MEDS Ed™

Welcome to:

Fentanyl: what to know – what to do – what's coming.

Our program will begin at 8:00 am!

Join our next Session: ***Substance use disorder in hospice, palliative care, and beyond.*** **Click to enroll!**

Join Our Next Session!

April 27th

Substance use disorder in hospice, palliative care, and beyond.

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Past sessions on video: http://www.careoregon.org/medsed

MEDS Ed™

Survey Completion for 2.5 Hours CME Credit:

Surveys will be emailed to all participants after the session

American Academy of Family Physicians – Prescribed credit, American Medical Association (AMA) Physician's Recognition Award (PRA) Category 1 Credits **2.5 hours**	**Oregon Board of Pharmacy –** Recognizes credits to toward CE hours requirements for license renewal! **2.5 hours**	**National Association of Social Workers –** LCSW CEU credits **2.5 hours**

Agenda (approximate timing)

5 minutes	**Welcome – Introduction** **Stacie Andoniadis (she/her) –** **Substance Use Disorder Integration Program Manager – CareOregon**
45 minutes	**Dr. Amanda Risser, MD, MPH, Senior Medical Director of Substance Use Disorder Services at Central City Concern** **Fentanyl Overview – What are we seeing? What is coming?**
45 minutes	**Jennifer Hartley PhD, MD, MSOM, Medical Director, Withdrawal Management – Fora Health Treatment & Recovery**
30 minutes	**Emily Skogrand, PharmD, Oregon Health & Science University Clinical Pharmacist**
30 minutes	Additional Q&A

Learning Objectives Include:

Participants will gain an:

- Understanding of how emerging additives like xylazine may impact the future of the fentanyl crisis.
- Understanding of best practices for OUD management in hospital and outpatient settings.
- Understanding of how to transition from fentanyl to buprenorphine/sublocade.

Introduction

Stacie Andoniadis (she/her) – Substance Use Disorder Integration Program Manager – CareOregon

Fentanyl: Overview

what are we seeing? what is coming?

Amanda Risser, MD MPH (she/her)

(Family, Preventive, Addiction Medicine)

Sr. Medical Dir. of SUD services, Central City Concern

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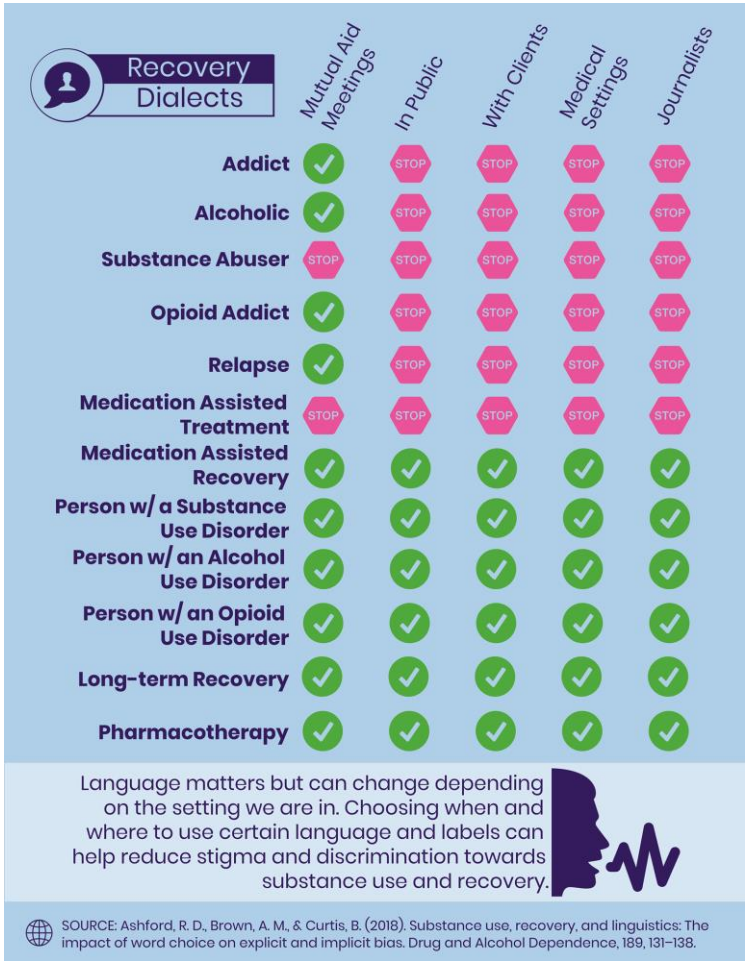
CareOregon

LANGUAGE and Drug Use

Linguistic research has shown that language can PROMOTE and MITIGATE stigma. Especially certain words like:

- "ABUSE"
- Language that is not person-first ("addict" "alcoholic")
- Clean/dirty
- Relapse vs Recurrence of use.

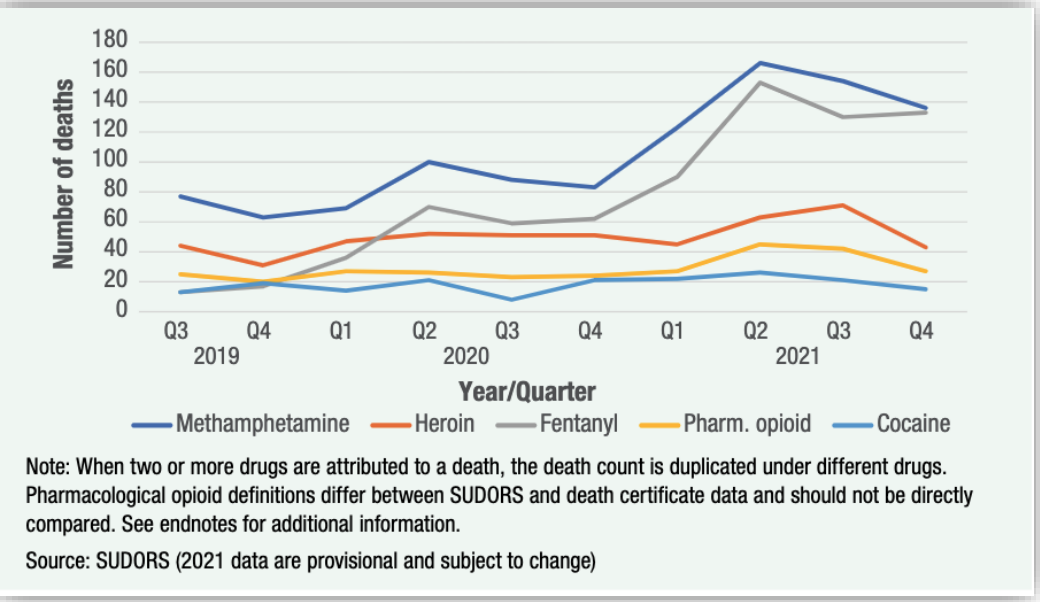


Fentanyl in Oregon

- We've been expecting fentanyl to arrive on the W. Coast since it started becoming an issue in the NE in 2017 and in Vancouver BC in 2015/2016.
- Fentanyl entered our state's drug supply in 2019.
- Fentanyl overdose deaths in Oregon increased by 600% in 2021 (509 individuals) compared to 2019 (71 individuals)- driven by fentanyl.

Data from OHA

Unintentional and undetermined overdose deaths by drug involved and quarter, July 2019-December 2021



Note: When two or more drugs are attributed to a death, the death count is duplicated under different drugs. Pharmacological opioid definitions differ between SUDORS and death certificate data and should not be directly compared. See endnotes for additional information.

Source: SUDORS (2021 data are provisional and subject to change)

From OHA publication "2022 Opioids and the Ongoing Drug Overdose Crisis in Oregon"
https://sharedsystems.dhsoha.state.or.us/DHSForms/Served/le2479_22.pdf

What is Fentanyl?

- A synthetic opioid: fentanyl and analogs.
- Unusual effects at receptor level- **high tolerance** to euphoric/analgesic effects in regular users **without** decreasing sensitivity to respiratory depression.
- Dangerous for incidental users, even when smoked.
- Lipophilic, distributes into tissues: short acting & long-acting characteristics.
- Dopamine activity more like methamphetamines than heroin.

What forms does it come in? How is it used?

Pressed pills, 30 mg oxycodone look-alike

Generally smoked: foil pipe or glass pipe, also swallowed.

Fentanyl Powder: can be smoked or injected

What else are we seeing?

- CONCURRENT use of fentanyl and methamphetamines is common.
- Non-fatal overdoses managed with Narcan by peers is common.
- Drug users are distressed about change in drug supply, safer supply is NOT available even when actively sought.

What else are we seeing?

- Increasing numbers of folks are INJECTING and we expect most users to resume injection use in the next 1-2 years
- Fentanyl has adulterated many other drugs: main contributor to teen and young adult overdoses when they think they're using alprazolam, Adderall, oxycodone.

What do we **expect** to see?

- Xylazine or "tranq dope" skin conditions (chronic wounds, infections) related to Xylazine.
- Novel synthetic benzodiazepine adulteration of fentanyl: "benzodope"
- A transition from smoked fentanyl to injected fentanyl.

Xylazine

A new adulterant we're expecting to come to our region (and may have already)

- Xylazine is an animal tranquilizer that has been an adulterant in opioids used on the east coast
- It causes localized vasoconstriction in the skin. This can occur remote from injection sites.
- INTOXICATION – sedation, bradycardia, hypotension, altered mental status, unconsciousness
- Is a concern both because of the intoxication and withdrawal syndrome but also because of the complication of wounds that are slow to heal and at risk for infection.
- Not seeing much morbidity yet- sporadic and not too severe so far in Oregon.
- We will likely see more as folks transition to injecting fentanyl.

Emerging: Sublocade

Sublocade is a monthly injection of long-acting buprenorphine that requires a 5-7 days of SL buprenorphine prior to injection.

Especially helpful for:

- Folks who have trouble transitioning on to and then staying on sublingual buprenorphine.
- Folks whose medication is frequently lost or stolen.
- People at high risk of overdose and/or who have experienced serious consequences of opioid use.
- People who are entering a jail system that doesn't support MOUD.

Sublocade and SL supplementation

- As we gain experience, we're learning that many folks are requiring SL supplementation in the first weeks to months.

- Research shows us that people who are not stabilized on SL buprenorphine prior to Sublocade injection are more likely to require SL supplementation.

- Some options:
  - 8-24 mg supplemental buprenorphine X 1-12 weeks
  - Maintain folks on 300 mg Sublocade for longer than 2 months is an option

Emerging: Methadone Demand

- There is some indication that methadone may be more acceptable for some fentanyl users
    - Some advantages to initiation compared to traditional buprenorphine starts.
    - Some advantages to treatment of withdrawal and cravings at appropriate doses.
    - In some communities affected by fentanyl: methadone treatment enrollment increased by 30-40% as fentanyl penetrated the drug supply.

Methadone is a fantastic medication! Significant barriers exist for many!

Emerging:
buprenorphine dosing > 24 mg

Low barrier providers in similar communities to ours (Olympia, Washington) or more remote communities (Ilwaco, Washington) have learned that around 20-30% of their buprenorphine patients are requiring doses of buprenorphine > 24 mg to treat their cravings and withdrawal symptoms.

High dose buprenorphine:

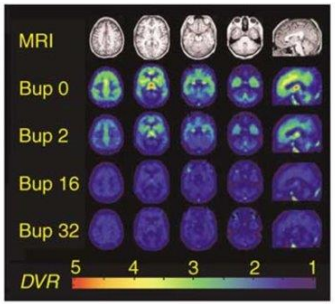
What is the evidence?

What about the 24 mg ceiling?

24 mg ceiling dosing based on studies done prior to 2003 (fentanyl entered drug supply nationally ~ 2013)

Slides from Cundiff et al.

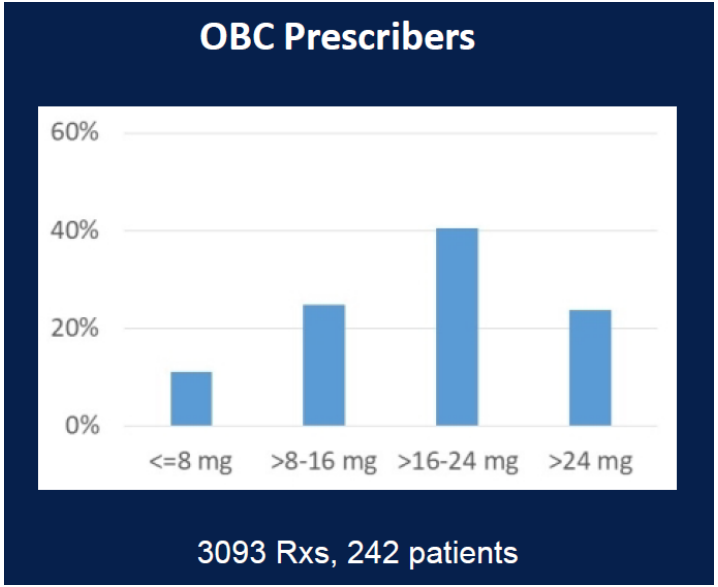
MU RECEPTOR OCCUPANCY (2003)



- Five heroin-dependent volunteers [no fentanyl!]
- Mu receptor occupancy (relative to placebo):
  - –2 mg/day: 27-47%
  - –16 mg/day: 80-92%
  - –32 mg/day: 89-98%

Greenwald et al, 2003

If we up titrate to effect, what should we expect?



This is unpublished data from an ASAM presentation from the April 2022 annual meeting. This shows that while the most individuals (40%) received dosing between 16-24 mg, a little over 20% are receiving dosing > 24 mg. I would expect our normal curve at CCC to be similar.

Fentanyl- near maximal receptor occupancy has clinical significance

MU RECEPTOR OCCUPANCY CONCLUSIONS

- **Buprenorphine dose-dependently increased mu receptor occupancy**
- **High receptor occupancy correlated with improved therapeutic effect: decreased opioid withdrawal and reward symptoms.**
- **Near-maximal effect occurred at 32 mg/day**

Slides from Cundiff et al, 2004

What about dosing > 32 mg

This will be rare!

32 mg seems like a “true” ceiling for most folks according to the data available at this time.

However, with individual variability in absorption and other physiologic variation, doses up to 36 mg are occasionally needed:

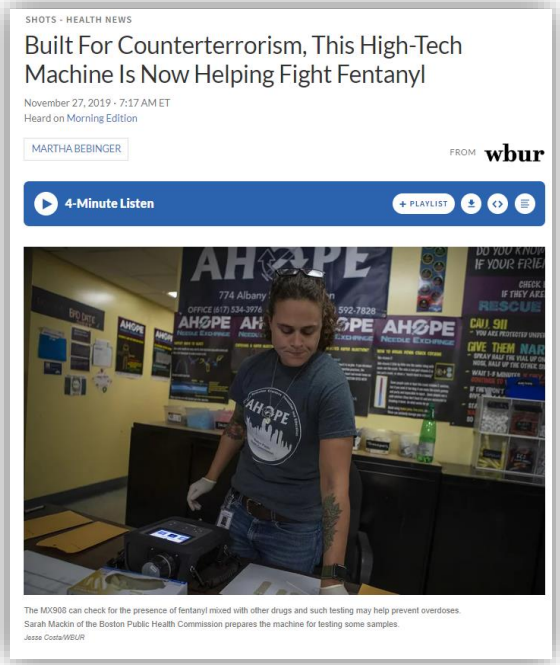
- Pregnancy, early recovery from high dose fentanyl use (first 3-6 months)
- During acute pain exacerbations.

ALSO, in the first few days of transition from fyl to buprenorphine.

Hot Topic: drug checking, drug supply

Fentanyl test strips and mass spectrometry: the drug supply is UNSAFE, how do folks stay safer?

- These machines can help identify adulterants and particularly risky substances in drugs that individuals are using.
- They can link with public health and help us follow trends and respond to emerging issues.
- In our community: Outside In's Drug Users Health Services has a mass spectrometer.

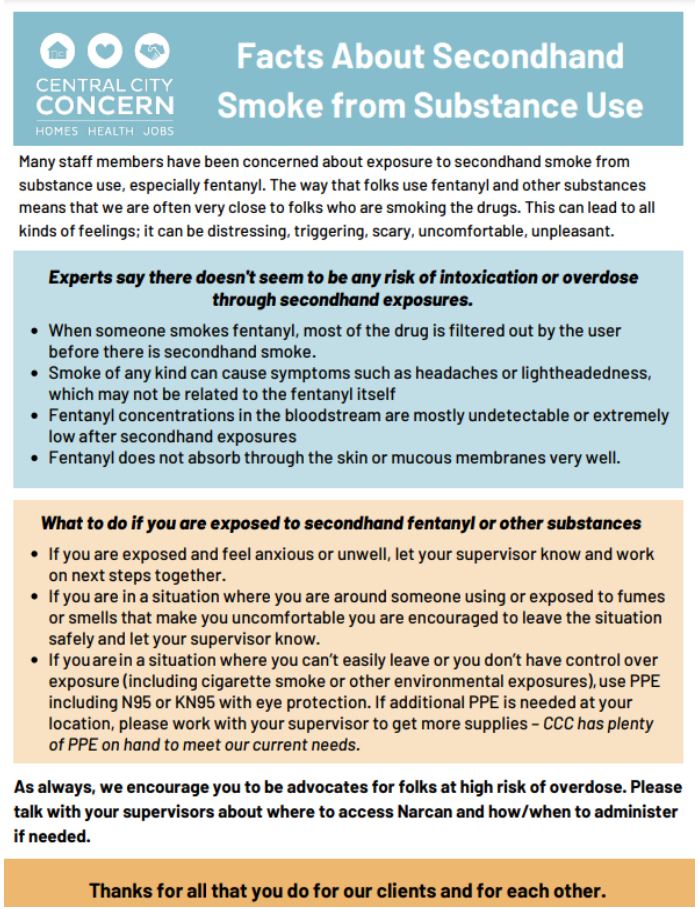


[NPR story about drug checking]

Hot Topic: topical or secondhand exposure to fentanyl.

"If I'm exposed to fentanyl smoke or if I touch fentanyl, am I at risk?"

- Short answer: no
- Stories about folks dying or becoming unconscious from second hand or topical exposure have all ended up being attributable to other etiologies: fainting, also using drugs, etc.



CENTRAL CITY CONCERN
HOMES HEALTH JOBS

Facts About Secondhand Smoke from Substance Use

Many staff members have been concerned about exposure to secondhand smoke from substance use, especially fentanyl. The way that folks use fentanyl and other substances means that we are often very close to folks who are smoking the drugs. This can lead to all kinds of feelings; it can be distressing, triggering, scary, uncomfortable, unpleasant.

Experts say there doesn't seem to be any risk of intoxication or overdose through secondhand exposures.

- When someone smokes fentanyl, most of the drug is filtered out by the user before there is secondhand smoke.
- Smoke of any kind can cause symptoms such as headaches or lightheadedness, which may not be related to the fentanyl itself
- Fentanyl concentrations in the bloodstream are mostly undetectable or extremely low after secondhand exposures
- Fentanyl does not absorb through the skin or mucous membranes very well.

What to do if you are exposed to secondhand fentanyl or other substances

- If you are exposed and feel anxious or unwell, let your supervisor know and work on next steps together.
- If you are in a situation where you are around someone using or exposed to fumes or smells that make you uncomfortable you are encouraged to leave the situation safely and let your supervisor know.
- If you are in a situation where you can't easily leave or you don't have control over exposure (including cigarette smoke or other environmental exposures), use PPE including N95 or KN95 with eye protection. If additional PPE is needed at your location, please work with your supervisor to get more supplies – *CCC has plenty of PPE on hand to meet our current needs.*

As always, we encourage you to be advocates for folks at high risk of overdose. Please talk with your supervisors about where to access Narcan and how/when to administer if needed.

Thanks for all that you do for our clients and for each other.

A note on overdose: recognition and response

Call 911 immediately if a person exhibits **ANY** of the following symptoms:

- Slumped over and not breathing
- Their face is extremely pale and/or feels clammy to the touch
- Their body goes limp
- Their fingernails or lips have a purple or blue color
- They start vomiting or making gurgling noises
- They cannot be awakened or are unable to speak
- Their breathing or heartbeat slows or stops

Respond according to Basic Life Support Training- assess Airway, Breathing, and respond with CPR or breathing support as appropriate.

CONSIDER Narcan if you have it available – it won't hurt someone not affected by opioids.

Fentanyl to Buprenorphine:
Practical Tools for Successful Transitions!

Jennifer Hartley PhD, MD (she/her) – Medical Director, Withdrawal Management – Fora Health Treatment & Recovery

Jennifer.Hartley@forahealth.org

Learning Objectives:

- Understand the practical challenges of fentanyl to buprenorphine transitions
- Understand the transition options available & how to help your patients think through what is the best approach for them
- Gain practical tools to help your patients through the process successfully and comfortably

Deep breath break –

- Transitioning patients onto buprenorphine from fentanyl can feel overwhelming.
- Yes, it can be challenging.
- It’s POSSIBLE!!!

The challenges:

- Fentanyl is STRONG.
- It is lipophilic and may remain stored in fat, “leaking” out over time.
- The withdrawal starts sooner, but precipitated withdrawal can occur much further out from last use, when compared with heroin withdrawal.
- Severe restlessness & anxiety often associated with withdrawal are difficult to manage.
- There is fear stemming from bad experiences and a belief that “you can’t get onto bupe from fentanyl”

Things that have changed –

- COWS is unreliable as a measure of when to start buprenorphine
  - Make sure patient has at least 2 objective signs of withdrawal

- Traditional 4 mg induction doses don't work well – they can precipitate withdrawal, and then it is very hard to get through the withdrawal.
  - Higher induction doses can be more effective

- Patients may require doses higher than 24 mg buprenorphine, at least initially, to adequately treat withdrawal and cravings.

Things that have changed –

The withdrawal experience can feel very different

- Restlessness can predominate and begin within several hours of last use

  "I feel like I need to get out of my skin"

- Severe back pain can occur

  "The dope is coming out of my back"

- Intense anxiety remains after maintenance dose of buprenorphine achieved

  "Don't you have anything that can make me feel better?"

Have a clear GAME PLAN –

- Know your patient
- Know your strategies
- Know your adjuncts
- Know your resources

Overview of fentanyl > buprenorphine options:

- Standard
  - COWS-based
  - Time-based
- Low Dose
- High Dose
- Combination: Low/High

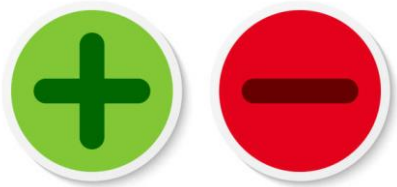
Let’s begin with the basics…

Some review and a bit of new

Standard: (home or WM setting)

- Patient reaches COWS of 16 with 2-3 objective WD symptoms
  - OR – Patient waits at least 48 hours
- Induction dose of 8 mg buprenorphine
- Increase by 8 mg doses q 20 min to 24– 32 mg

Standard:



ADVANTAGES

- Familiar approach
- Easy to keep track of hours
- No cutting tabs/films required
- Only need one size tablet

DISADVANTAGES

- Takes several days to stabilize
- Hard to be in withdrawal for that long
- Still possible to precipitate withdrawal and easy to give up at that point

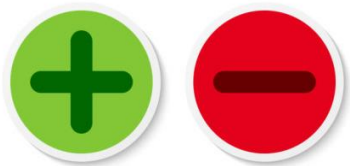
Low Dose:

- Patient starts small doses of buprenorphine while continuing to use fentanyl

- Day 1: 0.5 mg SL q 6 hours
- Day 2: 1 mg SL q 6 hours
- Day 3: 2 mg q 6 hours
- Day 4: 3 mg q 6 hours
- Day 4: 4 mg q 6 hours

- Day 5: Stop fentanyl use and take 24 mg buprenorphine + 8 prn

Low Dose:



ADVANTAGES

- Allows patient to “ease into things”
- Can be less frightening to begin
- Theoretically lower chance of precipitating withdrawal

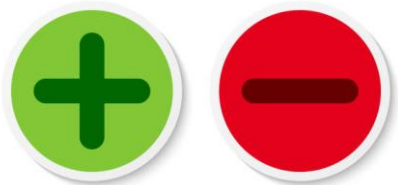
DISADVANTAGES

- Requires 2 different dose tabs
- Can be hard to stick to the “quit date”
- Most complicated method
- Takes a long time
- Anecdotally, some patients can have some withdrawal w 2 mg tabs

High Dose: (Home or WM setting)

- Wait at least 12 hours
- COWS of 16 + at least 2 objective signs of opiate withdrawal
  - Dilated pupils
  - Palpable piloerection
  - Runny nose
  - Diarrhea
- Give 16 mg buprenorphine
- Additional 8 mg as needed to 32 mg

High Dose:



ADVANTAGES

- Rapid transition
- Only one size tablet needed
- Overall simple process

DISADVANTAGES

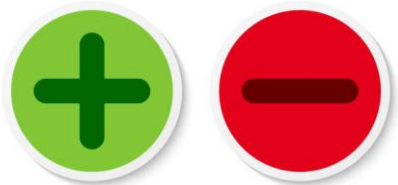
- Can be difficult for some to self-assess readiness
- If precipitated withdrawal occurs, likely to be severe

Low-High Combination

(Home or WM setting)

- Stop use of fentanyl
- 1 mg SL q 4-6 hours for 24 hours – or more – until in too much withdrawal to wait any longer
- Take 16-24 mg buprenorphine
- Additional 8 mg prn to 32-40 mg

Low-High Combination



ADVANTAGES

- Relatively rapid
- Initial low doses reduce fear around taking high dose
- Resensitization/upregulation of mu receptors with low doses may make high dose induction easier

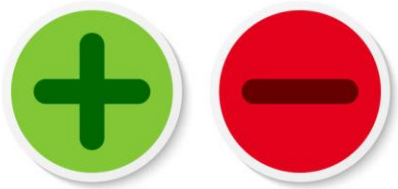
DISADVANTAGES

- Requires 2 different dose tabs
- Requires tracking time & number of doses

Quick Start: (Home setting)

- Patient self administers intranasal naloxone
- Immediately upon feeling withdrawal symptoms: take 24 mg buprenorphine
- Additional 8 mg bupe as needed

Quick Start:



ADVANTAGES

- Most rapid transition (under an hour)
- Can get onto maintenance bupe dose immediately

DISADVANTAGES

- For a short time, patient feels extremely miserable
- Requires high distress tolerance to manage

How do I choose which one to use?

- One size does NOT fit all –

- Get to know your patient (this is WELL WORTH the time ☺)
  - Past experiences
  - Current life situation
  - Goals: What's most important to them about their bupe start?

- Ask your patient what they have tried before and what they prefer

Assess Social/Emotional factors

- Any previous bad experiences?
- Safe place to be?
- Support resources – another person to be present and/or give meds & water/food?
- Trusting relationship with provider?
- Motivation level/Distress tolerance?
- Length of time patient has available to complete transition?

Assess medical considerations

- Withdrawing from other substances as well?

- Any other comorbidities?
  - HTN (severe/untreated)
  - COPD
  - Cardiac abnormalities
  - Psychiatric conditions
  - Chronic pain

Assess use pattern

- Number of blues daily

- Fentanyl powder?
  - Daily or less frequent?

- Any IV use of powder?
  - How frequently?

Assume that heroin is at least partially fentanyl powder

Reasons to consider inpatient withdrawal management:

- Concurrent regular use of alcohol or benzodiazepines
- H/O severe precipitated withdrawal/severe anxiety about process
- Unhoused and/or inappropriate housing situation (sole caregiver for children, etc.)
- Severe comorbidities
  - Uncontrolled HTN
  - Severe asthma
  - Anything serious that is triggered by stress!
- Overall low distress tolerance
- Very high use pattern with daily IV fentanyl use

To optimize outpatient success

- Switch from IV use to smoking at least one week prior to buprenorphine transition
- Taper over a week or two if using greater than 30 blues daily or fentanyl powder daily
- Sleeping helps. Start transition when very tired!
    - In the evening or stay up all night if starting in the morning

So, you're going to do this at home –

Great! *Proceed with confidence:*

- Once you've decided on a transition method, consider your comfort medications.
- Will the patient take them on a schedule or as needed?
- What adjuncts are important to the patient?
- What are you comfortable prescribing?

Helpful Adjunctive Medications:

- *For muscle spasms:*
  - Tizanidine: 2 mg QID
  - Methocarbamol: 1000 mg QID
- *For diarrhea:*
  - Loperamide: 2 mg QID
- *For nausea:*
  - Ondansetron: 4 mg tabs, 1-2 tabs QID
  - Promethazine: 25 mg TID
- *For anxiety:*
  - Clonidine: 0.1-0.2 mg QID
  - Diphenhydramine: 50 mg QID
  - Hydroxyzine: 50 mg QID

Helpful Adjunctive Medications:

- *For stomach cramps:*
  - Hyoscyamine 0.125 mg – 1-2 tabs QID
  - Dicyclomine: 20 mg QID
- *For restlessness/agitation:*
  - Gabapentin: 300 – 600 mg QID
  - Olanzapine: 5 mg BID or TID
- *For pain:*
  - Ibuprofen: 800 mg QID
  - Acetaminophen: 1000 mg QID
- *For sleep:*
  - Trazodone: 50-100 mg QHS (can also help w anxiety)
  - Quetiapine: 50-100 mg QHS
  - Mirtazapine: 15 mg QHS

Expert tip:

- For High Dose or Low/High Dose transitions, scheduling adjuncts can be very helpful.
- A support person to give the meds is ideal.
- If patient self-administers, a pill box is terrific.
- In either case, write out the schedule.

Getting ahead of withdrawal symptoms is easier than catching up, when a patient is already miserable and terrified!

Provide visual instructions

- Paper template
- Have the patient write down their own notes
- SOWS, adjunct list/schedule, affirmations

Tips for Withdrawal Management Setting:

- Build a structured “container” around the experience
- Identify and leap at the first sign of restlessness!
  - *Watch for the “telltale toe twitch”*
- Plan for some precipitated withdrawal and have a clear plan to manage
  - *Consider IM lorazepam*

Expert tip:

Don’t use 4 mg buprenorphine doses. They are large enough to precipitate withdrawal and get into a big hole but not large enough to get out of the hole successfully.

Non-Pharmaceutical Comfort Care:

- Aggressive Hydration
  - Sparkling water, Gatorade, herbal tea, ginger infusion, broth, Jell-O, popsicles
  - Have water bottles or flexible straws on hand
- Massage, especially back and calves
  - Try Vicks, Icy Hot, Tiger Balm
- Hot water bottle
- Walking/Stretching
- Shower/Bath
- Fan
- Essential Oils (do not put directly onto skin)
- Weighted blankets
- NADA acupuncture protocol with ear seeds
- Soft space/surroundings
- Human or pet companionship
- Music

Consider prescribing buprenorphine monoproduct for starts:

- Standard of care in inpatient settings
- Intolerance to naloxone exists and may be more common than we know
  - Nausea/vomiting
  - Headache
- When starting higher doses these symptoms are likely to be more severe
- Can switch to buprenorphine/naloxone at follow-up visit

Review sublingual technique:

- Moist mouth
- Nothing acidic before or after
- Take medication while sitting up
- Allow to dissolve fully & hold saliva for several minutes if possible
  - *Then it's okay to spit out saliva – remind patients!*
- Tucking the chin can help
- Crushing tabs can help – consider in WM setting or at home with the right patient

If precipitated withdrawal happens:

- Two strategies:
  - Push through with more bupe & adjuncts
  - Take a break, treat symptoms with adjuncts
- Talk these through with your patient ahead of time.
- It is also okay to just stop and try again with another plan.

Consider prescribing:

- 1-2 mg lorazepam

  or
- 10-20 mg diazepam

  or
- 25-50 mg chlordiazepoxide

to be used for any precipitated withdrawal

Expert tip:

For precipitated withdrawal:

Give 2 mg lorazepam with 16 mg buprenorphine

Additional helpful adjuncts for Precipitated Withdrawal (PW)

- If nauseated – 8 mg ondansetron
- If restless – 600 mg gabapentin
- If anxious – 5 mg olanzapine, 0.2 mg clonidine
- Severe back pain – 800 mg ibuprofen + 1 gram acetaminophen

Consider an office-based start:

- Make plan and send prescriptions for buprenorphine and adjuncts
- Start low dose at home for 1-2 days
- Have patient stop using the day before
- Patient comes into office with medications for high dose + adjuncts
  - Give benzodiazepine in the office with high dose buprenorphine
- Observe for 1-2 hours

Medical follow-up:

- Prepare your patient for adjustment period after induction of possibly several days
- Encourage rest, hydration/nutrition, and gentle exercise
- Plan for likely 32 mg dosing at least initially
- Have a ”Plan B”

Social follow-up:

- Provide follow-up number
- Call to check in within a day or two
- Engage peer support if possible

And never, never, NEVER underestimate…

The tremendous power of your attention, kindness, compassion and

LOVE

in helping people through this process.

This support can be the medicine that makes the difference!

References:

- Randal, Adam, et al. 2023. “Enhancing Patient Choice: Using Self-administered Intranasal Naloxone for Novel Rapid Buprenorphine Initiation” *Journal of Addiction Medicine* (September 23) DOI: 10.1097

- Gregg, Jessica, et al. 2023. “The Naloxone Component of Buprenorphine/Naloxone: Discouraging Misuse, but at What Cost?” *Journal of Addiction Medicine* (January) DOI: 10.1097

Hospital Management of Opioid Use Disorder

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CareOregon

Hospital Management of OUD

- Hospital is a reachable moment for treatment of OUD
  - At least 1 in 9 hospitalized patients in the US have an SUD
  - Many – especially in rural areas- don't have access to care elsewhere or experience large gap time to community treatment
  - Hospitalized pts with OUD die at rate similar to heart attacks (8% mortality)

- Interprofessional addiction consult services (ACS) improve patient and provider experience and outcomes, make hospitals more trauma-informed and responsive to needs of people who use drugs

- All hospitals should offer OUD basics, including acute withdrawal management and medications for OUD

- Confusion exists around legality of methadone and buprenorphine prescribing

Language Matters!

Reduce stigma by using the right words to chart

Avoid	Use
ABUSE, addict, drug abuser, junkie	Person with opioid use disorder, patient
Clean or dirty urine test	Negative or positive urine test, appropriate UDS, expected UDS
Opioid substitution therapy, MAT	Medication for opioid use disorder (MOUD)
Drug seeking	Reporting pain or cravings
Being clean	In remission or recovery

Fentanyl

Pharmacokinetics

- **Potent**
  - 30-50x more potent than heroin
  - 80-200x more potent than morphine
  - Very high affinity at the mu receptors
    - Euphoria, analgesia and respiratory depression

- **Lipophilic**
  - Rapidly crosses the BBB
  - Stored in fat cells and slowly leak out over days 7-14 days after last use, especially with recurrent use

Hospital Admission

Two important things to think of first

Supportive Medications

Naloxone

Naloxone

Administration

1. Check signs of overdose
    1. Slow, irregular breathing
    2. Blue/purple fingertips or lips
    3. Unresponsive to sternal rub
2. Remove nasal spray from package and place in person's nose
3. Press down on plunger
4. Place in rescue position
5. Call 911
6. Repeat in 2 minutes
7. Tell person that you administered Narcan once they respond

Naloxone

Risk Factors for Overdose

- Mixing opioid with alcohol or benzodiazepines
- Lowered tolerance after hospitalization, incarceration or drug treatment
- Co-occurring acute illness
- Change in drug supply
- History of overdose
- Using in a new environment

Naloxone and Fentanyl

- Increased need for *multiple doses* to reverse OD
- Higher doses are likely needed to exceed fentanyl concentrations in the CNS
- **Still effective in reversing fentanyl OD!**
- Commercially available as a 4 mg and 8 mg nasal spray
  - **Both covered on CareOregon formulary**
- Send prescription to pharmacy early in admission in case of patient directed discharge

Acute Withdrawal Management

Opioids:

- Opioids or buprenorphine are the mainstay of withdrawal management!
  - Methadone
  - Buprenorphine
  - Short acting full opioid agonist

- Partner with patients to determine which would be most helpful for them and what worked in the past

- Supportive Mediations

Acute Withdrawal Management

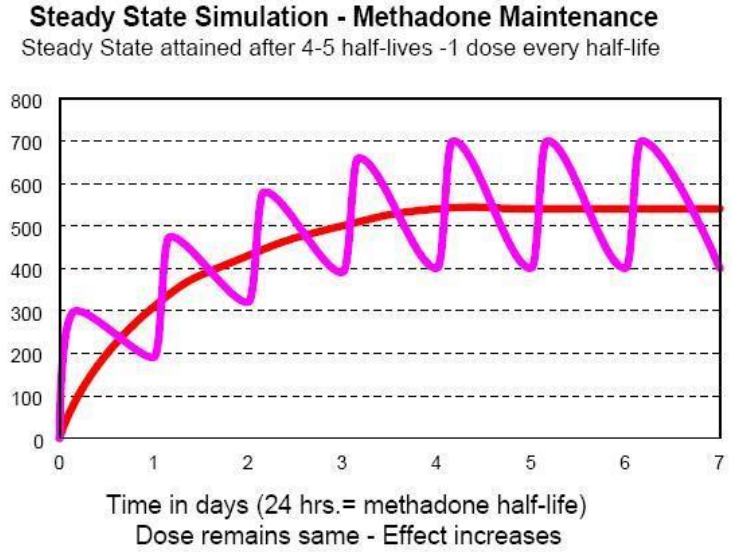
Supportive Medications

Medication	Indication
Tizanidine 2-4 mg every 6h as needed	Muscle spasms
Clonidine 0.1-0.2 mg 3 times daily as needed	Sweating or agitations
Hydroxyzine 25-50 mg every 4h as needed	Anxiety
Ondansetron 4 mg every 8h as needed	Nausea
Hyoscyamine 0.125 mg every 6h as needed	Abdominal cramping
Loperamide 2 mg 4 times daily as needed	Diarrhea

Methadone

Dosing Basics

- Full opioid agonist
- **Peaks in ~4 hours**
- Half life of 8-65 hours > long duration of action
- Reaches steady state at 4-7 days > requires careful dose titration
- Drug –drug interactions
- Controversy over when to check QTc
  - Use QTcF, not QTcB!
  - Reasonable to check baseline QTc
  - Generally, avoid if >500msec baseline
  - Risk vs Benefit discussion with patient if prolongation occurs with therapy



In the graph above the wavy line represents the blood levels of methadone as well as the "effect" it has on the individual patient.

Methadone

Is it legal to initiate or adjust methadone doses during hospitalization?

Yes!

Methadone

- 21 CFR limits methadone to federally licensed opioid treatment programs (OTP) for treatment of opioid use disorder BUT……

This section is NOT intended to impose ANY limitations on physicians or authorized hospital staff to administer to dispense narcotic drugs in a hospital to maintain or detoxify a person as an incidental adjunct to medical or surgical treatment of conditions other than addiction

- Allows for more freedom with methadone management in the hospital setting

Methadone

Induction Guidance:

- Don’t forget about your supportive medications!
- Partner with patient to discuss which are their most bothersome symptoms and let them know what they have available on their MAR
- Encourage patient to ask for specific medications
- Schedule medications if appropriate
- Utilize short acting opioids to manage withdrawal or craving while up titrating methadone

Methadone

Standard Induction:

Day	Scheduled methadone dose	As needed	Total daily dose
1	20-30 mg	10 mg x1 after 4 hours	40 mg
2	40 mg	10 mg x1 after 4 hours	50 mg
3	50 mg	10 mg x1 after 4 hours	60 mg
4	60 mg – Hold at 60mg and increase by 5-10 mg every 3-5 days		

Methadone

High Tolerance Induction:

- 10+ pressed fentanyl tablets a day or using powered fentanyl IV
- No clear standard
- Key is to rely heavily on appropriate doses of short acting opioids
    - Consider scheduling
- Use as needed methadone doses with clear max dose limits
    - Allows patient to decide when and if they are needed
- Spilt methadone dosing
    - If sedated 4 hours after dose, decrease the next dose

Methadone

High Tolerance Induction:

Day	Total methadone dose	Full agonist
1	40 -50mg	Oxycodone 15-30 mg q4h as needed
2	60 mg	Oxycodone 15-30 mg q4h as needed
3	80 mg	Oxycodone 15-30 mg q4h as needed
4+	Increase by 10-20 mg every 4 days to a max of 140mg	Oxycodone 10-20 mg q4h as needed

Methadone

Rapid Titration:

- Exclusions
  - End organ failure (ESRD, Cirrhosis)
  - Ventricular arrhythmias or QTc> 500
  - Concurrent use of benzodiazepine or alcohol
  - Age >65
  - Strong CYP 3A4 inhibitors

Methadone

Discharge Considerations:

- Adds extra complexity in care transitions and discharges planning
  - Many OTPs are closed on weekends
  - Limited hours or days for intake appointments
  - Often a barrier to SNF placement
- Best practice is to connect with methadone maintenance treatment on discharge
- Can not *prescribe* methadone
- ALWAYS prescribe naloxone
- If patient is not going to continue methadone at discharge, make sure they get their dose before they leave
  - Reduced tolerance and rushing to use> big overdose risk!

Methadone

72-hour Dispensing:

- 21 CFR had allowed for up to 72 hours of methadone ADMINISTRATION outside of OTP while arrangements were being made for follow up
- Updated federal code in 2021 to allow DISPENSING of opioids for up to 72 hours
- Eased discharge difficulties and saves hospital days
- Tricky to implement as it is outside of standard hospital workflow

Methadone

72-Hour Dispensing:

1- Apply for DEA exemption

- Pharmacy or Medical Director emails **ODLP@dea.gov**
- Request an exception to dispense 3 days of opioids to prevent withdrawal pursuant to 21 CFR 1306.07(b)
- Information should include institution name, address, DEA number
- Email does not need to include individual provider names

2- Find a pharmacy champion

- Process is heavily reliant on pharmacy for much of the work
- Helpful to have them available during initiation phase for real time troubleshooting

Methadone

72-hour Dispensing:

3- Dispensing Procedure

Procedure should contain step by step instructions of manipulations required in EMR

4- Develop Clinician workflows

Determine a standard for providers to communicate that methadone take home doses are needed

Develop standard EMR documentation of patient education

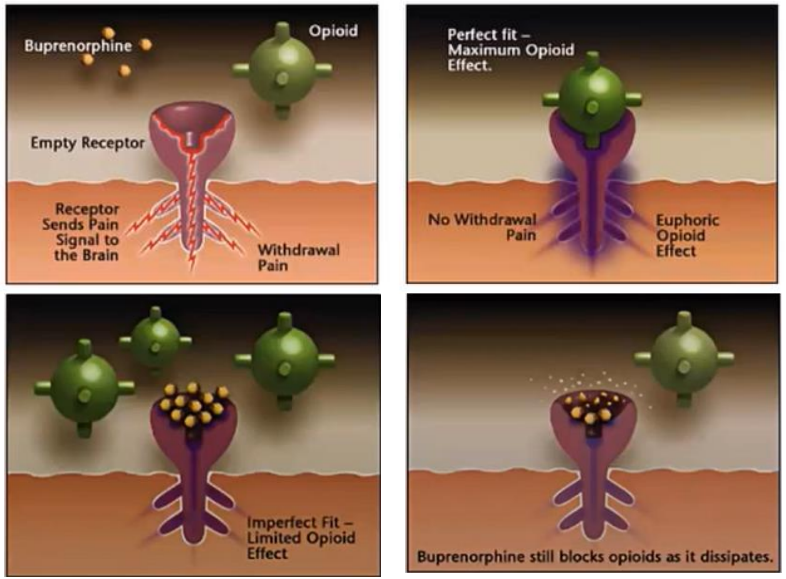
You were {started/continued} on methadone during your hospitalization. We dispensed (#) days of (#) mg of methadone to you at the time of hospital discharge with the plan for your methadone intake at the Opioid Treatment Program (specific name) on (date, time). Please do not throw out your empty containers. Bring them to your first visit at the methadone clinic to show clinicians there who may ask for them as proof of dose confirmation

5- Educate!

Buprenorphine

Basics:

- Partial opioid agonist
- High affinity at the mu receptor
  - Displaces other opioids from the mu receptor
  - Blocks other opioids from activating the mu receptor
- Long half life
  - Slowly dissipates from receptor
  - Blocking effects last for ~ 36 hours
- Ceiling effect
  - Effects max ~ 32 mg



Adapted from slide by Todd Korthuis, MD.

Buprenorphine

Administration:

- Tablets
  - Place under tongue
  - Keep under tongue for a minimum of 10 minutes and until tablet is completely dissolved
  - Do NOT need to swallow the saliva
  - Naloxone is not readily absorbed
- Films
  - Can be placed under the tongue or on the cheek
  - Do not overlap multiple films
  - Allow the film to fully dissolve

Buprenorphine

Administration in the Hospital:

- Not in medication cup!

- Put standard language on buprenorphine administration instructions on your EMR
  - DO NOT crush, chew or swallow whole. RN to observe administration. Place tablet under tongue until completely dissolved (may take up to 10 minutes). If 2 or more tablets are needed per dose, all may be placed under the tongue at once in different places. Do not eat or drink until tablets completely dissolved.

- Repeat full dose if accidentally swallowed
  - Bioavailability is very poor!

Buprenorphine

Multiple different ways to transition on to buprenorphine:

- Low dose induction
  - Greatly reduces the incidence of withdrawal, even in the setting of fentanyl
  - Takes at least 3 days to complete transitions
  - Complicated ordering if not utilizing an order set
  - May require formulary additions: patch, low dose films, quartering tablets
- Traditional induction
  - Withdrawal occurs
- California or Boulder Quick start
  - Withdrawal occurs
  - May be beneficial in ED

Buprenorphine

Critical to partner with patient on which method feels right for them!

Buprenorphine

Standard Low Dose Induction:

Day	Buprenorphine frequency	Total Daily Dose	Full Agonist
1	20 mcg/hr patch	~0.48 mg	Continue
2	1 mg twice daily x 2 doses	2 mg	Continue
3	2 mg twice daily x 2 doses	4 mg	Continue
4	4 mg twice daily x 2 doses	8 mg	Continue
5	6 mg twice daily x 2 doses	12 mg	Continue or stop
6	8 mg twice daily	16 mg	Continue or stop

Buprenorphine

Rapid Low Dose Induction:

Day	Buprenorphine schedule	Total daily dose	Full agonist	
1	20 mcg/hr patch	~0.48 mg	Continue	Leave on for full 7 days
2	1 mg three times daily	3 mg	Continue	0900-1500-2100
3	1 mg every 3 hrs x 6 doses	6 mg	Continue	0800-2300
4	1 mg once at 0600 8 mg once at 0900	9 mg	Stop or continue as appropriate for pain control	Can give additional buprenorphine dose in evening if needed

Buprenorphine

Low Dose Induction IV:

Day	Buprenorphine Schedule	Full Agonist
1	0.15 mg IV q6h x 2 doses	Continue
1	0.3 mg IV q6h x 2 doses	Continue
2	0.6 mg IV q6h x 2 doses	Continue
2	4 mg SL q6h x 2 doses	Continue
3	8 mg SL twice daily	Stop or continue if appropriate

Buprenorphine

Low dose induction:

How do I get 0.5 mg?

- Consider hospital policy
  - Stability for spilt films at 7 days but not quartered
  - Can nurses quarter tablet on the floor or it spilt dosing restricted to pharmacy
- Add patch to formulary
  - 20 mcg/hr patch = ~480 mcg buprenorphine per day
- Add Belbucca
  - Different bioavailability
  - 0.5m of Suboxone= ~ 225 mcg of Belbucca
- IV
  - Shorter duration of action so needs to be given more frequently

Buprenorphine

Traditional Induction:

- COWS of at least 14 in setting of fentanyl
- Supportive medications are very important!
- Preemptively have discussion with patient and describe how you will manage
  - Often confusing to give more of the medication that caused them feel awful
- Higher starting doses in setting of fentanyl

Buprenorphine

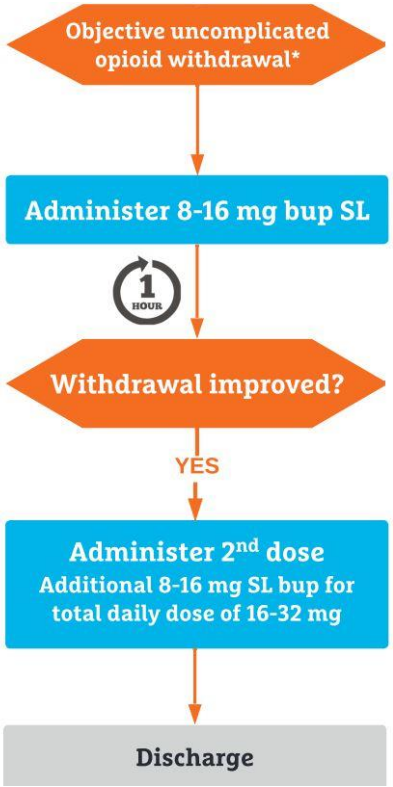
Traditional Induction:

Day	Scheduled	As Needed	Max Daily Dose
1	4-8 mg once COWS> 14	2-4 mg every 1 hour as needed for cravings/pain	16 mg
2	Total daily dose given on day 1 once in the morning	2 mg every 2 hours as needed for craving/pain	20 mg
3	Total daily dose given on day 2 once in the morning	2 mg every 2 hours as needed for craving/pain	24 mg
4	Total daily dose given on day 3 once in the morning		32 mg

Buprenorphine

California Bridge Quick Start:

- ED setting
- High risk of precipitated withdrawal in setting of fentanyl use
- Recommend treated precipitated withdrawal with an additional 16 mg of buprenorphine



Buprenorphine

Boulder Quick Start:

Induces withdrawal with self-administered naloxone

Buprenorphine 24 mg given immediately after naloxone

May not be ideal for inpatient initiation

Event	Time Elapsed, min	Time Between Events, min	COWS*
Last use of fentanyl	120 min prior		0
Premedication with clonidine 0.2 mg and gabapentin 600 mg	0	120	0
4 mg (1 spray) intranasal naloxone	36	36	NS†
GI upset ("stomach not feeling right")	38	2	NS
COWS measured	42	4	9
Vomiting (2 episodes of vomitus, 3 episodes of dry heaving)	45	3	NS
24/6 mg sublingual buprenorphine-naloxone at once	50	5	28
Buprenorphine-naloxone fully dissolved. Subjective withdrawal symptoms 0–10; he states that he is at a 4. Feeling tired.	60	10	NS
Discontinued visit to sleep	65	5	NS

Buprenorphine

In setting of fentanyl:

- Often need higher doses to control cravings> go up to **32 mg**!
- Higher risk of experiencing buprenorphine precipitated withdrawal if taken within 48 hours of last fentanyl use

	Buprenorphine* (N = 685)			Methadone† (N = 199)		
Odds of Severe Opioid Withdrawal Symptoms After Fentanyl Use	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Within 24 h of using fentanyl	5.202	1.979–13.675	0.001	0.616	0.117–3.247	0.568
Within 48 h of using fentanyl	3.352	1.237–9.089	0.017	0.300	0.035–2.606	0.275
Within 72 h of using fentanyl	2.222	0.780–6.329	0.135	0.316	0.036–2.750	0.297
Within 1 wk of using fentanyl	2.133	0.687–6.620	0.190	0.250	0.019–3.342	0.295

*Buprenorphine (also known as Belbuca, Buprenex, Butrans, Probuphine, Sublocade, Suboxone, and Zubsolv).
†Methadone (also known as Methadose).

Perioperative Buprenorphine

Continue!

- ASAM National Practice Guidelines
  - Discontinuation of buprenorphine before surgery is not required, Higher potency of full agonist opioids can be used perioperatively for analgesia
- Great harms in stopping or interrupting treatment
  - 50-90% incidence of returning to use or OD
- Vulnerable time for patients
- 1 mg of buprenorphine ~ 20 mg of morphine
- Spilt dose into TID
- Utilize appropriate doses of full agonist

Buprenorphine

Discharge Considerations:

- **No more X waiver!**
  - Any provider with scheduled III prescribing privileges can prescribe
- Prior authorization no longer required for doses above 24 mg for CareOregon patients
- Ensure prescription will last until follow up appointment
- Prescribe naloxone!

Patient Case

34 yo female presents to ED for treatment of abscess:

History: HepC and OUD> endorses using 10-15 mg of fentanyl tablets a daily. Previously on methadone and buprenorphine

Medications: Vancomycin 1gm q8h, Oxycodone 5 mg q6 hours prn pain

Labs: unremarkable. QtcF: 455 msec, blood cx + for MRSA

Exam: She endorses that she feels very anxious and restlessness. Noted to be sweating and tachycardic

Patient Case

Day 1

Methadone 30mg once and 10 mg q4h x 2 prn withdrawal/cravings or pain

Buprenorphine 20 mcg patch once

Oxycodone 15-30 mg q4h prn moderate pain or withdrawal, cravings

Supportive mediations

Day 2

Methadone 40 mg once and 10 mg q4h x 2 prn withdrawal/cravings or pain

Buprenorphine/ naloxone 1 mg SL TID

Oxycodone 15-30 mg q4h prn moderate pain or withdrawal, cravings

Supportive mediations

Patient Case

Day 3

Methadone 50 mg once and 10 mg q4h x 2 prn withdrawal/cravings or pain

Buprenorphine/naloxone 1 mg q3h x 6 doses

Oxycodone 15-30 mg every 4 hours as needed for moderate pain or withdrawal, cravings

Supportive medications

Day 4

Methadone 50 mg once

Buprenorphine/naloxone 1 mg at 0600
8 mg at 0900
8 mg at 1400

Oxycodone 15 mg every 4 hours as needed for moderate pain or withdrawal, cravings

Supportive medications

Patient Case

Day 5

Buprenorphine/naloxone 8 mg TID

Oxycodone 15 mg q4h prn moderate pain or withdrawal

Discharge Plan

Buprenorphine/naloxone 32 mg once daily

Naloxone Nasal Spray

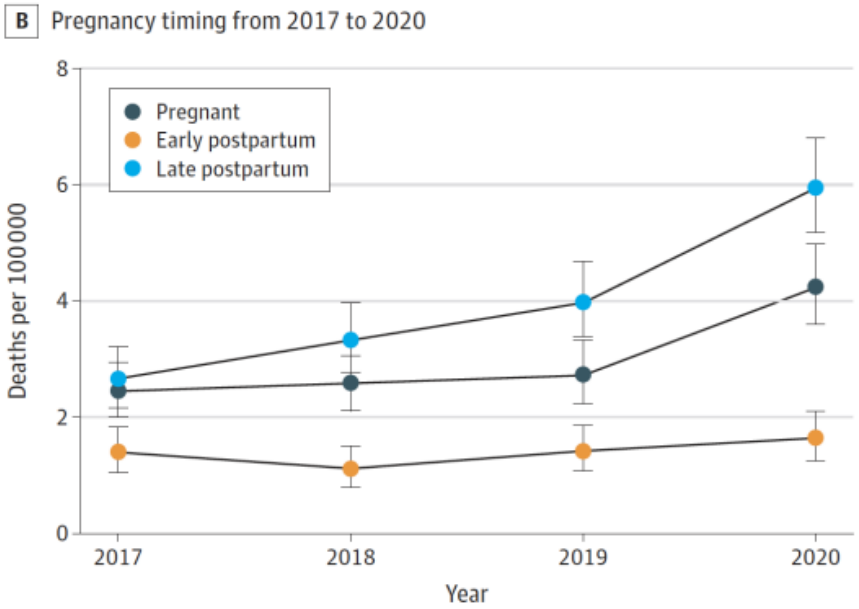
Linezolid 600 mg BID

Follow up in 3 days with PCP

Pregnancy

- 81% increase in pregnancy associated OD deaths since 2017
- Highest rise in postpartum

- Metabolic changes in pregnancy
  - Blood volume increases by 40-45%
  - Increase in CYP 3A4 metabolism > this can persist for 8-12 weeks post partum
  - Decrease in albumin
  - GFR increases by 25%



Pregnancy

- **ACOG recommends opioid agonist therapy with no preference of buprenorphine or methadone**

- Methadone
  - Plasma levels decline as soon as 10 weeks but biggest change in 3rd trimester
  - Spilt dosing and titrate!
  - Don’t immediately reduce dose postpartum!

- Buprenorphine
  - Spilt dosing
  - Titrate up to 32 mg
  - Mono product

- Naloxone at discharge!

Pregnancy

Rapid Methadone Titration

- Case report in 24-week pregnant patient

Day	Scheduled MMT (mg)	PRN MMT (mg)	Total MMT dose (mg)
1	30	10, 10, 10	60
2	30	10, 10, 10	60
3	30	10, 10, 10	60
4	60	10, 10, 10	90
5	60	10, 10, 10	90
6	60	10, 10, 10	90
7	90	0	90

- VERY LIMITED DATA!

Full Agonist Therapy

Not comfortable with either methadone or buprenorphine?

- Case series of 23 patients evaluated safety of short acting opioids for hospitalized patients with OUD
- Daily MME= 20-35 mg of oxycodone every 4 hours
- Naloxone administration was documented once in the operating room, over-sedation was documented once after unsanctioned opioid use, and there were no falls
- Lower patient directed discharges
- 65% of patient transitioned to methadone or buprenorphine at discharge

Thakrar, A.P., Uritsky, T.J., Christopher, C. *et al.* Safety and preliminary outcomes of short-acting opioid agonist treatment (sOAT) for hospitalized patients with opioid use disorder. *Addict Sci Clin Pract* 18, 13

Discharge Considerations

How to prepare for patient-directed discharge:

- Send naloxone RX early in stay and deliver to patient room if possible
- Have oral antibiotic treatment options noted in chart
- Harm reduction supplies

Harm Reduction

What is it?

- Evidence-based
- Set of practical strategies and ideas aimed at reducing negative consequences with substance use
- Values that people are the experts in their own experiences
- “Acknowledges that many people are not able to willing to abstain from drug use and that abstinence should not be a precondition to help.”

HarmReduction.org

Harm Reduction

Partner with person on what they are most concerned about:

- Naloxone
- Sterile syringes
- Smoking over IV use
- Fentanyl test strips
- Wound care kits
- Safer sex
- Oral care

Wound Care Kit

Safer Sex Kit and Oral Care Kit

Syringes and Sharps Containers

Harm Reduction

Resources:

Neverusealone.com

NextDistro.org

Harmreduction.org

Help!

OHSU Addiction Consult Line

503-494-4567

Ask for **addictions consult line** to be connected with an addiction physician

Help!

Targeted education or assistance in developing order sets or policies

Skogrand@ohsu.edu

References

1: Englander, H., Dobbertin, K., Lind, B.K. et al. Inpatient Addiction Medicine Consultation and Post-Hospital Substance Use Disorder Treatment Engagement: a Propensity-Matched Analysis. J GEN INTERN MED 34, 2796–2803 (2019). https://doi.org/10.1007/s11606-019-

2: Botticelli MP, Koh HK. Changing the Language of Addiction. *JAMA.* 2016;316(13):1361–1362. doi:10.1001/jama.2016.11874

3:Lexicomp Online,. Waltham, MA: UpToDate, Inc.; July 30, 2021. https://online.lexi.com. Accessed Feb 19, 2023.

4: Button D, Hartley J, Robbins J, et al. Low-dose buprenorphine initiation in hospitalized adults with opioid use disorder: a retrospective cohort analysis. J Addict Med 2022;16(2):e105–e111

5: Sokolski E, Skogrand E, Goff A, Englander H. Rapid Low-dose Buprenorphine Initiation for Hospitalized Patients With Opioid Use Disorder. J Addict Med. 2023 Jan 17. doi: 10.1097/ADM.0000000000001133. Epub ahead of print. PMID: 36728082.

6: Varshneya, Neil B. PhD; Thakrar, Ashish P. MD; Hobelmann, J. Gregory MD; Dunn, Kelly E. PhD, MBA; Huhn, Andrew S. PhD, MBA. Evidence of Buprenorphine-precipitated Withdrawal in Persons Who Use Fentanyl. Journal of Addiction Medicine ():, November 23, 2021. | DOI: 10.1097/ADM.0000000000000922

7: Randall, Adam DNP, FNP-C; Hull, Ilana MD, MSc; Martin, Stephen A. MD, EdM, FASAM, FAAFP. Enhancing Patient Choice: Using Self-administered Intranasal Naloxone for Novel Rapid Buprenorphine Initiation. Journal of Addiction Medicine ():10.1097/ADM.0000000000001073, September 23, 2022. | DOI: 10.1097/ADM.0000000000001073

8: 21 CFR 1306.07 -- Administering or dispensing of narcotic drugs., n.d., Code of Federal Regulations

9: Buresh M, Nahvi S, Steiger S, Weinstein ZM. Adapting methadone inductions to the fentanyl era. J Subst Abuse Treat. 2022 Oct;141:108832. doi: 10.1016/j.jsat.2022.108832. Epub 2022 Jun 27. PMID: 35870437.

11: Randa Abdelal, A. Raja Banerjee, Suzanne Carlberg-Racich, Neyla Darwaza, Diane Ito & Josh Epstein (2022) The need for multiple naloxone administrations for opioid overdose reversals: A review of the literature, Substance Abuse, 43:1, 774-784, DOI: 10.1080/08897077.2021.2010252

12: Sarah Ickowicz & Mark McLean (2022) Case report: rapid inpatient methadone titration during pregnancy, Journal of Substance Use, 27:4, 418-421, DOI: 10.1080/14659891.2021.1953167

13: Moss, R.B., Carlo, D.J. Higher doses of naloxone are needed in the synthetic opioid era. *Subst Abuse Treat Prev Policy* **14**, 6 (2019). https://doi.org/10.1186/s13011-019-0195-4

Q&A

Questions submitted via Chat feature

Join Our Next Session!

April 27th

Substance use disorder in hospice, palliative care, and beyond.

Click to enroll!

Past sessions on video: http://www.careoregon.org/medsed

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- Survey will be emailed to all enrolled participants

Thank you!