Opioid Angst in the Pain Clinic:

Why This Is Hard for Patients and Clinicians, and What We Can Do to Optimize Care and Outcomes

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Dr Rudolf is board certified in pain medicine, addiction medicine, medical acupuncture, and family medicine and has been practicing at Swedish Pain Services in Seattle for over 20 years. The clinic offers multidisciplinary care for chronic pain and common associated comorbidities such as substance use and mental health disorders.

He served as medical director of an inpatient SUD treatment program for 13 years and has published an innovative treatment protocol for opioid withdrawal. He has served as a member of the board of directors of the WA Society of Addiction Medicine and served as chair of the American Society of Addiction Medicine pain and addiction committee for 4 years. He is a clinical associate professor at the University of WA School of Medicine.

No disclosures or conflicts of interest.

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Disclosures:

Dr. Bicket reports consulting fees from Daniels Health which are ongoing

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NO DISCLOSURES

The Patients We're Talking About When Mental Models Collide

Opioids are the problem

→ Stopping = progress

Uncertainty • Risk management • Fear

Current practice reality

Opioids are the solution

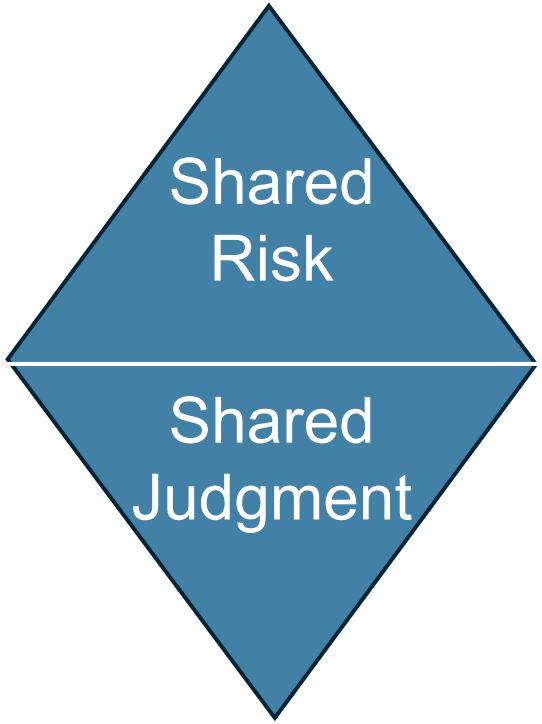
→ Continuation = care

Manhapra *Subst Abus* 2018;39:152, 10.1080/08897077.2017.1381663

Good Intentions, Shared Risk

Patients

- Relief
- Function
- Stability



Clinicians

- Safety
- Scrutiny
- Responsibility

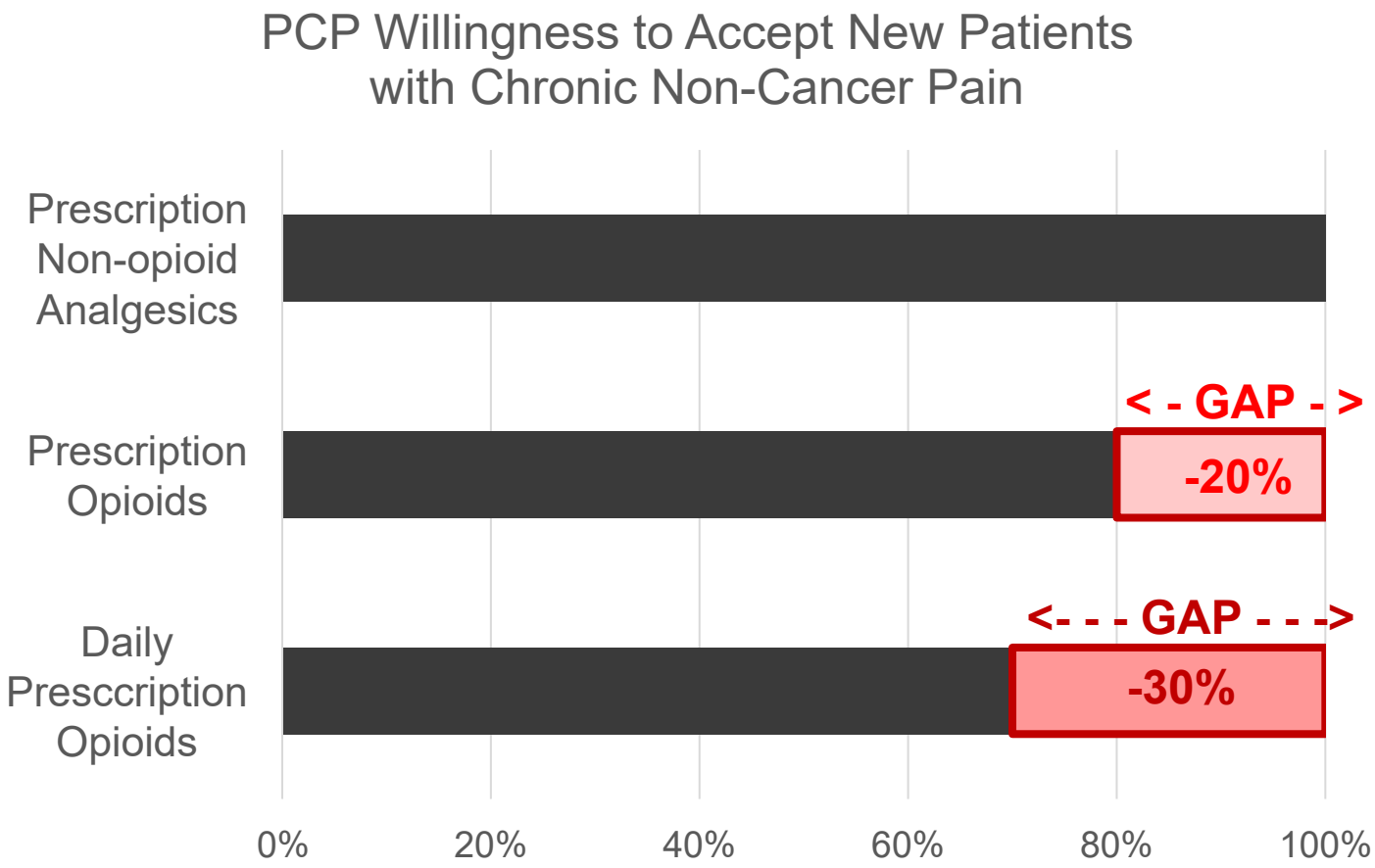
> *"I just want to get through my day …"*

> *"I don't want to hurt anyone."*

Matthias et al. *Patient Educ Couns* 2013;93:197, 10.1016/j.pec.2013.06.021

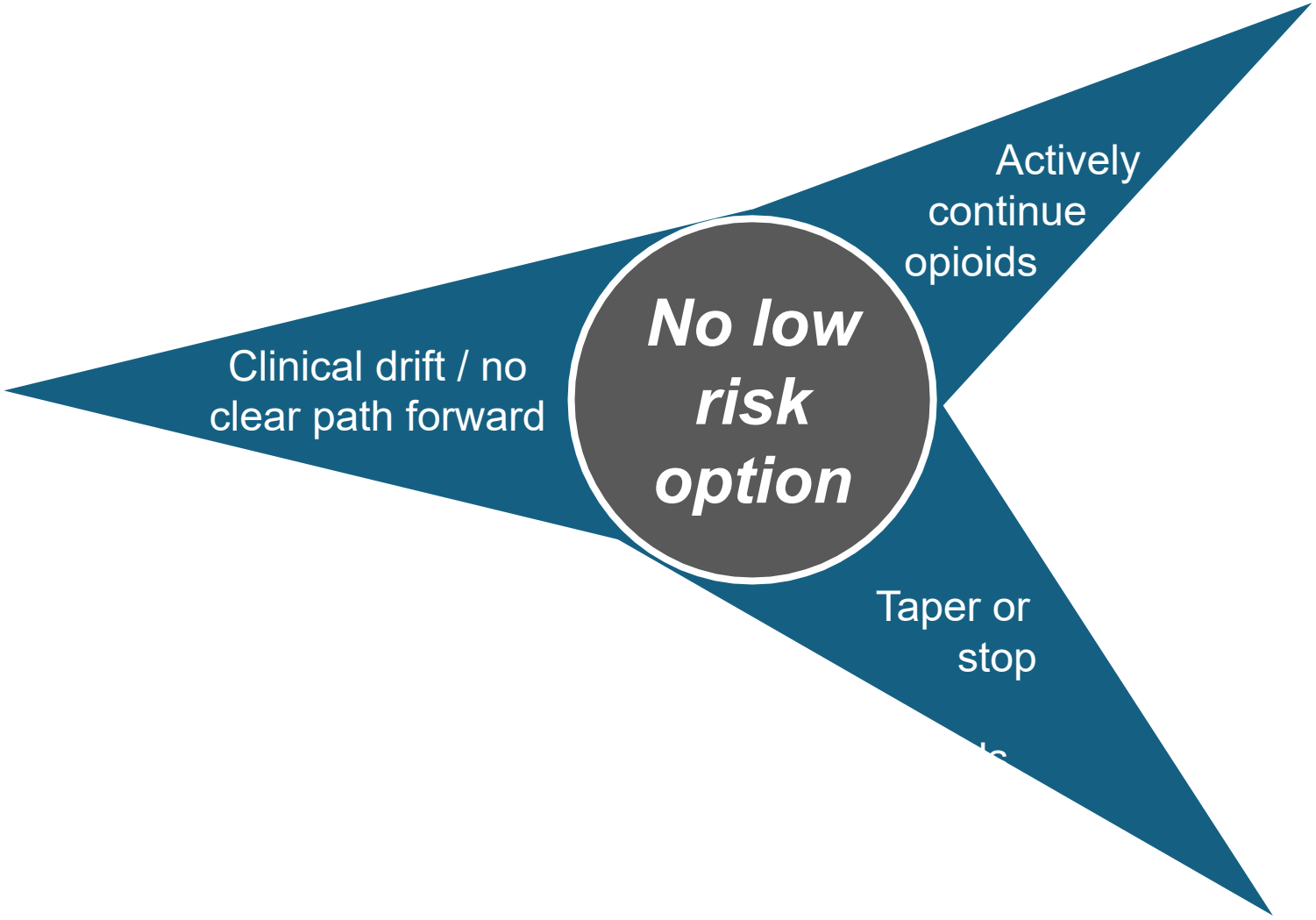
Prescription Opioids Now Carry Stigma

- Not just attitudes
  → access
- Not just discomfort
  → exclusion



Bicket et al. *Health Aff Sch* 2024;12:6, 10.1093/haschl/qxae086

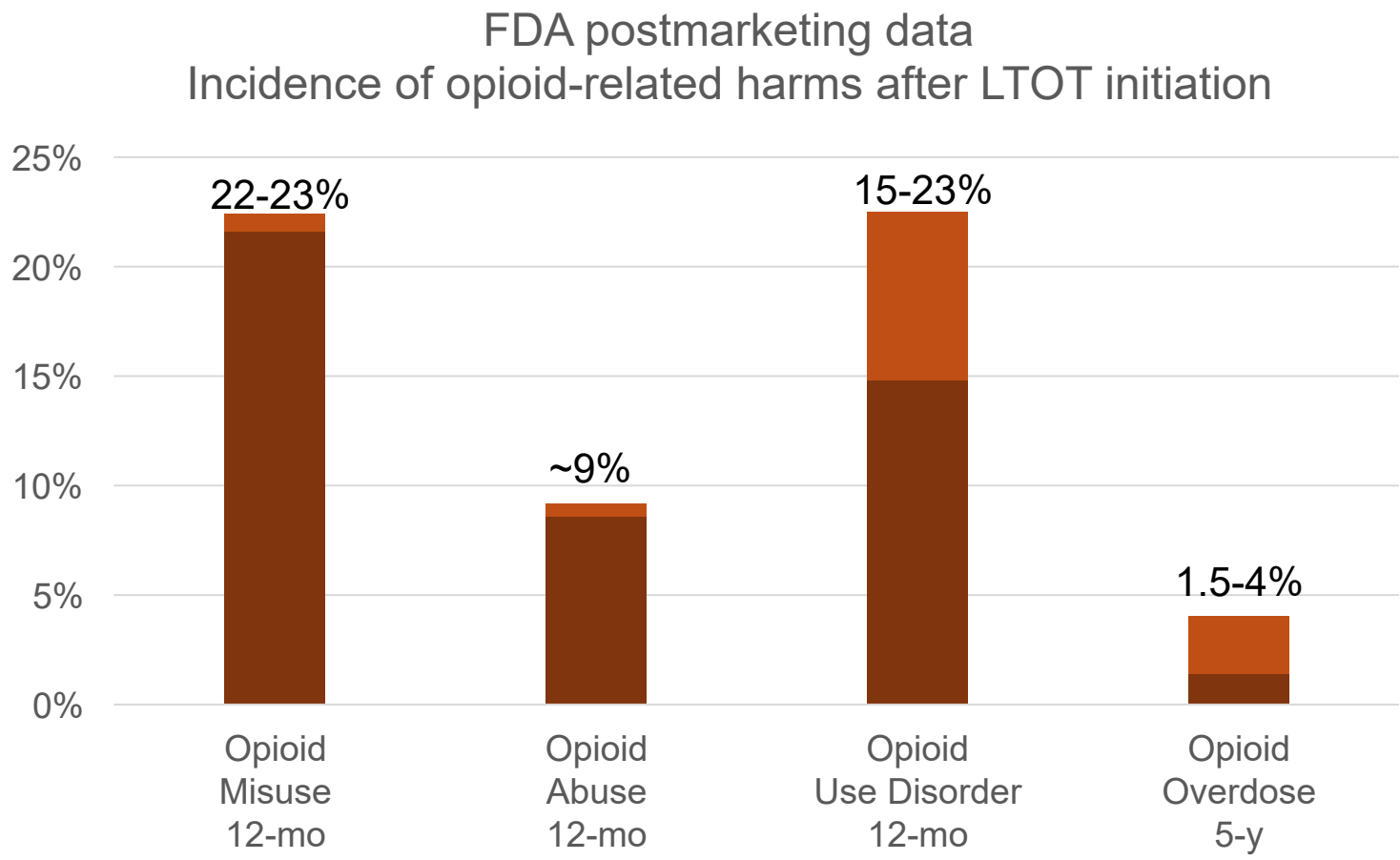
Pain Clinicians Practice Inside a Bind



What the Evidence Actually Says About Long-term Opioid Therapy (LTOT)

- We Can Quantify Risk, But Not Benefit
- Robust postmarketing evidence on misuse, OUD, overdose
- Little high-quality evidence for sustained functional benefit

JAMA



Bicket, Bateman. *JAMA* 2025;334:1057, 10.1001/jama.2025.13225

Clearly Labeling Prescription Opioid Risks

FOR IMMEDIATE RELEASE
July 31, 2025

Contact: HHS Press Office

202-690-6343

Submit a Request for Comment

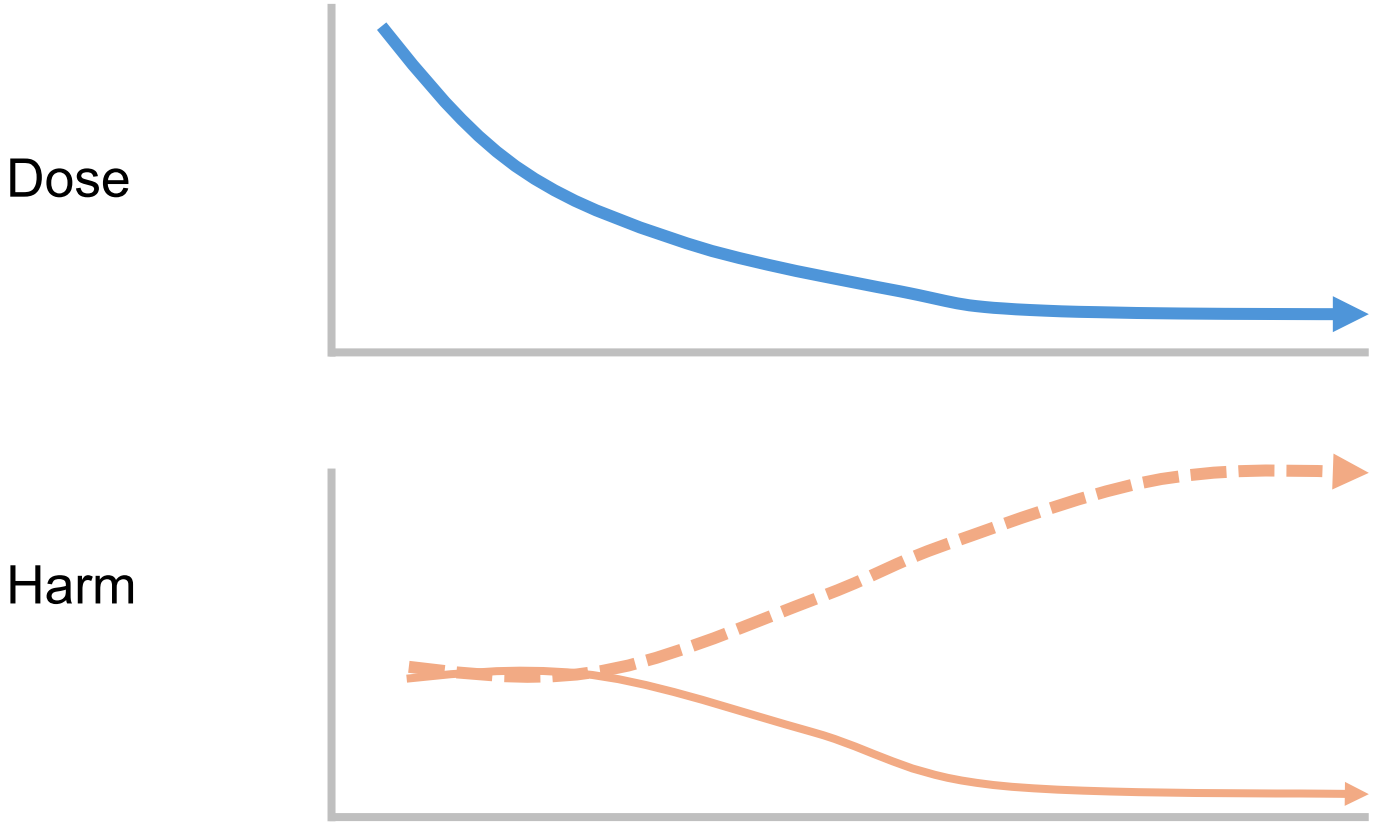
FDA Requires Major Changes to Opioid Pain Medication Labeling to Emphasize Risks

"The death of almost one million Americans during the opioid epidemic has been one of the cardinal failures of the public health establishment," said **FDA Commissioner Marty Makary, M.D., M.P.H.** "This long-overdue labeling change is only part of what needs to be done — we also need to modernize our approval processes and post-market monitoring so that nothing like this ever happens again."

Tragically, the new drug application for OxyContin was initially approved without study data supporting its long term use to treat pain in many patient populations for which it has been prescribed. The updated labeling change reflects robust data from two large FDA-required observational studies, called postmarketing requirements (PMR) 3033-1 and 3033-2, which recently provided new data on how long-term opioid use can lead to serious side effects. After reviewing those results, public comments, medical research and recognizing the absence of adequate and well-controlled studies on long-term opioid effectiveness, the FDA decided to require safety labeling changes to help health care professionals and patients make treatment decisions rooted in the latest evidence.

https://www.hhs.gov/press-room/fda-updates-opioid-risk-labels.html

Opioid Tapering Is Not a Neutral Intervention



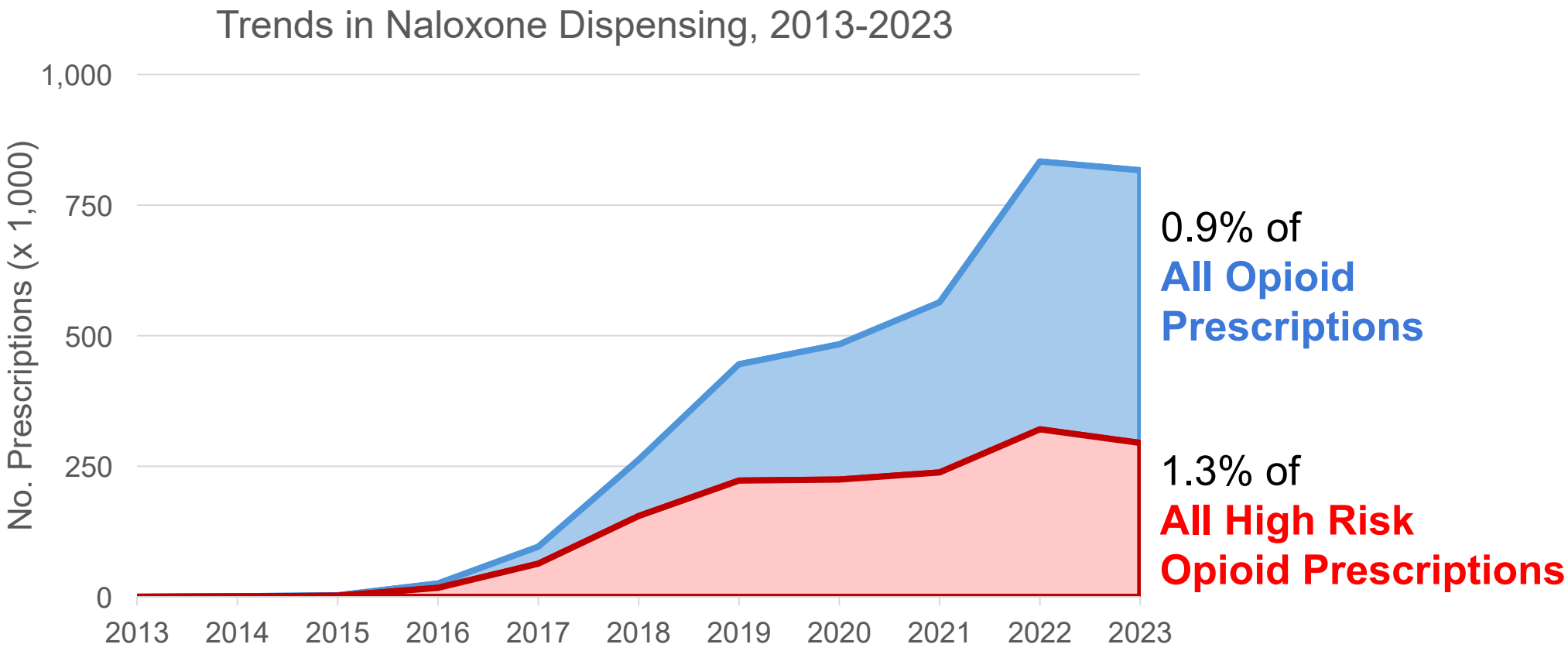
Dose ↓

does not always equal

Harm ↓

Coffin, Barreveld. *NEJM* 2022; ;386:611, 10.1056/NEJMp2115244

Overdose Prevention Still Fails LTOT Patients

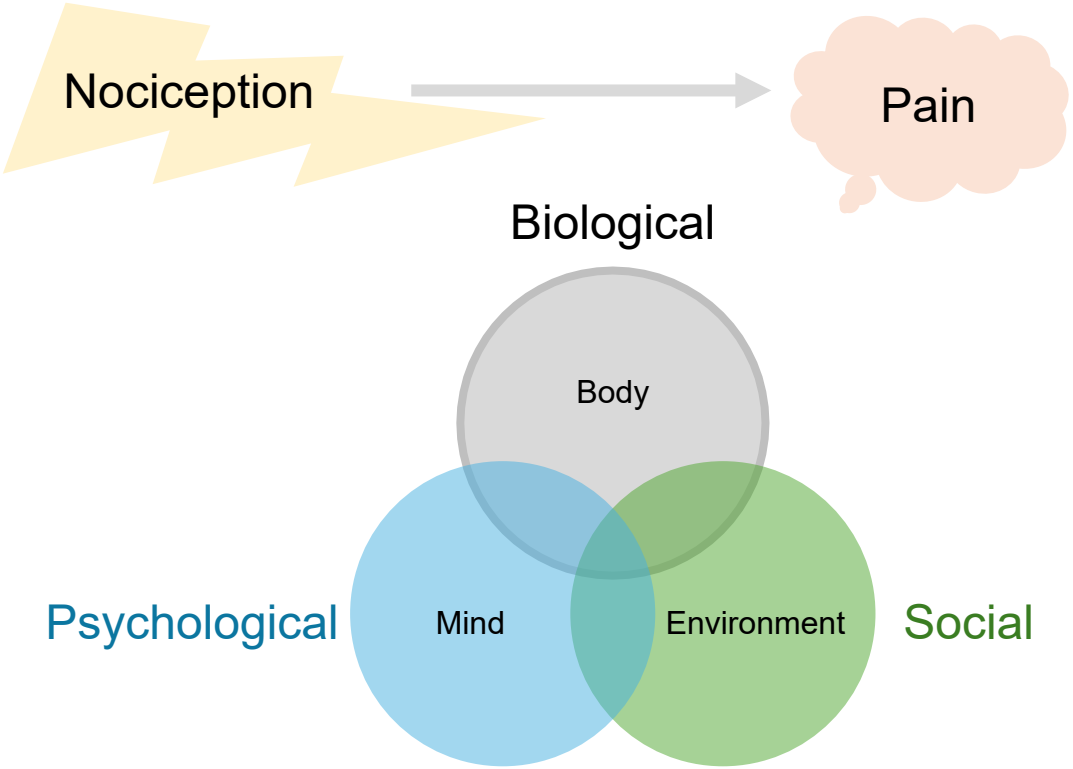


Beck et al. *Reg Anesth Pain Med* 2025, 10.1136/rapm-2025-106911

Pain Care Centered on Medications

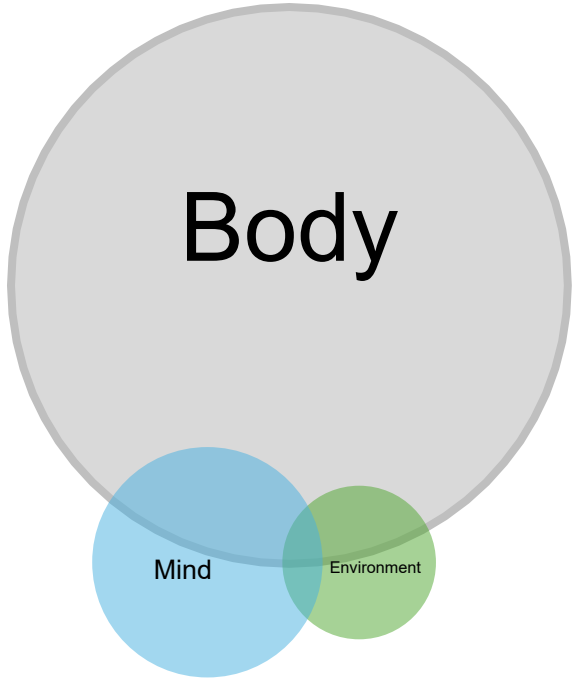
Biopsychosocial Framework

What we aim to practice



The Bio, Bio, Bio Model

What our systems often deliver



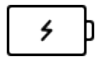
Gatchel et al. *Psychol Bull* 2007;133:581, 10.1037/0033-2909.133.4.581

When DSM-5 Criteria Meet Pain Clinic Reality

Observed Behaviors


Early refills


Dose escalation


Running out


Medication focus

Diagnostic Interpretation?
-> OUD
-> Physiologic dependence
-> Overlap

Multiple Mechanisms

Uncontrolled pain

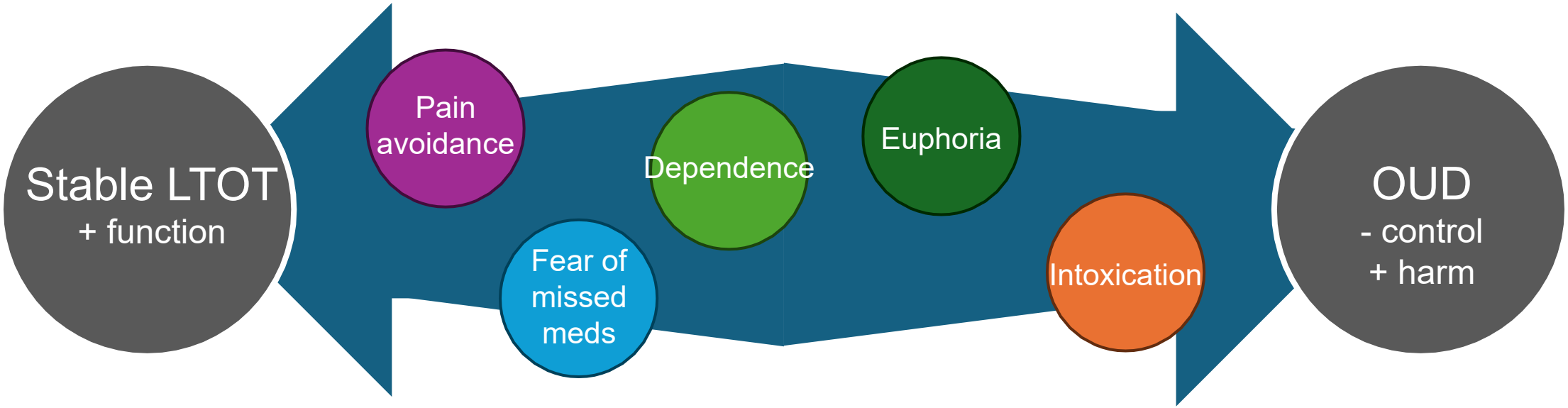
Avoiding withdrawal

Anxiety, catastrophizing

Disorganized systems

Biomedical focus on pain

Opioid-Related Risk Exists on a Spectrum



Complex Persistent Opioid Dependence CPOD As An Evolving Concept

CPOD describes patients who have:

- Long-term opioid exposure
- Physiologic dependence
- Functional or emotional reliance on opioids
- Instability with dose reduction
- That does not firmly map to OUD

What CPOD Is and Is Not

CPOD is:

- Descriptive, not diagnostic
- Clinically pragmatic
- Focused on stability and safety

CPOD is not:

- A DSM diagnosis
- A way to avoid diagnosing OUD
- A moral judgment

Manhapra et al. *JGIM* 2020 Dec;35:964, 10.1007/s11606-020-06251-w

Why Some Find CPOD Clinically Useful

What CPOD Changes in Practice

- Creates room to adjust the plan before labels harden
- Allows pain clinicians to stay engaged rather than deferring or referring prematurely
- Helps patients hear concern without accusation or redefining

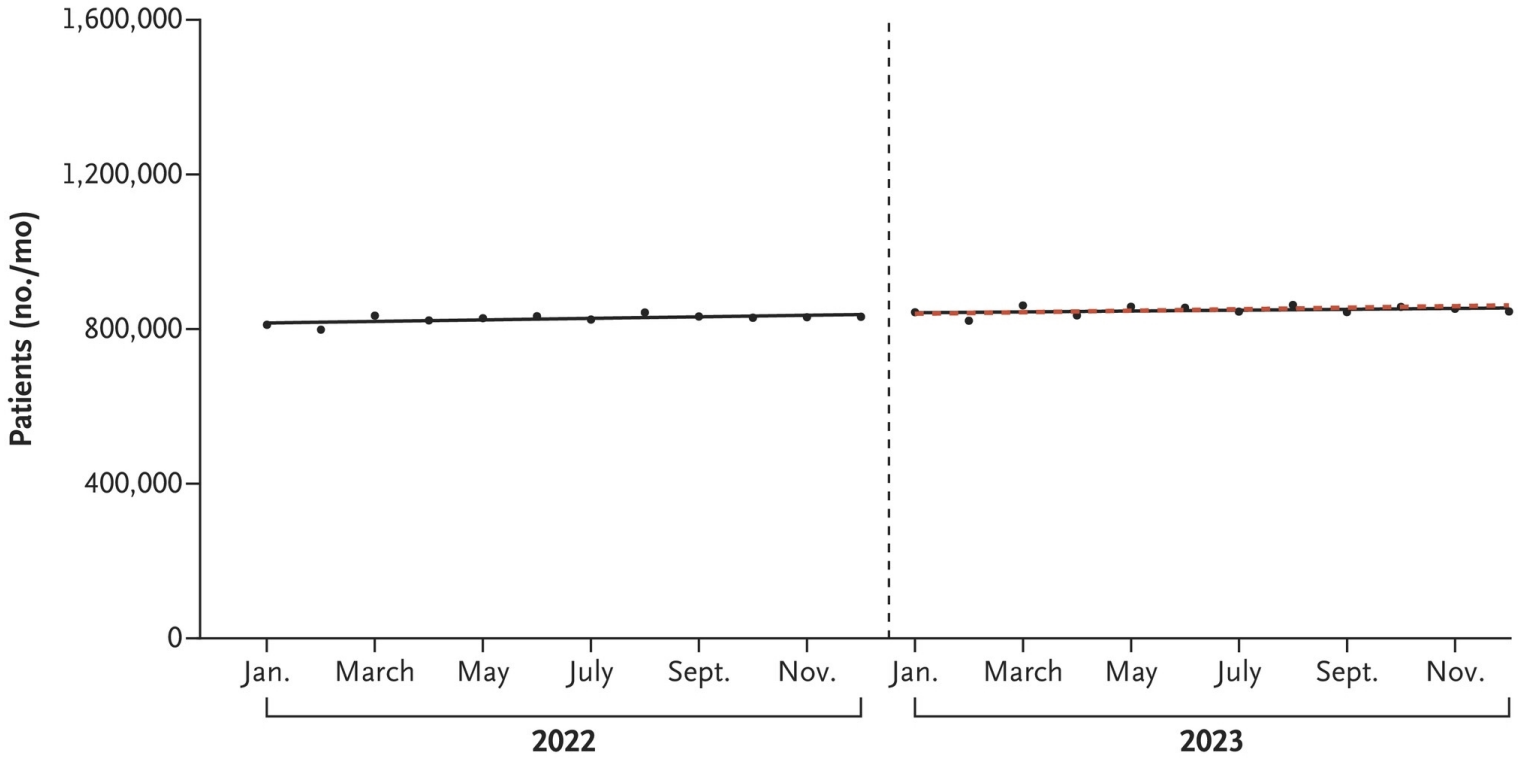
What CPOD Does Not Claim

- That action should be delayed until a diagnosis is fully settled
- That opioid use disorder isn’t present or possible
- That addiction medicine principles don’t apply

Manhapra. *Curr Treat Options Oncol* 2022;23:921, 10.1007/s11864-022-00985-x.

Setting the Stage for Safer, More Stable Care

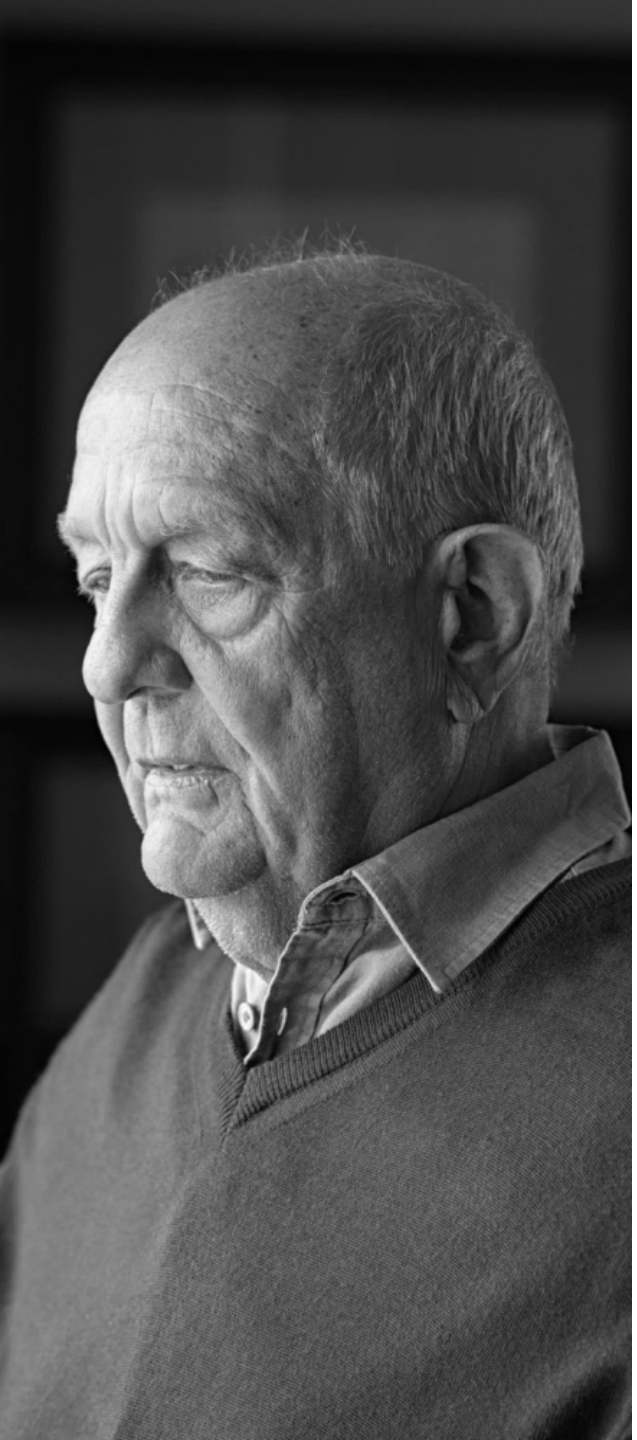
Monthly No. of Patients Filling Buprenorphine



No change after waiver removal

The NEW ENGLAND JOURNAL of MEDICINE

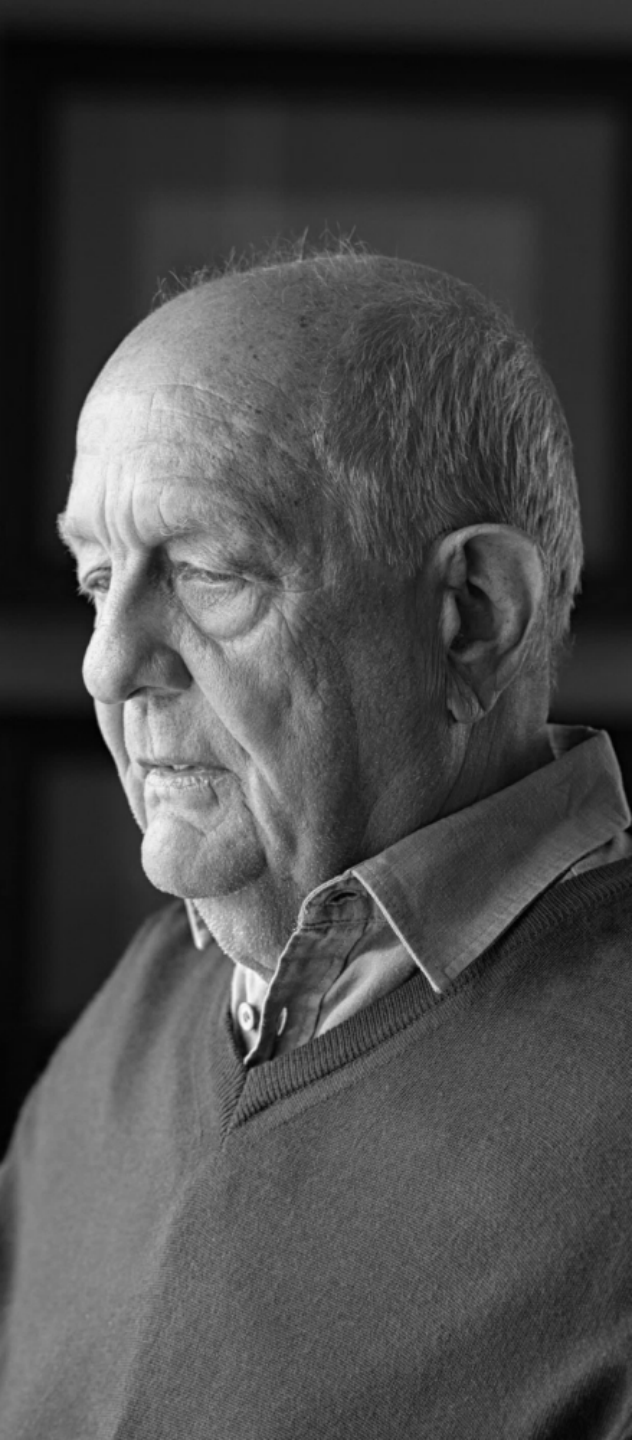
Chua et al. *NEJM*. 2024;390:1530, 10.1056/NEJMc2312906



Case Study: Tony

“I’ve been stable on these meds for a long time.”

66-year-old male with h/o alcohol use disorder in remission for over 10 years, now on chronic opioid therapy for past 6 years for lumbar DDD with right L5 radicular leg pain and bilateral knee DJD.



Case Study: Tony

- History: 3 lumbar surgeries including L3-S1 fusion in 2019
- Low back and right leg pain shooting to calf
- *“I have bad lumbar nerve scarring. Worst the surgeon had ever seen.”*

Medications

Oxycodone 10 mg, 1 Q4-6 hrs, max 6/ day x 10 years
#180/30 days

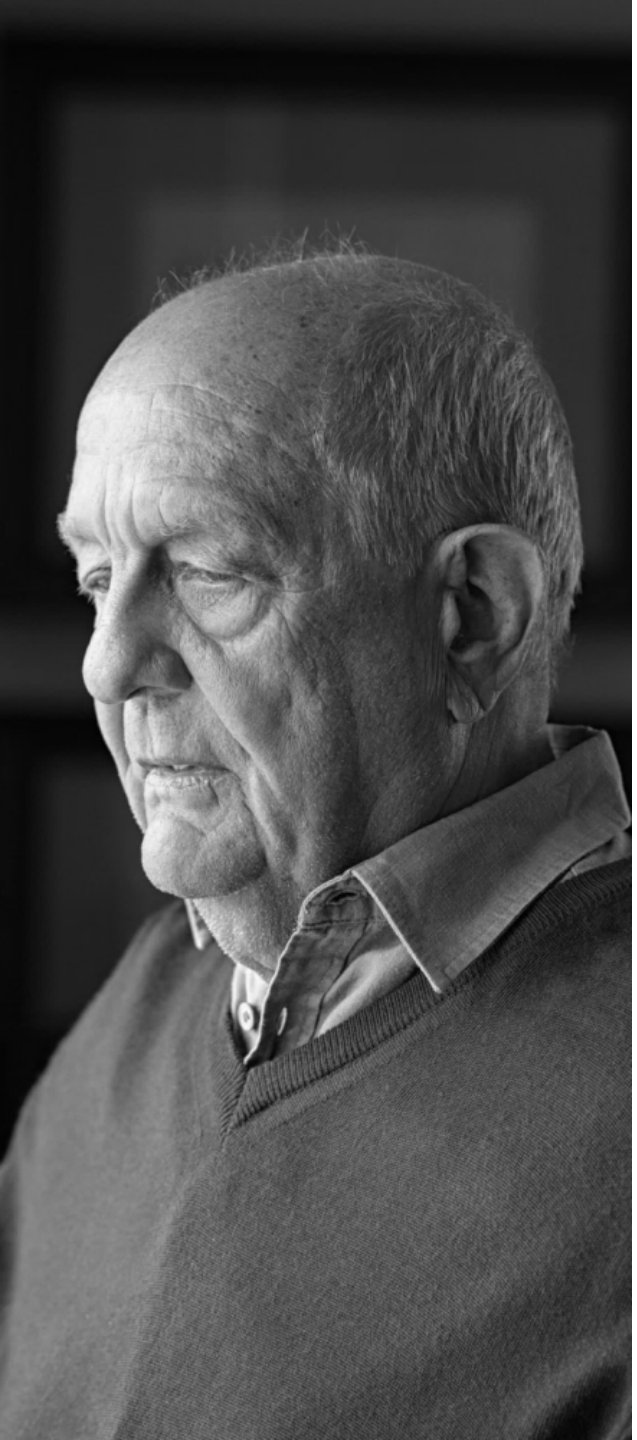
Alprazolam 1mg QHS x 3 years

Social

ETOH: past “problem,” none

Tobacco: quit in treatment 10 yrs

Wife supportive, no SUD hx



Case Study: Tony

- Though historically he has been adherent without red flags over 5 years working together, PCP recently became concerned about *multiple requests for early refills* reportedly due to unplanned out of town trips.

- His prescribed opioid, oxycodone, which is Rx'd at 10mg q4h as needed for pain (max 6/day), is *absent on urine tox screen* the next time seen, confirmed by GC/MS testing → PCP refers him to pain/addiction medicine.

- We discuss case hx and records in detail, do PE. Tony admits that he has been using 8/day recently because he needs to take 2 tabs in the AM to get adequate pain relief, and at least one dose overnight to avoid withdrawal. He therefore not surprisingly has been *running out several days early*.

Review Case Study

Review Tony 's history of chronic opioid therapy and alcohol use disorder as well as some of the red flags involved in his case.

Discussion Questions

- *Based on the information provided, does Tony's case align more with OUD, CPOD, or both? Why?*
- *How might this difference inform next steps?*

Time Allocated:

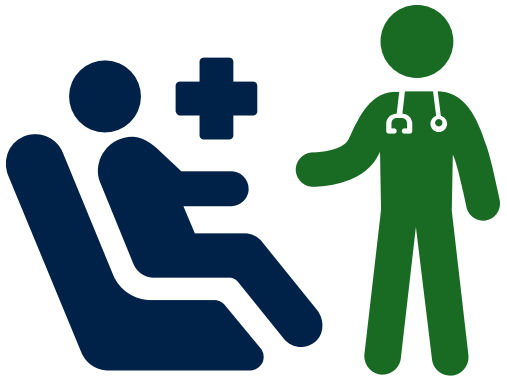
5 minutes

2019 HHS Pain Management Best Practices Interagency Task Force: *Role of Stigma*

Patients Face Stigma:

Patients with painful conditions and comorbidities such as anxiety, depression or substance use disorder (SUD) face additional **barriers to treatment** because of stigma.

Chronic pain is common among individuals with SUD, including opioid misuse, yet stigma remains a major barrier to implementation of programs and treatments for chronic pain or opioid use disorder, such as MOUD and naloxone.



Patients with co-occurring problematic opioid use and chronic noncancer pain report significant perceived ***stigma associated with buprenorphine and methadone treatment****.*

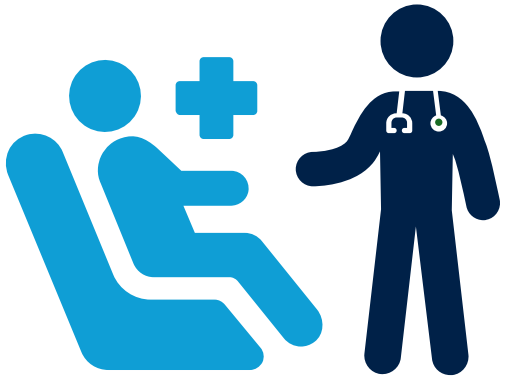
Jianguo Cheng, MD, PhD, FIPP, Molly Rutherford, MD, MPH, FASAM, Vanila M Singh, MD, MACM, The HHS Pain Management Best Practice Inter-Agency Task Force Report Calls for Patient-Centered and Individualized Care, Pain Medicine, Volume 21, Issue 1, January 2020, Pages 1–3, https://doi.org/10.1093/pm/pnz303

2019 HHS Pain Management Best Practices Interagency Task Force: *Role of Stigma*

Clinicians Face Stigma:

Clinicians who treat acute and chronic pain, particularly with opioids, may experience stigma from colleagues and society in general.

That stigma, in addition to fear of scrutiny from state medical boards and the Drug Enforcement Administration (DEA), may dissuade them from using opioids appropriately, **including buprenorphine**.



Stigma leads to over-referral and patient abandonment.

Jianguo Cheng, MD, PhD, FIPP, Molly Rutherford, MD, MPH, FASAM, Vanila M Singh, MD, MACM, The HHS Pain Management Best Practice Inter-Agency Task Force Report Calls for Patient-Centered and Individualized Care, Pain Medicine, Volume 21, Issue 1, January 2020, Pages 1–3, https://doi.org/10.1093/pm/pnz303

Normalizing Some of the Common Unintended Negative Consequences of Long Term Opioid Therapy (LTOT)

- Clear, non-judgmental PATIENT-CENTERED discussion of concerns about role of ongoing opioids in the plan
  - **Focus on potential unintended consequences on pain symptoms and overall functioning/QOL**
    - tolerance/hyperalgesia
    - withdrawal symptoms between doses, dysphoria and unstable pain control (hyperkatifeia*) → *negative reinforcement* to take another dose due to opponent processes
    - unstable mood/energy levels
    - impaired sleep (esp. common with short-acting opioids)

SOURCE: Koob GF. Drug Addiction: Hyperkatifeia/Negative Reinforcement as a Framework for Medications Development. Pharmacol Rev. 2021 Jan;73(1):163-201. doi: 10.1124/pharmrev.120.000083. PMID: 33318153

Treatment of Opioid Dependence Without OUD In Chronic Pain Patients

Original Investigation | Substance Use and Addiction

September 8, 2021

Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain

A Systematic Review

Victoria D. Powell, MD[1,2]; Jack M. Rosenberg, MD[3,4,5,6]; Avani Yaganti, BS[7]; et al

Author Affiliations | Article Information

JAMA Netw Open. 2021;4(9):e2124152. doi:10.1001/jamanetworkopen.2021.24152

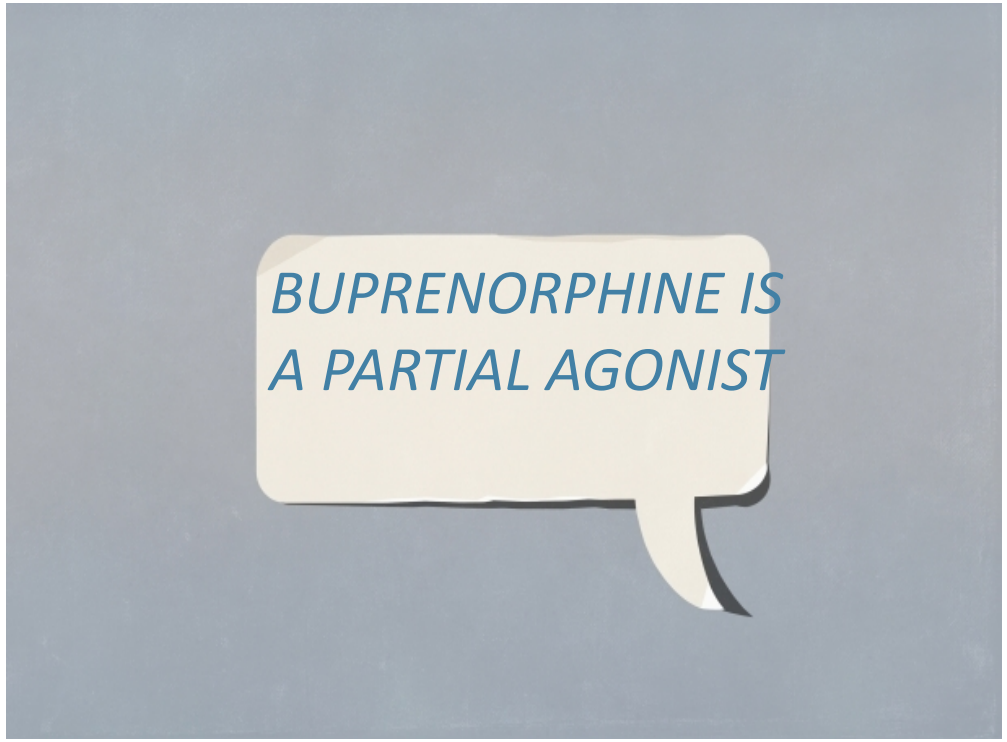
- **Buprenorphine should be proactively offered to treat pain/opioid dependence without OUD**
  - If presented confidently as a potentially effective and preferable option, pt may choose it rather than staying put or tapering
  - Transition can be handled in multiple ways

- Without red flags and patient resistant to changes, it may be reasonable to continue the usual opioid dose
  - Provide additional support if attempts to taper result in a deterioration in function and quality of life

Buprenorphine's Unique Pharmacologic Advantages in Safety and Sustainability for Chronic Pain

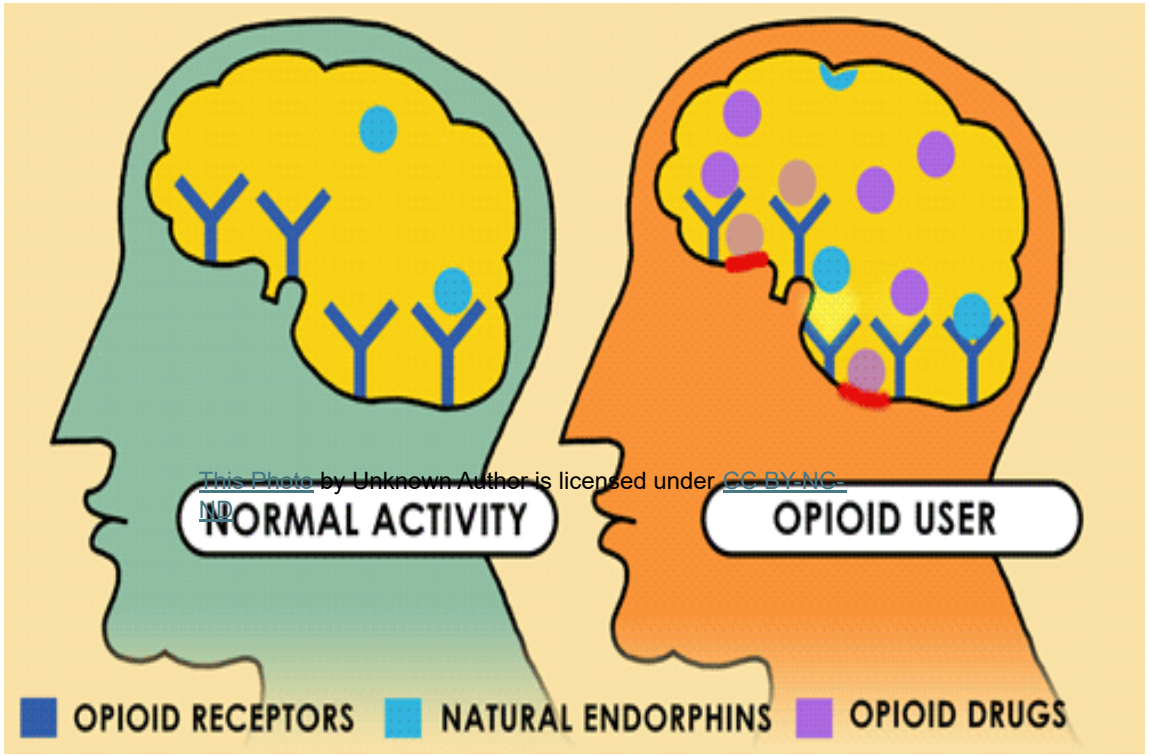
- *Structural* activity differences: intrinsic activity at the mu-OR is different from other opioids
  - **Effective analgesic threshold is met and maintained even with low % receptor occupancy (5-10%)= high intrinsic activity**, while adverse effects, risk of misuse/OUD/overdose are lower
  - **G-protein signaling leads to analgesia as with all other opioids, but with buprenorphine it does NOT lead to phosphorylation,** decreased signaling (desensitization), or gradual receptor downregulation → ***more sustainable*** **pain relief with buprenorphine**

QUESTION WHAT YOU HAVE BEEN TOLD ABOUT BUPRENORPHINE



- Partial agonism is defined by <u>low</u> intrinsic activity at the receptor (ie lower than a full agonist), BUT **buprenorphine has high intrinsic activity**, needing only 5-10% receptor occupancy to produce analgesia
  - Influenced by other factors like downstream signalling and OR density
- **“ceiling effect” exists for respiratory depression but *not for analgesia***

Buprenorphine's Unique Advantages in Safety and Sustainability for Chronic Pain (Cont.)



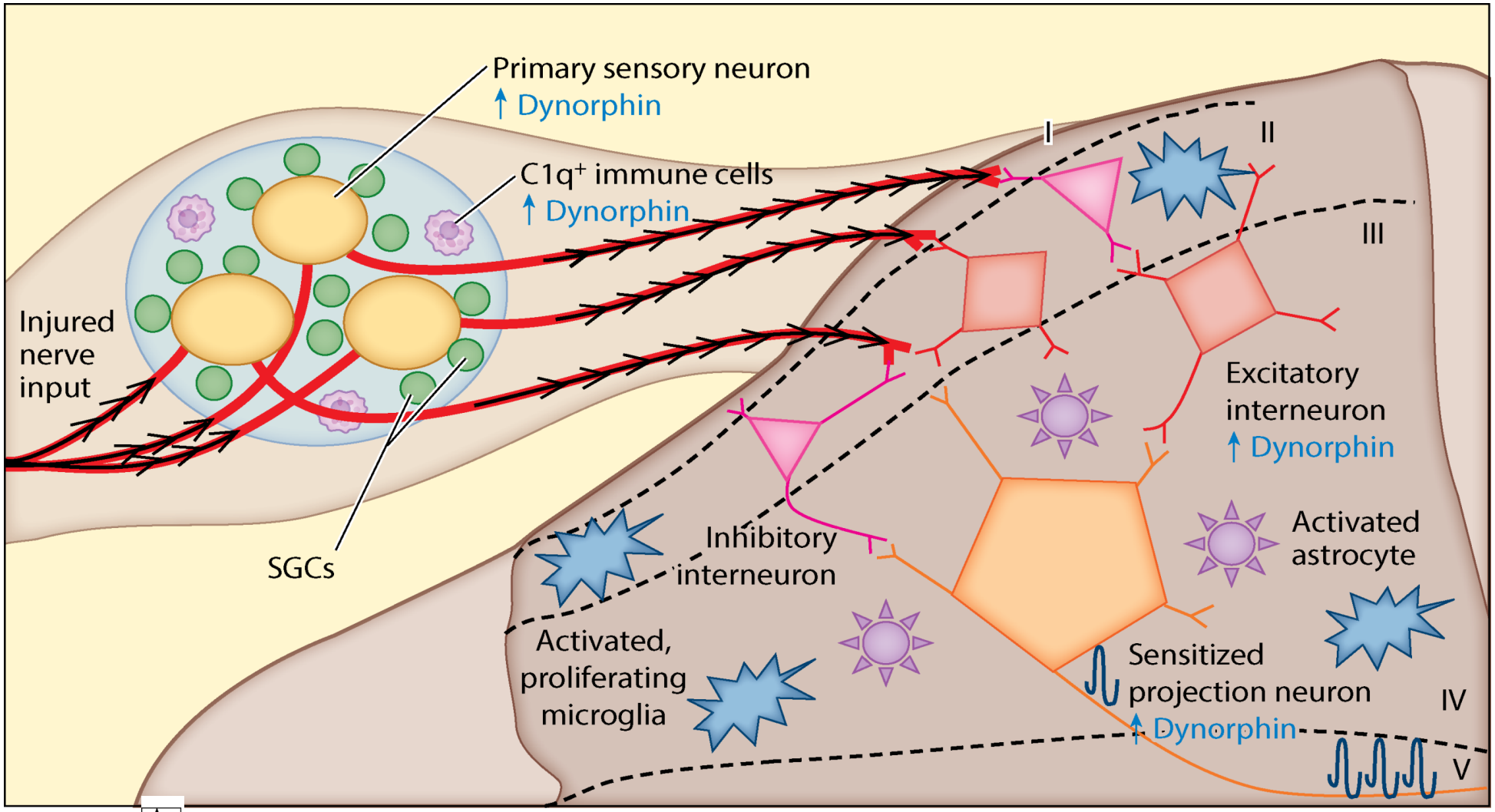
- *Tissue* activity difference: buprenorphine's active metabolite **norbuprenorphine mostly does not cross the blood brain barrier** (lipophobic)→ **minimal brain effect**
  - Affects primarily spinal-level opioid receptors, plus periphery
  - Spinal injection of naloxone blocks analgesia for buprenorphine, morphine and fentanyl; **supraspinal naloxone blocks morphine and fentanyl analgesia but not buprenorphine**

Buprenorphine Pharmacology Is Complex: Potent, Yet Safer and Less Impairing

- **Strong analgesic potency at mu-OR** (about 50x morphine)
  - *again*: **no analgesic ceiling up to at least 32mg** (Dahan, 2006)

- Binds distinct mu-OR subtype: arylepoxamide receptor (**AEAr**)
  - contains a particular *truncated protein* from the mu opioid receptor gene *Oprm1*
    - Mice lacking this protein displayed no analgesic effect from buprenorphine, while responding to morphine*
    - may be part of buprenorphine's typically lower cross-tolerance
      - **SOURCE:** Grinnell SG et al. Mediation of buprenorphine analgesia by a combination of traditional and truncated mu opioid receptor splice variants. Synapse. 2016; 70(10):395-407. PMID 27223691

Upregulation of *Dynorphin* in Chronic Pain: Agonist at *Kappa OR* → Pro-nociceptive and Dysphoric Effects



SOURCE: Podvin S, et al. 2016. Annu. Rev. Pharmacol. Toxicol. 56:511-33

Buprenorphine's Anti-Hyperalgesic Effects and Other Important Features in Pain Treatment

- Buprenorphine is a **kappa opioid receptor antagonist**
  - disrupts effect of dynorphin → **anti-hyperalgesia**

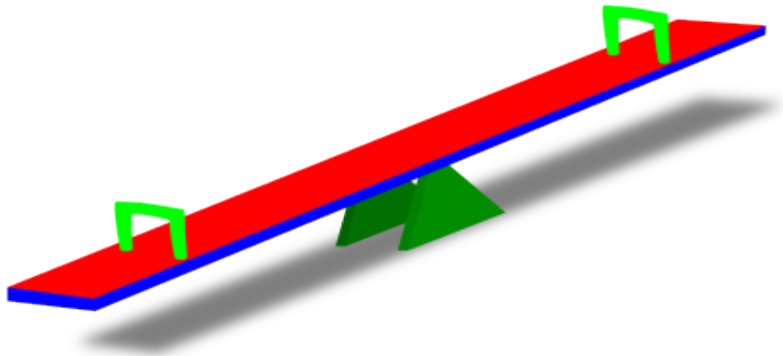
- Buprenorphine causes **sodium channel blockade** (Leffler 2012)
  - blocks voltage-gated sodium channels via the local anesthetic binding site → **anti-hyperalgesia**
  - New class of pain reliever starting with suzetrigine is selective peripheral sodium channel blocker (Nav1.8), FDA approved in January 2025

Recommending Buprenorphine for Treatment of Pain, OIH, *and* OUD/CPOD

- *Additional but less important opioid receptor activity of buprenorphine:*
  - *ORL-1 (nociceptin) receptor agonist*
    - unclear analgesic potency, some anti-hyperalgesia; no opioid adverse effects such as resp depression, itch
    - antagonist of dopamine transport → useful in non-opioid SUD tx? (Zaveri, 2016)
  - *Delta opioid receptor antagonist (weak)*
    - contributes to analgesia
    - improves negative emotional states (Pradhan, 2011)
    - helps limit tolerance and hyperalgesia (Gudin, 2020)

Recommending Buprenorphine for Treatment for Pain, OIH, *and* OUD/Complex Persistent Opioid Dependence

- High affinity, slow dissociation → **long half-life**
  - Pts appreciate stable opioid levels, lack of *negative reinforcement*
    - Many patients on LTOT are using a short-acting opioid routinely through the day→ they won't miss *ups and downs*
  - Implications on transitioning, especially to the high potency, rapid onset sublingual formulation



Buprenorphine Products FDA-Approved for Pain

- **Transdermal (Butrans™):** weekly transdermal patch
  - Better tolerated than sublingual in RCT
    - Skin irritation most common adverse effect
  - Effective for chronic pain of all causes including cancer
  - Lower dose of buprenorphine vs sublingual, range is 5mcg/hr → 20mcg/hr

- **Buccal (Belbuca™):** buccal film for chronic daily pain, usually dosed q12h; range 75mcg → 900mcg

- **Solution (Buprenex™):** solution used IV for <u>acute</u> pain in inpatient setting; this was original buprenorphine product introduced in 1981

Use of SL Buprenorphine for Pain

- **Is it OK to use sublingual off-label for pain? *YES!***
- *Why would you?*
  - Transition from high MED opioids (>90) → may require higher potency SL formulation to be perceived as effective
  - Cannot access other formulations FDA approved for pain through insurance (transdermal or buccal products)
  - Want to have some dosing flexibility (others must be fixed dose)

Use of SL Buprenorphine for Pain: Practical Tips

- Write “for pain” on Rx, “opioid dependence” for insurance authorization if asked
  - *Remember*, this is not the same as OUD, and the patient may feel less stigmatized
  - Pain typically not a covered indication for sublingual formulation
- Presence/absence of naloxone not clinically significant in pain context, though naloxone may contribute adverse effects

Buprenorphine Initiation Strategies

Traditional aka "Washout" or "Flying Dragon"

- Period of abstinence
- Wait until moderate (or worse) withdrawal – usually 12-24 hours (longer for fentanyl)
- Then start at 2 mg & titrate to therapeutic dose

Low Dose Initiation with Concurrent Full µOR Agonist

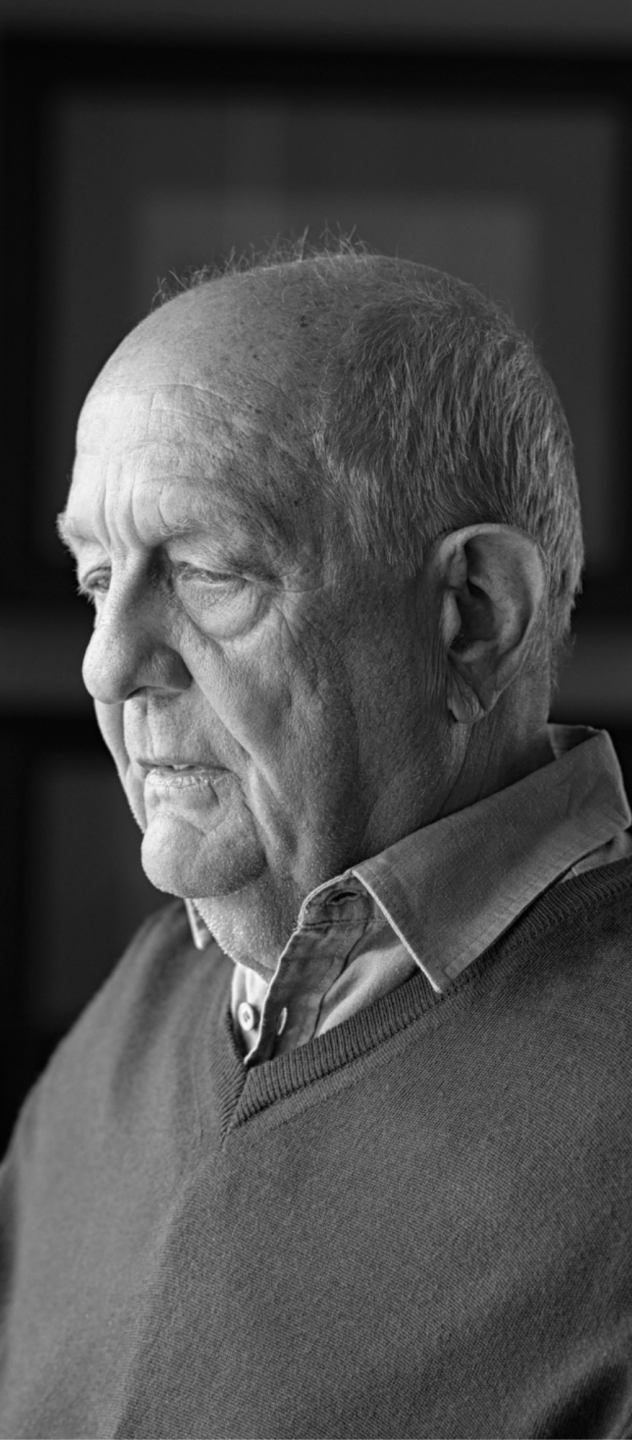
- Eliminates need for period of abstinence
- Gradual initiation of low doses (0.5 mg) with slow up-titration
- Concurrent full µOR agonist is managing withdrawal
- Once at therapeutic dose of bup, stop full µOR agonist

- 5-10 days to therapeutic dose

Rapid Low Dose Initiation

- Eliminates need for period of abstinence
- Start very low doses, every 3-4 hours, gradually increase dose
- "Sneak" on to the receptors
- Withdrawal symptoms managed with ancillary medications
- Minimizes full µOR agonist; may use as needed

- 2-4 days to therapeutic dose



What's Next for Tony?

Next steps:

- **Good candidate for buprenorphine**
  - Consider 2mg SL TID vs 150mcg buccal q12 vs 10mcg transdermal
  - Each has pros and cons, insurance factors
- Consider referring him to an interdisciplinary outpatient pain rehabilitation program
  - Includes counseling, PT/OT, biofeedback/relaxation training, medical mgmt
- Consider acupuncture trial
  - Strong evidence in LBP treatment
- Consider eval for spinal cord stimulator

Choices & Opportunities for Tony

“Isn’t Suboxone that stuff for addicts? I have real pain .”

Is Tony on board with your recommendations?

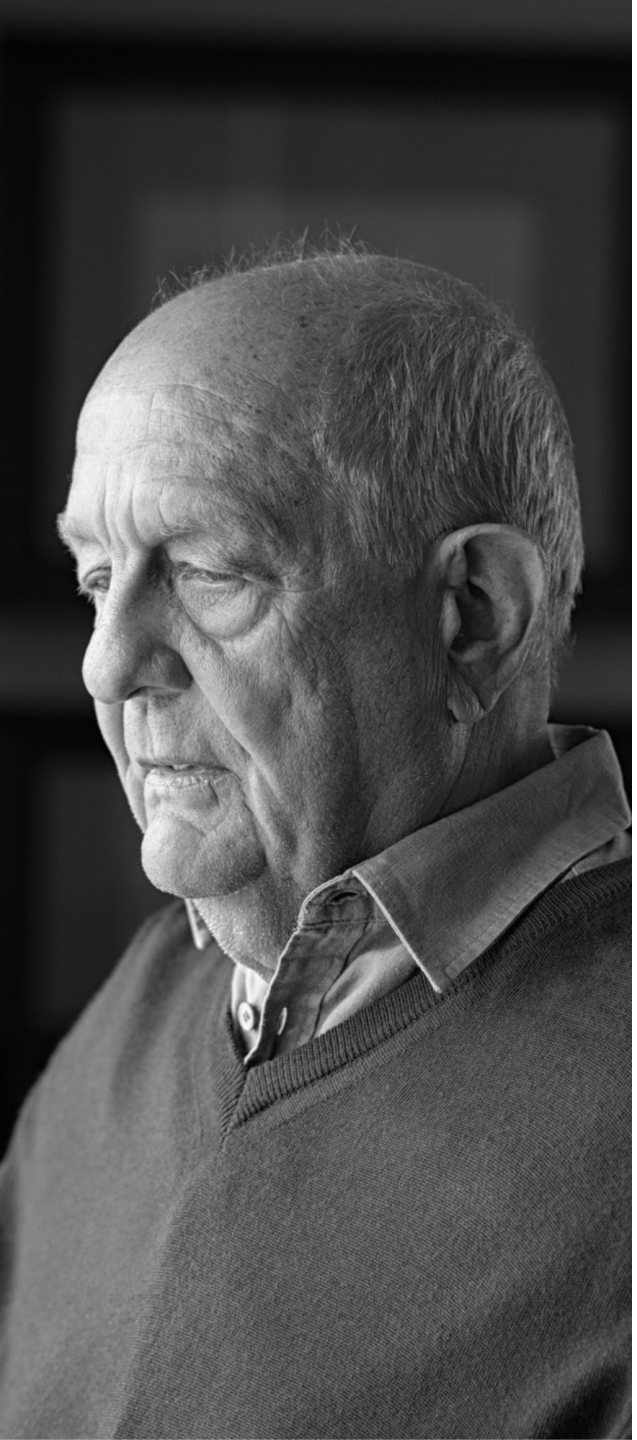
- **If he is resistant to buprenorphine: try to zero in on why**
  - gently challenge any inaccuracies in his understanding of potential benefits and appropriateness for him
  - Emphasize pharmacology and patient-centered concerns with current program
- *Where is “cognitive dissonance” about buprenorphine coming from?*
  - Internet, friend/family/acquaintance, medical source, or just plain fear of change?

Choices & Opportunities for Tony

1. **Transition to buprenorphine**, then re-evaluate pain and management options

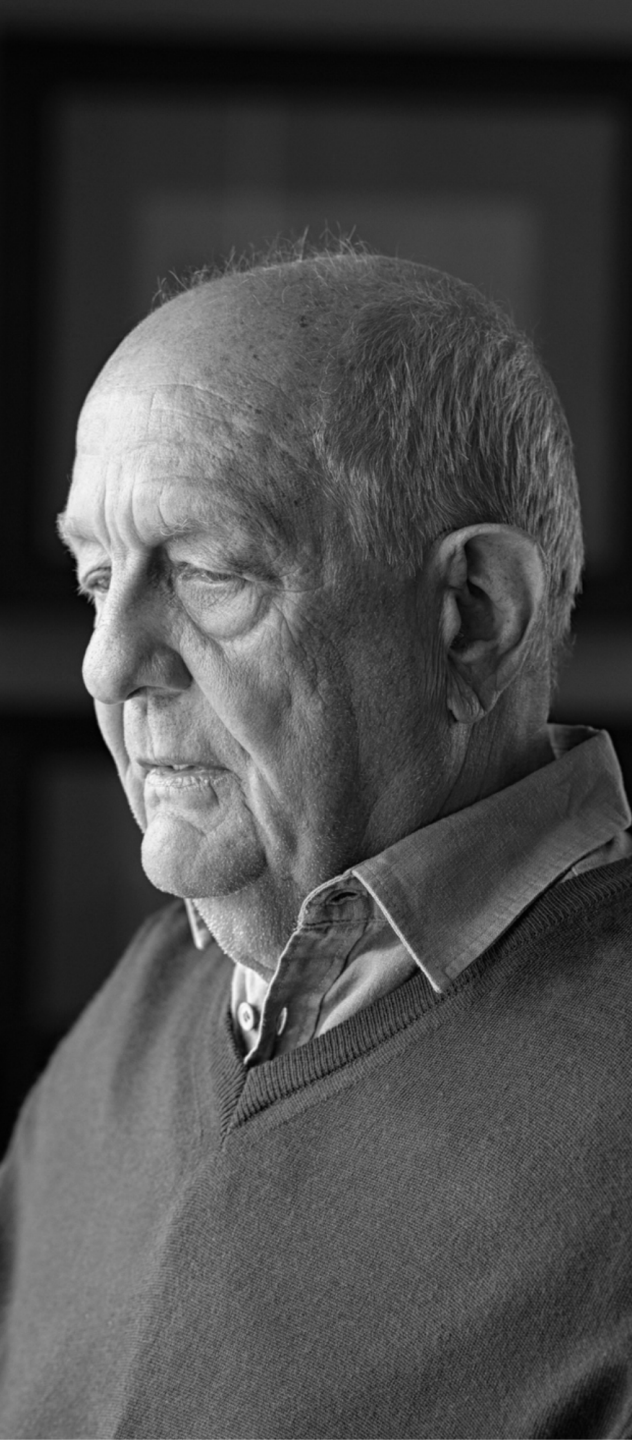
OR

2. Enact tight adherence measures, **then taper/discontinue opioids in a supportive fashion**
   - 1 or 2-week Rxs with gradually decreasing quantities
   - wife monitors med
   - add ancillary meds for pain/withdrawal (tizanidine, gabapentin) and sleep (trazodone or mirtazapine)
   - More frequent visits, urine tox screens
   - Still discuss referral to outpatient “pain rehabilitation” and/or acupuncture
   - Search “HHS opioid tapering schedule pdf”



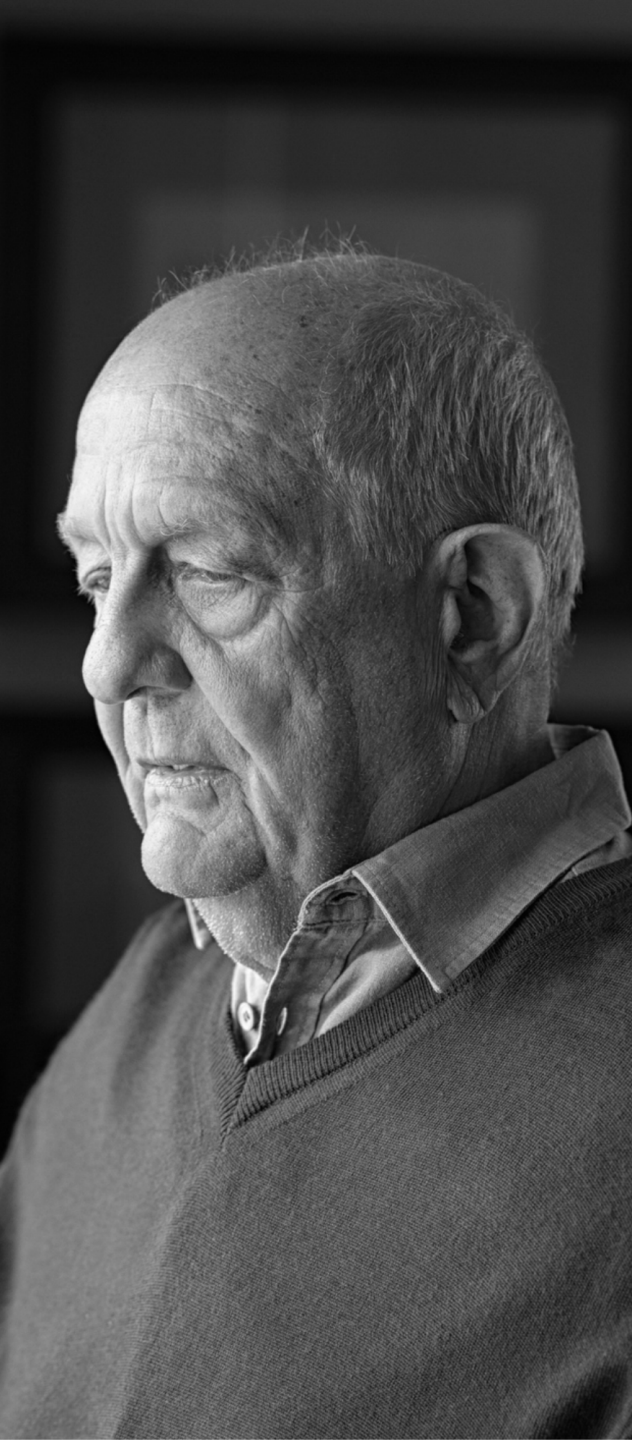
How Did Tony Do?

- Tony comes back for follow-up after two weeks. He was able to get started on SL bup and has been trying to be in a routine with 2mg TID dosing, though he is having significant adverse effects including nausea and sedation.
- Tony says, “I can fall asleep at any moment” and feels that his QOL is worse
- Tony feels that he can not continue this but wants to know what you recommend. He also asks if he should go back on oxycodone.



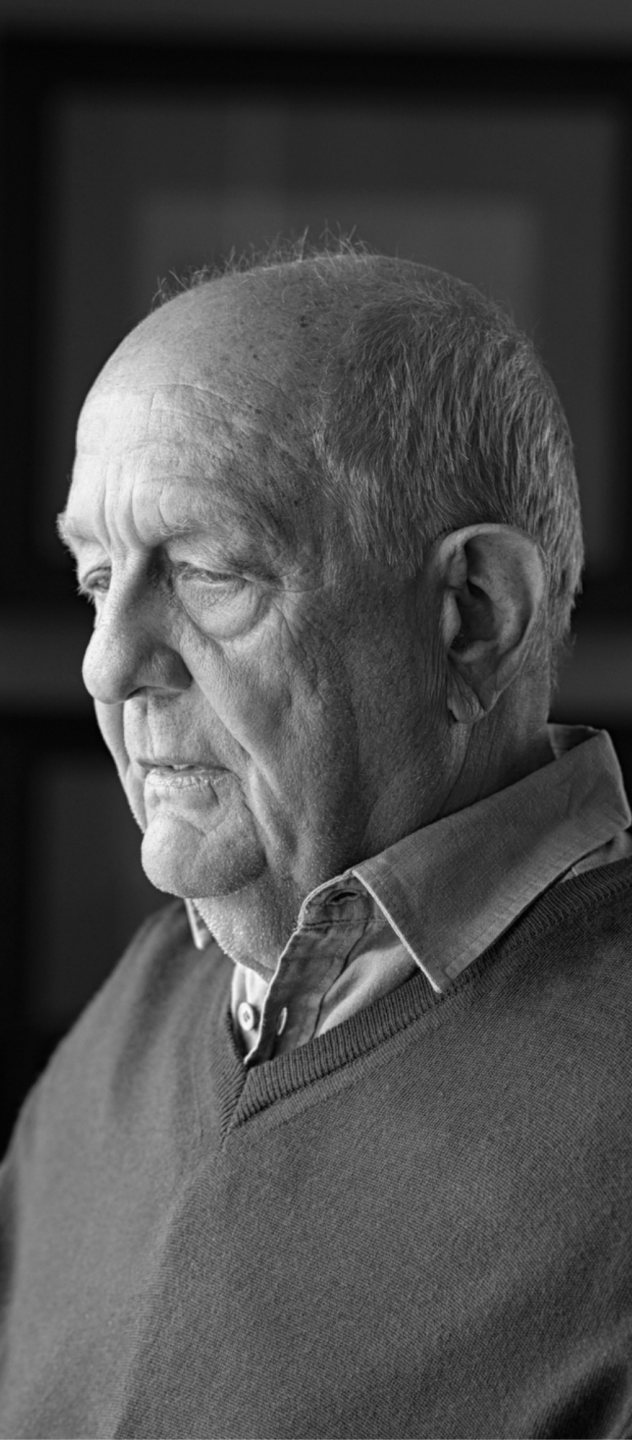
What to do next with Tony?

- You suggest initiating **transdermal** buprenorphine with the idea that the lower potency should allow for better tolerability and should still be helpful for pain
- He says one of his doctors tried him out on a fentanyl patch several years ago and he had severe skin rashes, so he prefers not to use a patch
- You then suggest the **buccal** formulation of buprenorphine given that it is also a lower dose range than sublingual, and he is willing. You start with 300mcg twice daily and stop SL



How Did Tony Do?

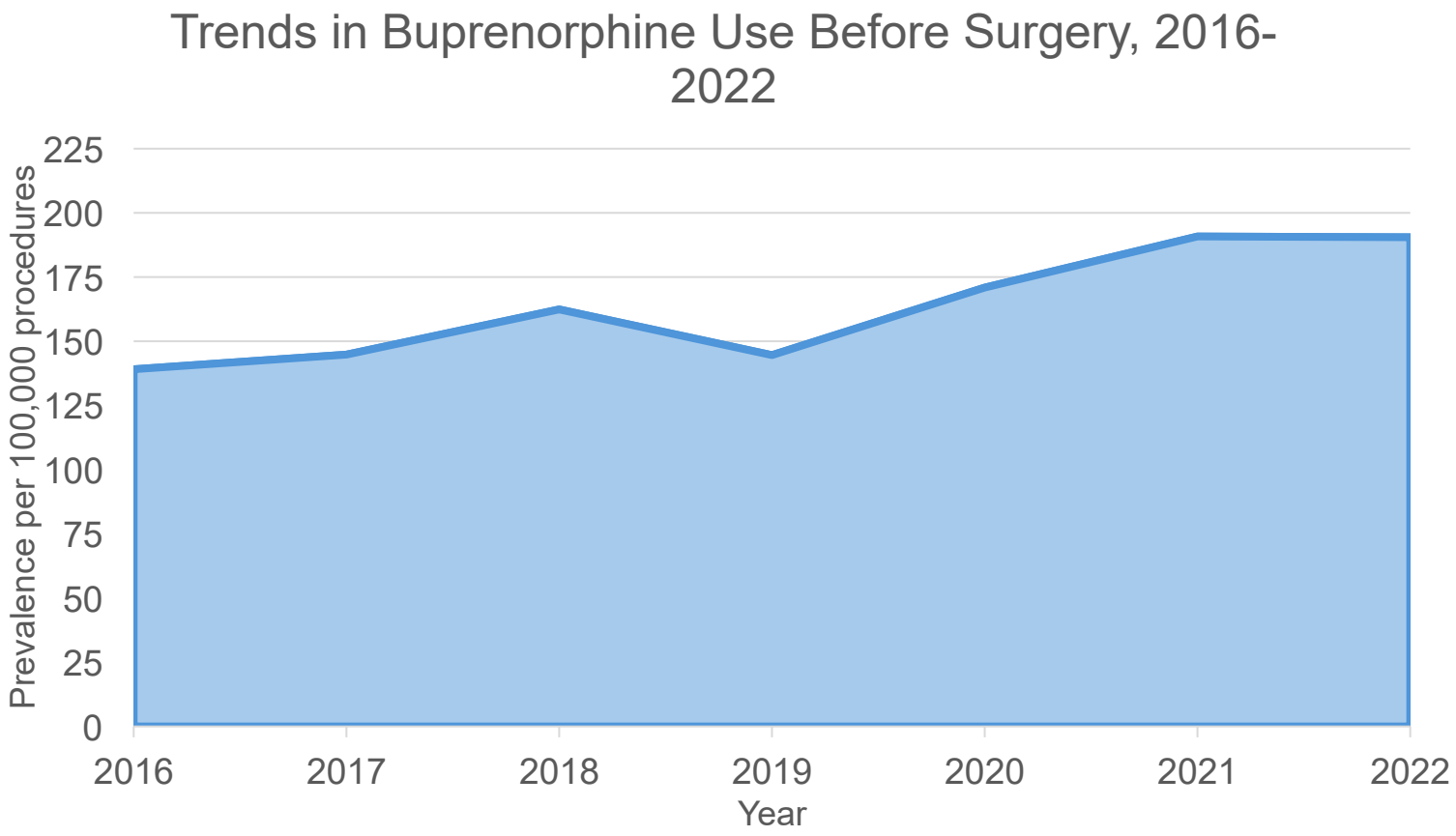
- Fortunately, after two more weeks Tony is feeling better on the buccal buprenorphine and thinks he can work with it. You agree to keep the dose stable for now and work on the rest of his pain management program (optimizing non-opioid medications, non-pharmacologic treatment, and self-care practices).
  - **THOUGHT EXPERIMENT:** *What if Tony reports he could not tolerate the buccal buprenorphine either?*
    - Tony says “I just can’t take this buprenorphine stuff. Can we please try something else or go back to oxycodone? This last month has been miserable!”



Tragedy Strikes

- 2 months later, Tony has been going to physical therapy and trying to go for walks around his neighborhood every day.
- One misty morning he catches his foot on the curb and falls, fracturing his R hip.
- **Ortho team consults and recommends surgery**.
  - They tell you they have some experience working with patients who are prescribed buprenorphine, and they typically recommend stopping it the day before surgery.
    - *Do you agree?*

More Surgical Patients On Buprenorphine



36% increase
Among commercially insured patients

Bicket et al. 2025, 10.1097/ALN.0000000000005771
Supported by NIH/NIDA R01DA057943

ANESTHESIOLOGY
NIH National Institute on Drug Abuse

Buprenorphine Maintenance Therapy: Continue or Stop?

- Discontinuation of buprenorphine exposes the patient to the substance of addiction and may lead to relapse

Review > J Subst Abuse Treat. 2015 May;52:48-57. doi: 10.1016/j.jsat.2014.12.011. Epub 2014 Dec 30.

Discontinuation of buprenorphine maintenance therapy: perspectives and outcomes

Brandon S Bentzley [1], Kelly S Barth [2], Sudie E Back [3], Sarah W Book [4]

Affiliations + expand

PMID: 25601365 PMCID: PMC4382404 DOI: 10.1016/j.jsat.2014.12.011

Free PMC article

> Br J Anaesth. 2019 Aug;123(2):e333-e342. doi: 10.1016/j.bja.2019.03.044. Epub 2019 May 29.

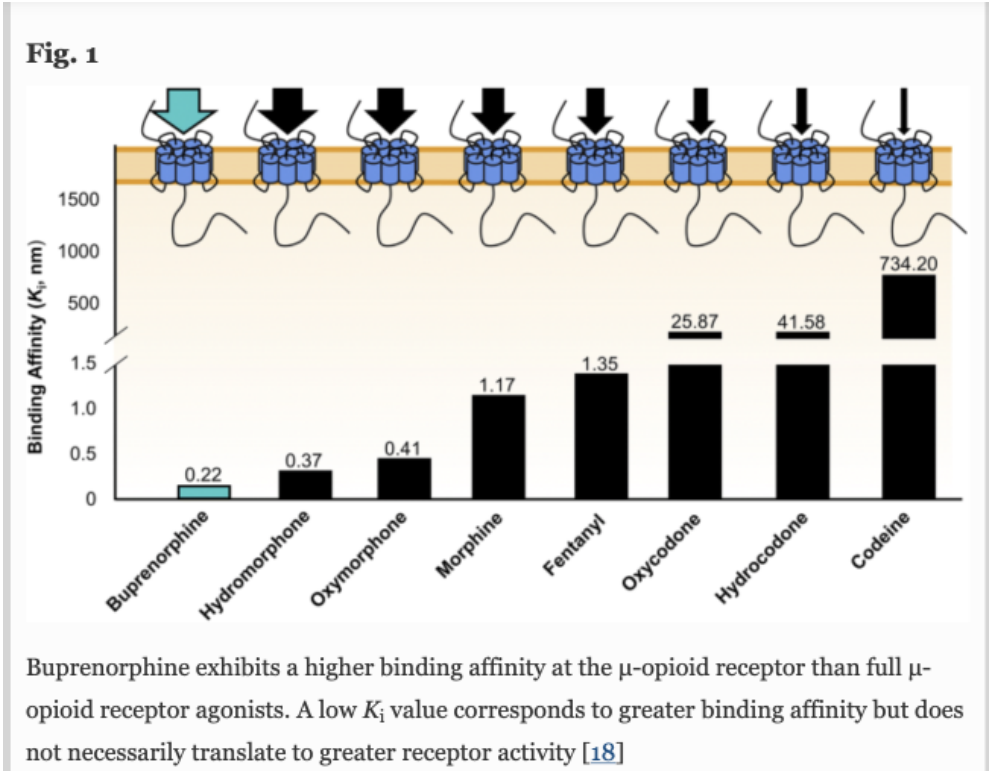
Perioperative Pain and Addiction Interdisciplinary Network (PAIN) clinical practice advisory for perioperative management of buprenorphine: results of a modified Delphi process

Akash Goel [1], Saam Azargive [2], Joel S Weissman [3], Harsha Shanthanna [4], John G Hanlon [5], Bana Samman [5], Mary Dominicis [5], Karim S Ladha [5], Wiplove Lamba [6], Scott Duggan [7], Tania Di Renna [5], Philip Peng [5], Clinton Wong [8], Avinash Sinha [9], Naveen Eipe [10], David Martell [11], Howard Intrater [12], Peter MacDougall [10], Kwesi Kwofie [13], Mireille St-Jean [14], Saifee Rashiq [15], Kari Van Camp [16], David Flamer [5], Michael Satok-Wolman [16], Hance Clarke [17]

- Continuing buprenorphine occupies the receptors making them unavailable for other opioids
  - Does this provide poorer analgesia?

Buprenorphine

- High binding affinity for the MOR
  - Will displace other opioid ligands
    - May precipitate withdrawal
  - Once in place prevents additional opioid binding



Buprenorphine exhibits a higher binding affinity at the μ-opioid receptor than full μ-opioid receptor agonists. A low K_i value corresponds to greater binding affinity but does not necessarily translate to greater receptor activity [18]

Gudin, J., Fudin, J. A Narrative Pharmacological Review of Buprenorphine: A Unique Opioid for the Treatment of Chronic Pain. *Pain Ther* **9,** 41–54 (2020). https://doi.org/10.1007/s40122-019-00143-6

Buprenorphine Receptor Binding

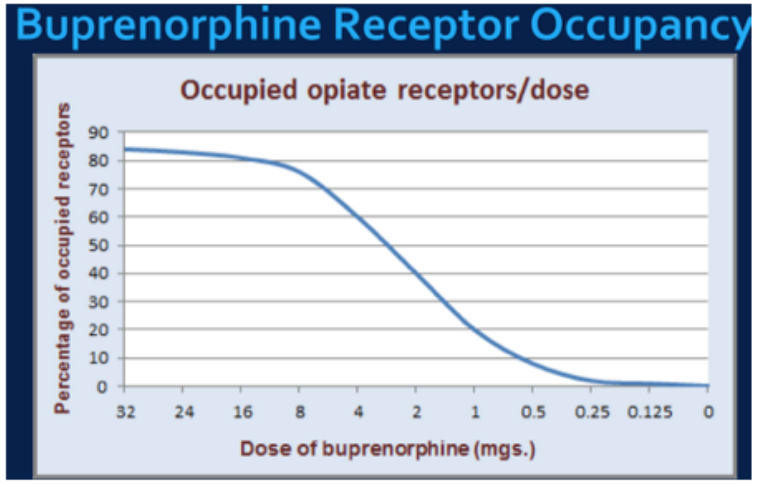


Table 2 Estimates of MOR occupancy based on buprenorphine dose

Dose	Low estimate (%)	High estimate (%)
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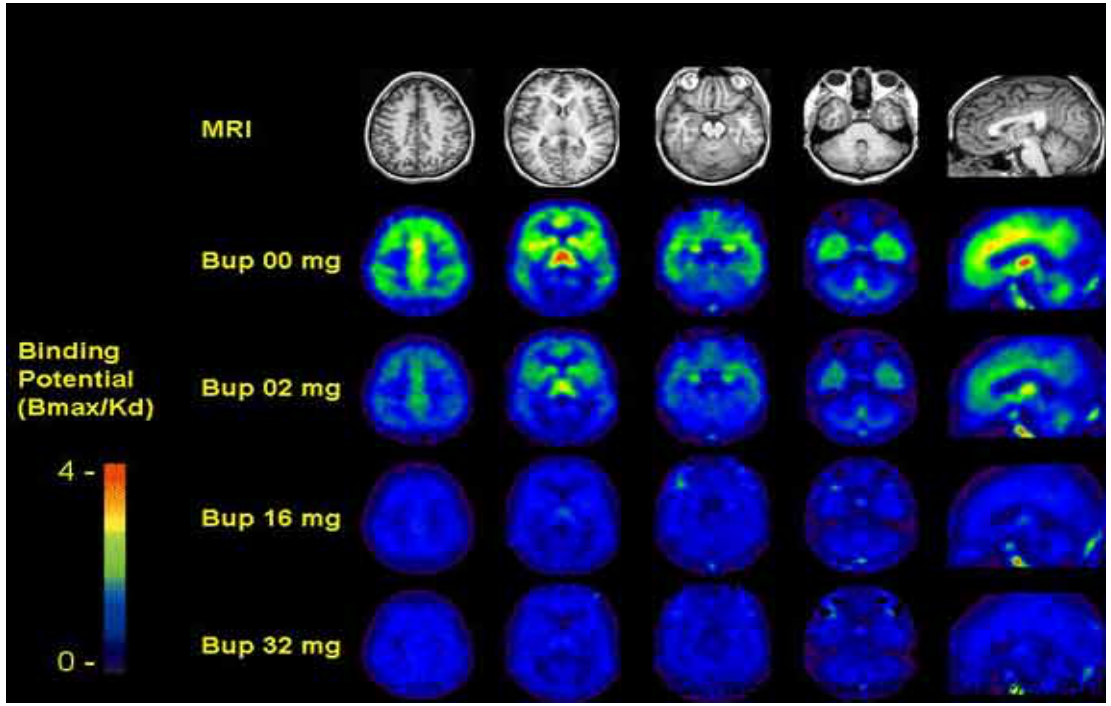

59%

20%

16%

Greenwald, M.K. et al. Effects of Buprenorphine Maintenance Dose on μ- opioid receptor availability. Neruopharmacology (2003) 28, 2000-2009
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Miller JC, Brooks MA, Wurzel KE, Cox EJ, Wurzel JF 3rd. A Guide to Expanding the Use of Buprenorphine Beyond Standard Initiations for Opioid Use Disorder. Drugs R D. 2023 Dec;23(4):339-362. doi: 10.1007/s40268-023-00443-5. Epub 2023 Nov 8. PMID: 37938531; PMCID: PMC10676346.

Can we Provide Adequate Analgesia?

Journal of
Clinical Pharmacy and Therapeutics

Journal of Clinical Pharmacy and Therapeutics, 2014, **39**, 577–583 doi: 10.1111/jcpt.12196

Commentary

The clinical analgesic efficacy of buprenorphine

R. B. Raffa* PhD, M. Haidery* PharmD, H.-M. Huang* PharmD, K. Kalladeen* PharmD, D. E. Lockstein* PharmD, H. Ono* PharmD, M. J. Shope* PharmD, O. A. Sowunmi* PharmD, J. K. Tran* PharmD and J. V. Pergolizzi†‡§ Jr MD

Temple University School of Pharmacy, Philadelphia, PA, †Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, ‡Department of Anesthesiology, Georgetown University School of Medicine, Washington, DC, and §Department of Pharmacology, Temple University School of Medicine, Philadelphia, PA, USA

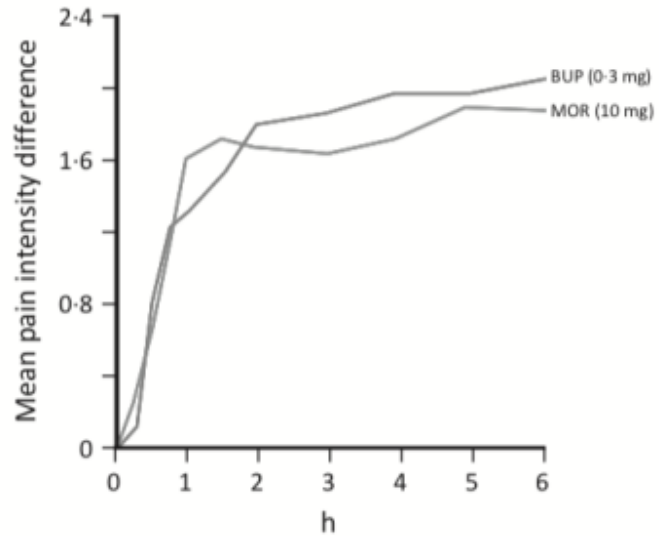


Fig. 1. The analgesic efficacy of i.m. buprenorphine (0·3 mg) was compared with that of i.m. morphine (10 mg) for post-operative pain relief in a randomized, double-blind, multiple-dose, non-crossover trial involving 60 patients (26M/34F; 17–78 years) scheduled for upper abdominal surgery. Post-op pain intensity was assessed using a visual analog scale (0 = none, 1 = slight, 2 = moderate, 3 = severe) and measured prior to the first dose of drug and every 15 min thereafter up to 2 h and every hour thereafter up to 6 h post-injection. Morphine and buprenorphine produced similar decreases in pain intensity. Redrawn from Tigerstedt and Tammisto.[16]

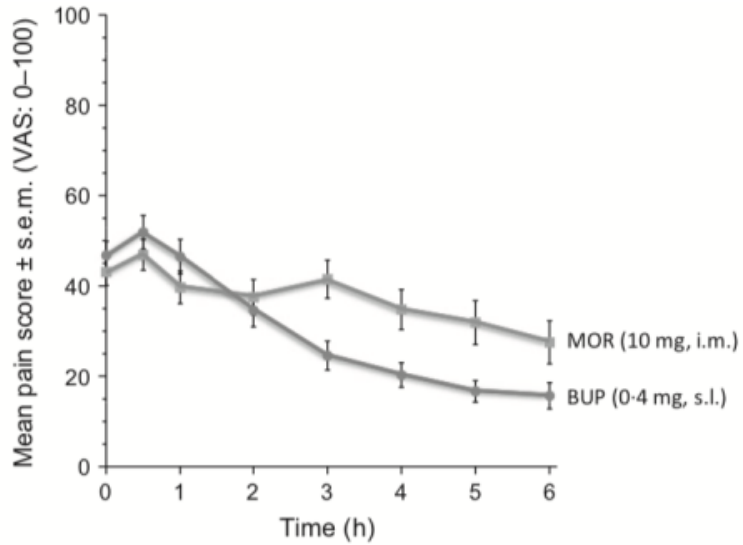


Fig. 2. The analgesic efficacy of s.l. buprenorphine (0·4 mg) was compared with that of i.m. morphine (10 mg) in a randomized, double-blind study of post-op pain of 101 patients (mean age: 40–45 years). Pain was measured using a 10-cm pain scale (0 = none, 10 = as much as imaginable). Buprenorphine produced the same pain relief as did morphine during the first 2 h and modestly greater pain relief from 2 to 6 h. Redrawn from Edge *et al.*[22]

Perioperative Buprenorphine and Methadone

- Pain relief and opioid requirements in the first 24 hours after surgery in patients receiving buprenorphine and methadone medication assisted treatment (MAT)
  - **No difference in pain** intensity ratings in patients who **continue or discontinue** on POD1
  - Patients who **discontinue** use **large quantities** of IV-PCA opioid
  - Authors recommend continuing buprenorphine
  - Buprenorphine provides significant analgesia

Macintyre PE et al. Anaesth Intensive Care 2013; 41:222-230

ANESTHESIOLOGY

Continuation *versus* Interruption of Buprenorphine/ Naloxone in Adult Veterans Undergoing Surgery: Examination of Postoperative Pain and Opioid Utilization in a National Retrospective Cohort Study

James M. Hitt, M.D., Ph.D., Peter L. Elkin, M.D., Oscar A. de Leon-Casasola, M.D.

Anesthesiology 2025; 142:320–31

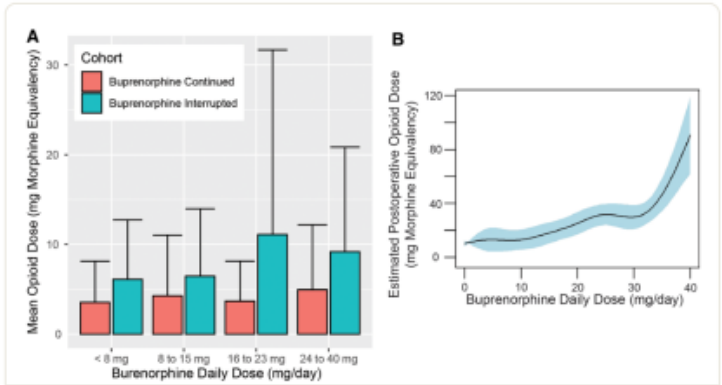


Fig. 4. (*A*) Mean ± SD postoperative opioid dose (milligram morphine equivalents) for patients for patients on different doses of buprenorphine. There was a noticeable dose–response association with buprenorphine greater than 16 mg/day in the interrupted group. (*B*) The predicted impact of buprenorphine dose on supplemental postoperative opioid doses from a generalized additive model, controlling for postoperative pain severity scale, sex, race, surgical year, and facility complexity rating. There was little impact of buprenorphine doses less than 10 mg/day, which was more pronounced at doses above 16 mg/day.

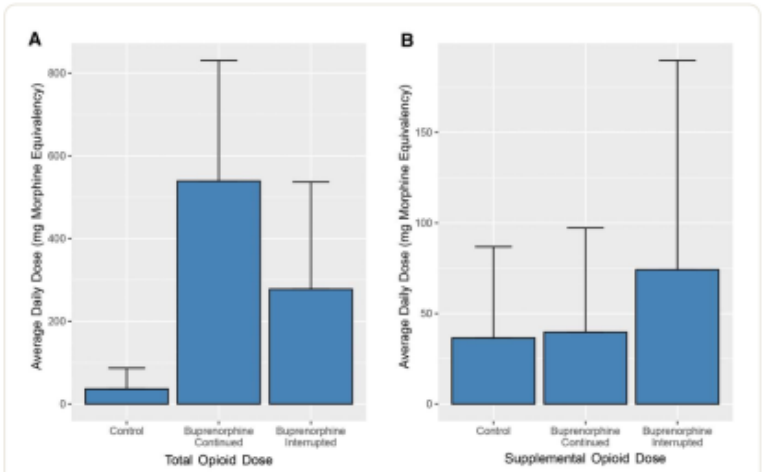


Fig. 3. Mean ± SD of postoperative opioid dose (milligram morphine equivalents) in the 2 weeks after surgery ($P < 0.001$ for pairwise comparisons after Bonferroni correction). (*A*) The mean of the average daily opioid dose for all opioids was highest in the buprenorphine continued cohort, followed by the buprenorphine interrupted group. (*B*) The exclusion of buprenorphine from the analysis shows that patients who continued buprenorphine did not require more supplemental postoperative opioid prescriptions of pure opioid agonists as compared to control ($P = 0.33$).

- Average post operative pain scores within 72 hours of sx were clinically similar in the 3 groups

Postop Pain Management

- No clear benefit to stopping and poses risk of relapse[1]
- Pts who discontinued buprenorphine have greater than 50% chance of relapse or death[2]
- Increased risk of overdose due to decrease in tolerance if discontinued[2]

1 2020 23E163-74
2. Bentzley et al: J Subst Abuse Treat 2015; 52:48-57

Continuing Chronic Buprenorphine Perioperatively is Associated With Reduced Postoperative Opioid Use

William J. Olney, BS, PharmD, BCCCP,[a,*]
Eric G. Johnson, PharmD, BCCCP,[a,b] *Cassidy Potts, PharmD,*[b]
J. Thomas Murphy, MD, FRCPC, FASAM,[c,d]
and Douglas R. Oyler, PharmD[b]

[a] *Department of Pharmacy, University of Kentucky Medical Center, Lexington, Kentucky*
[b] *University of Kentucky College of Pharmacy, Lexington, Kentucky*
[c] *Department of Anesthesiology, University of Kentucky Medical Center, Lexington, Kentucky*
[d] *University of Kentucky College of Medicine, Lexington, Kentucky*

- **Single-center retrospective** study at a **Level 1 trauma academic medical center**.
- Included: Adults on **outpatient buprenorphine** admitted with an operative booking.
- Groups:
  - **Continuation group** – buprenorphine maintained in hospital
  - **Withheld group** – buprenorphine stopped during admission
- **Primary outcome:** Any use of full μ-opioid agonists during admission days 1–7.
- **Secondary outcomes:** Length of stay (LOS), average pain scores (POD1 and POD7).

Outcomes

Primary Outcome: Opioid Requirements

- **43.4%** of patients who **continued buprenorphine** required **no full μ-agonists** during days 1–7.
- Only **3.1%** of those in the **withheld group** avoided full μ-agonists.
- **P < 0.001** → **Highly significant reduction** in opioid use when buprenorphine was continued.

Pain Scores

- No statistically significant difference in **average pain scores**:
  - POD1: **5.2 vs. 6.9** (P = 0.82)
  - POD7: **0 vs. 0** (P = 0.41)

Interpretation: **Continuation did not worsen pain control** and required fewer full agonists.

Length of Stay

- LOS showed **no significant difference**:
  - 4.7 days (2.8–6.6) vs. 6.1 days (4.0–8.2)
  - **P = 0.36**

Key points

Continuing buprenorphine perioperatively significantly reduces the need for supplemental full μ-agonists, without worsening pain or increasing LOS.

Pain scores remained **comparable** when buprenorphine was continued.

Findings support current evolving practice patterns and guidelines that favor **continuation rather than interruption** in most surgical patients with OUD.

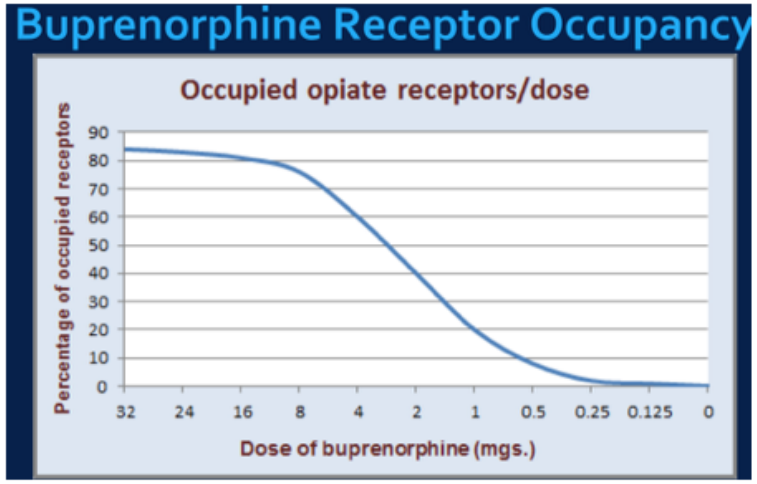
Does Dose, Diagnosis, or Type of Surgery Matter?

Buprenorphine Formulations

Formulation	Indication	Strengths	Frequency	Nalox
Sublingual tablet (generic)	Opioid dependence	2 mg; 8 mg	Once daily	N
Sublingual tablet, film (generic, Suboxone)	Opioid dependence	2 mg/0.5 mg; 4 mg/1 mg; 8 mg/2 mg; 12 mg/3 mg	Once daily	Y
Sublingual tablet (Zubsolv)	Opioid dependence	0.7 mg/0.18 mg; 1.4 mg/0.36mg 2.9 mg/0.71 mg; 5.7 mg/1.4 mg; 8.6 mg/2.1 mg; 11.4 mg/2.9 mg	Once daily	Y
Buccal film (Bunavail)	Opioid dependence	2.1 mg/0.3 mg; 4.2 mg/0.7 mg; 6.3 mg/1 mg	Once daily	Y
Buccal film (Belbuca)	Chronic pain	75 mcg; 150 mcg; 300 mcg; 450 mcg; 600 mcg; 750 mcg; 900 mcg	Every 12 hours	N
Intravenous (Buprenex)	Acute pain	0.3 mg/mL	Every 6 hours as needed	N
Subcutaneous extended release injection (Sublocade)	Moderate-to-severe opioid use disorder	100 mg/0.5 mL; 300 mg/1.5 mL	Monthly	N
Transdermal patch (Butrans)	Chronic pain	5 mcg/hr; 7.5 mcg/hr; 10 mcg/hr; 15 mcg/hr; 20 mcg/hr	Every 7 days	N

Warner NS, Warner MA, Cunningham JL, et al. A Practical Approach for the Management of the Mixed Opioid Agonist-Antagonist Buprenorphine During Acute Pain and Surgery. *Mayo Clin Proc*. 2020;95(6):1253-1267.

Buprenorphine Receptor Binding



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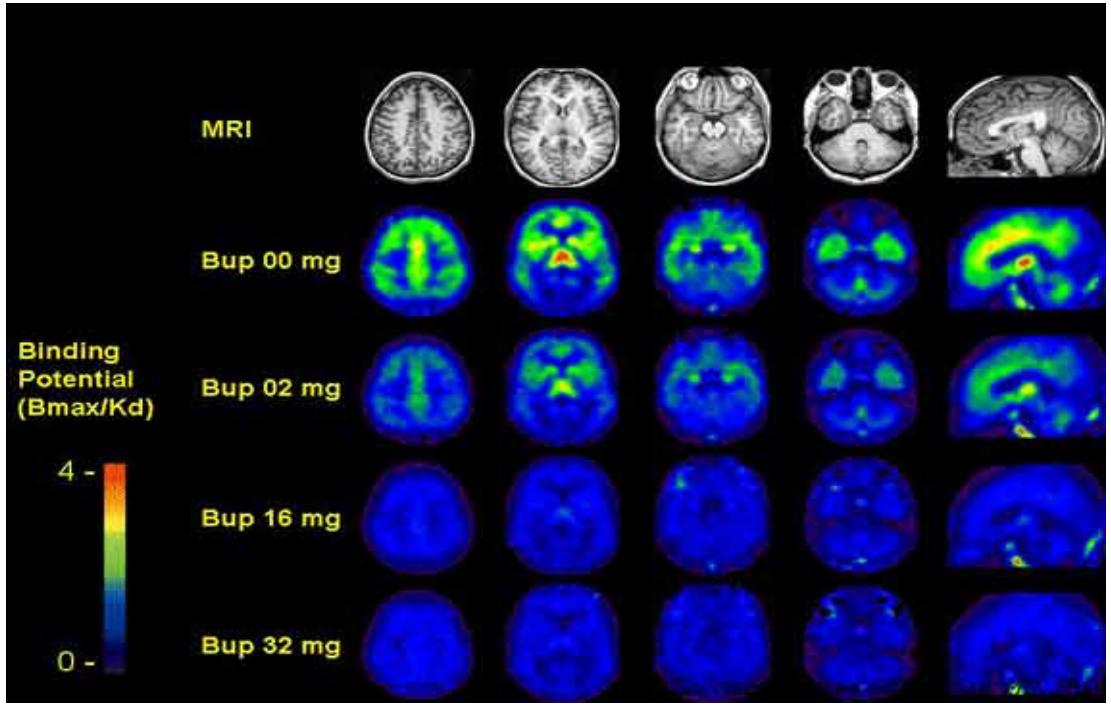

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The Efficacy of Buprenorphine in Preoperative and Postoperative Patients: A Literature Review

Keyur Patel [1], Paul Lee [1], Jessica Witherspoon [1], Kunnal Patel [1], Richard Jermyn [2]

1. College of Medicine, NeuroMusculoskeletal Institute, Rowan-Virtua School of Osteopathic Medicine, Stratford, USA
2. Physical Medicine and Rehabilitation, NeuroMusculoskeletal Institute, Rowan-Virtua School of Osteopathic Medicine, Stratford, USA

Corresponding author: Keyur Patel, patelk44@rowan.edu

- **Lumbar discectomy trial:** Sublingual buprenorphine given preoperatively significantly lowered postoperative pain scores at 1, 6, and 12 hours and reduced rescue analgesic use.
- **Knee arthroscopy:** Intra-articular buprenorphine resulted in lower pain scores at 12 and 24 hours and prolonged time to first rescue analgesic compared with dexmedetomidine.
- **Acute abdomen in opioid-dependent patients:** Sublingual buprenorphine produced lower pain scores and fewer withdrawal symptoms than IV morphine.
- **Transdermal formulations:**
- Buprenorphine 20 µg/hr patch provided superior 24-hour postoperative analgesia compared to fentanyl 25 µg/hr and buprenorphine 10 µg/hr.
- Combining a buprenorphine patch with diclofenac reduced the need for rescue analgesia after laparoscopic cholecystectomy.

What are you going to tell Tony?

Postoperative Pain Experience: Results from a National Survey Suggest Postoperative Pain Continues to Be Undermanaged

Jeffrey L. Apfelbaum, MD*, Connie Chen, PharmD†, Shilpa S. Mehta, PharmD†, and Tong J. Gan, MD‡

*Department of Anesthesia and Critical Care, The University Chicago Hospitals, Chicago, Illinois; †Pharmacia Corp., Skokie, Illinois; and ‡Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina

Table 2. Patient Concerns Before Undergoing Surgery

Concern[a]	Inpatient (n = 129)	Outpatient (n = 121)	Total (n = 250)
Pain after surgery	57%	61%	59%
Whether surgery would improve condition	47%	55%	51%
Full recovery from surgery	50%	41%	46%
Pain during surgery	36%	30%	33%
Treatment by health care professionals	32%	27%	30%
Don't know/refused	19%	12%	16%

[a] Patients could choose more than one concern.

Postoperative Pain Experience: Results from a National Survey Suggest Postoperative Pain Continues to Be Undermanaged

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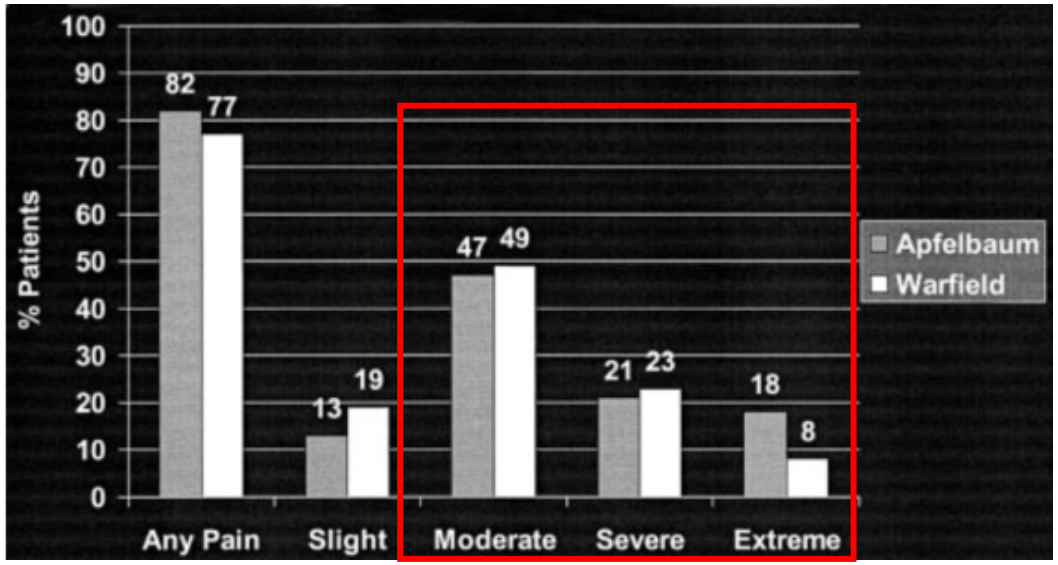

- Baseline Buprenorphine does not provide adequate surgical analgesia
  - Analgesic effect is 6-8 hours
- Pt’s still need additional periop analgesia

Education

- Assure pt that you understand that managing pain is primary goal
- Set realistic expectations
- Buprenorphine will be continued throughout the periop period
- A comprehensive multimodal tx plan will be used
- Additional pain medications may be used
  - Taper will be provided for any additional pain medications
- Coordination of care

Recommendations for Postoperative Management

Clinical Pearl: Buprenorphine home dose should not be routinely discontinued or tapered perioperatively

All surgery types (elective, urgent, emergent)

Buprenorphine Management

Mild/Moderate Pain:

- Home bupre-norphine dose can be split into two times per day/three times per day dosing to provide an analgesic effect.

Severe Pain:

- Home buprenorphine dose can be split into three times per day dosing to provide improved analgesic effect.
- Consider increasing dose of buprenorphine to 24-32 mg given in divided doses or using buprenorphine intravenous 0.3 mg every 6 hours prn
- Consider close monitoring if increasing or adding opiate for pain

Acute Pain with Other Opioids

- Maximize non-opioid strategies
- Treat acute pain with high affinity additional opioids as indicated in patients with OUD, avoid the opioid of past misuse
- Fentanyl derivatives and hydromorphone likely to be most effective due to high receptor affinity
- Consider close monitoring if increasing or adding opiate for pain

Nonopioid Pharmacological Management

- Regional anesthesia (Epidural catheter, Transversus Abdominus Plane block, peripheral nerve blocks with or without catheters including but not limited to erector spinae plane blocks, paravertebral block, femoral/adductor canal block, etc)
- Local infiltration by surgical team
- Intraoperative or postoperative ketamine/lidocaine/magnesium infusions
- Consider Dexmedetomidine if Intravenous sedation used postoperatively
- Topical agents (e.g. ice, lidocaine ointment or patches)
- NSAIDs when indicated (e.g. ketorolac, ibuprofen, etc)
- Intravenous vs. oral acetaminophen when indicated
- Antineuropathic agents when indicated or if comorbid anxiety (e.g. gabapentinoids, antidepressants such as TCAs, SNRIs, etc)
- Muscle relaxants as indicated (e.g. baclofen, tizanidine, cyclobenzaprine; avoid benzodiazepines or carisoprodol)

Non-Pharmacological Management

- Ice to surgical site
- Position change
- Relaxation strategies and mindfulness techniques for pain (e.g. guided "apps" such as the free app "Calm")
- Peer recovery support
- Distraction aligned with interests (e.g. reading, music, family and social support, etc)

Postoperative Disposition

- Post anesthesia care unit
- Discharge home if satisfactory pain control, coordinate buprenorphine dosing plan with prescriber
- Inpatient floor admission as applicable
- Consider ICU admission if uncontrolled pain and respiratory concerns

Multi-modal tx

<table>
<tr><th>Preoperative</th><th>Intraoperative</th><th>Postoperative</th></tr>
<tr><td>Provide preoperative education</td><td rowspan="4">Non-Opioid Medications
– Ketamine
– Lidocaine Infusion
– Acetaminophen
– NSAIDs
– Gabapentinoids
– Magnesium
– Dexmedetomidine
– Esmolol
– Muscle Relaxants</td><td>Clinical Opiate Withdrawal Scale monitoring and medications to treat opioid withdrawal symptoms (see Table 3)</td></tr>
<tr><td>Manage patient expectations</td><td>Acute pain service consultation</td></tr>
<tr><td>Consider preoperative pain consultation</td><td>Non-pharmacologic:
– Mindfulness Training
– Cognitive Behavioral Therapy
– Support Groups (e.g. Narcotics Anonymous)
– 12 Step Group Therapy
– Relaxation Strategies/ “Apps”
– Acupuncture</td></tr>
<tr><td rowspan="2">Coordinate care with MOUD provider or consider referral for OUD treatment</td><td rowspan="2">Local infiltration by surgical team</td><td rowspan="2">Topicals (ice, lidocaine ointment, lidocaine patches)</td></tr>
<tr><td rowspan="3">Regional Anesthesia Techniques
– Spinal Opioid Injection (Morphine/Hydromorphone)
– Epidural Catheter (Local Anesthetic +/- Opioid)
– Peripheral Nerve Block (single shot vs continuous catheter)</td></tr>
<tr><td>Involve family/support person, peer support, behavioral or counseling support as indicated</td><td>Discharge planning with MOUD provider</td></tr>
<tr><td>Optimize nutrition/hydration</td><td>Overdose Prevention Education and Nasal Naloxone Prescription (OPENP)</td></tr>
</table>

How do I Taper?

> Reg Anesth Pain Med. 2020 Jun;45(6):474-478. doi: 10.1136/rapm-2020-101324. Epub 2020 Mar 31.

Implementation of a patient-specific tapering protocol at discharge decreases total opioid dose prescribed for 6 weeks after elective primary spine surgery

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Tapering Instructions (Prescribed As-Needed)							
Prior 24-hour Oxycodone (mg)	Days 1-2	Days 3-4	Days 5-6	Days 7-8	Days 9-10	Days 11-12	Total Oxycodone 5 mg Tablets Prescribed (n)
10 mg	5 mg twice daily						4
20 mg	5 mg four times daily	5 mg twice daily					12
30 mg	5 mg six times daily	5 mg four times daily	5 mg twice daily				24
40 mg	10 mg four times daily	10 mg three times daily	5 mg four times daily	5 mg twice daily			40
50 mg	10 mg five times daily	10 mg four times daily	10 mg three times daily	5 mg four times daily	5 mg twice daily		60
60 mg	10 mg six times daily	10 mg five times daily	10 mg four times daily	10 mg three times daily	5 mg four times daily	5 mg twice daily	84

Figure 1 Discharge opioid prescribing and tapering protocol based on each patient's prior 24-hour oral opioid use.

JOURNAL ARTICLE

A Multidisciplinary Patient-Specific Opioid Prescribing and Tapering Protocol Is Associated with a Decrease in Total Opioid Dose Prescribed for Six Weeks After Total Hip Arthroplasty FREE

Mallika Tamboli, Edward R Mariano, MD, MAS, Kerianne E Gustafson, PA-C, Beverly L Briones, NP, Oluwatobi O Hunter, DNP, AG-ACNP, Rachel R Wang, MD, T Kyle Harrison, MD, Alex Kou, Seshadri C Mudumbai, MD, MS, T Edward Kim, MD ... Show more

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Summary

- Perioperative pain management can be achieved in pt's on Buprenorphine for analgesia or OUD
- Continuation of Buprenorphine is recommended
- Use of Muli-modal analgesia is encouraged
- If additional opioids or increase in buprenorphine occurred, provide taper back to preoperative dose
- Pt education is important

Questions or Comments?