Advances in the Management of Opioid Use Disorder

Katie Dunham, NP

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Disclosures

- The speaker has received honorarium for presentations on buprenorphine products through Indivior Pharmaceutical and Master Clinician Alliance.
- The speaker has been on an advisory board to Indivior Pharmaceutical on the topic of opioid use disorder.
- The speaker is an employee of Women's College Hospital and Nurse Educator for META:PHI, whose products will be discussed in this presentation.
- The speaker is a faculty of the University if Toronto, Bloomberg School of Nursing, for the course Mental Health and Addictions for Nurse Practitioners

- The speaker will work to highlight off-label discussion of treatments, and include brand and generic medication names throughout the presentation

Learning objectives

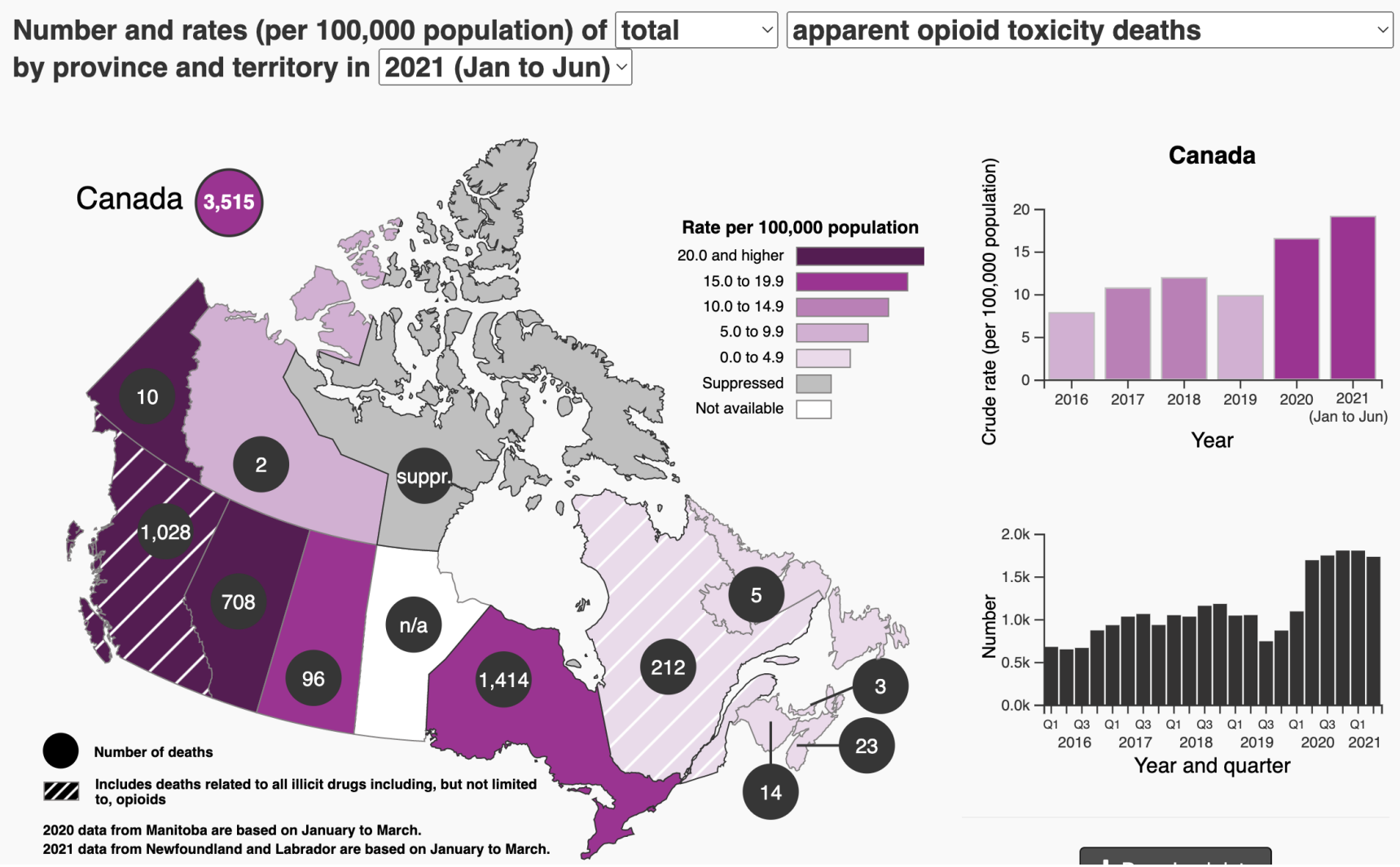
By the end of this session, the learner will be able to:

- Identify appropriate cases and protocols for macrodosing of buprenorphine, and quick starts of long-acting injectable buprenorphine.
- Determine the appropriate dose and titration rate for starting methadone alone, or in combination with SROM.
- Identify appropriate cases for OUD management with SROM as a stand-alone treatment option.

Agenda

- The state of OUD
- Physiology Review
- Quick-start buprenorphine
  - Macrodosing
  - Off-label long-acting injectable buprenorphine
- Methadone for people who use Fentanyl
  - Methadone + SROM
- Slow-release oral morphine (SROM)

The Opioid Epidemic in Canada



38, 514
apparent opioid toxicity deaths between January 2016
&
March 2023

Source: Public Health Agency of Canada https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/maps

The Opioid Epidemic in Canada

- Averaging **21** apparent opioid toxicity **deaths per day** so far in 2023

"Of all accidental opioid toxicity deaths so far in 2023 (January-March) **81% involved Fentanyl**"

- This is a 42% increase since 2016

Who?

– accidental opioid-related poisoning hospitalizations in Canada Jan-Mar 2023

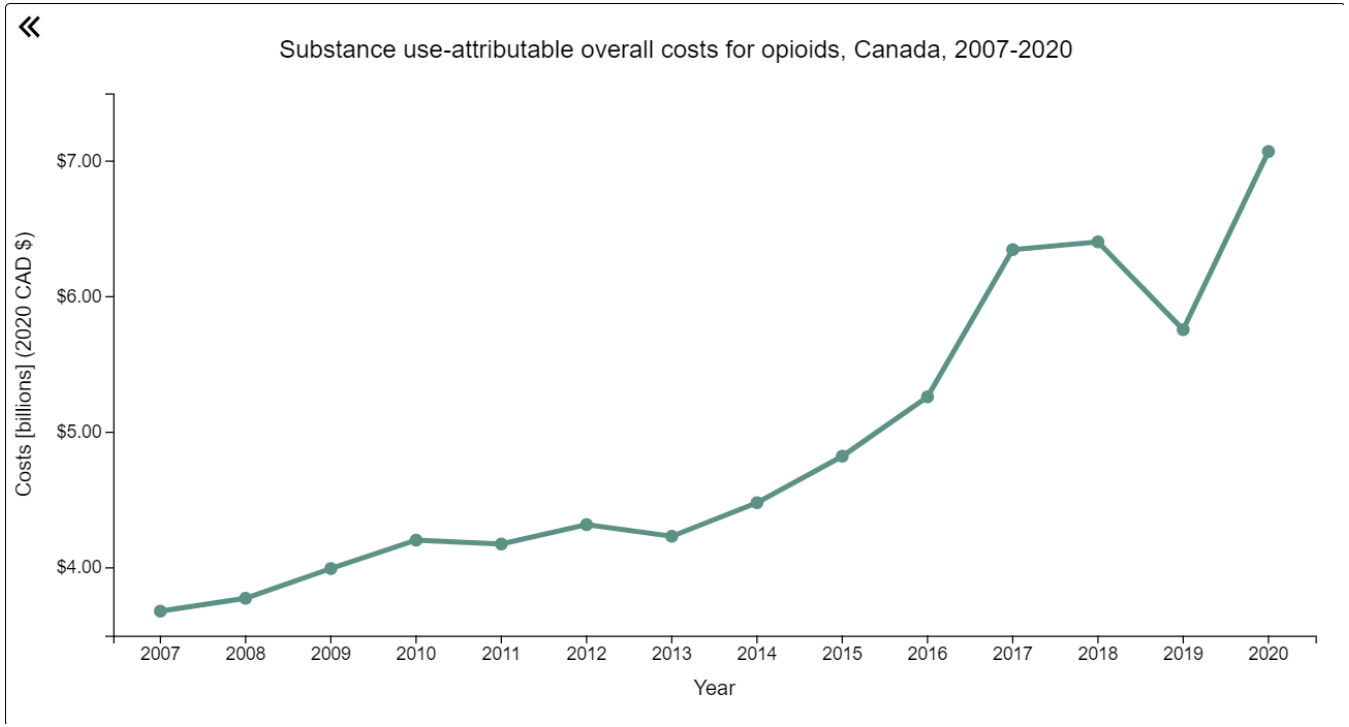
- 67% males
- 24% 30-39 years old
- 23% 60 years or more

Federal, provincial, and territorial Special Advisory Committee on the Epidemic of Opioid Overdoses. Opioid- and Stimulant-related Harms in Canada. Ottawa: Public Health Agency of Canada; September 2023. https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/

Cost

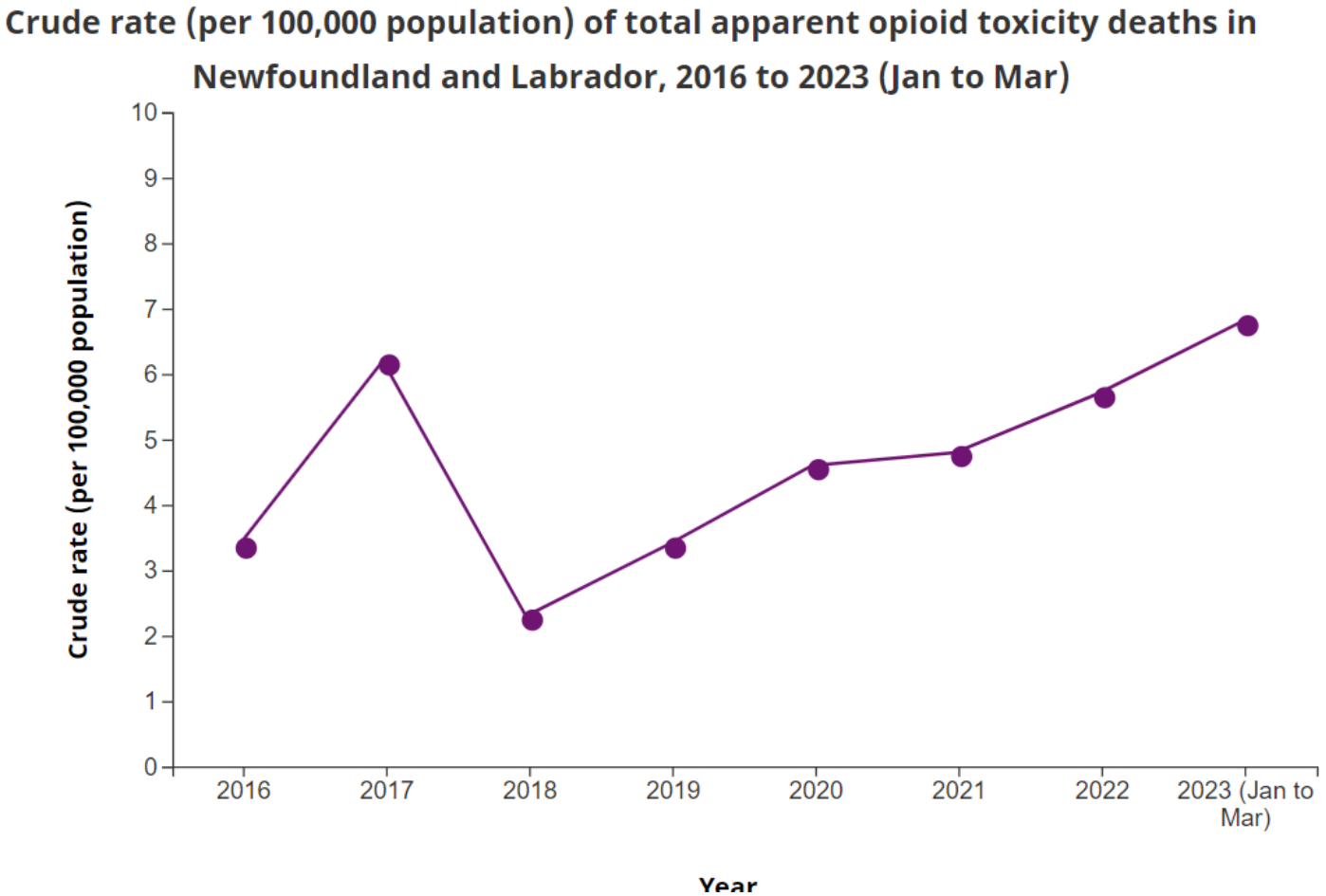
- There was a total of **37,697 opioid-related hospitalizations** from January 2016 to March 2023 in Canada (excluding Quebec)
- Average of **15 hospitalizations per day**
- Average length of stay was 3 days

$7.07 billion spent on opioid-related care in Canada in 2020



Canadian Substance Use Costs and Harms https://csuch.ca/explore-the-data/

The Opioid Epidemic in Newfoundland & Labrador



Source: Public Health Agency of Canada https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/maps

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Macrodosing

High-start buprenorphine starts

Microdosing

Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method

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Substance Abuse and Rehabilitation
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Number of times this article has been viewed

Robert Hämmig[1]
Antje Kemter[2]
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Barbara Gugger[1]
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Background: Buprenorphine is a partial μ-opioid receptor agonist used for maintenance treatment of opioid dependence. Because of the partial agonism and high receptor affinity, it may precipitate withdrawal symptoms during induction in persons on full μ-opioid receptor agonists. Therefore, current guidelines and drug labels recommend leaving a sufficient time period since the last full agonist use, waiting for clear and objective withdrawal symptoms, and reducing pre-existing full agonist therapies before administering buprenorphine. However, even with these precautions, for many patients the induction of buprenorphine is a difficult experience, due to withdrawal symptoms. Furthermore, tapering of the full agonist bears the risk of relapse to illicit opioid use.
Cases: We present two cases of successful initiation of buprenorphine treatment with the Bernese method, ie, gradual induction overlapping with full agonist use. The first patient began buprenorphine with overlapping street heroin use after repeatedly experiencing relapse, withdrawal, and trauma reactivation symptoms during conventional induction. The second patient was maintained on high doses of diacetylmorphine (ie, pharmaceutical heroin) and methadone during induction. Both patients tolerated the induction procedure well and reported only mild

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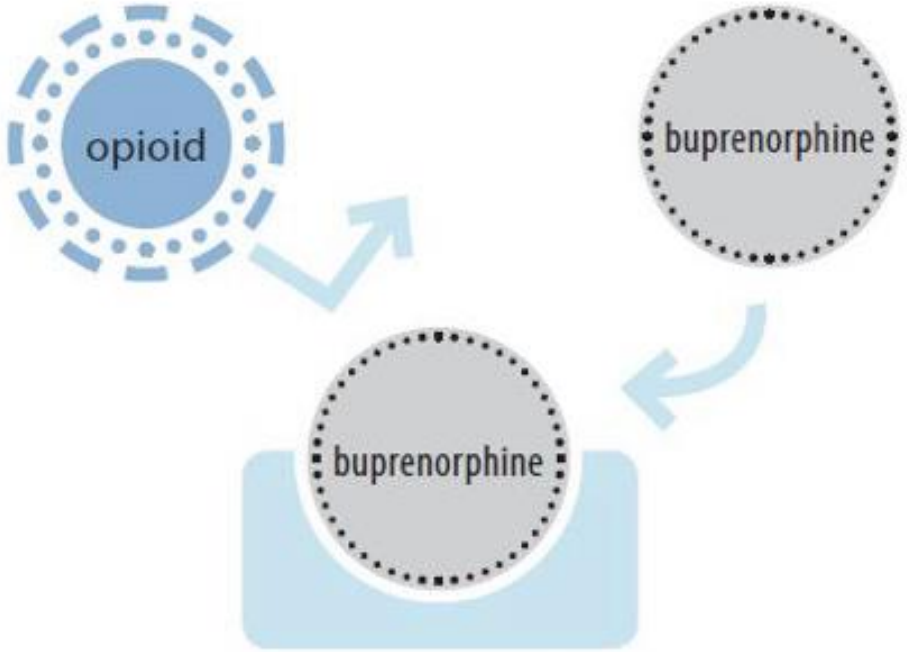
Mu Opioid Receptor Affinity

TABLE 1 Mu opioid receptor binding affinity

Drug	K_i (nM)
sufentanil	0.1380
buprenorphine	0.2157
hydromorphone	0.3654
morphine	1.168
fentanyl	1.346
methadone	3.378
oxycodone	25.87
codeine	734.2
tramadol	12,486

K_i denotes the binding affinity of opioid to mu opioid receptor. The smaller the K_i value, the stronger the binding affinity to receptor.

FIGURE 2 Mechanism of action of buprenorphine



buprenorphine has very high affinity for opioid receptors

Microdosing

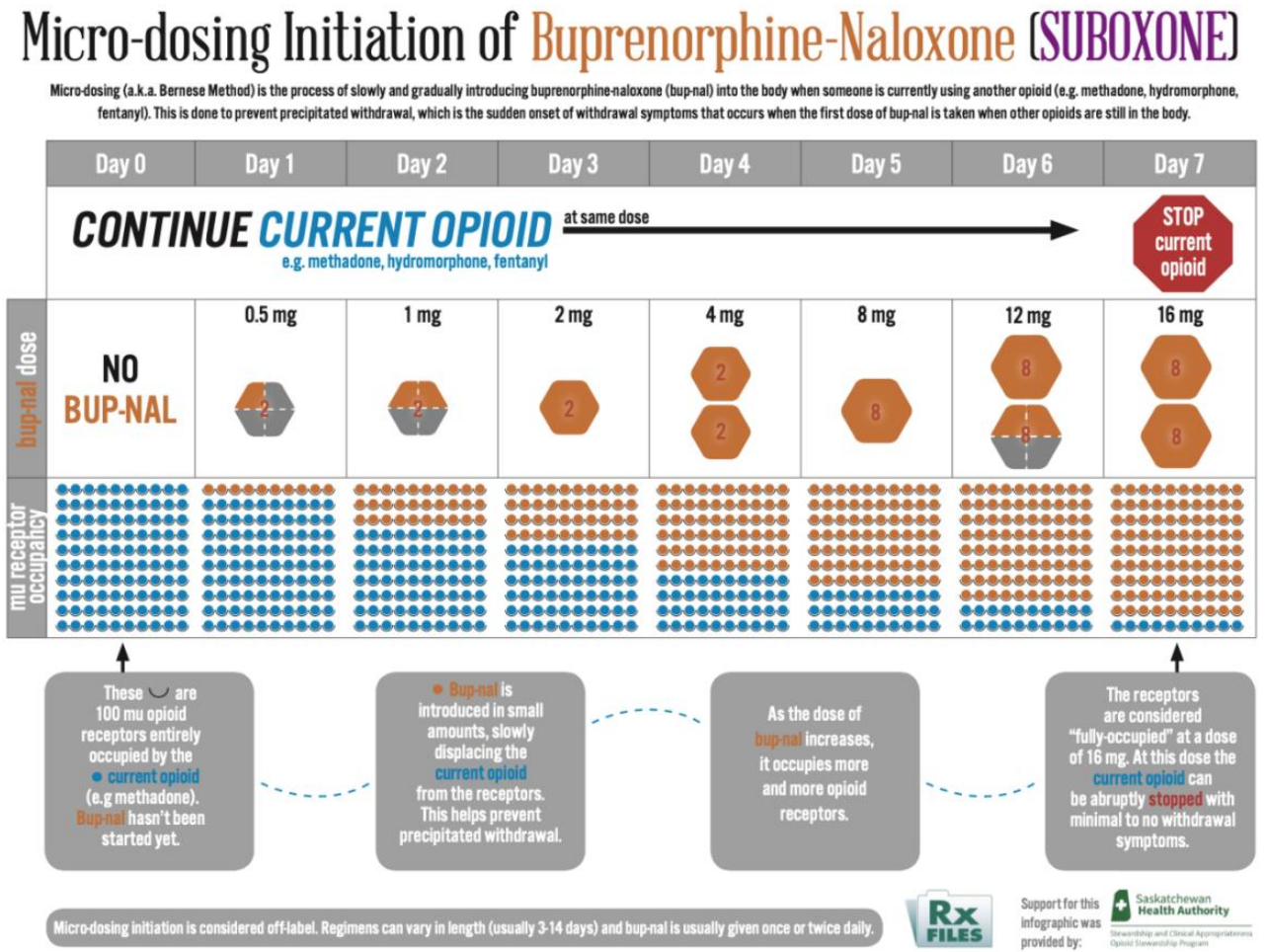


Image source: RxFiles Academic Detailing

Precipitated Withdrawal

There are no formal guidelines for the treatment of buprenorphine-precipitated withdrawal.

Recommendations are based on consensus and include the following options:

1) Non-agonist therapies, such as clonidine, ondansetron, and loperamide
2) Full-agonists, e.g. morphine
3) **High doses partial agonists, until full-agonist effects and withdrawal is relieved (e.g., 16-32mg)**

Macrodosing

Buprenorphine Macrodosing Initiation

Macrodosing is an alternative approach to initiating buprenorphine for patients who do not meet traditional criteria and for whom delays in treatment pose significant risk. Macrodosing should be reserved for people with high opioid tolerance. Higher initial and total Day 1 doses are off-label but have been shown to be effective in achieving therapeutic levels of buprenorphine.[1]

Contact ED substance use navigator/hospital to home coordinator if available.

Indications:
- **Patients in withdrawal from fentanyl use, or**
- **Patients who have had full naloxone reversal of an opioid overdose** (i.e., naloxone-induced withdrawal)

Are any exclusion criteria to buprenorphine macrodosing present?
- Allergy or hypersensitivity to buprenorphine or naloxone
- Reported methadone use in the last 72 hours
- Unable to provide informed consent
- Altered mental status, depressed level of consciousness, or delirium
- Acute intoxication
- Severe medical illness such as sepsis, respiratory distress, severe liver dysfunction
- Concurrent withdrawal from alcohol or benzodiazepines
- Elderly

NO / YES

Provide supportive care and re-evaluate.

OPTIONS:
- ☐ Consult addiction medicine if available; patient may be a candidate for **methadone** or **SROM**
- ☐ Offer RAAM referral/harm reduction resources
- ☐ Provide naloxone kit

Is patient awake with COWS ≥ 13
Has at least 18 hours elapsed since last fentanyl use?
(not necessary post-naloxone reversal)

YES / NO

OPTIONS:
- ☐ Offer home buprenorphine start
- ☐ Offer microinduction buprenorphine start
- ☐ Offer return to ED when in withdrawal for buprenorphine treatment
- ☐ Patient handouts about buprenorphine treatment, home start, microdosing
- ☐ Provide naloxone kit

Explain:
- Goal is to achieve full treatment dose within a matter of hours
- May experience transient worsening of withdrawal symptoms before relief
- For patients in naloxone-induced withdrawal macrodosing should be started as soon as possible

Provide 16mg buprenorphine SL as 2x8mg tablets → **Reassess in one hour**

Repeat buprenorphine 8–16mg q1–2h until withdrawal is resolved or sedation (recommended Day 1 maximum is 32mg)

- Discharge with prescription for total dose dispensed in the ED as daily observed dose until planned follow-up (max 7 days)
- Refer to RAAM/community clinic
- Dispense naloxone kit
- Buprenorphine handout
- Harm Reduction Info Sheet

- **See High-Dose Buprenorphine Initiation ("Macrodosing") Reference Guide for ED Providers**
- **See Buprenorphine Reference Guide for further information**

High-Dose Buprenorphine Initiation ("Macrodosing") for ED Providers

RATIONALE FOR MACRODOSING BUPRENORPHINE

High-dose buprenorphine (also referred to as *macrodosing*) is an alternative approach to initiating buprenorphine for patients who would benefit from achieving a full therapeutic dose rapidly. Many patients seen in the ED post-overdose would benefit from buprenorphine for treatment of opioid use disorder and prevention of overdose; however, use of fentanyl within 48 hours of presentation is an exclusion for standard buprenorphine initiation. Moreover, standard initiation suggests a maximum Day 1 dose of 16mg of buprenorphine; this dose is generally inadequate to provide relief of withdrawal symptoms for people who use fentanyl, which likely increases the risk of treatment discontinuation post-discharge.

Macrodosing as an alternative approach to treating withdrawal and initiating buprenorphine has been described as part of the CA Bridge program in California for patients who had undergone reversal of opioid overdose with naloxone (1). The protocol suggests an initial dose of 16mg for patients in withdrawal post-naloxone followed by subsequent doses of 8–16mg for a total Day 1 dose of up to 32mg (2). The pharmacological explanation is that buprenorphine at high enough doses provides relief of withdrawal symptoms and blockade against full-agonist opioids still in circulation that have been temporarily displaced by naloxone. The same rationale can be applied to withdrawal from opioid use without naloxone reversal: at doses of 16mg or higher, there is enough buprenorphine to provide relief of withdrawal symptoms after the full-agonist opioids are displaced from the mu-receptors, whereas lower doses (2–8mg) displace other full-agonist opioids without providing relief. Essentially, higher initial doses effectively bypass precipitated withdrawal and achieve a full therapeutic dose within hours.

It should be noted that there have been no clinical trials to date comparing the effectiveness of high-dose initiation to other initiation protocols, and that 24mg is the maximum daily dose of buprenorphine recommended in the product monograph in Canada. Nonetheless, high-dose buprenorphine has been shown to be safe and well tolerated (3), and clinicians using this protocol in Ontario have reported success in the ED setting in patients post-overdose and those in withdrawal from fentanyl (4).

Macrodosing initiation could therefore result in more patients starting buprenorphine in the ED and more patients continuing with outpatient buprenorphine treatment. Another advantage of high-dose buprenorphine initiation is that it allows for the early administration of depot buprenorphine (Sublocade®), a monthly extended-release injectable buprenorphine treatment option (see Depot Buprenorphine Information Sheet) that provides higher and more constant serum buprenorphine levels than sublingual dosing (5) and eliminates the need for frequent pharmacy attendance.

https://www.metaphi.ca/wp-content/uploads/MacrodosingOnePager.pdf
https://www.metaphi.ca/wp-content/uploads/MacrodosingPrimer.pdf

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Case Study: Macrodosing

Patient presents to your community addiction clinic in opioid withdrawal.
Reports daily fentanyl use, smoked, 1-3 points per day.
Last use ~30 hours ago.
COWS 18.
Has been on buprenorphine before, 2 years ago, for 1 month at 12 mg.

Buprenorphine 8 mg tablets
Mitte: 12 tablets
Refills: 0
Instructions: Take two tablets SL immediately, then take half to one tablet SL every 1 hour as needed for withdrawal to a max of 32 mg on day 1. STOP if sedated. Repeat total day 1 dose on day 2, plus another half to one tab as needed to a max of 32 mg. Follow-up with the clinic on day 3

Macro after opioid reversal

Rapid transition from methadone to buprenorphine using naltrexone-induced withdrawal: A case report

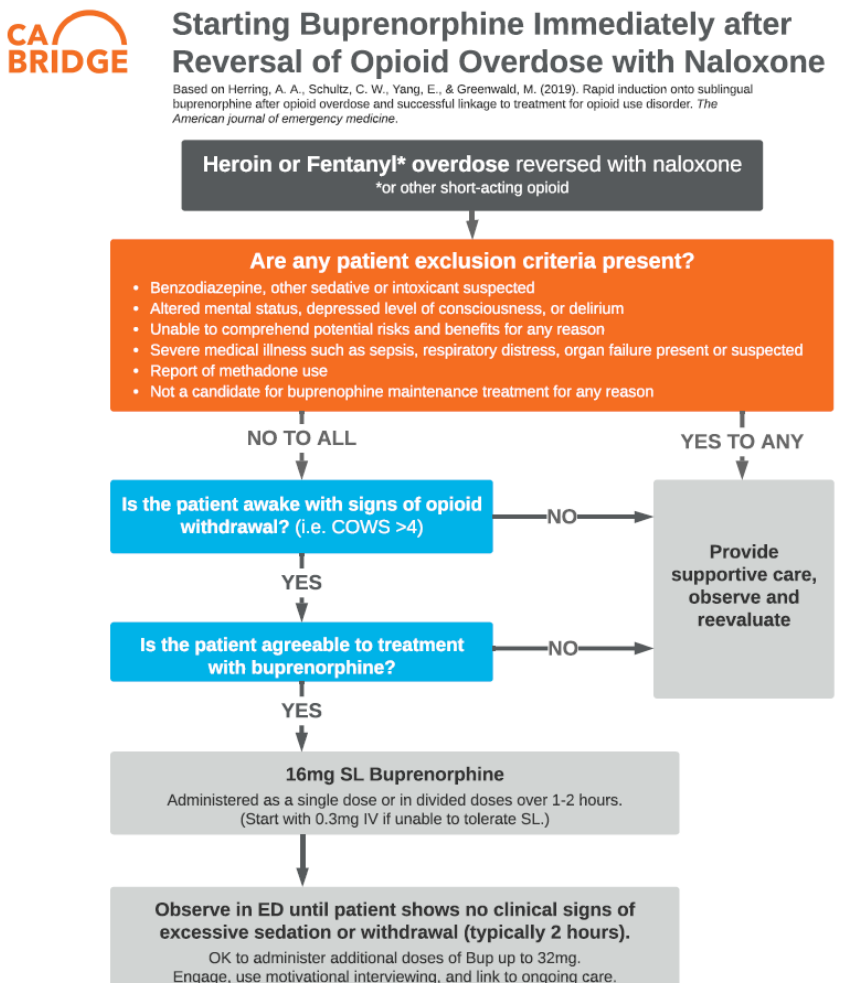
Heather Burrell Ward, Brian S. Barnett & Joji Suzuki

To cite this article: Heather Burrell Ward, Brian S. Barnett & Joji Suzuki (2019): Rapid transition from methadone to buprenorphine using naltrexone-induced withdrawal: A case report, Substance Abuse, DOI: 10.1080/08897077.2019.1573776

To link to this article: https://doi.org/10.1080/08897077.2019.1573776

Published online: 19 Mar 2019.

Macro after opioid reversal – in hospital



https://bridgetotreatment.org/resource/starting-buprenorphine-immediately-after-reversal-of-opioid-overdose-with-naloxone/

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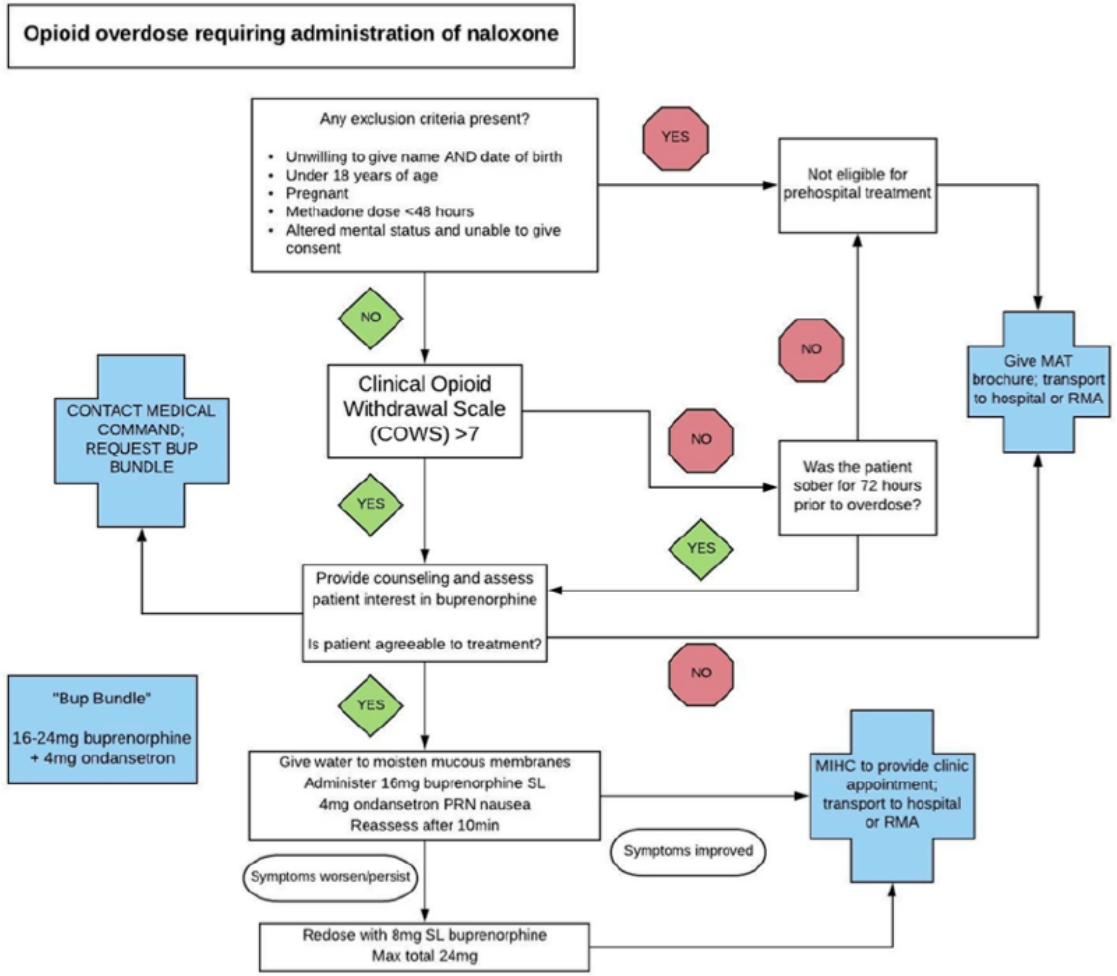
Macro after opioid reversal – EMS/Paramedic Protocols



Gerard G. Carroll , Deena D. Wasserman , Aman A. Shah , Matthew S. Salzman , Kaitlan E. Baston , Rick A. Rohrbach , Iris L. Jones & Rachel Haroz (2021) Buprenorphine Field Initiation of ReScue Treatment by Emergency Medical Services (Bupe FIRST EMS): A Case Series, Prehospital Emergency Care, 25:2, 289-293, DOI: 10.1080/10903127.2020.1747579

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Off-label Injectable Buprenorphine

Use before 7 days sublingual buprenorphine

Injectable buprenorphine

A guide to the use of depot buprenorphine

INTRODUCTION

Subcutaneous 28-day depot buprenorphine injection (hereafter BUP-XR, trade name Sublocade) is an alternative mode of delivering buprenorphine that can be a good choice for people who have difficulty attending a pharmacy regularly, use high- potency opioids such as fentanyl, or experience withdrawal symptoms or side effects with sublingual buprenorphine/naloxone (BUP-SL). BUP-XR is on the Ontario Drug Benefit (ODB) formulary as a Limited Use drug (LU 577), as well as most other provincial formularies, the NIHB program, and most private plans. In this document, we summarize the evidence for BUP-XR's effectiveness and adverse effects and present a practical guide for its use based on our collective initial experience with this product and current research. Given the relative novelty of depot products, much of the current research is industry sponsored, and information here is subject to change as new research becomes available. For a full discussion of depot buprenorphine's pharmacology and side effects, please refer to the product monograph (1).

EVIDENCE OF EFFECTIVENESS

BUP-XR vs. placebo

An industry-sponsored phase three randomized trial showed that BUP-XR was **significantly more effective than placebo at reducing opioid use** (2). At week 24, 41% of the 100mg group and 43% of the 300mg group had urine samples negative for illicit opioids, compared to 5% for the placebo group ($p < 0.0001$). High-dose BUP-XR may be particularly effective for people who inject opioids. A post-hoc analysis (3) of an industry-sponsored controlled trial (4) showed that people injecting opioids receiving 300mg monthly had more days of continuous abstinence than those receiving 100 mg monthly. This difference was not found for subjects who were using oral opioids. The industry-sponsored study (4) found that participants on 300mg and 100mg had improved satisfaction scores, higher percentage of employment, and fewer hospital days per person-year compared to placebo. Additionally, in a rollover open-label phase three multicentered study (5) of flexible 300mg and 100mg BUP-XR dosing, 61.5% of the 257 previously placebo-controlled and 75.8% of 412 de novo participants were abstinent, with retention rates of 50.6% and 50.5% for the rollover and de novo participants respectively.

BUP-XR vs. BUP-SL vs. methadone

A 24-week placebo-controlled trial compared BUP-SL to a different depot buprenorphine injection product not currently available in Canada (6). The proportion of opioid-negative urine samples was higher in the depot buprenorphine group (35.1%) than in the BUP-SL group (28.4%, $p < 0.001$), and treatment completion rates in the two groups were similar. The results of this trial do not necessarily apply to the depot product approved in Canada.

A six-month observational study conducted in Canada compared patient characteristics and overdose (OD) events on depot buprenorphine, BUP-SL, and methadone (7). Those on depot buprenorphine had the highest adherence and lowest nonfatal OD events, but authors recognize a patient selection bias. Those on methadone (at doses of 15–210mg) had the highest rate of OD events, but also the highest rates of injection drug use, HIV, hepatitis C, and mental health disorders. Furthermore, while BUP-XR had the greatest adherence, methadone demonstrated the highest retention at six months.

Sublocade Treatment: What to Know and Expect

WHAT IS SUBLOCADE?

- Sublocade (or *the shot*) is one way of taking buprenorphine, a medication used to treat addiction to opioids (heroin, fentanyl, or pain pills). Many people know buprenorphine by the brand name Suboxone, which is a tablet taken daily under the tongue.
- Sublocade is buprenorphine taken as a monthly injection. Once injected into the body, the liquid buprenorphine turns into a solid gel, called a depot. The depot gradually releases buprenorphine at a steady rate throughout the month.

WHAT IS IT LIKE TO TAKE SUBLOCADE?

- A health care professional will give you the medication as an injection in your abdomen every four weeks.
- The injection may be uncomfortable. Some people describe a hot or burning feeling when the medication is injected. Using an ice pack on the area before and after the injection usually helps to make it less painful.
- After the injection, the medication forms a small bump under the skin. The bump can last from four weeks up to a few months, but it will gradually go away.
- After the injection, most people feel completely normal, but some people feel a little bit sleepy for a few days. Over the month, most people feel very level and don't notice any withdrawal symptoms. If you do notice withdrawal symptoms, these can be managed by speaking with your health care provider.
- If you miss a dose, it can be given up to two weeks late.

IS SUBLOCADE RIGHT FOR ME?

- Sublocade can be a good choice for people who...
  - ...don't want to attend a pharmacy every day or every week.
  - ...travel frequently.
  - ...don't like the taste or feel of Suboxone.
  - ...experience withdrawal symptoms or cravings on Suboxone. (The concentration of buprenorphine in the blood is higher and more constant with Sublocade than with Suboxone. This means it may be more effective at relieving withdrawal symptoms and cravings, especially in people who have higher opioid tolerance, such as those who use fentanyl.)
- Sublocade can be given to people who take Suboxone 8mg or higher.
- Sublocade has not been studied in pregnancy. Talk to your health care provider about birth control and pregnancy testing before starting Sublocade.

https://www.metaphi.ca/wp-content/uploads/Guide_DepotBuprenorphine.pdf https://www.metaphi.ca/wp-content/uploads/DepotBuprenorphineInitiation.pdf
https://www.metaphi.ca/wp-content/uploads/WMS_4.7_SublocadeDischarge_v2.pdf https://www.metaphi.ca/wp-content/uploads/Handout_SublocadeTreatment.pdf

Off-label injectable buprenorphine

Growing body of evidence

Mariani et al, 2020
Case series
5 participants
received BUP-XR on days two and three of BUP-SL with no
(PW) no adverse

Peckham et al, 2021
Case series
10 participants
received BUP-XR day seven of BUP-SL
No PW, 9 got supplemental BUP-SL for withdrawal & cravings

Mariana et al, 2021
open-label trial
5 participants
Received BUP-XR within 185min of BUP-SL initiation
No PW no adverse events (no sedation)

Hassman et al, 2022
open-label phase four rapid initiation study
24 participants
Received BUP-XR one hour after a single 4mg
2 cases of PW, improved within 12h

On-label recommendations are to proceed with BUP-XR after induction and stabilization on BUP-SL ≥ 8mg for seven days.

To be considered for early administration of BUP-XR, ensure the following conditions are met:

1) **The client can tolerate buprenorphine.**
   The client has been exposed to buprenorphine without adverse events such as hypersensitivity.
2) **The client tolerates ≥ 8mg buprenorphine.**
   The client has tolerated at least 8mg of BUP-SL without respiratory depression or sedation. **If not tolerant of ≥ 8mg BUP-SL DO NOT proceed with BUP-XR**.
3) **The client is not at risk for precipitated withdrawal.**
   Monitor the client for severely worsening withdrawal, typically occurring within 1h of BUP-SL administration (limited research showed that when worsening withdrawal occurred after BUP-XR, it was mild to moderate and resolved with symptomatic support within 12h).

***NOTE:** If the above conditions are met, BUP-XR can be provided. Same or next day BUP-XR initiation should be considered for those at highest risk of treatment discontinuation and opioid harms. Initiation before discharge is appropriate for those in live-in settings (e.g., withdrawal management). Longer periods of stabilization should be considered for those with a precaution as listed above, e.g., elderly.

Has the client been on BUP-SL ≥ 8mg for at least seven days OR does the client meet the three criteria for early administration as listed above?

Mariani JJ, Mahony A, Iqbal MN, Luo SX, Naqvi NH, Levin FR. Case Series: Rapid Induction Onto Long Acting Buprenorphine Injection for High Potency Synthetic Opioid Users. Am J Addict. 2020;29(4):345-8.
Peckham AM, Kehoe LG, Gray JR, Wakeman SE. Real-world outcomes with extended-release buprenorphine (XR-BUP) in a low threshold bridge clinic: A retrospective case series. J Subst Abuse Treat. 2021;126:108316.
Mariani JJ, Mahony AL, Podell SC, Brooks DJ, Brezing C, Luo SX, et al. Open-label trial of a single-day induction onto buprenorphine extended-release injection for users of heroin and fentanyl. Am J Addict. 2021;30(5):470-6.
Hassman H, Strafford S, Shinde SN, Heath A, Boyett B, Dobbins RL. Open-label, rapid initiation pilot study for extended-release buprenorphine subcutaneous injection. Am J Drug Alcohol Abuse. 2022:1-10.

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Case Study: Macrodosing

Patient presents to your community addiction clinic in opioid withdrawal.
Reports daily fentanyl use, smoked, 1-3 points per day.
Last use ~30 hours ago.
COWS 18.
Has been on buprenorphine before, 2 years ago, for 1 month at 12 mg.

Started buprenorphine SL
Day 1 buprenorphine 16 mg + 8 mg
Day 2 buprenorphine 24 mg + 4 mg
Day 3 long-acting injectable buprenorphine 300 mg

More off-label use

Giving the second injection before 26 days

Giving the injection the same day SL buprenorphine is started

Starting with two 300 mg injections up front

Starting the injection without SL buprenorphine induction

Methadone for people who use fentanyl

High dose/quick start Methadone, Methadone + SROM

Case Study: Methadone for people who use fentanyl

Patient presents to your community addiction clinic wanting treatment.
Reports daily fentanyl use, smoked, 3-5 points per day.
Has tried methadone and buprenorphine before, but use didn't change, so eventually stopped treatment.

Considerations: did they get to a high enough dose of methadone or buprenorphine?

Options:
Buprenorphine
-micro – will the patient stick with treatment long enough to get to an effective dose?
-macro - can the patient abstain for 18+ hours?
Methadone
-can be started today – how long will it take to get to an effective dose?

Methadone for people who use fentanyl

- There is evidence that fentanyl users have high early drop out rates in the first few weeks of methadone treatment
- Fentanyl is so potent that many fentanyl users require high methadone doses (100 mg+) to get substantial relief of withdrawal and cravings
- Yet methadone must be titrated gradually to avoid toxicity:
  - Starting dose of methadone is 30 mg, with increases of 10-15 mg every 3-5 days
  - It would take at least two to three weeks to reach 100 mg, and much longer if the patient misses doses and require restarts
- A higher starting dose (40 mg) will shorten the titration time somewhat

https://www.metaphi.ca/wp-content/uploads/Guide_MethadoneForFentanyl.pdf
https://www.metaphi.ca/wp-content/uploads/Guide_MethadoneForFentanyl_PlainLanguage.pdf

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Methadone for people who use fentanyl

- Adding SROM to methadone may help retain patients in treatment
- SROM reaches a peak in 10 hours after ingestion, helping withdrawal symptoms during early methadone titration
- Initial dose 200mg, with dose increases of 50-100 mg every 2 days
- Once therapeutic dose of methadone + SROM reached, SROM can be maintained or tapered
- Limited evidence, but clinical experience in Ontario has been positive
  - Srivastava A, Kahan M. Methadone and Slow Release Oral Morphine for fentanyl users: Two case reports. Canadian Journal of Addiction, August 2023
  - META:PHI: Methadone treatment for fentanyl users. Bromley L et al, 2022.

https://www.metaphi.ca/wp-content/uploads/Guide_MethadoneForFentanyl.pdf
https://www.metaphi.ca/wp-content/uploads/Guide_MethadoneForFentanyl_PlainLanguage.pdf

Methadone for people who use fentanyl

https://www.metaphi.ca/wp-content/uploads/Guide_MethadoneForFentanyl.pdf

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Methadone for people who use fentanyl

Highlights

- Starting doses of 30mg
- Increasing by 15mg every 3-5 days
- Addition of SROM 200mg, inc q2 days by 50-100mg at a time
- Alternate methadone and SROM dose increases
- Dose adjustment after 4 consecutive missed methadone doses, to 50% or 30mg
- Don’t delay a dose increase for an ECG
- Take-home doses can be started after 1 month
- Consider leaving a 30mg dose restart order at the pharmacy
- Consider phone assessments or script to promote treatment continuation

https://www.metaphi.ca/wp-content/uploads/Guide_MethadoneForFentanyl.pdf
https://www.metaphi.ca/wp-content/uploads/Guide_MethadoneForFentanyl_PlainLanguage.pdf

METAPHI
MENTORING, EDUCATION, AND CLINICAL TOOLS FOR ADDICTION
PARTNERS IN HEALTH INTEGRATION

Case Study: Methadone for people who use fentanyl

Patient presents to your community addiction clinic wanting to treatment.
Reports daily fentanyl use, smoked, 3-5 points per day.
Has tried methadone and buprenorphine before, but use didn't change, so eventually stopped treatment.

Day 1
Methadone 30mg + **SROM 200mg** (MEQ 440) *using Methadone:SROM 1:8
Day 2
Methadone 30mg + SROM 200mg
Day 3
Methadone 30mg + **SROM 300mg** (MEQ 540)
Day 4
Methadone 45mg + SROM 300mg (MEQ 660)
Day 5
Methadone 45mg + **SROM 400mg** (MEQ 760)
Day 6
Methadone 45mg + SROM 400mg
Day 7
Methadone 60mg + SROM 400mg (MEQ 880) *if fentanyl:morphine 1:100, then MEQ starting was much higher

Slow-Release Oral Morphine

Slow-release oral morphine (SROM)

- Some evidence from controlled trials that SROM is of comparable effectiveness to methadone
- Can be used for patients who refuse methadone or buprenorphine, or when these medications were ineffective or had side effects
- Equivalence roughly 1 mg methadone = 8 mg SROM
- Fentanyl users often need a dose of 1000+ mg/day
- Observed dosing recommended, at least until the patient has stopped high risk opioid use; capsules can be injected
- META:PHI is preparing guidelines on SROM

Case Study: SROM

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Has tried methadone and buprenorphine before, but use didn't change, so eventually stopped treatment. Refuses to return to clinic if methadone or buprenorphine are all you have to offer.

Consider SROM

SROM

Opioid tolerance	Starting Dose	Dose Increases
Low-tolerance High risk for toxicity	30-50mg	50mg q2days
Moderate tolerance	100-150mg	100mg q2days
High tolerance	200-400mg	100mg daily 200mg q2days Slow increase at ~800mg

SROM

Day	Lower & Slower	Higher & Faster
1-2	50mg	400mg
3-4	100mg	600mg
5-6	150mg	800mg
7-8	200mg	900mg
9-10	250mg	950mg

Case Study: SROM

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Sample script

Kadian 100mg capsules
Two capsules by mouth once daily for 2 days
Instructions: Open capsules and sprinkle beads into cup, wash down with water or apple sauce.
Observed daily dosing. Fax clinic with missed doses.

Case Study: SROM

Patient presents to your community addiction clinic wanting to treatment.
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Has tried methadone and buprenorphine before, but use didn't change, so eventually stopped treatment. Refuses to return to clinic if methadone or buprenorphine are all you have to offer.

Day	
1	200mg
2	300mg
3-4	400mg
5-7	600mg
8-15	800mg

Previous recommendations, 40% reduction with 2 consecutive missed doses

Thank you!

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