Beyond Withdrawal:
Optimizing Pain in the Opioid Tolerant Patient

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April 25, 2026 4:45-6:00pm

Disclosure Information

- Presenter 1: Joseph D'Orazio, MD
  - Presenter 1 Disclosures: No disclosures

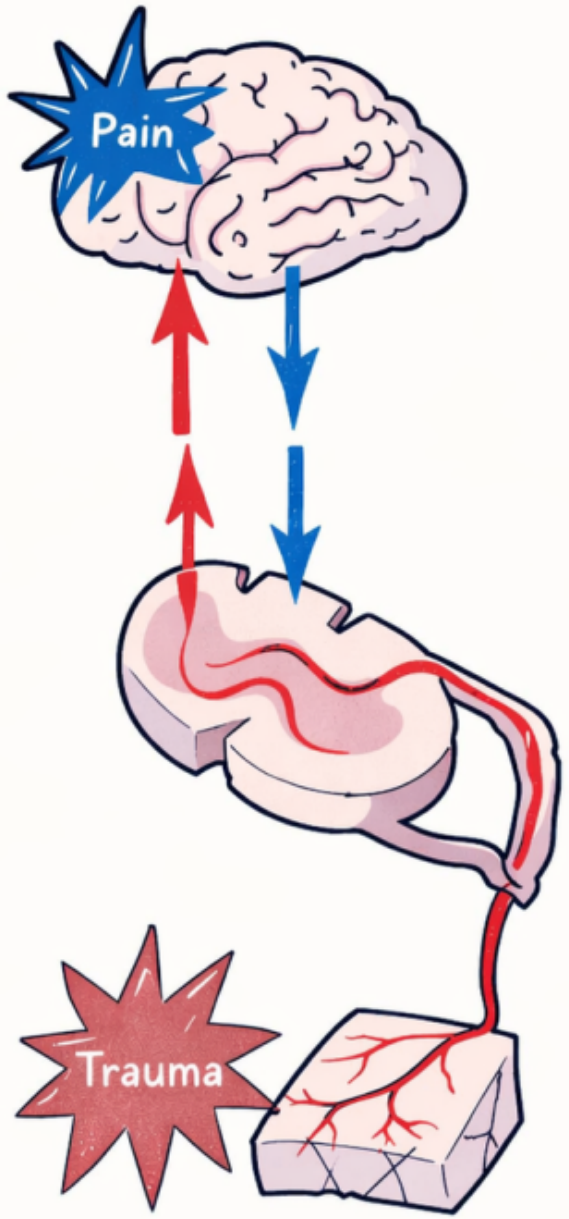
- Presenter 2: Christine Collins, MD
  - Presenter 2 Disclosures: No disclosures

Learning Objectives

- Explore the interplay between withdrawal and analgesia
- Outline a practical strategy of a basal-bolus opioid approach
- Emphasize the roles of long and short acting opioids as treatments for opioid use disorder and as therapeutic tools for analgesia
- Describe safe use of patient-controlled analgesia (PCA) pumps
- Analgesia in the perioperative period for patients with severe opioid tolerance
- Highlight multimodal, non-opioid approaches that are essential for comprehensive care, including pharmacotherapy and regional anesthesia

Why do we make patients in pain wait for relief when we have tools that can help them now?


Biological
Psychological
PAIN
Social
Environmental
Lifestyle



Receptors

Mu NMDA

TRPV1 GABA D1-R

5-HT Alpha-2

Enzymes

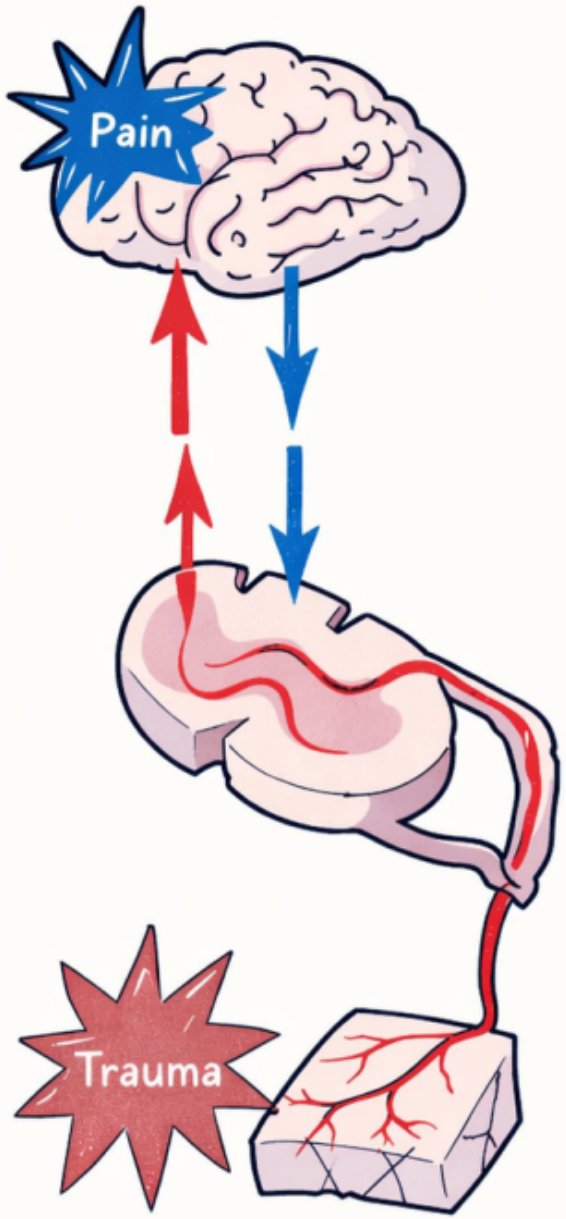
COX 1 COX 2

COX 3

Channels

Sodium Channels

Calcium Channels



Receptors

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NMDA

TRPV1

GABA

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Alpha-2

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Channels

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Calcium Channels

Opioid Analgesia

Opioids

Pharmaceutical

Oxycodone

Hydrocodone

Morphine

Hydromorphone

Fentanyl

Codeine

Non-Pharmaceutical Opioids

Illicitly manufactured fentanyl

Pressed fentanyl tablets

MME (Morphine Milligram Equivalents)

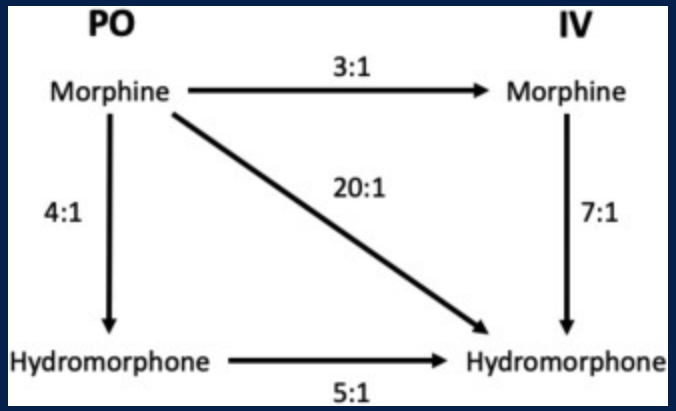
Conversion Table

Opioid	Conversion Factor
Fentanyl IV	300
Morphine PO	1
Morphine IV	3
Oxycodone PO	1.5
Hydromorphone IV	20
Hydromorphone PO	5
Methadone PO	4.7*

Quick References

Opioid	PO	IV
Morphine	30	10
Oxycodone	20	
Hydromorphone	7.5	1.5

Opioid	Dose
Morphine PO	30 mg
Morphine IV	10mg
Hydromorphone PO	7.5mg
Hydromorphone IV	20mg
Oxycodone PO	30mg



Mid-Atlantic "Dope"

- Core: opioid + alpha-2 agonist
- Opioid
  - Fentanyl 10-13mg per bag
- Alpha-2 agonist
  - Xylazine → medetomidine

- Other contaminants:
  - Carfentanil, nitazenes, brorphine, local anesthetics

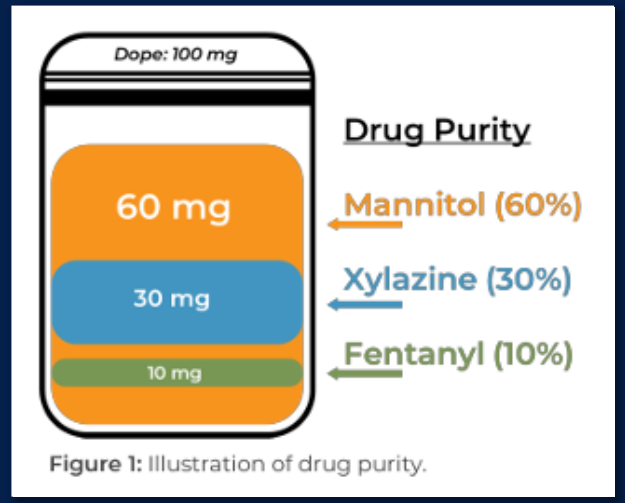


Figure 1: Illustration of drug purity.

Courtesy of CFSRE

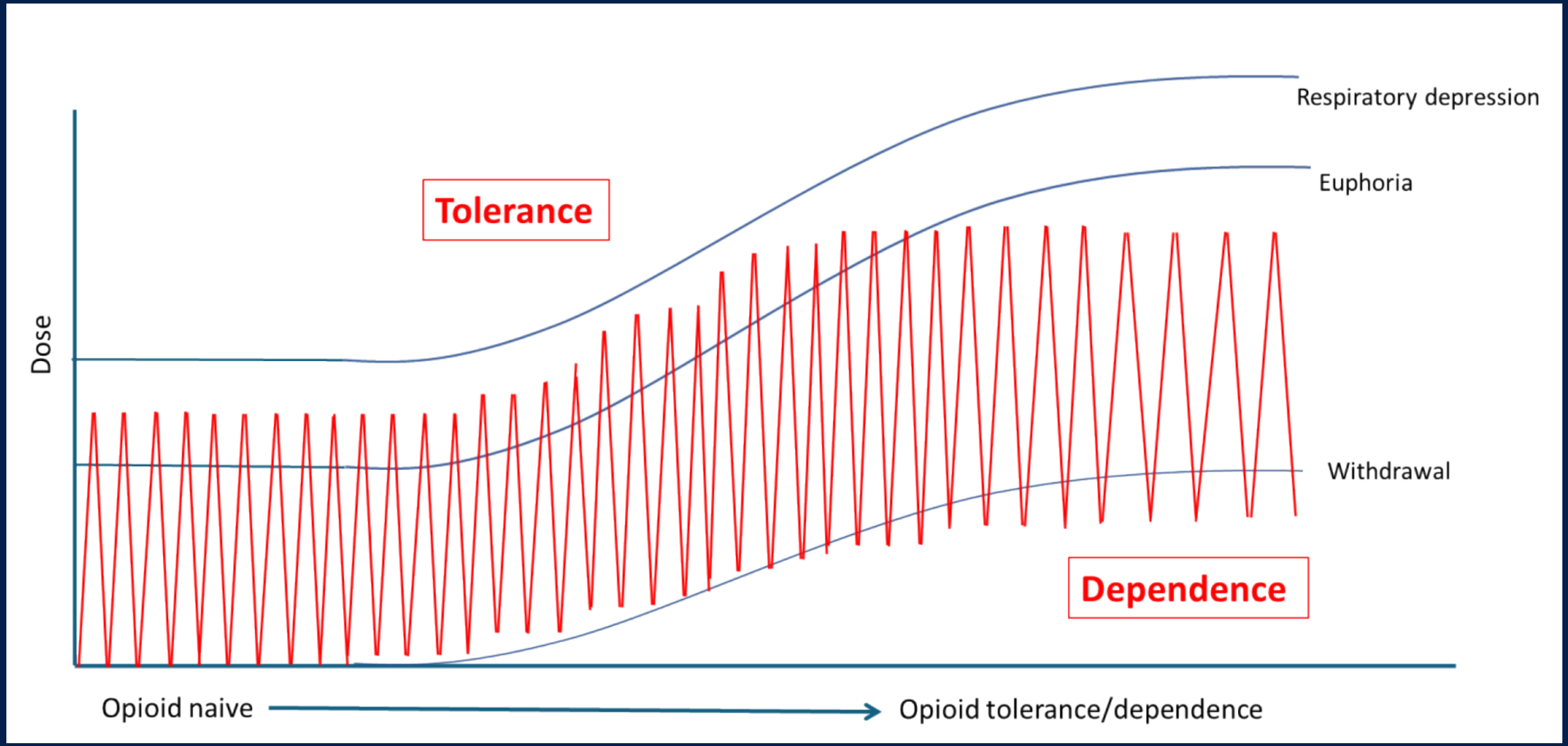
Krotulski AJ, Papsun DM, Logan BK. Drug Checking Quarterly Report – Mid-Atlantic Region. Center for Forensic Science Research and Education (CFSRE).

MME per Day Comparison of Opioids

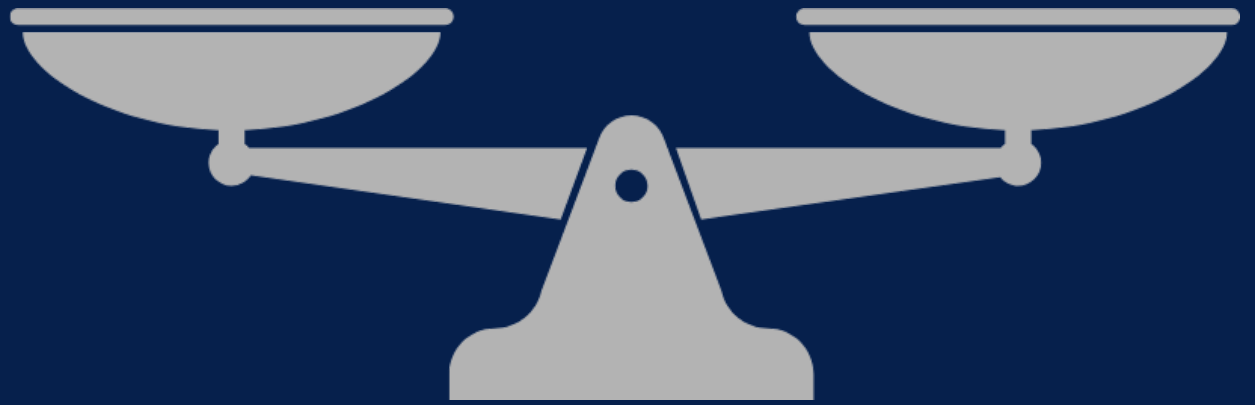
Bag of Philadelphia dope:
~ fentanyl 10,000mcg

Equivalent to:
hydromorphone 60mg IV
oxycodone 800mg

Opioid Tolerance and Dependence

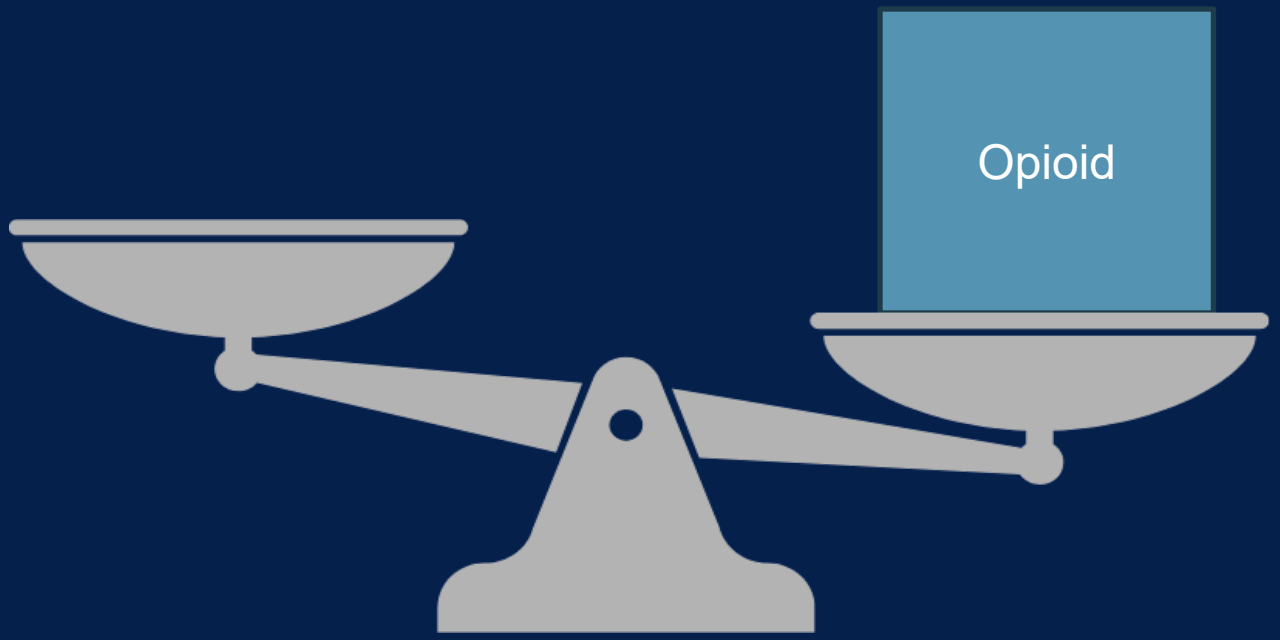


Opioid Naïve



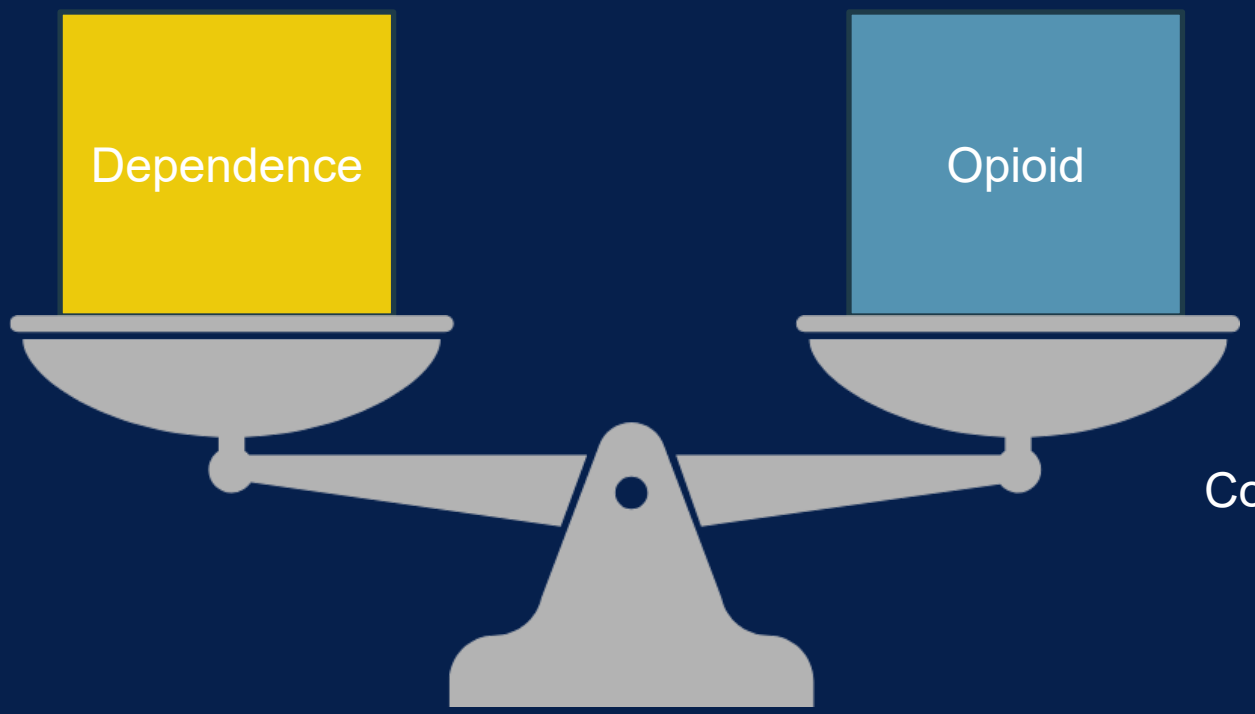
"Normal"

Opioid Naïve



Drug Effect
Analgesia
Euphoria

Opioid Dependence/Tolerance



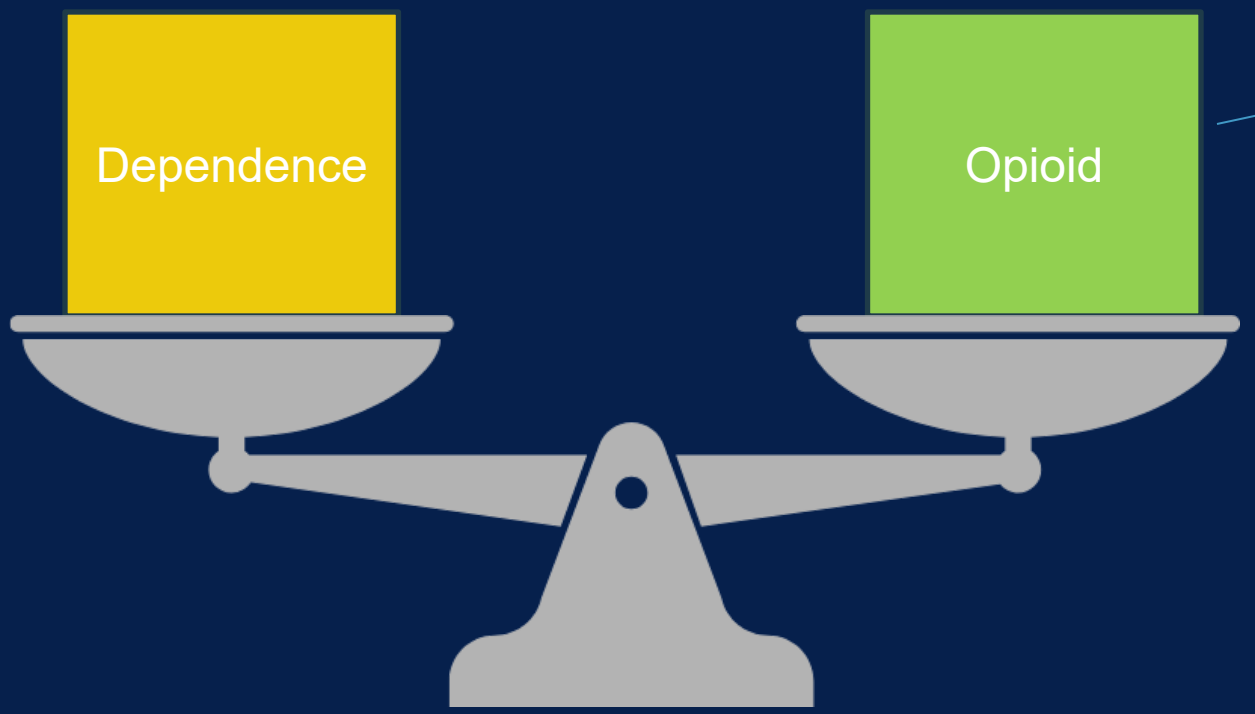
Consider: Chronic pain

"Normal"
No analgesia

Opioid Withdrawal

Withdrawal

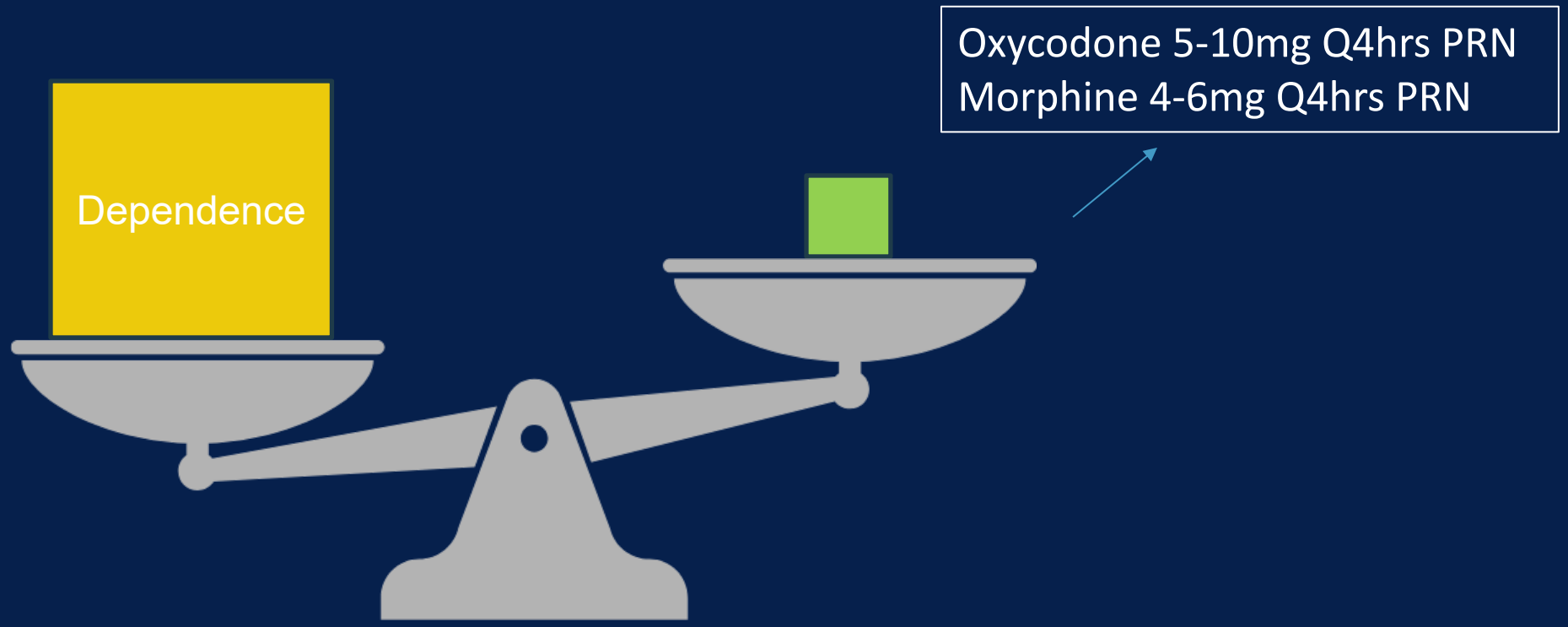
Opioid Withdrawal Management



Methadone
Buprenorphine
Oxycodone
Hydromorphone

"Normal"
Not intoxicated
No analgesia

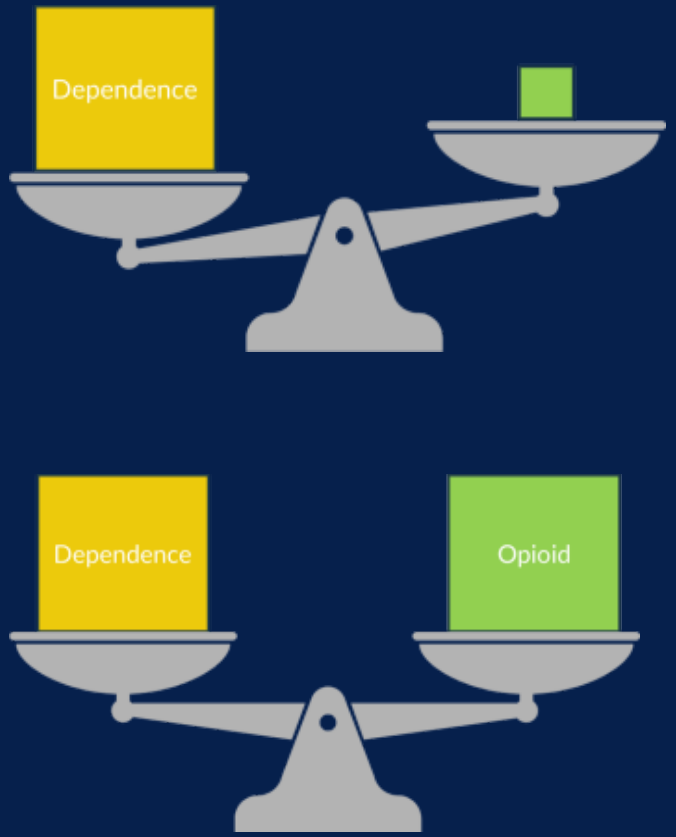
Inadequate Withdrawal and Pain Management



Withdrawal

Case Presentation

- Patient presents with fractured femur after fall from standing
- Team initially administers oxycodone 5 - 10mg PRN without significant relief overnight
- Over the weekend, the team identifies the patient is on methadone 100mg daily from a methadone clinic but does not restart it
- Pain continues to worsen throughout the day even with an increase in oxycodone to 15mg PRN
- Team eventually discontinues the oxycodone and administers methadone 100mg PO daily



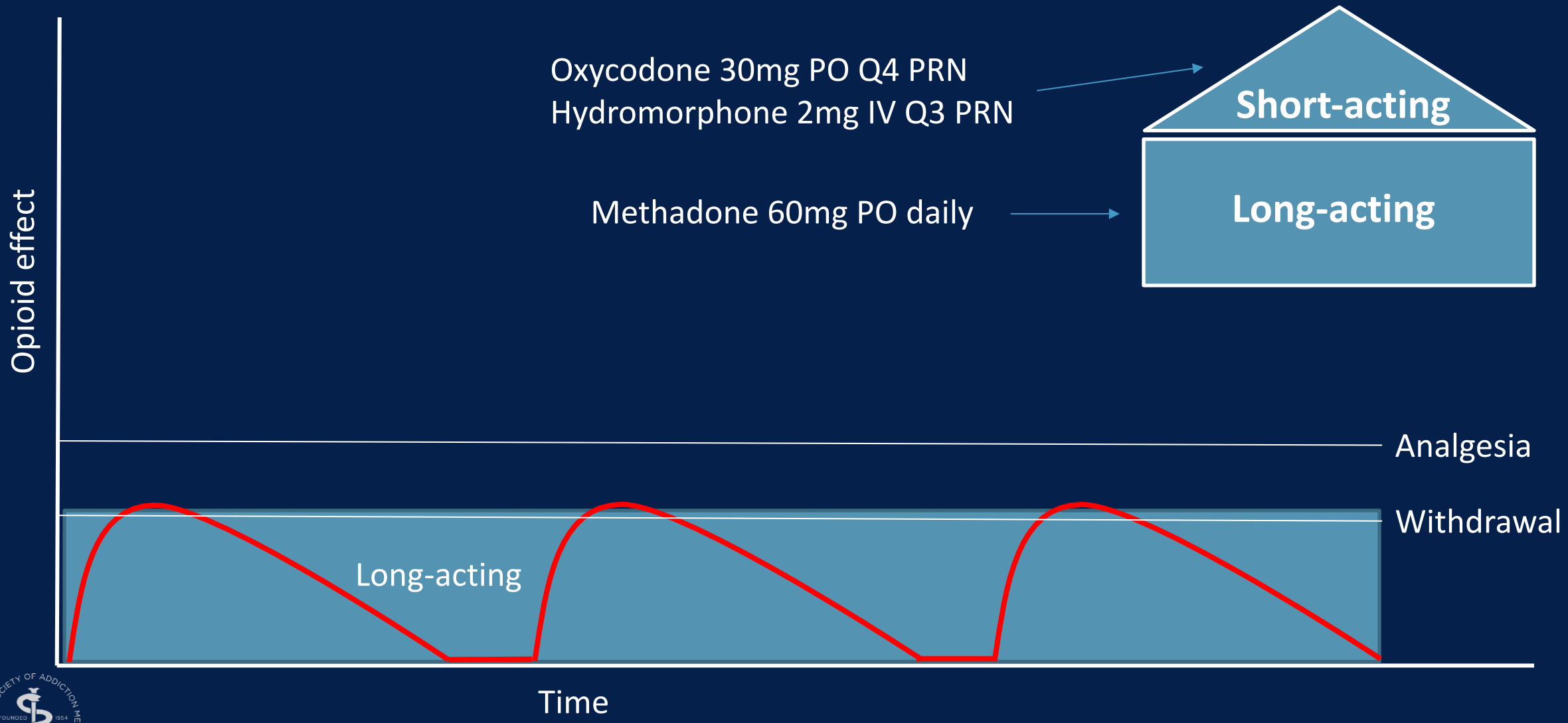
Pain Control in Setting of Opioid Dependence/Tolerance

Pain and Withdrawal Interplay: "Fill the Bucket"

- Basal/bolus approach
  - Long-acting/continuous infusion opioids for management of dependence
  - Short-acting opioids to provide analgesia
- Long-acting opioids
  - Methadone, buprenorphine, oxycodone CR, fentanyl patch, hydromorphone continuous infusion…
- Short-acting opioids
  - Oxycodone, hydromorphone, morphine

Swarm RA, Paice JA, Anghelescu DL, Are M, Bruce JY, Buga S, Chwistek M, Cleeland C, Craig D, Gafford E, Greenlee H, Hansen E, Kamal AH, Kamdar MM, LeGrand S, Mackey S, McDowell MR, Moryl N, Nabell LM, Nesbit S; BCPS; O'Connor N, Rabow MW, Rickerson E, Shatsky R, Sindt J, Urba SG, Youngwerth JM, Hammond LJ, Gurski LA. Adult Cancer Pain, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2019 Aug 1;17(8):977-1007. doi: 10.6004/jnccn.2019.0038. PMID: 31390582.

Opioid Withdrawal Treatment: Short-Acting Alone vs Basal Bolus



Ratio of Basal to Bolus Dose

- Calculating the short-acting dose for pain control for patients with opioid dependence
  - Calculate the total daily opioid dose, 10-20% of total daily dose as single bolus dose

Examples:

Oxycodone CR 100mg TID (450 MME) plus oxycodone 30mg PRN (45 MME)

Fentanyl 100mcg patch (200 MME) plus oxycodone 15mg PRN (22.5 MME)

Methadone 100mg daily (428 MME) plus oxycodone 30mg PRN (45 MME)

Hydromorphone 1mg/hr IV (24mg = 480 MME) plus 2.4mg (48 MME) IV bolus

Comments:

Imbalances: inadequate pain control, wide peaks/troughs

Be aware of hospital culture

Groninger H, Schisler RE. Pharmacologic management of pain at the end of life. *Am Fam Physician.* 2014;89(1):26-32.

Case Presentation

- 68-year-old female presents after fall.
- Reports she fell and has been down for 48hours. Xray reveals a hip fracture.
- She missed two doses of methadone from her clinic and feeling sick.
- Confirmed dose from her clinic is 100mg, last dose 2 days ago.

- What medications and doses are you administering?
- Give methadone 100mg home dose to match dependence
- Determine the short-acting dose for analgesia
  - Methadone 100mg = 428 MME
  - Give 10% of total daily dose as a bolus dose
    - For oxycodone: 10% of 428 MME = 42.8 MME ÷ 1.5 = oxycodone 28.5mg
    - For hydromorphone IV: 42.8 MME ÷ 20 = hydromorphone 2.1mg

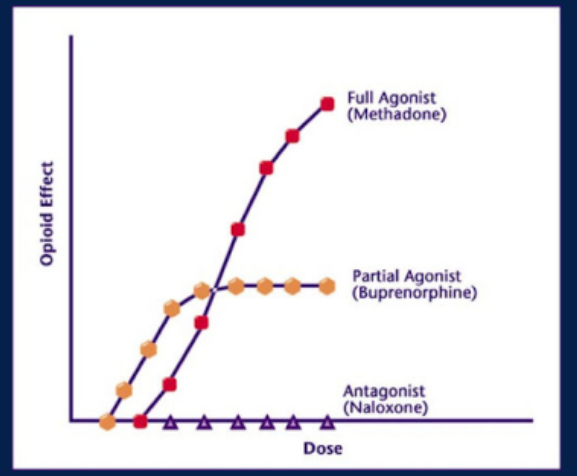
Methadone

- Pharmacology – mu, kappa, and delta receptor agonist. NMDA receptor antagonist
- Pharmacokinetics – Long-acting opioid 8-59 hour half-life (24hrs)
- Duration of action – 24-36 hours
- Duration of action for analgesia – 4-8 hours
- Typically dosed Q4-8 hours for pain control initially
- Rapid onset for withdrawal management, abstinence not required
- QTc prolongation - worse during induction and >100mg

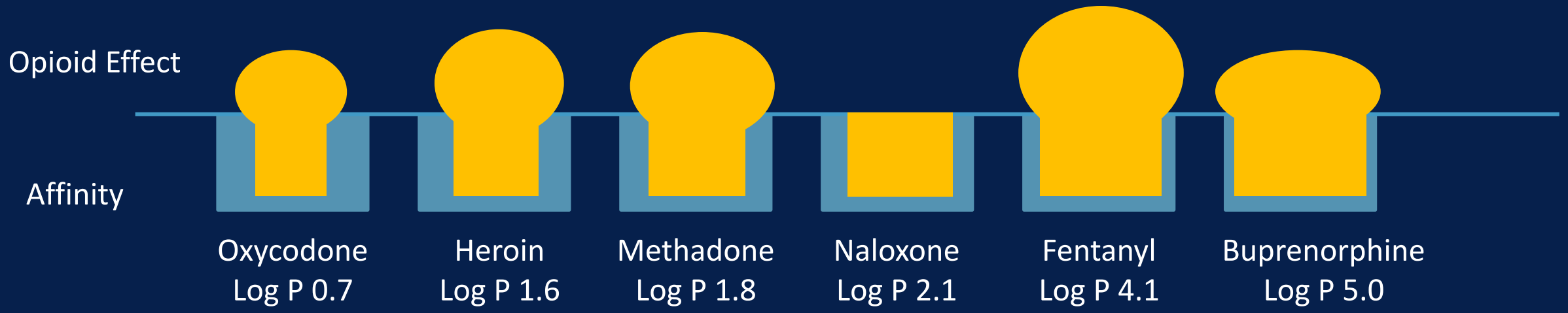
- Highly regulated drug for the treatment of opioid use disorder
  - Dispensed from a methadone clinic as outpatient only – not an office-based therapy
  - Typically dose as a daily medication from methadone clinics
  - No restrictions for use to manage withdrawal or for OUD as a secondary diagnosis in the hospital

Buprenorphine

- Pharmacology: partial mu agonist, ceiling effect
  - Low risk for overdose and misuse
- Pharmacokinetics: long-acting opioid
- Duration of action: 20–73 hour half-life (38hrs)
- Duration of action for analgesia: 6 hours
- Formulations: bupe/nlx, bupe mono
  - Long-acting injectables
  - Microgram doses- buccal and transdermal
- Abstinence required to start this medication
  - Risk of precipitated withdrawal in setting of dependence



Comparing Opioid Affinity & Effect

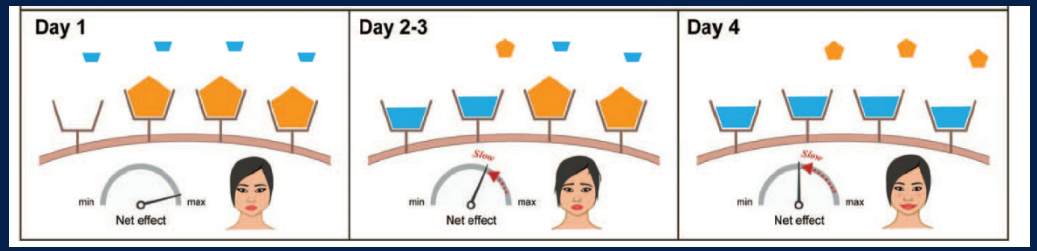


PubChem https://pubchem.ncbi.nlm.nih.gov/

Case Presentation

- 42-year-old male presents after autoped accident with multiple injuries
- Reports using fentanyl 10 bags/day IV
- Moderate withdrawal and severe pain
- Receiving oxycodone 15mg PRN pain
- Declines buprenorphine initially for multiple reasons – current pain and requirement for abstinence to start buprenorphine induction.
  - “I’m not stopping opioids! I’m in pain!”

Buprenorphine Microinduction

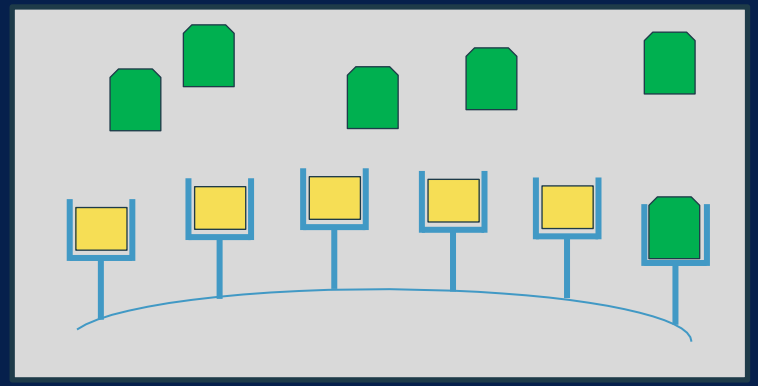


Buprenorphine 3-Day Microinduction	
Day 1	Buprenorphine (Belbuca) 300mcg Q3 x 8 doses
Day 2	Buprenorphine (Belbuca) 750mcg Q3 x 8 doses
Day 3	Buprenorphine 12mg SL x 1

Analgesia in Setting of Buprenorphine Maintenance

- Buprenorphine plus short-acting opioids
  - Adding tolerant dose short-acting opioids to buprenorphine can provide some added analgesia
  - 80 % of receptors are occupied at 16mg/day

  - Example regimen:
    - Buprenorphine/naloxone 4/1mg QID
    - Oxycodone 30mg PO Q4 PRN pain
    - Hydromorphone 2mg IV PRN dressing changes



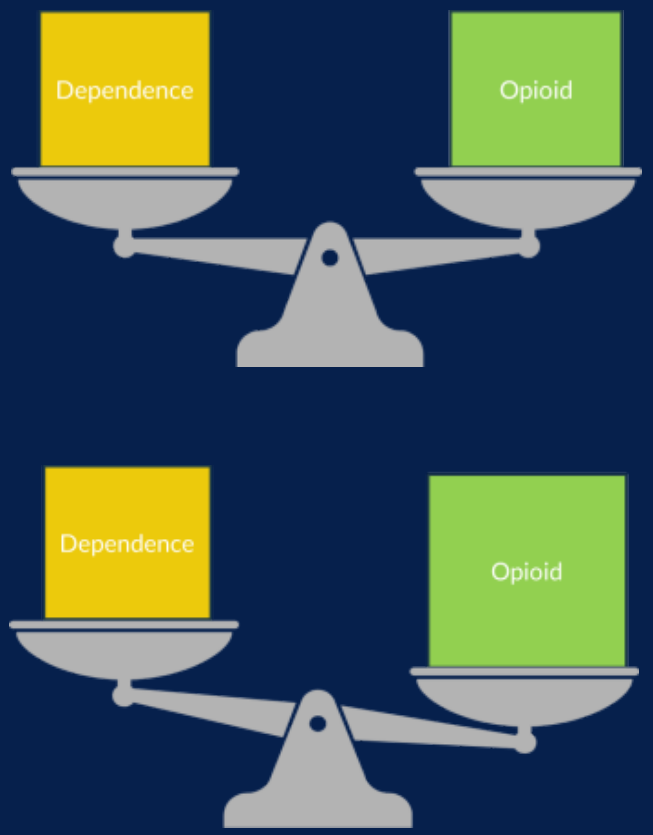
- Buprenorphine (yellow) stable on opioid receptor
- Adding tolerant dose oxycodone (green) provides added analgesic effect

Harrison TK, Kornfeld H, Aggarwal AK. Perioperative Considerations for Medications for Opioid Use Disorder: Buprenorphine, Methadone, or Naltrexone. Anesthesiol Clin. 2025 Dec;43(4):645-658. doi: 10.1016/j.anclin.2025.07.004. Epub 2025 Sep 13. PMID: 41233100.

Analgesia in Setting of Buprenorphine Maintenance

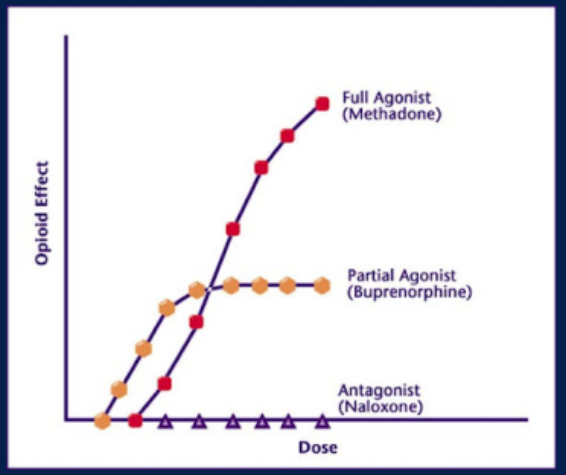
“Buprenorphine won’t treat my pain”

- Patient experience of getting onto buprenorphine from fentanyl
  - Misconception about buprenorphine
- “Tipping the scale” for patients on lower dose buprenorphine
  - Increasing total daily dose provides more opioid effect
- Splitting the dose
  - More frequent dosing improves pain control
  - Duration of action of analgesia for buprenorphine: 6hrs
  - 4mg QID >>> 8mg BID even though both are 16mg/day



Case Presentation – Perioperative Care

- 62-year-old female presents for total knee replacement in recovery on buprenorphine 32mg/day x years
- Complaining of uncontrolled pain despite tolerant dose opioids x 2 days
- On history, she reports that she did not take any buprenorphine day of surgery to avoid “blocking” opioids for pain and has refused buprenorphine since admission
- On evaluation, patient is experiencing mild withdrawal symptoms and appears uncomfortable
- Plan to reintroduce buprenorphine 16mg/day as 4mg QID, continue tolerant dose opioids, and wean PRN opioids to off as tolerated as outpatient



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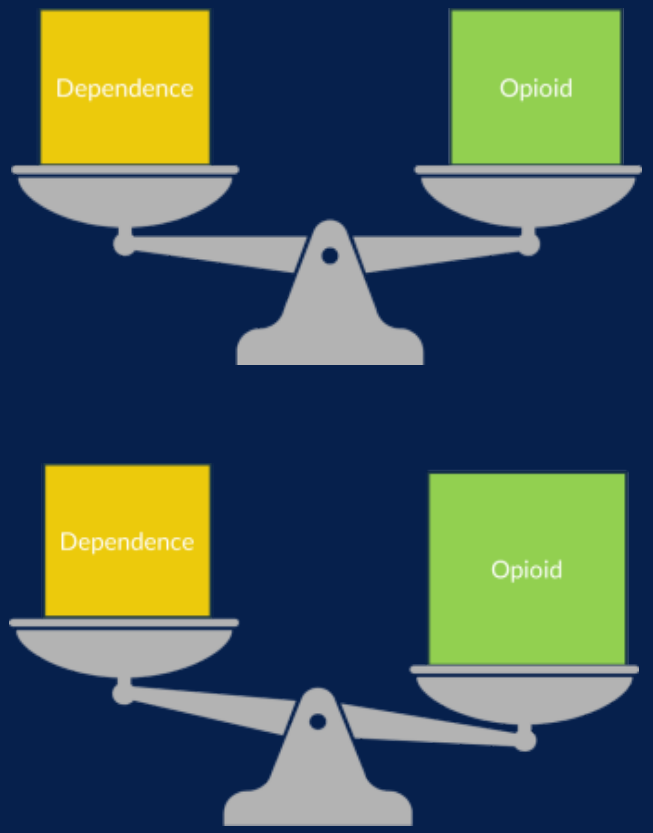
Analgesia in Setting of Methadone Maintenance

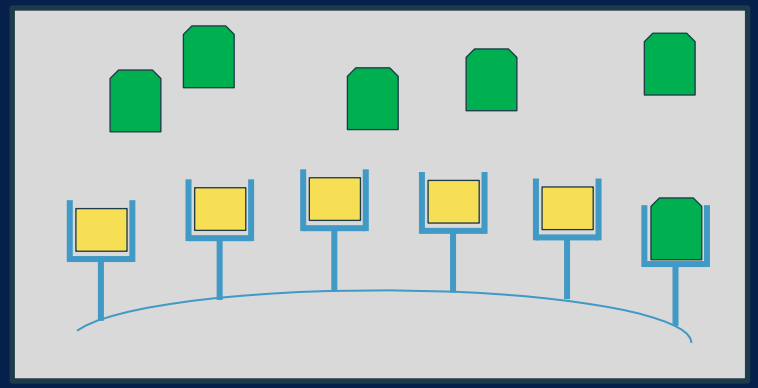
"I need to be on methadone because I have pain"

- Patient experience with methadone opioid effect
  - Misconception that methadone will always provide them the same pain control
- "Tip the scale"
  - Increasing total daily dose provides more opioid effect
- Splitting the dose
  - Duration of action of analgesia for methadone: 4-8hrs
  - Split dosing more effective for pain control



Analgesia in Setting of Methadone Maintenance

- Methadone plus short-acting opioids
  - Adding tolerant dose short-acting opioids to methadone can provide some added analgesia
  - High potency/affinity opioids displacing methadone
    - No risk of precipitated withdrawal
  - Example regimen:
    - Methadone 100mg PO daily (or 50mg BID)
    - Oxycodone 30mg PO Q4 PRN pain
    - Hydromorphone 2mg IV PRN dressing changes



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Other Full-Agonist Treatment: Oxycodone CR

Oxycodone CR 100mg PO Q8 hours scheduled

WITHDRAWAL/DEPENDENCE

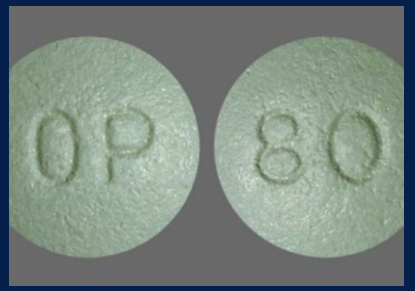
Tolerant dose short-acting opioids PRN for pain

Oxycodone 30mg Q4 PRN mild/moderate/severe pain

Hydromorphone 2mg IV Q3 PRN breakthrough pain

PAIN

Oxycodone CR



- Especially useful for patients not able to take methadone due to QTc prolongation and are able to take PO
- While short-acting IV opioids can provide rapid relief, focus on titrating oxycodone CR for sustaining relief
- Oxycodone CR 100mg equivalent to methadone 40mg

Swarm RA, Paice JA, Anghelescu DL, Are M, Bruce JY, Buga S, Chwistek M, Cleeland C, Craig D, Gafford E, Greenlee H, Hansen E, Kamal AH, Kamdar MM, LeGrand S, Mackey S, McDowell MR, Moryl N, Nabell LM, Nesbit S; BCPS; O'Connor N, Rabow MW, Rickerson E, Shatsky R, Sindt J, Urba SG, Youngwerth JM, Hammond LJ, Gurski LA. Adult Cancer Pain, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2019 Aug 1;17(8):977-1007. doi: 10.6004/jnccn.2019.0038. PMID: 31390582.

Case Presentation

- Patient with chronic pain (chronic pancreatitis) and no use disorder on oxycodone CR 60mg TID and Oxycodone 20mg Q4 PRN at home, admitted for bowel obstruction
- NPO, cannot give oxycodone CR or oxycodone
- While pain is adequately controlled initially with hydromorphone pushes, staff reports his pain is getting more difficult to control and requiring more frequent dosing.
- Plan for hydromorphone PCA pump temporarily
  - Hydromorphone PCA 0.6mg/hr, 0.3mg Q10min (2.4mg)

Hydromorphone PCA Pump

Hydromorphone 1mg/hr IV continuous infusion — WITHDRAWAL/DEPENDENCE

Hydromorphone 0.5mg Q10 min demand boluses — PAIN

- Titrate continuous infusion for withdrawal, titrate boluses for pain
- Hybrid: LA opioid plus bolus only PCA pump

- Benefits:
  - Patient autonomy, on demand therapy
  - Reduces nursing resource for medication administration
  - Re-aligns nursing therapeutic relationship
  - Safest way to administer high-dose opioids

Macintyre PE. Safety and efficacy of patient-controlled analgesia. Br J Anaesth. 2001;87:36-46

Discharge Planning on Opioids

- Patients in recovery or no use disorder
- Patients not in recovery

<u>Overall strategies</u>

- Smallest effective dose for shortest period of time
- Involve support system to monitor/dispense medication
- Frequent check-ins
- Monitoring with drug screening if necessary
  - UDS pitfalls: medications recently administered in the hospital
- Chronic opioids
  - Wean slowly to off as able – typically recommended 10% per month

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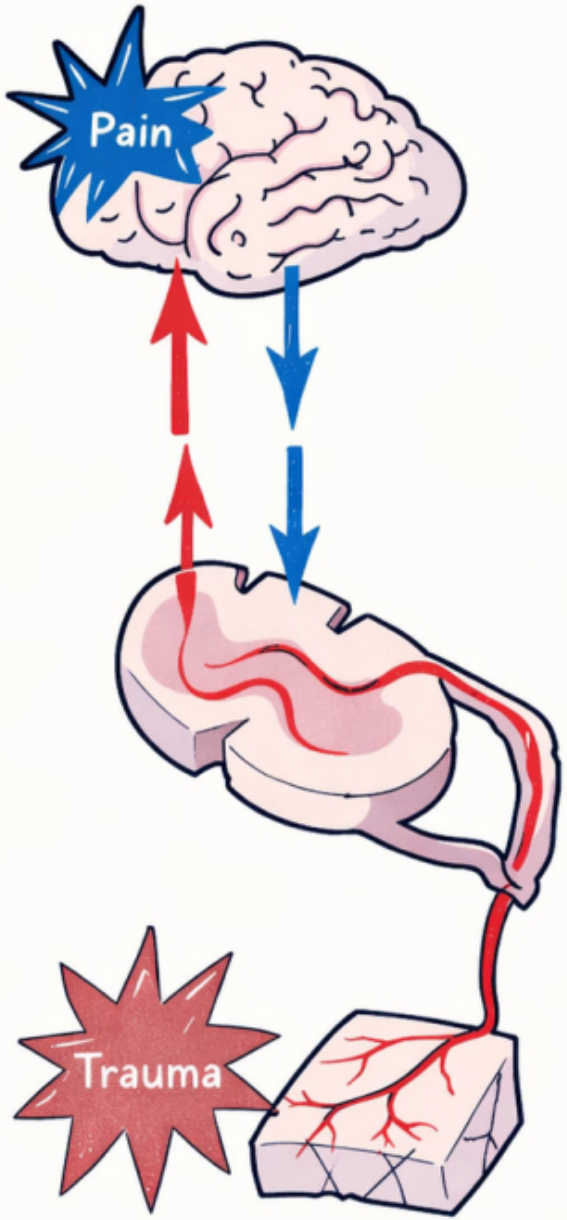
Outpatient Opioid Pain Management & SUD

- Screening for risk to develop OUD before opioids are started – Careful risk assessment
- Boundaries
  - "Pain contracts" → opioid treatment agreement (therapeutic collaboration > punitive)
  - Drug screening, pill counts, early refills procedure, off-hours/weekend refills, admissions to hospital, dose adjustments
  - Engagement with other treatments – PT, diet, non-opioid medications, injections, etc…
- Care plans for elective surgeries
  - Care coordination to continue MOUD peri-op
  - Coordinate peri-op pain control: opioids, opioid-free, or opioid-less plans
  - Discharge planning post-op
- Adjustments to opioid care plans
  - Slow, thoughtful adjustment to dose with basal bolus balance in mind
  - Medication availability at local pharmacy

Opioid Sparing Pharmacology

Opioid Sparing Pharmacology: Guide



Receptors

Mu NMDA

TRPV1 GABA D1-R

5-HT Alpha-2

Enzymes

COX 1 COX 2

COX 3

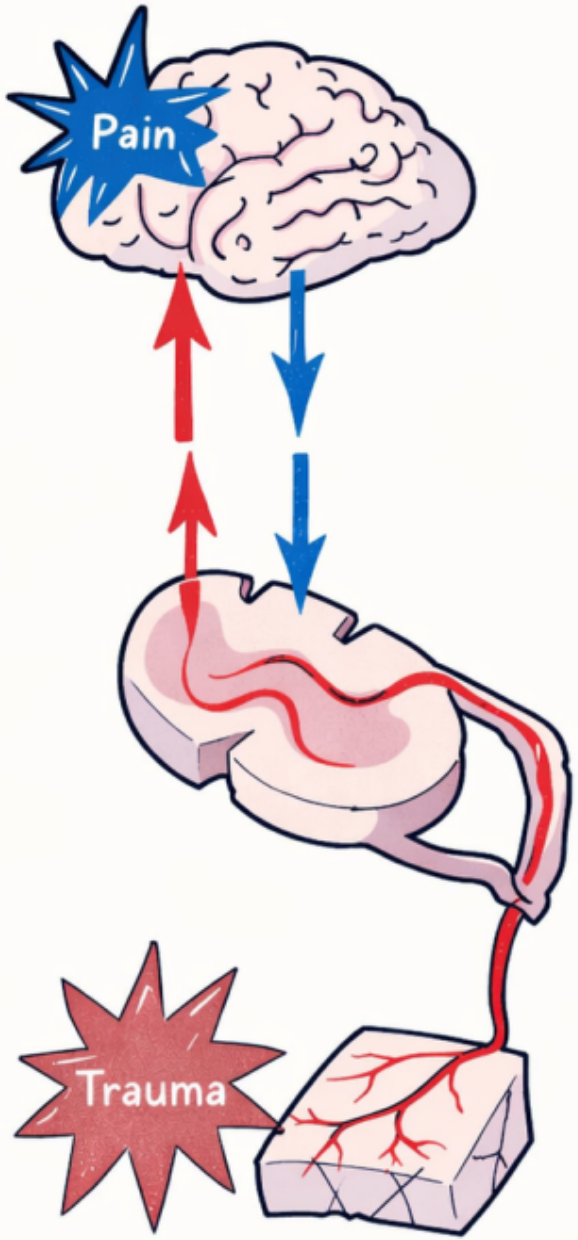
Channels

Sodium Channels

Calcium Channels

Acetaminophen: OUD Pearls

- Schedule early
- Dose smart: 1000 mg q6hrs
- Liver disease: consider <2 g a day
- Avoid "hidden" acetaminophen
- Pair with NSAID when safe



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NSAIDs: OUD Pearls

- Schedule with acetaminophen "base"
- Dose to analgesic ceiling
  - Ex: ibuprofen 400 mg q6hrs
- Know when to avoid
- Consider Cox-2 selective in high-risk patients

Case Presentation

32-year-old with OUD on **buprenorphine/naloxone** presents with a **closed ankle fracture**. Pain improved after hematoma block, however continues to have mild pain (2/10). Patient wants to avoid opioids.

Maximize Receptors and Enzymes!

- Step 1: Safety Checklist
- Step 2: Set the base Regimen
  - APAP 1000 mg q6hrs, Ibuprofen 400 mg q6hrs
- Step 3: Reassess and Escalate as needed

What if this patient has an AKI, is on anticoagulation, and has a history of bariatric surgery?

Don't forget the skin!

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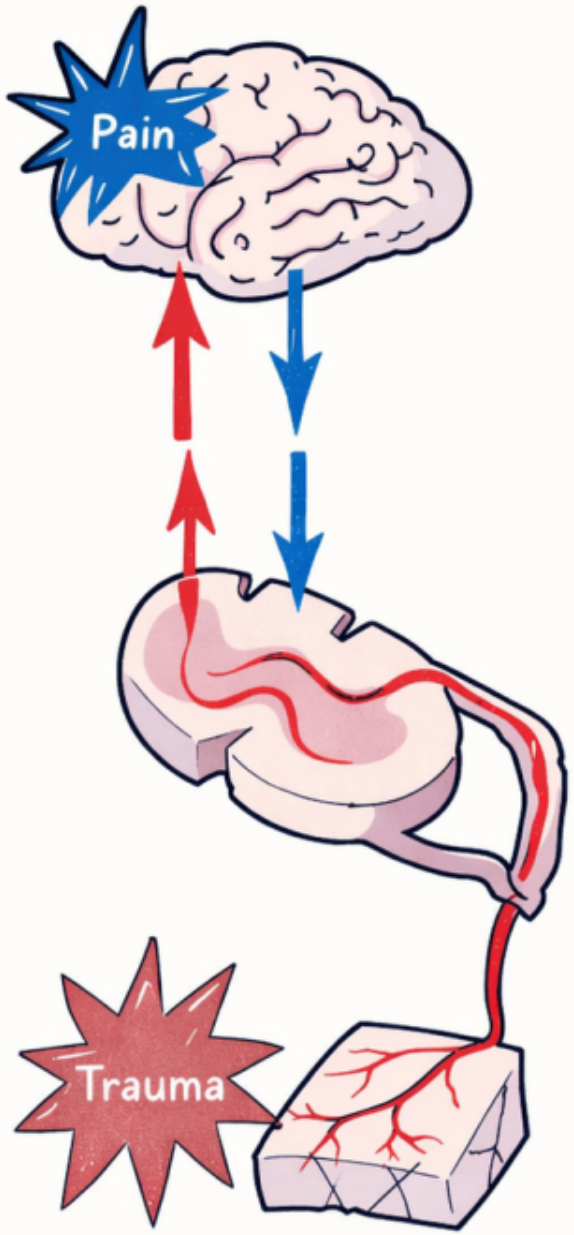
FOUNDED 1954
ASAM

Case Progression:

(Post-op day 1 after ORIF):

- Incisional pain is controlled, but patient now reports burning/tingling over the dorsum of the foot with allodynia. Pain 6/10, worse at night.



Receptors

Mu NMDA

TRPV1 GABA D1-R

5-HT Alpha-2

Enzymes

COX 1 COX 2

COX 3

Channels

Sodium Channels

Calcium Channels

Gabapentin: OUD Pearls

- Use for Neuropathic Pain patterns
- Dose low and titrate up
- Watch for renal impairment
- Reassess

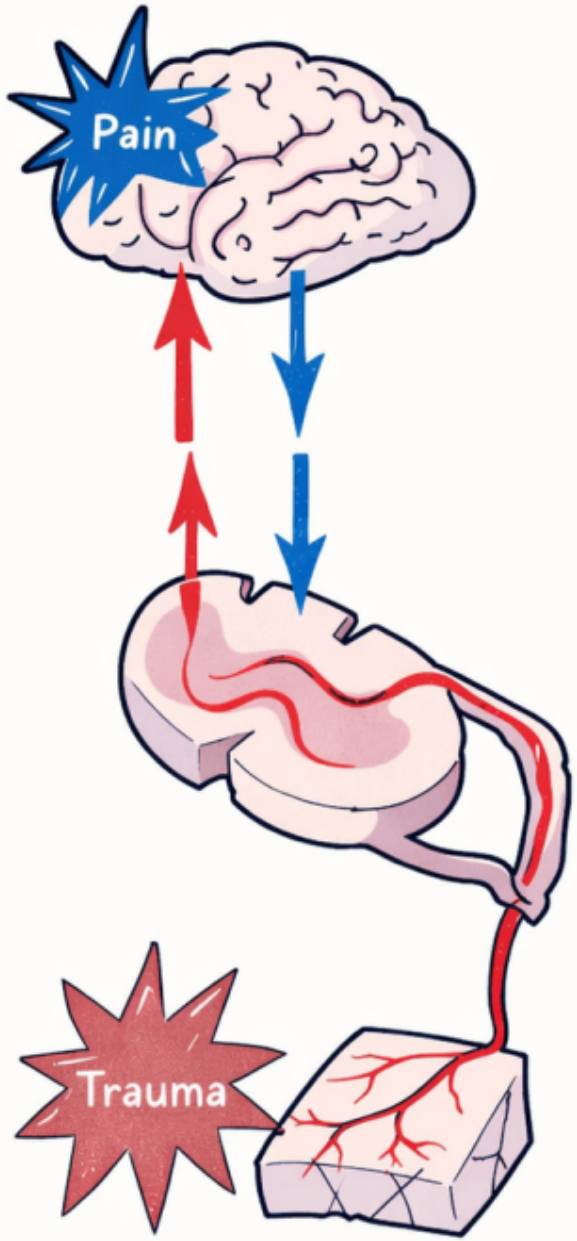
The Top 300 Drugs of 2022

2022

Rank	Drug Name	Total Prescriptions (2022)	Total Patients (2022)	Annual Change
1	Atorvastatin	109,582,746	27,935,702	0
2	Metformin	86,747,907	19,536,027	0
3	Lisinopril	82,513,967	20,314,304	↑ 1
4	Levothyroxine	82,431,914	18,130,331	↓ 1
5	Amlodipine	70,766,211	17,789,649	0
6	Metoprolol	65,245,216	15,542,999	0
7	Albuterol	59,075,269	19,265,334	0
8	Losartan	53,555,510	13,150,031	0
9	Omeprazole	52,132,950	13,802,111	0
10	Gabapentin	40,141,486	9,889,546	0

Case Progression:

Neuropathic symptoms improve, but the patient now reports **new tight, cramping pain** in the **calf and peroneal muscles** with **spasm worse with ankle movement/physical therapy**.



Receptors

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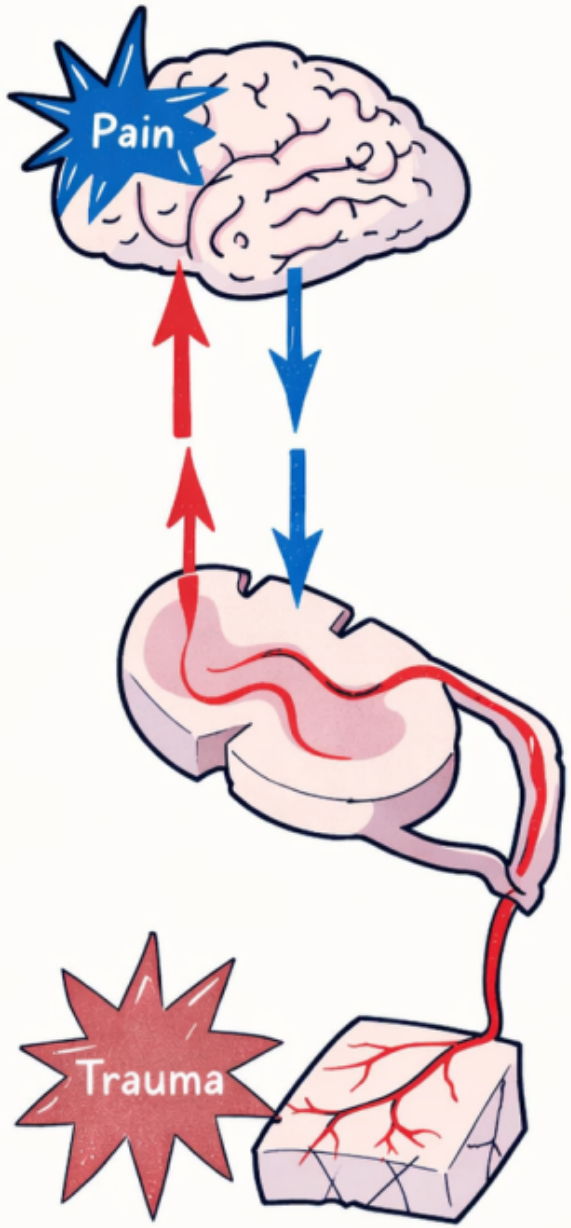
Muscle Relaxers: OUD Pearls

- Use for true muscle spasm
- Use with a strategic plan
- Monitor for sedation
- Treat the underlying cause

Case 2:

45-year-old with OUD on **methadone 110 mg daily** presents with an **ankle fracture** after a fall. Pain **10/10**, tachycardic, guarding. Last methadone dose taken this morning. Pain refractory to multiple doses of IV fentanyl and hydromorphone. "nothing is helping".



Receptors

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Calcium Channels

Ketamine: OUD Pearls

- Use for refractory pain/hyperalgesia
- IV has greatest evidence for pain
- Carefully dose
- Monitor for adverse events

Case Progression:

Pain improves with ketamine infusion over 3 hours. Patient is going to be transferred from the ED to the medical floors. He asks if there is anything else that can be done to help with pain.

Regional Analgesia

Headache

- Sphenopalatine Nerve
- Occipital Nerve

Neck Pain

- Superficial Cervical Plexus

Back Pain

- Trigger Point
- Erector Spinae

Chest Pain

- Parasternal
- Serratus Anterior
- Erector Spinae

Abdominal Pain

- TAP Block
- Subcostal
- Erector Sheath

Upper Extremity

- Brachial Plexus
- Ulnar, Radial, Median Nerve
- AC Shoulder Joint
- Glenohumeral joint
- Subacromial Bursa

Lower Extremity

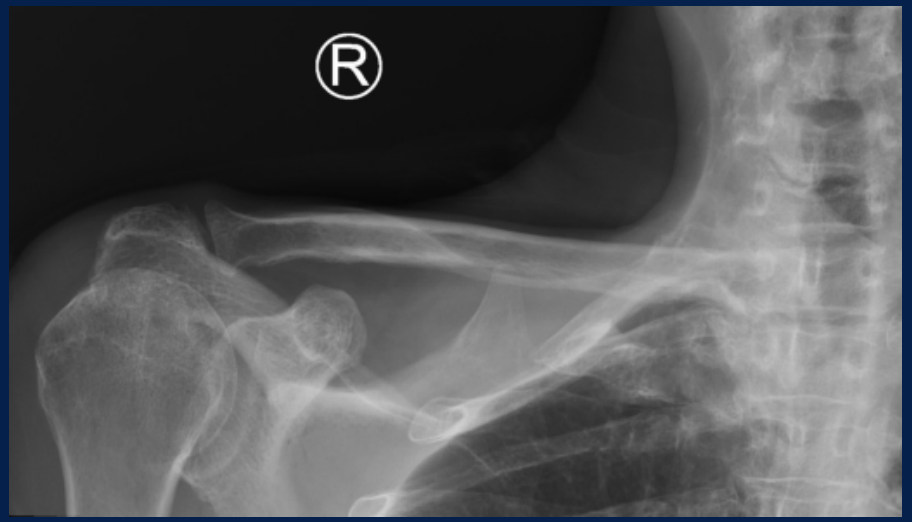
- Fascia Iliaca
- Femoral Nerve
- Suprapatellar recess
- PENG
- Popliteal
- Posterior Tibial

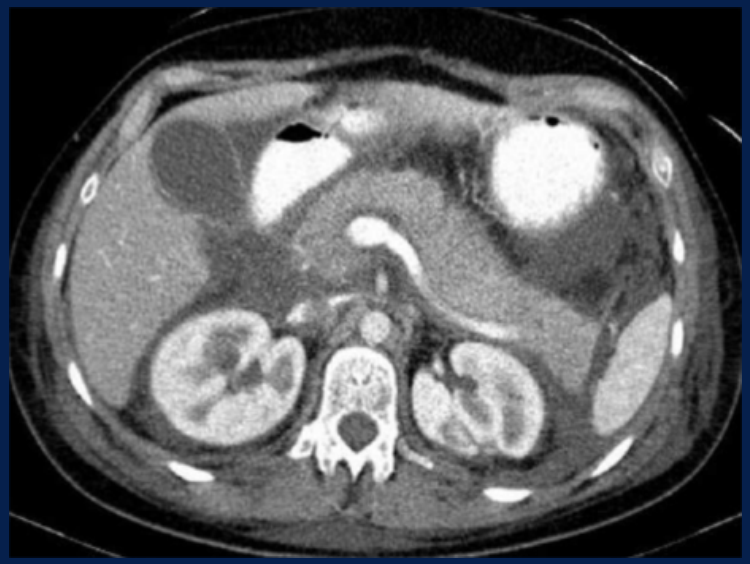
Abdominal Pain

- TAP Block
- Subcostal
- Rectus Sheath
- Erector Spinae

Why do we make patients in pain wait for relief when we have tools that can help them now?

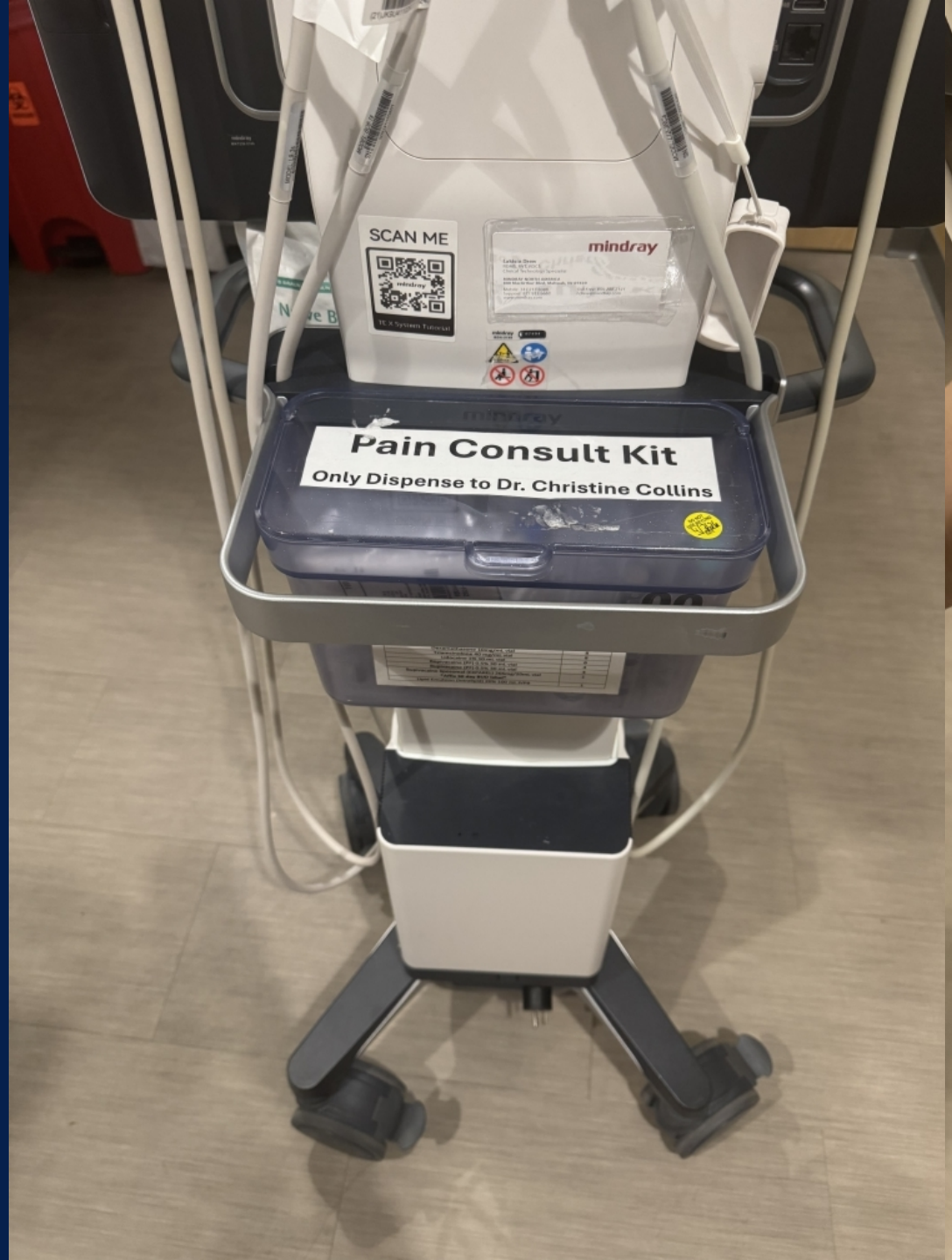
Addiction Medicine Run Block Service

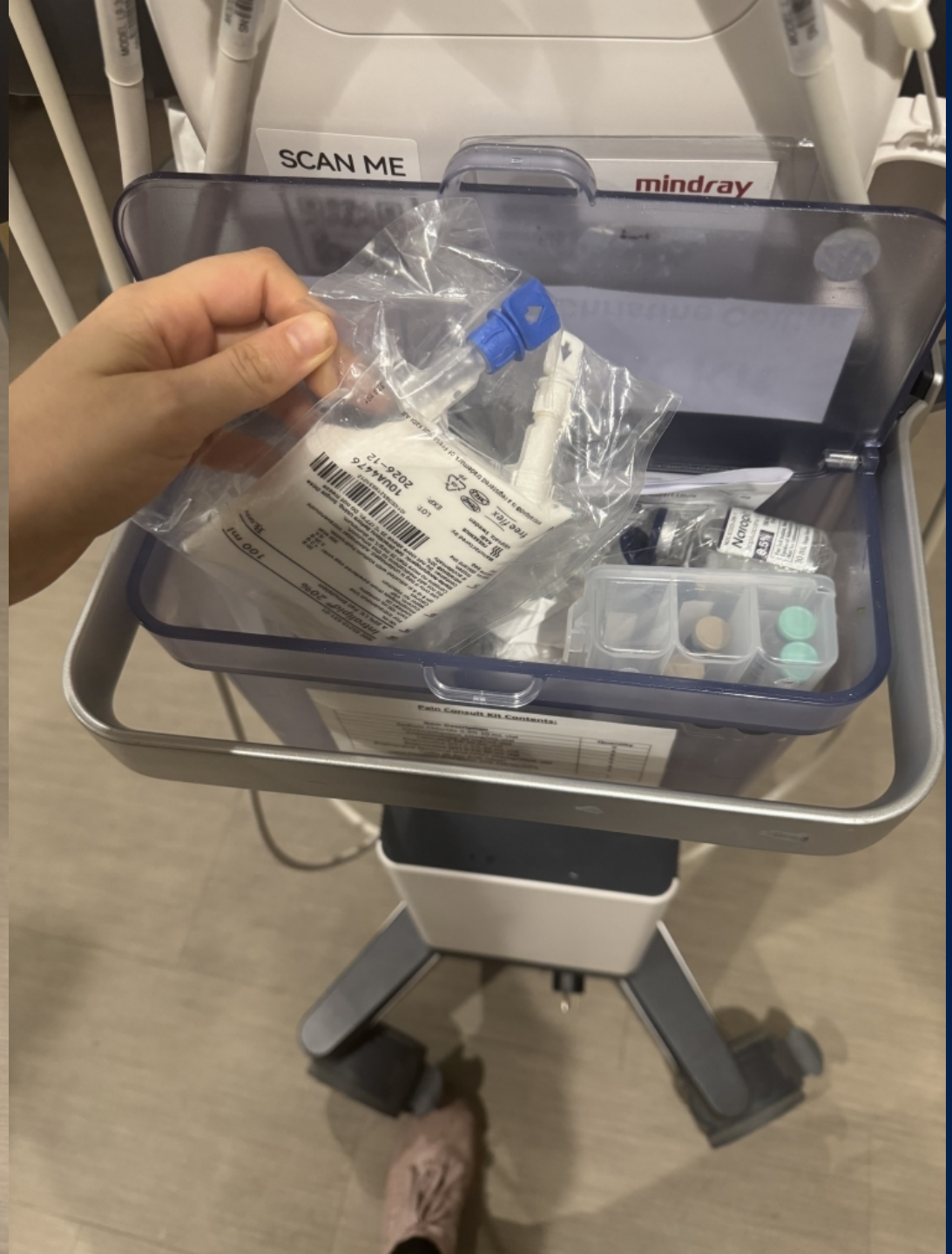


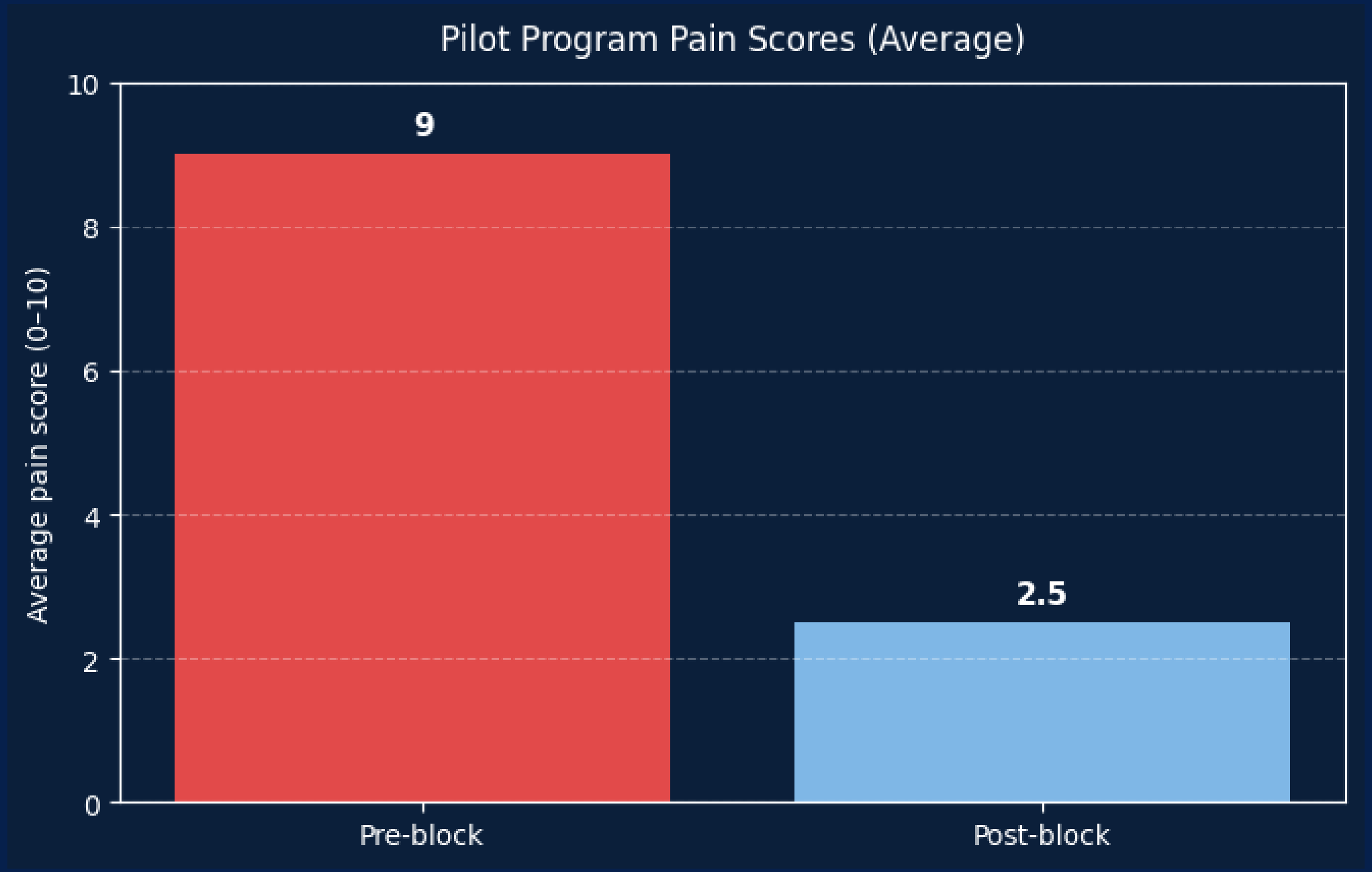


Pilot Program

- 0.3 FTE: Coverage
- Consult made to addiction medicine
- Inclusion criteria met for regional anesthesia
- Patient evaluated – block performed at the bedside


SCAN ME
mindray
Pain Consult Kit
Only Dispense to Dr. Christine Collins


SCAN ME
mindray


Pilot Program Pain Scores (Average)
Average pain score (0–10)
10
8
6
4
2
0
9
2.5
Pre-block
Post-block

Challenges

- Patient caution about procedure
- Staff training and comfort
- Resources
- Measuring Outcomes
- Billing

Final Takeaways/Summary

- **Treat Pain and Withdrawal Simultaneously by using a Basal–Bolus Opioid Strategy**
  - Target long-acting opioids to manage withdrawal and short-acting opioids for analgesia
- **Dose Analgesia Based on Tolerance**
  - Breakthrough doses should be 10–20% of the total daily opioid dose
- **Continue MOUD in the Hospital/Peri-operatively**
  - Methadone and buprenorphine should usually be continued during perioperative care. Acute pain should be treated in addition to maintenance therapy, not instead of it.

Final Takeaways/Summary

- **Optimize Non-Opioid and Multimodal Analgesia**
  - Effective pain control requires a multimodal base: Acetaminophen, NSAIDs, Neuropathic agents (e.g., gabapentin), Muscle relaxants, Ketamine for refractory pain
- **Match Therapies to Pain Patterns**
  - Neuropathic → gabapentinoids
  - Muscle spasm → muscle relaxants
  - Hyperalgesia/refractory pain → ketamine
  - Focal pain → regional anesthesia

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