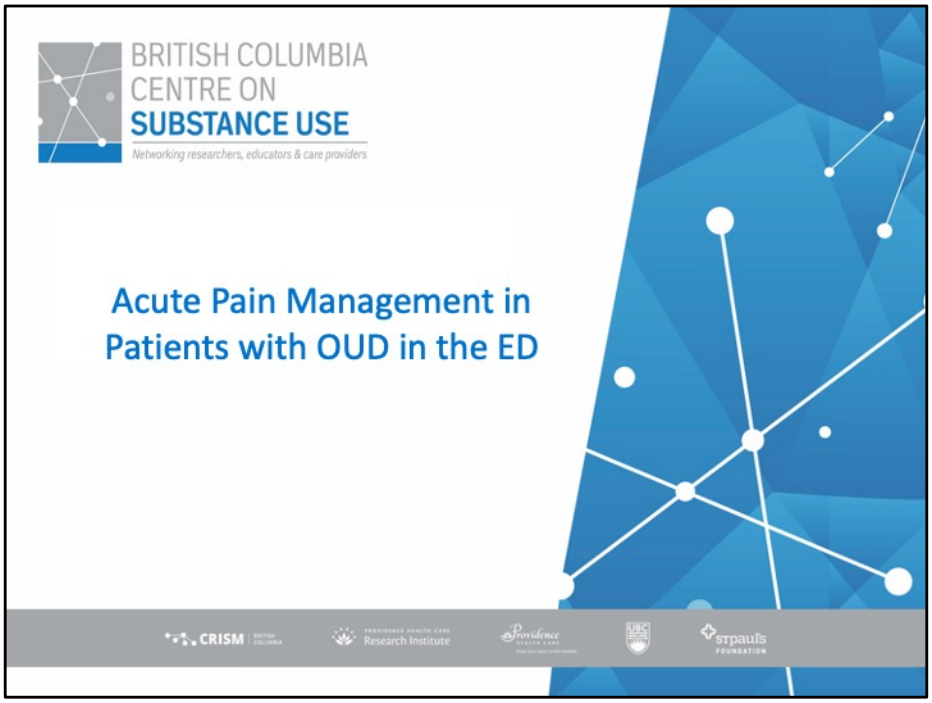

BRITISH COLUMBIA
CENTRE ON
SUBSTANCE USE
Networking researchers, educators & care providers
Acute Pain Management in
Patients with OUD in the ED
CRISM
Research Institute
Providence
stpauls
FOUNDATION

We respectfully acknowledge the land on which we work is the unceded traditional territory of the Coast Salish Peoples, including the traditional territories of xʷməθkwəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and Sə́l̓ílwətaɬ (Tsleil-Waututh) Nations

Disclaimer

Some of the protocols described in this presentation have been developed in response to the ongoing opioid crisis due to fentanyl in the illicit drug supply and may not be represented in current BCCSU Guidelines.

This includes innovative and novel approaches specific to emergency settings that are based on clinical experience. There is currently little evidence or research into the effectiveness of some of these protocols, therefore clinical judgement is advised.

Learning Objectives

1. Highlight differences in pain experience and management with patients with opioid use disorder (OUD)
2. Review an approach to pain management in the ED, including ordering opioids
3. Discuss an approach to specific scenarios, such as patients on buprenorphine and iOAT

Opioid Tolerance and Pain Experience (1)

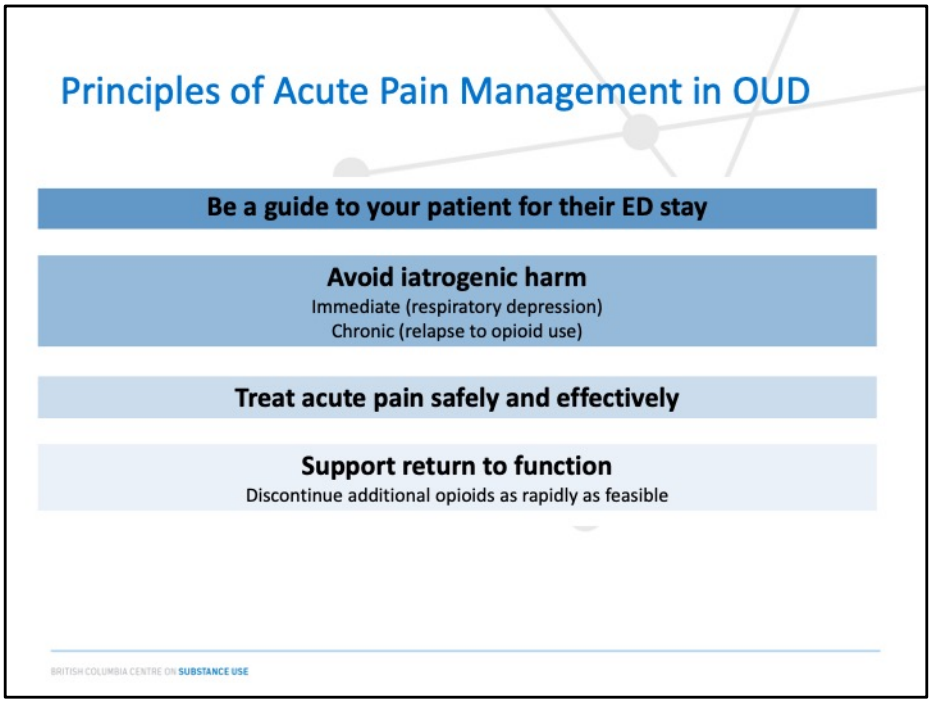
- A significant proportion of patients with OUD will experience chronic pain
  - >50% of patients on OAT report chronic pain
- Less likely to divulge being on OAT due to fear of stigma, which can result in less optimal pain management
- When experiencing pain, patients with OUD will have:
  - Greater pain sensitivity and severity
  - Less pain tolerance
  - Less non-pharmacologic coping strategies for pain

Opioid Tolerance and Pain Experience (2)

- Suboptimal pain treatment has been associated with the following consequences :
  - Decreased retention to treatment on OAT
    - However, many are on suboptimal doses of their OAT
  - Increased rates of self treatment (e.g., utilization of illicit opioids to self treat their pain)

Evidence and Guidance

- Most of the evidence that guides management of acute pain in patients with concurrent OUD are reviews based on:
  - Case series and expert consensus
  - Post-operative period studies



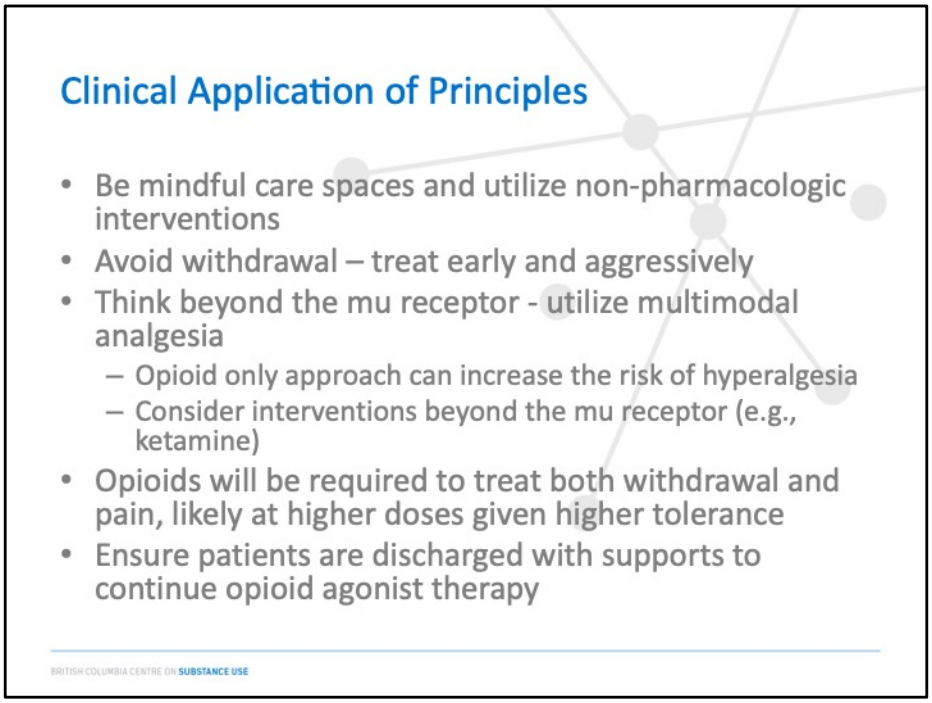
A guiding foundation was created by the Mayo Clinic (Warner et al 2020), who developed a four-pillar approach to pain management.

1. <u>Guide your patient through their ED stay:</u>
    - Describe the journey of their ED stay, which can include investigations and what diagnosis you are considering.
    - Validate and recognize their pain.
    - Discuss the steps you'll take to address their pain, including what tools are at their disposal (e.g., PRN medications, safer consumption sites).
2. <u>Avoid iatrogenic harms when ordering medications:</u>
    - Immediate or acute: opioids can cause respiratory depression. Consider starting low and titrating to effect with frequent re-assessments.
    - Chronic: discuss discharge planning to support the patient in being safe in the community and aligns with their treatment goals. This can include initiation or continuation of opioid agonist therapy.
3. <u>Utilize all tools available to you to treat pain safely and effectively</u>
    - Continue to practice evidence-based principles of pain management, such as ordering basal analgesia, developing treatment plans targeting the type of pain presentation and considering multi-modal analgesia.

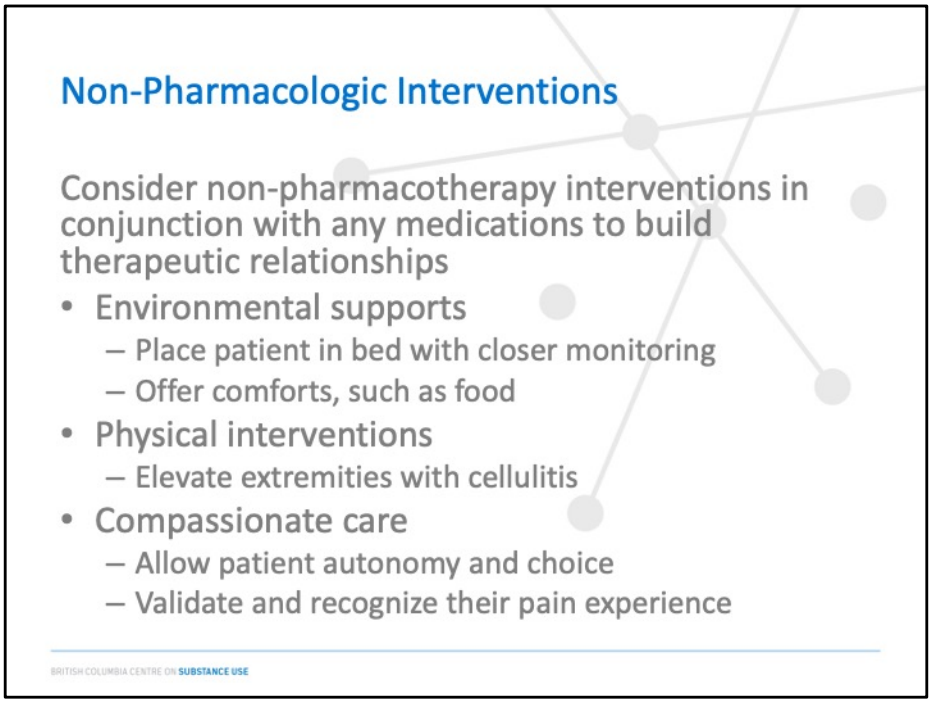
- Recognize the need for opioids to treat withdrawal and pain, likely at higher doses.

1. <u>Support your patient in early return to function and safety</u>
    - Ensure continuation of life saving treatments, such as opioid agonist therapy
    - Recognize that immediate release (IR) opioids and/or increases in OAT may be required on discharge but organize close reassessment to discontinue IR as early as feasibly possible.

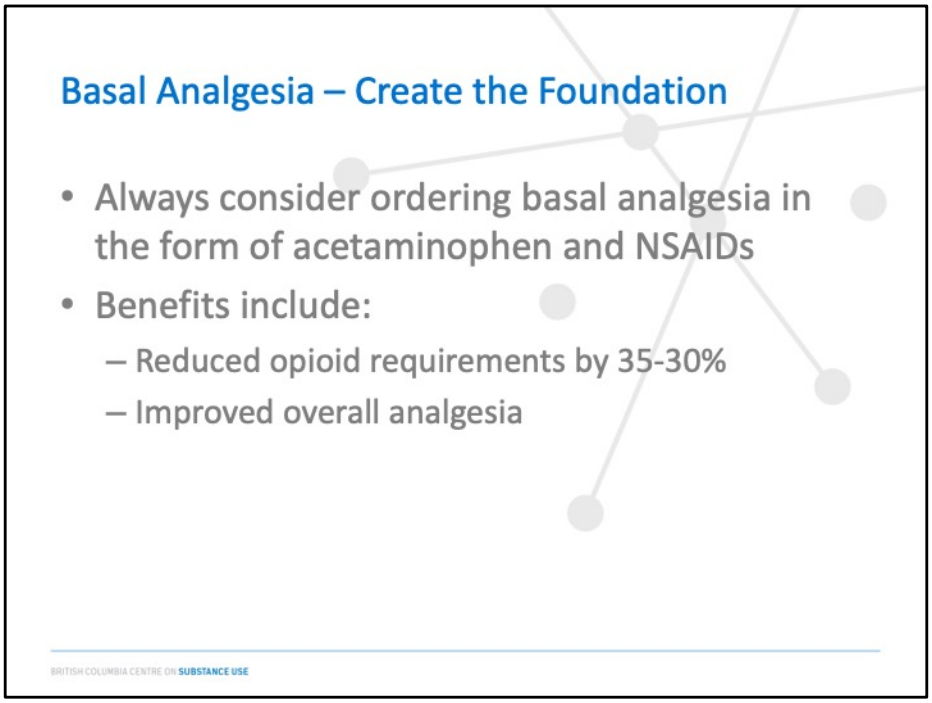
Warner NS, Warner MA, Cunningham JL, Gazelka HM, Hooten WM, Kolla BP, Warner DO. A Practical Approach for the Management of the Mixed Opioid Agonist-Antagonist Buprenorphine During Acute Pain and Surgery. Mayo Clin Proc. 2020 Jun;95(6):1253-1267. doi: 10.1016/j.mayocp.2019.10.007. Epub 2020 Feb 13. PMID: 32061413.



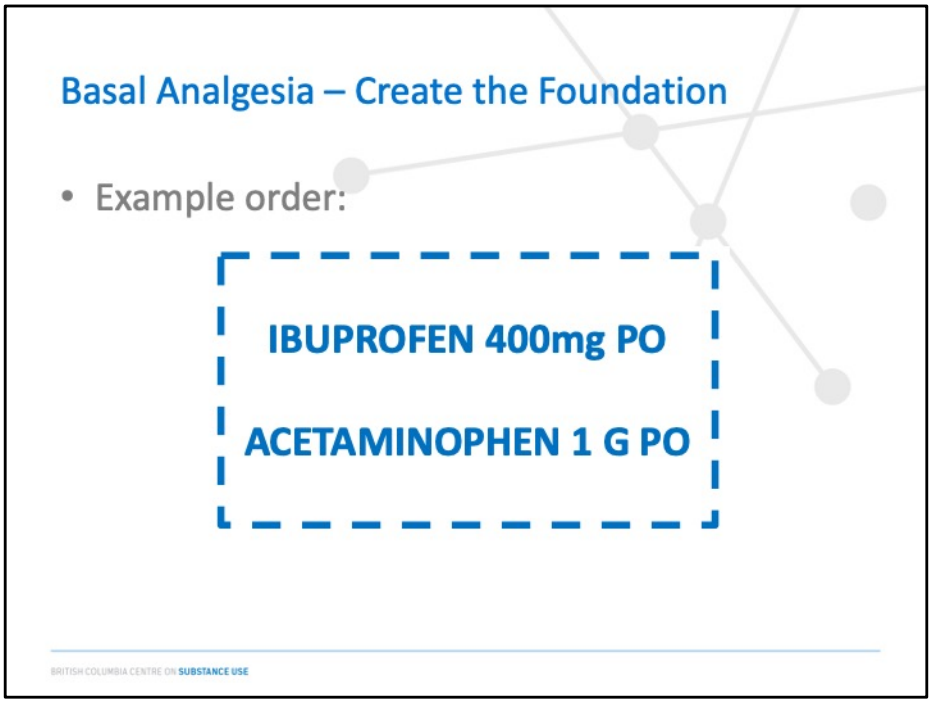
- Opioid-induced hyperalgesia is defined as state of hypersensitization caused by exposure to opioids, causing paradoxical pain with increasing opioid administration.
    - It occurs in patients with OUD only when administration of opioids escalate beyond what is required for withdrawal and pain management.
    - It presents clinically as escalating or unchanged pain despite significant escalation of opioids in a short time frame (<24 hours) in the absence of objective withdrawal symptoms.



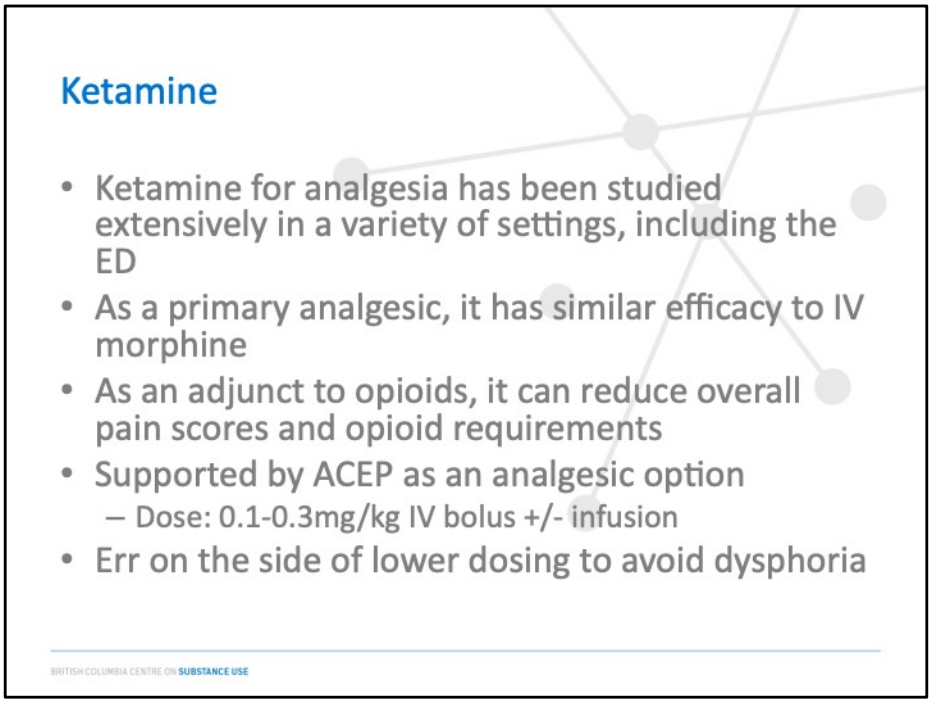
1. <u>Environmental supports</u>
    - Ensure your patient is in a calm environment.
    - Transfer them to a bed to allow for closer monitoring to titrate medications quickly.
    - Provide for their other needs, such as giving food.
    - Consider having a person with lived experience at the bedside to provide support.
2. <u>Physical interventions</u>
    - Continue physical interventions or supports that are recommended for the specific diagnosis, such as elevating a limb with cellulitis to mitigate pain from swelling
3. <u>Compassionate care</u>
    - Allow the patient autonomy and choice around their care. The emergency department may not be able to fully meet their needs, and patients may need to self treat.
    - Express compassion early in the visit by validating their pain experience and explaining next steps, including any possible delays.
    - Please refer to the modules around trauma informed care on https://www.bccsu.ca/edcare/



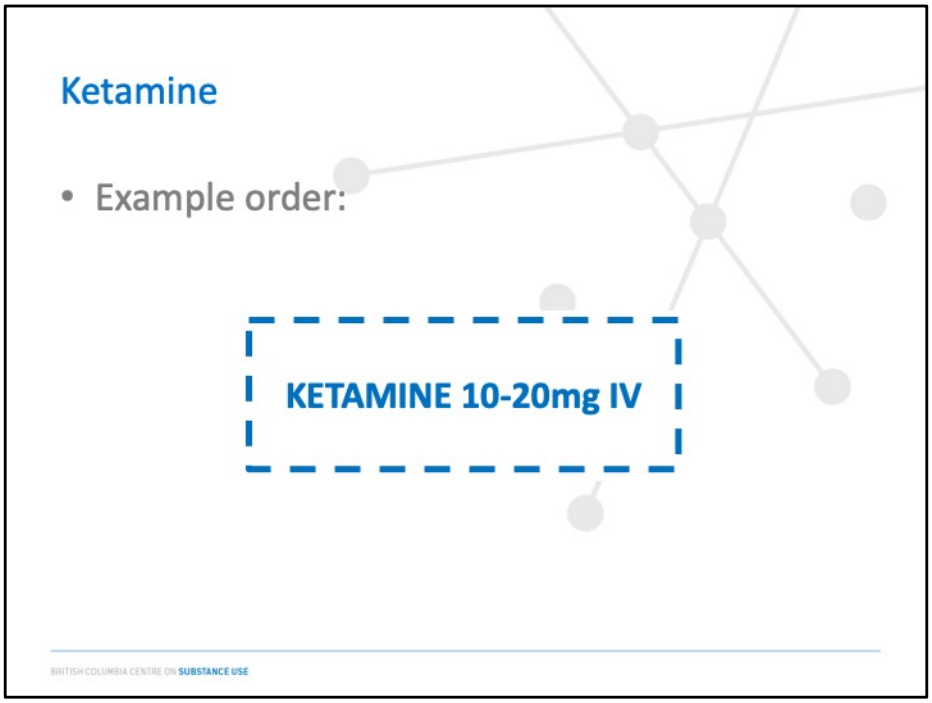
- For MSK related pain presentations, basal analgesia may provide equal pain reduction with or without opioids



- In patients with a prolonged stay in the ED or who ERPs are submitting admission orders, consider ordering these medications as regular rather than PRN to ensure their administration concurrently with opioids



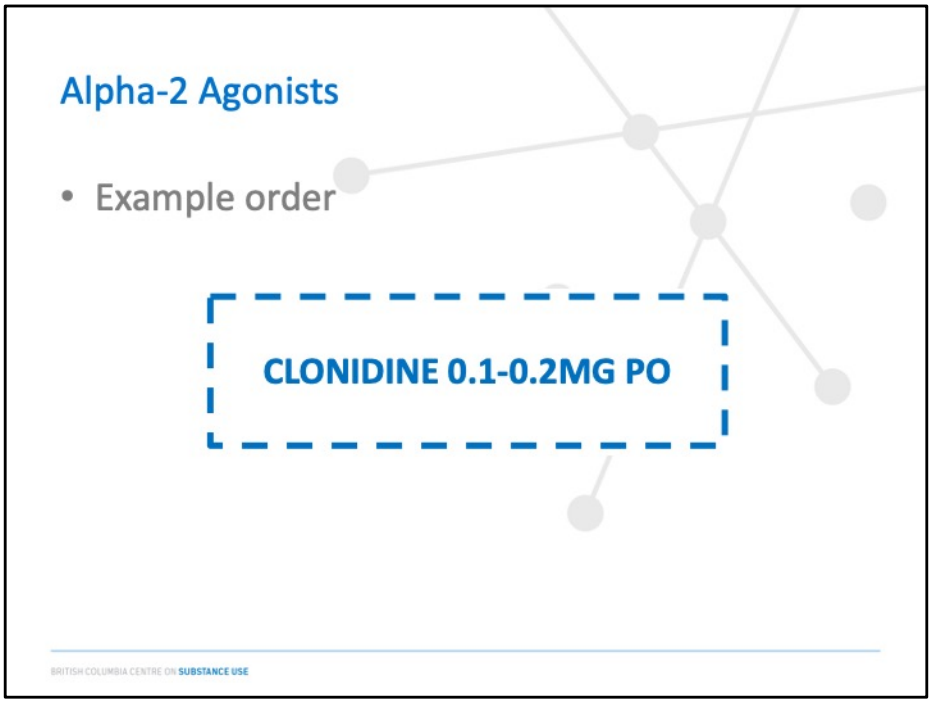
- Ketamine for analgesia has been studied in several different settings, including the ED and has been showed to be an effective analgesic through NMDA antagonism.
- In the RCT assessing its role as an adjunct, 25% of patients were noted to have prior opioid use and the intervention remained similarly effective (Bowers et al 2017).
- It is supported by ACEP, and they recommend bolus dosing of 0.1-0.3mg/kg IV followed by an infusion as needed
- A common side effect associated with larger doses of ketamine is dysphoria. This is generally poorly tolerated by patients with OUD – provide the lower dose range to avoid this side effect.



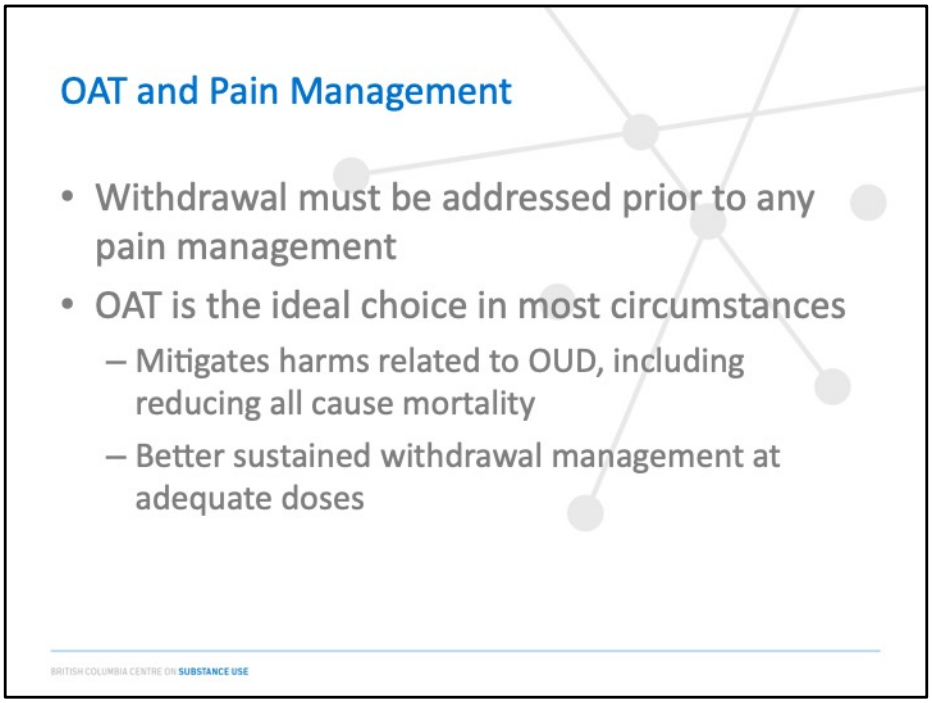
- This would be the dose provided as a bolus dose IV initially.
    - For prolonged stays and in the context of severe pain, a ketamine infusion can be initiated, but should be reassessed in 24 hours.

Alpha -2 Agonists

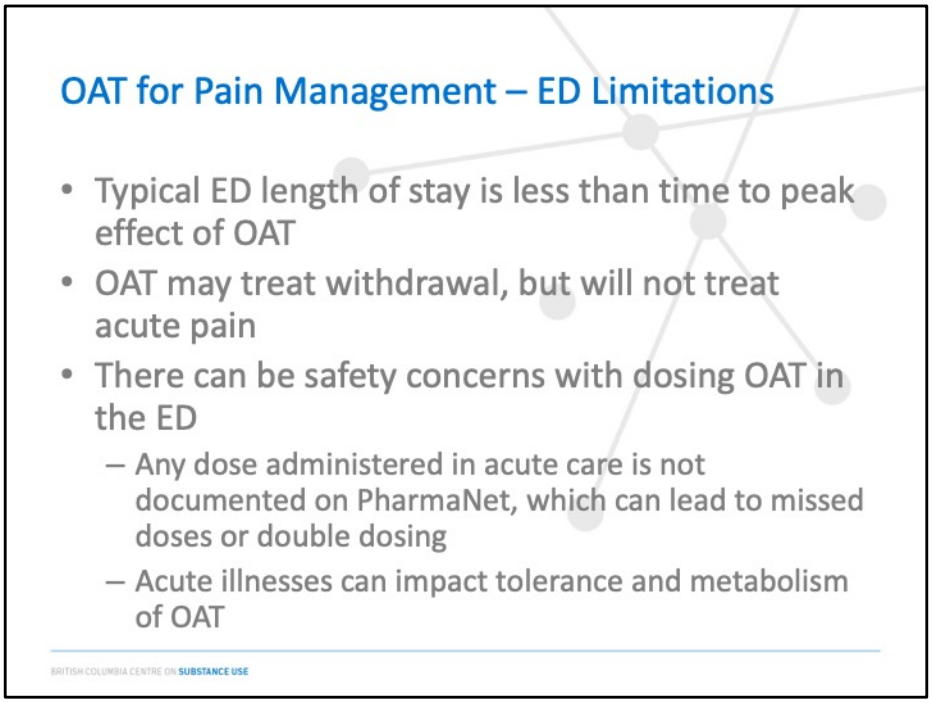
- Considered an adjunct for opioid sparing
- Includes medications such as dexmedetomidine and clonidine
- Most evidence is from the post-operative period using dexmedetomidine
- Postulated to reduce pain scores and opioid requirements through reduced anti-nociception



- Although dexmedetomidine has been studied more extensively, there are barriers to its implementation in the ED such as cost, monitoring and training requirements.
- Clonidine is an alternative. However, its side effects can be more pronounced such as bradycardia, somnolence, and hypotension. Measure blood pressure and heart rate prior to administering this medication.
- This can be provided every 6 hours as needed.
- Avoid prolonged administration due to risk of rebound hypertension.



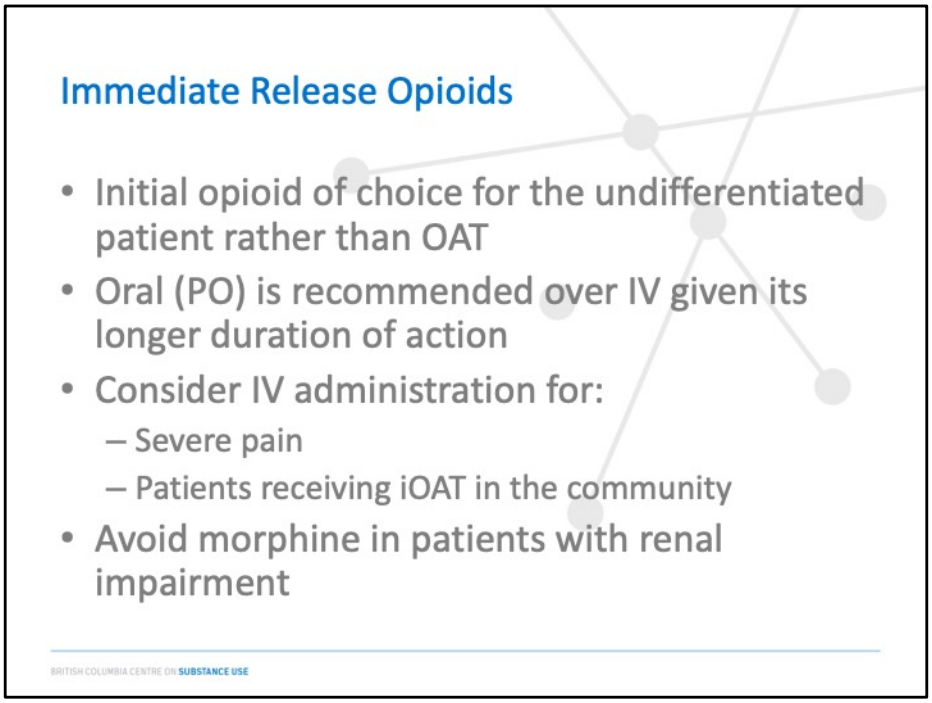
- In order to address pain, withdrawal must be treated adequately in order to “fill the sink”.
- This is accomplished through opioids.
    - IR opioids can address withdrawal quickly, but not in a sustained fashion
    - OAT (opioid agonist therapy) can provide better sustained withdrawal management, but requires patients to reach adequate maintenance doses to truly derive benefit
- OAT remains the ideal choice given it will (at maintenance doses):
    - Reduce all cause mortality, and mitigate harms related to OUD
    - Provide better sustained withdrawal management



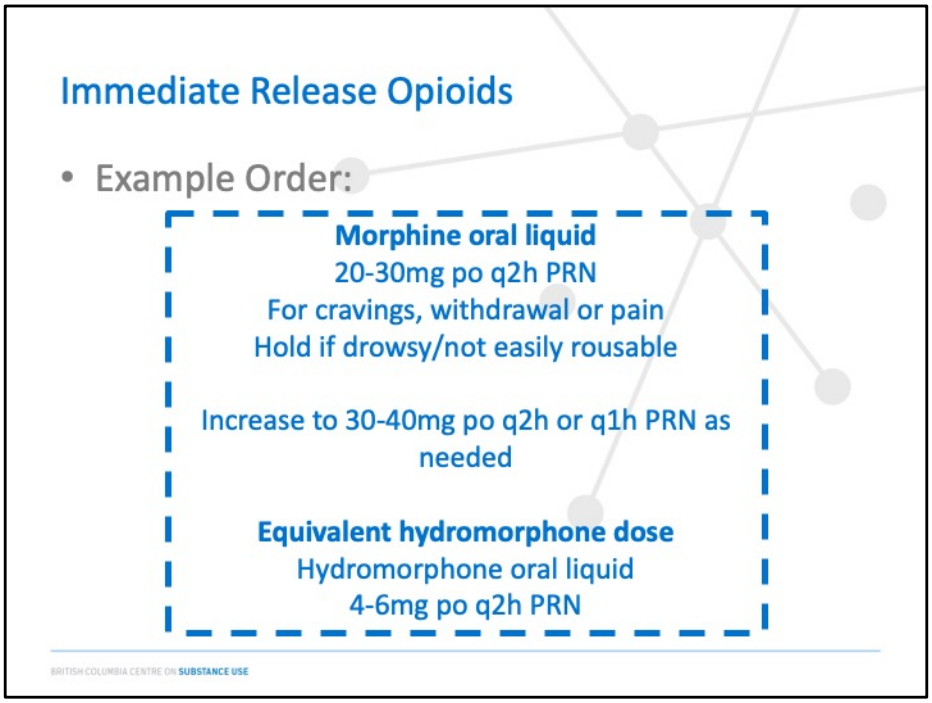
- Although OAT can be a key factor in successful pain management by addressing withdrawal, it does have its limitation
    - For patients who will be discharged from the ED, a typical length of stay is 3-4 hours. Most OAT have a peak effect at 3 hours or more. Taking in account delays in ordering and administration, the benefit of a single dose of OAT may not be noted.
    - OAT will treat withdrawal only when a patient is at adequate maintenance doses. Many patients are at suboptimal doses or have recently been initiated on therapy.
    - OAT will not adequately treat acute pain without other interventions.
- Safety consideration when providing doses of OAT in the ED can also offset perceived benefit
    - Any doses administered in acute care is not registered on PharmaNet.
        - PharmaNet is used by community providers and pharmacist to guide dosing, including dose increases or continuation of prescriptions.
    - If their usual community pharmacy is not notified of the dose administration, it can lead to
        - Double dosing if the patient presents on the same day

- Documentation of missed doses and the possibility of a dose reduction and/or cancelation of prescription depending on number of prior days missed

Please see modules on OAT (methadone, SROM) for further information on initiation and titration

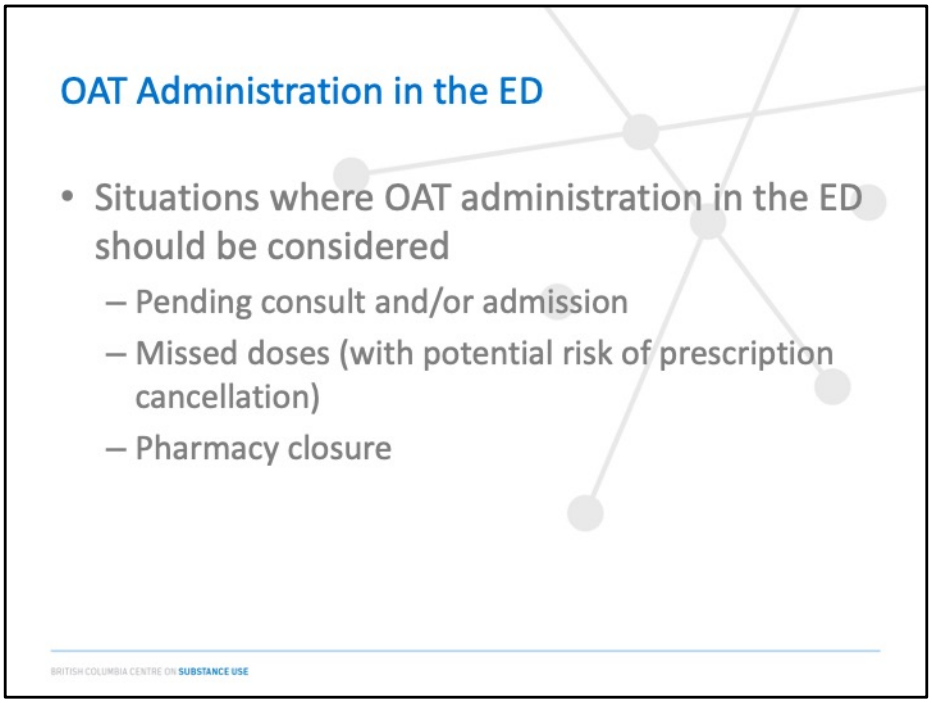


- Given some of these limitations of using OAT for pain management, IR opioids is the preferred initial opioid for the undifferentiated patient in the ED, and those with anticipated short stay.
- Oral administration is preferred given its longer duration of action, leading more sustained relief relative to IV.
- However, parenteral administration is preferred when:
    - Severe pain requires more immediate relief (IV peak effect is 10-15 minutes)
        - This should be closely followed by administration of oral opioids
    - Patients are receiving iOAT in the community
- Morphine should be avoided if the patient is at risk or has renal impairment due to accumulation of metabolites.

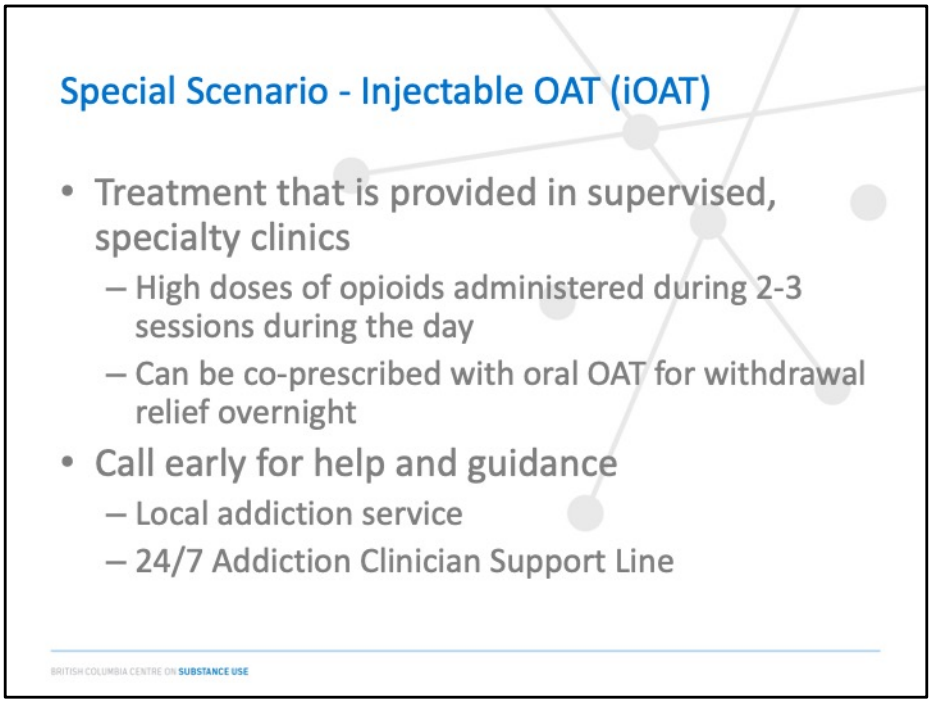


- This example is a starting point for patients with unclear tolerance, and for settings with lack of experiencing initiating and monitoring higher doses of opioids.
    - There is no standard approach in how to order IR opioids doses.
- A starting order for morphine is typically 20-30mg q2h as needed
    - This starting dose is not outside typical ordering ranges - morphine by weight-based dosing is typically 0.1-0.5mg/kg (average 0.2-0.3mg/kg)
        - For the average 70 kg patient, that equals to 20mg (14-21 mg)
    - For many patients, this is likely underdosing for their needs, especially in the absence of OAT
        - Discuss this with your patient and reassess them frequently for dose escalation
- A starting frequency is q2h
    - Peak effect of oral opioids is 80-90 minutes
    - This allows for post peak assessment if sedation is a concern
- If the dose in effective, next steps should be to:
    - Increase the amount by 10-20mg until an effective dose is reached and/or
    - Reduce the frequency from q2h to q1h. This will allow some dose stacking if there is no concern for sedation (e.g., the need to assess at peak effect prior to next dose)

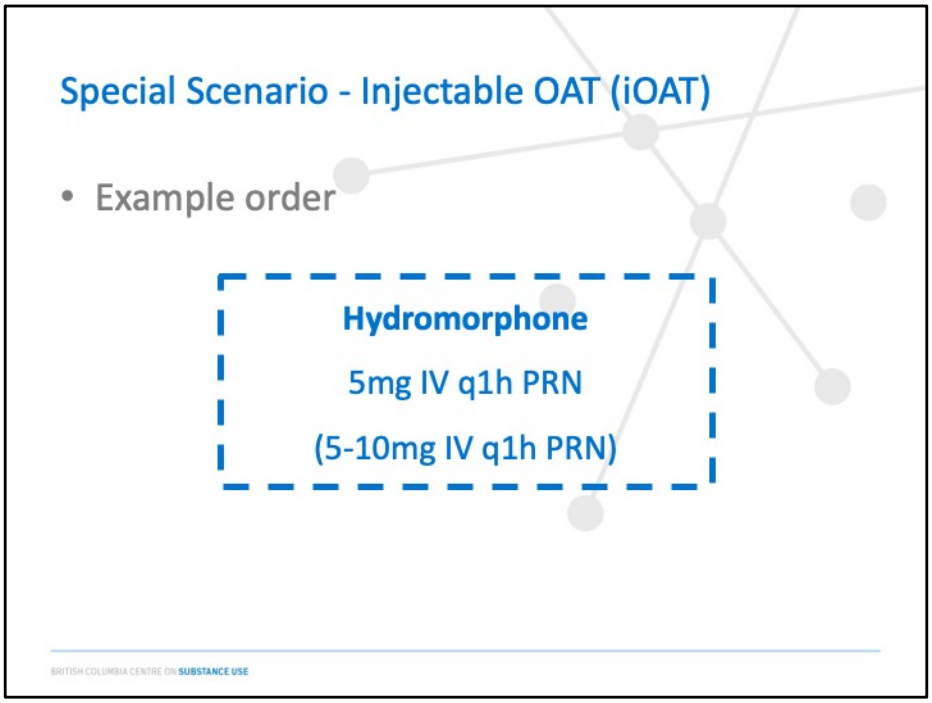
- Oral liquid is preferred to minimize diversion, but is not required
    - Equivalent in tab form can be ordered
- The same approach can be used if ordering hydromorphone



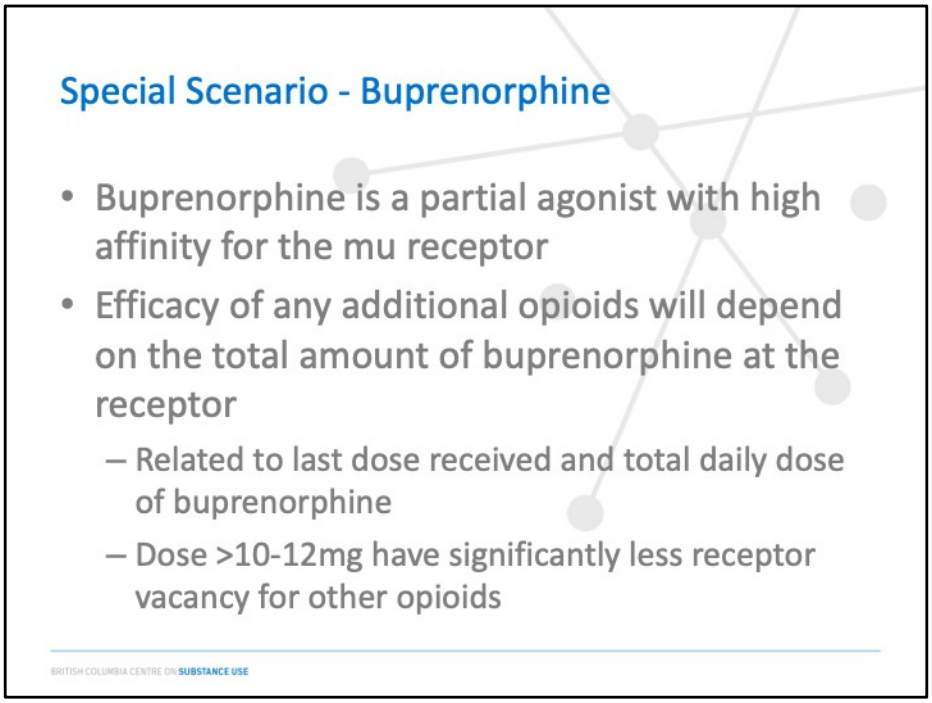
- OAT administration should be considered in the ED when the benefits likely outweigh the harms of lack of PharmaNet documentation. These include scenarios such as:
    - Referral for admission or consultation due to the prolonged duration in hospital
    - Missed doses due to the risk of a cancelled prescription or inability to obtain their OAT otherwise (see modules on OAT for further details)
    - Pharmacy closure making the risk of double dosing negligible, and a patient would not receive their dose otherwise
- Each hospital will have its own protocol for administration of OAT in acute care. These will include safeguards to minimize medication errors (such as pre-printed orders).
    - If unsure, contact your inpatient addiction service if available, or the 24/7 Addiction Clinician Hotline.



- Injectable OAT is a treatment that is provided in a supervised, specialty clinic
    - High doses of opioids (either hydromorphone or diacetylmorphine) are provided during 2 or 3 sessions throughout the day
    - The dose range is 30-200mg of IV hydromorphone equivalents for each session
    - Patients are often co-prescribed oral OAT to help treat any withdrawal overnight, but it is not a requirement
    - Please see module related to iOAT for further details
- This is a specialty treatment. Call early for guidance around dosing regimen and amount.
- For pain management, high doses of IV opioids are required
    - Hydromorphone is preferred due to its higher potency. It reflects the treatment being received in the community.
    - Start small but reassess frequently to scale up to effect.

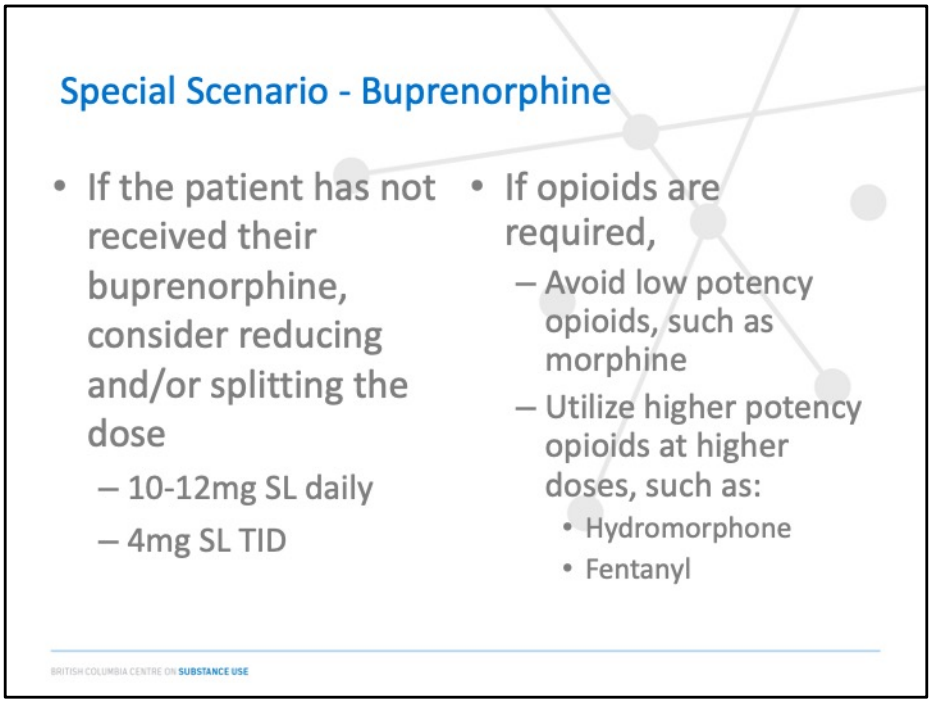


- Start at 5mg IV q1h PRN
    - Ensure the patient will be reassessed at 15-20 minutes if any concerns about sedation
    - This starting dose is conservative to take in account any changes in patient tolerance and/or provider discomfort around higher doses of IV opioids
    - For those who are awake and have visible signs of withdrawal, start at the higher range noted in brackets below.
        - Patients often require doses of 20mg or greater for analgesia.
    - Consider ordering PRN naloxone orders as a safeguard.
- Low threshold to obtain guidance from your local addiction consultant or the 24/7 addiction clinician line.



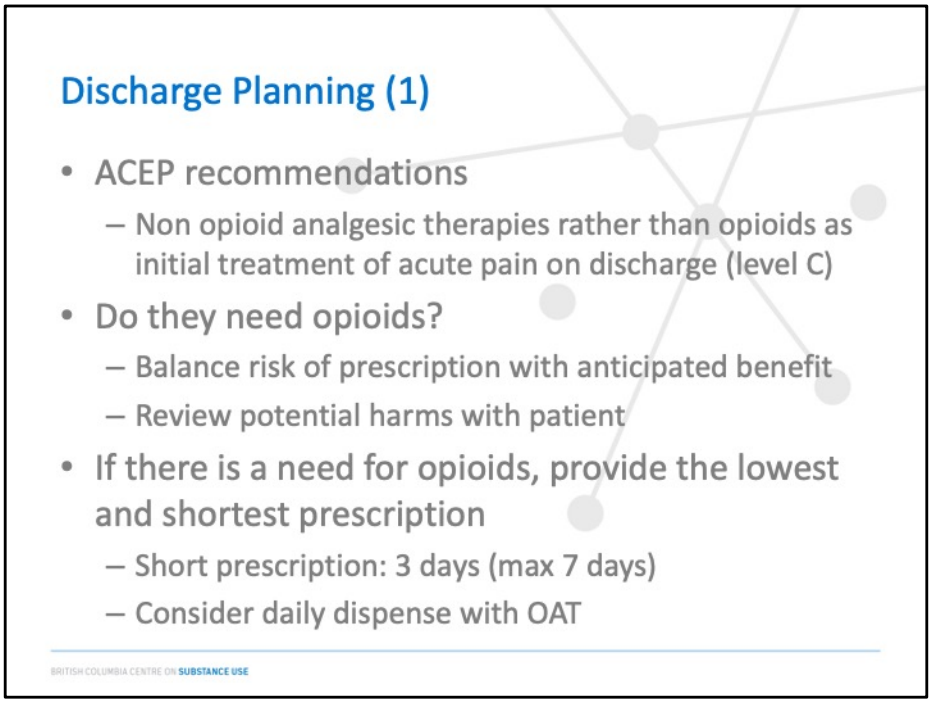
- Dose response to any IR opioid will vary depending on the total amount of receptors that are not occupied by buprenorphine, which is related to:
    - Time since last dose (>24 hours will have better receptor vacancy)
    - Total daily dose
- Doses above 10-12mg will have significantly less receptor availability. This requires larger doses of higher potency opioids (hydromorphone, fentanyl) to have any effect.

Warner NS, Warner MA, Cunningham JL, Gazelka HM, Hooten WM, Kolla BP, Warner DO. A Practical Approach for the Management of the Mixed Opioid Agonist-Antagonist Buprenorphine During Acute Pain and Surgery. Mayo Clin Proc. 2020 Jun;95(6):1253-1267. doi: 10.1016/j.mayocp.2019.10.007. Epub 2020 Feb 13. PMID: 32061413.



- If the patient has not received their buprenorphine, or they require admission orders:
    - Verify the timing of the last dose of buprenorphine.
    - If additional opioids are required, buprenorphine/naloxone should be continued and possibly lowered to 10-12mg daily to allow sufficient receptor availability while avoiding withdrawal that occurs with complete cessation of OAT
        - This can be achieved by
            - Reducing their total daily dose to 10-12mg daily
            - Reducing and splitting their dose to 4mg SL TID or 3mg SL QID
                - This allows some analgesic benefits from buprenorphine (analgesia will occur for the first few hours only) and reducing the duration of effect (<12 hours)
    - If no additional opioids will be required, continue buprenorphine/naloxone at the patient's usual dose.
- These strategies are recommended when ordering IR opioids:
    - Avoid lower potency opioids such as morphine.

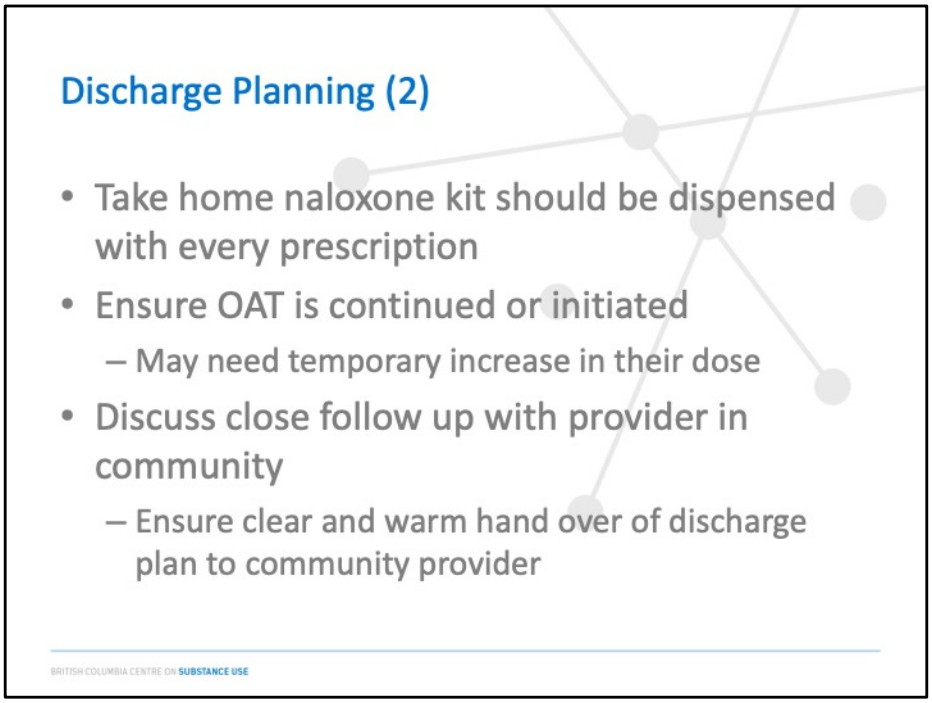
- Utilize higher potency opioids at higher doses such as hydromorphone (oral or IV) or fentanyl (IV) for breakthrough severe pain.
    - There is no standard dosing recommendation, but a conservative start would be hydromorphone 4-8mg po q2h PRN. Many patients will require doses of 16mg or above to perceive any effect.



- An ACEP guideline has provided the following recommendations around pain medications on discharge:
    - A trial of non opioid analgesia as first line therapy given less associated severe adverse effects and risks
        - This may not be appropriate for all pain presentations, such as fractures
        - This may not be appropriate for all patients (contraindications to medications such as NSAIDs)
    - Any opioid prescription is not without risk
        - Balance the anticipated benefits (pain relief) and potential harms
        - Review above with patient, including predicted duration of prescription and pain progression
    - If an opioid prescription is required, the lowest dose and shortest duration is recommended
        - Patients with OUD may require higher doses than typical due to tolerance.
        - Ideal duration is not known. It is recommended no longer than 7 days based on evidence linking higher rates of chronic opioid use with longer prescriptions. If feasible for the patient and the

condition, a 3-day prescription with close reassessment in the community is advised. This is not based on evidence, nor is there consensus amongst experts for this approach.
    - To minimize the number of pills dispensed, daily dispensing with or without OAT can provide another safeguard (similar to how risk mitigation pharmaceuticals are prescribed – see module).
- These recommendations are based on lower quality evidence, and always emphasize the importance of anticipated benefits and possible harms to proceed with any decision for prescribing opioids on discharge.

American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Opioids, Hatten BW, Cantrill SV, Dubin JS, Ketcham EM, Runde DP, Wall SP, Wolf SJ. Clinical Policy: Critical Issues Related to Opioids in Adult Patients Presenting to the Emergency Department. *Ann Emerg Med*. 2020 ;76(3):e13-e39. doi: 10.1016/j.annemergmed.2020.06.049. PMID: 32828340.



- Discuss life saving interventions:
    - Provide a take home naloxone kit and harm reduction supplies
    - Offer opportunities to initiate OAT if interested, and to support continuation of OAT without disruptions
        - In discussion with their usual provider or local addiction consultant, a transient increase in their OAT may be required to assist in pain management. However, OAT is not considered a pain management strategy on its own.
- Discuss the importance of close follow up with their usual community provider to reassess their pain and ensure continuation of OAT
    - Clear communication to both patient around expectations for ongoing IR opioid prescriptions and to their community provider around diagnosis, next anticipated steps and discussion with patients are key to a warm handover.

•If you need support managing precipitated withdrawal, inducting a patient on to buprenorphine/naloxone, or providing any other aspect of addiction and substance use care, you can call the 24/7 addiction medicine support line.

• The 24/7 addiction medicine clinician support line provides telephone consultation for physicians, nurse practitioners, nurses, mid-wives, and pharmacists who provide addiction and substance use care. It is available 24/7, 365 days a year. The number to call is 778-945-7619. More information can be found at www.bccsu.ca/24-7.

- The Provincial Opioid Addiction Treatment Support Program contains modules with more information on opioid use disorder and opioid agonist treatments, including buprenorphine/naloxone. This program is available online and it is free of charge.

References (1)

- American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Opioids, Hatten BW, Cantrill SV, Dubin JS, Ketcham EM, Runde DP, Wall SP, Wolf SJ. Clinical Policy: Critical Issues Related to Opioids in Adult Patients Presenting to the Emergency Department. *Ann Emerg Med*. 2020 ;76(3):e13-e39. doi: 10.1016/j.annemergmed.2020.06.049. PMID: 32828340.
- Balzer N, McLeod SL, Walsh C, Grewal K. Low-dose Ketamine For Acute Pain Control in the Emergency Department: A Systematic Review and Meta-analysis. Miner J, ed. *Acad Emerg Med*. 2021;6:198–11. doi:10.1111/acem.14159.
- Bowers KJ, McAllister KB, Ray M, Heitz C. Ketamine as an Adjunct to Opioids for Acute Pain in the Emergency Department: A Randomized Controlled Trial. Miner J, ed. *Acad Emerg Med*. 2017;24(6):676-685. doi:10.1111/acem.13172.
- Chan AKM, Cheung CW, Chong YK. Alpha-2 agonists in acute pain management. *Expert Opin Pharmacother*. 2010;11(17):2849-2868. doi:10.1517/14656566.2010.511613.
- Wheeler et al. Adjuvant Analgesic Use in the critically ill: a systemic review and meta-analysis. *Critical Care Explorations*. 2020;2(e0157):1-8.
- Chang AK, Bijur PE, Esses D, Barnaby DP, Baer J. Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department. *JAMA*. 2017;318(17):1661-1667. doi:10.1001/jama.2017.16190.
- Coutens B, Derreumaux C, Labaste F, et al. Efficacy of multimodal analgesic treatment of severe traumatic acute pain in mice pretreated with chronic high dose of buprenorphine inducing mechanical allodynia. *European Journal of Pharmacology*. 2020;875:172884. doi:10.1016/j.ejphar.2019.172884.
- Dunn KE, Finan PH, Tompkins DA, Fingerhood M, Strain EC. Characterizing pain and associated coping strategies in methadone and buprenorphine-maintained patients. *Drug and Alcohol Dependence*. 2015;157(C):143–149. http://doi.org/10.1016/j.drugalcdep.2015.10.018
- Helander EM, Menard BL, Harmon CM , et al. Multimodal Analgesia, Current Concepts, and Acute Pain Considerations. February 2017:1-10. doi:10.1007/s11916-017-0607-y.

References (2)

- Horn A, Kaneshiro K, Tsui BCH. Preemptive and Preventive Pain Psychoeducation and Its Potential Application as a Multimodal Perioperative Pain Control Option. *Anesthesia & Analgesia*. 2020;130(3):559-573. doi:10.1213/ANE.0000000000004319.
- Karlow N, Schlaepfer CH, Stoll CRT, et al. A Systematic Review and Meta-analysis of Ketamine as an Alternative to Opioids for Acute Pain in the Emergency Department. Miner J, ed. *Acad Emerg Med*. 2018;25(10):1086-1097. doi:10.1111/acem.13502.
- Koller G, Schwarzer A, Halfter K, Soyka M. Pain management in opioid maintenance treatment. *Expert Opin Pharmacother*. 2019;20(16):1993-2005. doi:10.1080/14656566.2019.1652270.
- Krebs EE, Gravely A, Nugent S, et al. Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain. *JAMA*. 2018;319(9):872–11. doi:10.1001/jama.2018.0899.
- Scott G, Gong J, Kirkpatrick C, Jones P. Systematic review and meta-analysis of oral paracetamol versuscombination oral analgesics for acute musculoskeletal injuries. *Emerg Med Australas*. 2020;33(1):107-113. doi:10.1111/1742-6723.13596.
- Tucker H-R, Scaff K, McCloud T, et al. Harms and benefits of opioids for management of non-surgical acute and chronic low back pain: a systematic review. *Br J Sports Med*. 2020;54(11):664-664. doi:10.1136/bjsports-2018-099805.
- Veazie S, Mackey K, Peterson K, Bourne D. Managing Acute Pain in Patients Taking Medication for Opioid Use Disorder: a Rapid Review. September 2020;1-9. doi:10.1007/s11606-020-06256-5.
- Voon P, Callon C, Nguyen P, Dobrer S, Montaner J, Wood E., Kerr T. Self-management of pain among people who inject drugs in Vancouver. *Pain Management*. 2014;4(1):27–35. http://doi.org/10.2217/pmt.13.62
- Wachholtz, A., & Gonzalez, G. Co-morbid pain and opioid addiction: Long term effect of opioid maintenance on acute pain. *Drug and Alcohol Dependence*. 2014;145:143–149. http://doi.org/10.1016/j.drugalcdep.2014.10.010
- Wardhan R, Chelly J. Recent advances in acute pain management: understanding the mechanisms of acute pain, the prescription of opioids, and the role of multimodal pain therapy. *F1000Res*. 2017;6:2065–10. doi:10.12688/f1000research.12286.1
- Warner NS, Warner MA, Cunningham JL, Gazelka HM, Hooten WM, Kolla BP, Warner DO. A Practical Approach for the Management of the Mixed Opioid Agonist-Antagonist Buprenorphine During Acute Pain and Surgery. Mayo Clin Proc. 2020 Jun;95(6):1253-1267. doi: 10.1016/j.mayocp.2019.10.007. Epub 2020 Feb 13. PMID: 32061413.
- Zeballos JL, Lirk P, Rathmell JP. Low-Dose Ketamine for Acute Pain Management. *Regional Anesthesia and Pain Medicine*. 2018;43(5):453-455. doi:10.1097/AAP.0000000000000810


BRITISH COLUMBIA CENTRE ON
SUBSTANCE USE
400-1045 Howe St
Vancouver BC
V6Z 2A9
www.bccsu.ca
CRISM
Research Institute
Providence
stpauls
FOUNDATION