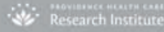
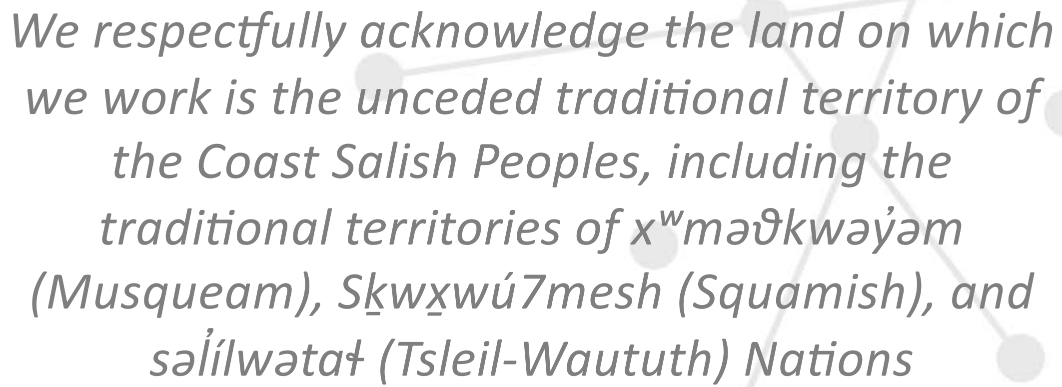
BRITISH COLUMBIA
CENTRE ON
SUBSTANCE USE
Networking researchers, educators & care providers

Overview of Slow-Release Oral Morphine (SROM)




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 (Musquem), Sḵwx̱wú7mesh (Squamish), and səl̓ílwətaɬ (Tsleil-Waututh) Nations

Outline

1. Slow-release oral morphine—the basics
   – Review of the evidence
   – Pharmacologic properties
   – Side effects
   – Prescribing: initiation, titration and missed doses
2. Emergency department presentations
   – Missed doses
   – Toxicity
   – Withdrawal

Slow-release Oral Morphine—The Basics

Review of the Evidence

- Slow-release oral morphine (SROM) has been shown to have a similar effectiveness at treating OUD as methadone
  - ↓ Opioid use
  - ↑ Retention in treatment
- Slow-release oral morphine may have additional benefits compared to methadone:
  - ↓ Cravings
  - Does not prolong QTc
  - Improved mood

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- The evidence thus far shows SROM as being non inferior to methadone, but there are several limitations.
  - The overall quality of the evidence remains low (small, unblinded trials of limited duration).
  - There is much less published data compared to the body of evidence supporting methadone.

1. Klimas J, Gorfinkel L, Giacomuzzi SM, Ruckes C, Socías ME, Fairbairn N, et al. Slow release oral morphine versus methadone for the treatment of opioid use disorder. Bmj Open. 2019;9(4):e025799.
2. Ferri M, Minozzi S, Bo A, Amato L. Slow-release oral morphine as maintenance therapy for opioid dependence. Cochrane Db Syst Rev. 2013;6(6):CD009879.
3. British Columbia Centre on Substance Use and B.C. Ministry of Health. A Guideline for the Clinical Management of Opioid Use Disorder. Published June 5, 2017. Available at: http://www.bccsu.ca/care-guidance-publications/
4. British Columbia Centre on Substance Use. Opioid use Disorder Practice Update. Published January 2022. Available at: https://www.bccsu.ca/covid-19/

SROM—Who?

- SROM is considered third line medication for OUD
  - Considered for patients who did not experience benefit, refused or have contraindications to first (buprenorphine/naloxone) and second line (methadone) therapy
- SROM should only be prescribed by those with clinical expertise

Pharmacologic Properties

- Long-acting medication through sustained release of immediate release opioid:
  - Slow release of morphine from polymer beads
  - Need intact gut and not to crush/alter beads
- Peak: 8.5-10 Hours
- Duration: 24+ hours in adequate doses
- Metabolism: liver
- Clearance: renal

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- Some sources reported peak effect being as short as 6-8 hours.
  - Current BCCSU guidelines state peak effect to be at 8.5-10 hours.

Side Effects

SROM has been associated with:

- ↑ rates of overdose/sedation in combination with sedatives (and other sedating medications)
- Constipation
- Abdominal discomfort/cramps
- Early studies indicate that SROM may be associated with ↑ rates of insomnia/fatigue

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- Most of the side effects listed are ***common to all forms of opioid agonist therapy***

Prescribing

	(1) Literature	(2) Standard Practice *High fentanyl use
Initiation	30–60mg	200mg
Titration	Q2days 30–60mg	Q1-2day 100mg
Stabilization	~ 300–800mg	>1000mg

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- Above prescribing protocol examples are based on the 2017 OUD guidelines from the BCCSU (1) and the BCCSU January 2022 practice update (2).
- SROM is prescribed as once daily dosing and daily witnessed ingestion in pharmacies
- The literature has typically studied lower doses for initiation and titration, and that was reflected in the previous 2017 BCCSU guidelines.
- In practice, with the increased use of fentanyl and individuals with high opioid tolerance, higher doses are often needed to achieve clinical effect.
- Highest prescribed dose in literature to date is 1200mg. However, clinical experiences has shown patients often require higher doses to manage symptoms (cravings and withdrawal) due to high tolerance from fentanyl.

1. British Columbia Centre on Substance Use and B.C. Ministry of Health. A Guideline for the Clinical Management of Opioid Use Disorder. Published June 5, 2017. Available at: http://www.bccsu.ca/care-guidance-publications/
2. British Columbia Centre on Substance Use. Opioid use Disorder Practice Update. Published January 2022. Available at: https://www.bccsu.ca/covid-19/

Prescribing—Missed doses

Missed doses (consecutive days)	Dose Reduction
0–1 day	No Change
2 days	40% reduction
3 days	60% reduction
4 days	80% reduction
5+ days	Restart

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- This table shows the reduction in dose that is required based on the number of consecutive days that a dose has been missed

Prescribing

- Typically prescribed as daily witnessed ingestion (DWI) in pharmacies
- Pre-COVID: capsules sprinkled (to reduce risk of diversion)
  - Requirement removed during COVID to minimize contact time in pharmacies
- Compared to methadone, SROM is not as widely prescribed or available in pharmacies
- There have been drug shortages in the past

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- Some patients may have carry doses in context of high clinical stability or have limitations in travelling to a pharmacy daily, such as rural areas.

2. . Emergency Department Presentations

Missed Doses

- CAEP position statement recommended that administration of missed doses of OAT in the ED should be provided to support continuation of care
- This should be considered in patients who:
  - Have prolonged stay in the ED
  - Missed doses due to pharmacy closure

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Koh, J. J. *et al.* CAEP Position Statement: Emergency department management of people with opioid use disorder. *Cjem* **22**, 768–771 (2020).

SROM Provision in the ED

- Doses provided in acute care do not appear on PharmaNet
  - Risk of double dosing if usual pharmacy not informed
  - Doses is marked as "missed" and may lead to dose reductions
- Prior to providing SROM, ensure the patient has appropriate tolerance
  - Acute medical illness (sedation, respiratory illness, sepsis, liver dysfunction)
  - Renal impairment

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- PharmaNet is a province wide, central data system where any prescription dispensed in a community pharmacy will be entered. Healthcare providers can access this data system to review medication history and confirm any missed doses for opioid agonist therapy such as methadone.
  - Its validity is contingent of the pharmacist or a delegate entering the information.
  - Other jurisdictions may have similar regional pharmacy databases, and the approach would remain the same for providers.

SROM Provision in the ED

- When providing a dose of SROM in the ED:
  - Follow your hospital protocol
  - Confirm the patient's usual pharmacy
    - Notify of dose provided in the ED
  - Review PharmaNet for last 7 days to assess the appropriate dose
    - Check for missed doses and daily amount
  - Ensure that the order specifies to "open capsules and sprinkle"

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PharmaNet Refills for DIN 00843512

Patient: Clowes, Sophia D | Female | DOB: 10-Mar-1972 | PHN: 9015894292

Fill Date	Status	Doctor	Qty	Drug	DIN	Manufacturer	Local	Directions
20-Apr-2015	Filled	Cullen	5.0	**Yohimbine Hcl 6 MG Tablet**	**00843512**	Rougier Pharma	Yes	TAKE 1 TABLET ONCE A DAY
02-Mar-2015	Filled	Cullen	5.0	**Yohimbine Hcl 6 MG Tablet**	**00843512**	Rougier Pharma	Yes	TAKE 1 TABLET ONCE A DAY
07-May-2014	Filled	Cullen	5.0	**Yohimbine Hcl 6 MG Tablet**	**00843512**	Rougier Pharma	Yes	TAKE 1 TABLET ONCE A DAY
07-May-2014	Not Filled	Cullen	5.0	**Yohimbine Hcl 6 MG Tablet**	**00843512**	Rougier Pharma	Yes	TAKE 1 TABLET ONCE A DAY
07-May-2014	Reversed	Cullen	5.0	**Yohimbine Hcl 6 MG Tablet**	**00843512**	Rougier Pharma	Yes	TAKE 1 TABLET ONCE A DAY
05-May-2014	Filled	Cullen						

Detail | Close

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- This is a photo of how the doses will show in PharmaNet.
- For medications that are daily witnessed ingestions, each dose administered will be a separate entry
- Missed doses will be documented as either “reversed” or as lack of any entry for that day.

Transition of Care

- Review harm reduction and safer use with the patient
  - Provide the patient with a THN kit
- Provide information about OAT clinics or low barrier clinics if patient not already connected to care
- Forward a note to the patient’s usual provider about the dose received in the ED

SROM Initiation (1)

Must refer to provider with expertise

- Initiating SROM requires:
  - Completion of POATSP
  - Prescription on harmonized prescription pad
  - More detailed assessment to candidacy of treatment, such as reviewing risk and benefit of initiation of therapy

- POATSP (Provincial Opioid Addiction Treatment Support Program) is a comprehensive education and training program from the BCCSU (BC Centre on Substance Use) that provides the tools for providers in BC to prescribe oral opioid agonist therapy (buprenorphine/naloxone, methadone, and slow-release oral morphine) and injectable opioid agonist therapy.
- There are similar programs available in each province, where ability to prescribe certain oral opioid agonist therapies is contingent on completing this training.
- Given this is considered to date a more specialized treatment option, a referral to or review with a provider with expertise is recommended.
  - This can be done in the ED or arranging for next day clinic follow up if available.

SROM Initiation (2)

- Assessment should include
  - Diagnosis of OUD
  - Determining tolerance and risk of opioid toxicity
  - Medication and co-morbidities review:
    - History of Renal impairment?
    - Concurrent sedative use (Alcohol/Benzo)?
    - Prior trials of OAT?
  - UDT recommended
- Consider barriers to continuation in community
  - Limited providers with capability to prescribe
  - Follow organizational referral pathways

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- Given this is considered to date a more specialized treatment option, a referral to or review with a provider with expertise is recommended.

Initiation—Special Scenario

- Consider initiation of SROM in high-risk patient where this might facilitate their stay
  - Prolonged stay in the ED or requiring admission
- It requires review with designated addiction specialist or a POATSP-trained provider
  - Contact addiction consult team or 24/7 Addiction Clinician Support Line
- Use PPO for safety and monitoring
- Follow your hospital or health authority protocol

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- There are similar programs available in each province, where ability to prescribe certain oral opioid agonist therapies is contingent on completing this training.
- 24/7 Addiction clinical support line provides telephone consultation around substance use care to health care providers (physicians, nurse practitioners, nurses, midwives and pharmacist) in British Columbia.

SROM Toxicity

- Toxicity may occur due to:
  - Changes in clearance (renal impairment eGFR <30)
  - Concurrent sedatives
  - Non-prescribed use (dissolving or crushing/chewing diverted pellets)
- Symptoms of SROM toxicity include:
  - Signs and symptoms of opioid poisoning
  - +/- Myoclonus
- Treatment should include:
  - Monitoring +/- naloxone infusion

- Naloxone infusion may be required due to the prolonged duration of action

SROM Withdrawal

- SROM has a late peak, which may be interpreted as a lack of effect by some patients
  - Take care to not interpret this as SROM withdrawal
- Withdrawal may be present at inadequate doses, especially when titrating or due to dose reduction from missed doses
- If opioid withdrawal present, consider treatment with IR opioids
  - Morphine preferred: morphine oral liquid 20-30mg po q2h PRN

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See withdrawal management module for further details

References

1. Klimas J, Gorfinkel L, Giacomuzzi SM, Ruckes C, Socías ME, Fairbairn N, et al. Slow release oral morphine versus methadone for the treatment of opioid use disorder. Bmj Open. 2019;9(4):e025799.
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4. British Columbia Centre on Substance Use. Opioid use Disorder Practice Update. Published January 2022. Available at: https://www.bccsu.ca/covid-19/
5. Koh JJ, Klaiman M, Miles I, Cook J, Kumar T, Sheikh H, Dong K, Orkin AM, Ali S, Shouldice E. CAEP Position Statement: Emergency department management of people with opioid use disorder. CJEM. 2020 Nov;22(6):768-771. doi: 10.1017/cem.2020.459. PMID: 33028446.

24/7 Addiction Medicine Clinician Support Line

Telephone consultation for physicians, nurse practitioners, nurses, mid-wives, and pharmacists providing addiction and substance use care.

Available 24/7, 365 days a year. More info at www.bccsu.ca/24-7.

CALL 778-945-7619

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- 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.

Provincial Opioid Addiction Treatment Support Program

Provincial Opioid Addiction Treatment Support Program

Online Course

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- 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.

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