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1.0 Introduction

The purpose of this guideline is to ensure that patients who are at risk of developing withdrawal symptoms can be weaned off opioids and benzodiazepines in a timely fashion. It is appropriate that when discontinuing opioids and benzodiazepines, practitioners are cognizant of the potential as well as the clinical effects of withdrawal.

Target Users

- Nurses, Nurse Practitioners.
- Staff Physicians, Residents, Fellow.
- Pharmacists.

Target Patient Population


These guidelines are intended for children at risk of withdrawal:

- Any neonate with postnatal exposure to opioids or benzodiazepines for 5 days or more.
 - Neonates with antenatal exposure are not included in this guideline. (Refer to the withdrawal algorithm for Neonatal Abstinence Syndrome).
- Any infant or child who has had exposure to opioids or benzodiazepines for 5 days or more.

Caution should be exercised to ensure that the child does not require the drugs for pain and sedation management. If the child undergoes a procedure that requires any pain or sedation medication then this should be taken into consideration within the weaning process.

2.0 Definitions

1. **Physical dependence** is defined as the need for continued administration of a drug to prevent the development of a withdrawal syndrome.
2. **Tolerance** is defined as a state in which the given dose of a drug becomes ineffective or where increase dosage of the drug is required to produce the same analgesic or sedative effect.
3. **Withdrawal** includes the physical signs and symptoms that manifest when the administration of an opioid or benzodiazepine is withdrawn after persistent use. This phenomenon may occur with the usage of these agents for as short as five consecutive days or occasionally even after only three days. The onset and course of the withdrawal state are related to the type of medication and dose being used immediately before cessation or reduction of use.

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Common Agents associated with withdrawal

Commonly used agents associated with withdrawal symptoms include opioids and benzodiazepines. Other agents associated with withdrawal include clonidine, dexmedetomidine, barbiturates and chloral hydrate.

Risk factors for withdrawal


Risk factors for developing opioid or benzodiazepine withdrawal include:

- Neonate, infant or child who has required opioids and/or benzodiazepines for 5 days or more.
- Neonate, Infant or child who has required high doses or multiple agents.
- Neonate, infant or child who has had previous experience of withdrawal.
- Infants less than 6 months of age.

Signs and Symptoms of Withdrawal

Below are clinical features that have been described with withdrawal of opioids and benzodiazepines. It is clinically difficult to distinguish between signs of opioid and benzodiazepine withdrawal.

CNS irritability	GI disturbances	Autonomic dysfunction
Poor sleep pattern Tremors Muscle spasms/aches Irritability Hallucinations Dilated pupils Seizures	Diarrhea Vomiting Abdominal pain Uncoordinated suck/swallow Gagging	Sweating Fever Yawning Hiccups Goosebumps/ chills Increased secretions Tachycardia Tachypnea Hypertension

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3.0 Clinical Practice Recommendations

The grading system in Table 1 serves as a guideline for the user about the hierarchy of evidence available to support each recommendation; with meta-analysis considered to be the highest level of evidence and expert opinion considered to be the lowest level of evidence that can be used to support a CPG.

Table 1: Grades of Recommendation

A	Recommendation supported by at least one randomized controlled trial, systematic review or meta-analysis.
B	Recommendation supported by at least one cohort comparison, case study or other experimental study.
C	Recommendation supported by expert opinion or experience of a consensus panel.

3.1 Withdrawal Assessment (Grade B)


The first step in withdrawal management is to conduct a withdrawal assessment using a validated tool called the WAT 1 (Franck and Curley 2007). The WAT 1 should be started on the first day of weaning in patients who are ready to commence a weaning plan and who have received opioids and/or benzodiazepines by infusion, intermittent IV dosing or oral dosing for prolonged periods (e.g. 5 days or more).

When using the WAT 1 the following factors should be taken into consideration:

- Natural course of the illness.
- Patient baseline.
- Other potential contributing factors (e.g. environment).
- Scores should be interpreted on their trend over time.

Steps to use the WAT 1

- Obtain a baseline withdrawal score using the WAT 1 before any of the drugs are weaned.
- Chart a pain score as per hospital [policy](#) (e.g. q4 hourly).
- Score every 12 hours at 06:00 and 18:00 hours - based on bedside staff clinical judgement the need for more frequent assessment may be necessary- increase to q4-8h if withdrawal scores are high and intervention is required.
- Withdrawal is correlated with a score > 3. Inform physician if scores are > 3 and use the withdrawal management plan as a guideline to direct care.
- Continue scoring q12h until 72 hours after the last opioid/benzodiazepine administered in the wean plan.

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WITHDRAWAL ASSESSMENT TOOL VERSION 1 (WAT – 1)

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Patient Identifier														
	Date:													
	Time:													
Information from patient record, previous 12 hours														
Any loose /watery stools	No = 0 Yes = 1													
Any vomiting/wretching/gagging	No = 0 Yes = 1													
Temperature > 37.8°C	No = 0 Yes = 1													
2 minute pre-stimulus observation														
State	SBS ¹ < 0 or asleep/awake/calm = 0 SBS ¹ > +1 or awake/distressed = 1													
Tremor	None/mild = 0 Moderate/severe = 1													
Any sweating	No = 0 Yes = 1													
Uncoordinated/repetitive movement	None/mild = 0 Moderate/severe = 1													
Yawning or sneezing	None or 1 = 0 >2 = 1													
1 minute stimulus observation														
Startle to touch	None/mild = 0 Moderate/severe = 1													
Muscle tone	Normal = 0 Increased = 1													
Post-stimulus recovery														
Time to gain calm state (SBS ¹ ≤ 0)	< 2min = 0 2 - 5min = 1 > 5 min = 2													
Total Score (0-12)														


3 indicators obtained from the nursing documentation in the **previous 12 hours** are scored with one point:

- **Loose/watery stools**, which are not consistent with the patient’s age, medical condition or baseline pattern.
- **Vomiting/wretching/gagging** that cannot be attributed to other causes or interventions.
- **Temperature elevation** that remains >37.8 more frequently than not during the previous 12 hours and not associated with infection.

5 indicators assessed during a **2 minute observation** of the patient at rest are scored with one point:

- **State behavior** based on observation (asleep/awake/calm = 0 or awake/distressed = 1).
- **Tremors** that are moderate to severe and cannot be attributed to another clinical cause.
- **Sweating** that is observed and not related to an appropriate temperature regulation response.
- **Uncoordinated/repetitive movements** that are moderate to severe including head turning, leg or arm flailing or torso arching.

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- **Yawning/sneezing** that is observed more than once in the 2 minute observation period.

2 indicators assessed during a **progressive arousal stimulus** scored with one point:

- **Startle to touch** that is severe.
- **Muscle tone** that is increased.

1 indicator assessed during an **observation period** following the stimulus scored with up to two points:

- Time to return to calm state that is greater than 5 minutes will receive 2 points.
- If the time to return to calm state is 2-5 minutes, it will receive 1 point.

Higher scores indicate more withdrawal symptoms; lower scores indicate fewer withdrawal symptoms. Interpretation is based on their trend over time. A score greater than 3 indicates withdrawal. Scoring should be done q12h.


(Adapted from: Curley et al. State behavioral scale: A sedation assessment instrument for infants and young children supported on mechanical ventilation. *Pediatr Crit Care Med* 2008; 7(2): 107-114.)

3.2 Prevention of Withdrawal (Grade B)

The goal of withdrawal prevention is to have a patient who is not agitated or distressed, who has met their pain management goal and is not overly sedated.

Initial Steps

- Decision made to wean sedative and analgesic agents based on clinical situation of the child.
- Order withdrawal scoring (WAT-1) q12h.
- Assessment should be done of all regular and PRN sedative and analgesics medications being used to determine which agents will need to be weaned.
- This includes reviewing:
 - Opioids: Infusion and bolus doses.
 - Benzodiazepines: lorazepam midazolam, diazepam – infusions and bolus doses.
 - Other sedatives: dexmedetomidine, clonidine, chloral hydrate.
- Calculations should be made taking into account:
 - All agents used for sedation and analgesia.
 - Age of the child.
 - Weight of the child.
 - Total duration of use.
 - Patient history.

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- Withdrawal symptoms have been reported with all agents used for sedation and analgesia so a carefully planned weaning regimen taking into account all medications must be considered for every patient.

3.3 Withdrawal prevention guidelines (Grade B)

Algorithms have been developed to help guide the weaning process with the aim of prevention of withdrawal symptoms. If the child/infant has been exposed to opioids and/or benzodiazepines for 5 days or more then wean using an appropriate algorithm.

The [algorithms](#) cover the following scenario:


- Opioid only wean.
- Opioid and benzodiazepine wean.
- Benzodiazepine only wean.

3.4 Order of drugs to wean (Grade C)

- General recommendations is as follows:
 - Wean Opioid until at 50% of dose at start of wean.
 - Begin weaning diazepam dose once opioid is at 50% of dose at start of wean.
 - Continue daily opioid and benzodiazepine wean.
 - If on clonidine, this preferably should not be weaned until Opioid and Benzodiazepine has been successfully discontinued.
- Note: Above is a general guideline and will need to be tailored to patient's clinical situation. For example, in some situations it may be more important to wean the sedative first if there is an ongoing requirement for analgesia.

3.5 Converting to Enteral dosing of analgesics and sedative and how to wean (Grade C)

- An early goal in weaning should be to convert all medications to enteral formulation.
- This should be done as early as possible once a child is able to tolerate enteral medications and not likely to have significant periods of being nil by mouth.
- [Conversion formulas](#) are provided to help facilitate the conversion from IV to enteral for both opioids and benzodiazepines.
- Once enteral formulation has been established, you can continue the same % wean that was being weaned while in IV form.
- Once you get to low enough doses, the weaning involves increasing the interval between the doses rather than reducing the dose further.


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- For enteral morphine the suggestion is to wean:
 - Until at a dose of 0.1mg/kg q4h.
 - Once at 0.1mg/kg q4h, keep the same dose and increase the dosing interval to q6h for 24 hours (or same period you were weaning previously i.e. if was weaning every 48 hours then would do this for 48 hours).
 - You would then continue to increase the interval between the doses from q6h to q8h then to q12h and then to q24h before ceasing.
 - Each step would be for 24 hours or the same time period that you were weaning previously e.g. every 48 hours etc.
- For enteral hydromorphone the suggestion is to wean:
 - Until at a dose of 0.02mg/kg q4h.
 - Once at 0.02mg/kg q4h, then increase the interval from q4h to q6h for 24hrs (or same period of time you were weaning previously).
 - You would continue to increase the interval between the doses from q6h to q8h to q12h and then to q24h before ceasing.
- For enteral diazepam, the suggestion is to wean:
 - Until at a dose of 0.05mg/kg q6h.
 - Once at 0.05mg/kg q6h then increase the interval from q6h to q8h for 24 hours (or same period of time you were weaning previously i.e. if was weaning every 48 hours then would do this for 48 hours).
 - You would continue to increase the interval between the doses from q8h to q12h and then to q24h before ceasing.
 - Each step would be for 24 hours or the same time period that you were weaning previously e.g. every 48 hours etc.
- Note: it is often at these smaller doses that it is difficult to wean off the drug without symptoms of withdrawal. If this is the case, you may need to slow the wean further. Some suggestions would be:
 - Dropping the % wean: e.g. 5% wean every 24hours instead of 10% wean.
 - Increasing the interval between weans: e.g. going from q24h to q48h.
 - IF weaning opioids and benzodiazepines: wean off one drug at a time or switch to alternate day weans if both were being weaned daily.

3.6 Management of Withdrawal (Grade B)

3.6.1 Introduction

- Diagnosis of Withdrawal Syndrome is a diagnosis of exclusion.

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- Changes in clinical status e.g. new infection can cause signs and symptoms that can be mistaken for withdrawal.
- WAT-1 scores > 3 or increasing trends in the scores should increase awareness about possibility of withdrawal but patient should be assessed to ensure no other cause of clinical change is present.
- Management for Withdrawal Syndrome once it is diagnosed should consist of
 - Non- Pharmacological Measures.
 - Pharmacological Measures.

3.6.2 Non-Pharmacological Measures that can be utilized to reduce withdrawal (Grade C)

Reduce environmental stimuli at patient's bedside including noise, light and handling.


- Swaddle infants. Some infants may settle with holding, rocking and a pacifier.
- Frequent feedings.
- Appropriate fluid therapy to prevent dehydration.

3.6.3 Pharmacological Measures to treat withdrawal (please refer to [algorithms](#)) (Grade B)

- It is often difficult to determine which medication is contributing to withdrawal. Benzodiazepine and opioid withdrawal can present very similarly.

General principle for management of withdrawal symptoms:

- Adopt non pharmacological measures wherever possible.
- Pharmacological Principles of withdrawal management are as follows:
 - Give a bolus of the medication being weaned. If weaning both opioid and benzodiazepines, start with a bolus of opioid first to see if this controls the symptoms.
 - Increase the dose of the agent being weaned back to the previous dose where there were no withdrawal symptoms.
 - Hold the wean for 24 hours.
 - Then commence slower wean than was being used previously.
 - Adjuncts to assist with weaning should only be added once above has failed. There is only a small group of patients in which adjuncts will be needed to facilitate weaning.


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Specific Management Suggestions for withdrawal:

- Reduce environmental stimuli at patient's bedside including noise, light and handling.
- Once diagnosis of withdrawal is confirmed:
 - Give dose of opioid that is being weaned (Give 50% of current oral or IV dose of opioid up to maximum of morphine 0.1mg/kg IV or fentanyl 0.5mcg/kg) and increase the infusion back to previous dose.
 - If symptoms do not resolve with above step and patient is also weaning from benzodiazepine, give dose of lorazepam 0.1mg/kg and consider increasing routine diazepam.
 - Ensure all symptoms resolve and hold wean for 24 hours.
 - Once symptoms have been controlled then weaning of sedatives/ analgesics needs to be slowed. For example:
 - Reduce opioid wean to 10% q48h or 5% q24h
 - If concurrent wean of opioid and benzodiazepine had been ongoing, hold benzodiazepine wean until opioids are weaned further then recommence benzodiazepine wean on alternate days to the opioid wean
 - Can also consider weaning only one drug at a time.

3.7 Adding Adjuncts to assist with weaning of opioids and benzodiazepines (Grade B)

- This should not be used as initial step. Any adjunct that is added will result in another medication that needs to be weaned for the patient and hence increase time on medications, so should only be reserved if necessary.
- Initial management is to slow the wean as outlined above.
- In a small number of patients this may not work and you are unable to wean the opioid and/or benzodiazepine despite using a slower wean.
- These patients may benefit from addition of an adjunct to assist with weaning.
- These include:
 - Clonidine.
 - Benzodiazepines (Diazepam) – if not already on it or increasing the dose if already on it.
 - Dexmedetomidine (restricted).
- Clonidine is a selective alpha-2 adrenergic agonist. Orally and parenterally administered clonidine results in sedative, analgesic and anxiolytic effects without causing respiratory depression. In combination with opioids or benzodiazepines, clonidine often allows for a reduction in the doses of these agents.


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3.8 Weaning Clonidine:

- When clonidine is part of the analgesic/sedative combination, then this should be the last drug to wean. This is because clonidine will help to facilitate weaning of opioids and benzodiazepines.
- The clonidine dose should remain the same until opioid and/or benzodiazepine is completely weaned off.
- Once Opioid and/or benzodiazepine have been successfully discontinued, then the clonidine should be weaned over 7-10 days to avoid rebound hypertension.
- Suggestion for wean:
 - Wean down to 1mcg/kg per dose every 6 hours and then increase the interval between doses to q8h, q12h and then q24h then cease. Each step would be for 24 hours.
- **Note:** Some patients may be on clonidine as part of their management for their underlying disease (e.g. single ventricle patients). In these patients, clonidine should not be weaned.

3.9 Weaning Chloral Hydrate:

- Long term use of chloral hydrate has not been well studied.
- It is thought that dependence and hence withdrawal can occur with long term use of chloral hydrate however it is not known if a weaning regimen is required for chloral hydrate.
- In patients who require an opioid and benzodiazepine wean, it is likely that they would have also been using regular chloral hydrate.
- If the patient is being established on a formal benzodiazepine wean that includes diazepam it is unlikely you will need to formally wean the chloral hydrate as mechanism of action would be similar.
- Chloral hydrate should be kept on the prn order in the initial few days while appropriate doses of opioids and benzodiazepines are being titrated for the patient.
- Suggested dose of chloral hydrate during weaning should be 10-20mg/kg q6h prn po/ng.
- As weaning of sedatives occur chloral hydrate prn interval should be reduced (q12 to q24h).

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4.0 Implementation of CPG

Facilitators to implementation

- Education within Critical Care Units (CCCU/CCU/NICU) and with CCRT team.
- CCRT team as a bridge to the wards with their role to increase education on the wards on a patient by patient basis.
- Acute Pain service to provide support on the wards.
- iLearn modules for withdrawal monitoring.
- iLearn module for withdrawal prevention.
- Target education for specific wards with high number of patients who are weaning from analgesics and sedatives.

Organizational barriers to implementation

- Large amount of clinical areas to target.
- Handover challenges between patients transferring from different units on weaning plans (ie critical care unit to the ward) and ensuring transfer of information occurs.

Potential economic impact

- Reduce critical care length of stay by having children safely being able to transfer to the ward on a safe weaning regimen without signs of withdrawal.
- Potential to reduce length of stay in the hospital if drugs can be effectively weaned off without withdrawal symptoms.
- Potential to send children home earlier on a specified controlled wean of their drugs once familiarity established with the guideline.


Key review criteria/indicators for monitoring and audit purposes

- Monitoring use of WAT-1 on the wards.
- Collecting data on each child weaning to identify what steps are working and which ones need to be readdressed and then reformatting the guidelines to reflect this new knowledge (quality improvement project).

5.0 Related Documents

[Weaning Algorithms](#)

[Opioid and Benzodiazepines Conversion Formulas](#)

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6.0 Statement of Evidence

- Literature search was conducted in Medline to identify any papers related to withdrawal and weaning of analgesics and sedatives in pediatric patients. All papers were reviewed.
- In addition literature search was also conducted to gain information on the pharmacokinetics and pharmacodynamics of each drug involved to help assist with recommendations in which there was limited evidence.
- Other centers were also contacted to obtain their practices for weaning of analgesics and sedatives to help provide insight into recommendations. All recommendations were reviewed and agreed upon by all the teams involved (Critical Care, NICU and Acute Pain service).
- In addition, we did a pilot of the first version of these guidelines and obtained data on successful and unsuccessful recommendations which allowed this version of the guideline to be adapted to reflect this evidence.

7.0 Guideline Group and Reviewers

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Attachments:

[CPG - Weaning Algorithm April 2015.pdf](#)

[APPENDIX -Conversion Calculators_CPG_Dec18_2014.pdf](#)