META:PHI's New Guidance for Methadone Prescribing

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October 22 2025

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MENTORING, EDUCATION, AND CLINICAL TOOLS FOR ADDICTION
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Disclosure of Financial Support

- This program has received in-kind support from META:PHI in the form of logistical support
- Potential for conflict(s) of interest:
  - Andrew McLeod and Anita Srivastava have received an honorarium from META:PHI for work in developing the guidance being discussed in this program
  - Jennifer Wyman has received salary support from META:PHI for work in developing the guidance being discussed in this program.

Presenter Disclosure

- We have no relationships to disclose

Mitigating Potential Bias

- Jennifer Wyman, Anita Srivastava 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 peer review of the guideline

- Contributors:

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Objectives

1.Describe the considerations in selecting a starting dose and titration protocol for methadone in a RAAM/outpatient setting

2. Identify situations when higher dose methadone starts and restarts may be appropriate

3. Implement strategies to support patient/client engagement in care

Background

- Last provincial guidelines in Ontario were written in 2011 and rescinded in 2021.
- New guidelines needed to address:
  - High numbers of opioid-related toxicity deaths and very high opioid tolerance
  - Low treatment engagement and retention rates
  - New practitioners and new care settings

- Extensive literature review regarding methadone with a focus on OAT in the context of the current unregulated drug supply-> **consensus-based document**
  - Reviewed by prescribers, pharmacists, nurses, clinic administrators, and people with lived/living experience of methadone therapy

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
- Plan for most appropriate pharmacy, write longer prescriptions

Treatment retention

"It's hard to keep making the effort when your dose isn't helping- or available"

- Communication between community and hospital/correctional/treatment settings
- Prescription notes:
  - Note exceptions to usual prescribing practices
  - May start this prescription at any time in the duration of the prescription (i.e. seven days)
  - Do not cancel prescription unless patient misses 4 or more consecutive doses
  - Patient does not have ID – provide description
  - Specify how to contact prescriber in case of questions to minimize the likelihood of Rx being held

Evidence and experience with starting doses >30mg methadone

- META:PHI 2021: methadone 30mg + SROM up to 300mg
- BCCSU 2023: initial dose up to 40mg for individuals with very high tolerance who use fentanyl and have previous experience with methadone
- SAMHSA 2024: Day 1 dose up to 50mg based on individualized assessment
- Steiger 2024: 40/60/80 mg with dose increases up to 20mg every 3 days for people reporting daily fentanyl use (n=93)
- Stone 2018: 30mg Day 1 followed by increases of 10mg daily for two days, then q7 as required (n=154)
- Taylor 2022: Day 1 40mg, Day 2 50mg, Day 3 60mg (n=142)

Framework for decisions re dose initiation and titration

- Goal: to reach an effective dose in a manner that is timely, collaborative, and considers the patient's comfort, risk profile and function

- When determining initial doses and titration plans, the clinician should consider:
    - opioid tolerance
    - risks of toxicity
    - the risks of not being on methadone
    - clinician experience

Opioid Tolerance

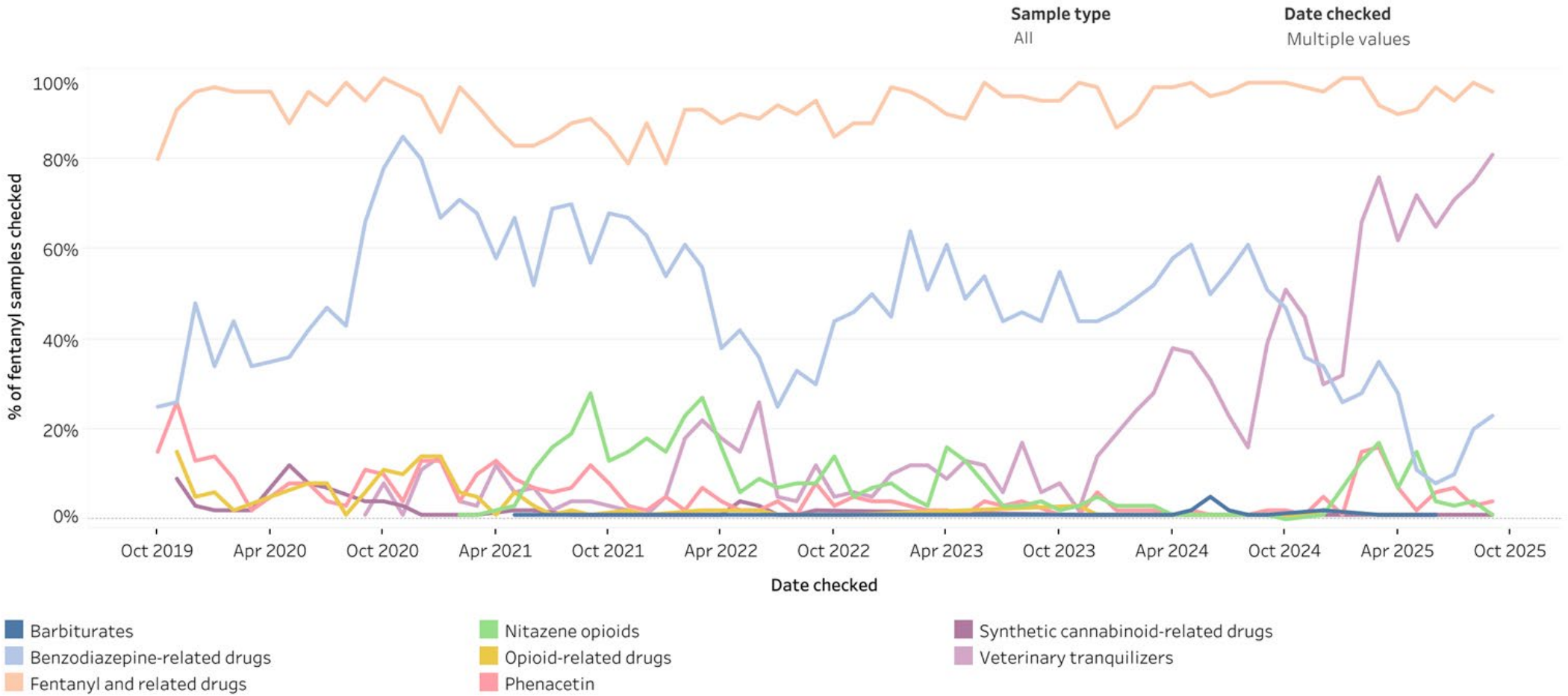
Category	Descriptor
Low tolerance	Use of low-potency opioids (e.g. codeine) or low doses of moderate-potency opioids (e.g. oxycodone 20-40mg/day, generally <100MME). Also includes intermittent use of higher-potency opioids, including smoked/injected.
Moderate tolerance	Oral use of higher doses of moderate-potency opioids,(e.g. oxycodone 120-160mg/day, HM 32-64mg/day, generally 100-300MME when known). Not regularly using fentanyl (recognizes that people may be exposed through use of tablets that are not of pharmaceutical origin).
High tolerance	Daily or near daily use of heroin or fentanyl (<1gm/day, smoked or injected) Regular injection use of morphine or hydromorphone High doses of moderate-potency opioids taken orally (e.g. HM 64mg/day or more)
Very high tolerance	Daily use of fentanyl 1gm/day or more, smoked or injected

Risk for Toxicity Considerations

High Risk of Toxicity	Advanced age, frailty, significant alcohol or benzodiazepine use (i.e., use that causes intoxication or sedation), advanced COPD, severe liver dysfunction, recent start of sedating medications, interruptions in opioid use resulting in loss of tolerance.
Risk of Toxicity	Moderate alcohol or benzodiazepine use, concurrent use of medications that are sedating or interact with methadone by prolonging the half-life, sleep apnea, liver dysfunction.
No Major Risk Factors for Toxicity	No concurrent health conditions, substance use, or medications that increase risk.

Factors	Initial Dose	Titration	Comments
No/low tolerance OR High risk of toxicity	5-10mg	5-10mg q3-5 days	Strongly consider buprenorphine
Moderate tolerance AND Risk of toxicity	10-20mg	10mg q3-5 days	Example: Oxycontin 80mg x 3/day, hydromorphone 8mg x 8/day
Moderate tolerance AND No major risk factors for toxicity	20-30mg	< 80mg: 10-15mg q3-5 days ≥ 80mg: up to 10mg q5-7 days	
High tolerance AND Risk of toxicity	20-30mg	< 80mg: 10-15mg q3-5 days ≥ 80mg: up to 10mg q5-7 days	
High tolerance AND No major risk factors for toxicity	30-40mg	<80mg: 15mg q3-5 days ≥80mg: 10mg q5-7 days	
Very high tolerance AND No major risk factors for toxicity	40-50mg	<80mg: 15mg q3-5 days ≥80mg: 10-15mg q5-7 days	Daily fentanyl use of ≥1gm plus evidence of recent experience of high-dose methadone at a steady state *

Be Aware of Changes in the Drug Supply- https://drugchecking.community



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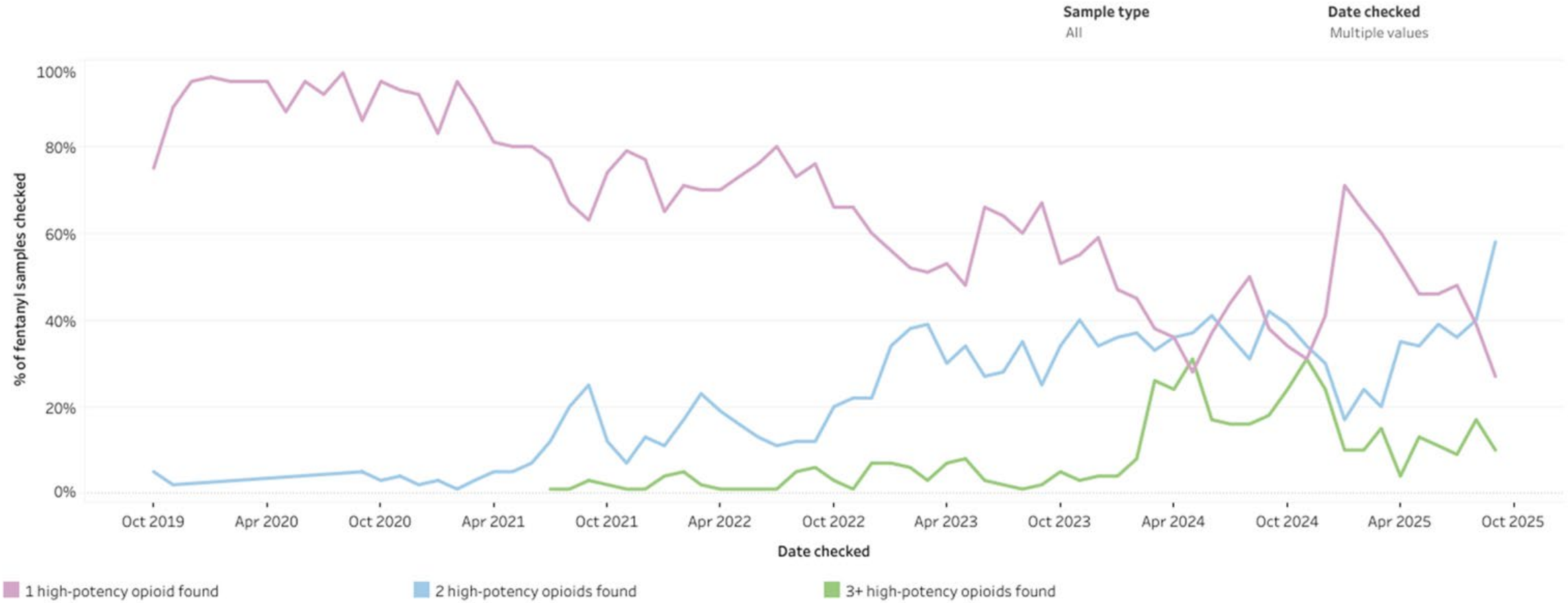
Number of high-potency opioids in expected fentanyl samples



Amount of drugs found

Expected drug	Drug found	10 mg vs percent	Date checked
Fentanyl	Fentanyl	% of total sample	Multiple values

Month	# of drug samples	Average* amount found (%)	Amount found in 50% of the samples was between (%)	Minimum amount found (%)	Maximum amount found (%)
All	3,352	3.0%	1.3% - 6.5%	0.1%	85.7%
Oct 2025	49	1.1%	0.7% - 1.6%	0.1%	13.5%
Sep 2025	94	1.0%	0.5% - 2.2%	0.1%	13.9%
Aug 2025	72	1.4%	0.8% - 2.6%	0.1%	18.1%
Jul 2025	55	0.6%	0.4% - 1.6%	0.1%	14.0%
Jun 2025	36	0.4%	0.2% - 1.2%	0.1%	9.5%
May 2025	50	1.0%	0.4% - 1.7%	0.2%	29.8%
Apr 2025	63	0.6%	0.3% - 1.6%	0.1%	8.7%
Mar 2025	114	1.4%	0.9% - 2.2%	0.1%	16.3%
Feb 2025	163	1.6%	0.8% - 2.2%	0.1%	20.4%
Jan 2025	137	2.0%	0.6% - 7.3%	0.1%	79.4%
Dec 2024	91	1.3%	0.8% - 8.6%	0.1%	37.6%
Nov 2024	113	0.7%	0.2% - 2.6%	0.1%	31.3%
Oct 2024	109	1.3%	0.4% - 3.7%	0.1%	29.2%
Sep 2024	32	3.4%	0.6% - 7.1%	0.4%	26.5%
Aug 2024	41	5.0%	3.3% - 11.6%	0.3%	28.9%
Jul 2024	50	4.4%	1.8% - 7.9%	0.3%	48.7%
Jun 2024	63	3.2%	1.0% - 6.5%	0.3%	49.0%
May 2024	54	2.8%	1.4% - 5.7%	0.1%	59.6%
Apr 2024	61	4.9%	1.9% - 9.7%	0.4%	36.0%
Mar 2024	47	5.8%	1.5% - 8.0%	0.1%	14.9%
Feb 2024	38	4.7%	2.9% - 8.2%	0.3%	70.6%
Jan 2024	90	6.0%	2.9% - 12.9%	0.3%	83.1%

Three main risk factors for Iatrogenic OD

- Low Opioid Tolerance
- Higher Starting Dose*
- Sedating drugs or substances

**vast majority of iatrogenic methadone toxicity cases in first two weeks tx*

Micky

- 40yo M - on methadone 130mg up to approximately 1 month ago, then stopped attending
- Using fentanyl 1gm + daily, smoking and injecting
- Crystal meth/crack – smoking, not daily
- No alcohol, BZD use

Medical Issues:

- Cellulitis L hand
- Bipolar

- UDS: + EDDP, +FYL, + COC, + MA, + BZD, +HM - OXY, - BUP

Considerations

- Opioid tolerance – daily use of at least 1gm of fyl = very high tolerance
- Risks for toxicity:
    - health conditions – no apparent risks re methadone
        - EKG fr 6 months ago, QTc 437
    - medications (off for past month)
        - aripiprazole 20mg OD
        - lorazepam 1mg BID
- Social hx:
    - criminal charges during period of use, not sure whether he'll be going to jail
    - couch surfing for now

Micky Continued

Very high tolerance AND No major risk factors for toxicity	40-50mg	<80mg: 15mg q3-5 days ≥80mg: 10-15mg q5-7 days	Daily fentanyl use of ≥1gm plus evidence of recent experience of high-dose methadone at a steady state *

- Plan to start methadone at 50mg
- Choose a pharmacy that is accessible to him, with flexible hours
- Review goals/importance of daily dosing, observing for sedation, strategies for managing fentanyl and CM use and reducing risks – review naloxone kit, access to inhalation and injection equipment and disposal
- Would you restart aripiprazole and lorazepam?
- Would you plan to have antibiotic daily dispensed with methadone as well?

Other questions

- UDS: is it necessary to get both MTD and EDDP, or is EDDP good enough?
- How do you factor benzodiazepine contamination into higher methadone starting doses? Does it put the patient at more risk of toxicity?
- Does Mickey's stimulant use concern you? What would you do if the QT was prolonged?
- Mickey misses doses frequently and isn't getting 3 consecutive doses. Is there anything that can be done to increase his dose?

Penny

63yo F, using fentanyl daily – snorts between ½- 1 gm/day

- Frequent ”small” ODs, near ODs
- No other regular substance use except tobacco
- On methadone over many years, more recently off OAT
- Just retried BUP XR but is continuing to experience withdrawal and cravings despite more frequent injections, resulting in ongoing use

Medical Issues:

- HIV+, remote endocarditis, remote Hepatitis C (cleared)

- UDS: + BUP, FYL, MOP, HM, BZD - EDDP, COC, MA, OXY

Considerations

- Shared decision-making re next OAT choice -> methadone
- Opioid tolerance – daily use of .5-1gm of fyl = high tolerance
- Risks for toxicity:
    - age
    - health conditions – no COPD, apparently normal liver function
    - medications:
        - enalapril
        - clonazepam .5mg BID longstanding
        - Bictarvy (bictegravir + tenofovir alafenamide + emtricitabine)

- Social history: Supportive housing, partner uses alcohol but not opioids

Drug interaction and QT checkers – Page 14 Methadone Guidance doc

- CYP450 inducers and inhibitors: **U.S. Food and Drug Administration website** https://www.fda.gov/drugs/drug-interactions-labeling/drug-development-and-drug-interactions-table-substrates-inhibitors-and-inducers
- QTC prolongation: **Credible Meds** https://www.crediblemeds.org
- Medication interaction checkers:
  - **Credible Meds**
  - Drugs.com's **Drug Interaction Checker** **https://www.drugs.com/drug_interactions.html**
  - Medscape's **Drug Interaction Checker** **https://reference.medscape.com/drug-interactionchecker**
  - Toronto General Hospital's **HIV/HCV Drug Therapy Guide** **https://hivclinic.ca/app/**

Penny Continued

High tolerance AND No major risk factors for toxicity	30-40mg	<80mg: 15mg q3-5 days ≥80mg: 10mg q5-7 days	

- Plan to start methadone at 40mg
- Choose a pharmacy that is accessible to her, with flexible hours
- Review goals/importance of daily dosing, observing for sedation, strategies for managing fentanyl use and reducing risks
- EKG + blood work
- Plan follow up in 4 days

Nicky

- 35yoF on 60mg methadone for almost 3 months
- Has been having a hard time getting to pharmacy -> doses not being increased
- Comes in after an ED visit for vaginal bleeding – 15 weeks pregnant
- Wants to continue the pregnancy, but is fearful because of previous negative experiences with obstetrical providers and CAS
- Since ED visit trying hard to reduce use but feeling significant withdrawal

- UDS + EDDP, FYL, BZD, + HM - MOP, COC, MA, BUP, OXY

Considerations

- Why is she having a hard time getting to the pharmacy?
- Opioid tolerance: until recently using 2-5pts of fentanyl most days, but over past week has reduced significantly
- Risks for toxicity: none
- Risks of withdrawal – pregnancy loss,

- Social history:
  - Stable housing, partner does not live with her, uses opioids
  - Kids 2 and 5 with grandparents

- Check last doses: missed 2 days ago but has had last 2 days and 4 of 5

Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
30 mg	30 mg	30 mg	miss	30 mg	45 mg
30 mg	30 mg	miss	30 mg	30 mg	45 mg
60 mg	60 mg	60 mg	miss	60 mg	75 mg
60 mg	60 mg	miss	60 mg	60 mg	75 mg
60 mg	miss	60 mg	miss	60 mg	60 mg*

*No increase on Day 6; dose can be increased when the patient has had four doses in the past five days.

(Bromley et al. 2021, p. 11, Table 2)

- How much would you increase her dose?

Criteria for Take-Home Doses

- Ability to store carries securely
- Amount of time on methadone
- Clinical and psychosocial stability
- Frequency of missed doses
- Recent substance use patterns
- Urine drug screen results

SIX GUIDING QUESTIONS FOR MAKING DECISIONS ABOUT CARRIES

1. Can the carries be kept **safe**?
2. **How long** has the person been taking methadone?
3. How is the person managing their responsibilities(i.e., **stability**)?
4. Does the person take **most of their observed doses**?
5. Are the person's recent **substance use patterns** lower or higher risk?
6. What do the person's **urine drug tests** show?

BASED ON THE ANSWERS TO THESE QUESTIONS, SOMEONE MIGHT BE ELIGIBLE FOR…

No carries (potential risks outweigh potential benefits)	Up to **3 non-consecutive** carries ~~Su~~ M ~~Tu~~ W ~~Th~~ F ~~Sa~~	**4 to 6** carries	**7 or more** carries

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Nicky Continued

- Start her with 3 carries – work with her to choose the most appropriate days
- Plan next dose increase before next visit
- When would you consider split doses? What do you do about carries with split doses?
- OB referral
- Other supports: Special diet, transportation, social work

More questions from September webinar

- What about the sugar in methadone mixed with Tang?
- *When do you consider testosterone replacement for people on OAT?
- *When do you stop extending methadone prescriptions?
- How do you manage virtual care for patients on methadone?
- Are there minimum standards for an EMR if you're prescribing methadone?
- How do you manage methadone overdose?
- *What is your approach if someone wants to taper methadone? If they are experiencing sweats and restlessness, when would you prescribe clonidine vs increasing the dose?

Summary

- Utilize a framework to guide decision-making with space for clinician judgement, self-awareness regarding prescribing experience, and patient input
- Choose starting dose and titration based on tolerance and risks of toxicity
- Offer options for follow-up (phone/video)
- Be proactive about communicating with patient and pharmacy
- Apply judgement and flexibility about dosing and carries as appropriate

Thanks!

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