; as a sedative agent for short diagnostic and therapeutic procedures; or as an analgesic for painful procedures.

   - Ketamine produces a clinical state of 'dissociative anaesthesia', which is a trance-like cataleptic state through dissociation between the cortical and limbic system. During dissociative anaesthesia, patient's eyes may remain open with a disconnected stare and probable nystagmus. These actions produce a combination of sedation, amnesia and analgesia making it useful for paediatric painful and painless procedures.

4. Other Pharmacological Effects

   a. *Central Nervous System:*
      - Ketamine can cause nystagmus, increase in muscle tone and spontaneous involuntary limb movement.
      - In patients with abnormal CSF drainage, it elevates intracranial pressure.
      - Seizures may be precipitated in susceptible patients.
      - Hallucinatory emergence occurs in up to 50% adults but in less than 10% in young children. Excessive noise or stimulation should be avoided during recovery.
      - Such adverse reactions could be prevented in older children by administration of benzodiazepines which however will prolong recovery due to synergistic effects. Routine co-administration of benzodiazepines is not recommended.
      - Adverse reaction of emergence phenomenon can be managed with intravenous Midazolam at low dose (0.03mg/kg).

   b. *Respiratory System:*
      - Ketamine preserves laryngeal and pharyngeal reflexes when given within recommended dose range.
      - However, it stimulates salivary and tracheobronchial secretions and sensitizes cough and gag reflexes. Life threatening side effects, such as laryngospasm and aspiration can occur during sedation using ketamine.
      - Ketamine should not be used in patients with upper/lower respiratory tract infection or excessive salivation. Concomitant use of an anticholinergic, e.g. atropine, can decrease airway secretions. Routine co-administration is not recommended.
      - Although spontaneous respiration, muscle tone of the tongue and larynx, cough and swallowing reflexes are usually preserved by ketamine, adverse effects such as apnoea, respiratory depression with decreased respiratory rate and tidal volume, as well as oxygen desaturation have been reported. These complications can occur during rapid intravenous bolus of exceptionally high doses (e.g. 2 mg/kg) causing conversion to general anaesthesia, and in ill or preterm infants.
      - Ketamine causes potent relaxation on bronchial smooth muscles, making it an ideal anaesthetic and analgesic agent in patients with asthma.

Personnel administering ketamine should be familiar with airway management. Muscle paralysis and endotracheal intubation may be required in severe laryngospasm with airway compromise.

c. *Cardiovascular System:*
- Ketamine has sympathomimetic actions through inhibiting the reuptake of catecholamines, thus resulting in mild to moderate increases in blood pressure, heart rate, and cardiac output.
- However, its direct vasodilatory effects (through smooth muscle relaxation) may result in hypotension in the critically ill who has depleted catecholamine stores.
- Although there is no conclusive evidence that ketamine increases pulmonary vascular resistance, the use of ketamine in children with pulmonary hypertension should be cautious

d. *Others:*
- Ketamine can cause increased intra-ocular pressure
- Ketamine can cause nausea and vomiting
- In case of intractable post-procedure vomiting, IV ondansetron (0.1mg/kg- maximum 4mg) can be considered

5. Recommended Dose and Administration
- Ketamine is commonly given through the intravenous or intramuscular route. It can also be given by oral, rectal or intranasal routes at higher doses but with less predictable onset of action and recovery time.
- For sedation and analgesia using ketamine, the recommended dose for intravenous use is 1-2 mg/kg IV with additional bolus doses of 0.5-1 mg/kg, up to a maximum total dose of 4 mg/kg IV over 20 minutes for difficult patients. (See Point 7. Precautions)
- Lower initial dose (e.g. 0.5 mg/kg) is used if adjuvant sedatives (e.g. midazolam) are also given.
- Ketamine may also be given IM at 2-4 mg/kg.
- For longer procedures, infusion of 2-20 microgram/kg/min may be required.
- The onset times vary with the route of administration (30-60 seconds for IV; 5-20 minutes for IM).

6. Contraindications [86-104]
- Absolute (Risk almost always outweigh benefit)
  - Age younger than 3 months *(higher risk of airway complications)*
  - Known or suspected schizophrenia, psychosis *(can exacerbate condition)*
- Relative (Risk may outweigh benefit)
  - Major procedures stimulating the posterior pharynx (e.g. endoscopy) *(increased risk of laryngospasm)*
  - History of airway instability, tracheal surgery, or tracheal stenosis *(higher risk of airway complications)*
  - Active pulmonary infection or disease, including upper respiratory infection/ asthma *(increased risk of laryngospasm)*
  - Known or suspected cardiovascular disease, including angina, heart failure, or hypertension *(exacerbation caused by sympathomimetic properties)*
  - Central nervous system abnormalities with hydrocephalus or abnormal CSF drainage *(increased intracranial pressure)*
  - Uncontrolled epilepsy *(precipitation of seizures)*
  - Glaucoma or acute globe injury *(increased intraocular pressure with ketamine)*
  - Porphyria, thyroid disorder, or thyroid medication *(enhanced sympathomimetic effect)*

7. Precautions
- Unless appropriate monitoring, personnel with appropriate training in advanced life support, resuscitative equipment and drugs are readily available, ketamine should not be administered in high bolus doses at and above 1.5 mg/kg.

- ***Fentanyl***

1. Fentanyl has replaced morphine and pethidine as the opioid of choice for analgesia/sedation for procedures in children.

2. Intravenous fentanyl is a potent pure opioid (i.e. 100 times more potent than morphine) with no amnesic properties.

3. Its high lipid solubility allows for onset within 30 seconds and a peak effect at 2-3 minutes. It has a brief clinical duration of 20-40 minutes when given in small doses owing to its rapid redistribution to skeletal muscle, fat and other inactive sites. It has no active metabolites.

4. In preterm and term infants, fentanyl's clearance is decreased and its half-life is increased

5. Its pharmacological effects can be fully reversed by opioid antagonists and is frequently used with a short-acting anxiolytic (such as midazolam).

6. Doses must be given in small aliquots and carefully titrated to avoid chest wall and glottic rigidity.

7. When carefully titrated and appropriately monitored, fentanyl has few adverse effects.

8. Chest wall rigidity is a centrally mediated idiosyncratic reaction that can interfere with respiratory function. The mechanism of action is partially modulated by GABA pathways at the spinal level. It can be reversed with naloxone or muscle relaxants.

9. Chest wall rigidity is quite rare and has only been described when higher doses (3-4 microgram/kg) were given in boluses for sedation in neonates.

10. Other adverse reactions from fentanyl include bradycardia, dysphoria, delirium, nausea, vomiting, pruritus, urinary retention, hypotension, and smooth muscle spasm. Close post-procedural observation is required because respiratory depression can outlast analgesia.

III. COMMONLY USED DRUGS FOR REVERSAL

- ***Flumazenil***

1. Flumazenil is a specific benzodiazepine receptor antagonist and will rapidly reverse the sedative and respiratory effects of benzodiazepines (e.g. midazolam)

2. Children who are taking benzodiazepines for epilepsy may develop seizure rapidly if flumazenil is given. It should also be used with caution in patients with benzodiazepine dependence.

3. The recommended dose of flumazenil is 0.01 mg/kg (up to max of 0.2 mg) every minute to a maximum cumulative dose of 0.05 mg/kg or max of 1 mg intravenously (max 2 mg in ICU setting).

4. Antagonism begins within 1 to 2 minutes and lasts approximately 1 hour.

5. Because re-sedation after 1 hour may occur, the child must be carefully monitored for at least 2 hours. Repeat dose of flumazenil may be necessary.

6. It should be noted that flumazenil will not antagonize respiratory depression due to opioids (e.g., fentanyl).

7. Flumazenil should not be administered for the routine reversal of the sedative effects of benzodiazepines but reserved for reversal of respiratory depression.

- ***Naloxone***

1. Mu-receptor opioid antagonist specifically reverses the respiratory and analgesic effects of opioids and should be readily available when opioids (e.g., fentanyl) are used.

2. It should not be used for routine reversal of the sedative effects of opioids but reserved for reversal of respiratory depression or respiratory arrest.

3. It may be given intravenously or intramuscularly. The initial dose for respiratory depression is 10 microgram/kg titrated to effect every 2-3 minutes. Up to 100 microgram/kg may be required for severe respiratory depression or respiratory arrest.

4. Adverse reactions from reversal of analgesia include pain, tachycardia, hypertension, delirium, and pulmonary oedema.

5. Children on long-term opioid therapy should be given opioid reversal agents in low doses and with extreme caution because withdrawal seizures and delirium may occur.

6. Children given naloxone may have opioid effects reappear after 1 hour. *If naloxone is used, then the child should be observed for a minimum of 2 hours*. Repeated doses of naloxone may be necessary and titrate according to clinical response.

IV. COMMONLY USED LOCAL ANAESTHETIC DRUGS

General Principles and Maximum Recommended Doses:

1. Local anaesthetics play a critical role in analgesia for painful procedures and greatly reduce requirements for systemic opioid when administered topically or by local infiltration.

2. For local skin infiltration, local anaesthetic solution containing adrenaline 1:200,000 (5 microgram/ml) is often used as a vasoconstrictor to lengthen the duration of blockade, decrease bleeding, and reduce systemic toxicity by decreasing vascular uptake. The toxicity of local anaesthesia is additive when used in combination. No more than the maximum amount (mg/kg) should be drawn up in a syringe to avoid accidental overdose.

3. Solutions with adrenaline **must not** be used in parts of the body with compromised blood supply or supplied by end-arteries, such as **fingers, toes, nose, ears or penis**. There is a possibility of producing arterial vasoconstriction and subsequent ischaemic gangrene distal to the site of injection.

4. Local anaesthetic can obtund airway reflexes when sprayed in the mouth for bronchoscopy or gastrointestinal endoscopy.

A. Lignocaine

1. Lignocaine is the most commonly used local anaesthetic drug by non-anaesthesiologists.

2. Lignocaine has a rapid onset and an intermediate duration of action. The onset of action is 1-5 minutes following subcutaneous infiltration.

3. The rate of absorption depends on the dose, the route of administration and the vascularity of the injection site. For example, intercostal blocks give the highest peak plasma concentrations, while abdominal subcutaneous injections give the lowest.

4. The addition of adrenaline considerably slows the absorption of lignocaine. Peak plasma concentrations are reduced by 50% following subcutaneous injection if adrenaline 1:200000 (5 microgram/ml) is added.

5. Injection should always be made slowly with frequent aspirations to avoid inadvertent intravascular injection which can produce cerebral symptoms even at low dose. Drowsiness may be an early sign of CNS toxicity.

6. Signs and symptoms of toxicity include restlessness, anxiety, tinnitus, dizziness, blurred vision and tremors.

7. For children and adolescents, typically solutions with concentration <2% should be used (allow for larger volumes); maximum dose: 5 mg/kg/dose, not to exceed the recommended adult maximum dose of 300 mg/dose; do not repeat within 2 hours [Lexicomp].

8. Lignocaine is also available as a 10% topical spray which delivers 10mg of Lignocaine on each actuation. The maximum recommended dose is 3 mg/kg (e.g., up to 6 metered doses for a child weighing 20 kg).

B. EMLA Cream

1. EMLA cream is a *E*utectic *M*ixture of *L*ocal *A*naesthetics (Lignocaine 2.5% and Prilocaine 2.5%).

2. When placed on the skin for 60 minutes, it is useful for reducing the pain of skin incision, intravenous cannula insertions and lumbar punctures.

3. Absorption of large amounts of Prilocaine can cause methaemoglobinaemia.

4. It should be applied only to normal intact skin in appropriate doses.

5. <u>Dosage:</u>
   - The dose should not exceed 1 gram per 10 cm^2 of application area.
   - Age 0-3 month: the maximum application area is 10 cm^2 (1 gram) over maximum of 1 hour.
   - Age 3-12 month: the maximum application area is 20 cm^2 (2 gram) over maximum of 1 hour.
   - Age 1-6 year: the maximum application area is 100 cm^2 (10 gram) over maximum of 5 hours.
   - Age 6-12 year: the maximum application area is 200 cm^2 (20 gram) over maximum of 5 hours.

6. The duration of action is 1-2 hours after the cream is removed.

7. Adverse reactions include erythema, itching, rash, and methaemoglobinaemia. It also causes blanching of the skin, which can make intravenous access difficult.

8. It is contraindicated in neonates with gestational age of < 37 weeks and in children with congenital or idiopathic methaemoglobinaemia, or in infants under the age of 12 months who are receiving treatments with methaemoglobinaemia-inducing drugs (e.g., Phenytoin, Phenobarbital, and Sulfonamides). Patients with glucose-6-phosphate dehydrogenase deficiency are also more susceptible to drug induced methaemoglobinaemia, therefore, caution is advised.

SECTION D: APPENDICES AND REFERENCES

APPENDIX A

University of Michigan Sedation Scale (UMSS)

Score	Characteristics
0	Awake and alert
1	Minimally sedated: tired/sleepy, appropriate response to verbal conversation and/or sound
2	Moderately sedated: somnolent/sleeping, easily aroused with light tactile stimulation or a simple verbal command
3	Deeply sedated: deep sleep, arousable only with significant physical stimulation
4	Unarousable

APPENDIX B

American Society of Anesthesiologists (ASA) Physical Status Classification

Class I	A normal healthy patient
Class II	A patient with mild systemic disease (e.g. a child with controlled reactive airway disease)
Class III	A patient with severe systemic disease (e.g. a child who is actively wheezing)
Class IV	A patient with severe systemic disease that is a constant threat to life (e.g. a child with status asthmaticus)
Class V	A moribund patient who is not expected to survive without the operation (e.g. a patient with severe cardiomyopathy requiring heart transplantation)
Class VI	A declared brain-dead patient whose organs are being removed for donor purposes

APPENDIX C

Factors That May Be Associated with Difficulty in Airway Management Include, but Are Not Limited to:

- Previous problems with anaesthesia or sedation
- Stridor
- Snoring or apnoea
- Dysmorphic facial features (e.g., Pierre Robin syndrome, trisomy 21)
- Craniofacial abnormalities
- Significant obesity (especially involving the neck and facial structures)
- Short neck, limited neck extension, large neck mass
- Tracheal deviation
- Small mouth, protruding incisors, loose or capped teeth, high arched palate
- Macroglossia
- Tonsillar hypertrophy
- Nonvisible uvula
- Micrognathia
- Retrognathia
- Trismus

APPENDIX D

Calculation of Post-Conceptual Age

Gestational age is calculated from the first date of the LMP. Actual age is the time since birth.
Post-Conceptual Age (PCA) = Gestational age + Actual age

Example: PCA = Gestational age 33 weeks + 17 weeks old = 50 weeks

A widely accepted guideline is to admit and monitor all infants younger than 60 weeks' post-conceptual age for 12 to 24 hours after anaesthesia and surgery. In general, the younger the patient's gestational and post-conceptual ages, the greater the risk for postoperative apnoea attack.

Similar precaution may be advised for infant with PCA < 60 weeks after sedation and procedure.

APPENDIX E

Fasting

1. The longstanding tradition of fasting before elective surgery and procedural sedation has minimal scientific support and was instead prompted by early reports of aspiration [105] and the logical presumption that regurgitation of gastric contents cannot physically occur if the stomach is empty [77, 106-108]. There are no prospective, controlled trials to guide decision making concerning the impact of fasting intervals on aspiration; therefore, conclusions regarding association or causal relationships rely on observational series and indirect evidence. There is no conclusive evidence to support assertions about safe fasting intervals and thus current fasting recommendations from prominent specialty societies [75, 77, 109-114] are largely consensus driven (Table 1).

Table 1: Current elective fasting guidelines from selected prominent specialty societies*

	Clear Liquids	Breast Milk	Infant Formula	Nonhuman milk	Light meal
Association of Paediatric Anaesthetists of Great Britain and Ireland, European Society for Paediatric Anaesthesiology, L'Association Des Anesthesistes-Reanimateurs Pediatriques d'Expression Francaise 2018 [61]	1h	4h	6h	not specified	6h
American Society of Anesthesiologists 2017 [22]	2h	4h	6h	6h	6h
American Academy of Pediatrics 2016 [51]	2h	4h	6h	6h	6h
American Academy of Pediatric Dentistry 2016 [96]	2h	4h	6h	6h	6h
Academy of Medical Royal Colleges 2013 [97]	2h	4h	not specified	not specified	6h
European Society of Anaesthesiology 2011 [23]	2h	4h	6h	6h	6h

*Emergency Procedures

- American College of Emergency Physicians 2014 [98]: "Do not delay procedural sedation in adults or pediatrics in the Emergency Department based on fasting time."
- Royal College of Anaesthetists and The College of Emergency Medicine 2012 [99]: "Fasting is not needed for minimal sedation or moderate sedation where verbal contact is maintained. For deeper levels of sedation the fasting rules for general anaesthesia form an accepted baseline. For an emergency procedure in the absence of fasting any decision to proceed should be based on urgency and the target depth of sedation coupled with a careful assessment of aspiration risk."

2. Indeed, shorter fasting periods for clear liquids before general anaesthesia have resulted in lower gastric volumes in both adults [115] and children [116]. Additionally, gastric volumes and pH at the time of induction vary greatly regardless of fasting, particularly in children [117-134]. Clear liquids administered up to two hours prior to surgery do not adversely affect gastric volume or pH [121, 123, 126, 127, 135-137].

3. Regurgitated clear liquids appear to represent little risk of aspiration morbidity, regardless of volume. Clear liquids are generally considered to include water, fruit juices without pulp, clear tea, and black coffee [111, 112, 138]. Aspiration of acidic particulate matter or solid food, on the other hand, is known to result in pulmonary damage and is thus of greater importance [77, 139]. The mean gastric emptying time after breakfast in preschool children is 4 hours, [140] and is similar at 4 versus 6 hours [118]. When comparing apple juice, 2% fat milk, and a high protein drink (Ensure Clear™), an ultrasound study of older children found that stomachs were essentially empty 3 to 3.5 hours later, discounting the apparent merit of differentiating clear versus non-clear liquids [141].

4. In many nations pre-operative fasting recommendations were shortened two decades ago from "nothing by mouth after midnight" to 2 hours for clear liquids and 6 hours for solids. This major reduction did not result in a proliferation of aspiration. Indeed, over time this incidence has decreased [108]. More recently, many hospitals have encouraged patients to drink carbohydrate-rich fluids within the 2 hours before elective surgery [142-144], as recommended by the European Society of Anaesthesiology [40]. Again, no resulting surge in aspirations has been evident [111, 142-144]. In 2018 multiple European societies jointly issued a statement recommending clear liquids up to 1 hour prior to elective anaesthesia in children [75, 145, 146].

5. In general, studies showed that the risk of pulmonary aspiration in non-high risk procedural sedation is very low (Table 2). Also, the risk of aspiration during sedation is almost certainly lower than that during general anaesthesia [80]. The best available study is a 139,142-patient, multi-center registry of paediatric sedation using primarily propofol, with an overall aspiration incidence of 1:13,914 with zero mortality [72].

Table 2: Literature estimates of aspiration risk during procedural sedation

Study	Population	Principal Agent	Endoscopy?	Total Subjects	Aspiration overall	Aspiration during non-fasted procedures	Aspiration mortality
Bhatt [39]	Children	Ketamine	No	6295	None	None	None
Beach [19]	Children	Propofol	Some	139,142	1:13,914	1:12,701	None
Chiaretti [40]	Children	Propofol	Some	36,516	None	None	None
Friedrich [41]	Adults	Propofol	All	15,690	1:541	Not stated	None
Rajasekaran [42]	Children	Propofol	All	12,447	None	None	None
Agostoni [43]	Mixed	Propofol	All	17,999	1:1,000	Not stated	None
Dean [44]	Mostly adults	Propofol	None	62,125	None	Not stated	None
Green [45]	Children	Ketamine	None	8282	None	None	None
Rex [46]	Adults	Propofol	All	646,080	Not stated	Not stated	None
Horiuchi [47]	Adults	Propofol	All	10,662	None	None	None
Vespasiano [48]	Children	Propofol	None	7304	1:7,304	Not stated	None
Onody [49]	Mostly Children	Nitrous oxide	Some	35,828	None	None	None
Tohda [50]	Adults	Propofol	All	27,500	1:6,875	Not stated	None
Sanborn [51]	Children	Pentobarbital	None	16,467	1:8,234	None stated	None
Walker [52]	Adults	Propofol	All	9152	1:9,152	Not stated	None
Gall [53]	Children	Nitrous oxide	Some	7511	None	None	None

*To include just the largest studies, we display those with 5000 or more patients. We also exclude studies which report duplicate subsets of patients.

No estimate for aspiration mortality associated with procedural sedation is available; however, there were only nine sedation-associated aspiration deaths reported in the medical literature from 1985 to 2016, only one of which was for a non-endoscopic procedure [147]. None of these nine deaths were in children or in low-risk adult patients [80].

6. Fasting does not guarantee that gastric emptying is complete [70].

7. On the other hand, unnecessary long fasting may aggravate the feeling of hunger and stress, especially in small children, and resulted in reduction of sedation efficacy [65] and failure of procedural sedation [66, 67].

8. Although it is possible that pre-procedural restrictions on solid food (rather than liquids) may be protective, current evidence suggests that there may be trivial or no impact from either food or liquid restriction, with the greater contributing factor being the prior identification of patients with risk factors (Table 3) and increased precautions with their airway management [80].

9. For URGENT procedures in a child who has not been adequately fasted, the benefits of the procedures must be balanced against the possible risk of aspiration. URGENT procedural sedation should NOT be delayed based on fasting time alone [64, 71-73].

10. Based on a recent international multidisciplinary consensus statement on fasting before procedural sedation in adults and children, which is the first consensus statement published to provide fasting recommendations specific to procedural sedation only, (the recommendations are based on extensive literature search and consensus developed using Delphi methodology) [80, 148-150], the fasting recommendation [80] as below is currently undergoing peer's review and new updates to our practice may be available soon.

Table 3:

Risk factors reported more than once and not specifically refuted elsewhere (Quality of evidence – Moderate)	Greater comorbidities in children
Risk factors reported in a single study and not refuted elsewhere (Quality of evidence – Moderate)	Infants 12 months of age or less Obstructive sleep apnoea in children Oesophageal endoscopy / Bronchoscopy in children
Clinical features found to not be risk factors, with no conflicting data (Quality of evidence – Moderate)	Emergency procedure in children Absence of fasting in children Upper respiratory infection in children Pregnancy in teenagers

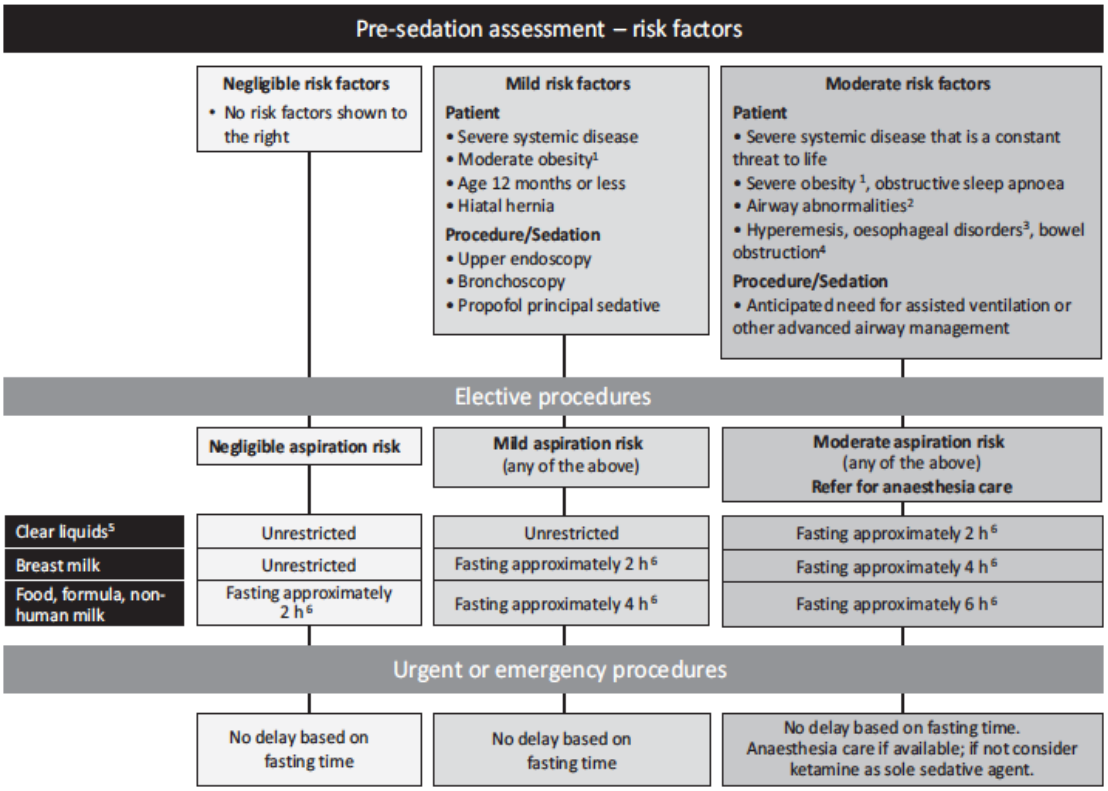


Figure 1 Algorithm linking risk stratification and fasting guidance. Notes: (1) Suggested definitions for moderate obesity are a body mass index (BMI) of 30–39 $kg.m^{-2}$ in adults or from the 85th up to the 95th BMI percentile based on age/sex in a child, and for severe obesity a BMI of 40 $kg.m^{-2}$ or higher in an adult or at the 95th percentile or greater in a child. (2) Includes micrognathia, macroglossia and laryngomalacia; (3) Includes gastroparesis, achalasia, atresia, stricture and tracheoesophageal fistula; (4) Includes ileus, pseudo-obstruction, pyloric stenosis and intussusception. (5) Clear liquids are generally considered to include water, fruit juices without pulp, clear tea, black coffee and specially prepared carbohydrate-containing fluids. (6) Fasting intervals are not absolute, with exceptions permissible when the volumes of oral intake are minor, or the fasting time reasonably close.

APPENDIX F

Non-pharmacological strategies

Non-pharmacological techniques have been implemented for long to reduce the stress and anxiety of children during clinical procedures. It is involved in both preprocedural preparation and intraprocedural period. Family-centered approach is essential, where the clinicians can work collaboratively with children and their parents to achieve the best medical outcomes and psychological well beings.

There are limited randomized control trials comparing pharmacological and non-pharmacological strategies for sedation in painless procedures in paediatric patients. The recommendations from large-scale prospective and retrospective studies and recent review articles are summarized as below.

A retrospective review done by Atonov revealed a high success rate when using feed and wrap technique for MRI in infants aged 3 months or younger. It was less effective in preterm infants and those undergoing spinal MRI [151]. The result was comparable with other previous studies on the use of feed and wrap technique in young infants undergoing radiological imaging.

A review article written by Dong in 2019 supported modification of environment for different aged children and participation of child life specialists to reduce sedation for children undergoing MRI [152]. Another review article by Janos in 2019 supported the use of environmental modification, use of pacifier, swaddling and feeding, and coaching by child life specialists in radiology suites for children [153].

By the use of MR-compatible audio-visual system, a retrospective study in 2009 showed that there was a significant reduction in need for sedation in paediatric patients aged 4-10 years old [154]. There was also a reduction in wait time for sedation. They concluded that the A/V system provided a safer option without the risk of sedation, provided a positive patient experience, was cost effective and did not affect the image quality. The result was in line with Harned and Strain, who published an article in 2001 showing significant reduction in need for sedation for those above 3 years old undergoing MRI with the use of an audio-visual system. There was also a 17% decrease in MRI room time [155].

Child life specialists are essential in providing effective coping and emotional support through play, preparation, education and self-expression activities [156]. Trained child life specialists, in a prospective trial of children between the age of 1 and 12 years, played an important role in relieving the anxiety, distress, and perception of pain, and in improving both parental and patient experience [157].

Experience in a local hospital showed that Hospital Play Service has significantly reduced the need for oral sedation in painless procedures such as echocardiogram [158]. It involved psychological preparation, environment modification, personalized distraction technique and positive rewards. Another local study showed that painless procedures such as radionuclide thyroid scan and renal scintigraphy (DMSA scan) could be performed in young infants after a feed without oral sedation [159]. Both studies showed comparable success rate in performing the procedures without pharmacological sedation. Sedation risk could be reduced with satisfactory feedback from both parents and health care professionals.

For painful procedures, patients more commonly experience anxiety, distress and fear. In the long term it may result in reduced compliance to subsequent health care service, abnormal behaviour in children or even post-traumatic stress disorder in extreme cases [160]. Combination strategies, involving physical, psychological and pharmacological approaches would reduce their stress. A Cochrane systematic review published in 2018 studied the effectiveness of psychological interventions for needle-related procedural pain and distress in children and adolescents. There was evidence supporting the efficacy of distraction, hypnosis, combined cognitive behaviour therapy and breathing intervention [161]. Despite low-quality evidence, the potential benefits of reduced pain or distress support the evidence in favour of using these interventions in clinical practice. Another Cochrane systemic review performed in 2015 studied non-pharmacological management of procedural pain in infants and young children [162]. Sixty-three studies were included involving 4905 participants. The most established evidence was for non-nutritive sucking, swaddling/facilitated tucking, and

rocking/holding. However, the evidence was of low quality, and more research will be needed to study non-pharmacological management of acute pain in infancy.

There are difficulties in using non-pharmacological strategies in paediatric sedation [160]. Firstly, its daily application is limited by the busy hospital environment. There may be insufficient time, manpower and space to apply non-pharmacological strategies. Secondly, there is no single technique that could be effective for all children. It needs to be individualized by trained personnel. Finally, there are limited large sample size randomized trials to study the efficacy of different non-pharmacological strategies. In the future, more large-scale research on potential efficacy and application of non-pharmacological strategies is needed. More research is also needed for children with medical complexities who require multiple and repeated procedures.

Oral sucrose given pre-emptively to neonate or young infants before painful procedure has been shown to have mild analgesic effect in various studies. This can be considered to facilitate the procedure without altering patient's sedation level. Detail discussion of the evidence of analgesic effect of oral sucrose is beyond the scope of the present recommendation.

Recommendations:

1. Non-pharmacological strategies can be considered as an adjunct or to replace pharmacological sedation in selected patients, taking into consideration of individual patient characteristics, technical availability and feasibility in different settings. These strategies may include child-friendly environment, feed and wrap technique in infancy, distraction with audio-visual system, and participation of trained child life specialists. (Weak recommendation, low quality of evidence)

2. For painful procedures, techniques such as distraction, hypnosis, combined cognitive behaviour therapy, and breathing interventions may be helpful in older children, whereas sucking-related intervention and swaddling may benefit preterm babies and neonates. (Weak recommendation, low quality of evidence)

APPENDIX G

Paediatric Flexible Bronchoscopy

1. Paediatric flexible bronchoscopy is often performed in ICU, bronchoscopy suite or other high dependency environment because of the monitoring capability and experience of the clinicians and nursing staff.

2. Topical Lignocaine is applied to pharynx and tracheobronchial tree, usually by spray, nebuliser or atomizer device.

3. Atropine is often administered as an antisialagogue.

4. IV sedation by Ketamine, Midazolam and Fentanyl has been used with varying success.

5. Many of these children have significant comorbidities. Some of these children may already be intubated and receiving ventilatory support in ICU.

6. Availability of dedicated experienced medical staff to provide sedation, airway support and monitoring is essential to allow the bronchoscopist to focus on the procedure itself.

7. If available, dedicated anaesthesiologist to administer intravenous or inhalational anaesthesia and to manage airway is recommended. The use of a variety of airway device (facemask, laryngeal mask airway, intubation or spontaneous breathing tubeless technique) may allow flexibility to the bronchoscopist.

APPENDIX H

Emergency Equipment † That May Be Needed to Rescue a Sedated Patient:

Intravenous Equipment

- IV cannulae (e.g., 24-, 22-, 20-, 18-, 16-gauge)
- Tourniquets
- Alcohol wipes
- Adhesive tape
- Assorted syringes (e.g., 1-, 3-, 5-, 10-mL)
- IV tubing
- Paediatric drip set
- Adult drip set
- Extension tubing
- Injection port or 3-way stopcocks
- IV fluid e.g. Lactated Ringer solution, Normal saline solution, etc.
- IV needles (e.g., 25-, 23-, 21-, and 18-gauge)
- Intraosseous needle
- Sterile gauze pads

Airway Management Equipment

- Face masks (infant, child, small adult, medium adult, large adult)
- Self-inflating breathing bag and valve set (infant, child, adult)
- Oropharyngeal airways (size 000, 00, 0, 1, 2, 3, 4)
- Nasopharyngeal airways (available in sizes 12F to 36F. Alternatively, for infants and small children, a shortened endotracheal tube may be used.)
- Laryngeal mask airways (sizes 1, 1.5, 2, 2.5, 3, and 4)
- Laryngoscope handles (with extra batteries)
- Laryngoscope blades
  - ✧ Straight (Miller) No. 0, 1, 2, and 3
  - ✧ Curved (Macintosh) No. 1, 2 and 3
- Video laryngoscopes (items be made available within short period of time)

- Endotracheal tubes (2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, and 6.0 uncuffed and 3.0, 3.5,4.0,4.5,5.0, 5.5, 6.0, 6.5. 7.0. 7.5 and 8.0 cuffed)
- Bougie and Stylet (appropriate sizes for endotracheal tubes)
- Water soluble lubricant e.g. KY Jelly
- Suction catheters (appropriate sizes for endotracheal tubes)
- Yankauer-type suction
- Gastric tubes
- Nebuliser with medication kits
- Gloves (sterile and nonsterile, latex free)

† The choice of emergency equipment may vary according to individual or procedural needs.

† Non ferromagnetic airway equipment will be required for sedation in MRI suite

APPENDIX I

Drugs* That May Be Needed to Rescue a Sedated Patient

- Adrenaline (1:10 000)
- Amiodarone
- Atropine
- Chlorpheniramine
- Diazepam
- Dopamine
- Dobutamine
- Ephedrine
- Flumazenil
- Glucose (10% or 50%)
- Hydrocortisone
- Lignocaine (cardiac Lidocaine, local infiltration)
- Naloxone
- Oxygen
- Ondansetron
- Rocuronium
- Salbutamol (intravenous and for inhalation)
- Sodium bicarbonate
- Suxamethonium

* The choice of emergency drugs may vary according to individual or procedural needs.

APPENDIX J

Capnographic monitoring

Methods

A systematic review of the literature was conducted to assess the clinically important outcomes associated with the use of capnography in children. Important outcomes include the effectiveness of capnography in reducing serious complications in children during sedation as well as adverse effects of using capnography (Table 1).

Published literature was identified by searching the following bibliographic databases from inception to June 2019: MEDLINE with in-process records and daily updates, Embase, Cochrane Library, and PubMed. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's Medical Subject Headings (MeSH), and keywords. Search concepts included capnography, capnometry, and carbon dioxide monitoring of patients undergoing procedural sedation. Methodological filters were applied to limit retrieval to systematic reviews, meta-analyses, randomized controlled trials, controlled clinical trials, or economic studies.

Google and other Internet search engines were used to search for additional Web-based materials. Two reviewers screened citations, selected articles for inclusion, extracted data, and performed risk of bias assessment. If consensus could not be reached, the Working Group was consulted. GRADE assessment and conclusion was performed by the Working Group.

Study Inclusion Criteria

Studies for inclusion in our analysis were selected using the "PICO" criteria shown in Table 1. There is no time frame limitation in the literature search. Only randomized controlled trials (RCTs) were included in the analysis.

Study Exclusion Criteria

All non-randomized controlled trials (non-RCTs) are excluded from analysis. However, even though non-RCTs are excluded, all relevant studies retrieved in the literature search were appraised and useful information were extracted and presented in "Discussions". If the primary objective of the study was to assess other aspects of paediatric sedation (e.g., comparison of different sedation medications with capnography as assessment tool) without assessing the impact of capnography, the study was excluded.

Results

A total of 15 full-text articles after the initial screen were retrieved [51, 56, 57, 163-174]. Twelve articles were excluded (10 articles were non-RCTs; 1 article recruited non-paediatric patients; and 1 article studied sedation medication rather than capnography). Three RCTs were included for analysis [163-165].

Table 1: Inclusion Criteria for Clinical Review:

PICO	Research Question
Population	Healthy children (age 0- 18 years old), non-intubated, who are sedated for a diagnostic or interventional procedure
Intervention	Capnography (ETCO2 monitoring)
Comparators	● No capnography monitoring ● Standard monitoring (pulse oximetry, pulse rate, blood pressure, visual assessment ● Capnography performed but real-time capnography readings concealed from operator
Outcome	**Critical or important outcomes:** ● Severe desaturation ● Moderate desaturation ● Apnoea ● Hypoventilation requiring bagging / intubation ● Cardiac/ Respiratory arrest ● Intolerable to capnographic monitoring ● Procedure cannot be completed **Less important outcomes:** ● Mild desaturation ● Mild hypoventilation
Study setting	Patients undergoing diagnostic or interventional procedure in hospital setting (Emergency Department, Endoscopy suite, ward)
Study Design	Randomized controlled studies Non-randomized controlled studies were also appraised and relevant data included in "Discussions" but are not included in the analysis

Study and patient characteristics

The 3 RCTs were published in 2006, 2015, and 2017 respectively, and performed at the Paediatric Outpatient Endoscopy Unit, the Emergency Department, and the Paediatric Post-anaesthesia Care Unit (PACU) respectively. All studies were conducted in the USA, with sample size between 154 and 201 (Table 2).

All 3 RCTs assessed the effectiveness of capnography compared with standard monitoring. In both the intervention and the comparison groups, capnography was used in addition to standard monitoring. In the intervention group, the capnography monitor was visible to the treatment team, whilst the monitor was hidden from sight of the treatment team, but available to researchers in the comparison group. The capnography devices used for ETCO2 monitoring in the included studies were one of the following: (1) Nellcor OxiMax NPB (2) Phillips MP20 monitor (3) CapnoStream 20. All devices were sidestream, portable, and multi-parameter models (measuring two or more parameters, such as ETCO2, SpO_2, respiratory rate, heart rate, ECG, temperature), connected to the patient via an oral or nasal cannula.

Outcomes in these randomized studies included persistent hypoventilation, staff interventions, oxygen desaturations, timely interventions, abnormal ventilation, and adverse events. The statistical analysis included a comparison of the primary outcome between intervention and control groups using chi-square test, or Fisher's exact test for categorical variables and Student t test for continuous variables. Mann-Whitney test was used for non-parametric distributions. One study performed an intention-to-treat analysis [165]. Multivariate regression analyses were performed to control for the following possible confounding variables: age, sex, ethnicity, procedure type, duration of procedure, provider, respiratory rate, baseline oxygen saturation and ETCO2, use of shoulder roll at the start of the procedure, level of sedation, length of sedation, and sedative dose.

The mean/median ages for the three RCTs were 8, 10 and 14 years old respectively. The percentage of male subjects was just over 50% (54% -59%) in the studies. Procedure types requiring sedation included emergency room procedures (fracture reduction, laceration repair, joint reduction, incision and drainage of abscess, arthrocentesis, etc., and endoscopic procedures (endoscopy, colonoscopy). Sedation agents used included ketamine, midazolam and fentanyl. Depth of sedation was documented in one study as Ramsey sedation score 2-4 [165]. This study included patients with ASA score I-II (indicating relatively healthy subjects). The other two included subjects with American Society of Anaesthesiology Classification I-III [163, 164]. Co-morbid conditions (snoring, OSA) was mentioned in one study only [163].

Table 2: Details of the study characteristics of the 3 randomized controlled studies on clinical effectiveness of ETCO2 monitoring for Paediatric Patients undergoing procedural sedation:

Author, publication year	Study type Sample size (n) Patient characteristics	Setting	Sedation Airway	Intervention group	Comparator group	Outcome
Langhan 2017	Randomized controlled trial (RCT) N= 201 **Inclusion criteria**: -Age 1-20 y.o. -Undergoing general anaesthesia for elective surgery and cared for in the PACU **Exclusion criteria:** -Need for post-op assisted ventilation via ET tube/ tracheostomy -Urgent surgical procedures -Surgery that precludes use of nasal cannula -Diseases with abnormal ETCO2 or pulse oximetry	Paediatric post anaesthesia care unit (PACU)	**Sedatives:** post general anaesthesia **Airway:** Native airway (non-intubated)	Standard monitoring + Capnography available (Capnography used + visible to treatment team) Alarms set for ETCO2 below 30mmHg and above 50mmHg	Standard monitoring + Capnography not available (Capnography used but not visible to treatment team)	**Primary outcome:** -Frequency of respiratory depression -hypopnoeic hypoventilation (ETCO2 </= 30mmHg for > 30 s without rise in resp rate > 50%) -Bradypneic hypoventilation (ETCO2 >/= 50mmHg for > 50 secs) -Apnoea (ETCO2= 0mmHg for minimum 20 secs) -Oxygen desaturations -Staff interventions
Langhan 2015	Randomized controlled trial (RCT) N=154 **Inclusion criteria:** -Age 1-20 y.o. (Paediatrics only) - IV sedation given **Exclusion criteria:** -Intubation -Administration of baseline O2 -Conditions with abnormal ETCO2 -Intolerance of nasal cannula -Crying > 20% of sedation	Emergency Dept of tertiary centre	**Sedatives:** Ketamine Midazolam **Airway:** Native airway (non-intubated)	Standard monitoring + Capnography available (Capnography used + visible to treatment team)	Standard monitoring + Capnography not available (Capnography used but not visible to treatment team. Alarms silenced)	**Primary outcome:** -Hypoventilation (capnograph<30 mmHg or > 5-mmHg) -Intervention by staff -Oxygen desaturations (SpO_2 <95%) **Secondary outcome:** -Persistent hypoventilation -Timely intervention
Lightdale 2006	Randomized controlled trial (RCT) N= 163 **Inclusion criteria:** -Age 6m – 19 yrs -Pts undergoing procedures at an outpatient endoscopy unit -ASA class I to II **Exclusion criteria:** -ASA class III to V -Received general anaesthesia -Seizure disorder -Use of mood altering/ chronic pain medications	Outpatient endoscopy Unit at a Children's hospital Procedure: GI endoscopy (upper and lower?)	**Sedatives:** Midazolam, Fentanyl **Airway:** Native airway (non-intubated)	Standard monitoring + Capnography (Capnography is used but not visible to treatment team) Independent observer indicated with raised hand if capnography waveforms absent for 15 seconds	Standard monitoring + Capnography (Capnography is used but not visible to treatment team) Independent observer indicated with raised hand if capnography waveforms absent for 60 seconds	**Primary outcome:** -Oxygen desaturation (SpO_2 <95% for > 5 seconds) **Secondary outcome:** -Abnormal ventilation -Termination of procedure -Adverse events (need for bag & mask ventilation, reversal of sedation, seizures)

Risk of bias assessment

All 3 RCTs had adequate sequence generation and allocation concealment. Patients and treatment teams were blinded to treatment allocation in 1 study [165] (physicians were signalled by an independent investigator if hypoventilation was detected by the capnography device for > 15 seconds in the intervention group and > 60 seconds in the control group), but staff may be able to "guess" the group allocation from the frequency of alert. Blinding was not possible in the other 2 studies [163, 164]. Outcome assessors were not blinded to group allocation in all 3 studies. In one study [164], the research team needed to recruit more patients after initial randomization, whilst data were lost for 10 patients in another study [163], which led to risk of bias for the intention-to-treat principle. One study had reporting bias that the outcome of interventions used for hypoxia in each group was not reported [165]. In one study, there was significant difference in baseline respiratory rate between the 2 groups [164] (Table 3).

Data analysis and synthesis

Hypoventilation and oxygen desaturation are the primary outcomes in all 3 trials. However, the definition of hypoventilation is not unified across studies. The significance of transient hypoventilation is not known and the Working Group considered this not an important outcome. On the other hand, the definition of oxygen desaturation is less varied among the 3 studies. In 2 studies [164, 165], oxygen desaturation is defined as SpO_2 < 95%. In a third study [163], desaturation is categorized into "mild oxygen desaturation" (SpO_2 < 95% when receiving supplemental O_2 or SpO_2 < 93% in room air), "moderate oxygen desaturation" (SpO_2 < 90% when receiving supplemental O_2 or SpO_2 < 90% in room air), or "severe desaturation" (SpO_2 < 85% when receiving O_2 or SpO_2 < 80% in room air). Severe oxygen desaturation is considered a critical outcome and moderate desaturation is considered an important outcome by the Working Group, as it leads to hypoxia, and known to be associated with adverse effect. The results of the data analysis on oxygen desaturation are shown in Table 4.

In 2 studies [163, 164], there was no significant difference in oxygen desaturation between the capnography and the comparison group. One study demonstrated reduced occurrence of oxygen desaturation in the capnography group [165]. Combined analysis of the 3 RCTs (Figure 3) demonstrated moderate heterogeneity among studies (I^2 = 0.7). Therefore, the random effects model was used for meta-analysis (Figure 1). There was no significant difference in desaturation between the capnography and comparison groups (Risk ratio 0.89, 95% CI 0.47-1.68).

Table 3: Risk of bias assessment of RCTs for clinical effectiveness of ETCO2 monitoring for Paediatric Patients undergoing procedural sedation:

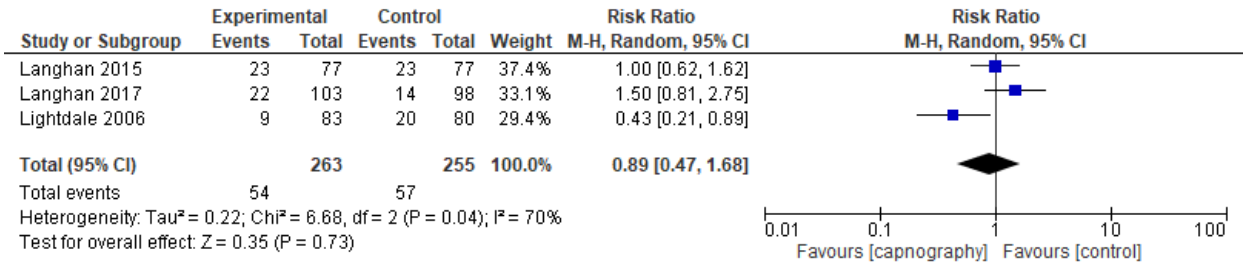
Study	Critical appraisal	Risk of bias
Langhan 2017 RCT	**Selection bias:** -Randomization by statistician in blocks of 6 -Allocation concealment performed, patients allocated to treatment arms using sequentially numbered, sealed, opaque envelopes	**Low**
	Performance bias: Patients and treatment teams are not blinded to group allocation	**High**
	Detection bias: Outcome assessors are not blinded to group allocation	**High**
	Reporting bias: No indication of selective outcome reporting	**Low**
	Attrition bias: -Data for 10 patients (4 from treatment group, 6 from comparison group) was lost □ violation of Intention-to-treat (ITT) principle	**High**
	Other bias: No evidence of other bias	**Low**
	Remarks: Study may be under-powered to detect severe hypoxia and severe adverse events	
Langhan 2015 RCT	**Selection bias:** -Randomization by statistician in blocks of 6 -Allocation concealment performed, patients allocated to treatment arms using sequentially numbered, sealed, opaque envelopes	**Low**
	Performance bias: Patients and treatment teams are not blinded to group allocation	**High**
	Detection bias: Outcome assessors are not blinded to group allocation	**High**
	Reporting bias: No indication of selective outcome reporting	**Low**
	Attrition bias: -Patients excluded after randomization and team needed to recruit more patients afterwards -> violation of intention-to-treat principle -Incomplete follow up: Monitoring period is very short, may not pick up events after the initial period	**High**
	Other bias: Significant difference in baseline respiratory rate between the 2 groups	**High**
	Remarks: Study may be under-powered to detect severe hypoxia and severe adverse events	
Lightdale 2006 RCT	**Selection bias:** -Randomization performed by independent observers, based on permutated blocks of 2,4,6,8 and stratified by procedure type. -Allocation concealment performed, patients allocated to treatment arms using sequentially numbered, opaque sealed envelopes	**Low**
	Performance bias: Patients and treatment teams are blinded to group allocation, but blinding is not very robust (staff may be able to "guess" the group allocation from the frequency of alert	**Unclear**
	Detection bias: Outcome assessors are not blinded to group allocation	**High**
	Reporting bias: Frequency of interventions used for hypoxia in each group is not reported	**High**
	Attrition bias: Intention to treat principle observed. No patients lost to follow up	**Low**
	Other bias: No evidence of other bias	**Low**
	Sample size: Target sample size (n= 173) is not achieved **Precision:** Confidence interval (CI) for logistic regression analysis is very large, indicating poor precision **Directness:** Use of capnography is not directly assessed, therefore this study cannot be translated directly into clinical practice	

Key: ITT= Intention to treat RCT= Randomized controlled trial

Table 4: Summary of findings for oxygen desaturation

Primary outcome (+ Definition)	**Intervention**	**Comparator**	**Risk ratio (95% C.I.)**	**P-value**
Study 1: Langhan 2017 (RCT)				
	Standard monitoring + visible capnography	**Standard monitoring**		
Mild desaturation <95%	15/103 (15%)	7/98 (7%)		0.09
Moderate desaturation <90%	5/103 (5%)	5/98 (5%)		0.94
Severe desaturation <85%	2/103 (2%)	2/98 (2%)		1.00
Any desaturation	**22/103 (21.4%)**	**14/98 (14.3%)**	**1.50 (0.81, 2.75)**	0.2
Primary outcome (+ Definition)	**Intervention**	**Comparator**	**Risk ratio (95% C.I.)**	**P-value**
Study 2: Langhan 2015 (RCT)				
	Standard monitoring + capnography visible	**Standard monitoring**		
Oxygen desaturation (SpO_2 < 95%)	**23/77 (29.9%)**	**23/77 (29.9%)**	**1.00 (0.62, 1.62)**	**1.0**
Primary outcome (+ Definition)	**Intervention**	**Comparator**	**Risk ratio (95% C.I.)**	**P-value**
Study 3: Lightdale 2006 (RCT)				
	Signaled when capnography waveforms absent for 15 secs	**Signaled when capnography waveforms absent for 60 secs**		
Oxygen desaturation (SpO_2 < 95%) for > 5 secs	**9/83 (10.8%)**	**20/80 (25%)**	**0.43 (0.21, 0.89)**	**0.024**

Figure 1: Meta-analysis of primary outcome for 3 RCTs (Forest Plot)- oxygen desaturation



In addition to any oxygen saturation, other outcomes including apnoea, hypoventilation, and termination of procedure were also analyzed. The evidence profile for these outcomes is presented in Table 5.

Table 5: Evidence profile of the effect of capnography on different outcomes

Quality assessment						Effect					
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Capnography**	**Control**	**RR (95% CI)**	**Absolute (95% CI)**	**Quality of evidence**	**Importance**
Severe desaturation											
1	RCT	serious	not serious	serious	serious	2/103 (1.9%)	2/98 (2.0%)	0.95 (0.14-6.62)	**0 fewer per 1,000** (from 40 fewer to 40 more)	+ (very low)	critical
Apnoea											
1	RCT	serious	not serious	serious [b]	serious	30/103 (29.1%)	28/98 (28.6%)	1.02 (0.66-1.57)	**10 more per 1,000** (from 120 fewer to 130 fewer)	+ (very low)	critical
Termination of procedure											
1	RCT	serious	not serious	not serious	serious	0/83 (0.0%)	0/80 (0.0%)	not estimable	**NA**	++ (low)	critical
Hypoventilation requiring bagging											
2	RCT	serious	not serious	not serious	serious	0/160 (0.0%)	0/157 (0.0%)	not estimable	**NA**	++ (low)	critical
Moderate desaturation											
1	RCT	serious	not serious	serious	serious	5/103 (4.9%)	5/98 (5.1%)	0.95 (0.28-3.19)	**0 fewer per 1,000** (from 60 fewer to 60 more)	+ (very low)	important
Any desaturation											
3	RCT	serious	serious	not serious	serious	54/263 (20.5%)	57/255 (22.4%)	0.89 (0.47-1.68)	**20 fewer per 1,000** (from 90 fewer to 50 more)	+ (very low)	important
Any hypoventilation											
1	RCT	serious	not serious	not serious	serious	58/103 (56.31%)	60/98 (61.2%)	0.92 (0.73-1.16)	**50 fewer per 1,000** (from 190 fewer to 90 more)	++ (low)	not important

Important information obtained from studies not included in review

In addition to results obtained from the studies included, review of excluded studies also yielded some important information. No adverse event of capnography was reported in all the studies. Two studies reported that capnographic monitoring is well tolerated in most patients [36, 170]. However, one study reported a high incidence of false positive events in capnography [166]. Another study [174] reported that baseline ETCO2 could not be obtained in 20% of patients with developmental delay, as the patients could not co-operate. These highlight the practical difficulty in applying capnography to paediatric patients

Discussion

Although capnography monitoring is recommended in adult patients undergoing sedation for procedures, there are not many studies on the use of capnography in children. From the current systematic review, most of the studies on capnography in paediatric sedation are of low or very low quality. Even though there are three RCTs on this topic, there is heterogeneity among the studies, as well as significant risk of bias in all of them. At the same time, there are no standardized definitions for important outcomes like oxygen desaturation, hypoventilation, and abnormal ventilation. Ideally, larger scale RCTs with clear-cut definitions of outcome would provide more important information.

One very important outcome parameter used in most studies is oxygen desaturations, as it can lead to potentially serious sequelae. From this review, capnography does not significantly decrease or eliminate desaturations. Thus, unlike the situation in adults, there is no adequate evidence to recommend routine capnography.

Another concern is whether significant side effects are associated with paediatric capnography. As capnography is non-invasive, the risk of physical harm to the patient is minimal. However, some patients (especially those with developmental delay), may be unable to tolerate the nasal cannula and become very irritable, thus leading to procedure failure. Also, routine capnography monitoring may pick up episodes of subclinical, transient hypoventilation which are not associated with desaturations or other serious sequelae.

If intervention is given (e.g., waking the child) for all these episodes, it may lead to repeated interruptions in the procedure.

There is low level of evidence from 1 study [165] on the use of capnography in decreasing mild and transient desaturation (SPO_2<95% for >5 secs) in GI endoscopy procedure.
As patients with conditions of ASA class III to V or with abnormal ETCO2 / pulse oximetry or requiring baseline O_2 were excluded in the reviewed studies, the effect of capnography on children with co-morbidities (e.g., those with syndromal diagnosis and congenital upper airway obstruction, e.g., Pierre Robin sequence) was not assessed.

Summary
A comprehensive search of MEDLINE, Pubmed, EMBASE and Cochrane Library identified 3 relevant paediatric RCTs comparing addition of capnography to routine oximetry monitoring for children undergoing procedural sedation. The combined results showed that compared with no capnography, those who received capnography monitoring are not significantly different in frequency of successful procedure and oxygen desaturation (low to very low quality of evidence). Subgroup analysis suggested that for children undergoing deep sedation for endoscopy, those who received capnography have fewer transient and mild desaturations (low level of evidence). The included trials have overall serious risk of bias and low precision in most outcome estimates and results were inconsistent among studies.

Recommendations

1. We suggest that capnography is not routinely required for healthy children undergoing procedural sedation. (Weak recommendation, low to very low quality of evidence)
2. As patients with conditions of ASA class III to V or with abnormal ETCO2 / pulse oximetry or requiring baseline O_2 were excluded in the reviewed studies, there is no evidence-based recommendation. The use of capnography in children with co-morbidities (e.g., those with syndromal diagnosis and congenital upper airway obstruction, e.g., Pierre Robin sequence or with abnormal ETCO2 or pulse oximetry) would need to be based on clinical judgement. (No recommendation)
3. We suggest capnography may be considered in the procedural sedation for GI endoscopy procedure. (Weak recommendation, low quality of evidence)

** The detail use of capnography and interpretation of its wave forms can be found from various references [81] and is beyond the scope of this recommendation. **

APPENDIX K

Chloral hydrate

Chloral hydrate (CH) has slow onset of action which is around 30 minutes after oral administration. The duration of action is up to 4-8 hours. Sedation by CH is not always successful. In about 10-20% of procedures, CH failed to sedate the child adequately.

CH is safe in general, but side effects occur in 5-10% of children including vomiting and paradoxical excitation. Major side effects such as respiratory depression and cardiovascular instability have been reported in about 1% of cases in the literature, especially at higher doses.

CH should be given only in facilities capable of resuscitation. Safety precaution including pre-sedation assessment, and close monitoring after oral administration are recommended.

Because of prolonged sedative effects after taking CH, the patient requires a longer period of post-sedation observation and discharge is allowed only when the patient meets discharge criteria.

To review the "2013 Recommendation", we examined and appraised recently published systemic reviews and meta-analyses on the use of CH and provided opinions to update the recommendations.

In the review we aimed to answer the following clinical question:

"Is chloral hydrate effective and safe compared with other sedatives for procedural sedation in children?"

We identified and included three recent systemic reviews and meta-analyses:

- Safety and efficacy of chloral hydrate for procedural sedation in paediatric ophthalmology: a systematic review and meta-analysis. A Mataftsi, et al. Br J Ophthalmol. 2017 [175]

- Chloral hydrate as a sedating agent for neurodiagnostic procedures in children. CY Fong, et al. Cochrane Database Syst Rev. 2017 [176]

- Efficacy of chloral hydrate oral solution for sedation in pediatrics: a systematic review and meta-analysis. Z Chen, et al. Drug Design, Development and Therapy 2019 [177]

Efficacy of CH compared to other sedative agents and non-pharmacological intervention, and different doses of oral CH

Summary of each meta-analysis

Safety and efficacy of chloral hydrate for procedural sedation in paediatric ophthalmology: a systematic review and meta-analysis.
Mataftsi A, et al. Br J Ophthalmol. 2017

Objectives:
- To review the efficacy of CH in achieving paediatric ophthalmic examinations under sedation
- To review the drug's safety of its use in children

Databases searched:
Medline (PubMed), EMBASE, Web of Science, Scopus, CENTRAL, Google Scholar and Trip database, to 1 October 2015. Only RCTs were included in the meta-analysis. Observational studies were included in assessment of safety.

Studies included:

- 13 RCTs were found that compared CH to another agent, but none of which specifically concerned ophthalmic procedures.
- 8 /13 compared CH to oral, intranasal and sublingual midazolam
- 5 /13 compared CH to another sedative (oral promethazine, oral melatonin, oral hydroxyzine, IV pentobarbital, or an IM cocktail of atropine, meperidine, promethazine and secobarbital).

Summary of efficacy of CH

- Overall, CH (50 to 100mg/kg) was more successful in achieving sedation (OR 3.49, 95% CI 1.32 to 9.21; 13 studies); this result was significant when CH was compared to midazolam alone (OR 5.77, 95% CI 1.42 to 23.52; 8 studies) but not significant when it was compared to another sedative (OR 1.83, 95% CI 0.50 to 6.69; 5 studies).

- Meta-regression revealed no significant effect of mean age or CH dosage on the summary outcome.

  The included RCTs presented significant heterogeneity in many areas. Risk of bias assessment revealed that the majority of trials failed to meet the criteria set by the Cochrane Collaboration. Thus, interpretation of results is difficult, given the high probability of bias.

Chloral hydrate as a sedating agent for neurodiagnostic procedures in children.
CY Fong, et al. Cochrane Database of Systematic Reviews 2017

Objectives:
To assess the effectiveness and adverse effects of CH as a sedative agent for non-invasive neurodiagnostic procedures in children.

Databases searched
MEDLINE (OVID SP) (1950 to July 2017), the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library, Issue 7, 2017), Embase (1980 to July 2017), and the Cochrane Epilepsy Group Specialized Register (via CENTRAL). Only RCTs included.

Included studies

- 13 single centre RCTs included (up to July 2017). The number of children ranged from 40 to 582, with a total of 2390 children.

- 5 trials were conducted on neuroimaging studies (brain CT or brain MRI); 8 were conducted on EEG studies.

There were ten comparisons:

CH group and dose	**Other agents / other doses of CH**
50 mg/kg or 100 mg/kg	oral dexmedetomidine
75 mg/kg	intravenous pentobarbital
75 mg/kg or 100mg/kg	orally or intranasal midazolam
50 mg/kg	oral melatonin
60 mg/kg	music therapy
50 mg/kg	oral hydroxyzine hydrochloride
70 mg/kg	oral promethazine
50 mg/kg	rectal midazolam
100 mg/kg	CH 70 mg/kg
100 mg/kg	CH 50 mg/kg

Summary of efficacy of CH:

- Children who received CH had lower sedation failure when compared with oral promethazine (RR 0.11, 95% CI 0.01 to 0.82; 1 study, moderate-quality evidence).

- Children who received CH had more sedation failure when compared with music therapy (RR 17.00, 95% CI 2.37 to 122.14; 1 study, very low quality evidence)
- Sedation failure rates were similar between CH, and oral dexmedetomidine, oral hydroxyzine hydrochloride, IV pentobarbital and oral midazolam.

- Chloral hydrate 100 mg/kg had lower sedation failure than chloral hydrate 50mg/kg, (RR 0.23, 95% CI 0.05 to 0.99; 1 study) and no difference when compared with chloral hydrate 70 mg/kg (RR 0.46, 95% CI 0.19 to 1.09; 1 study).

Efficacy of chloral hydrate oral solution for sedation in pediatrics: a systematic review and meta-analysis.
Chen Z, et al. Drug Design, Development and Therapy 2019

Objective:
To evaluate systematically the efficacy of CH oral solution in paediatrics for sedation

Databases searched
PubMed, EMBase, Cochrane Library and four Chinese electronic databases (China National Knowledge Infrastructure, WanFang Database, Chinese Biomedical Literature Database, VIP Database for Chinese Technical Periodicals). Only RCTs included.

Included studies

- 24 RCTs, with total 3564 subjects, published between 2000 and 2017 were included

- dose range of CH oral solution is 25–100 mg/kg

- comparison: placebo, no intervention, or other sedatives (midazolam, diazepam, oral or intranasal dexmedetomidine, barbiturates)

- 3/24 RCTs involved painful procedures (2 lumbar puncture, 1 suture of face)

Summary of efficacy of CH:

- sedative effect of CH (25-100mg/kg) was better than midazolam (oral 0.5mg/kg, intranasal 0.2-0.5mg/kg, sublingual 0.3mg/kg, iv 0.2mg/kg) (RR 1.63, 95% CI 1.48 to 1.79; 8 studies)

- there was no significant difference in the success rate of sedation between CH (25-100mg/kg) and diazepam (oral, 5.0 mg per dose, im 0.1-0.2mg/kg, iv 0.3-0.5mg/kg) (RR 0.93, 95% CI 0.80 to 1.08; 3 studies), dexmedetomidine (oral 2-3mcg/kg, intranasal 1-3mcg/kg) (RR 0.92, 95% CI 0.80 to1.06; 4 studies) and barbiturates (im phenobarbital 5mg/kg, iv pentobarbital 2-5mg/kg, rectal thiopental 25mg/kg) (RR 1.03, 95% CI 0.94 to 1.13; 5 studies)

The sedation success rate of CH in different procedures in RCTs included in Chen's (2019) meta-analysis:

	%
Hearing test	95.12%
ECG	93.62%
MR scan	88.54%
Ophthalmic testing	85.92%
Lumbar puncture	80.43%
CT scan	78.26%
Dental examination	76.05%

Summary and limitation of the 3 meta-analyses:

Meta-analysis	**procedures**	**Number of RCTs**	**Year of publication of RCTs**	**Total number of subjects**	**Comparisons**
Fong 2017	neurodiagnostic	13	up to July 2017	2390	other sedative agents and non-drug, different doses of CH
Mataftsi 2017	all	13	Up to Oct 2015		Other sedative agents
Chen 2019	all	24	up to 2017	3564	Placebo, and other sedative agents

There were a total of 32 RCTs included in the afore-mentioned systematic reviews. We noted that there are overlaps of primary source articles among the three meta-analyses:
4 RCTs are included in all 3 meta-analyses
4 RCTs overlapped in Fong's and Mataftsi's meta-analyses
4 RCTs overlapped in Fong's and Chen's meta-analyses
2 RCTs overlapped in Chen's and Mataftsi's meta-analyses

Meta-analysis	**Efficacy of CH**	**Adverse effect**	**Opinions on efficacy**	**Opinion on safety**	**limitations**
Fong 2017	Yes	Yes	• CH better than oral promethazine • similar between CH, and oral dexmedetomidine, hydroxyzine , iv pentobarbital and oral midazolam	requires further study	• wide variation 'risk of bias' profiles • evaluation of efficacy of the sedative agents was underpowered • Most RCTs are of very low quality or low quality
Mataftsi 2017	Yes	No	• CH better than midazolam • Similar between CH and promethazine, melatonin, hydroxyzine, pentobarbital, or a cocktail of atropine, meperidine, promethazine and secobarbital	fairly safe	• the RCTs have significant heterogeneity in many areas • majority of RCTs failed to meet assessment criteria for risk of bias
Chen 2019	Yes	No	• CH was better than	--	• overall quality of the

			midazolam • similar between CH and diazepam, oral and intranasal dexmedetomidine, barbiturates		included RCTs was not satisfactory • some studies had compelling levels of heterogeneity

Summary of efficacy of CH from the three meta-analyses:

- CH is an effective sedative agent.
- Successful rate of sedation by CH is approximately 90% (range 76 to 95 % according to one meta-analysis).
- High dose CH (100mg/kg) may be more effective than low dose (50mg/kg).
- Compared with other sedatives, CH may be more effective than midazolam (oral, iv, im, intranasal) and promethazine (oral).
- CH may be equally effective when compared to diazepam (oral, iv, im), dexmedetomidine (oral and intranasal), hydroxyzine (oral) and barbiturates (iv, im).

Adverse effects of chloral hydrate:

Chen et al. did not perform comparison of adverse effects (AE) of CH with other sedative agents [177].

Fong et al. [176] found that when CH was compared to oral dexmedetomidine, there was an increased risk of overall adverse events (RR 7.66, 95% CI 1.78 to 32.91; 1 study, low-quality evidence), and nausea and vomiting (RR 12.04, 95% CI 1.58 to 91.96; 1 study, low-quality evidence). The authors commented that adverse effects of CH required further study.

Mataftsi et al. [175] performed a systemic analysis on adverse effects of CH, which included 91 observational studies published up to October 2015. The authors reported adverse events in 24,265 sedation episodes, where CH was the sole sedative agent used.

Major	Airway misalignment/stridor/ laryngospasm	37	(0.152%)
	Respiratory distress	52	(0.214%)
	Apnoea	59	(0.243%)
	Central nervous system depression	6	(0.025%)
	Cardiovascular instability	86	(0.354%)
	Pulmonary aspiration	2	(0.008%)
	Need for endotracheal intubation	10	(0.041%)
	Oral laceration	4	(0.016%)
	Oesophageal/gastric ulcerations	7	(0.029%)
	Death	2	(0.008%)
Minor	Oxygen desaturation/hypercarbia	423	(1.743%)
	Prolonged sedation	200	(0.824%)
	Dizziness/sleepiness	121	(0.499%)
	Post-discharge sleep disturbances	50	(0.206%)
	Ataxia/unsteadiness	196	(0.808%)
	Loss of appetite	22	(0.091%)
	Paradoxical reaction	491	(2.023%)
	Emesis/nausea	808	(3.330%)
	Immediate defecation/diarrhoea	33	(0.136%)
	Rash	14	(0.058%)

*(*our working group had classified severity of adverse events into major and minor as in the above table.)*

Overall minor AE occurred in approximately 10%, most commonly nausea, vomiting, prolonged sedation, excitement/restlessness and paradoxical reaction.

Major AE was rare (1.1%) and included central nervous system depression, respiratory or airway complications, cardiovascular events, gastrointestinal complications and two deaths.
Severe AE, including two deaths, were related to comorbidity, overdose or aspiration.

Five studies reported on oxygen saturation decrease in intervention and control groups. The synthesis of this outcome did not reveal any difference between CH and other sedatives (OR 1.16, 95% CI 0.40 to 3.35; 5 studies).

GRADE assessment of current evidence

Certainty assessment						
№ of studies	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall certainty of evidence**
Sedation failure						
32 RCTs in 3 SRs	serious [a]	serious [b]	not serious	serious [c]	none	⊕◯◯◯ VERY LOW
Adverse effects						
18 RCTs in 2 SRs; 91 observational studies in 1 SR;	serious [a]	serious [b]	not serious	serious [c]	none	⊕◯◯◯ VERY LOW

CI: Confidence interval; **RCT**: randomized controlled trial; **SR**: systematic review

Explanations
a. Most studies had unclear or high risk of bias.
b. Studies were very heterogeneous in the patient characteristics, procedures performed, comparative sedatives used, dosing of sedatives, and outcome measures.
c. Most relative risks had wide confidence intervals.

Recommendation on the use of chloral hydrate as a sedative agent in children

We suggest chloral hydrate as first-line agent in children who require sedation for non-painful procedures. (Weak recommendation, very low quality of evidence)

This recommendation is based on overall assessment of evidence that:

1. Chloral hydrate is a more effective or equally effective sedation agent compared with other alternatives in children.

2. Chloral hydrate has vast amount of information on safety. Chloral hydrate is a fairly safe drug for sedation in children. There is no evidence that serious adverse effects are excessive compared with alternative sedation agents.

3. Chloral hydrate has a low cost compared with alternatives.

Limitations of the recommendations

As mentioned by authors of the 3 meta-analyses, the overall quality of the included RCTs was not satisfactory. In many RCTs blinding of participants and personnel assessment was not performed. Allocation concealment and other biases were ambiguous in the majority of trials.

Some studies had significant levels of heterogeneity, which was caused by dose of the treatment and control groups, age of the child, type of procedures, and outcome measures.

Caution should be exercised in the use of oral chloral hydrate because of the low quality and limited evidence associated with the RCTs in the meta-analyses.

Chloral hydrate may be associated with more adverse effects compared with dexmedetomidine in some situations.

Formal economic analyses are not available for chloral hydrate as compared with alternative sedation agents.

Unanswered issues related to the use of chloral hydrate in children

Although chloral hydrate has been used for many years at different dosage and with different monitoring arrangement, there are still many issues that required further study:

- Efficacy of CH in various age and patient groups in various painless procedures
- Adverse events in various age and patient groups and different oral doses
- Overall safety of CH use in children with the implementation of safety measures and being used at the current recommended dosage
- Cost-effectiveness analysis

APPENDIX L

Intranasal dexmedetomidine

There are limited choices on non-intravenous paediatric sedation agents. Chloral hydrate has been used for decades, with limited supplies in some countries.

Dexmedetomidine is an alpha-2 adrenergic receptor agonist with minimal respiratory depression. It has sedative, anxiolytic and analgesic properties. It can enhance endogenous sleep by decreasing noradrenergic output from locus ceruleus. It has a shorter half-life of two hours than chloral hydrate with the active metabolite trichloroethanol.

Recommended dosage:
Age: more than 1 month
Initial dosage: 2-3microgram/kg INTRANASALLY 30 minutes before procedure
Rescue dosage: 1-2microgram/kg
Maximum dosage: 4microgram/kg

Need to be applied through an atomizer

Preparation

1. Use undiluted IV dexmedetomidine 100mcg/ml solution
2. Draw up corresponding volume of dexmedetomidine ordered plus an additional 0.1ml into a syringe (The extra 0.1ml is to account for the dead space of the atomizer)
3. Attach the atomizer to the syringe via the luer-lock connector on the syringe
4. Briskly compress the syringe plunger and deliver half of the medication dose into each nostril to maximize dispersion and absorption area

Alternative method of slowly dripping from a needleless syringe onto the nasal mucosa while in a recumbent position have been used successfully as premedication before anaesthesia [178-181] or for sedation [182]. Preliminary studies comparing the effectiveness of dripping method against application via MAD have mixed results with equal or slight benefit in the MAD group [85, 183]. Further confirmation of the dripping method effectiveness would be desirable for a more cost-effective use of the medication.

Adverse effect monitoring
Side effect may occur in less than 5% of patients. Desaturation requiring oxygen supplementation occurred in 0-6% of patients [184-187]. Patients need to be monitored for bradycardia and hypotension. In studies reported, no child has clinically significant bradycardia or hypotension requiring intervention.

Literature Search
We performed literature search to review existing evidence on the use of intranasal dexmedetomidine for procedural sedation in children. We formulated the following PICO question for this review purpose.

1. Is intranasal dexmedetomidine (IN DEX) effective and safe when compared with chloral hydrate (CH) for procedural sedation in children?
2. Is dexmedetomidine effective and safe when used as rescue therapy for children who have failed chloral hydrate?

We used search terms “dexmedetomidine”, “intranasal “AND “child”, and databases including Pubmed, EMBASE, OVID Medline, and Google Scholar were searched during 2010-2019. Those with search term “anaesthesia” were excluded. Studies not comparing dexmedetomidine with chloral hydrate were also excluded. Retrospective case series were excluded. In the search as 2019, no systematic review or meta-analysis was found. A total of six RCT reports were identified. One report was excluded as it had a duplicated patient pool with another RCT by the same group. Another RCT was excluded as dexmedetomidine was used as premedication rather than sedation agent for CT scan. Finally, four RCTs were included for the first PICO question and one RCT was included for the second PICO question.

PICO Question 1

Is IN DEX effective and safe when compared with CH for procedural sedation in children?

Studies included

(i) Miller J, Xue B, Hossain M, et al. Comparison of dexmedetomidine and chloral hydrate sedation for transthoracic echocardiography in infants and toddlers: A randomized clinical trial. Pediatric Anesthesia. 2016;26(3):266-272. [185]

(ii) Cao Q, Lin Y, Xie Z, et al. Comparison of sedation by intranasal dexmedetomidine and oral chloral hydrate for pediatric ophthalmic examination. Pediatric Anesthesia. 2017;27(6):629-636. [184]

(iii) Yuen VM, Li BL, Cheuk DK, et al. A randomized controlled trial of oral chloral hydrate vs. intranasal dexmedetomidine before computerized tomography in children. Anaesthesia. 2017;72(10):1191-1195. [186]

(iv) Reynolds J, Rogers A, Medellin E, Guzman JA, Watcha MF, Cravero J. A prospective, randomized, double-blind trial of intranasal dexmedetomidine and oral chloral hydrate for sedated auditory brainstem response (ABR) testing. Pediatric Anesthesia. 2016;26(3):286-293. [187]

Study characteristics and key efficacy findings are summarized as below:

Study	Procedure	No. of subjects	Age (months)	Intervention (IN DEX)	Control (CH)	Efficacy in intervention group	Efficacy in control group
Cao 2017	eye exam	144	10-25	2mcg/kg	80mg/kg	86%	64%
Miller 2016	TTE	150	3.2-34.1	DEX2-2mcg/kg DEX3-3mcg/kg	70mg/kg	DEX2 – 100% DEX3 – 96%	96%
Reynolds 2016	AABR	85	23.3 (95%CI: 19.5-27.2)	3 +/-1 mcg/kg	50+/-25mg/kg	89%	66%
Yuen 2017	CT	196	8-70	3mcg/kg	50mg/kg	74%	76%

(a) Patients excluded in the above studies:
   a. Allergy to Dexmedetomidine or chloral hydrate
   b. Cardiac arrhythmia, bradycardia, second degree heart block
   c. American Society of Anaesthesiologist (ASA) physical status 3 or more

(b) Efficacy of IN DEX vs CH as a primary agent:

When IN DEX 2mcg/kg is compared to chloral hydrate, the sedation failure rate is lower with a faster onset time (Figures 1 and 2). However, when used at a higher dose IN DEX 3mcg/kg, a superior effect in sedation failure rate cannot be demonstrated, though sedation onset time was faster in the IN DEX group (Figures 3 and 4). A possible explanation can be due to level of heterogeneity in the procedures involved, which may require a variable degree of sedation involved to complete the procedures. Another explanation is the small sample size involved in the studies which did not demonstrate the true effects of these agents.

Figure 1. Failed sedation rate comparing IN DEX 2mcg/kg vs CH as a primary agent

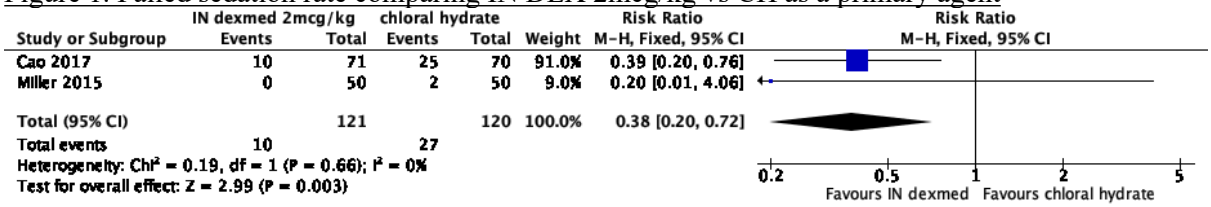


Figure 2. Failed sedation rate comparing IN DEX 3mcg/kg vs CH as a primary agent

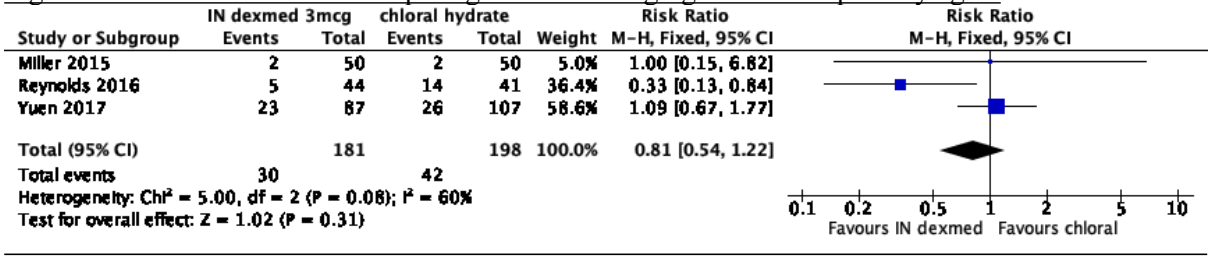


Figure 3. Onset time of sedation comparing IN DEX 2 mcg/kg vs CH as a primary agent

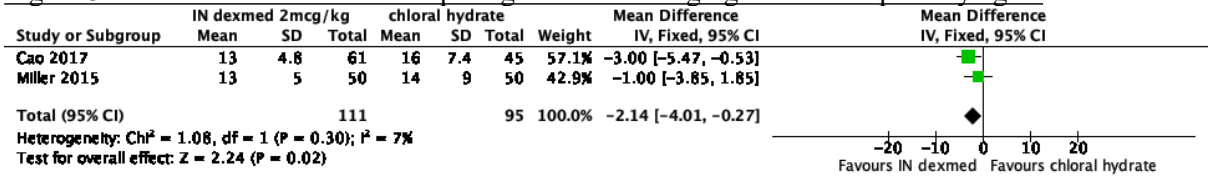
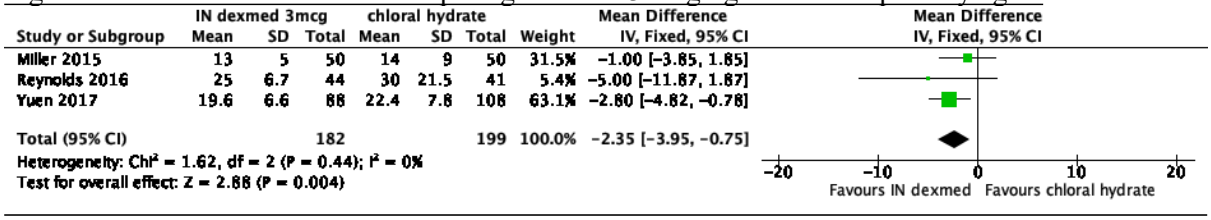


Figure 4. Onset time of sedation comparing IN DEX 3 mcg/kg vs CH as a primary agent

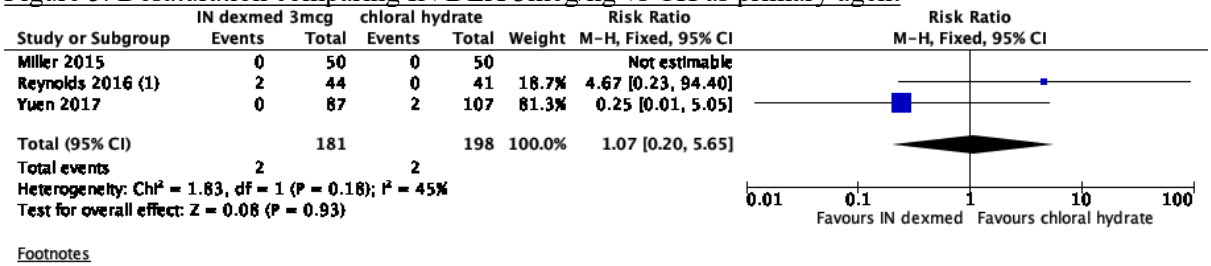


(a) Adverse Effects comparing IN DEX vs CH as primary agent

There is no significant difference in the adverse event of desaturation when comparing IN DEX and CH (Figure 5). In the studies involved, no adverse events of significant desaturation or bradycardia requiring interventions were noted in both study arms.

The risk of vomiting after chloral hydrate is high (6% CH vs 0% IN DEX; p = 0.03) [186]; (24% CH vs 0% IN DEX; p <0.001) [184]. Those who are more prone to gastrointestinal side effects may be more preferable to use IN DEX as sedation agent.

Figure 5. Desaturation comparing IN DEX 3mcg/kg vs CH as primary agent



Footnotes
(1) O2, repositioning

(b) Risk of bias in studies involved

Figure 6. Risk of bias summary for each included study

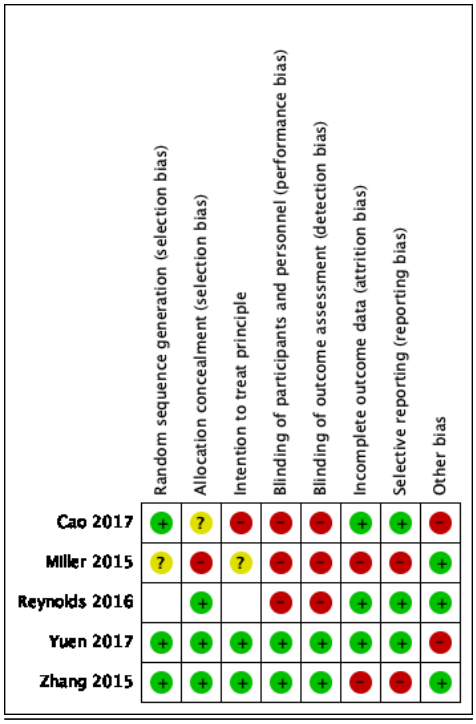
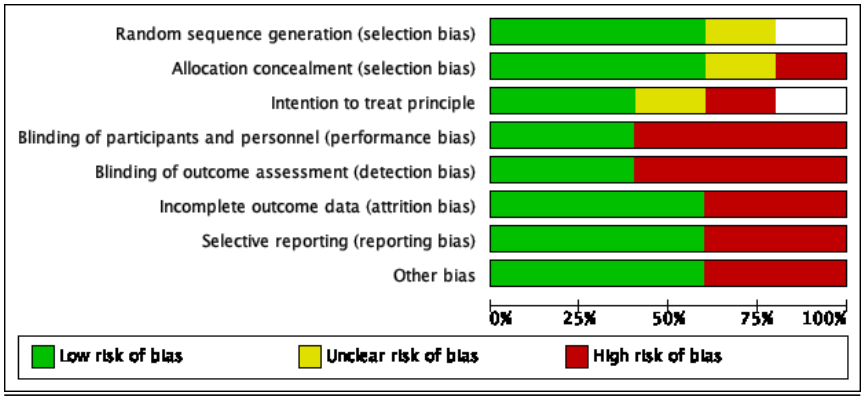


Figure 7. Risk of bias graph for each risk of bias item presented as percentages across all included studies.



Summary of findings and evidence profile for IN DEX 2mcg/kg vs CH as primary agent

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IN dexmed 2mcg/kg	chloral hydrate	Relative (95% CI)	Absolute (95% CI)		
Failed sedation for procedure												
2	randomised trials	serious	not serious	not serious	serious [a]	none	10/121 (8.3%)	27/120 (22.5%)	**RR 0.38** (0.20 to 0.72)	**140 fewer per 1,000** (from 180 fewer to 63 fewer)	⨁⨁◯◯ LOW	CRITICAL
Onset time of sedation												
2	randomised trials	serious	not serious	not serious	serious	none	111	95	-	MD **2.14 minutes fewer** (4.01 fewer to 0.27 fewer)	⨁⨁◯◯ LOW	NOT IMPORTANT
Any desaturation												
2	randomised trials	serious	serious	not serious	serious	none	3/120 (2.5%)	7/121 (5.8%)	**RR 0.47** (0.13 to 1.63)	**31 fewer per 1,000** (from 50 fewer to 36 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Desaturation requiring intervention												
1	randomised trials	serious	not serious	not serious	serious	none	0/50 (0.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	CRITICAL
Bradycardia/ hypotension requiring intervention												
1	randomised trials	serious	not serious	not serious	serious	none	0/71 (0.0%)	0/70 (0.0%)	not estimable		⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Summary of findings and evidence profile for IN DEX 3mcg/kg vs CH as primary agent

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IN dexmed 3mcg/kg	chloral hydrate	Relative (95% CI)	Absolute (95% CI)		
Failed sedation for procedure												
3	randomised trials	serious	serious	not serious	serious [a]	none	30/181 (16.6%)	42/198 (21.2%)	**RR 0.81** (0.54 to 1.22)	**40 fewer per 1,000** (from 98 fewer to 47 more)	⨁◯◯◯ VERY LOW	CRITICAL
Onset time of sedation												
2	randomised trials	serious	not serious	not serious	serious	none	138	158	-	MD **2.2 minutes fewer** (3.85 fewer to 0.55 fewer)	⨁⨁◯◯ LOW	NOT IMPORTANT
Any desaturations												
1	randomised trials	serious	not serious	not serious	serious [a]	none	2/50 (4.0%)	3/50 (6.0%)	**OR 0.65** (0.10 to 4.09)	**20 fewer per 1,000** (from 54 fewer to 147 more)	⨁⨁◯◯ LOW	IMPORTANT
Desaturation requiring intervention												
3	randomised trials	serious	serious	not serious	serious	none	2/181 (1.1%)	2/198 (1.0%)	**OR 1.07** (0.21 to 5.59)	**1 more per 1,000** (from 8 fewer to 44 more)	⨁◯◯◯ VERY LOW	CRITICAL
Bradycardia/ hypotension requiring intervention												
2	randomised trials	serious	not serious	not serious	serious	none	0/131 (0.0%)	0/148 (0.0%)	not pooled	see comment	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

New evidence of IN DEX as primary agent

Two systemic reviews were published in 2020 on IN DEX as primary agent [188, 189]. Poonai et al. [188] compared IN DEX with non-IV sedation agents including oral chloral hydrate, oral/ intranasal midazolam, oral/ intranasal ketamine. For painful procedures, IN DEX can adequately sedate 61.2% vs 47.1% patients among other non-IV formulations. In non-painful procedures, IN DEX can adequately sedate 84.1% vs 72.0% among other non-IV formulations.

Adverse effects were reported in 18 trials included. Comparing IN DEX with other non-IV formulations, bradycardia was reported in 2.2% vs 1%; hypotension 1.2% vs 1.5%; oxygen desaturation 0.5% vs 2% and vomiting 0.4% vs 7.9% respectively.

Certainty Assessment							No. Patients		Effect		Certainty	Importance
No. Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	IND	Other sedatives	Relative (95% CI)	Absolute (95% CI)		
Adequacy of Sedation												
18	Randomized trials	Not serious[a]	Serious[b]	Serious[c]	Not serious	None	1086 of 1362 (79.7%)	398 of 622 (64.0%)	Not pooled	See comment	⊕⊕◯◯ Low	Critical
Need for Additional Sedation												
5	Randomized trials	Not serious[a]	Not serious	Serious[c]	Not serious	None	22 of 223 (9.9%)	47 of 167 (28.1%)	Not pooled	See comment	⊕⊕⊕◯ Moderate	Critical
Onset of Sedation												
11	Randomized trials	Serious[d]	Serious[e]	Not serious	Not serious	None	IND range 7 to 31 minutes; intranasal comparator range 7 to 44.2 minutes				⊕⊕◯◯ Low	Important
Duration of Sedation												
6	Randomized trials	Serious[d]	Not serious	Not serious	Not serious	None	IND range 41 to 91.5 minutes; intranasal comparator range 77 to 85.9 minutes				⊕⊕⊕◯ Moderate	Important
Length of Stay												
4	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	IND range 76.8 to 156 minutes; intranasal comparator range 95 to 144 minutes				⊕⊕⊕⊕ High	Important
Analgesia												
1	Randomized trials	Not serious	Serious[f]	Not serious	Serious[g]	None	Overall significant difference in the mean (SD) FLACC score during dental procedures between IND 1 μg/kg (3.8 [0.8]), IND 1.5 μg/kg (3.7 [0.9]), intranasal midazolam (5.6 [1.1]), and intranasal ketamine (3.5 [0.7]) ($P < .001$).				⊕⊕◯◯ Low	Important
Adverse Effects												
18	Randomized trials	Serious[h,i,j]	Not serious	Not serious	Not serious	None	67 of 127 (9.2%)	98 of 591 (16.6%)	Not pooled	See comment	⊕⊕⊕◯ Moderate	Critical
Acceptance of IN Administration												
4	Randomized trials	Serious[k]	Not serious	Not serious	Not serious	None	IND well accepted by 199 of 264 (75.4%) participants with no reports of aborting administration because of refusal. Authors of 1 study reported intranasal midazolam was well accepted by 42 of 42 (100%) participants.				⊕⊕⊕◯ Moderate	Important

Adapted from Poonai et al. Intranasal Dexmedetomidine for Procedural Distress in Children: A Systematic Review [188]

Recommendations on using IN DEX as a primary agent

We suggest the use of intranasal dexmedetomidine as a primary agent in children 1 month to 5 years old in selected situations where IN DEX may show a more favourable side effect profile, e.g., in children prone to vomiting or potential ease of administration with intranasal formulation. (Weak recommendation, low to very low quality of evidence)

The efficacy and safety profile of IN DEX outside this age range for procedural sedation has not been demonstrated with randomized controlled trials.

PICO Question 2

Is Dexmedetomidine effective and safe when used as rescue therapy for children who have failed chloral hydrate?

Study included:

(i) Zhang W, Wang Z, Song X, et al. Comparison of rescue techniques for failed chloral hydrate sedation for magnetic resonance imaging scans—additional chloral hydrate vs intranasal dexmedetomidine. *Pediatric Anesthesia*. 2016;26(3):273-279. [190]

Study characteristics and key efficacy findings are summarized as below:

Study	Procedure	No subjects	Age (months)	Intervention (IN DEX)	Control (CH)	Efficacy in intervention group	Efficacy in control group
Zhang 2016	MRI scan	150	1-6	DEX 1- 1mcg/kg DEX 2- 2mcg/kg	25mg/kg	DEX 1 – 94% DEX 2 – 98%	80%

Summary of findings and evidence profile for IN DEX 1mcg/kg vs CH as rescue therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IN dexmed 1mcg/kg	chloral hydrate	Relative (95% CI)	Absolute (95% CI)		
Failed sedation for procedure												
1	randomised trials	serious	not serious	not serious	serious	none	3/50 (6.0%)	10/50 (20.0%)	**RR 0.30** (0.09 to 1.03)	**140 fewer per 1,000** (from 182 fewer to 6 more)	⨁⨁◯◯ LOW	CRITICAL
Onset time of sedation												
1	randomised trials	serious	not serious	not serious	serious	none	45	37	-	MD **0.5 minutes more** (1.17 fewer to 2.17 more)	⨁⨁◯◯ LOW	NOT IMPORTANT
Any desaturation												
1	randomised trials	serious	not serious	not serious	serious	none	0/50 (0.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	IMPORTANT
Desaturation requiring intervention												
1	randomised trials	serious	not serious	not serious	serious	none	0/50 (0.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	CRITICAL
Bradycardia/ hypotension requiring intervention												
1	randomised trials	serious	not serious	not serious	serious	none	0/50 (0.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Summary of findings and evidence profile for IN DEX 2mcg/kg vs CH as rescue therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IN dexmed 2mcg/kg	chloral hydrate	Relative (95% CI)	Absolute (95% CI)		
Failed sedation for procedure												
1	randomised trials	serious	not serious	not serious	serious	none	1/50 (2.0%)	10/50 (20.0%)	**RR 0.10** (0.01 to 0.75)	**180 fewer per 1,000** (from 198 fewer to 50 fewer)	⨁⨁◯◯ LOW	CRITICAL
Onset time of sedation												
1	randomised trials	serious	not serious	not serious	serious	none	45	37	-	MD **0.5 seconds fewer** (2.16 fewer to 1.16 more)	⨁⨁◯◯ LOW	NOT IMPORTANT
Any desaturation												
1	randomised trials	serious	not serious	not serious	serious	none	0/50 (0.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	IMPORTANT
Desaturation requiring intervention												
1	randomised trials	serious	not serious	not serious	serious	none	0/50 (0.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	CRITICAL
Bradycardia/hypotension requiring intervention												
1	randomised trials	serious	not serious	not serious	serious	none	0/50 (0.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

In patients who failed chloral hydrate (50mg/kg) as the primary sedation agents, use of IN DEX as a rescue sedation may be superior to additional doses of chloral hydrate (25mg/kg). The efficacy may be dose dependent with higher proportion of patients successfully treated in higher dose (2mcg/kg) than lower dose (1mcg/kg) but the difference was not statistically significant.

There was no significant intergroup difference in sedation induction time. However, time to wake up for low dose (1mcg/kg) IN DEX rescue group (61.8 +/-11.2 min) was significantly shorter compared to high dose (2mcg/kg) IN DEX (91.5 +/-15.6 min) or additional doses of chloral hydrate (85.9 +/- 14.6min) ($P<0.001$).

Desaturation was not observed in the included patients in all groups. There was also no clinically significant inter-group hemodynamic disturbance observed. Though IN DEX showed a modest reduction in heart rate (10% in CH; 15.9% in DEX 1mcg/kg; 24.3% in DEX 2mcg/kg; $P< 0.01$) and blood pressure (15.8% in CH; 21.1% in DEX 1mcg/kg; 25.3% in DEX 2mcg/kg; $p< 0.01$) when compared to chloral hydrate group, none of these patients required clinical intervention.

Recommendations of using IN DEX as a rescue agent

Intranasal dexmedetomidine can be considered as a rescue agent in patients failing chloral hydrate as the primary agent, in selected populations, e.g., in children prone to vomiting or potential ease of administration with intranasal formulation. (Weak recommendation; low quality of evidence)

Clinical effect may be dose dependent. Possible side-effects of bradycardia and hypotension needs to be acknowledged though reports of clinically significant events requiring intervention are not common.

REFERENCES:

1. American Academy of Pediatrics, et al., *Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update.* Pediatrics, 2006. **118**(6): p. 2587-602.
2. Hong Kong Academy of Medicine. *Guidelines on Procedural Sedation* 2019.
3. American Academy of Pediatrics Committee on Drugs., *Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: addendum.* Pediatrics, 2002. **110**(4): p. 836-8.
4. American Society of Anesthesiologists Task Force on Sedation Analgesia by Non-Anesthesiologists., *Practice guidelines for sedation and analgesia by non-anesthesiologists.* Anesthesiology, 2002. **96**(4): p. 1004-17.
5. Gross, J.B., et al., *Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea.* Anesthesiology, 2006. **104**(5): p. 1081-93; quiz 1117-8.
6. Cravero, J.P., et al., *Incidence and nature of adverse events during pediatric sedation/anesthesia for procedures outside the operating room: report from the Pediatric Sedation Research Consortium.* Pediatrics, 2006. **118**(3): p. 1087-96.
7. Malviya, S., et al., *Depth of sedation in children undergoing computed tomography: validity and reliability of the University of Michigan Sedation Scale (UMSS).* Br J Anaesth, 2002. **88**(2): p. 241-5.
8. Cote, C.J., et al., *Adverse sedation events in pediatrics: a critical incident analysis of contributing factors.* Pediatrics, 2000. **105**(4 Pt 1): p. 805-14.
9. D'Agostino, J. and T.E. Terndrup, *Chloral hydrate versus midazolam for sedation of children for neuroimaging: a randomized clinical trial.* Pediatr Emerg Care, 2000. **16**(1): p. 1-4.
10. Dachs, R.J. and G.M. Innes, *Intravenous ketamine sedation of pediatric patients in the emergency department.* Ann Emerg Med, 1997. **29**(1): p. 146-50.
11. Green, S.M., et al., *Ketamine sedation for pediatric gastroenterology procedures.* J Pediatr Gastroenterol Nutr, 2001. **32**(1): p. 26-33.
12. Malviya, S., T. Voepel-Lewis, and A.R. Tait, *Adverse events and risk factors associated with the sedation of children by nonanesthesiologists.* Anesth Analg, 1997. **85**(6): p. 1207-13.
13. Biban, P., et al., *Adverse effect of chloral hydrate in two young children with obstructive sleep apnea.* Pediatrics, 1993. **92**(3): p. 461-3.
14. Greenberg, S.B., et al., *High-dose chloral hydrate sedation for children undergoing MR imaging: safety and efficacy in relation to age.* AJR Am J Roentgenol, 1993. **161**(3): p. 639-41.
15. Greenberg, S.B., E.N. Faerber, and C.L. Aspinall, *High dose chloral hydrate sedation for children undergoing CT.* J Comput Assist Tomogr, 1991. **15**(3): p. 467-9.
16. Vade, A., et al., *Chloral hydrate sedation of children undergoing CT and MR imaging: safety as judged by American Academy of Pediatrics guidelines.* AJR Am J Roentgenol, 1995. **165**(4): p. 905-9.
17. Mayers, D.J., et al., *Chloral hydrate disposition following single-dose administration to critically ill neonates and children.* Dev Pharmacol Ther, 1991. **16**(2): p. 71-7.
18. Malviya, S., et al., *Prolonged recovery and delayed side effects of sedation for diagnostic imaging studies in children.* Pediatrics, 2000. **105**(3): p. E42.
19. Burtin, P., et al., *Population pharmacokinetics of midazolam in neonates.* Clin Pharmacol Ther, 1994. **56**(6 Pt 1): p. 615-25.
20. Jacqz-Aigrain, E. and P. Burtin, *Clinical pharmacokinetics of sedatives in neonates.* Clin Pharmacokinet, 1996. **31**(6): p. 423-43.
21. Litman, R.S., R.J. Berkowitz, and D.S. Ward, *Levels of consciousness and ventilatory parameters in young children during sedation with oral midazolam and nitrous oxide.* Arch Pediatr Adolesc Med, 1996. **150**(7): p. 671-5.
22. Yaster, M., et al., *Midazolam-fentanyl intravenous sedation in children: case report of respiratory arrest.* Pediatrics, 1990. **86**(3): p. 463-7.
23. Krauss, B. and S.M. Green, *Sedation and analgesia for procedures in children.* N Engl J Med, 2000. **342**(13): p. 938-45.
24. Blouin, R.T., et al., *The effect of flumazenil on midazolam-induced depression of the ventilatory response to hypoxia during isohypercarbia.* Anesthesiology, 1993. **78**(4): p. 635-41.
25. Flogel, C.M., et al., *The effects of large-dose flumazenil on midazolam-induced ventilatory depression.* Anesth Analg, 1993. **77**(6): p. 1207-14.
26. The Flumazenil in Intravenous Conscious Sedation with Midazolam Multicenter Study Group I., *Reversal of central nervous system effects by flumazenil after intravenous conscious sedation with midazolam: report of a multicenter clinical study.* Clin Ther, 1992. **14**(6): p. 861-77.

27. McDuffee, A.T. and J.D. Tobias, *Seizure after flumazenil administration in a pediatric patient.* Pediatr Emerg Care, 1995. **11**(3): p. 186-7.
28. Moro-Sutherland, D.M., et al., *Comparison of intravenous midazolam with pentobarbital for sedation for head computed tomography imaging.* Acad Emerg Med, 2000. **7**(12): p. 1370-5.
29. Neidhart, P., et al., *Chest wall rigidity during fentanyl- and midazolam-fentanyl induction: ventilatory and haemodynamic effects.* Acta Anaesthesiol Scand, 1989. **33**(1): p. 1-5.
30. Olkkola, K.T., K. Hamunen, and E.L. Maunuksela, *Clinical pharmacokinetics and pharmacodynamics of opioid analgesics in infants and children.* Clin Pharmacokinet, 1995. **28**(5): p. 385-404.
31. Kennedy, R.M., et al., *Comparison of fentanyl/midazolam with ketamine/midazolam for pediatric orthopedic emergencies.* Pediatrics, 1998. **102**(4 Pt 1): p. 956-63.
32. Billmire, D.A., H.W. Neale, and R.O. Gregory, *Use of i.v. fentanyl in the outpatient treatment of pediatric facial trauma.* J Trauma, 1985. **25**(11): p. 1079-80.
33. Fahnenstich, H., et al., *Fentanyl-induced chest wall rigidity and laryngospasm in preterm and term infants.* Crit Care Med, 2000. **28**(3): p. 836-9.
34. Muller, P. and C. Vogtmann, *Three cases with different presentation of fentanyl-induced muscle rigidity--a rare problem in intensive care of neonates.* Am J Perinatol, 2000. **17**(1): p. 23-6.
35. American Academy of Pediatrics Committee on Drugs., *Naloxone dosage and route of administration for infants and children: addendum to emergency drug doses for infants and children.* Pediatrics, 1990. **86**(3): p. 484-5.
36. Tobias, J.D., *End-tidal carbon dioxide monitoring during sedation with a combination of midazolam and ketamine for children undergoing painful, invasive procedures.* Pediatr Emerg Care, 1999. **15**(3): p. 173-5.
37. Green, S.M., et al., *Intravenous ketamine for pediatric sedation in the emergency department: safety profile with 156 cases.* Acad Emerg Med, 1998. **5**(10): p. 971-6.
38. Green, S.M., et al., *Intramuscular ketamine for pediatric sedation in the emergency department: safety profile in 1,022 cases.* Ann Emerg Med, 1998. **31**(6): p. 688-97.
39. Merola, C., et al., *An audit of adverse events in children sedated with chloral hydrate or propofol during imaging studies.* Paediatr Anaesth, 1995. **5**(6): p. 375-8.
40. Motamed, F., et al., *Midazolam-ketamine combination for moderate sedation in upper GI endoscopy.* J Pediatr Gastroenterol Nutr, 2012. **54**(3): p. 422-6.
41. Tosun, Z., et al., *Propofol-ketamine vs propofol-fentanyl for sedation during pediatric upper gastrointestinal endoscopy.* Paediatr Anaesth, 2007. **17**(10): p. 983-8.
42. Berkenbosch, J.W., et al., *Use of a remifentanil-propofol mixture for pediatric flexible fiberoptic bronchoscopy sedation.* Paediatr Anaesth, 2004. **14**(11): p. 941-6.
43. Kannikeswaran, N., et al., *Sedation medication received and adverse events related to sedation for brain MRI in children with and without developmental disabilities.* Paediatr Anaesth, 2009. **19**(3): p. 250-6.
44. Weber, F., H. Hollnberger, and J. Weber, *Electroencephalographic Narcotrend Index monitoring during procedural sedation and analgesia in children.* Paediatr Anaesth, 2008. **18**(9): p. 823-30.
45. Motas, D., et al., *Depth of consciousness and deep sedation attained in children as administered by nonanaesthesiologists in a children's hospital.* Paediatr Anaesth, 2004. **14**(3): p. 256-60.
46. Malviya, S., T. Voepel-Lewis, and A.R. Tait, *A comparison of observational and objective measures to differentiate depth of sedation in children from birth to 18 years of age.* Anesth Analg, 2006. **102**(2): p. 389-94.
47. McDermott, N.B., et al., *Validation of the bispectral index monitor during conscious and deep sedation in children.* Anesth Analg, 2003. **97**(1): p. 39-43, table of contents.
48. Malviya, S., et al., *Sedation and general anaesthesia in children undergoing MRI and CT: adverse events and outcomes.* Br J Anaesth, 2000. **84**(6): p. 743-8.
49. Lightdale, J.R., *Sedation and analgesia in the pediatric patient.* Gastrointest Endosc Clin N Am, 2004. **14**(2): p. 385-99.
50. Slonim, A.D. and F.P. Ognibene, *Amnestic agents in pediatric bronchoscopy.* Chest, 1999. **116**(6): p. 1802-8.
51. Langhan, M.L., et al., *Detection of hypoventilation by capnography and its association with hypoxia in children undergoing sedation with ketamine.* Pediatr Emerg Care, 2011. **27**(5): p. 394-7.
52. Sammartino, M., et al., *Capnography and the bispectral index-their role in pediatric sedation: a brief review.* Int J Pediatr, 2010. **2010**: p. 828347.
53. Metzner, J. and K.B. Domino, *Risks of anesthesia or sedation outside the operating room: the role of the anesthesia care provider.* Curr Opin Anaesthesiol, 2010. **23**(4): p. 523-31.
54. Langhan, M., *Continuous end-tidal carbon dioxide monitoring in pediatric intensive care units.* J Crit Care, 2009. **24**(2): p. 227-30.

55. Nagler, J. and B. Krauss, *Capnography: a valuable tool for airway management.* Emerg Med Clin North Am, 2008. **26**(4): p. 881-97, vii.
56. Yarchi, D., et al., *Assessment of end-tidal carbon dioxide during pediatric and adult sedation for endoscopic procedures.* Gastrointest Endosc, 2009. **69**(4): p. 877-82.
57. Anderson, J.L., et al., *Capnography and depth of sedation during propofol sedation in children.* Ann Emerg Med, 2007. **49**(1): p. 9-13.
58. Atkins, D., et al., *Grading quality of evidence and strength of recommendations.* BMJ, 2004. **328**(7454): p. 1490.
59. Guyatt, G.H., et al., *What is "quality of evidence" and why is it important to clinicians?* BMJ, 2008. **336**(7651): p. 995-8.
60. Guyatt, G.H., et al., *GRADE: an emerging consensus on rating quality of evidence and strength of recommendations.* BMJ, 2008. **336**(7650): p. 924-6.
61. Schunemann, H., et al., *GRADE handbook: handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach*. 2013.
62. National Institute for Health and Clinical Excellence. *Sedation in children and young people*. 2019.
63. ASGE Standards of Practice Committee, et al., *Guidelines for sedation and anesthesia in GI endoscopy.* Gastrointest Endosc, 2018. **87**(2): p. 327-337.
64. *Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018: A Report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons, American College of Radiology, American Dental Association, American Society of Dentist Anesthesiologists, and Society of Interventional Radiology.* Anesthesiology, 2018. **128**(3): p. 437-479.
65. Ghaffar, S., et al., *Sedation for pediatric echocardiography: evaluation of preprocedure fasting guidelines.* J Am Soc Echocardiogr, 2002. **15**(9): p. 980-3.
66. Keidan, I., et al., *The effect of fasting practice on sedation with chloral hydrate.* Pediatr Emerg Care, 2004. **20**(12): p. 805-7.
67. Hoffman, G.M., et al., *Risk reduction in pediatric procedural sedation by application of an American Academy of Pediatrics/American Society of Anesthesiologists process model.* Pediatrics, 2002. **109**(2): p. 236-43.
68. Walker, R.W., *Pulmonary aspiration in pediatric anesthetic practice in the UK: a prospective survey of specialist pediatric centers over a one-year period.* Paediatr Anaesth, 2013. **23**(8): p. 702-11.
69. Habre, W., et al., *Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe.* Lancet Respir Med, 2017. **5**(5): p. 412-425.
70. Hellstrom, P.M., P. Gryback, and H. Jacobsson, *The physiology of gastric emptying.* Best Pract Res Clin Anaesthesiol, 2006. **20**(3): p. 397-407.
71. Bhatt, M., et al., *Association of Preprocedural Fasting With Outcomes of Emergency Department Sedation in Children.* JAMA Pediatr, 2018. **172**(7): p. 678-685.
72. Beach, M.L., et al., *Major Adverse Events and Relationship to Nil per Os Status in Pediatric Sedation/Anesthesia Outside the Operating Room: A Report of the Pediatric Sedation Research Consortium.* Anesthesiology, 2016. **124**(1): p. 80-8.
73. Agrawal, D., et al., *Preprocedural fasting state and adverse events in children undergoing procedural sedation and analgesia in a pediatric emergency department.* Ann Emerg Med, 2003. **42**(5): p. 636-46.
74. Frykholm, P., et al., *Preoperative fasting in children: review of existing guidelines and recent developments.* Br J Anaesth, 2018. **120**(3): p. 469-474.
75. Thomas, M., et al., *Consensus statement on clear fluids fasting for elective pediatric general anesthesia.* Paediatr Anaesth, 2018. **28**(5): p. 411-414.
76. Lambert, E. and S. Carey, *Practice Guideline Recommendations on Perioperative Fasting: A Systematic Review.* JPEN J Parenter Enteral Nutr, 2016. **40**(8): p. 1158-1165.
77. Cote, C.J., et al., *Guidelines for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures: Update 2016.* Pediatrics, 2016. **138**(1).
78. The Royal Children's Hospital Melbourne (RCH). *Procedural Sedation for Ward and Ambulatory Areas Guideline*. 2016.
79. The Sydney Children's Hospital Network. *Practice Guideline: Procedural sedation (Paediatric ward, clinic and imaging areas)*. 2019.
80. Green, S.M., et al., *An international multidisciplinary consensus statement on fasting before procedural sedation in adults and children.* Anaesthesia, 2020. **75**(3): p. 374-385.
81. Long, B., A. Koyfman, and M.A. Vivirito, *Capnography in the Emergency Department: A Review of Uses, Waveforms, and Limitations.* J Emerg Med, 2017. **53**(6): p. 829-842.

82. Cote, C.J., et al., *Guidelines for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures.* Pediatrics, 2019. **143**(6).
83. Cravero, J.P. and M.G. Roback *Procedural sedation in children outside of the operating room*. UpToDate, 2020.
84. Roback, M.G., et al., *Tracking and Reporting Outcomes Of Procedural Sedation (TROOPS): Standardized Quality Improvement and Research Tools from the International Committee for the Advancement of Procedural Sedation.* Br J Anaesth, 2018. **120**(1): p. 164-172.
85. Xie, Z., et al., *Sedation effects of intranasal dexmedetomidine delivered as sprays versus drops on pediatric response to venous cannulation.* Am J Emerg Med, 2017. **35**(8): p. 1126-1130.
86. Green, S.M., et al., *Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update.* Ann Emerg Med, 2011. **57**(5): p. 449-61.
87. *The Royal College of Emergency Medicine : KETAMINE PROCEDURAL SEDATION FOR CHILDREN IN THE EMERGENCY DEPARTMENT Best Practice Guidelines*. 2020.
88. Bourgoin, A., et al., *Safety of sedation with ketamine in severe head injury patients: comparison with sufentanil.* Crit Care Med, 2003. **31**(3): p. 711-7.
89. Bourgoin, A., et al., *Effects of sufentanil or ketamine administered in target-controlled infusion on the cerebral hemodynamics of severely brain-injured patients.* Crit Care Med, 2005. **33**(5): p. 1109-13.
90. Schmittner, M.D., et al., *Effects of fentanyl and S(+)-ketamine on cerebral hemodynamics, gastrointestinal motility, and need of vasopressors in patients with intracranial pathologies: a pilot study.* J Neurosurg Anesthesiol, 2007. **19**(4): p. 257-62.
91. Bar-Joseph, G., et al., *Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension.* J Neurosurg Pediatr, 2009. **4**(1): p. 40-6.
92. Caricato, A., et al., *Racemic ketamine in adult head injury patients: use in endotracheal suctioning.* Crit Care, 2013. **17**(6): p. R267.
93. Green, S.M. and B. Krauss, *Clinical practice guideline for emergency department ketamine dissociative sedation in children.* Ann Emerg Med, 2004. **44**(5): p. 460-71.
94. Chang, L.C., et al., *The emerging use of ketamine for anesthesia and sedation in traumatic brain injuries.* CNS Neurosci Ther, 2013. **19**(6): p. 390-5.
95. Zeiler, F.A., et al., *The ketamine effect on ICP in traumatic brain injury.* Neurocrit Care, 2014. **21**(1): p. 163-73.
96. Gregers, M.C.T., et al., *Ketamine as an Anesthetic for Patients with Acute Brain Injury: A Systematic Review.* Neurocrit Care, 2020.
97. Gardner, A.E., F.J. Dannemiller, and D. Dean, *Intracranial cerebrospinal fluid pressure in man during ketamine anesthesia.* Anesth Analg, 1972. **51**(5): p. 741-5.
98. Wyte, S.R., et al., *Ketamine-induced intracranial hypertension.* Anesthesiology, 1972. **36**(2): p. 174-6.
99. List, W.F., et al., *Increased cerebrospinal fluid pressure after ketamine.* Anesthesiology, 1972. **36**(1): p. 98-9.
100. Shaprio, H.M., S.R. Wyte, and A.B. Harris, *Ketamine anaesthesia in patients with intracranial pathology.* Br J Anaesth, 1972. **44**(11): p. 1200-4.
101. Gibbs, J.M., *The effect of intravenous ketamine on cerebrospinal fluid pressure.* Br J Anaesth, 1972. **44**(12): p. 1298-302.
102. Kochanek, P.M., et al., *Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines, Executive Summary.* Pediatr Crit Care Med, 2019. **20**(3): p. 280-289.
103. Kolenda, H., et al., *Ketamine for analgosedative therapy in intensive care treatment of head-injured patients.* Acta Neurochir (Wien), 1996. **138**(10): p. 1193-9.
104. Albanese, J., et al., *Ketamine decreases intracranial pressure and electroencephalographic activity in traumatic brain injury patients during propofol sedation.* Anesthesiology, 1997. **87**(6): p. 1328-34.
105. Mendelson, C.L., *The aspiration of stomach contents into the lungs during obstetric anesthesia.* Am J Obstet Gynecol, 1946. **52**: p. 191-205.
106. Green, S.M. and B. Krauss, *Pulmonary aspiration risk during emergency department procedural sedation--an examination of the role of fasting and sedation depth.* Acad Emerg Med, 2002. **9**(1): p. 35-42.
107. Green, S.M., et al., *Fasting and emergency department procedural sedation and analgesia: a consensus-based clinical practice advisory.* Ann Emerg Med, 2007. **49**(4): p. 454-61.
108. Ljungqvist, O. and E. Soreide, *Preoperative fasting.* Br J Surg, 2003. **90**(4): p. 400-6.
109. Academy of Medical Royal Colleges. *Safe Sedation Practice for Healthcare Procedures*. 2013.
110. Royal College of Anaesthetists. *Safe Sedation of Adults in the Emergency Department*. 2012.
111. Smith, I., et al., *Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology.* Eur J Anaesthesiol, 2011. **28**(8): p. 556-69.

112. *Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration: Application to Healthy Patients Undergoing Elective Procedures: An Updated Report by the American Society of Anesthesiologists Task Force on Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration.* Anesthesiology, 2017. **126**(3): p. 376-393.
113. Godwin, S.A., et al., *Clinical policy: procedural sedation and analgesia in the emergency department.* Ann Emerg Med, 2014. **63**(2): p. 247-58 e18.
114. *Guideline for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures: Update 2016.* Pediatr Dent, 2016. **38**(5): p. 77-106.
115. Brady, M., S. Kinn, and P. Stuart, *Preoperative fasting for adults to prevent perioperative complications.* Cochrane Database Syst Rev, 2003(4): p. CD004423.
116. Brady, M., et al., *Preoperative fasting for preventing perioperative complications in children.* Cochrane Database Syst Rev, 2009(4): p. CD005285.
117. Van de Putte, P., et al., *When fasted is not empty: a retrospective cohort study of gastric content in fasted surgical patientsdagger.* Br J Anaesth, 2017. **118**(3): p. 363-371.
118. Schmitz, A., et al., *Residual gastric contents volume does not differ following 4 or 6 h fasting after a light breakfast - a magnetic resonance imaging investigation in healthy non-anaesthetised school-age children.* Acta Anaesthesiol Scand, 2012. **56**(5): p. 589-94.
119. Schmitz, A., et al., *Gastric emptying after overnight fasting and clear fluid intake: a prospective investigation using serial magnetic resonance imaging in healthy children.* Br J Anaesth, 2011. **107**(3): p. 425-9.
120. Schmitz, A., et al., *Fasting times and gastric contents volume in children undergoing deep propofol sedation--an assessment using magnetic resonance imaging.* Paediatr Anaesth, 2011. **21**(6): p. 685-90.
121. Cook-Sather, S.D., et al., *Overweight/obesity and gastric fluid characteristics in pediatric day surgery: implications for fasting guidelines and pulmonary aspiration risk.* Anesth Analg, 2009. **109**(3): p. 727-36.
122. Ingebo, K.R., et al., *Sedation in children: adequacy of two-hour fasting.* J Pediatr, 1997. **131**(1 Pt 1): p. 155-8.
123. Nicolson, S.C., A.T. Dorsey, and M.S. Schreiner, *Shortened preanesthetic fasting interval in pediatric cardiac surgical patients.* Anesth Analg, 1992. **74**(5): p. 694-7.
124. Cote, C.J., et al., *Assessment of risk factors related to the acid aspiration syndrome in pediatric patients-gastric ph and residual volume.* Anesthesiology, 1982. **56**(1): p. 70-2.
125. Schreiner, M.S., A. Triebwasser, and T.P. Keon, *Ingestion of liquids compared with preoperative fasting in pediatric outpatients.* Anesthesiology, 1990. **72**(4): p. 593-7.
126. Splinter, W.M., J.A. Stewart, and J.G. Muir, *Large volumes of apple juice preoperatively do not affect gastric pH and volume in children.* Can J Anaesth, 1990. **37**(1): p. 36-9.
127. Splinter, W.M., J.D. Schaefer, and I.H. Zunder, *Clear fluids three hours before surgery do not affect the gastric fluid contents of children.* Can J Anaesth, 1990. **37**(5): p. 498-501.
128. Splinter, W.M., J.A. Stewart, and J.G. Muir, *The effect of preoperative apple juice on gastric contents, thirst, and hunger in children.* Can J Anaesth, 1989. **36**(1): p. 55-8.
129. Maekawa, N., et al., *Effects of 2-, 4- and 12-hour fasting intervals on preoperative gastric fluid pH and volume, and plasma glucose and lipid homeostasis in children.* Acta Anaesthesiol Scand, 1993. **37**(8): p. 783-7.
130. Phillips, S., et al., *High-risk residual gastric content in fasted patients undergoing gastrointestinal endoscopy: a prospective cohort study of prevalence and predictors.* Anaesth Intensive Care, 2015. **43**(6): p. 728-33.
131. Schmidt, A.R., et al., *Gastric pH and residual volume after 1 and 2 h fasting time for clear fluids in childrendagger.* Br J Anaesth, 2015. **114**(3): p. 477-82.
132. Bouvet, L., et al., *Ultrasound assessment of the prevalence of increased gastric contents and volume in elective pediatric patients: A prospective cohort study.* Paediatr Anaesth, 2018. **28**(10): p. 906-913.
133. Sharma, G., et al., *Preoperative assessment of gastric contents and volume using bedside ultrasound in adult patients: A prospective, observational, correlation study.* Indian J Anaesth, 2018. **62**(10): p. 753-758.
134. Leviter, J., et al., *"Full Stomach" Despite the Wait: Point-of-care Gastric Ultrasound at the Time of Procedural Sedation in the Pediatric Emergency Department.* Acad Emerg Med, 2019. **26**(7): p. 752-760.
135. Schwartz, D.A., et al., *Gastric contents in children presenting for upper endoscopy.* Anesth Analg, 1998. **87**(4): p. 757-60.
136. Soreide, E., et al., *Pre-operative fasting guidelines: an update.* Acta Anaesthesiol Scand, 2005. **49**(8): p. 1041-7.

137. Sandhar, B.K., et al., *Effect of oral liquids and ranitidine on gastric fluid volume and pH in children undergoing outpatient surgery.* Anesthesiology, 1989. **71**(3): p. 327-30.
138. Soreide, E., E. Bjornestad, and P.A. Steen, *An audit of perioperative aspiration pneumonitis in gynaecological and obstetric patients.* Acta Anaesthesiol Scand, 1996. **40**(1): p. 14-9.
139. Thomas, M. and T. Engelhardt, *Think drink! Current fasting guidelines are outdated.* Br J Anaesth, 2017. **118**(3): p. 291-293.
140. Sumpelmann, A.E., et al., *Ultrasound assessment of gastric emptying after breakfast in healthy preschool children.* Paediatr Anaesth, 2017. **27**(8): p. 816-820.
141. Du, T., et al., *Gastric emptying for liquids of different compositions in children.* Br J Anaesth, 2017. **119**(5): p. 948-955.
142. Song, I.K., et al., *Ultrasound assessment of gastric volume in children after drinking carbohydrate-containing fluids.* Br J Anaesth, 2016. **116**(4): p. 513-7.
143. Andersson, H., B. Zaren, and P. Frykholm, *Low incidence of pulmonary aspiration in children allowed intake of clear fluids until called to the operating suite.* Paediatr Anaesth, 2015. **25**(8): p. 770-777.
144. Tudor-Drobjewski, B.A., et al., *Randomised controlled trial comparing preoperative carbohydrate loading with standard fasting in paediatric anaesthesia.* Br J Anaesth, 2018. **121**(3): p. 656-661.
145. Fawcett, W.J. and M. Thomas, *Pre-operative fasting in adults and children: clinical practice and guidelines.* Anaesthesia, 2019. **74**(1): p. 83-88.
146. Linscott, D., *SPANZA endorses 1-hour clear fluid fasting consensus statement.* Paediatr Anaesth, 2019. **29**(3): p. 292.
147. Green, S.M., K.P. Mason, and B.S. Krauss, *Pulmonary aspiration during procedural sedation: a comprehensive systematic review.* Br J Anaesth, 2017. **118**(3): p. 344-354.
148. McCracken, G.C. and A.F. Smith, *Breaking the fast for procedural sedation: changing risk or risking change?* Anaesthesia, 2020.
149. Zdravkovic, M., C.A. Hagberg, and N. Chrimes, *Consensus statement on fasting before procedural sedation - underestimating the threat to patient safety?* Anaesthesia, 2020. **75**(6): p. 829-830.
150. Green, S.M., et al., *Consensus statement on fasting before procedural sedation - underestimating the threat to patient safety? A reply.* Anaesthesia, 2020. **75**(6): p. 830-832.
151. Antonov, N.K., et al., *Feed and Wrap MRI Technique in Infants.* Clin Pediatr (Phila), 2017. **56**(12): p. 1095-1103.
152. Dong, S.Z., M. Zhu, and D. Bulas, *Techniques for minimizing sedation in pediatric MRI.* J Magn Reson Imaging, 2019. **50**(4): p. 1047-1054.
153. Janos, S., et al., *Free-breathing unsedated MRI in children: Justification and techniques.* J Magn Reson Imaging, 2019. **50**(2): p. 365-376.
154. Lemaire, C., G.R. Moran, and H. Swan, *Impact of audio/visual systems on pediatric sedation in magnetic resonance imaging.* J Magn Reson Imaging, 2009. **30**(3): p. 649-55.
155. Harned, R.K., 2nd and J.D. Strain, *MRI-compatible audio/visual system: impact on pediatric sedation.* Pediatr Radiol, 2001. **31**(4): p. 247-50.
156. Hearst, D., *Non-pharmacological Distraction Techniques as Sedation Adjunct*, in *Pediatric Sedation Outside of the Operating Room*, K.P. Mason, Editor. 2015, Springer: New York, NY. p. 655-674.
157. Tyson, M.E., D.D. Bohl, and J.G. Blickman, *A randomized controlled trial: child life services in pediatric imaging.* Pediatr Radiol, 2014. **44**(11): p. 1426-32.
158. Ng, H.Y., et al. *Hospital Play Service can Decrease Sedation Use for Children Undergoing Echocardiography in Tseung Kwan O Hospital*. in *Hospital Authority Convention* 2019. Hong Kong.
159. Poon, K.H., et al. *Option of "no sedation" for babies in nuclear medicine – continuous quality improvement project*. in *28th International Conference of The International Society for Quality in Health Care* 2011. Hong Kong.
160. Leroy, P.L., et al., *Beyond the drugs: nonpharmacologic strategies to optimize procedural care in children.* Curr Opin Anaesthesiol, 2016. **29 Suppl 1**: p. S1-13.
161. Birnie, K.A., et al., *Psychological interventions for needle-related procedural pain and distress in children and adolescents.* Cochrane Database Syst Rev, 2018. **10**: p. CD005179.
162. Pillai Riddell, R.R., et al., *Non-pharmacological management of infant and young child procedural pain.* Cochrane Database Syst Rev, 2015(12): p. CD006275.
163. Langhan, M.L., F.Y. Li, and J.L. Lichtor, *The impact of capnography monitoring among children and adolescents in the postanesthesia care unit: a randomized controlled trial.* Paediatr Anaesth, 2017. **27**(4): p. 385-393.
164. Langhan, M.L., et al., *A randomized controlled trial of capnography during sedation in a pediatric emergency setting.* Am J Emerg Med, 2015. **33**(1): p. 25-30.
165. Lightdale, J.R., et al., *Microstream capnography improves patient monitoring during moderate sedation: a randomized, controlled trial.* Pediatrics, 2006. **117**(6): p. e1170-8.

166. Boriosi, J.P., et al., *The utility of the pretracheal stethoscope in detecting ventilatory abnormalities during propofol sedation in children.* Paediatr Anaesth, 2019. **29**(6): p. 604-610.
167. Hart, L.S., et al., *The value of end-tidal CO2 monitoring when comparing three methods of conscious sedation for children undergoing painful procedures in the emergency department.* Pediatr Emerg Care, 1997. **13**(3): p. 189-93.
168. Kim, G., et al., *Ventilatory response during dissociative sedation in children-a pilot study.* Acad Emerg Med, 2003. **10**(2): p. 140-5.
169. Langhan, M.L., F.Y. Li, and J.L. Lichtor, *Respiratory depression detected by capnography among children in the postanesthesia care unit: a cross-sectional study.* Paediatr Anaesth, 2016. **26**(10): p. 1010-7.
170. McQuillen, K.K. and D.W. Steele, *Capnography during sedation/analgesia in the pediatric emergency department.* Pediatr Emerg Care, 2000. **16**(6): p. 401-4.
171. Tobias, J.D. and A. Kavanaugh-McHugh, *Oximetry and capnography during sedation for transesophageal echocardiography.* Clin Pediatr (Phila), 1995. **34**(10): p. 565-6.
172. Yldzdas, D., H. Yapcoglu, and H.L. Ylmaz, *The value of capnography during sedation or sedation/analgesia in pediatric minor procedures.* Pediatr Emerg Care, 2004. **20**(3): p. 162-5.
173. Campbell, S.G., et al., *End-tidal capnometry during emergency department procedural sedation and analgesia: a randomized, controlled study.* World J Emerg Med, 2016. **7**(1): p. 13-8.
174. Kannikeswaran, N., X. Chen, and U. Sethuraman, *Utility of endtidal carbon dioxide monitoring in detection of hypoxia during sedation for brain magnetic resonance imaging in children with developmental disabilities.* Paediatr Anaesth, 2011. **21**(12): p. 1241-6.
175. Mataftsi, A., et al., *Safety and efficacy of chloral hydrate for procedural sedation in paediatric ophthalmology: a systematic review and meta-analysis.* Br J Ophthalmol, 2017. **101**(10): p. 1423-1430.
176. Fong, C.Y., et al., *Chloral hydrate as a sedating agent for neurodiagnostic procedures in children.* Cochrane Database Syst Rev, 2017. **11**: p. CD011786.
177. Chen, Z., et al., *Efficacy of chloral hydrate oral solution for sedation in pediatrics: a systematic review and meta-analysis.* Drug Des Devel Ther, 2019. **13**: p. 2643-2653.
178. Akin, A., et al., *Dexmedetomidine vs midazolam for premedication of pediatric patients undergoing anesthesia.* Paediatr Anaesth, 2012. **22**(9): p. 871-6.
179. Cimen, Z.S., et al., *Comparison of buccal and nasal dexmedetomidine premedication for pediatric patients.* Paediatr Anaesth, 2013. **23**(2): p. 134-8.
180. Gyanesh, P., et al., *Comparison between intranasal dexmedetomidine and intranasal ketamine as premedication for procedural sedation in children undergoing MRI: a double-blind, randomized, placebo-controlled trial.* J Anesth, 2014. **28**(1): p. 12-8.
181. Wang, S.S., et al., *The sedative effects and the attenuation of cardiovascular and arousal responses during anesthesia induction and intubation in pediatric patients: a randomized comparison between two different doses of preoperative intranasal dexmedetomidine.* Paediatr Anaesth, 2014. **24**(3): p. 275-81.
182. Ghai, B., et al., *Comparison of oral midazolam with intranasal dexmedetomidine premedication for children undergoing CT imaging: a randomized, double-blind, and controlled study.* Paediatr Anaesth, 2017. **27**(1): p. 37-44.
183. Li, B.L., et al., *A comparison of intranasal dexmedetomidine for sedation in children administered either by atomiser or by drops.* Anaesthesia, 2016. **71**(5): p. 522-8.
184. Cao, Q., et al., *Comparison of sedation by intranasal dexmedetomidine and oral chloral hydrate for pediatric ophthalmic examination.* Paediatr Anaesth, 2017. **27**(6): p. 629-636.
185. Miller, J., et al., *Comparison of dexmedetomidine and chloral hydrate sedation for transthoracic echocardiography in infants and toddlers: a randomized clinical trial.* Paediatr Anaesth, 2016. **26**(3): p. 266-72.
186. Yuen, V.M., et al., *A randomised controlled trial of oral chloral hydrate vs. intranasal dexmedetomidine before computerised tomography in children.* Anaesthesia, 2017. **72**(10): p. 1191-1195.
187. Reynolds, J., et al., *A prospective, randomized, double-blind trial of intranasal dexmedetomidine and oral chloral hydrate for sedated auditory brainstem response (ABR) testing.* Paediatr Anaesth, 2016. **26**(3): p. 286-93.
188. Poonai, N., et al., *Intranasal Dexmedetomidine for Procedural Distress in Children: A Systematic Review.* Pediatrics, 2020. **145**(1).
189. Li, L., et al., *Intranasal dexmedetomidine versus oral chloral hydrate for diagnostic procedures sedation in infants and toddlers: A systematic review and meta-analysis.* Medicine (Baltimore), 2020. **99**(9): p. e19001.

190. Zhang, W., et al., *Comparison of rescue techniques for failed chloral hydrate sedation for magnetic resonance imaging scans--additional chloral hydrate vs intranasal dexmedetomidine.* Paediatr Anaesth, 2016. **26**(3): p. 273-9.

Paediatric Procedural Sedation Record

Affix Patient's Label

Diagnosis:

Date / Time of Procedure:

Procedure:

Please "√" the box (s) where appropriate

Allergy history:	☐ **Nil**	☐ **Drug**	☐ **Food:**	☐ **Others:**

Brief history:
Completed by Doctor:

Significant past health:

ASA: ☐ **I** Healthy ☐ **II** Mild systemic disease ☐ **III** Severe systemic ☐ **IV** Life threatening ☐ **V** Moribund

Prematurity <37 weeks (see App.D*)	☐ No	☐ Yes (<60weeks post-conceptual age)	☐ Yes (> 60 weeks PCA)	
Sedation history:	☐ Nil of significant	☐ Failed previously	☐ Adverse event:	
Physical examination:				
General condition:	☐ Satisfactory	☐ Serious	☐ Critical	
Hydration state:	☐ Normal	☐ Dehydrated	☐ Oedematous	
Colour:	☐ Normal/Pink	☐ Pale	☐ Jaundice	☐ Cyanotic
Respiratory system:	☐ Normal	☐ Distress	☐ Wheezing	☐ Others:
Respiratory support:	☐ Nil	☐ Oxygen	☐ NIV	☐ MV
Airway:	☐ Patent	☐ Compromised:	☐ Difficult (see App.C*)	☐ Tracheostomy
Cardiovascular system:	☐ Normal	☐ Abnormal:		
Abdomen:	☐ Normal	☐ Abnormal:		
Mental state:	☐ Alert/Calm	☐ Confused	☐ Fear/Anxious	☐ Uncooperative
Others:				

*refer to "Practice Recommendations for Procedural Sedation in Paediatric Specialty Outside Operation Room" 2020

Assessed risk of sedation (Sec. BII*):	☐ Standard risk	☐ Increased risk (presence of experienced doctor recommended)	
Sedation plan: (can tick more than one)	☐ Oral sedation	☐ IV sedation	☐ Intranasal sedation

Obtain informed consent for the procedure/test and sedation: ☐ **Yes** ☐ **No**

Aspiration risk (Sec. BIII*) : ☐ **Negligible** ☐ **High Risk**

Fasting plan (Sec. BIII*):___hrs for clear fluid,____hrs for breast milk,____hrs for formula milk/light meal,_____hrs for heavy meal

Monitoring and escort required:	
Escort required during transport	☐ **PCA** ☐ **Nurse** ☐ **Doctor**
Monitor required:	☐ **Yes** ☐ **No**
• Continuous SpO_2, HR, RR monitor until discharge	☐ **Yes** ☐ **No**
• Continuous ECG monitor until discharge	☐ **Yes** ☐ **No**
Other : e.g. continuous $ETCO_2$ monitor until discharge for high risk cases	☐ **Yes** ☐ **No**

Isolation precautions: ☐ Standard ☐ Contact ☐ Droplet ☐ Airborne

Doctor Name (staff no): **(** **)** Signature:

Pre Procedure condition:

BW: kg BH: cm Surface area: m^2

Temp: ^0C AR: /min RR: /min SpO_2: % BP: / mmHg

Mobility: ☐Walk in ☐ Wheelchair ☐ Carried by caretaker ☐ Others

Conscious state: ☐ Awake ☐ Confused ☐ Agitated ☐ Sedated ☐ Comatose

Last food: _____ /_____ /_____:_____hr Last drink: ____/ ____ /_____ _____ :____hr

Pre Procedure SIGN IN:	**Procedural TIME OUT (Immediate before procedure)**
☐ Confirm patient identity	☐ Patient's name and ID
☐ Consent	☐ Explanation and informed consent for the procedure/test is available
☐ Screening evaluation (brief history / past health / allergy history/sedation history/physical examination)	☐ Any allergy or alert
☐ Confirm fasting (App. E)	☐ Check drug expiry date and dosage
☐ Steroid cover	
☐ IV site ready (Site _____Size_____G)	

Nurse Name (staff no): **(** **)** Signature:

IV SEDATION CHECKLIST (if IV Sedation is planned)

To be filled in by the doctor / nurse administering intravenous sedation on the day of procedure

Age or size appropriate airway equipment		
ETT size:_____	□ No	□ Checked
Mask Size	□ No	□ Checked
Oral Airway Size	□ No	□ Checked
Self-inflating Bag / Valve	□ No	□ Checked
Suction	□ No	□ Checked
Direct Laryngoscopy	□ No	□ Checked
IV patency	□ No	□ Checked

Reversal drugs:

Flumazenil available □ No □ Yes

(0.01 mg /kg up to 0.2 mg every min to max total 1 mg intravenously)

Naloxone available □ No □ Yes

(10 microgram/kg, titrate to effect every 2 to 3 min)

E Trolley/Resuscitation Box available □ No □ Yes

Other Resuscitative Drugs □ No □ Yes

Doctor Name (staff no): **(** **)** Signature:

Nurse Name (staff no): **(** **)** Signature:

Sedation and treatment record (Optional / Refer to MAR)

BH: **cm** **BW:** **kg** **Surface area:** **m²**

Date/ Time	**Order**	***Dosage***	***Prescribed by (Signature/Staff no)***	***Given at (Time)***	***Given by (Signature/Staff no)***	***Checked by (Signature/Staff no)***
	NPO till conscious					
	Antibiotic cover:	mg				
	Steroid cover:	mg				
Sedation drugs:						
	Chloral hydrate po (1st dose)	mg				
	Chloral hydrate po (2nd dose)	mg				
	(Chloral hydrate 30-50 mg/kg for neonates, others 50-75 mg/kg; addition 25 mg/kg, max total dose of 100 mg/kg or 2 gm)					
	Midazolam iv (1st dose)	mg				
	Midazolam iv (2nd dose)	mg				
	Midazolam iv (3rd dose)	mg				
	(Midazolam0.05-0.1 mg/kg iv, repeated at 2-3 min interval, max total dose of 0.6 mg/kg or 6mg for 6m-5yo, max total 0.4mg/kg or 10mg for >6yo)					
	Ketamine iv / im (1st dose)	mg				
	Atropine iv	mg				
	Ketamine iv (2nd iv dose)	mg				
	(Ketamine 1-2 mg/kg iv, addition dose of 0.5-1 mg/kg, up to max 4 mg/kg ± pre-med with 0.01-0.02 mg/kg Atropine)					
	Dexmedetomidine intranasal	mcg				
	Dexmedetomidine intranasal (2nd dose)	mcg				
	(Dexmedetomidine 2-3mcg/kg, max total 200mcg in total and up to 100mcg per nare)					
	Fentanyl iv	mcg				
	(Fentanyl 1-2mcg/kg/dose, max 50mcg/dose)					

Observation chart

Assessed by:_____(Nurse Name/Rank) Signature:_____Time:_____Date:_____.

TIME (Q_min.) Moderate sedation Q10-15mins. Deep sedation Q5mins.													
HR													
SpO_2													
$ETCO_2$													
RR													
ABP / NBP													
UMSS*													
Others													

*(*APPENDIX A: UMSS: 0 Awake and alert; 1 Minimally sedated: tired/sleepy, appropriate response to verbal conversation and/or sound; 2 Moderately sedated: somnolent/sleeping, easily aroused with light tactile stimulation or a simple verbal command; 3 Deeply sedated: deep sleep, arousable only with significant physical stimulation; 4 Unarousable)*

Post Procedure SIGN OUT Checklist

Completed Procedure/Intervention checklist				□ Yes	□ No
Patient is able to maintain airway, breathing well and SpO2 satisfactory				□ Yes	□ No
Stable BP / heart rate / RR	□ Yes	□ No	Patient is easily arousable	□ Yes	□ No
Escort required	□ PCA	□ Nurse	□ Doctor		
Continue O_2 supplement to ward	□ Yes	□ No	Continuous SpO_2 in ward	□ Yes	□ No
Monitoring in ward: SpO_2 / BP /P / RR / Conscious level Q____H			□ 24 hours in-patient observation needed		

Other Notes / $ETCO_2$ monitoring if required / Plan:

Assessed by:_____(Doctor Name/Rank) Signature:_____Time:_____Date:_____.

_____(Nurse Name/Rank) Signature: _____Time:_____Date:_____.

Checklist for Discharge Home

☐ All vital signs (temp, HR, BP, RR, SpO_2, +/- $ETCO_2$) have returned to normal levels

☐ Patient is awake (or has returned to baseline level of consciousness)

☐ Nausea, vomiting and pain have been adequately managed

☐ Discharge information explained to patient or parent

Discharge information sheet given? □ Yes □ No

Other Notes:

Checked by:_____(Doctor Name/Rank) Signature: _____Time:_____Date: _____.

_____(Nurse Name/Rank) Signature:_____Time:_____Date: _____.

The adverse event and outcome of procedural sedation in Generic Clinical Form

☐ **No adverse events during sedation or recovery.** ***(form completed)***

☐ **Yes, unplanned interventions or outcomes occurred.** ***(check all that apply below)***

Assessed by: _____ (Doctor Name/Rank) Signature: _____ Time:_____ Date:_____

	Intermediate	Report to AIRS
Airway/ Breathing	☐ Positive pressure ventilation ☐ Naloxone or flumazenil ☐ Oral airway	☐ Tracheal intubation ☐ Neuromuscular blockade ☐ Pulmonary aspiration
Circulation	☐ Bolus IV fluids	☐ Chest compressions ☐ Vasoactive drug administration
Neuro	☐ Anticonvulsant administration	☐ Neurological deficit
Sedation Quality & Patient Experience	☐ Sedation insufficient ☐ Escalation of care of hospitalization ☐ Provider dissatisfied ☐ Patient/ family dissatisfied	Sentinel events ☐ Death

Suspected Etiology
- ☐ Apnea
- ☐ Respiratory depression
- ☐ Upper airway obstruction
- ☐ Laryngospasm
- ☐ Hypotension
- ☐ Bradycardia
- ☐ Cardiac arrest
- ☐ Seizure or seizure-like movements
- ☐ Patient active resistance or need for restraint
- ☐ Sedation complication
- ☐ Unpleasant recovery reaction/ agitation
- ☐ Unpleasant recall

☐ OTHER _____

☐ OTHER _____

Modified with approval from the TROOPS continuous quality-improvement form. British Journal of Anaesthesia 2018, 120(1): 167