

Part One

1. Welcome to an episode where we'll review something we all probably wish we knew less about: Prescription Opioid Overdose
 - a. Here we'll:
 - a.i. Go over some compelling statistics;
 - a.ii. Review the classic presentation of opioid OD;
 - a.iii. Talk though Narcan dosing options;
 - a.iv. Run a case;
 - a.v. Discuss observation times and the disposition of an opioid OD patient *and*
 - a.vi. Review a bunch of cool best-practice guidelines for how to optimize use of the opioids that we have in our formularies.
 - b. The good news that there's a lot that we can do, for ourselves, for medicine and most importantly, for our patients, to optimize management, maximum good outcomes and minimize harm.
2. But First, some bad news:
 - a. **Drug overdose currently the leading cause of injury death in the United States.**¹
 - a.i. From 2000 to 2014 nearly half a million Americans died from drug overdoses.²
 - a.ii. **Every 6 out of 10 deaths from drugs was an opioid drug death.**
 - a.ii.1. Most of those opioid drug deaths were from **oxycodone and hydrocodone.**^{3, 4}
 - b. What's important to remember about the morbidity and mortality from opioids?
 - b.i. **"The number of opioid analgesic overdoses is proportional to the number of opioid prescriptions and the dose prescribed."**⁵
 - c. In 2012, we prescribers wrote 82.5 OPR prescriptions *per* 100 persons in the United States.⁶
 - c.i. Most Rx's were for oxycodone, hydrocodone, and methadone.
3. A lot of scripts mean a lot of ED Admissions from opioid ODs and a lot of calls to poison control.
 - a. In a four-year period, between 2004-8, 144% increase in ED visits due to *oxycodone overdose alone.*⁷
 - b. Analgesics were the #1 reason for calls to the poison control center in 2014⁸ and 2013⁹...and also 2012...you get the idea.
4. So **who is the risk group?** What are the biggest red flags?
 - a. One is **history of use and abuse**, obviously. That population always raises a flag.
 - b. Another population that should raise flags the **patients who historically get the most scripts.**
 - b.i. By age, these are the **45-54 and 55-64 year-old age groups.**
 - b.ii. By gender, its a slight majority female.¹⁰
 - c. The third big risk factor, besides age and history of use/abuse, is **polypharmacy.**

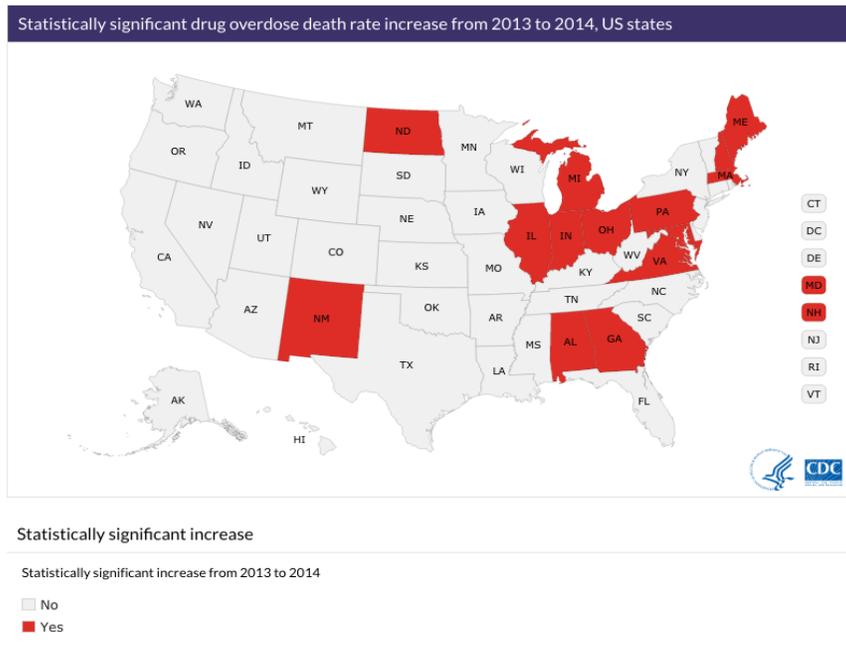


Figure 1 From the CDC

c.i. A 2015 study found that **patients who died from opioid ODs had an average of 21 prescriptions, from 4.5 different providers, and 3 different pharmacies.**¹¹

c.i.1. They were poly *everything*, not just polypharmacy.

d. The patient statistically most likely to OD on prescribed opioids is a 45-65 yo with polypharmacy.

5. Opioid Overdose Presentation

a. Recognition of the **opioid toxidrome**

a.i. Opioid toxicity is the classic triad of **respiratory depression, CNS depression, and miosis.**

a.ii. Pinpoint pupils and a RR of 4 should trigger suspicion of opioid OD every time.

a.ii.1. Let's look at each of these quickly.

b. **Opioid OD Triad Part 1: Respiratory Depression**

b.i. The respiratory depression is a **decrease in both tidal volume and respiratory rate.**

b.i.1. The effect is dose-dependent.

b.i.2. D/t reduced sensitivity of the user's respiratory medullary center.

b.i.2.a.i. Ingesting opioids makes the user's brain less aware that there's hypercapnea.

c. **Opioid OD Triad Part 2: Miosis**

- c.i.1. The miosis is due to stimulation of receptors in the Edinger-Westphal nucleus of the 3rd cranial nerve
 - c.i.1.a.i. If you haven't read those words since medical school you're not alone.
 - c.ii. **Miosis in opioid overdose is not universal.**
 - c.ii.1.a. Synthetic opioids like meperidine don't affect the Edinger-Westphal nucleus, nor will Lomotil, or diphenoxylate-atropine.
 - c.ii.1.a.i. **Miosis, while very common in classic opioid OD, may not be present in all cases of toxicity.**
 - d. **Opioid OD Triad Part 3: CNS depression**
 - d.i. That's due to stimulation of mu receptors.
 - d.i.1. Excitability happens too, especially when you reverse the high too quickly.
 - d.ii. Less well-known **other CNS symptoms:**
 - d.ii.1. Hypertonicity
 - d.ii.2. Myoclonus
 - d.ii.3. Parkinsonian symptoms
 - d.ii.4. Seizures have also been reported, particularly with the use of synthetic opioids like meperidine.
 - d.ii.4.a.i. As mentioned in Rosen's, the seizures are attributed to either hypoxia or accumulation of opioid metabolites like normeperidine.
 - e. Some lesser-known & substance-specific symptoms to watch out for.
 - e.i. **Mild orthostatic hypotension and relative bradycardia.**
 - e.i.1. The hypotension may be caused by histamine release.
 - e.i.1.a. According to Rosen's, can be treated with antihistamines or laying the patient down.
- 6. Let's try this out on a case.
 - a. **47-year-old woman** arrives via EMS.
 - a.i. Found down at home by her son who called EMS approximately 15 minutes prior.
 - a.ii. Hx: **Only pertinent history is chronic back pain** s/p multiple surgeries. According to her son, patient has been complaining recently of increased pain. He knows that **she takes something for it**, but doesn't know what.
 - a.iii. On arrival to the scene the BLS unit recorded VS: HR 42, RR 4, BP 102/65, satng 85 with a GCS of 7.
 - a.iv. **Gave 2 mg of Narcan IM.**
 - a.iv.1. En route, they got IV access.
 - a.v. VS on arrival 10 min later: HR 57, RR 7, BP 109/70, GCS 8.
 - b. **Our primary concern is ABCs, assessment, and stabilization.**

- b.i. Even if the patient is found down with a needle in their anti-cub and a long hx of opioid abuse, **the primary things that we're worried about** are the same things we're always worried about:
 - b.i.1. Hypoxia**
 - b.i.2. Cardiac arrest**
 - c. Whatever dose of Narcan you eventually decide to give, whatever route you decide to give it, the first steps with opioid-OD patients are the same first steps as with every patient: ABCs. Or CABs with a code.
 - c.i. Get on a monitor and oxygenate the heck out of them.**
 - c.i.1. If the heart's not working, pump it.
 - c.i.2. If they aren't oxygenating well, give O2.
 - c.ii. If they are apneic: bag them and start Narcan.
 - c.ii.1. That may buy us just a bit of time before intubating.
 - c.iii. If they have any respiratory effort:
 - c.iii.1. Throw on a NC plus a NRB. Crank it up to 15 LPM.
 - c.iii.2. Try a jaw thrust while you're getting the Narcan started.
 - c.iii.2.a. May help stimulate them to breath.
 - d. **We do all that for our patient.** Assess, stabilize, seek out, and treat easily reversible causes of AMS.
 - d.i.1. **Opioid OD and hypoglycemia**
 - d.i.1.a. And (maybe) thiamine deficiency.
 - e. **ABCs for this patient.**
 - e.i. We secure the airway.**
 - e.i.1. Airway patent.**
 - e.i.1.a. I like to throw in an OPA to keep it that way.
 - e.ii. Breathing**
 - e.ii.1. Still at 7/min.**
 - e.ii.2. We put the NC on, crank up the NRB and try a jaw thrust..**
 - e.ii.3. She is sating at 94% .**
 - e.iii. Circ**
 - e.iii.1. The patient is hooked up to a monitor.
 - e.iii.2. We getting and reading her first **EKG.**
 - e.iii.2.a. HR 62 regular sinus**
 - f. Getting a **finger stick.**
 - f.i. Fingertstick glucose is **80.**
 - g. Administering **Narcan.**
 - g.i. She's sating well, breathing at about 7/min.
 - g.ii. with no improvement in mental status we're going to give Narcan
 - g.ii.1. With the goal of safely waking the patient up to get a story.
7. Narcan, our good buddy the highly-competitive opioid receptor antagonist.
- a.i. There are dozens of possible doses and routes of administration.

- a.ii. What's the best choice for our patient?
- b. The best choice depends upon history and presentation.
- c. In general, there are *only two ways give Narcan*:
 - c.i. 1: Code Dosing**
 - c.i.1. 0.4 mg IV/IO/IM.**
 - c.ii. 2: Wake-up Dosing**
 - c.ii.1. Everyone not coding or apneic.**

8. Narcan Code Dosing

- a. If your patient is in arrest or apneic.**
 - a.i. **0.4 mg for an acute overdose.**¹² VERY acute overdose.
 - a.i.1. With apnea, seizure, and/or cardiac arrest.
 - a.ii. When I was an EMT when we found someone down we grabbed a handful of 1 ml vials of .4mg/ml Narcan and got to work.
 - a.ii.1. If the patient isn't breathing that may be appropriate.
- b. Any patient who is breathing merits something a gentler.**
 - b.i. Gentler = "Nice Narcan Wake-up" dosing.
 - b.ii. For the opioid OD patient with respiratory drive.
 - b.iii. For the ED physician who does not want their patient to be an angry, puking, mess.

9. Nice Narcan Wake-Up Dosing: For patient and physician comfort.

- a. Six routes and a lot of doses.**
- b. To choose correctly, keep it simple and remember the goals.
 - b.i. Goal #1: Titrate to adequate ventilation.**
 - b.ii. Goal #2: Ideally, the ability to give a good history.**
 - b.iii. Goal #3: Avoid precipitating an acute withdrawal.**
 - b.iii.1. Acute w/d is a harm that we should try to avoid.
 - b.iii.2. One of my captains used to put Narcan down the ET tube and the results were catastrophic.
 - b.iii.3. Steve Carroll, whose podcast this is, knows of a cancer patient who had Narcan slammed on for a bit of respiratory depression and later described it as "razor blades being jammed all over" his body.
 - b.iv. Opioid-OD patients often have altered mental status, so we don't consider the potential pain involved in acute withdrawal.
 - b.iv.1. We should.
- c. This patient is a great example: she is very altered, but she's also breathing. No reason to slam on the Narcan.**

c.i. She gets a Nice Narcan wake-up.

10. Nice Narcan Wake-ups 1 - 6

- a. Nice Narcan Wake-Up #1: Low IV dosing**
 - a.i. **Starting adult dose = 0.1 mg**

- a.i.1. **0.1 mg for the chronic user** who has gone a little too far, like our patient.
- a.ii. **Repeat or increase the dose every 2-3 minutes.**
 - a.ii.1. To a **max dose: 2-10 mg**
- b. Nice Narcan Wake-Up #2: Narcan by Neb**
 - b.i. **2 mg in 3 ml NS.**¹³
 - b.i.1. **If your patient is breathing > 6 times/min.**
 - b.i.2. There's a link to a paper that discusses [nebulized narcan](#) dosing and outcomes in the show notes.
- c. Nice Narcan Wake-Up #3: Gentle IVP.**
 - c.i. If the patient is breathing at all, instead of giving 0.4 mg or even 0.1 mg of Narcan, you can give **0.04mg by slow IVP.**
 - c.i.1. Dilute that 1 mg vial into a 10 ml syringe with 9 ml of NS, and push a 1 ml every 60 seconds.
 - c.i.2. This method & the rationale behind using it are described in the [ALIEM podcast](#).
- d. Nice Narcan Wake-up #4: Narcan IM**
 - d.i. IM Narcan is what I was raised on, so to speak.
 - d.ii. It's great if you don't have access, and even if you do. It's easy.
 - d.ii.1. In the field, we would start at **0.1-0.2 mg IM and titrate to effectiveness by re-dosing every 2 min.**
 - d.ii.1.a. 0.2-every-2 is easy to remember.
 - d.iii. It woke people up enough to give us a story while not precipitating AAS: Acute Anger Syndrome.
 - d.iv. IM has a milder onset of action than IV.
 - d.v. This technique is losing favor because now we have a great new technique to play with, something we've been working towards for a long time.
- e. Nice Narcan Wake-Up #5: Narcan IN**
 - e.i. Narcan without the needle. Just the antidote we've all been waiting for!
 - e.ii. Unlike Narcan neb or Gentle IVP, Narcan IN **CAN be given as a 1st-line to an apneic patient.**
 - e.ii.1. The history of trying to make IN Narcan work is kind of interesting.
 - e.ii.1.a.i. I'm putting [a link to a paper called in the show notes](#) if you're interested.
 - e.ii.1.a.ii. The short version is that people have been experimenting with introducing Narcan intranasally for years, in the field and in the department, without a lot of luck.
 - e.ii.1.a.iii. The bioavailability just wasn't high enough (~4%).

- e.ii.2. We finally upped the effective Narcan concentration in the atomizers, so IN Narcan is now being used basically everywhere we can get it to.
 - e.iii. **1 mg per nostril in each nare via atomizer for a total of 2 mg IN.**
 - e.iii.1. If the patient has some respiratory effort, **feel free to start with 1 mg in 1 nostril, and wait for 2 min to give the other 1 mg.**
 - e.iii.2. **Just be sure to minimize run-off after administration.**
 - e.iii.2.a. **I.E. lay the patient down**
 - e.iii.3. These doses are pre-measured in the kits, but if you're making it up yourself, get the concentration to 1 mg/mL.
 - e.iv. A lot of good news with IN Narcan
 - e.iv.1. Generally, it **works well as long as the nares are patent and the patient doesn't have any abnormal physiology.**
 - e.iv.2. There's **no risk of provider needle-stick**, which is a great thing in all patients and in this high-risk population in particular.
 - e.iv.3. IN Narcan is **a lot faster to administer than IV Narcan.**
 - e.iv.3.a.i. A little more than twice as fast.¹⁴
 - e.iv.4. With the lower bioavailability of the trans-nasal route, **reversal of the overdose should be a gentler process.**
 - e.v. The less good news with Narcan IN is that **non-response is still occasionally an issue.**¹⁵
 - e.v.1. Especially in a patient with a history of intra-nasal drug use, trauma, or recent URI.
 - e.v.2. In the field, if non-response occurs with IN Narcan, IM is the rescue route of choice.
 - e.v.3. In the hospital, if you've tried IN first-line, w/ no response, and the patient's respiratory effort is poor:
 - e.v.3.a. You can't go by neb.
 - e.v.4. If it's non-existent:
 - e.v.4.a. You can't go by IVP
 - e.v.5. And if you don't have good IV access:
 - e.v.5.a. You can't go IV.
 - e.vi. In that case, you might go IO, so let's talk about that really quickly.
- f. Nice Narcan Wake-Up #6: Narcan IO**
- f.i. Great for peds who got into the parents' oxycodone supply.
 - f.i.1. **Peds Narcan dosing is 0.1 mg/kg IV/IM/IN/IO up to 20 kg.**
 - f.ii. For adults if that's the access that you have.
 - f.ii.1. IO dosing for adults is the same as it is for Narcan IV: 0.1 for anyone not coding or apneaic, 0.4 mg for the code.
- g. Narcan IV infusion**

- g.i. In the field, we could usually find the effective dose rapidly enough. A problem arose if we had a transport of more than 30 minutes: the patient would sometimes become somnolent again.
 - g.i.1. That's because the half-life of Narcan is 30-90 minutes, which is shorter than the half-life of most opioids other than pure heroin.
 - g.i.2. As awesome as Narcan is, it's just an antagonist.
 - g.i.2.a. It doesn't actually remove any opioid from the patient's system.
 - g.i.2.b. Long-acting opioids may well need an infusion.
 - g.ii. In the department, this often becomes important when your patient has OD'd on methadone.
 - g.iii. Narcan infusion dosing and rate**
 - g.iii.1. ***2/3rd of the "Nice-Narcan Wake-Up", aka the effective dose, per hour.***
 - g.iii.2. Also: To prevent a precipitous drop in Narcan levels and having the patient drift off again, it is recommended that you ***administer 1/2 of the initial wake-up dose as a bolus 15 min after initiating continuous IV infusion.***¹⁶
 - g.iv. **This infusion rate is good for any initial route of administration, IM, IV, IO or IN.**
 - h. That was a lot of information. Let's review the routes and dosing again.
 - h.i. Narcan IV or IO for adults
 - h.i.1. 0.1 mg every 2 min for the chronic user.
 - h.i.2. 0.4 mg for the acute OD with apnea.
 - h.ii. Narcan by Neb
 - h.ii.1. 2 mg in 3 mL NS.
 - h.ii.2. Must be breathing >6/min.
 - h.iii. Narcan by IVP
 - h.iii.1. 0.04 mg per ML, push one 1ml/min.
 - h.iii.2. Draw the 0.4 mg vial into a 10 mg syringe, fill it up the rest of the way with NS.
 - h.iii.3. Must have some respiratory effort.
 - h.iv. Narcan IN
 - h.iv.1. Good for any situation as long as the nostrils are patent.
 - h.iv.2. 1 ml up each nare.
 - h.iv.3. Wait between nares if the patient has any resp. effort.
 - h.v. Narcan IM
 - h.v.1. We used to go 0.2mg every 2 min. You can start at 0.1 mg.
 - h.vi. Narcan IO for peds.
 - h.vi.1. 0.1 mg/kg up to 20 kg.
11. So that's all the routes and dosings. Nice x6 plus the code dose. What about onset?

- a.i. Expected onset of Narcan depends upon the dose and method of administration that you choose.
 - a.i.1. Whatever you choose, onset should be within 2 min.
 - a.i.1.a. Duration, as we said, 30-60 min.
 - a.i.ii. If opioids alone are the cause of the AMS, we should see some results pretty quickly.
 - b. If no improvement is seen in this patient with during the initial intervention, and our patient is still GCS < 8 with no gag reflex, we're in the middle of running an RSI.
12. What are we going to do for our patient, the 47 year old woman found down, who is breathing and has a pulse?
- a.i. She is a chronic user breathing at 7/min.
 - a.ii. We consider gentler approaches.
 - b. We start a Narcan neb with 2 mg in 3 ml NS, dropping the flow rate on the line so that we don't blow the lid off the acorn.
 - b.i. And our patient starts to come around!
 - c. Now we can move on to our usual diagnostic approach to AMS.
 - d. We'll go over that in Part 2 of this podcast:
 - d.i. We'll finish the initial assessment of a patient with AMS.
 - d.ii. Go through monitoring and disposition of this patient.
 - d.iii. Then hit those guidelines and recommendations we talked about at the beginning of this podcast. We'll also talk about the special case that is methadone overdose.
13. See you soon!

Part Two

Welcome back to part 2 of Prescription Opioid Overdoses. In part 1 we went over the problem that we have in this county with opioid OD; the prototypical patient demographics and presentation; and the routes and dosing of Narcan for either the code situation or the nice-wake up. Using this information, by the time we finished our initial stabilization of our 47-year-old female patient, she was on a Narcan neb at 2 mg/3 mL.

In this episode we'll finish caring for our patient, go over observation and dispo, talk about morphine OD and tx, and hit those opioid prescription guidelines I promised in the 1st episode.

1. **When last we left our patient** (47 year old woman found down at home, came into the department with HR 57, RR 7, BP 109/70, GCS 8. She got 2 mg of Narcan IM in the field, and another 2 mg by neb in the ED).
 - a. **Her VS improved, sating over 94, in reg sinus rhythm with a RR of 10.**
 - b. While we wait for her mental status to improve, **we move on from our initial assessment.**

2. During the secondary assessment, **even if we suspect opioid OD due to history, presentation and/or drug response, we keep all the usual AMS differentials in mind.**
 - a. No one is ever just drunk or just overdosed until proven otherwise.
 - b. The way that we assure ourselves that it is “just overdose” is to **run through the differential before finally concluding that none of the other possible etiologies fit.**

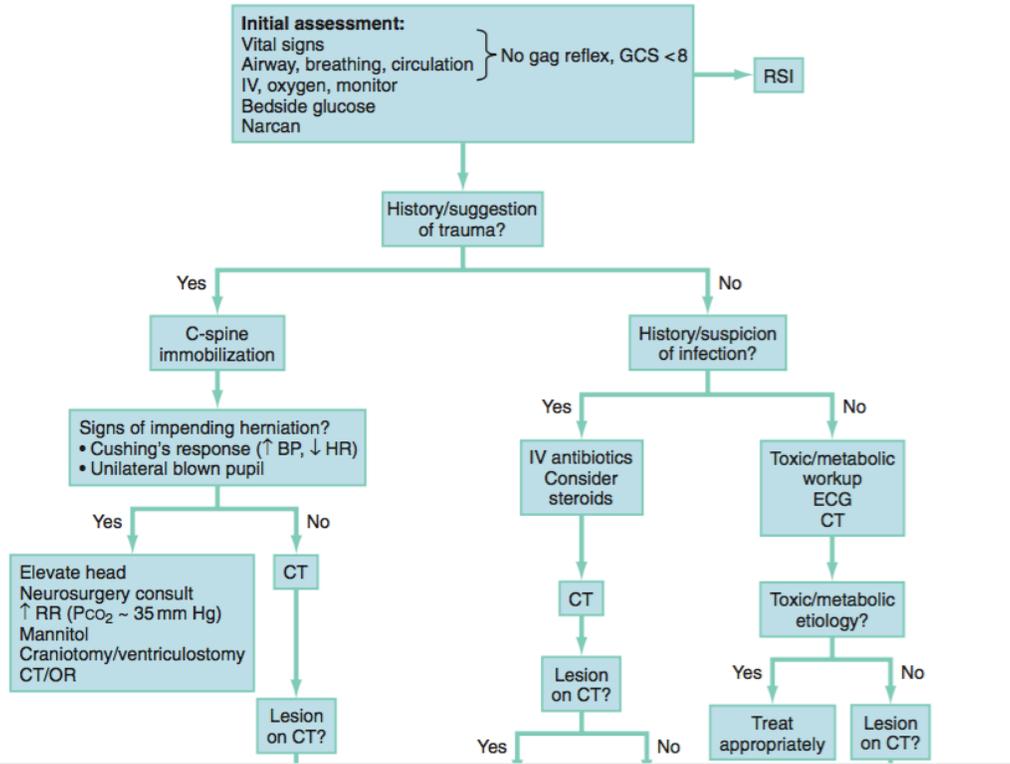


Figure 2 From Rosen's 7th Edition Page 136

Once we've tackled the ABCs, given Narcan, and seen an improvement in VS & MS, we can ask:

- c. **Are there other neurological findings that might support additional concern?**
 - c.i. Are her pupils are fixed?
 - c.i.1. They often are in opioid OD, but ALSO:
 - c.i.2. Are there **any other pathologic eye movements?**
 - c.i.2.a. Do we suspect mass effect?
 - c.ii. Is she very hypo or hypertensive?
 - c.iii. Any other signs of brain stem suppression?
 - c.iii.1. Does she need a neurosurgical team?
 - d. Are there **signs of trauma or major blood loss?**
 - e. Any reason to **suspect infection?**

- e.i. Does she have a high fever?
 - e.ii. A nasty-looking wound?
 - f. Good! **We ruled out major trauma, infection, and impending herniation** in this patient.
- 3. The Story
 - a. Our patient's AMS has resolved to the point where **she can give us a story.**
 - a.i. **She just got her prescription for oxycodone refilled, and may have taken too many.**
 - b. What kind of workup do we now do on our patient?
- 4. The Workup
 - a. **We do a good history, including screening for depression and suicidal ideation, other drugs, etc.**
 - b. **She gets a complete physical exam, including neuro exam AND PSYCH eval.**
 - c. We continue to keep **an eye on her respiratory status.**
 - c.i. Even though she may be talking, she may still be bradypneic.
 - c.i.1. If she's still breathing less than 12 times a minute, she may need more Narcan, or even bagging.
 - d. Our patient is breathing between 12 and 20 times a minute, so we can contemplate doing some more for her.
- 5. Labs
 - a. **What about Labs?** Do we order any?
 - a.i. According to Rosens, "Toxicology screens are often very expensive, and their use is not warranted in most routine drug overdoses."¹⁷
 - a.ii. We agree with that to a large extent. If someone presents with the classic S&S of opioid use and their decreased mental state resolves completely with Narcan administration, and they are denying other drugs, then a full tox screen is probably not necessary.
 - a.iii. While we're here, let's ask: When is a full toxicology screen most useful?
 - a.iii.1. Answer: A full tox screen is most useful in patients who:
 - a.iii.1.a. Present with their first psychotic episode or
 - a.iii.1.b. Are critically ill for an unknown reason when identification of an otherwise unsuspected toxin may change management.
 - a.iii.2. That's about it.
 - b. **This patient's story is consistent with her presentation and her sx have resolved post-Narcan-administration, so no labs are warranted.**
- 6. Before we move on, another word about Narcan.
 - a. In these cases, we're always in a rush to give it, and with good reason.
 - b. At the same time, we need to bear in mind that Narcan itself is not a risk-free maneuver.

- b.i. Caution should be exercised when administering naloxone to habitual users.
 - b.i.1. It may precipitate withdrawal with hypertension, tachycardia, and violent behavior.
- b.ii. Also, though it reverses AMS and the respiratory depression associated with opioid OD, it doesn't always reverse the hypotension.
 - b.ii.1. Giving Narcan does not allow us to fire and forget.
- b.iii. So we keep an eye on this patient for a while – but how long a while?

7. Post OD-observation times

- a. How long do we keep a patient like our 47 yo lady who is awake, breathing 14/minute, with a GCS of 15, no significant findings on PE, and no complaints?
 - a.i. Some patients will want to leave AMA.
 - a.i.1. If they truly have no physical findings – no ataxia or fever – and deny SI then they have a right to leave. D/C AMA.
 - a.ii. If they are willing to stay, **observation time depends on what caused the OD.**
 - a.ii.1. In this case, it was a **short-acting opioid**, so the **observation time is 4-6 hours after the last Narcan dose.**¹⁸
 - a.ii.2. If it was a **long-acting opioid** (methadone, fentanyl, etc), then the **observation time is 8 hours.**
 - a.iii. Before we move on to dispo, we should take a moment to discuss methadone.

8. Methadone is a beast all its own.

- a. Like heroin, it's an opioid receptor agonist.
 - a.i. It comes in tablets and syrup.
- b. A synthetic that's been engineered to be **long-acting.**
 - b.i. Heroin has a half-life of 30 minutes. So it's fast-on, fast-off.
 - b.ii. Methadone has a huge half-life range: *15-40 hours.*
 - b.ii.1. The average half-life is ~25 hours.**
 - b.ii.2. Peak plasma concentrations are usually seen ~15 hours after tablet ingestion.¹⁹
 - b.ii.3. Has a potent analgesic effect.
- c. Methadone is not a bad thing in and of itself.
- d. For 45 years, Methadone Maintenance Therapy (MMT) has been the standard of care for former heroin users attempting to abstain from their habit.
 - d.i. Opioid-dependent patients who are enrolled in MMT programs have 1/3 the mortality incidence of those who are not.²⁰
 - d.i.1. They have a higher quality of life, earn more money, and contract fewer infectious diseases.
- e. The rise of MMT has seen some concomitant rise in methadone toxicity (MDT).
 - e.i. The numbers make it very clear that MMT isn't really the problem.

- e.ii. Methadone is such a long-acting mu-receptor agonist that it inhibits the heroin-type high.
- e.iii. If you want to get high, you have to take a lot of other drugs to get around the methadone that's already there.
- f. Most of the recent trend of MDT comes from prescribing methadone *for pain*.
 - f.i. A 2012 paper in JAMA showed that **methadone was linked to 30% of the prescription painkiller deaths** in 2009.²¹
 - f.ii. That's really impressive, given that methadone constituted only 2% of the proscribed painkillers that year.
 - f.ii.1. Great at killing pain and people.
- g. **Why is methadone so good at killing people?**
 - g.i. **The peak analgesia & the peak respiratory suppression don't line up.**
 - g.i.1. Patients switching to methadone from morphine get their expected 4-8 hours of analgesia
 - g.i.2. The analgesic effect wears off, but the methadone is still on board.²²
 - g.ii. **It takes a long time to titrate up to continuous effective pain relief.**
 - g.ii.1. It's in those first two weeks of starting therapy that we see a lot of the morbidity and mortality from methadone in that initial exposure or re-exposure.
 - g.ii.1.a. One paper I read stated that chronic users can retain methadone in their livers, leading to longer duration of action even though the plasma concentration of methadone was low.²³
 - g.ii.2. The point is that the half-life of this drug is all over the place, even for habitual users, and does not match up well with the duration of analgesia.
 - g.iii. To make matters worse, because **the drug is so old it's really cheap, and so insurance companies have listed it as preferred.**²⁴
 - g.iii.1. Primary care doctors are being encouraged to use it even though it's a very hard drug to use correctly.
 - g.iii.2. You need baseline EKGs, follow-up EKGs, medication reconciliation, titration, and very, very close monitoring.
- h. **Morbidity and mortality from methadone**
 - h.i. Is dose-related and largely **d/t respiratory depression, QT prolongation, and Torsades de Pointes.**
 - h.i.1. There are numerous case studies of other strange events.
- i. **Risk factors for MDT include:**
 - i.i. **Recent initiation of therapy.**
 - i.ii. **High doses** (>80-200 mg/day).²⁵
 - i.iii. **Other drugs on board** that interfere with cyp450 metabolism and/or cause prolonged QT.

- i.iv. **Underlying long QT syndrome** at baseline.²⁶
 - i.v. **The syrup-form of methadone.**²⁷
 - j. MDT workup
 - j.i. If a patient on methadone presents with dizziness, weakness, syncope or AMS:**
 - j.i.1. Throw the 12 lead on ASAP.**
 - j.i.2. Look for co-ingestions.
 - j.i.3. Multiple Rx.
 - j.i.4. Be extra-suspicious if the story reveals that the methadone therapy is < 2 weeks old.
 - j.ii. Expect apnea. Get end-tidal CO2 monitoring.**
 - j.iii. Start the Narcan drip.**
 - j.iii.1. *2/3rd of the “Nice-Narcan Wake-Up”, aka the effective dose, per hour PLUS*
 - j.iii.2. *1/2 of the initial wake-up-nicely bolus dose 15 min after initiating continuous IV infusion.*²⁸
 - j.iv. **Expect that you'll be admitting this patient to the ICU.**
 - j.iv.1. He or she will need careful, continuous monitoring as the methadone is metabolized over the next 40 hours.
 - j.v. That's it for methadone.
 - k. How long do we observe our patient?
 - k.i. Our current patient was on an immediate-release form of oxycodone, so we observe her for 4 hours after her last Narcan dose, which we gave by neb.
 - k.i.1. Everything looks good, so we can start to consider dispo.

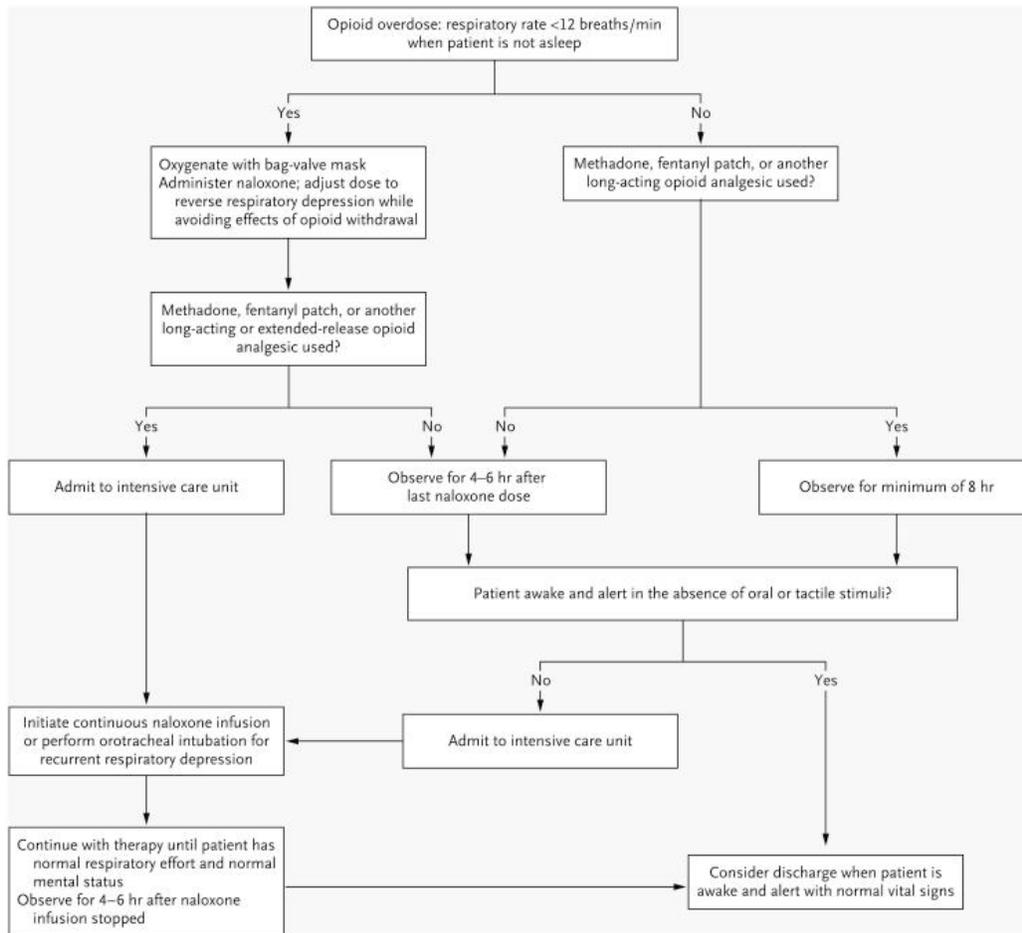


Figure 3: From Boyer, Edward W. "Management of Opioid Analgesic Overdose." *The New England journal of medicine* 367.2 (2012): 146-155. PMC. Web. 9 Mar. 2016.

9. Disposition of the Opioid OD patient

- a. After the 4-6 hours window, what happens?
- b. In theory, **patients with AMS secondary to recreational, accidental drug or alcohol OD can be discharged once their mental status returns to baseline.**
 - b.i. In other words, clinical sobriety can be a ticket to walk out the door.
 - b.i.1. But should it be a scot-free ticket?
- c. What we want is for these people not only to live long enough to walk out the door, but for them to not come back in the door again for this reason.
 - c.i. What can we do to try **maximize a good outcome?**
 - c.ii. We've got them for at least 4 hours. We may as well make the most of it.
- d. Our when it comes to a drug OD of any kind, we **must talk to the patient.**
 - d.i. **Call social services.**
 - d.i.1. Document the services that have been offered and accepted.
 - d.ii. What services?

- d.ii.1. In our case, the patient insists that the OD was accidental, but it still happened.
 - d.ii.2. Maybe she needs welfare checks.
 - d.ii.3. Maybe she needs more assistance at home in general.
 - d.ii.4. Maybe she needs an XR formulation. Or not.
 - d.iii. We can try to get or at least discuss these things with her or her PCP while she's in the ED.
 - e. We could also consider a proscription for Narcan.
 - e.i. That's one of the 4 CDC recommendations when it comes to addressing this epidemic.
 - f. So that's what we'll give her: a ticket in an envelope with a lot of other information after a conversation and a few calls to social services and her PCP.
10. Before we dive into the CDC guidelines, here's a rapid review of what we've covered so far since Part 1:
- a. Drug OD is the leading cause of injury death in the US, and more than half of those are d/t opioids. Most of those opioids are prescribed.
 - b. The highest-risk population/classic patients with opioid OD are 45-54 and 55-64 years-old, female slightly higher than male, with a history of abuse, and polypharmacy.
 - c. Your initial workup, history, and physical exam will allow you to differentiate between AMS from opioid OD and other etiologies that mimic opioid OD.
 - c.i. Those are, very quickly & very broadly: trauma, infection, and other toxic-metabolic issues.
 - c.i.1. Besides or in addition to opioids.
 - d. The classic presentation is respiratory and CNS depression *probably* with miosis.
 - d.i. Variations exist and miosis may not be present w/ a synthetic opioid OD.
 - e. Whatever the etiology of the CNS and respiratory depression, ABC's come first.
 - e.i. Get monitoring, good oxygenation, and good ventilation.
 - e.ii. Get a jaw thrust going.
 - e.ii.1. After that, move to Narcan.
 - f. If it's not a code situation, dose Narcan NICELY.
 - f.i. Start at 0.1 mg IM/IV/IO.
 - f.ii. Slow IVP, 1-2 ml of 0.04mg/ml.
 - f.iii. IN one nare at a time.
 - f.iv. If your patient is breathing > 6 times per minute, consider nebulized Narcan at 2 mg in 3 ml NS.
 - g. In all of these methods, wait a few minutes for a response before increasing or repeating the dose to a max of 10 mg.
 - h. When your patient is awake enough to give a story, *stop the Narcan UNLESS*
 - h.i. The story is that methadone was involved.

- i. With methadone OD, start a Narcan infusion at 2/3 the effective “wake up nicely” dose.
 - i.i. Expect an ICU admission.
 - j. For all short-acting opioids, after you have resuscitated the patient to a normal GCS and VS, they need to be observed for 4-6 hours after their last Narcan dose.
 - j.i. While we've got them in the ED, let's make the most of that time.
 - j.i.1. Call Social Services.
 - j.i.2. Educate them.
 - j.i.3. Get them a take-home naloxone Rx.
 - j.i.4. Try to recruit them to our side, which is the side of keeping them alive and actually fixing what's wrong with them.
 - k. The story we give them, the short version:
 - k.i. Chronic opioid therapy helps basically no one who stands any chance at getting better.
 - k.ii. Let's focus on function rather than focusing on taking the pain away.
 - k.iii. Set goals and expectations appropriately.
 - l. The story we give ourselves, the short version:
 - l.i. Let's not start opioids on people if there's any other alternative.
 - l.ii. Let's never start them without a checklist, a plan, and a lot of education.
 - l.iii. Let's never proscribe doses higher than 60 mg.
 - l.iii.1. Literature shows that people will either respond to 60 mg BID or they probably won't respond well to any dose.
 - l.iii.1.a. That's non-cancer pain.
11. Now on to the CDC recommendations (basically 2):
- a. #1: **Protect people with opioid use disorder – give Narcan to-go.**
 - a.i. *By expanding access and use of naloxone—a critical drug that can reverse the symptoms of an opioid overdose and save lives.*²⁹
 - b. #2: **Limit initiation into opioid misuse and addiction.**
 - b.i. *Opioid pain reliever prescribing has quadrupled since 1999. Providing health care professionals with additional tools and information—including safer guidelines for prescribing these drugs—can help them make more informed prescribing decisions.*
12. Both sound great. #2 sound tricky.
- a. What tools and information can help inform our opioid prescribing practices?
 - b. We have some guidance from the FDA.
 - b.i. Here are 4 suggestions from the FDA.**
13. **Suggestion #1: ANY patient who gets an opioid prescription gets an additional prescription for education.**
- a. So it's: here's your hydrocodone & here's your education.



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Focus on Prescriber Education

- Patient-Prescriber interaction critical opportunity to improve opioid use
 - Better discussions about use of opioids
 - Better discussion about how to avoid adverse effects of opioids
 - Better discussion about how to store and dispose of opioids
- Opioid prescribing is challenging
- Educating prescribers represents targeted opportunity to improve opioid use

Figure 4 From "Opioid Prescribing Practices and Pain Management"

- b. What's the message we should focus on with that **education**?
 - b.i. What opioids are really for.**
 - b.ii. How to use them properly.**
 - b.iii. The risks of using them properly *and* improperly.**
 - b.iv. How to properly store and dispose of them.**
 - c. This is a great chance to warn people not to leave their prescriptions around where they can be accidentally or intentionally ingested by anybody else.
 - c.i. This isn't just about pills.
 - c.ii. There have been more than two dozen cases of kids being exposed to fentanyl patches. 10 of these cases were fatal.³⁰
14. **Suggestion #2:** We *re-focus our prescribing practices away from a subjective pain* scale and more toward an assessment of how our patient's pain impacts them.
- a. In other words, the patient may say they have 10/10 pain, but if you ask them **what they can no longer do because of the pain.**
 - b. That answer is the one which will determine if opioids of any kind are warranted.
15. **Suggestion #3:** *Use a summary checklist when prescribing opioids.*
- a. We have one for you in the show notes.
 - b. It can help make sure that you've dotted your opioid I's and crossed your therapeutic T's.
 - b.i. That you've checked for pain and function together.
 - b.ii. That you've gone over a history of substance abuse.
 - b.iii. That you've documented all current prescriptions and noted all drugs with potential for abuse.
 - b.iv. That you've screened for depression.
 - b.v. That you've assessed for the side effects of opioids.

- b.v.1. The constipation, the worsening sleep apnea, the coordination impairment that affects driving, and so on.
 - c. It's all in the checklist.
16. **Suggestion #4:** *Stay on top of the latest guidelines for opioid use, risk mitigation, prescribing practices, etc.*
- a. Who makes the guidelines and where can we get them?
 - a.i. They are all available on the National Guidelines Clearinghouse Website.
 - a.ii. Your state may well have opioid dosing guidelines.
 - a.iii. Every major medical association has one.
 - a.iii.1. Ex: "Practice Guidelines for Chronic Pain Management, An Updated Report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine," 2010.
 - a.iv. You and your colleagues can check them out, agree on protocols, and later evaluate how well they are serving your department and your practice.
 - b. The guidelines can help steer your practice in a number of ways.
 - b.i. They can help define your maximum daily dose limits for each kind of opioid in your arsenal.
 - b.ii. The effects of opioids, good and bad, are almost entirely dose-related.
 - b.ii.1. For example, Washington State Opioid Dosing Guidelines state that more than 100 morphine equivalents a day associated with 9-fold increased risk of overdose (Level B Evidence)
 - b.ii.1.a.i. For that reason, those guidelines recommend limiting daily doses to 120 mg without consultation from a pain specialist.
 - c. In addition to looking up and knowing the prescribing guidelines, we can earn free CME that focuses on Risk Evaluation and Mitigation Strategies for Opioid Prescription
 - c.i. <https://search.er-laopioidrems.com/Guest/GuestPageExternal.aspx>
17. So again, here's what the CDC and the FDA have to say so far:
- a. **Protect Opioid users. Give them a naloxone take-home.**
 - b. **Seek opioid alternatives.**
 - c. **Prevent misuse with education. Tell people:**
 - c.i. **What opioids are really for.**
 - c.ii. **How to use them properly.**
 - c.iii. **The risks of using them improperly.**
 - c.iv. **How to properly store and dispose of them.**
 - d. **Re-focus function.**
 - e. **Use a summary checklist when prescribing.**
 - f. **Keep up with the guidelines.**
18. Remember how I said at the beginning of this podcast "this is the bad news"? Well, here is the good news: Most of these overdoses are from proscription drugs.

- a. We – doctors - proscribe these drugs.
 - b. We can positively affect the outcomes in our patients, and maybe do something to stem the tide of the opioid overdose epidemic.
 - c. To that end, we all need to sit down, talk about and answer for ourselves questions like: who gets opioids, when, why and how much.
 - c.i. The overwhelming evidence is that people who don't need them get them anyway.
 - c.i.1. One recent BMJ study estimated that 14-22% of pregnant women received an opioid prescription.³¹
 - c.i.2. WHY?
 - d. It is our prescribing practices that are doing this. We have the ability and the duty to turn the tide of the epidemic.
 - e. Let's look at the guidelines, choose our practices in advance in partnership with our departments, and talk to our patients.
 - e.i. Let's explain to them how low doses of meds work just as well as high doses for chronic pain.
 - e.ii. Let's explain how chasing pain with meds only makes things worse.
 - e.iii. Let's keep an eye out for red flags like lost or stolen scripts.
19. Lets work together on helping control this epidemic, and let's hope that someday we have a new class of drug to work with that's abuse-free, or at least abuse- deterrent.
- a. The FDA is currently sponsoring a search for abuse deterrent opioids, which would be a totally awesome, so we wish them a lot of luck.³²

Glossary of Addiction-Related Assessment Tools

ADDIS: alcohol and drug diagnostic instrument
PDUQ: prescription drug use questionnaire
ASI: addiction severity index
PMQ: pain medication questionnaire
Atluri six-point screening tool
POSIT: problem-oriented screening instrument for teenagers
CAGE/CAGE-AID: cut down, annoyed, guilty, eye-opener/ adjusted to include drugs RAFFT:
relax, alone, friends, family, trouble
CCI: chemical coping inventory
SASSI: substance abuse subtle screening inventory
Chabal five-point prescription opiate abuse checklist
SCID-P: alcohol and drug sections of the DSM-III-R
COMM: current opioid misuse measure
SISAP: screening instrument for substance abuse potential
CUAD: chemical use, abuse, and dependence scale
SMAST-AID: short Michigan alcoholism screening test/adapted to include drugs
DAPA-PC: drug abuse problem assessment for primary care
SOAPP: screener and opioid assessment for patients with pain
DAST: drug abuse screening test STAR: screening tool for addiction risk
DIRE: diagnosis, intractability, risk, efficacy
SUDDS: substance use disorder diagnostic schedule
KMSK scale: Kreek-McHugh-Schluger-Kellogg scale
TICS: two-item conjoint screen

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CHECKLIST FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

For primary care providers treating adults (18+) with chronic pain ≥ 3 months, excluding cancer, palliative, and end-of-life care

CHECKLIST

When **CONSIDERING** long-term opioid therapy

- Set realistic goals for pain and function based on diagnosis (eg, walk around the block).
- Check that non-opioid therapies tried and optimized.
- Discuss benefits and risks (eg, addiction, overdose) with patient.
- Evaluate risk of harm or misuse.
 - Discuss risk factors with patient.
 - Check prescription drug monitoring program (PDMP) data.
 - Check urine drug screen.
- Set criteria for stopping or continuing opioids.
- Assess baseline pain and function (eg, PEG scale).
- Schedule initial reassessment within 1–4 weeks.
- Prescribe short-acting opioids using lowest dosage on product labeling; match duration to scheduled reassessment.

If **RENEWING** without patient visit

- Check that return visit is scheduled ≤ 3 months from last visit.

When **REASSESSING** at return visit

Continue opioids only after confirming clinically meaningful improvements in pain and function without significant risks or harm.

- Assess pain and function (eg, PEG); compare results to baseline.
- Evaluate risk of harm or misuse:
 - Observe patient for signs of over-sedation or overdose risk.
 - If yes: Taper dose.
 - Check PDMP.
 - Check for opioid use disorder if indicated (eg, difficulty controlling use).
 - If yes: Refer for treatment.
- Check that non-opioid therapies optimized.
- Determine whether to continue, adjust, taper, or stop opioids.
- Calculate opioid dosage morphine milligram equivalent (MME).
 - If ≥ 50 MME/day total (≥ 50 mg hydrocodone; ≥ 33 mg oxycodone), increase frequency of follow-up; consider offering naloxone.
 - Avoid ≥ 90 MME/day total (≥ 90 mg hydrocodone; ≥ 60 mg oxycodone), or carefully justify; consider specialist referral.
- Schedule reassessment at regular intervals (≤ 3 months).

REFERENCE

EVIDENCE ABOUT OPIOID THERAPY

- *Benefits of long-term opioid therapy for chronic pain not well supported by evidence.*
- *Short-term benefits small to moderate for pain; inconsistent for function.*
- *Insufficient evidence for long-term benefits in low back pain, headache, and fibromyalgia.*

NON-OPIOID THERAPIES

Use alone or combined with opioids, as indicated:

- Non-opioid medications (eg, NSAIDs, TCAs, SNRIs, anti-convulsants).
- Physical treatments (eg, exercise therapy, weight loss).
- Behavioral treatment (eg, CBT).
- Procedures (eg, intra-articular corticosteroids).

EVALUATING RISK OF HARM OR MISUSE

Known risk factors include:

- Illegal drug use; prescription drug use for nonmedical reasons.
- History of substance use disorder or overdose.
- Mental health conditions (eg, depression, anxiety).
- Sleep-disordered breathing.
- Concurrent benzodiazepine use.

Urine drug testing: Check to confirm presence of prescribed substances and for undisclosed prescription drug or illicit substance use.

Prescription drug monitoring program (PDMP):

Check for opioids or benzodiazepines from other sources.

ASSESSING PAIN & FUNCTION USING PEG SCALE

PEG score = average 3 individual question scores (30% improvement from baseline is clinically meaningful)

Q1: *What number from 0–10 best describes your **pain** in the past week?*

0 = “no pain”, 10 = “worst you can imagine”

Q2: *What number from 0–10 describes how, during the past week, pain has interfered with your **enjoyment of life**?*

0 = “not at all”, 10 = “complete interference”

Q3: *What number from 0–10 describes how, during the past week, pain has interfered with your **general activity**?*

0 = “not at all”, 10 = “complete interference”

