BRITISH COLUMBIA CENTRE ON SUBSTANCE USE

Networking researchers, educators & care providers

Clinical Management of Medetomidine-related Presentations

Expanded Slide Deck

May 13, 2026

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Land Acknowledgement

The BCCSU respectfully acknowledges that the BCCSU office is situated on the traditional, unceded homelands of the xʷməθkwəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and səl̓ílwətaɬ (Tsleil-Waututh) Nations.

We recognize that the ongoing criminalization, institutionalization, and discrimination against people who use drugs disproportionately harm Indigenous Peoples, and that continuous efforts are needed to dismantle colonial systems of oppression. We see our work connected to these efforts and hope that this work today contributes to a system that provides safe, respectful, evidence-based care for all people.

Disclosures and Disclaimers

Mitigating Potential Bias

- All content developed as part of this session was reviewed for potential bias by the BCCSU.

Disclaimers

- This slide deck is not a substitute for the professional judgment of a health care professional and is not provincial clinical guidance. Health care professionals must take into consideration the circumstances of the patient and all applicable laws, regulations, and standards, including those set by relevant governing bodies. The BCCSU make no representation or warranty, and assumes no liability, for the contents of this document.
- This content is based in available published evidence in addition to clinical experience from addiction medicine clinicians in Philadelphia, Pennsylvania – as noted in the BCCSU webinar recording ("Clinical Management of Medetomidine-related Presentations") from May 11, 2026.
- The May 11 webinar recording contains case study and Q&A discussion that is not reflected in this slide deck.

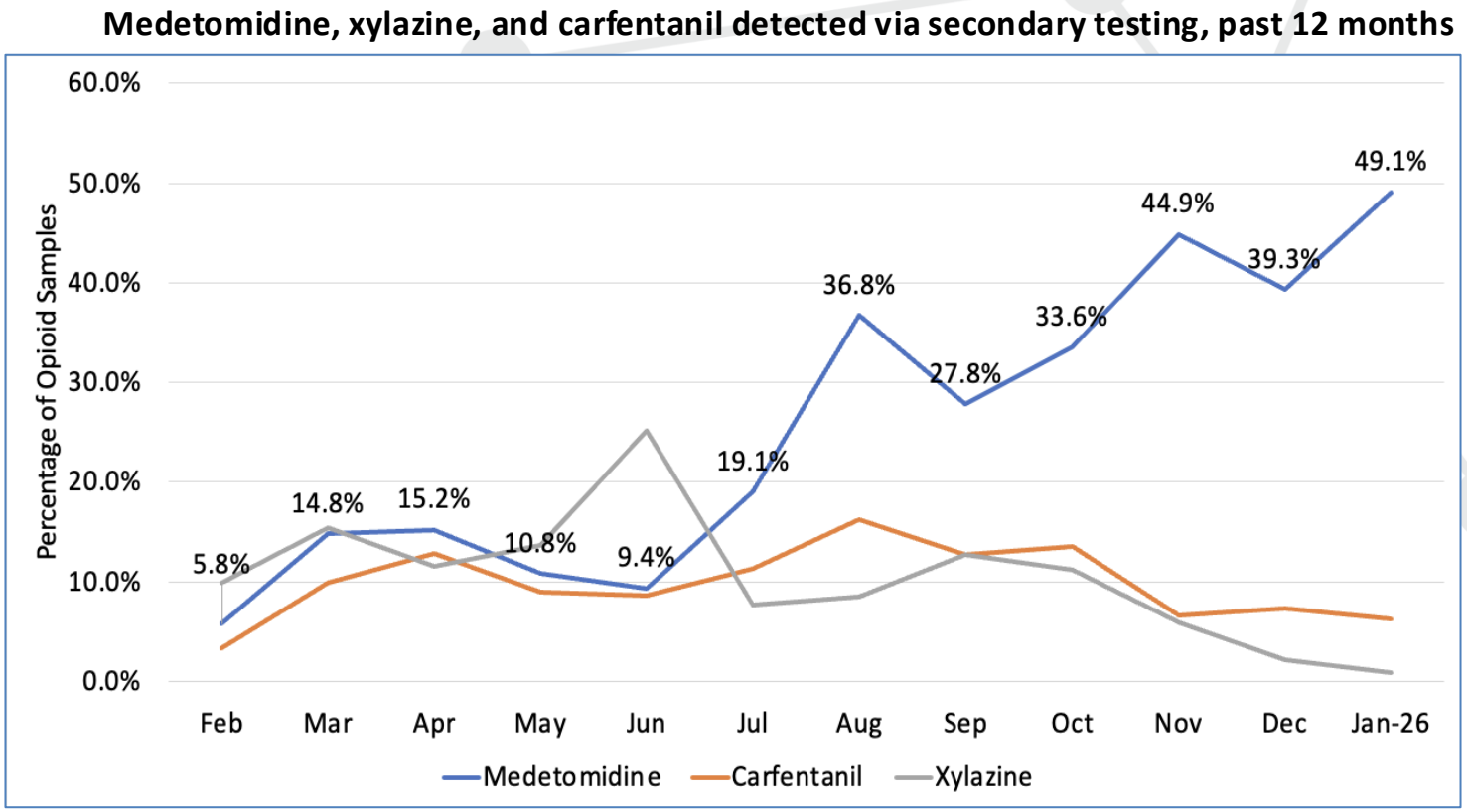
Overview

1. Medetomidine Pharmacology
2. Provincial & National Epidemiological Data
3. Medetomidine Effects
4. Managing Medetomidine-opioid Poisonings
5. Medetomidine Withdrawal & Management
6. Clinical Pearls

Medetomidine Pharmacology[1]

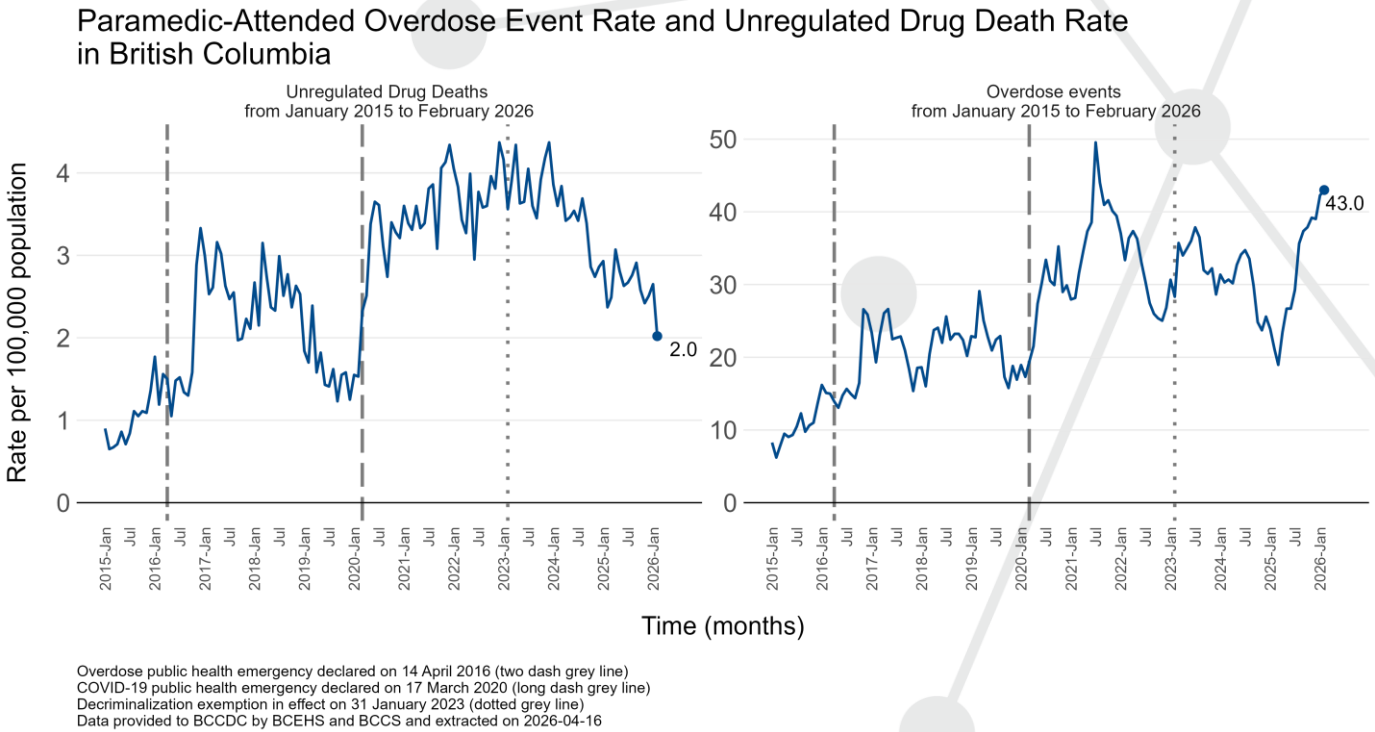
- Alpha-2 adrenergic agonist
- Approved for use in veterinary medicine for sedation and analgesia
- Racemic mixture with dexmedetomidine as the primary active enantiomer
- **Sympatholytic**: decreases norepinephrine, HR, BP
  - While biphasic cardiovascular impact can occur (initial HTN followed by hypotension & bradycardia), initial HTN rarely seen
    - May be influenced by co-occurring substance use
- **Very limited empirical data** on pharmacokinetics & -dynamics in humans and even more limited application to inhalation contexts

BC Drug Checking Trends[2]



- Increase in drug poisonings in Fall 2025, thought to be associated with an increase in medetomidine
- Medetomidine detected in samples with fentanyl, other opioids, xylazine, or benzodiazepines

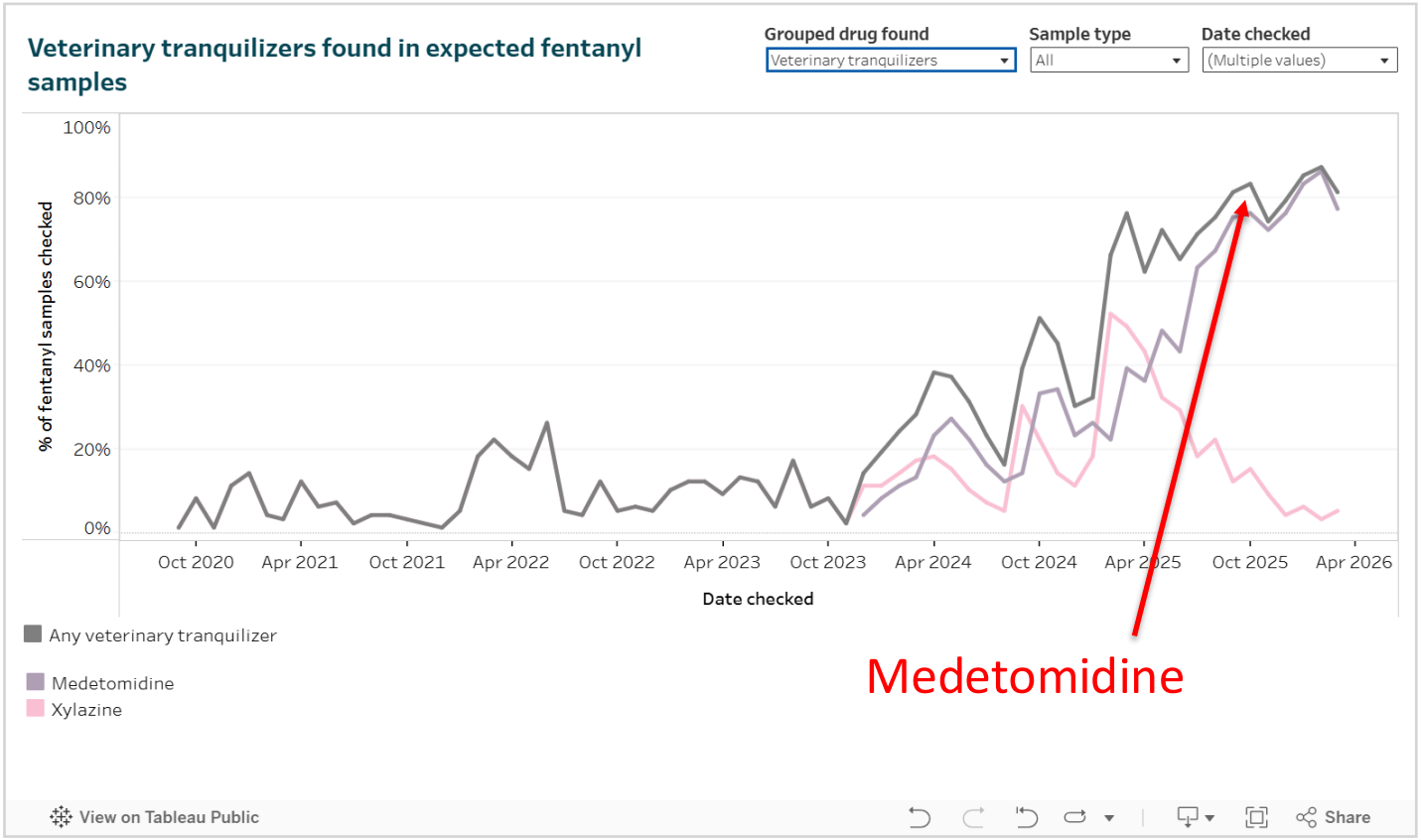
Paramedic-attended Opioid Overdoses in BC[3]



- In May 2025, BC started to see an increase in opioid overdoses attended by paramedics, which continued through the fall
- January, February, and March 2026 all had the highest one day totals ever for 911 calls related to drug poisonings

Other Provinces[4,5]

Toronto Drug Checking



- Most other Canadian provinces are also seeing substantial increases in medetomidine
- There was a 230% increase in law enforcement seized samples of medetomidine nationally in 2025 compared to 2024

Medetomidine Effects[2,6,7]

In BC, medetomidine is **almost always detected with other unregulated opioids, which may modify opioid-induced respiratory depression with additional sedation**

Bradycardia (severe)

Hypotension Can be initial brief HTN followed quickly by hypotension

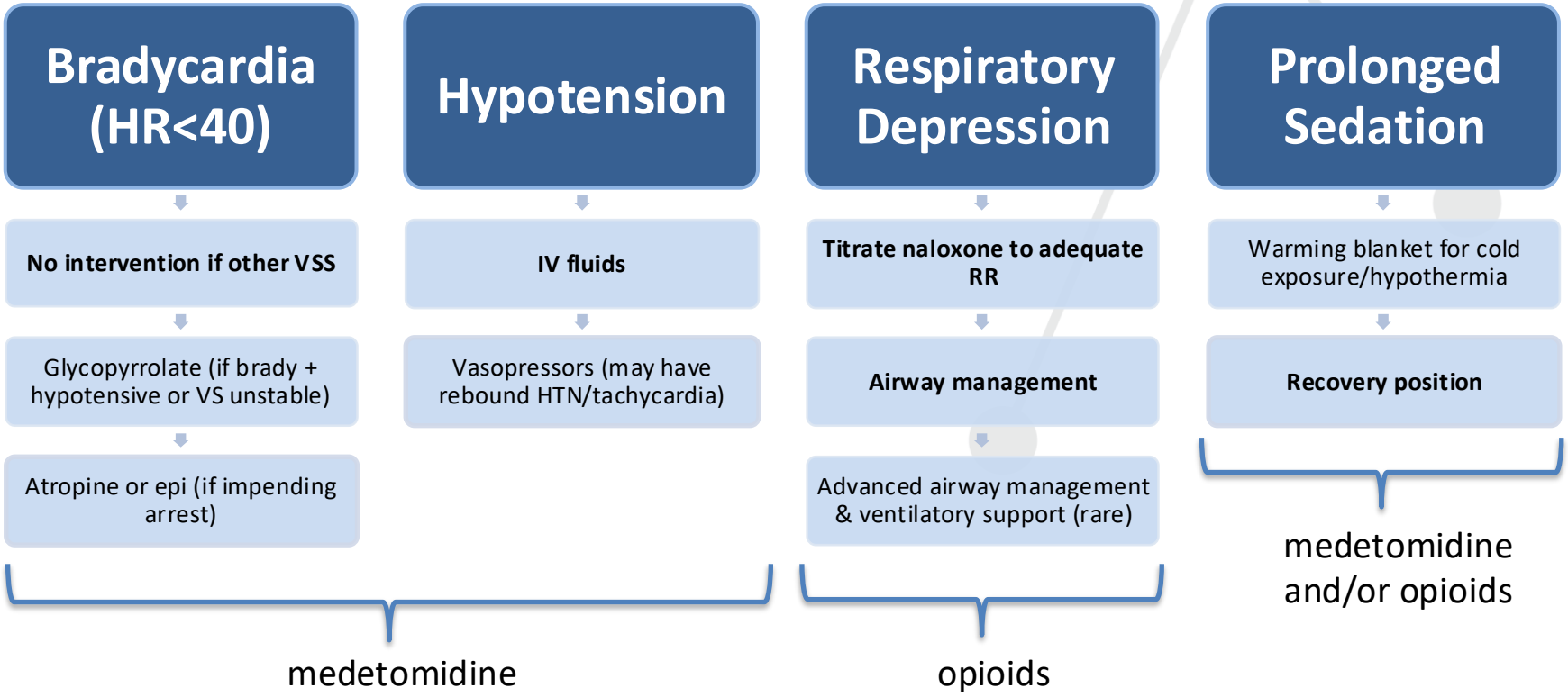
Prolonged sedation (non-responsive to naloxone)

- Effects can last from **90 minutes to several hours or longer**
- **Bradycardia ~3-9 hours** (despite being normotensive)

- **Not detected in routine panels**, toxicology screens, or UDS
- **Syndromic recognition**

Medetomidine-Opioid Poisonings[6-9]

No reversal agent for medetomidine approved for use in humans
Approach should be **led by clinical presentation and severity of symptoms**



Medetomidine Withdrawal[10-12]

Dependence may develop quickly

- Timing unclear given **lack of empirical evidence**
- **Likely varies based on intensity of use**

Rapid transition from intoxication to withdrawal (6-12 hours)

- Withdrawal **symptoms worsen over time**

Sudden discontinuation of medetomidine-adulterated opioids may lead to **severe withdrawal symptoms**

- May be **complicated by benzo withdrawal**

Medetomidine-opioid Withdrawal Syndrome[13]

Hallmark Features

- **Tachycardia** (e.g., 145bpm)
- **Profound hypertension** (e.g., 195/120)
- **Vomiting**
  - Often severe, non-responsive
  - More pronounced than with fentanyl withdrawal
  - Often coincides with rising HR & BP

Common Features

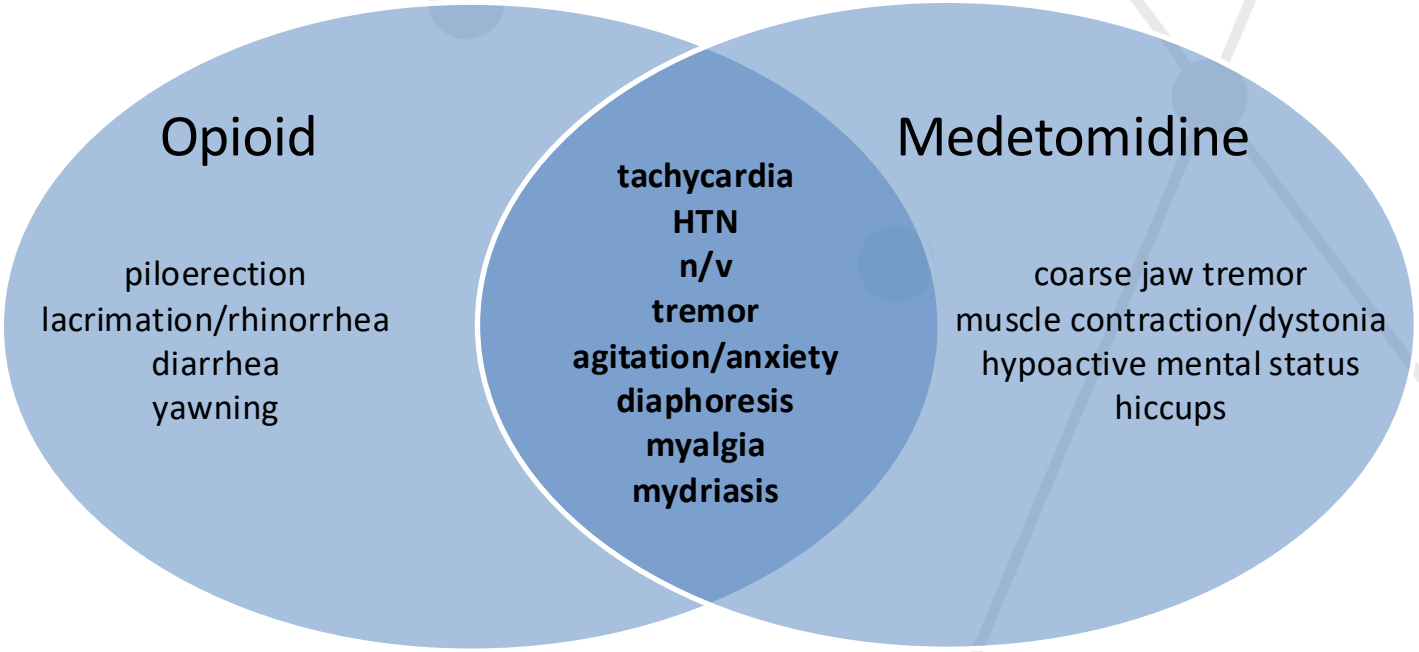
- **Disordered movements**
  - Hypokinesis
  - Myoclonus
  - Dystonia/dystonic posturing
  - Athetosis
- Coarse tremor (jaw)
- Features of typical opioid withdrawal, where:
  - COWS score may be diminished by hypokinesis/mutism
  - Can appear obstructionist, but actually unable to talk or move
- Hypoactive delirium/encephalopathy (severe cases)

Possible Features

- Mutism
- "pseudo-catatonia"
- Hyperthermia
- Hiccups
- Seizures (rare)
- "Brain zaps"
- Severe cravings
- Urinary retention
- Cardiomyopathy
- Demand NSTEMI
- PRES

Suspect medetomidine withdrawal if hallmark features are present *and m*arked sympathetic hyperactivity doesn't respond to benzodiazepines or phenobarbital

Comparing Opioid and Medetomidine Withdrawal Signs



- **Rapid onset of medetomidine withdrawal signs** as compared to a more gradual onset for opioid withdrawal
- **Rapid deterioration with medetomidine withdrawal** as compared to response to full opioid agonists for opioid withdrawal
- Medetomidine withdrawal symptoms precede severe opioid withdrawal; patients remains at **risk for precipitated withdrawal** despite significantly elevated COWS score

Medetomidine-Opioid Withdrawal Management: Pharmacotherapy[13-16]

Opioid Withdrawal	• Short and long-acting opioids (e.g., OAT) • Clonidine
Benzo Withdrawal	• Benzo taper • Phenobarbital
Medetomidine Withdrawal	• Clonidine • Dexmedetomidine • Other a2 agonists (e.g., tizanidine, guanfacine)
Vomiting	• Fast-acting PO (if tolerated) • Olanzapine (5-10mg IV) • Prochlorperazine (10mg IV) • Droperidol (2.5mg-5mg IV)
Hypertension	• Easily titratable IV agents such as esmolol, labetalol, or hydralazine

Managing Opioid Withdrawal[16]

Prioritize opioid withdrawal management

- Manage/prevent opioid withdrawal
- **Prevent self-initiated discharge** and return to unregulated opioid use

Full agonists preferred

- **Long-acting**: PO methadone/SROM or hydromorphone IV
- **Short-acting**: Oxycodone IR or Hydromorphone IV

Goal: COWS ≤ 5

- Titrate opioids to COWS score

Use alongside

- **Alpha-2 agonists (e.g., clonidine)**
- **Supportive care** (for sedation, cardiovascular effects, withdrawal)

Caution

- **Risk of precipitated withdrawal** despite significantly elevated COWS score
- **Monitor for prolonged QTc** (Hodges formula)

Medetomidine Withdrawal Management: Clonidine[13,14,16-18]

Demonstrated efficacy in managing medetomidine withdrawal

- Once stabilized following dexmedetomidine or in lieu of if not available

Dosing

- **If HR & BP reasonably controlled and no vomiting, consider** aggressively treating with **PO** (0.4-0.6mg q6h)
  - Limited success >0.8mg
- **Dynamic dosing for first 24h tailored to clinical presentation and SBP**
- **Taper off** by 0.1mg every 1-2 days based on VS
  - Consider discharge when at 0.3mg q8h

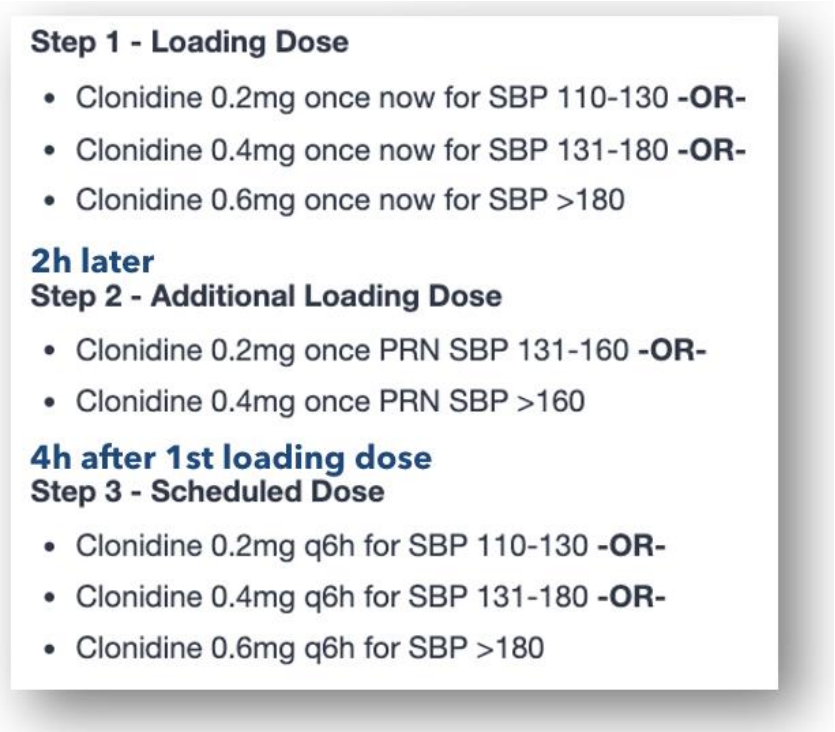
Caution

- If a2 agonist-naïve or concern for hypotension, try test dose first or lower dose with more frequent monitoring (e.g., q2-3h)
- May need a long outpatient taper (several weeks) with close VS follow-up

Sample Clonidine Dosing Protocol

Clonidine Loading Dose Protocol from the University of Pennsylvania Health System Philadelphia Hospitals, where:

- Medetomidine prevalence in local fentanyl supply is >80%, *and*
- Average medetomidine concentration is >10%



Step 1 - Loading Dose

- Clonidine 0.2mg once now for SBP 110-130 **-OR-**
- Clonidine 0.4mg once now for SBP 131-180 **-OR-**
- Clonidine 0.6mg once now for SBP >180

2h later
Step 2 - Additional Loading Dose

- Clonidine 0.2mg once PRN SBP 131-160 **-OR-**
- Clonidine 0.4mg once PRN SBP >160

4h after 1st loading dose
Step 3 - Scheduled Dose

- Clonidine 0.2mg q6h for SBP 110-130 **-OR-**
- Clonidine 0.4mg q6h for SBP 131-180 **-OR-**
- Clonidine 0.6mg q6h for SBP >180

✓

Loading dose protocol **takes advantage of clonidine pharmacokinetics to minimize toxicity risk** (e.g., hypotension in overtreatment)

!

Adapt dosing amounts and SBP parameters to local unregulated drug supply

Medetomidine Withdrawal Management: Dexmedetomidine[16,18]

Approved for ICU and perioperative settings

- May require transfer to ICU (if only approved for use in ICU settings)
- Some hospitals approved for use in ED settings

Most effective option for stabilizing severe medetomidine withdrawal

- **Use with cardiac monitoring**
- Once stabilized (~24-48hrs), use clonidine and other management strategies

Contraindications

- HR < 50bpm
- MAP < 65mmHg
- Second/third degree heart block
- Consider guanfacine or tizanidine if contraindicated

Dexmedetomidine: Sample Titration

START: 0.5mcg/kg/hr IV

TITRATE: +0.4 mcg/kg/hr q20 min to 1.5mcg/kg/hr

- **Titrate based on clinical effect** up to max 2.5 mcg/kg/hr

TARGET: SBP <180 mmHg

CONSIDER: clinical triggers for bolus (0.5mcg-1mcg/kg IV)

- Increased HR by >20% or >120bpm
- Increased SBP by >20% or >180mmHg
- Persistent vomiting, tremor, or minimal response to infusion

Withdrawal Management: Antiemetics[16]

Preferred (dopamine antagonists)

- **Olanzapine** (5-10mg IV)
  - Preferential in early treatment due to less QT prolongation
- **Prochlorperazine** (10mg IV)
  - Can be given IM, but IV preferred due to injection pain

Other options

- Droperidol (2.5mg-5mg IV/IM)

Caution

- **QT prolongation risk** (for all)
  - Less impact with olanzapine; greater risk with prochlorperazine

Withdrawal Management: Antihypertensives[16,19]

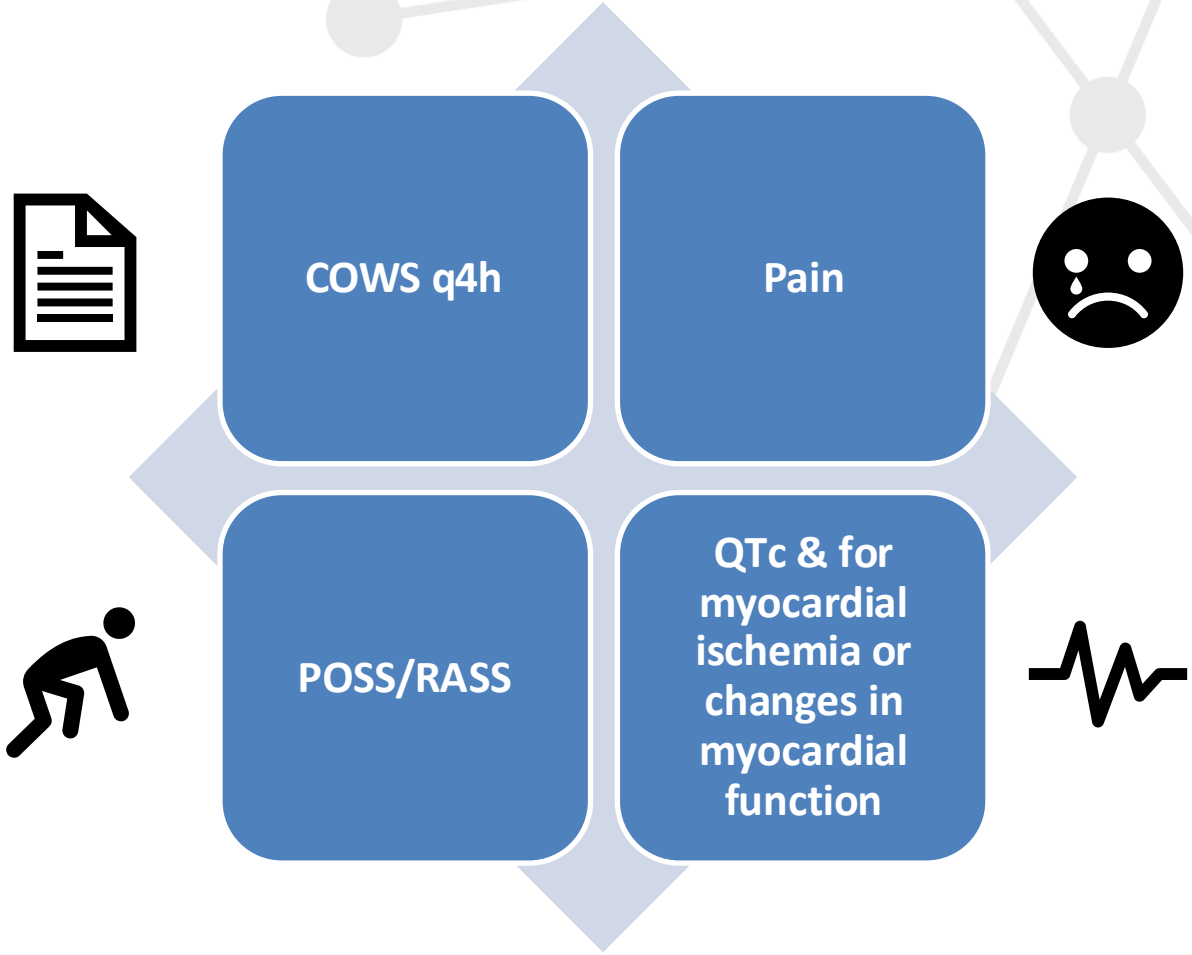
For persistent, severe HTN

- Treat with **short-acting, titratable antihypertensives** as per protocol for management of hypertensive emergency
  - **If highly suspicious of medetomidine withdrawal, do not wait to treat**: HTN and tachycardic emergency is inevitable with severe medetomidine withdrawal

Consider

- **Whole clinical picture**:
  - Whether max a2 agonist therapy reached (e.g., max dexmed dose)
  - Withdrawal symptoms outside of HTN are well controlled
- PO agents for patients tolerating PO medications (e.g., captopril)
  - **Short-acting CCB (e.g., nifedipine) not recommended** due to unpredictable response and higher mortality in HTN emergency
- If not tolerating PO: Easily titratable IV agents such as nicardipine, esmolol, labetalol, or hydralazine
- Co-use of methamphetamines
  - HTN/tachycardia syndrome may behave differently

Clinical Monitoring[16]



Systems Impacts: Philadelphia Experiences

ICU beds utilized for dexmed infusion for medetomidine withdrawal	Less capacity to accommodate non-withdrawal, critically-ill patients	Critically-ill patients transferred out
WDM facilities ill-equipped to respond to medetomidine withdrawal	Patients in medetomidine withdrawal transferred to ED	Less capacity in ED for non-withdrawal, emergency care; longer ED wait times; lost to care during transfer
Long outpatient clonidine tapers upon discharge to community	Community providers unprepared for related follow-up and monitoring requirements	Hypotension if not monitored (rare); lost to care +/- return to use; return to acute care with HTN

Clinical Pearls

Vomiting Signal	**Severe, non-responsive vomiting is hallmark sign of medetomidine withdrawal**; **can indicate escalating withdrawal** and need for alternative level of care (e.g., ICU with dexmed infusion)
Role of Naloxone	Still required to reverse opioid poisoning; **titrate to RR** (not wakefulness); **avoid excessive doses** due to precipitated withdrawal risk and associated patient trauma
Assess for Other Substances	**Unregulated opioid supply can often have benzos *and* medetomidine** plus opioids; benzo withdrawal & stimulant intoxication can further complicate clinical picture

Clinical Pearls

Clonidine Tolerability	Person not exposed to a2 agonists can become hypotensive with higher doses of clonidine (e.g., 0.3mg); **consider lower dose and redose q2-3h if unsure**
ICU Admission	Recommended for persistent HTN (**SBP>180**) *or* tachy (**HR>120**) *or* signs of end organ dysfunction *after* opioid agonists for WD *and* max tolerated PO *and* antiemetics; consider with PO intolerability and risk of losing airway (e.g., severe vomiting and sedation)
Monitor Myocardial Function	**Myocardial injury possible**; monitor for ischemia or changes to myocardial function

Clinical Pearls

Using Assessment Tools	**Hypoactive mental status** from medetomidine withdrawal **can complicate POSS/RASS assessments**; overlapping symptoms can impede accurate assessment (e.g., CIWA-B)
Plan for Discharge Management	Clonidine tapers can require weeks to months of close vital signs monitoring
Maintain Compassionate Care	The severity of medetomidine withdrawal can be very scary for patients, on top of fears of inadequate treatment and stigmatizing interactions; support continued engagement in care with compassionate treatment

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