Pain Management in patients on Medically Assisted Treatment for Opioid Use Disorder

Margaritaville 2023 ACP MO Chapter

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I have no **DISCLOSURES**

PLAN FOR TODAY:

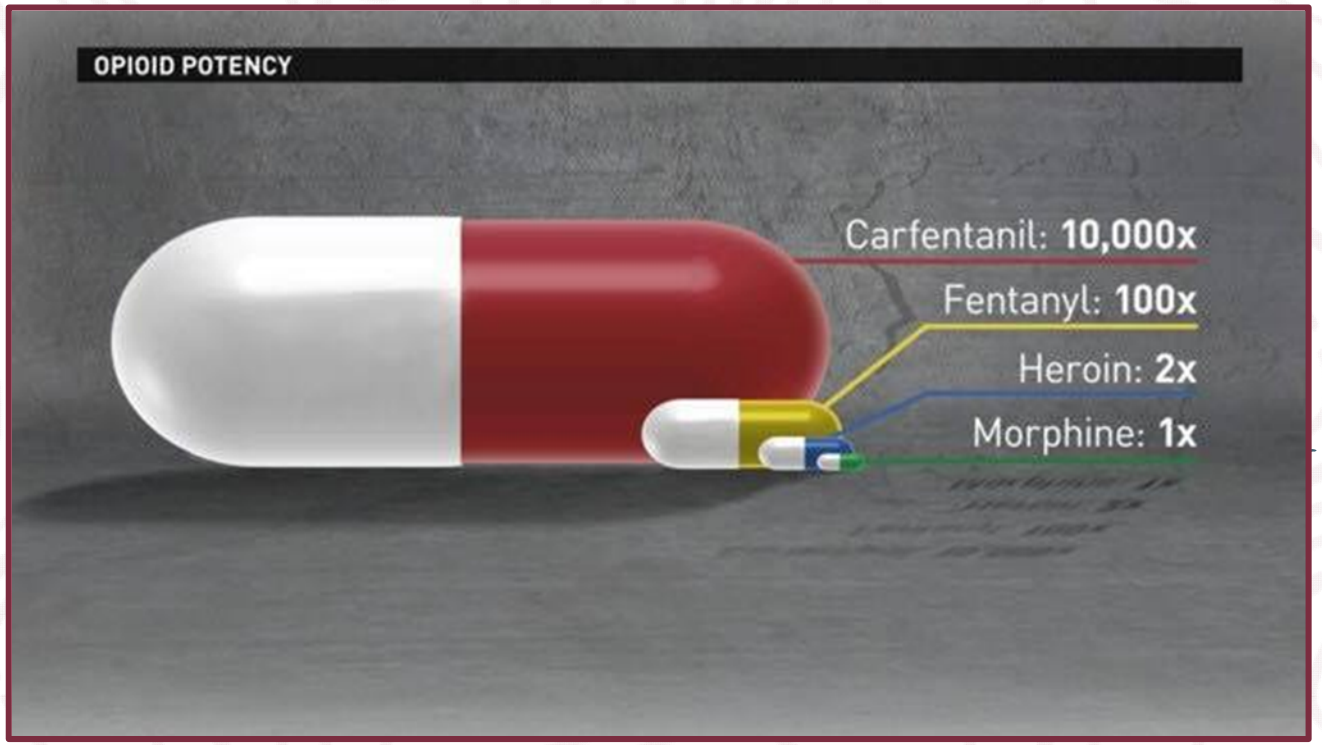
- *Basic understand of opioids and all that is Mu*
- *General concepts of Medically Assisted Treatment (MAT)*
- *Debunk old myths surrounding pain and MAT*

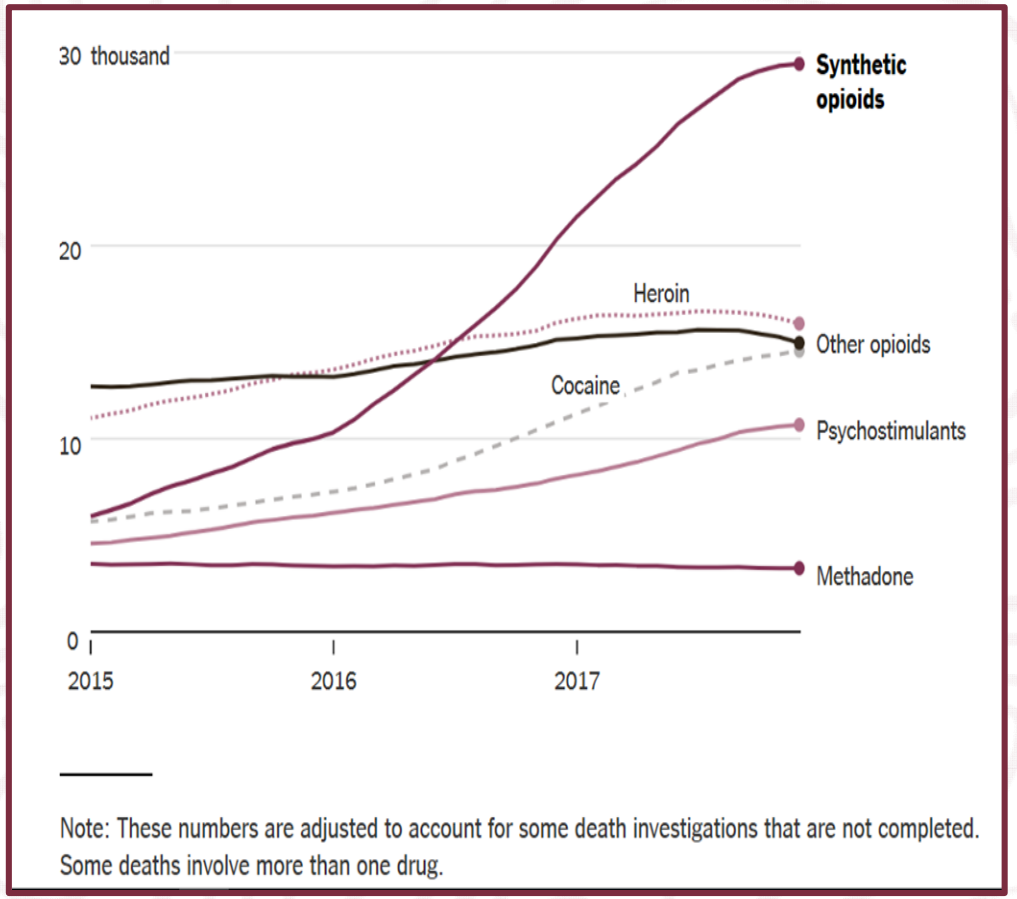
- *How to advise a patient on MAT having elective surgery*
- *What to do for a patient on MAT with acute pain emergency*

PLAN FOR TODAY:

- *Basic understanding of opioids and all that is Mu*

Opioids misuse





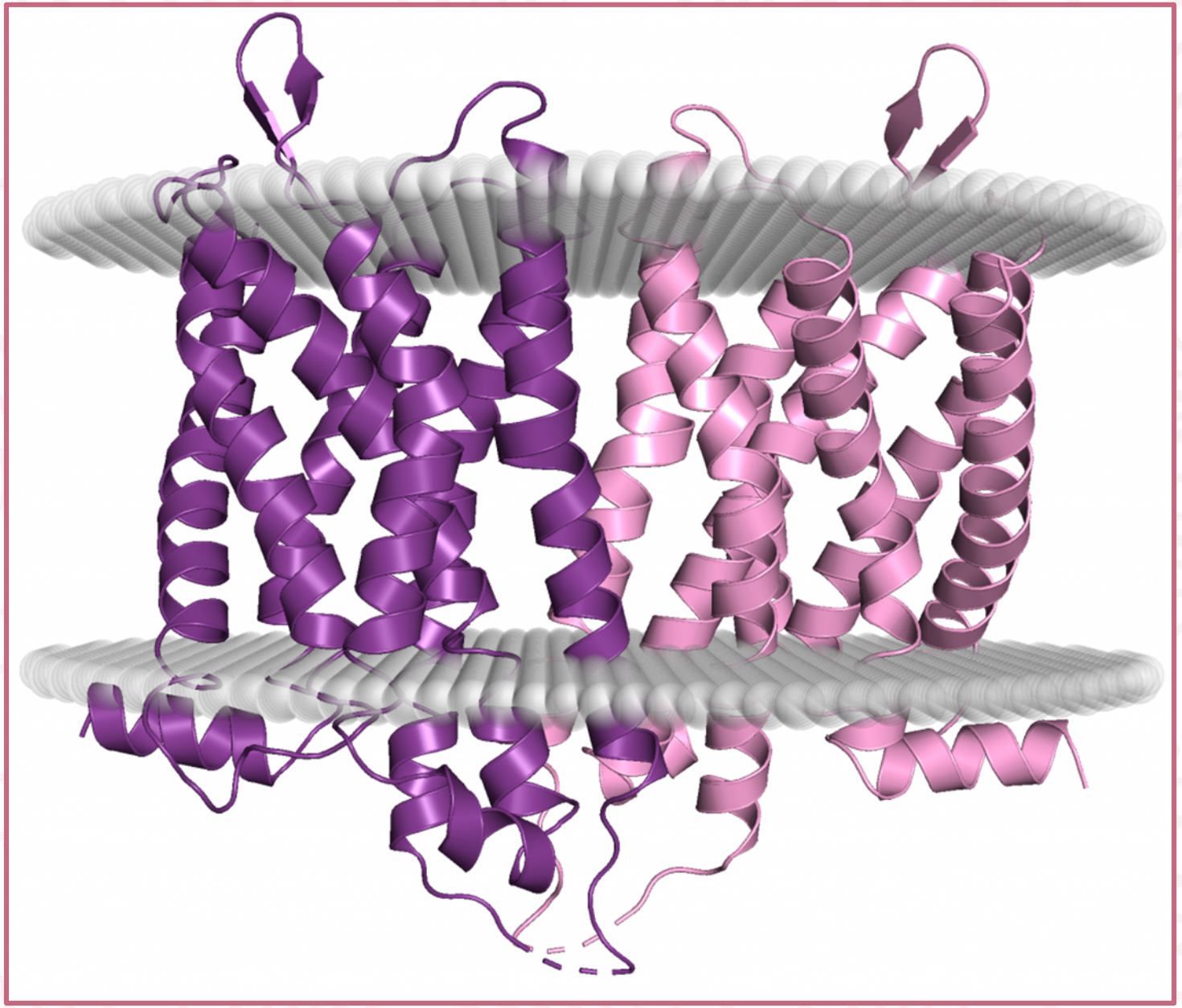
Opioid epidemic is killing our patients – 40 is the average age of a person who died in 2018

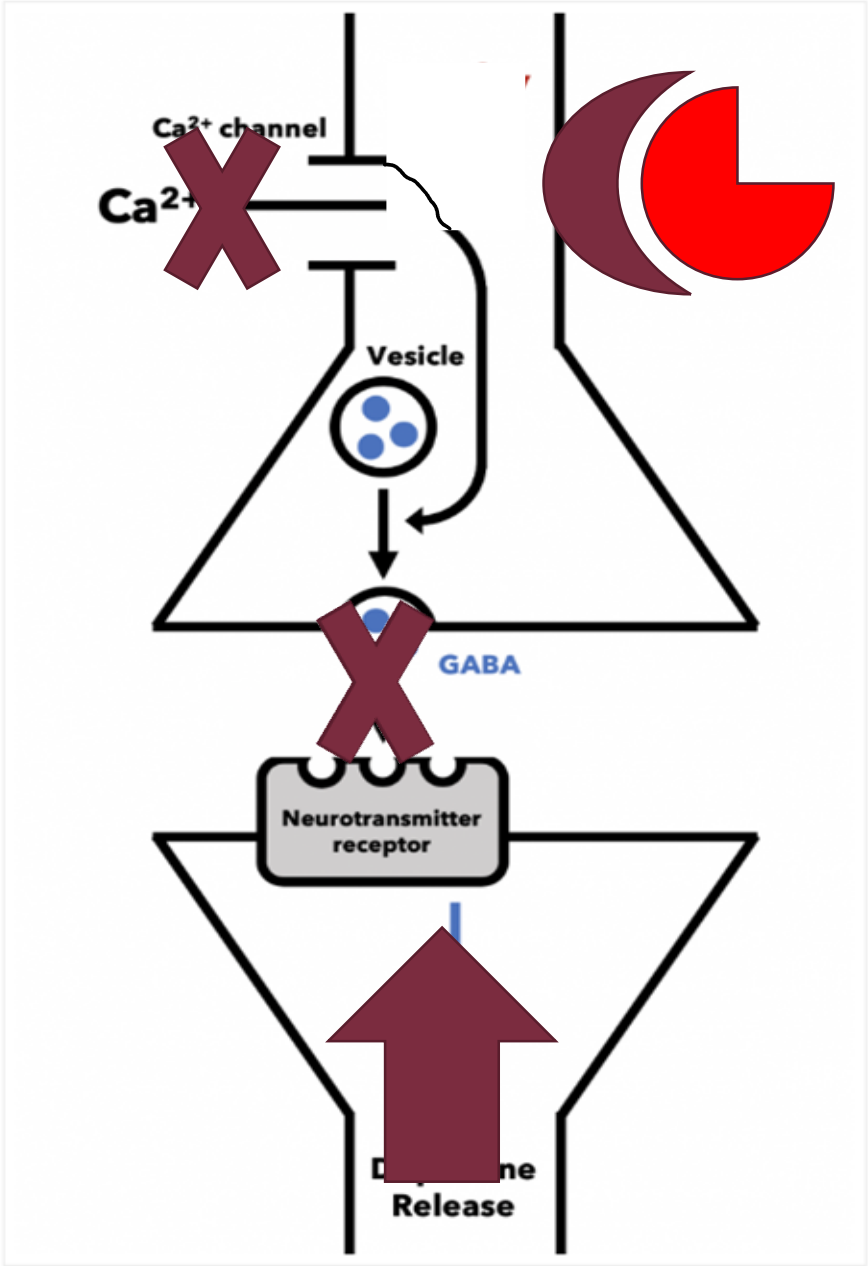
www.mohopeproject.org

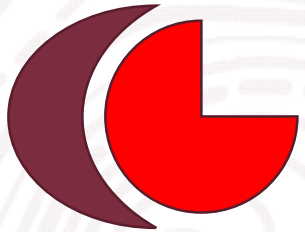
UNDERSTAND OPIOID RECEPTORS

Opioid-receptors

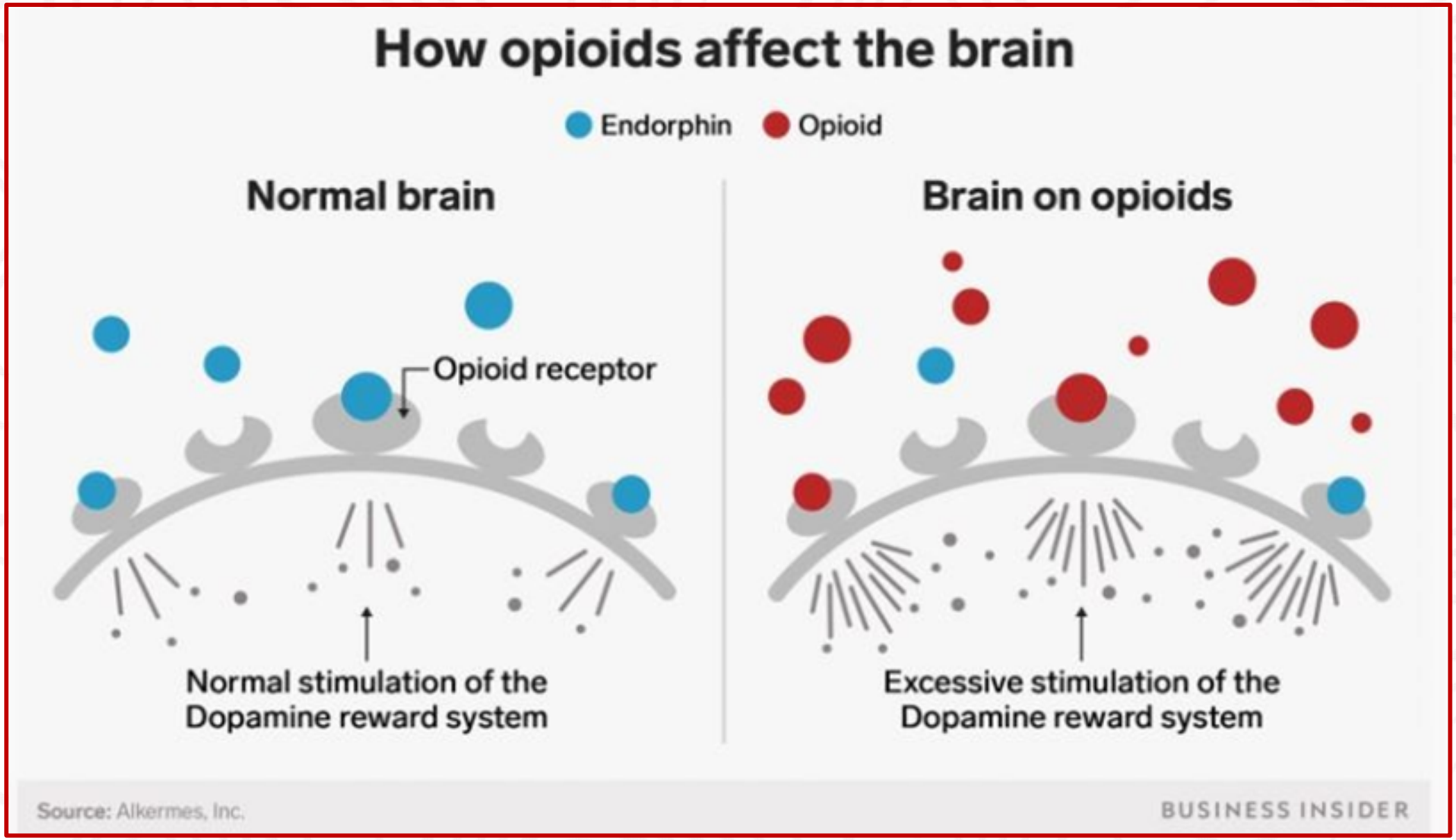
- There are three types of opioid receptors: mu (μ), delta (δ), and kappa (K).
- Opioid-receptor agonists produce analgesia by acting primarily at μ-receptors found in the **brain, brainstem, spinal cord, and primary afferent sensory neurons.**

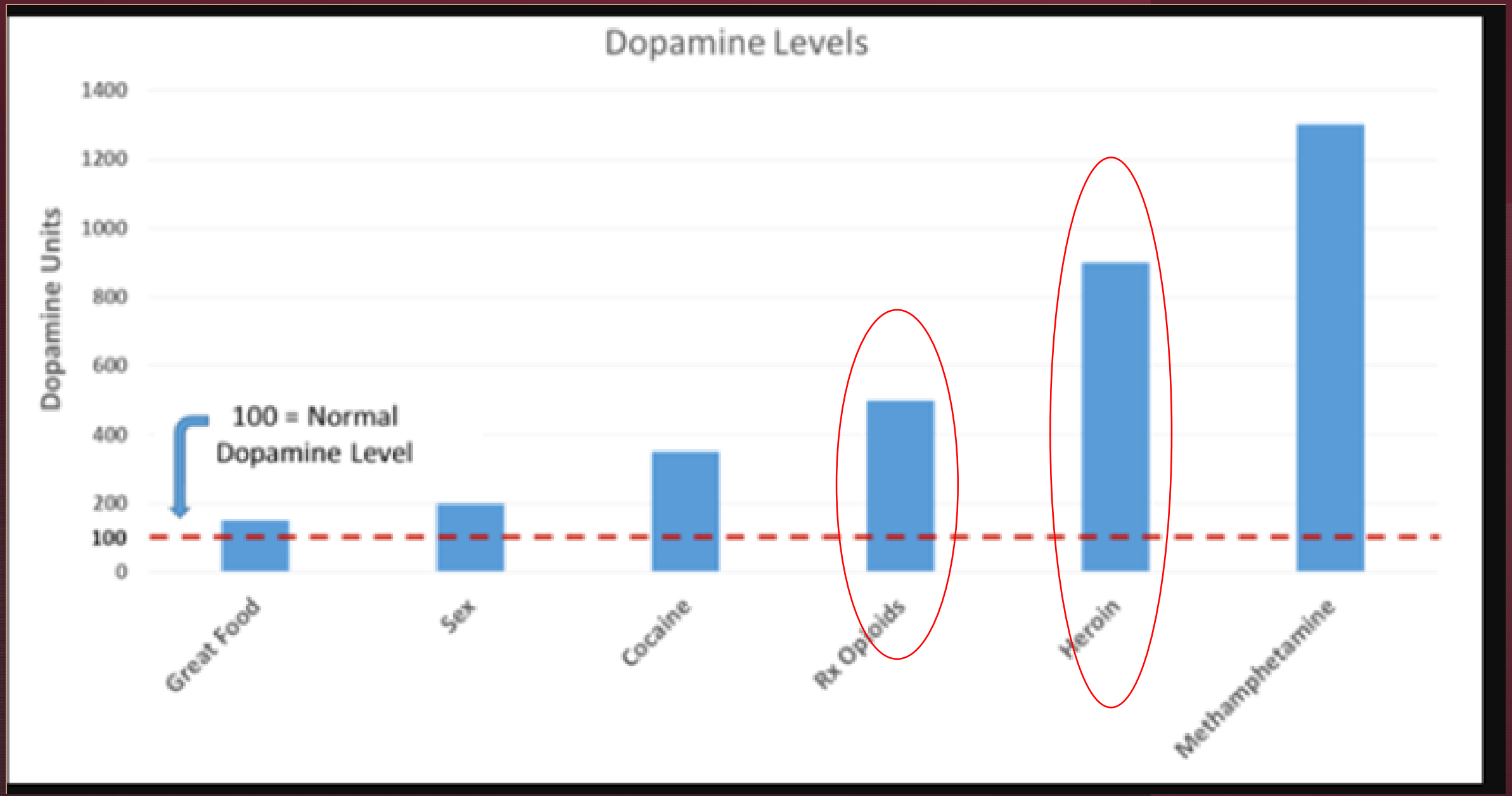



Ca2+ channel
Ca2+
Vesicle
GABA
Neurotransmitter receptor
Release

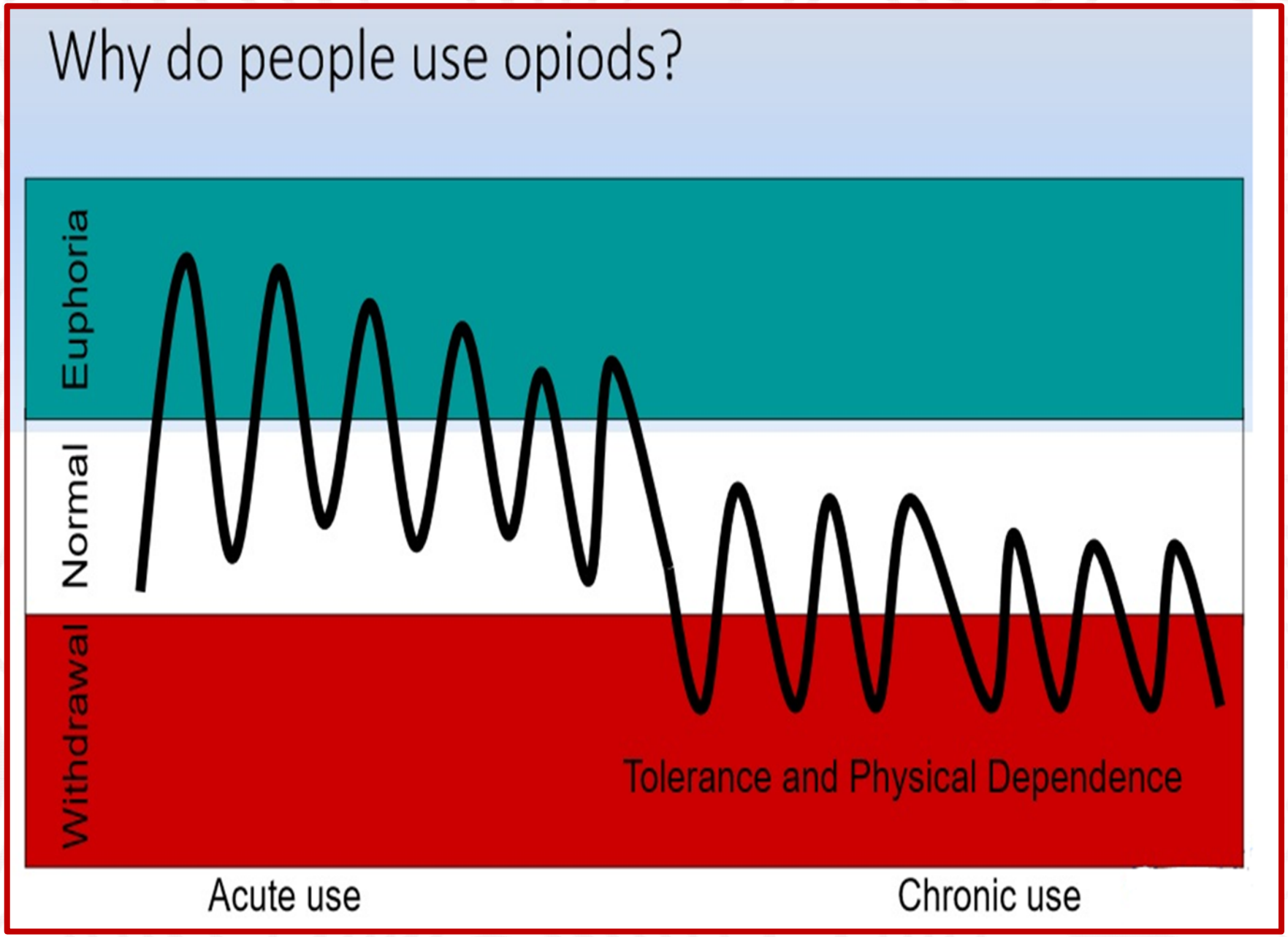


Mu R Opioid

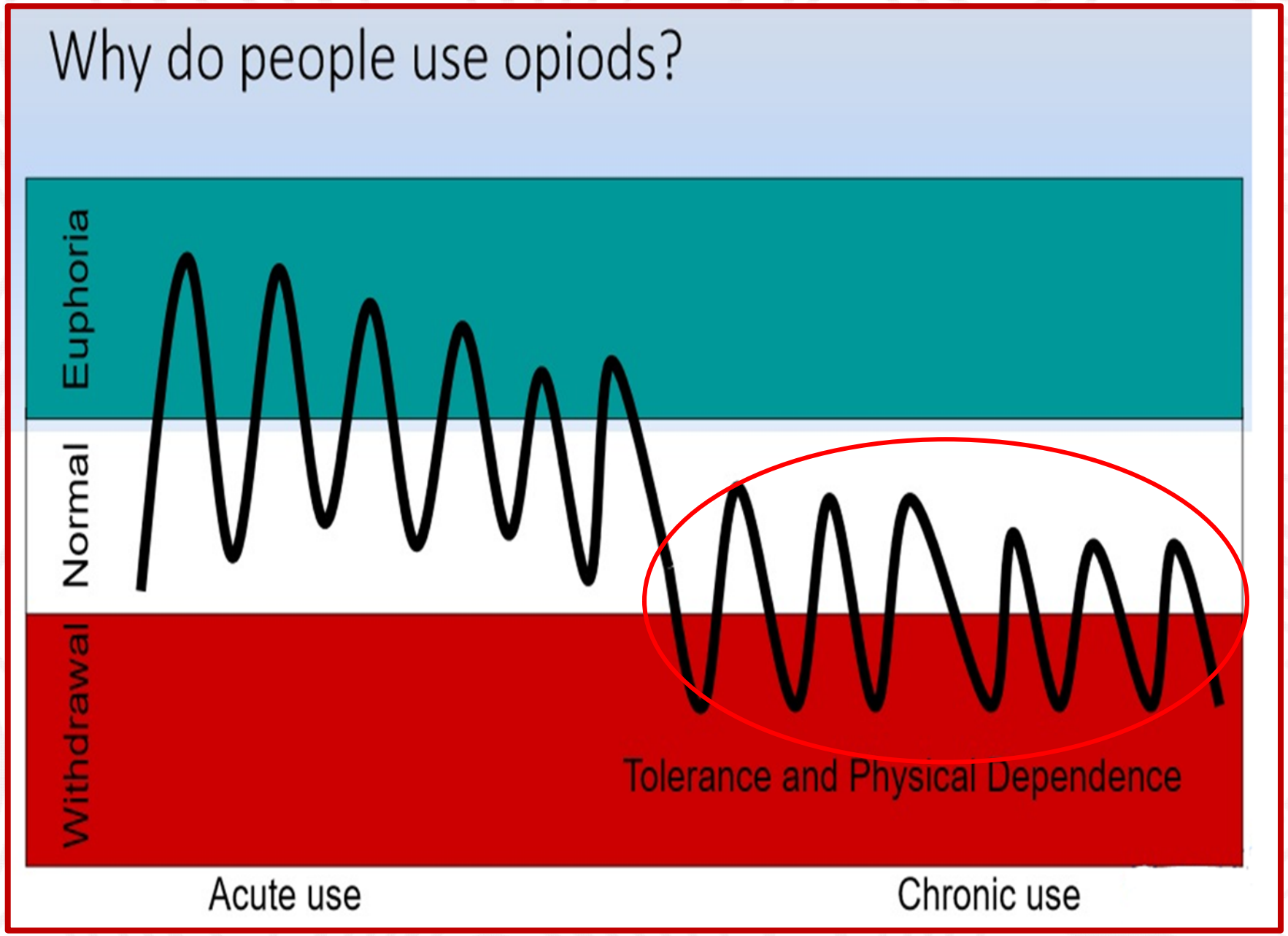

How opioids affect the brain
Endorphin
Opioid
Normal brain
Opioid receptor
Normal stimulation of the Dopamine reward system
Brain on opioids
Excessive stimulation of the Dopamine reward system
Source: Alkermes, Inc.
BUSINESS INSIDER


Dopamine Levels
Dopamine Units
1400
1200
1000
800
600
400
200
100
0
100 = Normal Dopamine Level
Great Food
Sex
Cocaine
Rx Opioids
Heroin
Methamphetamine

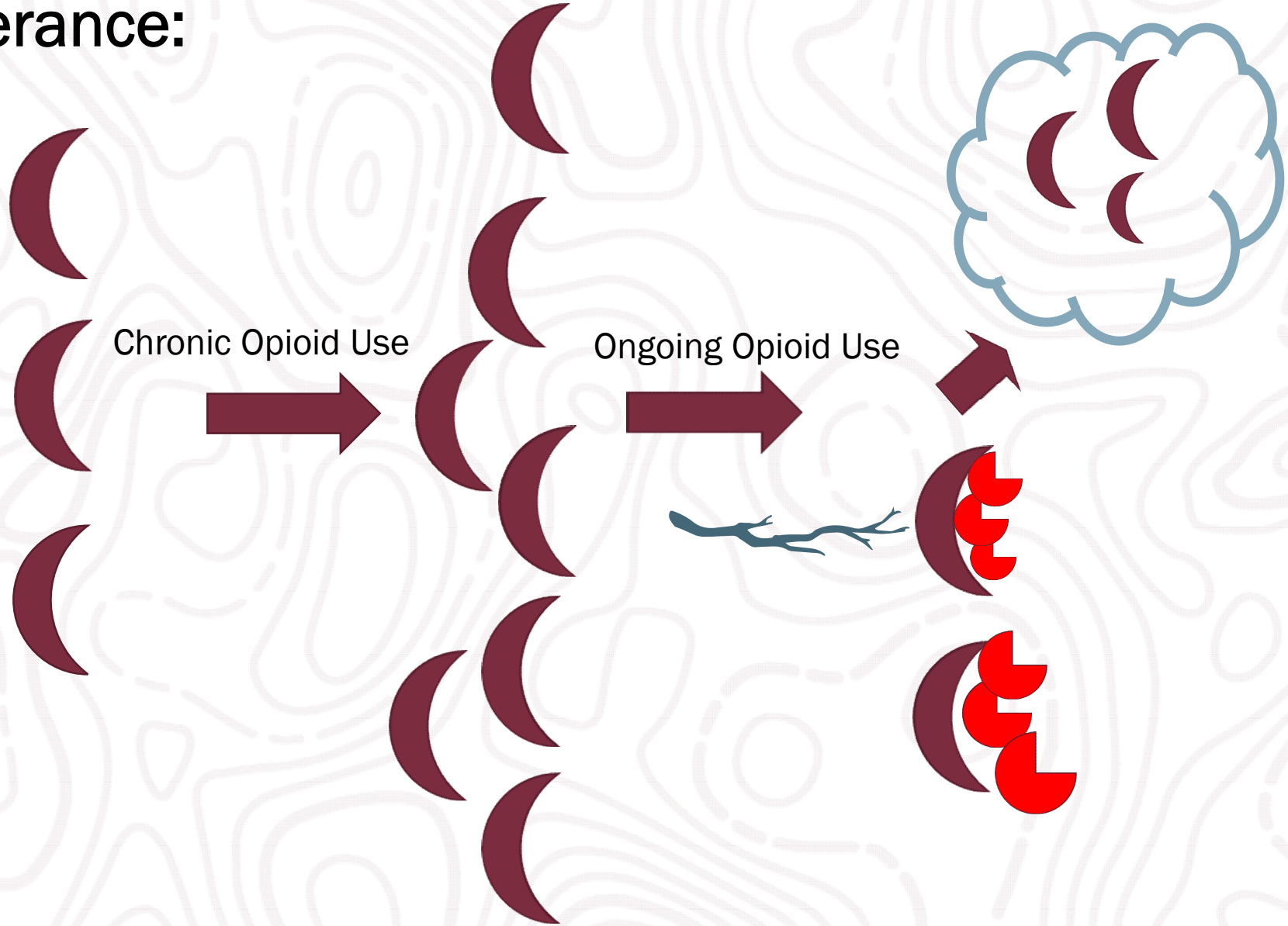
Why do people use opiods?



Why do people use opiods?



Tolerance:

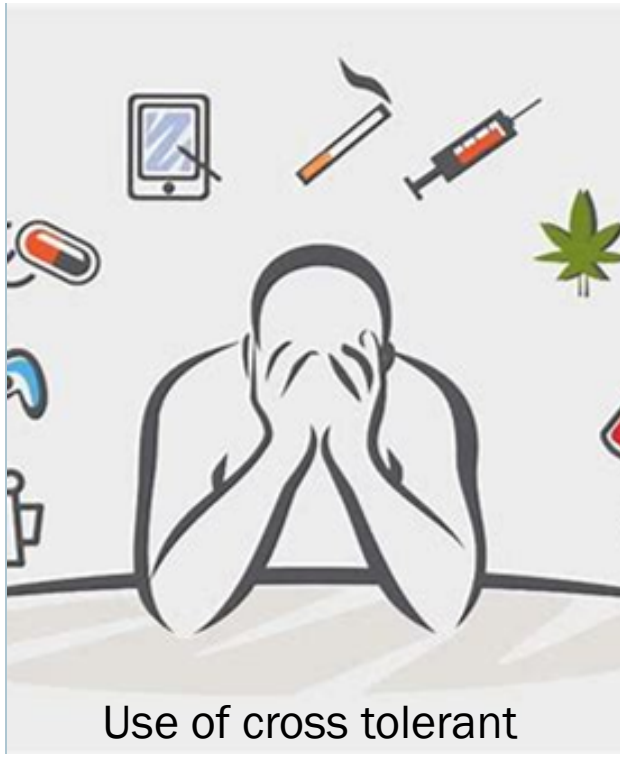


- *General concepts of Medically Assisted Treatment (MAT)*

OR rather GDMT (Guideline Directed Medical Therapy)

General concept of treating SUD

Suppress withdrawal



Use of cross tolerant medication

Reducing signs and symptoms withdrawal

“Comfort Medications”

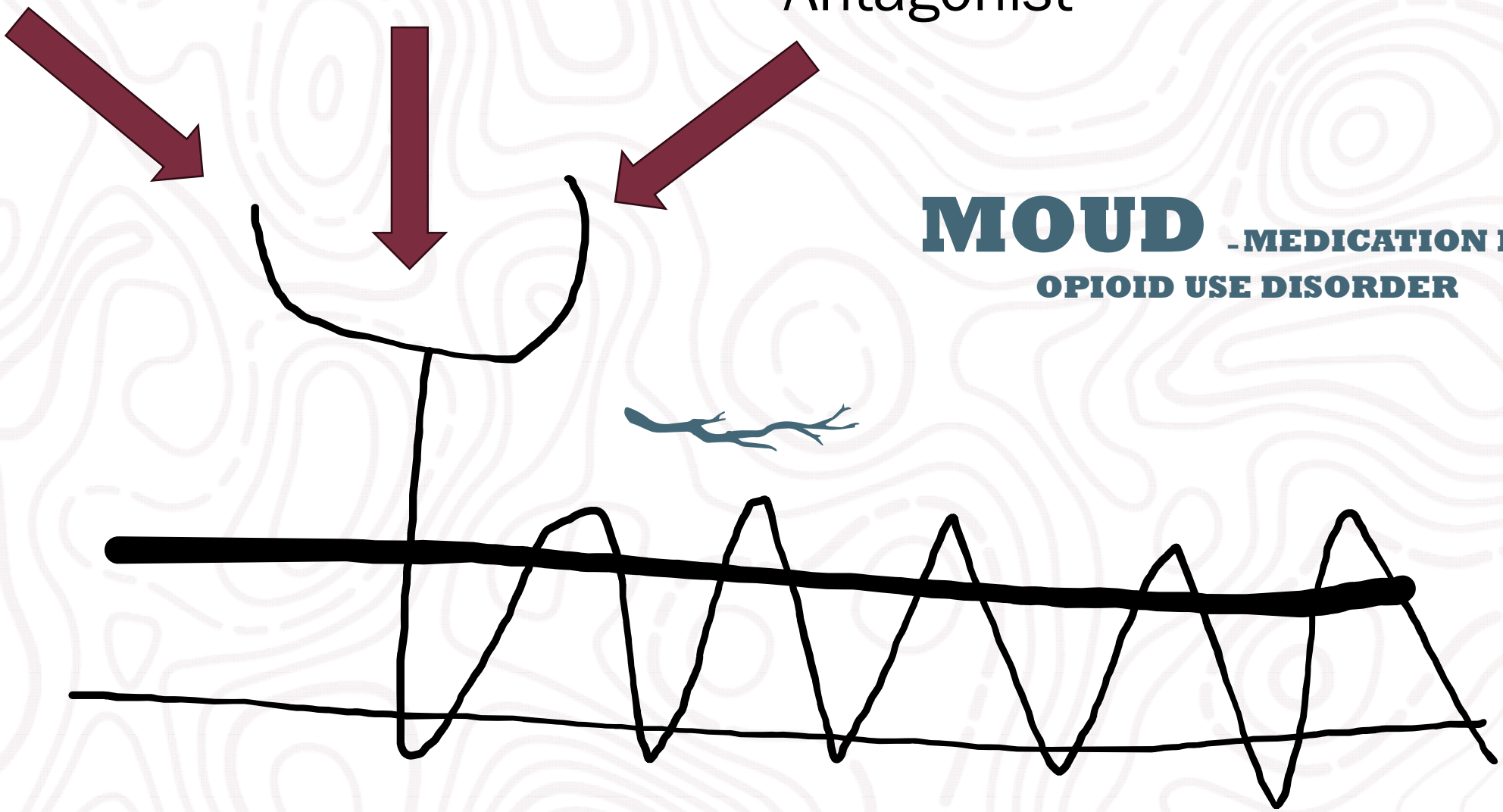
Relapse Prevention

Relapse comparable to rates relapse in other chronic illness. . Ongoing use of GDMT

Full Agonist

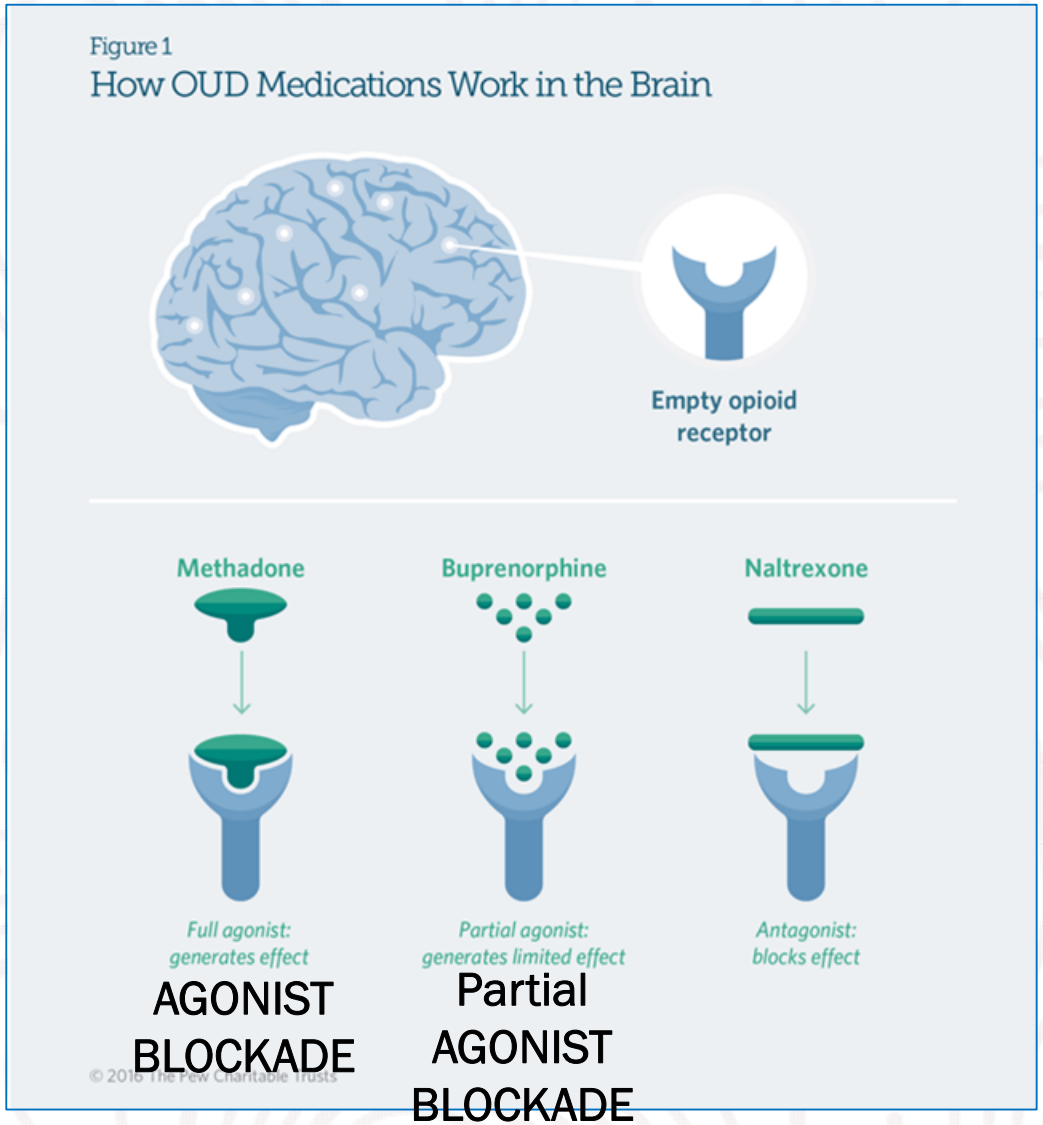
Partial Agonist

Antagonist



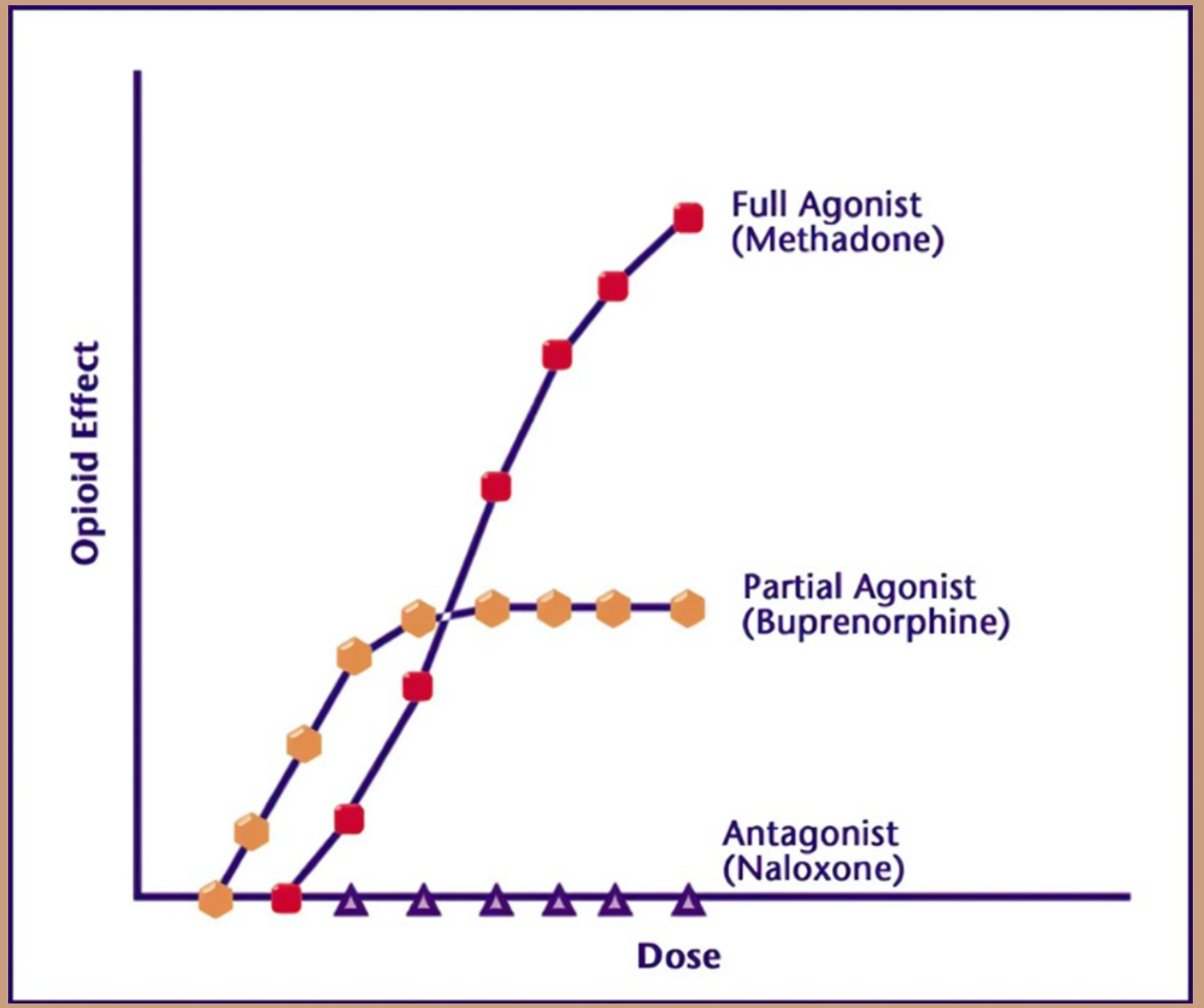
MOUD - MEDICATION FOR OPIOID USE DISORDER

MOUD FOR OUD

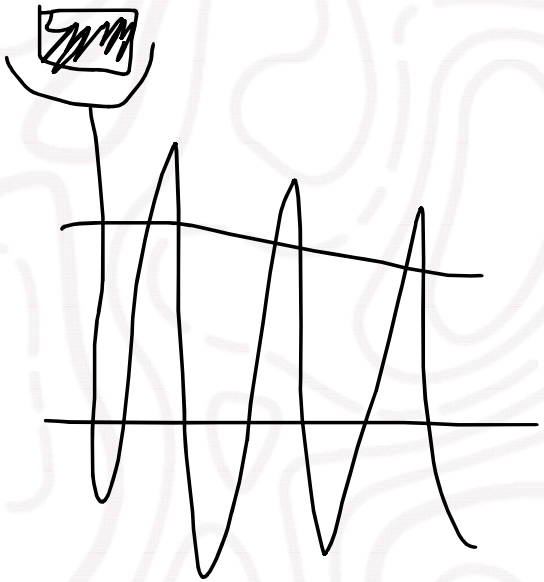


AGONIST BLOCKADE

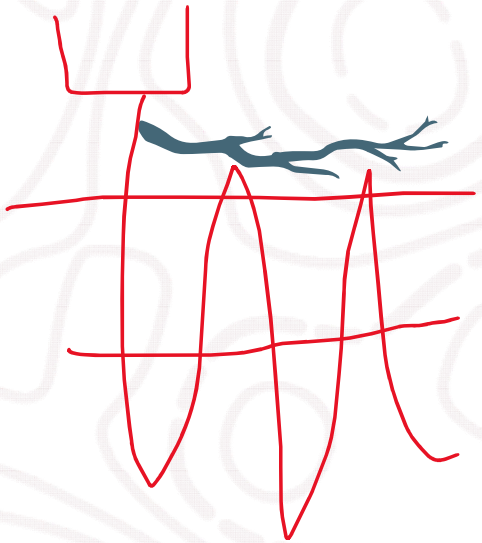
Partial AGONIST BLOCKADE


Opioid Effect
Full Agonist
(Methadone)
Partial Agonist
(Buprenorphine)
Antagonist
(Naloxone)
Dose

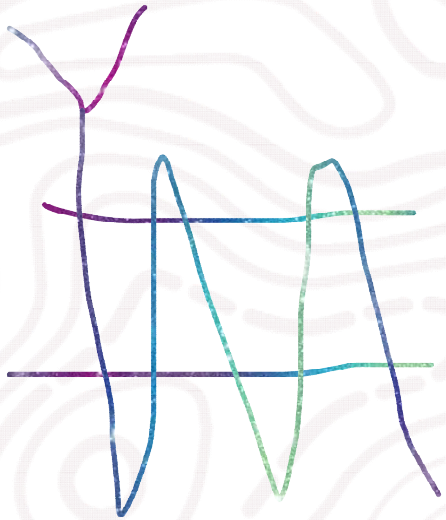
Buprenorphine
Agonist antagonist?



Mu Agonist

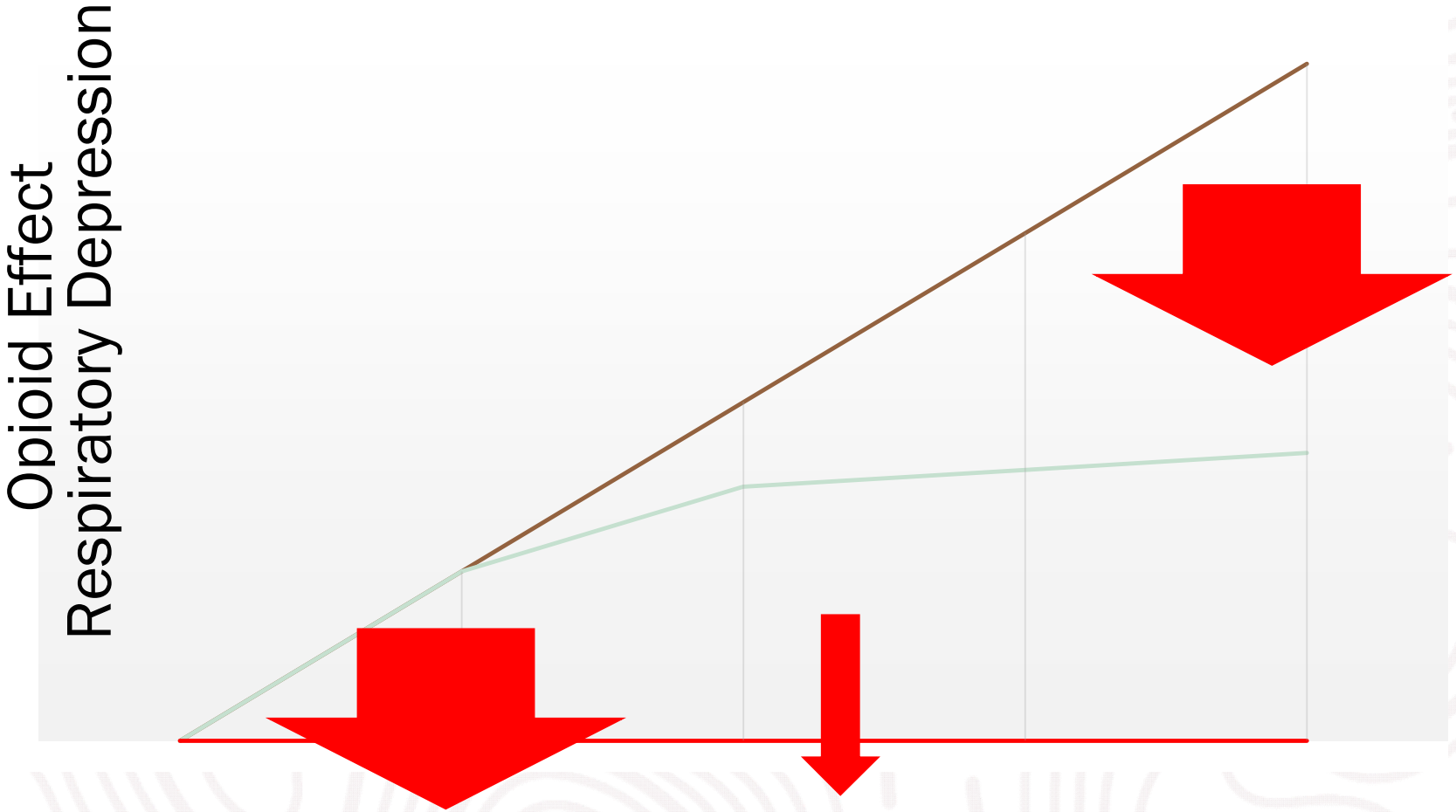


Delta Agonist

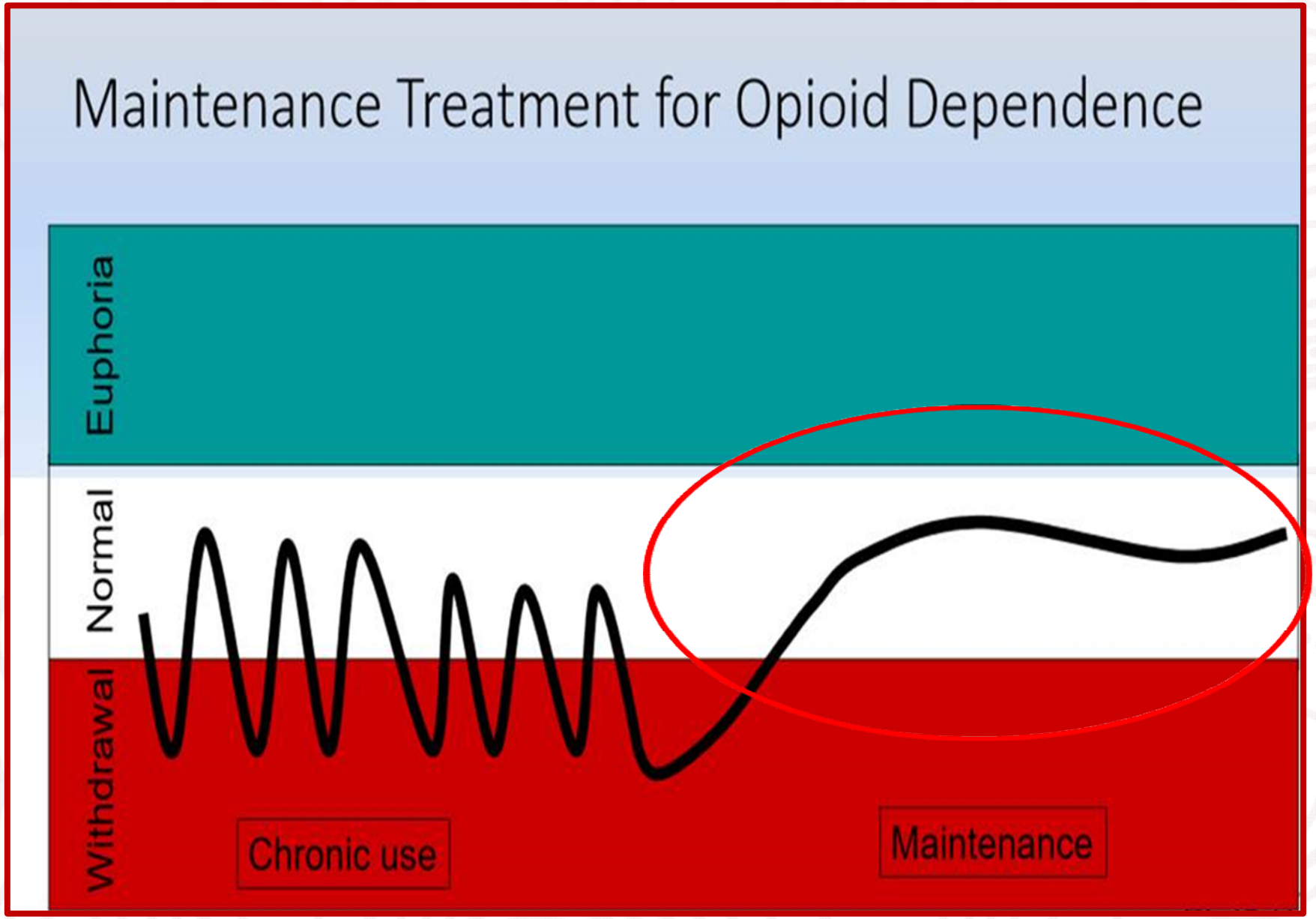


Kappa Antagonist

PARTIAL AGONIST VS FULL AGONIST



"Bup is a full agonist at lower doses, partial agonist at higher doses"


Maintenance Treatment for Opioid Dependence
Euphoria
Normal
Withdrawal
Chronic use
Maintenance

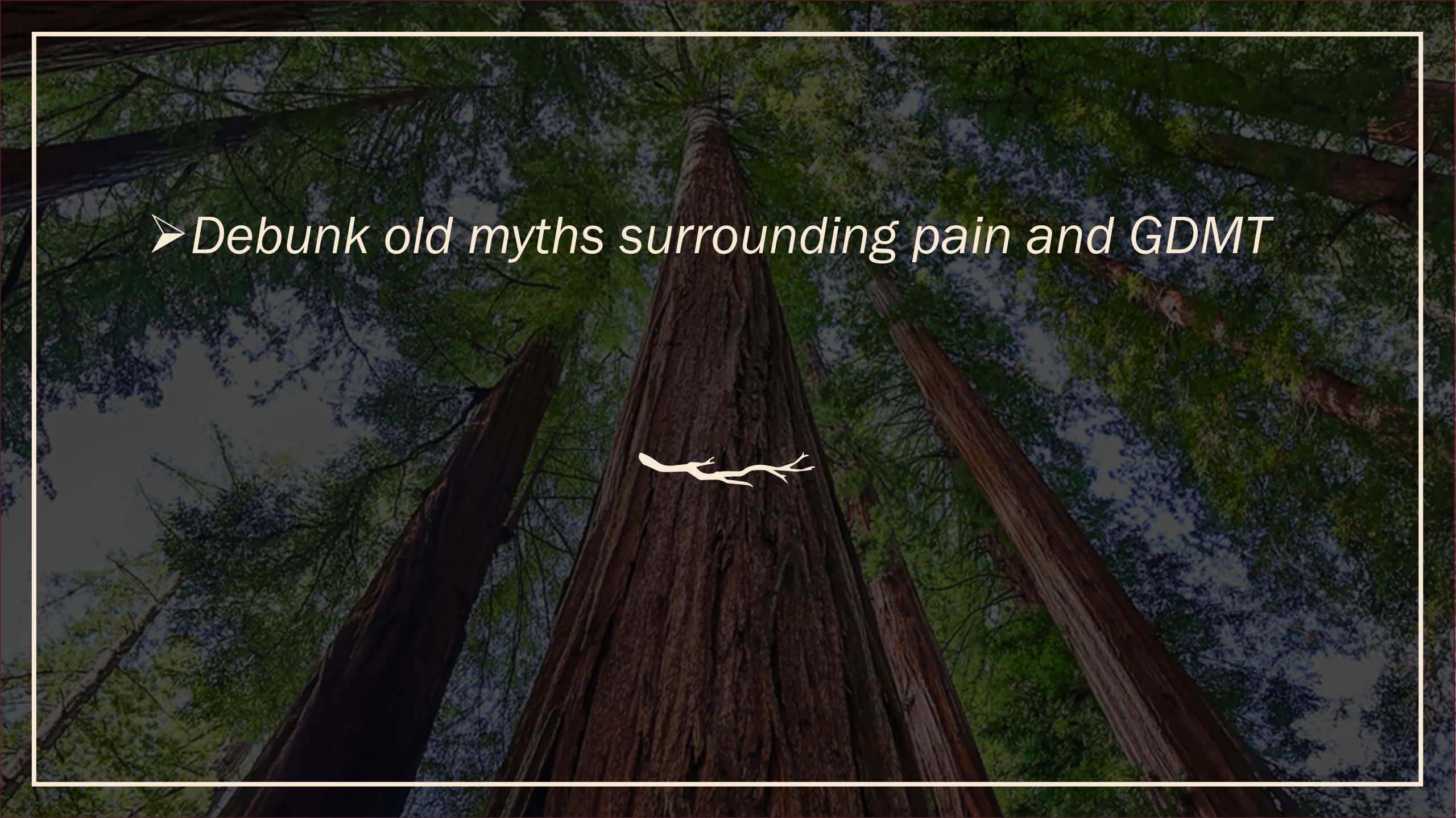
☺	Benefits in NNT
4	1 in 4 using low-dose buprenorphine (2 to 6 mg) had retention in treatment
3	1 in 3 using medium-dose buprenorphine (7 to 16 mg) had retention in treatment
2	1 in 2 using high-dose buprenorphine (≥ 16 mg) had retention in treatment

☹	Harms in NNT
	No study-related medication mortality was reported
	Uncertain adverse effects

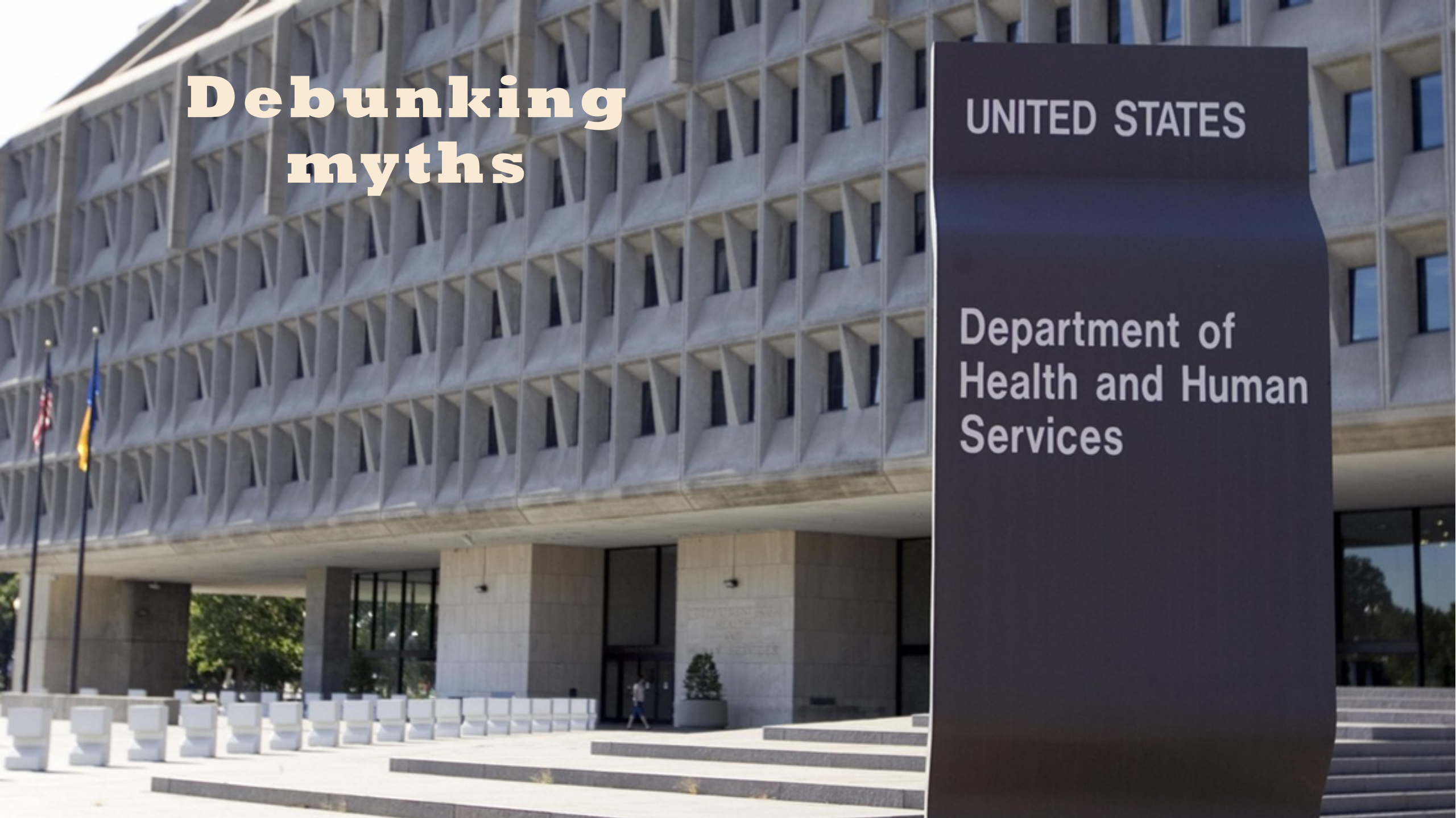
Screening reduces colorectal cancer mortality

Benefits in NNT	
450	Flexible sigmoidoscopy: 1 in 450 did not die from colorectal cancer
900	Fecal occult blood testing: 1 in 900 did not die from colorectal cancer

Harms in NNT	
1250	Flexible sigmoidoscopy: 1 in 1250 experienced an adverse outcome
3300	Fecal occult blood testing: 1 in 3300 experienced an adverse outcome


➢Debunk old myths surrounding pain and GDMT

Debunking myths



"While patients are taking opioid pain medications, the administration of buprenorphine generally should be discontinued."

"may be difficult to achieve analgesia"

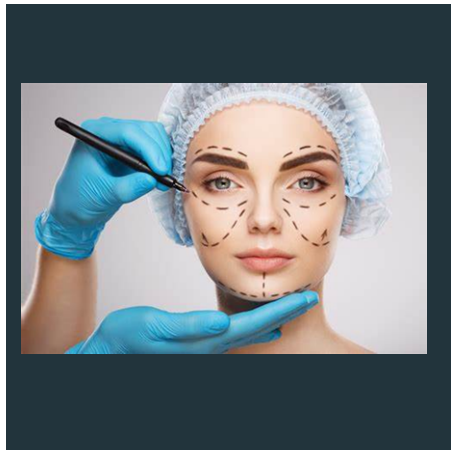
"Note that, until buprenorphine clears the body, it may be difficult to achieve analgesia with short-acting opioids in patients who have been maintained on buprenorphine, and higher doses of short-acting opioids may be required."

2015 ASAM National Practice Guidelines

"For severe acute pain, *discontinuing buprenorphine and commencing a high potency opioid* (such as fentanyl) is advisable."

Elective surgery

Surgery performed in advance



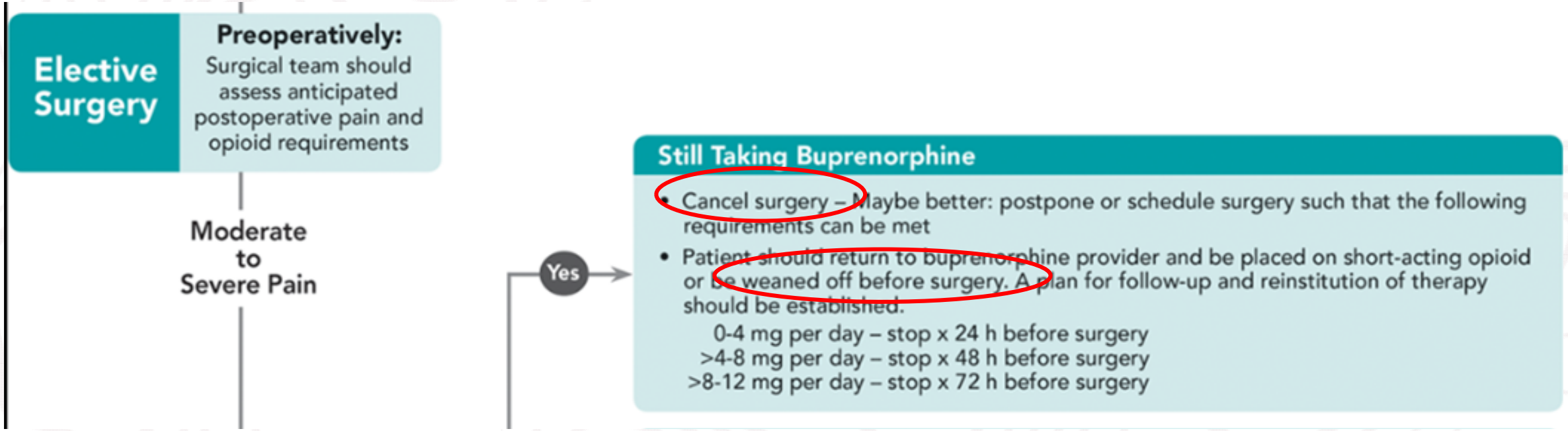
Stop 24-36h before

Restart post op when need for full opioid analgesia has passed

J Addict Med. 2015 Oc; 9(5): 358-36

Older Guidelines

University of Michigan Health System Protocol 2017



To Stop of Not. That Is the Question: Acute Pain Management for the Patient on Chronic Buprenorphine T Anthony Anderson, Aurora N A Quaye, E Nalan Ward, Timothy E Wilens, Paul E Hilliard, Chad M Brummett Anesthesiology 2017 Jun; 126(6): 1180-1186

If acute surgery:

Still Taking Buprenorphine

1. Discontinue buprenorphine
2. Start PCA – Will likely require high doses; may require some continuous opioid infusion. However, would avoid high-dose, continuous opioids and *instead allow* the patient to use PCA. Consult APS, PCA to be managed by Acute Pain Service (APS).
3. Patient should be in a monitored setting with close nurse monitoring (ICU, or monitored/moderate care setting)
    - Duration of ICU/monitored setting time will vary
    - Acetaminophen around the clock (ATC)
    - Consider gabapentin or pregabalin
4. Regional anesthesia – consider continuous catheters
5. Maximize adjuncts
    - Dexemedetomidine for ICU patients used according to ICU protocols
    - Acetaminophen around the clock (ATC)
    - Consider gabapentin or pregabalin
6. Continue traditional opioid therapy for postoperative pain after discharge. Coordinate follow-up with pain physician prescribing buprenorphine for eventual opioid wean and reinstitution of buprenorphine therapy.

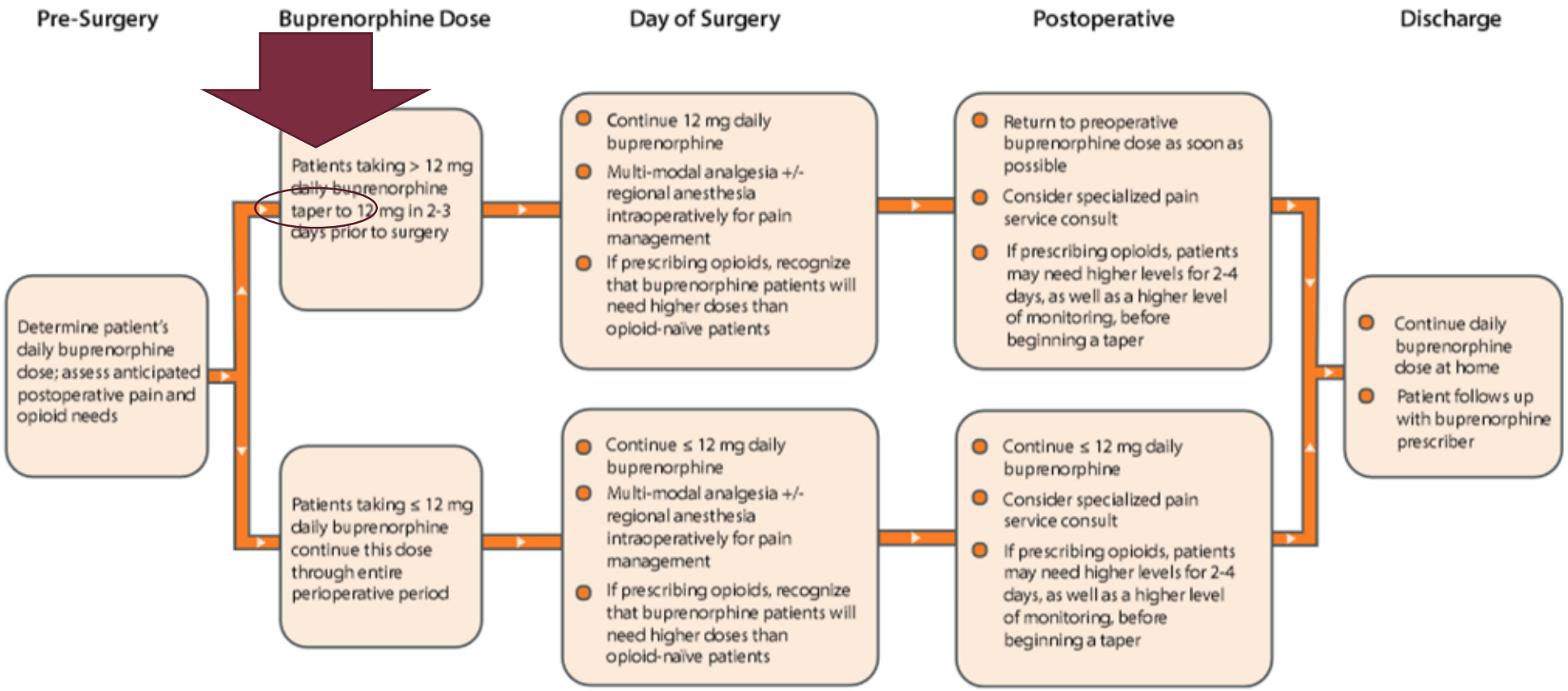


Figure 1 Perioperative Buprenorphine Protocol.

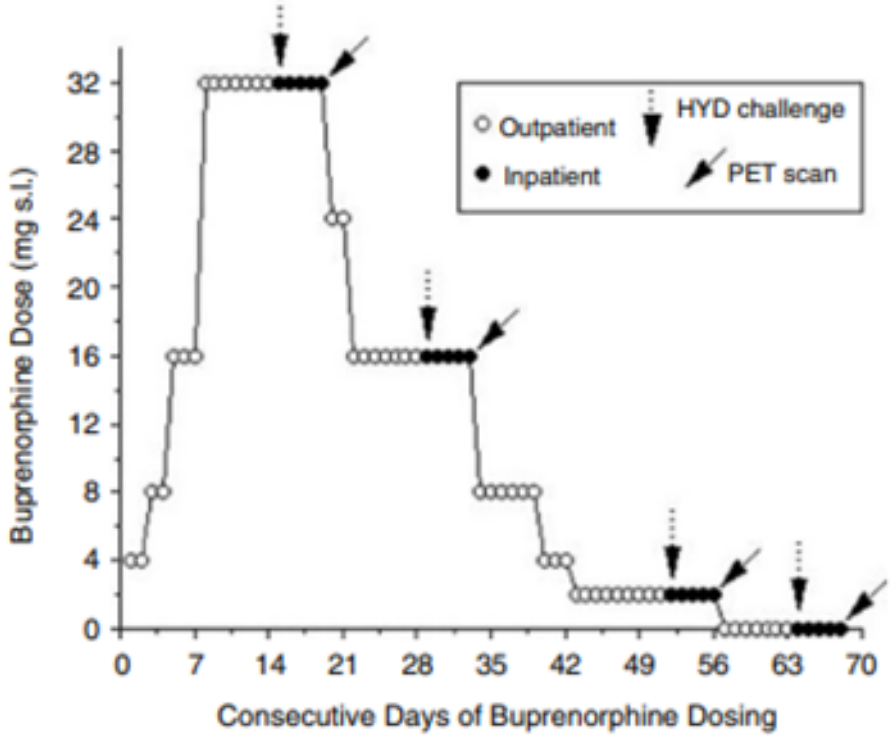
Taper to 12mg…

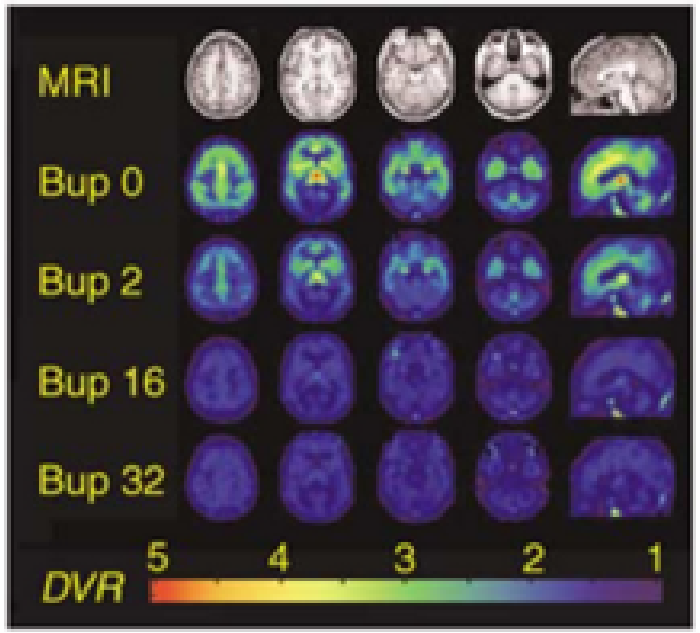
Quaye AN, Zhang Y. Perioperative Management of Buprenorphine: Solving the Conundrum. Pain Med. 2019 Jul 1;20(7):1395-1408. doi: 10.1093/pm/pny217. PMID: 30500943; PMCID: PMC7963209.

Receptor Occupancy?

Effects of Buprenorphine Maintenance Dose on μ-Opioid Receptor Availability, Plasma Concentrations, and Antagonist Blockade in Heroin-Dependent Volunteers

Mark K Greenwald*[,1], Chris-Ellyn Johanson[1], David E Moody[2], James H Woods[3], Michael R Kilbourn[4], Robert A Koeppe[4], Charles R Schuster[1] and Jon-Kar Zubieta[5]





vs affinity for the receptor

Medication	K_i (nM)
Codeine	734.2
Meperidine	450.1
Oxycodone	25.87
Methadone	3.378
Naloxone	1.518
Fentanyl	1.346
Morphine	1.168
Hydromorphone	0.3654
Buprenorphine	0.2157
Sufentanil	0.1380

Bottom line – you can displace bup with a higher affinity binding drug or if you use a high enough dose.

Don’t mess with the Buprenorphine

Burdening patients with additional preoperative instructions and tasks

requiring more clinic visits and care coordination between multiple providers (primary prescriber, surgeon, and anesthesiologist)

Delaying surgery to allow adequate time to taper

increased risk for relapse to opioid misuse and accidental overdose when buprenorphine is discontinued because they experience an opioid deficit while simultaneously gaining access to a new supply of full-opioid agonists

Re-induction on to buprenorphine is logistically complicated and labor intensive

Re-induction onto buprenorphine after surgery is likely to be physically painful and medically destabilizing

Forces them to endure a period of active opioid withdrawal before buprenorphine can be restarted

potential for discontinuity in care and patient nonadherence

Newer evidence – buprenorphine stopping vs not

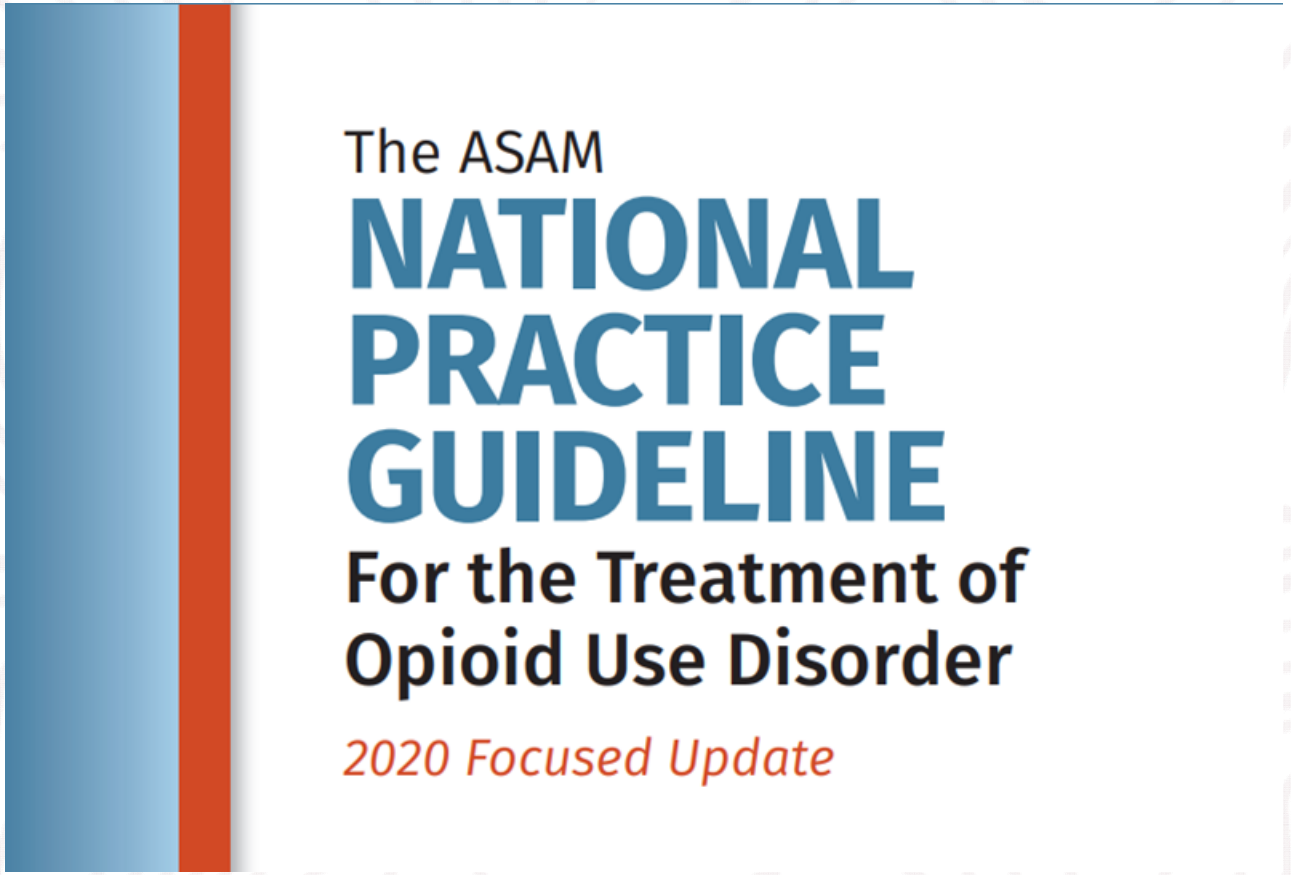
retrospective study of 55 patients on buprenorphine for chronic pain, dose ~ 16 mg

The number of opioid prescriptions dispensed was significantly higher with buprenorphine discontinuation (53% cont. vs 82% held, P = 0.011), as was MME dispensed (mean of 229 cont. vs mean of 521 held, P = 0.033). PACU pain scores were higher with buprenorphine discontinuation (mean 2.9 cont. vs mean 7.6 held, P < 0.001).

Quaye, A. N. A., et. al. (2020) **Perioperative Continuation of Buprenorphine** at Low–Moderate Doses Was Associated with Lower Postoperative Pain Scores and Decreased Outpatient Opioid Dispensing Compared with Buprenorphine Discontinuation, Pain Medicine, Volume 21, Issue 9, Pages 1955–1960, https://doi.org/10.1093/pm/pnaa020

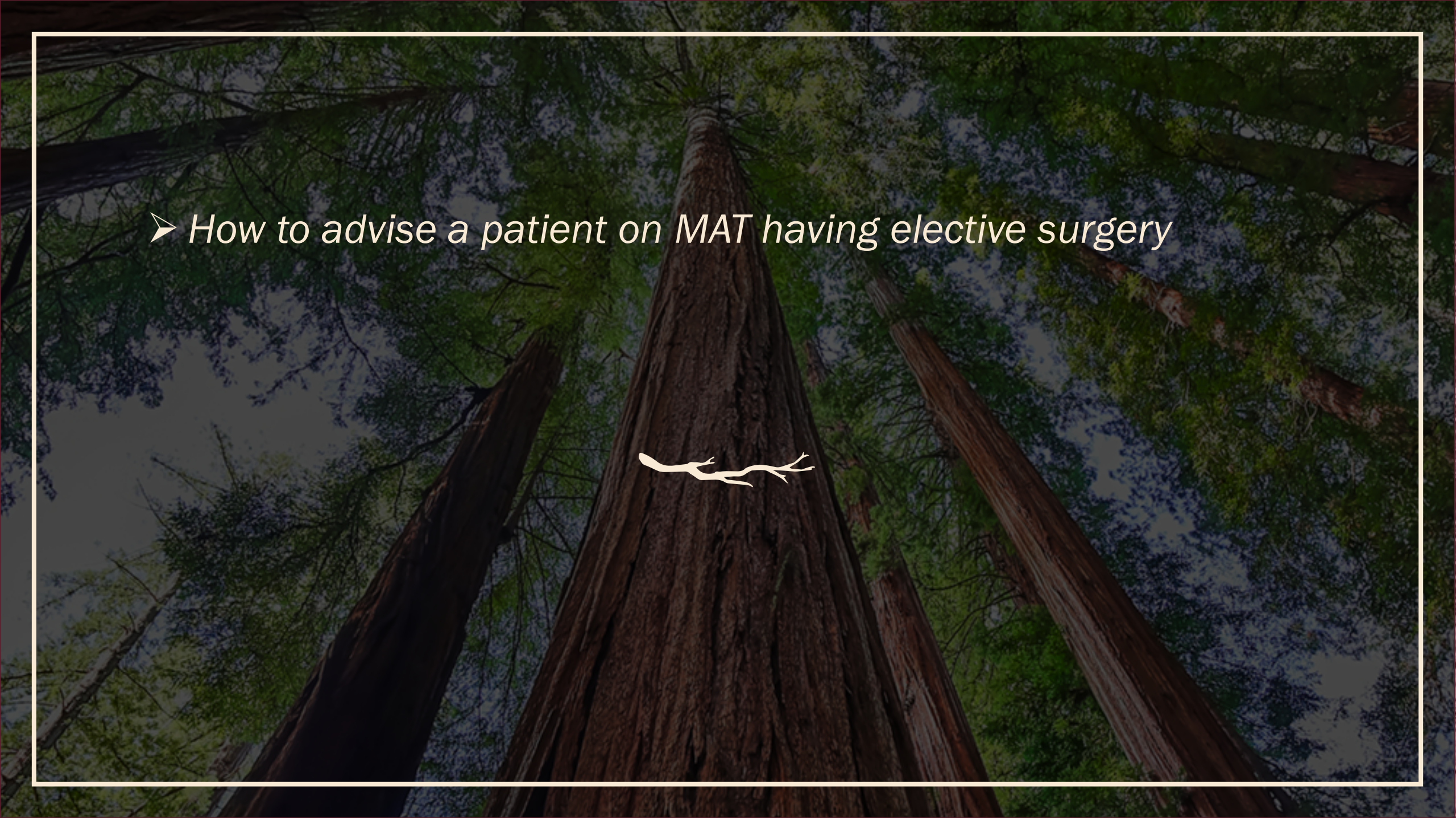
Principle no 1:
DON'T MESS WITH THE BUPRENORPHINE

Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction TIP 40 Center for the Substance Abuse Treatment 2002



"Discontinuation of methadone or buprenorphine before surgery is not required. Higher-potency intravenous full agonists opioids can be used perioperatively for analgesia in addition to the patient's regular dose of methadone or buprenorphine"

Analgesic or moderate doses of buprenorphine combined with opioid agonists can have an additive, instead of antagonistic, analgesic effect.


➢ How to advise a patient on MAT having elective surgery


DON'T STOP THE BUPRENORPHINE
NDC 0054-0177-13
30 Tablets
BUPRENORPHINE
HCl Sublingual Tablets
C III
8 mg*
PHARMACIST: Dispense with attached Medication Guide. Children who accidentally take buprenorphine HCl will need emergency medical care. Keep out of the reach of children.
Boehringer Ingelheim
Roxane Laboratories
℞ only

NON OPIOID TREATMENT

Acetaminophen

- Provided analgesic and opioid sparing
- Some studies show benefit when started pre-operatively
- No demonstrated benefit to IV formulation
- Don’t exceed recommended max dose – 4g/day
- Severe ROH, stable cirrhosis, low body weight reduce 2g/day

Gabriel RA, Swisher MW, Sztain JF, Furnish TJ, Ilfeld BM, Said ET. State of the art opioid-sparing strategies for post-operative pain in adult surgical patients. Expert Opin Pharmacother. 2019 Jun;20(8):949-961. doi: 10.1080/14656566.2019.1583743. Epub 2019 Feb 27. PMID: 30810425.

NON OPIOID TREATMENT

NSAIDS

- Provided analgesic and opioid sparing ~ 50% in morphine
- Significant pain relief at 24h and 48h
- Help pain and post op function – earlier return to oral intake, time to ambulation, decreased urinary retention
- 24h ketorolac => ibuprofen
- NSAID contraindications

Gabriel RA, Swisher MW, Sztain JF, Furnish TJ, Ilfeld BM, Said ET. State of the art opioid-sparing strategies for post-operative pain in adult surgical patients. Expert Opin Pharmacother. 2019 Jun;20(8):949-961. doi: 10.1080/14656566.2019.1583743. Epub 2019 Feb 27. PMID: 30810425.

NON OPIOID TREATMENT

NSAIDS and acetaminophen

- Provided analgesic and opioid sparing
- Synergistic? Studies differ..
- May be equivalent in efficacy to opioid
- Can increase mobility and reduce LOS

Ilyas AM, Miller AJ, Graham JG, Matzon JL. A Prospective, Randomized, Double-Blinded Trial Comparing Acetaminophen, Ibuprofen, and Oxycodone for Pain Management After Hand Surgery. Orthoped
2019 Mar 1;42(2):110-115. doi: 10.3928/01477447-20190221-02. Epub 2019 Feb 27. PMID: 30810754.
Sim V et al. How low can you go: Achieving postoperative outpatient pain control without opioids. J Trauma Acute Care Surg. 2019 Jul;87(1):100-103. doi: 10.1097/TA.0000000000002295. PMID: 31259

NON OPIOID TREATMENT

Lidocaine patch

- Provided analgesic
- One above and one below incision
- Post sternotomy, post C section
- Reduction in pain and total dose rescue opioid

de Queiroz VKP, da Nóbrega Marinho AM, de Barros GAM. Analgesic effects of a 5% lidocaine patch after cesarean section: A randomized placebo-controlled double-blind clinical trial. J Clin Anesth. 202
Oct;73:110328. doi: 10.1016/j.jclinane.2021.110328. Epub 2021 May 8. PMID: 33975094..
The 5% Lidocaine Patch for Decreasing Postoperative Pain and Rescue Opioid Use in Sternotomy: A Prospective, Randomized, Double-blind Trial, Sanghon Park et al

NON OPIOID TREATMENT

Gabapentinoids

- Binds to voltage gated calcium channels – decreasing substance P
- Dizziness (19%), gate disturbance (14%), somnolence (14%)
- Most research is single dose gabapentin given at time of surgery 600- 1200mg. 200mg tid after
- Higher doses in patients with OUD

Clarke HA, Katz J, McCartney CJ, Stratford P, Kennedy D, Pagé MG, Awad IT, Gollish J, Kay J. Perioperative gabapentin reduces 24 h opioid consumption and improves in-hospital rehabilitation but not po
discharge outcomes after total knee arthroplasty with peripheral nerve block. Br J Anaesth. 2014 Nov;113(5):855-64. doi: 10.1093/bja/aeu202. Epub 2014 Jun 30. PMID: 24980426.

NON OPIOID TREATMENT

Gabapentinoids- pregabalin

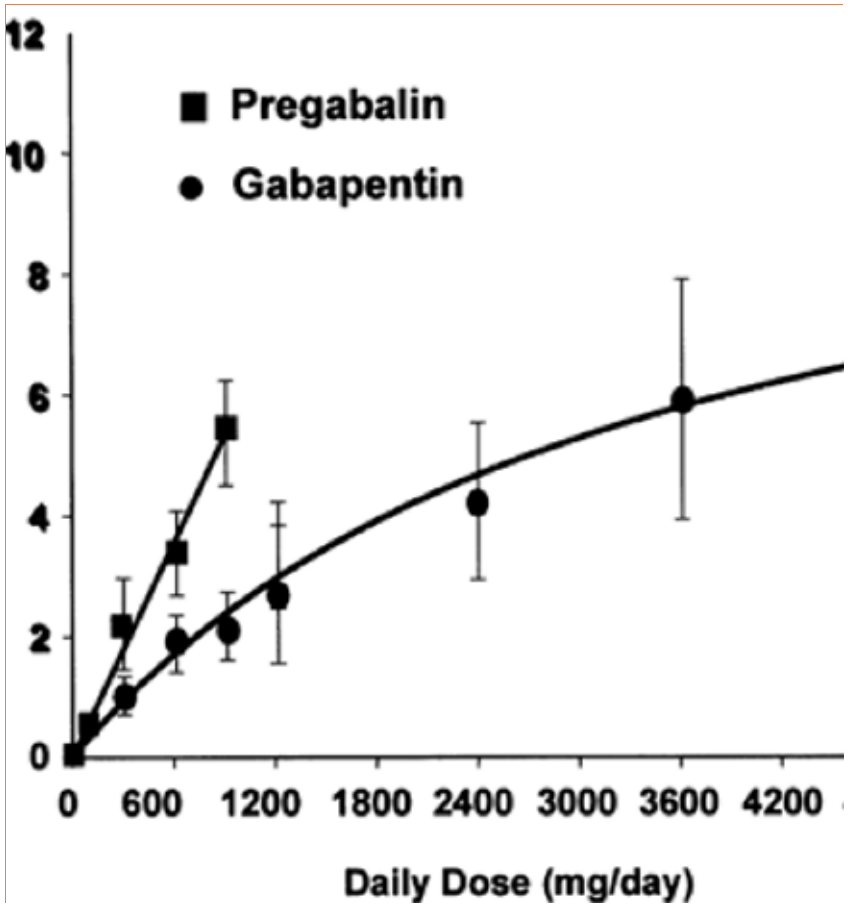
Binds to voltage gated calcium channels – decreasing substance P

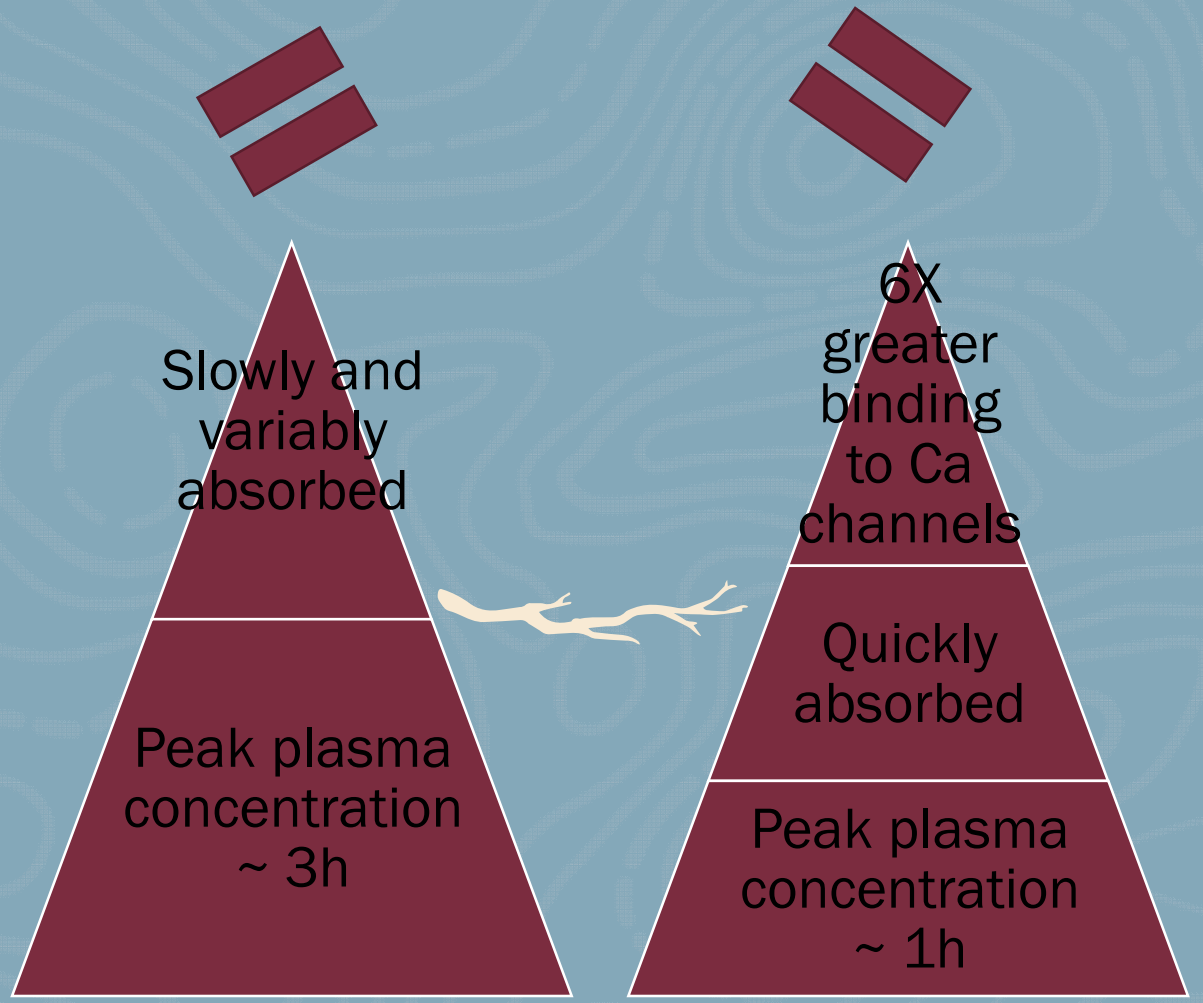
Blurred vision (1%), sedation (4%)

Better for pronociceptive procedures

Eipe N, Penning J, Yazdi F, Mallick R, Turner L, Ahmadzai N, Ansari MT. Perioperative use of pregabalin for acute pain-a systematic review and meta-analysis. Pain. 2015 Jul;156(7):1284-1300. doi: 10.1097/j.pain.0000000000000173. PMID: 25830925.

Gabapentin vs pregabalin?





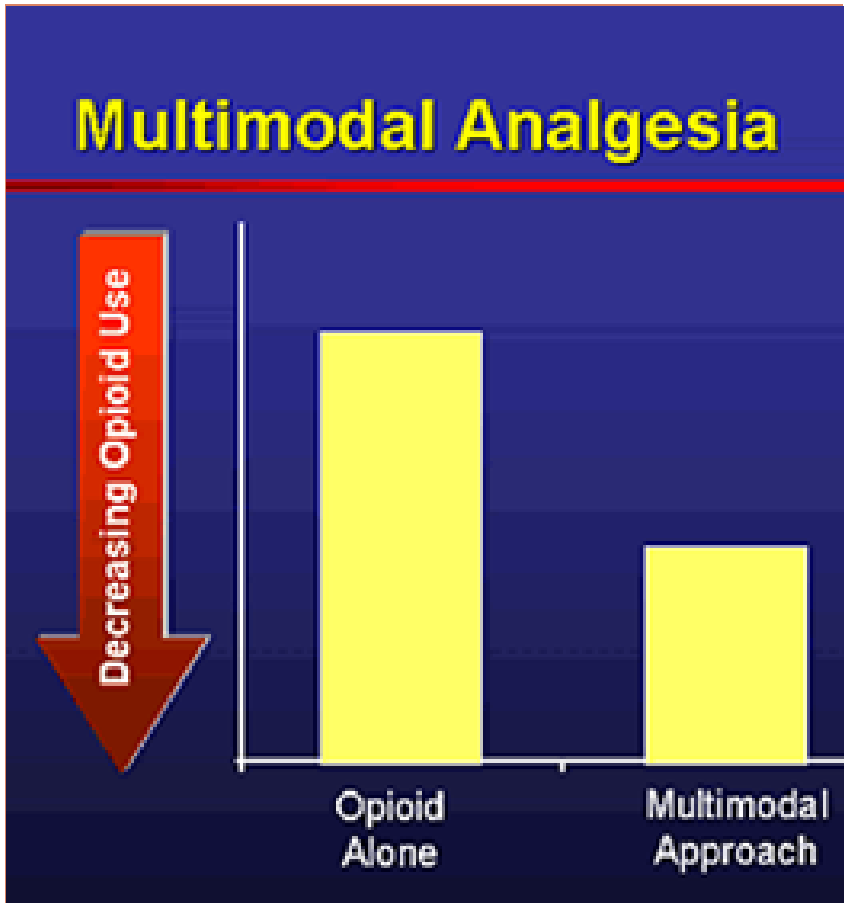
Bockbrader HN, Radulovic LL, Posvar EL, Strand JC, Alvey CW, Busch JA, Randinitis EJ, Corrigan BW, Haig GM, Boyd RA, Wesche DL. Clinical pharmacokinetics of pregabalin in healthy volunteers. J Clin Pharmacol. 2010 Aug;50(8):941-50. doi: 10.1177/0091270009352087. Epub 2010 Feb 10. PMID: 20147618.

NON OPIOID TREATMENT

ICU settings

- Ketamine – analgesic dosing
- dexmedetomidine
- Tizanidine
- IV Lidocaine during case

Gabriel RA, Swisher MW, Sztain JF, Furnish TJ, Ilfeld BM, Said ET. State of the art opioid-sparing strategies for post-operative pain in adult surgical patients. Expert Opin Pharmacother. 2019 Jun;20(8):94
doi: 10.1080/14656566.2019.1583743. Epub 2019 Feb 27. PMID: 30810425.



Consider Multimodal pain control – "controlled polypharmacy"

What if you do want to use Opioids?

OPIOIDS DONE WELL…

Continue:

or

<u>Can</u> (but don't have to):

- Increased efficacy for pain
- Divide prior dose to bid or tid:
  - Fewer hours where the dose may be waning
  - Less risk of respiratory suppression

For low dose patients(probably only relevant for patients on < 8mg), could consider giving more suboxone divided.

Usually only for minor surgery (e.g., dental) for a few days only.

Opioid treatment

Opioid agonists - Which one and how much?

Consider those with high affinity to Mu receptor (no published data to support this)

Medication	K_i (nM)
Codeine	734.2
Meperidine	450.1
Oxycodone	25.87
Methadone	3.378
Naloxone	1.518
Fentanyl	1.346
Morphine	1.168
Hydromorphone	0.3654
Buprenorphine	0.2157
Sufentanil	0.1380

More than usual!
2 or 3 or 4- or 5-times typical dosing
e.g., oxycodone 10-15mg q4h rather than 5mg”

Patients on buprenorphine – Ki (and receptor availability?)

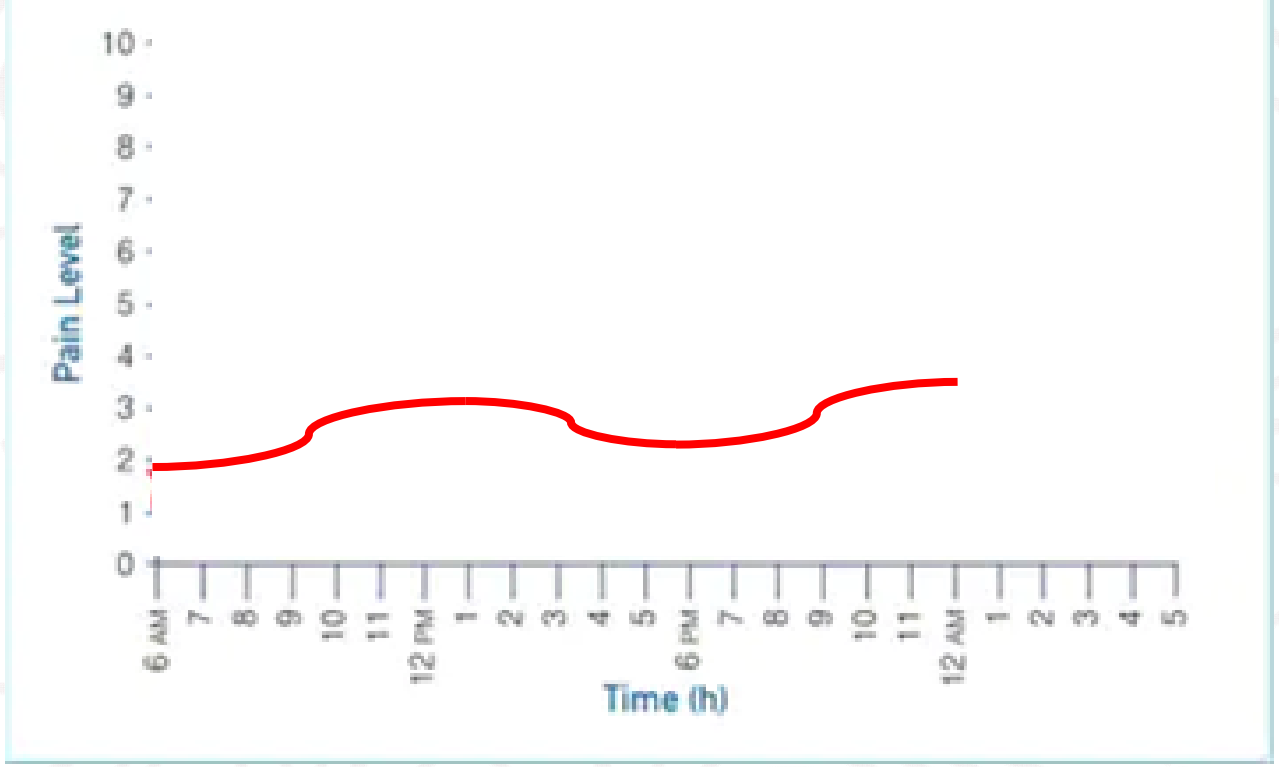
Patients on methadone – VERY opioid tolerant

Risk of overdosing patients on opioids alone is low

Buresh M, Ratner J, Zgierska A, Gordin V, Alvanzo A. Treating Perioperative and Acute Pain in Patients on Buprenorphine: Narrative Literature Review and Practice Recommendations. J Gen Intern Med. 2020 Dec;35(12):3635-3643. doi: 10.1007/s11606-020-06115-3. Epub 2020 Aug 21. PMID: 32827109; PMCID: PMC7728902.

OPIOIDS DONE WELL

What causes addiction; makes you want more of a drug??

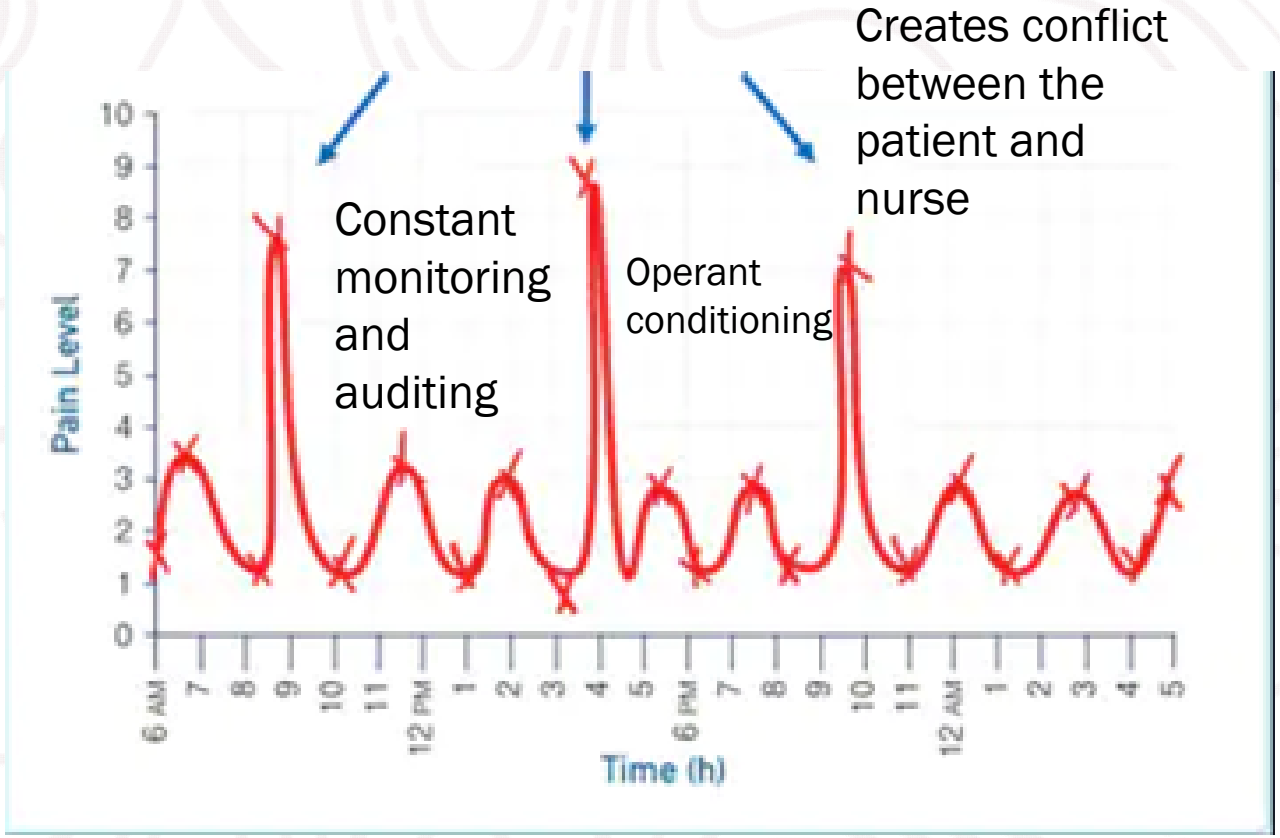


Reinforcing:

- Time of onset
- Rapid spikes
- Relief of pain

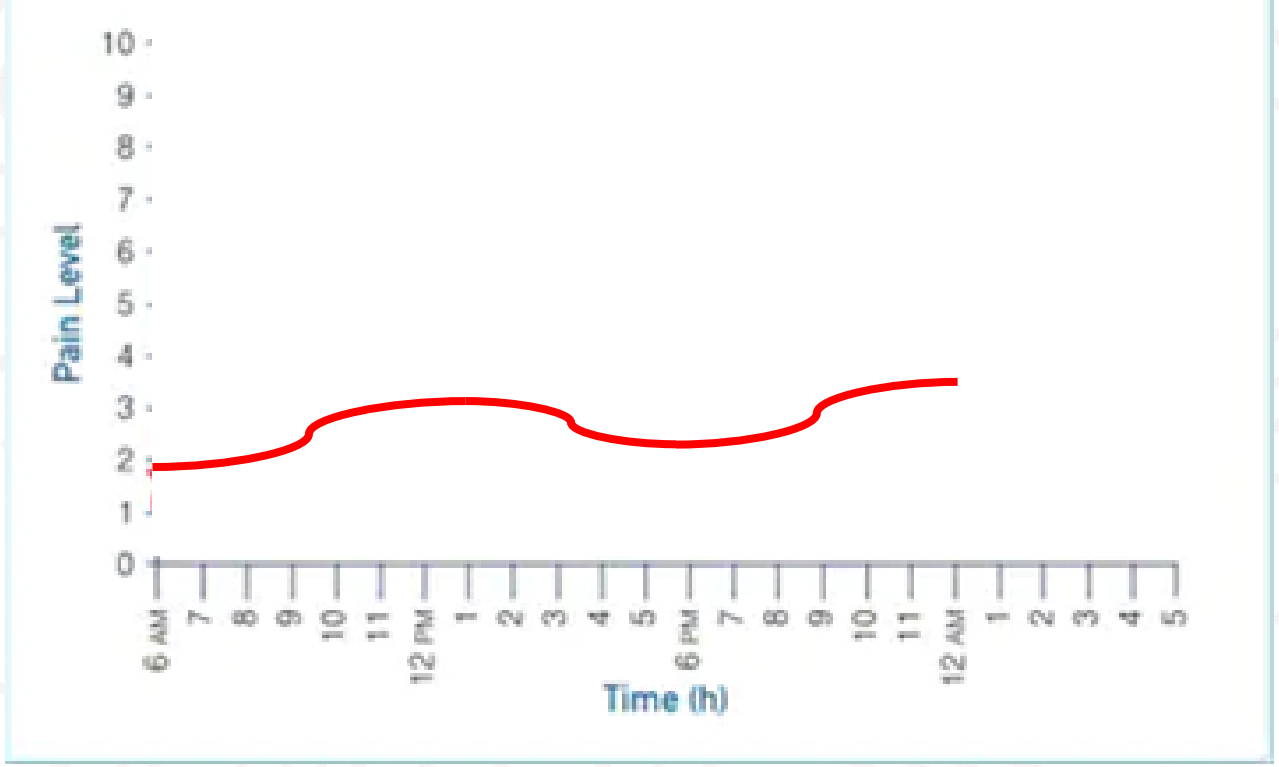
OPIOIDS DONE WELL

What causes addiction; makes you want more of a drug??



Reinforcing

OPIOIDS DONE WELL



Nursing patient interactions elegant and supportive.

OPIOIDS DONE WELL

My personal opinion/recommendations…

Oral medications when can:

Oral medication rather than IV medication whenever possibly can as have slower onset

PCA vs IV bolus if MUST use IV medications – frequent, small doses

Scheduled dosing rather than prn whenever possible.

RASS (Richmond Agitation Sedation Scale)		
4	Combative	Overtly combative, violent, immediate danger to staff
3	Very agitated	Pulls or removes tubes or catheters; aggressive
2	Agitated	Frequent non-purposeful mvmt, fights ventilator
1	Restless	Anxious but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Sustained awakening to voice (≥10sec)
-2	Light sedation	Briefly awakens with eye contact to voice (<10 sec)
-3	Moderate sedation	Movement or eye opening to voice but no eye contact
-4	Deep sedation	No response to voice but movement or eye opening to physical stimulation
-5	Cannot be aroused	No response to voice or physical stimulation

MANAGING POST OPERATIVE PAIN

Hydromorphone oral

4 or 6 mg PO q4h scheduled
4-8mg PO q4h prn

or

Hydromorphone PCA

0.4 -1mg dose q8 min
No maximum dose (patients will fall asleep)
Nurse bolus 1-2mg to start

1mg IV hydromorphone ~ 4-5mg PO hydromorphone

- Is an epidural/nerve block an option? Concentrations in CSF easily displace buprenorphine

PCA dosing:

May need higher than default dosing

Prepare patient for transition to PO medication – do the math!

What about Naltrexone?

Patents should stop oral Naltrexone 72h before scheduled surgery to allow 5 half-lives to pass, resulting in elimination of nearly 98% of the drug.

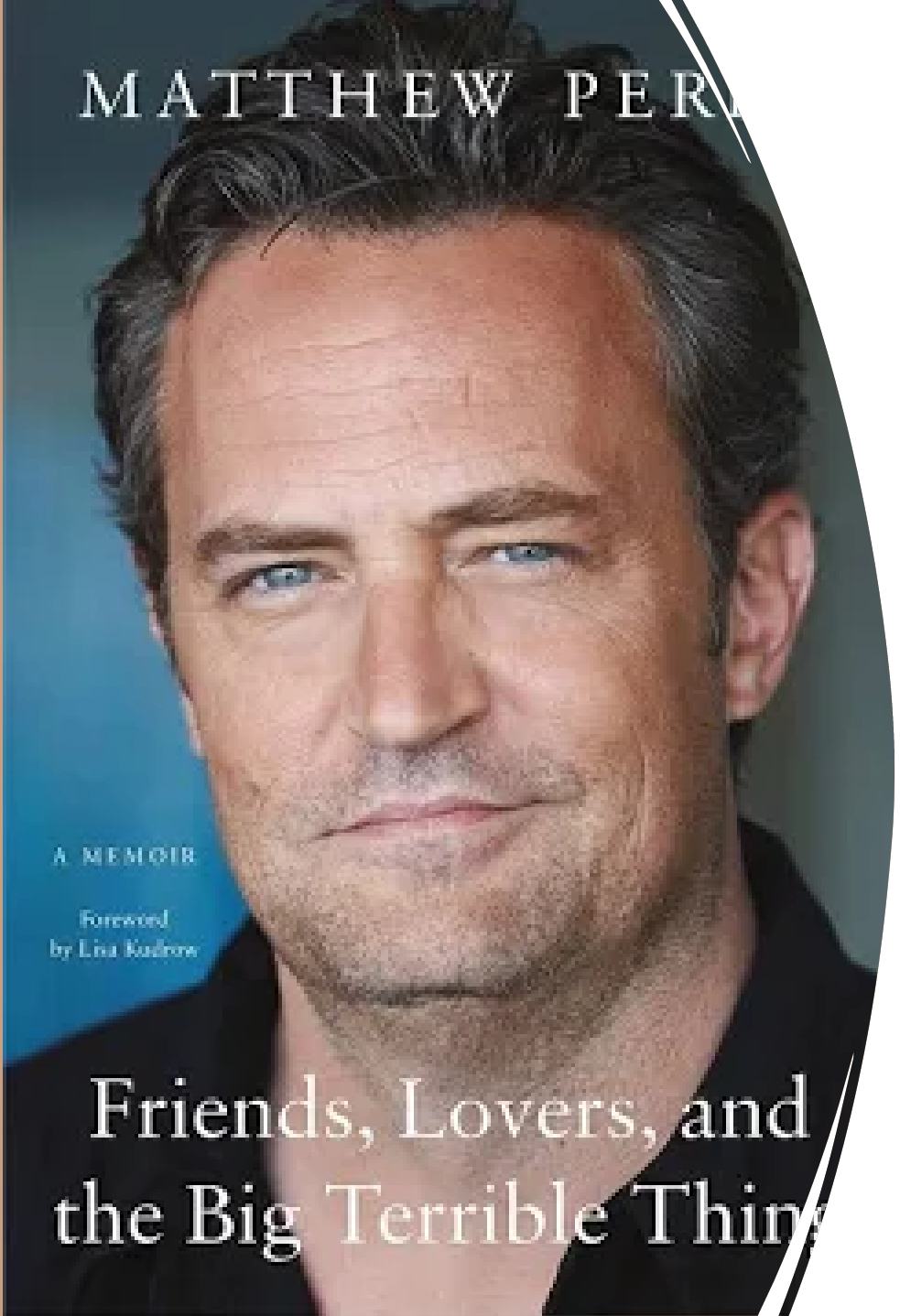
What about Vivitrol?

- When surgery is unscheduled, individuals on naltrexone may require up to 10-20-fold higher doses of opioids for pain relief when compared to individuals not on MAT.
- Need to probably lean heavily to regional/neuraxial analgesia, multimodal anesthesia.
- Some protocols using low dose ketamine

Vickers, AP and A Jolly. Naltrexone and problems in pain management. British Medical Journal 2006 Jan 21;332(7534):132-3.

- When surgery is scheduled, transition to oral and then *stop for 72h prior to scheduled surgery.

*Injectable intramuscular naltrexone ½-life=5 days, resulting in a 25-day time period for a 98% elimination of the drug.



“ADDICTS ARE NOT BAD PEOPLE. WE’RE JUST PEOPLE WHO ARE TRYING TO FEEL BETTER”.