New Guidelines for Methadone Prescribing

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- Presenter: Andrew McLeod
- Relationships with financial sponsors: Not applicable

Mitigating Potential Bias

- Jennifer Wyman and Andrew McLeod are contributors to the methadone guide. The methodology used for this guideline includes participation of individuals from an array of organizations and perspectives, including peer reviewed literature and planned peer review of the guideline.

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Objectives

1. Utilize the concepts of opioid tolerance and risk of toxicity in determining initial methadone doses and titration strategies
2. Identify elements of care that promote retention in treatment
3. Identify opportunities to improve access to methadone and transitions of care between settings

Background

In 2020 fentanyl and fentanyl analogues accounted for over 99% of of opioid overdose deaths in Ontario

Last CPSO guidelines were written in 2011 and rescinded in 2021.

Need new guidelines to address:

- high numbers of opioid and opioid-related toxicity deaths
- very high opioid tolerance
- low treatment engagement and retention

Methodology

Group:

- 5 physicians
- 2 PWLE of methadone treatment
- 1 NP
- 1 pharmacist

Terms of reference explicitly acknowledge the value of different types of experience and education and the partnership between all members of the group as co-creators of the new guidance document

Contents

- Principles of care, holistic care & treatment retention
- Methadone pharmacology
- Methadone initiation and titration, maintenance, and tapering & discontinuation
- Considerations for special conditions and populations
  - Mental health conditions
  - Concurrent substance use
  - Acute & chronic pain
- Setting specific considerations
  - Transitions of care
  - RAAM clinics, virtual care & primary care
  - Emergency department and inpatient settings
  - Prison
- Pharmacy considerations

Poll Question #1

- What is the highest starting dose of methadone you've prescribed?

20mg

25mg

30mg

35mg

40mg

50mg

other

Poll Question #2

- What's the highest dose you've used for a methadone restart?

- 30mg
- 40mg
- 50mg
- 60mg
- Other

Poll Question #3

- Do you co-prescribe methadone with SROM at initiation?
- Yes
- No

New CFR from SAMHSA 2024!

(ii) For each new patient enrolled in an OTP, the initial dose of methadone shall be individually determined and shall include consideration of the type(s) of opioid(s) involved in the patient's opioid use disorder, other medications or substances being taken, medical history, and severity of opioid withdrawal. The total dose for the first day should not exceed 50 milligrams unless the OTP practitioner, licensed under the appropriate State law and registered under the appropriate State and Federal laws to administer or dispense MOUD, finds sufficient medical rationale, including but not limited to if the patient is transferring from another OTP on a higher dose that has been verified, and documents in the patient's record that a higher dose was clinically indicated.

SAMHSA. (2024, February 1). *The Federal Register*. https://www.federalregister.gov/documents/2024/02/02/2024-01693/medications-for-the-treatment-of-opioid-use-disorder

Protocol	Initial dose	Titration	Indications/Comments
BCCSU	30-40mg	15mg every 3 days	Higher may be considered case by case Documented history of fentanyl and exp of methadone
Stone	30mg	Day 2 40 Day 3 50, then inc q7 days, max 20mg /week	Retrospective chart review n=154 Nursing daily assessments
Faster Paths (Taylor et al) Revised protocol	10-50 median 30 40	Day 2 median 40 Day 3 median 50 Day 2 50 Day 3 60	Chart abstractions N= 150 (142 unique patients) For high opioid tolerance and moderate to severe withdrawal
San Francisco outpatient (Steiger et al)	30+10	Day 2 60 Day 3-5 80 Day 6-8 100 Day 9 120 then wait 5 days	Retrospective chart review n= 65 High tolerance (daily fentanyl use), excluding CHF, CRF, COPD, cirrhosis
Baymark pilot (unpublished)	30+10 30+10	Day 2 60 Day 3 80 then wait 3 days Day 2 50, Day 3 60, Day 4 70, Day 5 80	N=100 High intensity Moderate intensity Highest peak doses ass'd with highest retention

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Steiger Case Series (2024)

- Retrospective chart review: rapid induction ordered for 93 patients and completed by 65
- Patient selection:
  - daily fentanyl use as their primary opioid
  - excluding those at higher risk of overdose (>65, heart failure, ESRD, cirrhosis, advanced pulmonary disease
  - concurrent substance use including benzodiazepines and alcohol was not an exclusion criterion

  Protocol:
  - Day 1 40
  - Day 2 60
  - Day 3 80
  - followed by dose increases of up to 20mg q3 days; average dose at day 7 was 89mg
- No reports of sedation, fatal or nonfatal overdoses, within 14 days of initiation

Overdose literature

- Single overdose:
  - Typically accidental ingestion in an intolerant individual or individual who lost tolerance

- Accumulated toxicity:
  - The combination of prescribed methadone with another medication
  - BZDs most commonly reported

- Deaths during the first two weeks of treatment usually occur because tolerance was overestimated OR other opioids/depressants were used with prescribed methadone
- Deaths > 2 weeks usually related to other drugs, especially BZDs

- Patients in whom the first dose suppresses withdrawal for full 24h may experience symptoms of toxicity as tissue stores accumulate

Considerations for Dose Initiation and Titration

- Opioid Tolerance
- Risk of toxicity
- Risks of not being on OAT

Opioid Tolerance

Low tolerance	Intermittent use, use of low-potency opioids (e.g. codeine) or low doses of moderate-potency opioids (e.g. oxycodone 20-40mg/day)
Moderate tolerance	Oral use of pharmaceutical or unregulated tablets (range 100-200MME when known) Not knowingly or regularly using fentanyl
High tolerance	Daily or near daily use of fentanyl (<1gm/day), injection use of morphine or hydromorphone
Very high tolerance	Daily use of fentanyl 1gm/day or more

Risk for Toxicity Considerations

- Age: 65 and older
- Concurrent health conditions: severe COPD, severe liver disease, conditions associated with QT prolongation
- Concurrent prescribed medications: medications that are sedating and/or prolong the half life of methadone
- Concurrent substance use: alcohol and benzodiazepine use at levels that cause sedation, e.g. ≥4 drinks daily, more than a moderate night-time dose of benzodiazepines
- Recent methadone experience: people on doses >90mg in the last 3 months may be considered for higher starting doses
- Recent overdoses: may be at increased risk of overdose with prescribed methadone but also increased benefit from rapid stabilization

Factors	Initial Dose	Titration	Comments
No/low tolerance High risk of toxicity	5-10mg	5-10mg q3-5 days	Strongly consider buprenorphine
Moderate tolerance Moderate risk of toxicity	10-20mg	10mg q3-5 days	Example: Oxycontin 80mg x 3/day, hydromorphone 8mg x 8/day
Moderate tolerance No major risk factors for toxicity	20-30mg	10-15mg q3-5 days	Typically keep dose increases to 10mg once at 80mg methadone
High tolerance Moderate risk of toxicity	20-30mg	10-15mg q3-5 days	Dose increases of 10mg once at 80-100 mg of methadone
High tolerance No major risk factors for toxicity	30-40mg	15mg q3-5 days	Dose increases of 10mg once at 80-100mg
Very high tolerance	40-50mg	15mg q3-5 days	Daily fentanyl use of ≥1gm plus evidence of previous methadone ≥90mg in the last 3 months

What about the methadone + SROM?

META:PHI 2021 *Methadone for People Who Use Fentanyl: Recommendations* suggested co-prescribing methadone and SROM (max 30 + 300mg) for people using fentanyl daily

Rationale at the time:

- Aimed to achieve an effective OAT dose more rapidly than using methadone alone
- Dose guidance on higher starting dose was negligible
- SROM peaks later than methadone
- No bioaccumulation with SROM

- Small number of case reports
- Observations of authors with LE: people who use fentanyl find SROM augments the methadone dose and helps with pain
- Prescribers' experience: seems to help people stabilize and some people prefer to stay on combination therapy rather than tapering SROM as methadone approaches effective dose

Methadone and short-acting opioids

Short-acting opioids can be considered:

- As a trial, with the goal of optimizing OAT
- For individuals using large amounts of fentanyl daily
- For people who have repeatedly discontinued or had difficulty engaging with OAT

Maximum methadone starting dose of 30mg in people also receiving short-acting opioids given the lack of information on accelerated methadone dosing and co-prescribed short-acting opioids.

Ideally all short-acting opioids are observed.

Take-home doses warrant the same considerations as take-home methadone doses with respect to storage and ability to manage medications safely.

Recommendation

- For people with high/very high opioid tolerance, discuss options, ideally using a **decision aid**:
  - Methadone 30mg + SROM 300
  - Methadone 40-50mg depending on tolerance/toxicity risks

- Considerations:
  - No bioaccumulation with SROM; can be increased every 2 days
  - SROM may be less risky than higher dose methadone in people with hepatic dysfunction or on medications that increase the half-life of methadone
  - SROM should not be prescribed to individuals with renal insufficiency
  - For people without ODB coverage, SROM may be more expensive or not covered than methadone
  - Carries may not be expedited as readily as with methadone due to risks of diversion
  - SROM may not be accepted as OAT in certain bed-based treatment programs

Poll Question #4

- Reflecting on these dose recommendations, I feel:

- Bored – I was already doing a version of this
- Frustrated – They don’t go far enough
- Apprehensive – They seem like a big leap
- Optimistic – This seems like a reasonable next step

It’s more than the dose

“Methadone: It saves your life, and without it, the other things aren’t necessarily effective. In the beginning when the medicine isn’t quite doing it, what keeps you going is the relationship with the practitioner and the trust. They weren’t trying to watch me pee. I could have an open conversation and tell them about my drug use, my relapses and everything and it wasn’t like “We’re going to take away this medication that’s stabilizing you and retrigger you”, but “what do you need to make it better and more effective?”

Ashley Smoke

Treatment retention

“OAT should not be a full-time job.”

- Convenient hours and options for drop-in visits as well as scheduled appointments
- Options for connecting with the clinic, e.g. texts and emails outside of appointments
- Having holistic care in the same setting
- Responsiveness to unexpected changes

Treatment retention

"Supports are what made me stop using completely: counseling, access to a psychiatrist, help finding a physiotherapist, having referrals even to a dentist."

- A safe environment: welcoming and clean, no one selling drugs inside/outside the clinic, no violence, no discriminatory language
- Holistic care such as mental health supports, primary care, referrals, peer support groups, clothing exchanges.
- Opportunities for shared decision making and collaborative goal setting

Treatment retention

"It's hard to get stable when you've got nothing to eat and nowhere safe to live."

- Hiring staff with lived experience of substance use
- Have snacks available
- Being treated like a human being

Case 1 - Mike

- 45yo M on methadone 110mg until about 3 months ago – lost his partner, Rx was discontinued after missed doses -> didn't make it back to clinic and discontinued treatment
- Using fentanyl 1gm+/day, smoking + injecting
- Uses crystal meth, no alcohol, no additional BZDs
- No other medications
- No known health conditions

- UDS + FYL, + BZD, +CM, + HM

Mike

Very high opioid tolerance AND known experience of methadone at a dose of at least 90mg for at least 5 days in the last 3 months:

Initial doses of up to 50mg may be considered

50mg x 3 days -> 65mg x 3 days -> 80mg x 3 days

What if he misses doses?

- After 4 weeks he's at 130mg, still using fentanyl though significantly decreased
- Getting almost all his doses, but missing Sunday consistently – pharmacy is open for 2 h only
- Goes out of town for some part-time work; misses 4 doses -> pharmacy cancels Rx , now off methadone for 6 days
- By guidelines: restart based on initial dosing criteria and increase by 10-15mg every 3-5 days

- Thoughts?

Steiger, Unpublished

Missed doses: once stabilized, all patients return to full dose by Day 2 as long as they haven't missed a week

- 3 missed days - reduce by 10%, return to full dose the next day (e.g. 115mg, then back to 130)
- 4 missed days – reduce by 20%, return to full dose the next day (e.g. 105 mg, then back to 130)
- 5 missed days – reduce by 30%, return to full dose the next day (e.g. 90mg, then back to 130)

- At a week, dec by 50% or "floor" of 60

Mike, continued

Was on 130mg, missed 6 days

- Start at 50mg, inc by 15mg q3 days
- Start at 50mg, inc by 15mg daily x 3 and hold until reassess
- Start at 60?

- What if he has another opportunity to get work out of town?
- What are your thoughts about carries?

Criteria	No carries	Up to 3 non-consecutive carries	4–6 carries	7–27 carries
Ability to store carries securely	-Living on the street or in unstable or unsafe housing -Unable to store carries in a manner and location that reduces the risk of inappropriate use	-Consistent and safe living environment -Able to store carries in a manner and location that reduces the risk of inappropriate use -Locked box		
Amount of time on methadone	< 4 weeks	> 4 weeks	> 12 weeks	-7–13 carries: 1 year, with at least 6 months of 6 carries -14–27 carries: 2 years, with at least 1 year of 13 carries
Stability	-Not stable or stability unknown -Active psychosis, suicidality	-Developing stability -Establishing routines around clinic/treatment expectations -Attending most appointments -No acute conditions that impair judgment or ability to manage carries safely	-Consistent clinical and psychosocial stability -Stable routines around clinic expectations and medication management -Dose is stable -Stable living situations, employment, or participation in other regular activities -No acute mental health conditions that impair judgement or ability to manage carries safely	
Frequency of missed doses	-Frequent	-Missing 2 doses per week at most	-Missed doses rare	
Recent substance use patterns	-Higher-risk use that is impacting health, physical safety and overall well-being -Intoxicated or sedated at appointments -Regular overdoses or blackouts/memory loss	-Lower-risk, not impacting immediate safety or health -In alignment with goals -Not intoxicated or sedated at appointments -No overdoses or blackouts/memory loss in the last month	-Lower-risk, not impacting immediate safety or health, and overall stability -In alignment with goals -Not intoxicated or sedated at appointments -No overdoses or blackouts/memory loss in the last 3 months	-No use of unregulated or unprescribed substances and no high-risk use of regulated or prescribed substances
Urine drug screen results	-Negative for methadone or indicative of tampering	-Positive for methadone -Consistent with self-reported substance use	-Positive for methadone -Consistent with self-reported substance use -Generally negative for unregulated and unprescribed substances	-Positive for methadone -Consistently negative for unregulated and unprescribed substances

Case 2 - Tom

- 35yo M released from jail 2 weeks ago; was on 40mg methadone while in corrections
- Used opioids before incarceration (pills > fentanyl) but not in past 3 months
- Prescription was sent to a pharmacy for 5 days, but he couldn't get there beyond Day 1 -> Rx was cancelled
- Bipolar, ADHD, AUD, cannabis use
- Medications:
  - Quetiapine XR 200mg
  - Trazodone 150mg
  - Gabapentin 300mg TID

- No fixed housing
- Reports drinking + some crack, no CM, no opioids
- UDS + EDDP, + HM, + COC, + BZD, - FYL

- Thoughts?

Tom

Moderate tolerance and moderate risk of toxicity: Initial dose of 10–20 mg

- Does not want buprenorphine
- Methadone 20mg with close attention to alcohol use and mental health
- Unsure what pharmacy he'll access -> give him printed prescription
- Rx up to 7 days
  - May start this prescription at any time in the duration of the prescription (i.e. seven days)
  - Do not cancel prescription unless patient misses 5 or more consecutive doses

- Naloxone kit, counseling re overdose risks d/r loss of tolerance, connection to supports, ensure continuity of other medications, follow-up plan

Case 3 – Jasmine

- 38yo F using approx. 1gm of fentanyl daily – mostly smoking + CM daily
- On methadone on and off, unsure of doses
- No prescription medications
- No other health conditions or active substance use
- Connecting Ontario: last dose 50mg 1 month ago, hasn't been above 60mg in past 3 months
- Moving back and forth between her mother's and BF's, unsure where she'll be staying and which pharmacy she wants to use, no consistent phone access
- No ID

- UDS + FYL, BZD, COC, CM

Dose initiation

High opioid tolerance and no major risk factors for toxicity:
Initial dose may be up to 40 mg

- Offered option of methadone 40 or methadone 30 + SROM 300
- Plan for most appropriate pharmacy
- Write Rx for methadone 40mg x 7 days
- Notes to pharmacist:
  - May start this prescription at any time in the duration of the prescription (i.e. seven days)
  - Do not cancel prescription unless patient misses 5 or more consecutive doses
  - Patient does not have ID – description

- Alternative contact # with permission + ensure she knows how to access team

Day 5 – Monday

- Made it to the pharmacy Friday & Saturday – missed Sunday
- Has not had Monday's dose yet
- Dose feels very low, lasting ? 4-5 hours, no sedation at all, ongoing use
- Cont methadone 40mg for another day and plan dose increase to 55mg Tuesday
- Plan for telephone visit Thursday

Day 7 - Friday

- Unable to reach the patient Thursday or Friday
- Per Connecting Ontario and pharmacy has had doses of 55mg for Tues, Wed, Thurs
- Thoughts?
  - Continue Rx?
  - Any dose adjustment?
  - Let mother know prescription is available?

Day 12 - Monday

- Telephone Visit
- Made it to the pharmacy Saturday – missed Sunday, hasn't been to the pharmacy yet
- Dose still feels very low, never sedated, continuing to use

Day 1 Tuesday	Day 2 Wednesday	Day 3 Thursday	Day 4 Friday	Day 5 Saturday	Day 6 Sunday
55mg	55mg	55mg	Missed	55mg	missed

- Thoughts?

Missed doses and dose titration

- Consider dose increases for patients who repeatedly face challenges achieving 3 consecutive doses, particularly those who have demonstrated tolerance to methadone and high potency opioids with:
  - A dose of 60mg or less
  - At least 4 doses in 5 days
  - Little withdrawal relief at the current dose
  - Ongoing fentanyl use
  - Lack of sedation

Next steps

- Rx 2 more days at 55
- Pre-plan dose increase to 70mg for Wednesday
- Note on the prescription:
  - Note dose increase after 2 consecutive doses per META:PHI guide
  - IF the patient does not attend Tuesday, continue 55mg
  - Please notify us of any missed doses
  - Contact the prescriber if any questions

- Explain to patient:
  - Hard but important to get to the pharmacy consistently – helps to get doses higher faster
  - When in doubt show up at the pharmacy

Summary

- What can clinicians do to provide person centered care in order to better support patients?

- Choose starting dose based on tolerance and risks of toxicity
- Offer phone/video options for follow-up
- Be proactive about communicating with patient and pharmacy
- Apply judgement and flexibility about dosing and carries as appropriate

Thanks!

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