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MACS Webinar

Challenging Case Presentations and Discussion on the Use of Buprenorphine for Pain

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MACS Pain Management Consultant
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Maryland Addiction Consultation Service (MACS)

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Acknowledgement

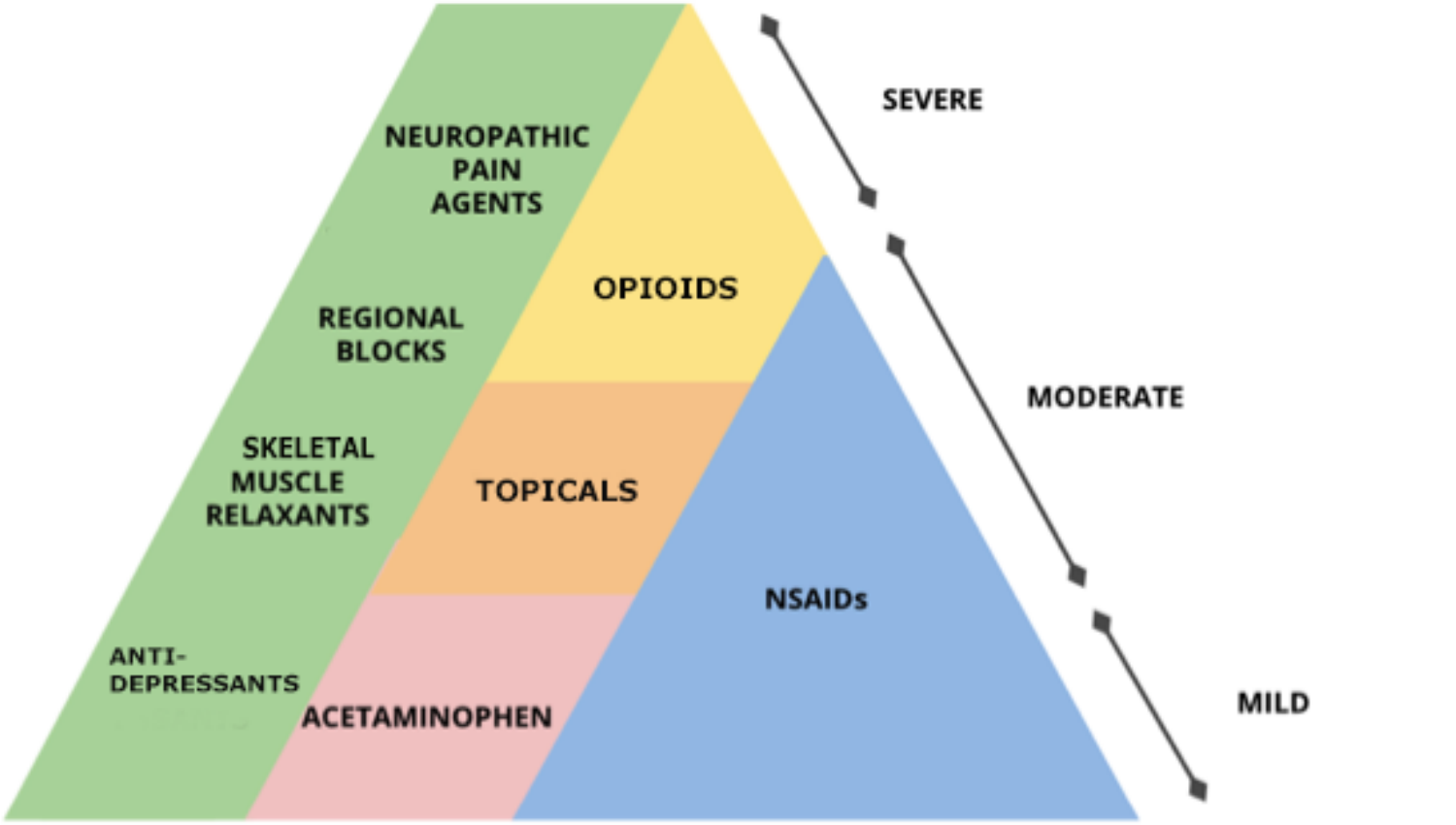
- To my patients, who have all taught me so much about doctoring, and about the experience of pain.

Objectives

- Learners will review example of patients on short acting medication being opioid dependent
- Learners will review that having addiction to one substance is commonly associated with addiction to another
- Learners will gain familiarity with use of buprenorphine for pain and clinical pearls for weaning from conventional opioids

Sir William Osler: “Listen to the patient. He is telling you the diagnosis.”

Pain Medication Treatment Framework



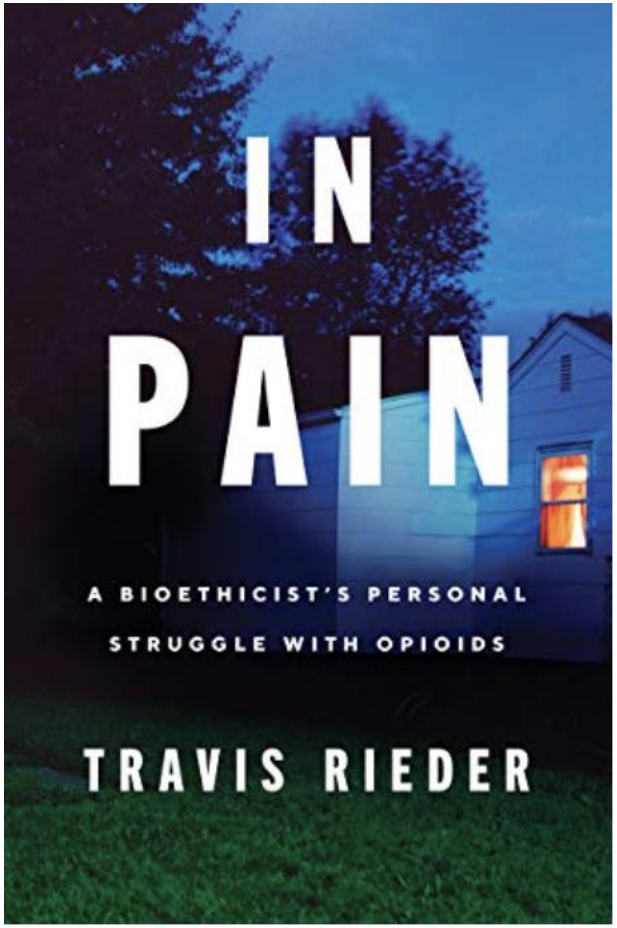
https://canadiem.org/approach-to-pain-management-in-the-ed/

Case 1 - Vivitrol:

- 40 yoM presented to the ER with shaking, pain, all over chills with onset same day after first shot of Vivitrol. Reported he had developed alcohol problems with loss of control. Sought couseling and treatment.
- Medication list included oxycodone 5/325 mg QID for pain. Patient reported taking it as prescribed without signs of misuse.
- Went to the ER for care and discharged after comfort treatment.

Case 1 Discussion

- Patient taking opioid for pain (even tramadol, oxycodone) may be dependent on the opioid
- Were you taught that opioid withdrawal lasts 72 hours?
  - For some medications symptoms will peak at 72h
- "Opioid withdrawal won't kill you, but it may make you want to die"
- Example: "In Pain" book



Case 2 - Medication overuse:

- 52-year-old female with history of back injury in high school and episodic low back pain since that time. Worsening low back pain. Presented for consult for pain management May 2020 after hospitalization with GI bleed (Hb 5.6) due to ibuprofen overuse.
- She had prior history of treatment with lumbar facet injection pain management several years ago with partial improvement.
- Chief complaint low back pain radiating into bilateral legs. Intermittent neck pain radiating to the arms.

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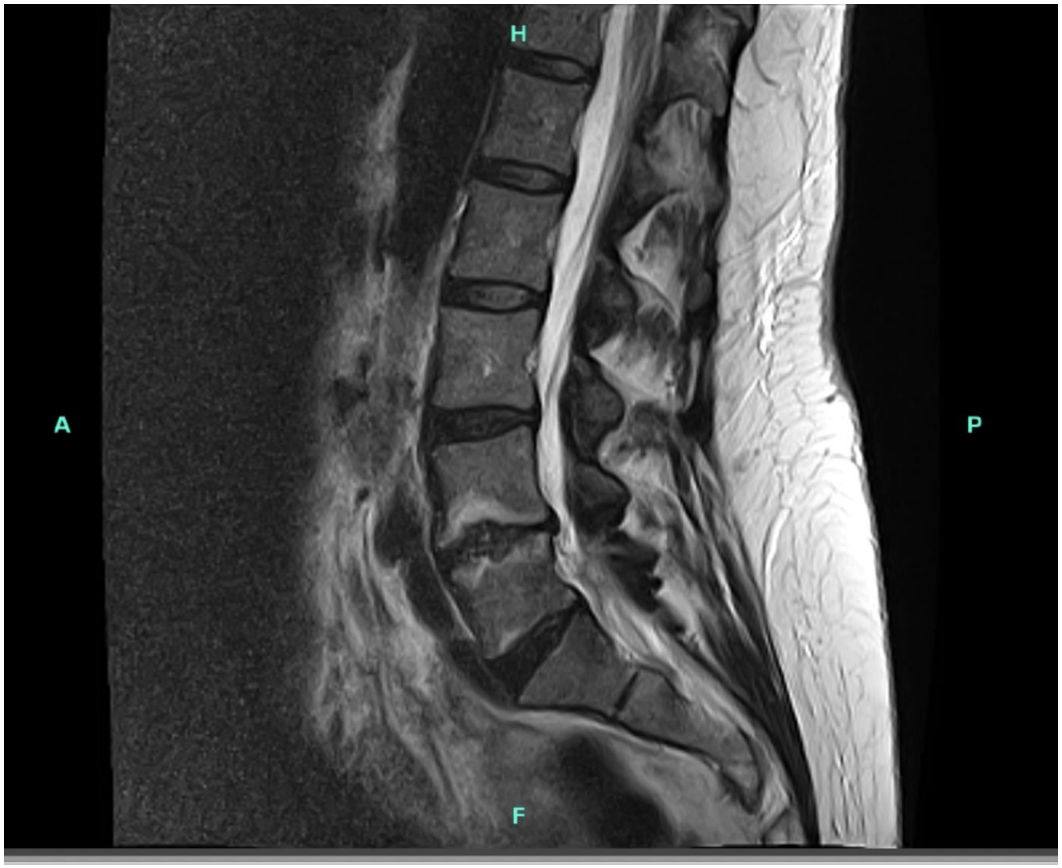
Case 2 - Lumbar MRI

L4-5: Mild progressive discogenic endplate changes as above. Mildly progressive mild-to-moderate facet arthrosis, right greater than left, and ligamentous hypertrophy. Shallow broad-based disk bulge. No central spinal canal stenosis. Mildly progressive right lateral recess narrowing with transiting nerve root abutment. Progressive mild-to-moderate bilateral neural foraminal narrowing without exiting nerve root abutment.
L5-S1: Mild progressive disk desiccation. Unchanged mild disk space narrowing. Mild to moderate right and severe left facet arthrosis similar to the prior examination. Shallow broad-based disk bulge. No spinal canal stenosis. Severe bilateral neural foraminal narrowing, left slightly greater than right, with bilateral exiting nerve root abutment and likely impingement similar to the prior examination.



Case 2 Continued:

- August 2020 she checked herself into alcohol rehab because she was finding she was drinking nightly to treat her pain. She said it was eye-opening to see folks with much worse problems. She was not even drinking daily but at the same time did not feel in control of it so she sought help. She did not take any pain medication while hospitalized at the rehab center but "I was dying" in pain
- Has a counselor and psych NP
- Most recent visit continuing PT with partial improvement. Planning for epidural injection. Planning spine surgery consult

Case 2 discussion:

- Don’t dismiss the patient - ”Just because the patient has mental illness doesn’t mean there is nothing wrong with them”
- Having one substance use problem is associated with increased risk for others – smoking, obesity, alcohol overuse, opioid use
- Substance misuse as a brain disease

Case 3 – Opioid naïve patient started on buprenorphine

- 42 yo patient with EDS/Joint hypermobility. She has had multiple spine surgeries.
- H/o anxiety. h/o childhood sexual trauma.
- Multifactorial chronic pain
- Wants to discuss analgesic options for pain but has failed many non-opioid treatments
- Is in counselling, sees primary care recently
- Discussed trial of 75 mcg buprenorphine buccal patch BID

Buprenorphine is an Analgesic

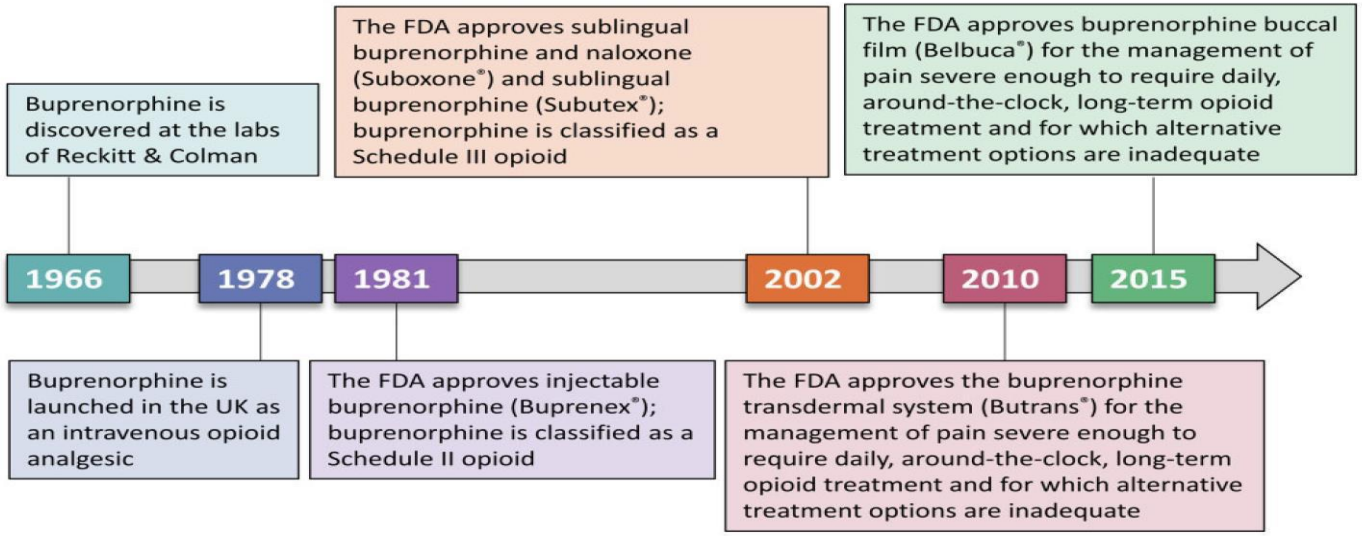
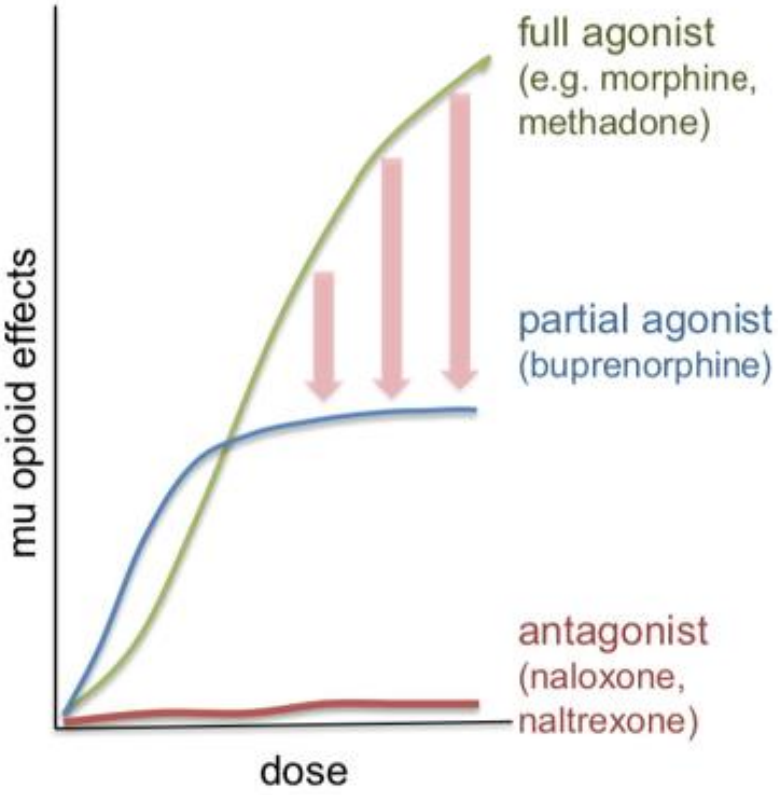
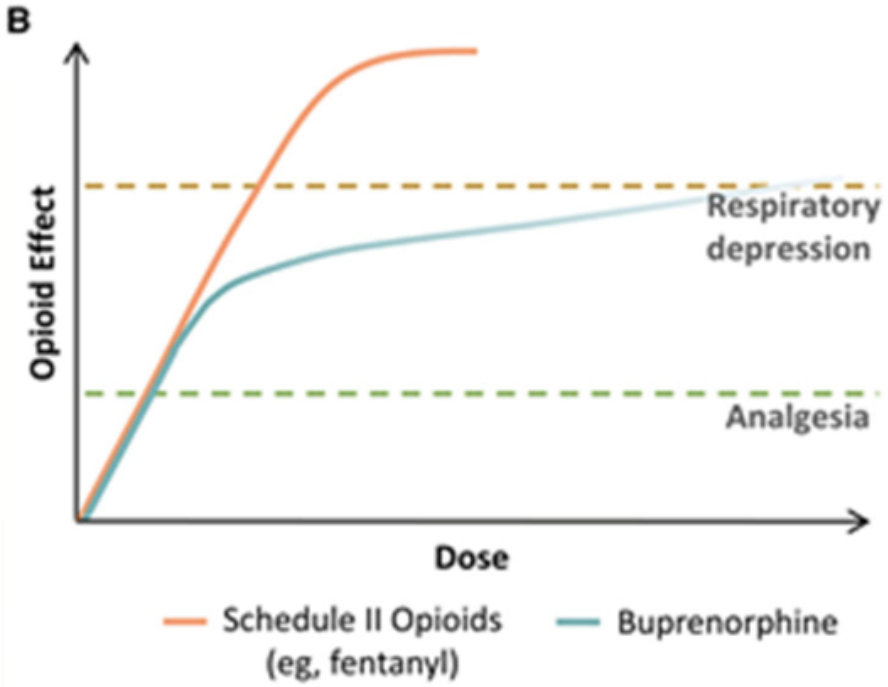


Figure 1. The history of buprenorphine. Buprenorphine was originally developed as an analgesic and was subsequently used for OUD before novel delivery systems allowed for approval in chronic pain management [8,9,12,13]. FDA=Food and Drug Administration; OUD=opioid use disorder.

Webster et al., Understanding Buprenorphine for Use in Chronic Pain: Expert Opinion. Pain Medicine, 0(0), 2020, 1–10 doi: 10.1093/pm/pnz356. Open access article

Mechanism of Buprenorphine vs other opioids





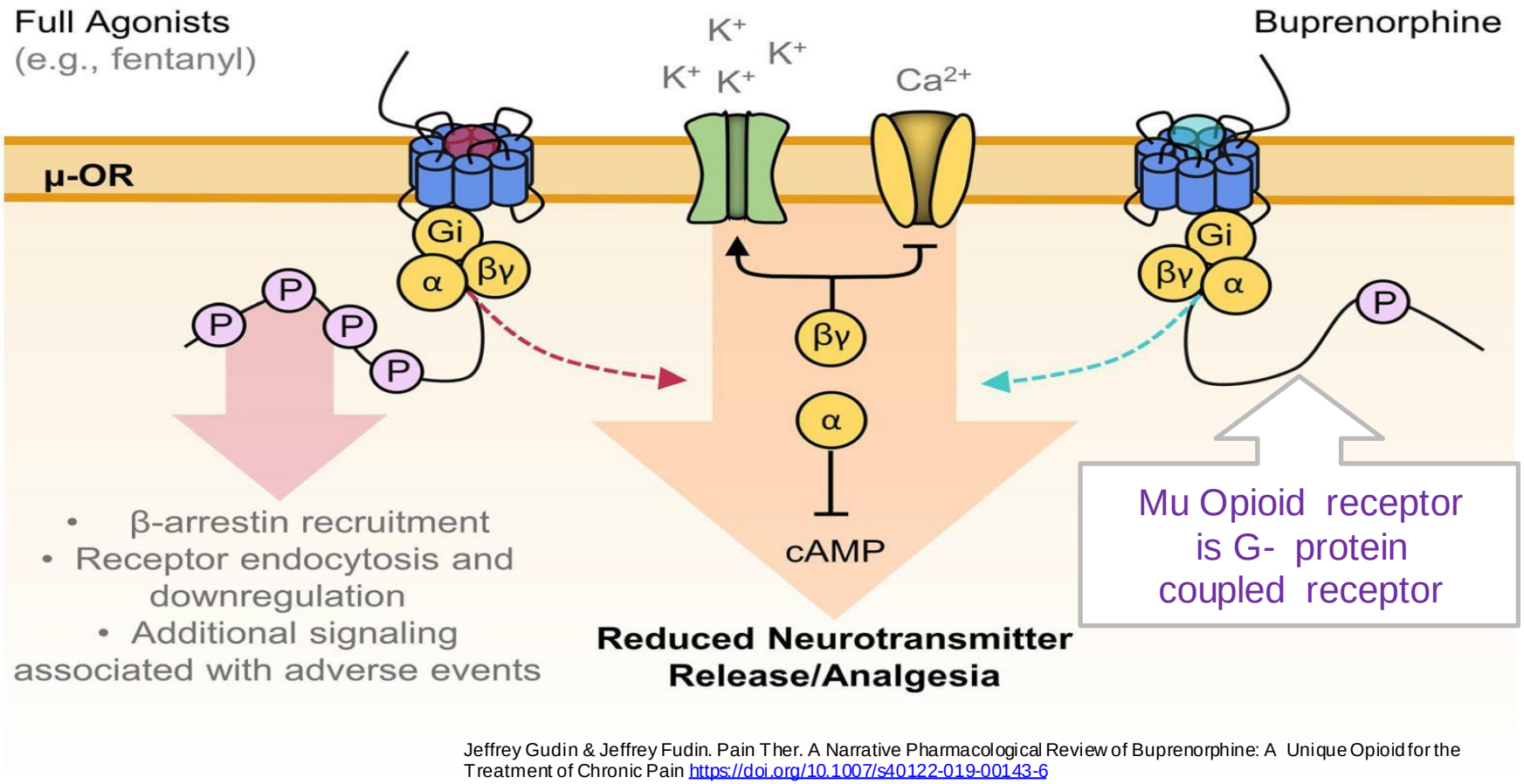
Case 3 Discussion

- Continues in counselling, sees primary care recently
- Started 75 mcg buprenorphine buccal patch BID with excellent pain relief and functional improvement. Able to run errands independently, cook for self which she was previously not able to do.

Case 4 – Rotation from C2 opioid to buprenorphine

- 77 year old male, history of Crohn's disease
- Currently prescribed Oxycontin 10mg 2x/day (for about 7 years) and Oxycodone 2.5mg at 6pm (22.5 mg oxycodone or about 34 MME)
- The pt is having a hard time getting his medication, sometimes the pharmacy does not have it, etc
- The pt wants to transition from these medications to buprenorphine. He reports a family member transitioned from pain medications to Suboxone and is doing well. The pt has never been on buprenorphine in the past.

1) Mechanism of Buprenorphine vs other opioids



Jeffrey Gudin & Jeffrey Fudin. Pain Ther. A Narrative Pharmacological Review of Buprenorphine: A Unique Opioid for the Treatment of Chronic Pain https://doi.org/10.1007/s40122-019-00143-6

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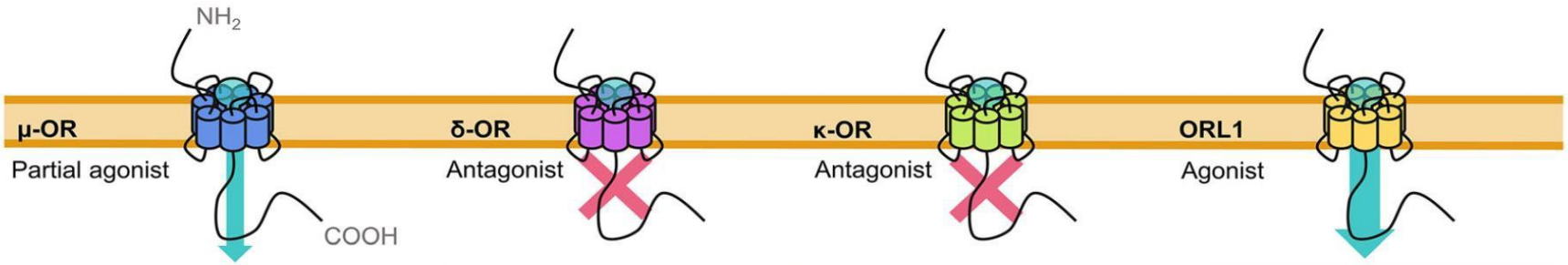
Buprenorphine works on Four Receptors



- Potent analgesia
- Ceiling on respiratory depression and euphoria
- Limited impact on GI motility
- Limited physical dependence, abuse potential, and withdrawal symptoms
- Reduced immunosuppression and impact on the HPA axis
- Reduction in suicidal thoughts, anxiety, and depression
- Limited dysphoria

- Anti-opioid effects
- Myocardial protection
- Limited impact on GI motility*
- Limited respiratory depression*

- Reduced depression, dysphoria, suicidal tendencies, anxiety, and hostility
- Limited potential for addiction* and tolerance
- Reduced immunosuppression

- Enhanced spinal analgesia
- Reduced supraspinal analgesia
- Diminished opioid-rewarding effects
- Limited potential for tolerance

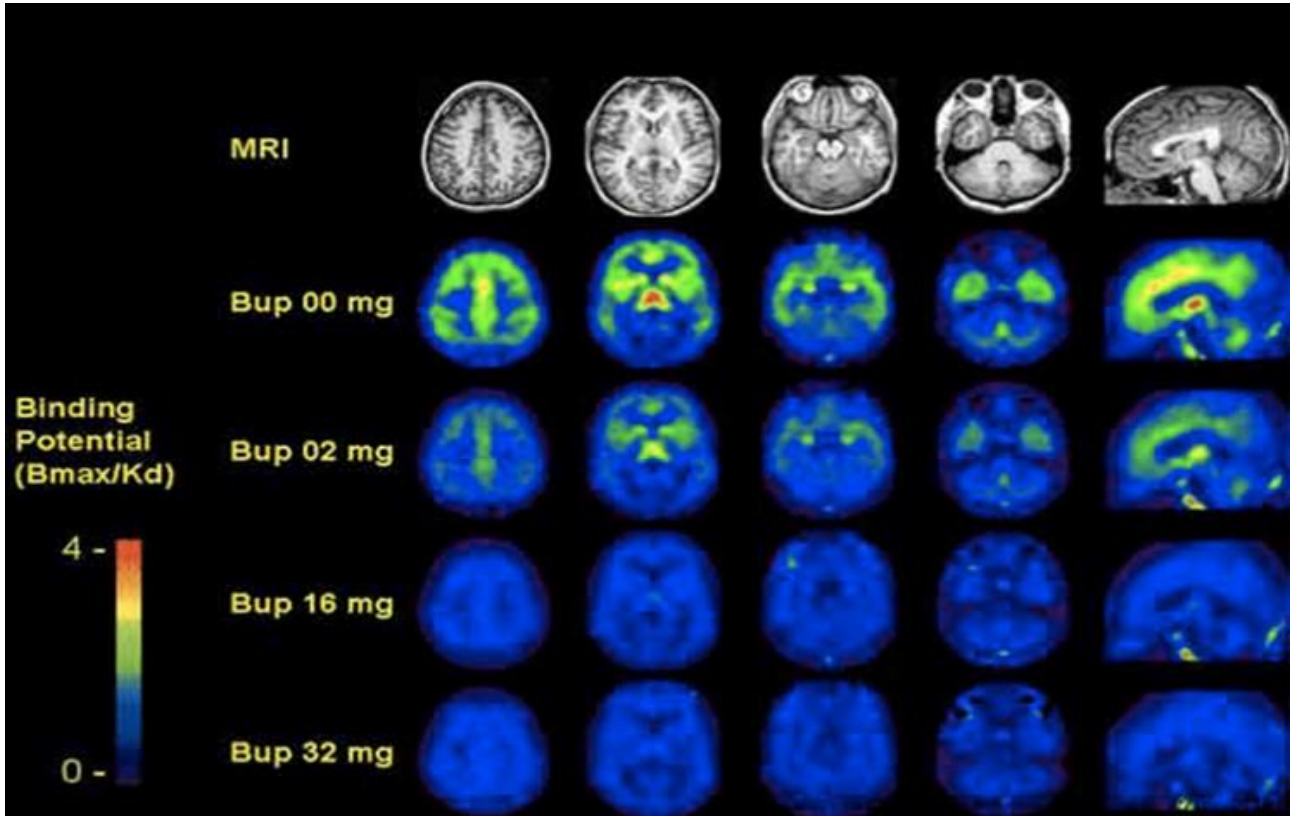
Jeffrey Gudin & Jeffrey Fudin. Pain Ther. A Narrative Pharmacological Review of Buprenorphine: A Unique Opioid for the Treatment of Chronic Pain https://doi.org/10.1007/s40122-019-00143-6

Requirements to write buprenorphine for pain vs writing buprenorphine for opioid use disorder

There are at least 3 ways to write it

- On label for OUD
  - Must use X number for OUD
- On label for pain
  - There are just 2 currently
    - Buprenorphine transdermal (Butrans 5-20 mcg/hr patch in US, higher in Europe)
    - Belbuca buccal film 75-900 mcg BID recommended dose
- Off label pain prescribing: Writing Buprenorphine FDA approved for OUD
  - generic buprenorphine tab
  - generic buprenorphine-naloxone tab or film
  - branded formulations

Buprenorphine Receptor Binding



Greenwald, M.K. et al. Effects of Buprenorphine Maintenance Dose on μ- opioid receptor availability. Neruopharmacology (2003) 28, 2000-2009

Characteristics of buprenorphine vs other opioids

- Mu-opioid receptor **partial** agonist with high affinity, long duration of action
  - High affinity means it will displace other opioids (and may precipitate withdrawal in the opioid tolerant on full agonist)
  - Decreased risk of respiratory depression
  - Ceiling effect (80% of receptors bound at 8-12mg dose; 95% receptors bound at 24mg dose)
- Kappa-opioid receptor antagonist
- Beta-arrestin and G-protein balance
- 24-60 hours half life for sublingual or buccal formulations
- Naloxone = very poor oral, sublingual, and buccal bioavailability; absorbed as injection or intranasally

Case 4 Discussion

- Considered multiple options:
  - Buprenorphine buccal or transdermal patch (Belbuca or Butrans) is one option - **on label** for pain
  - Generic buprenorphine tablet **off label** for chronic pain.
    - In that case the prescriber is not obligated to use their X number.
      - The pharmacy may still ask for it.
      - But it's not strictly required if Rx not for OUD
      - I tend to use X number due to adequate numbers on waiver and to avoid phone calls from the pharmacy.
      - Recommended 2 mg BID to TID, titrating to 8 mg 0.5 BID if needed
- For diagnosis to prescribe under in EMR, I tend to use the F11.20 which is opioid dependence and in our system doesn't specify OUD or not.
- Other considerations:
  - Would you be comfortable to rotate the person back on to oxycodone if after 2-4 weeks the patient does not think their clinical status is improved?

Case 4 Discussion

- Transitioned to buprenorphine 8-2 mg film 0.5 BID and increased to 0.5 TID (12 mg buprenorphine per day), remained at a stable dose one year later.

Case 5 – Risks of COT outweigh benefits

- 45 yo male with normal BMI, chronic low back pain. H/o MI at a young age.
- Running out of medication, requesting early refills
- No UDS positive for nonprescribed substances
- Works full time, coaches son's soccer team
- Workup negative for rheumatologic disease or inflammatory issues.

When Might Risks of Opioids Outweigh Benefits?

Consider if:

- Pain remains significant
- Suspect Opioid-induced Hyperalgesia
- PEG scores >5 consistently (or >15/30)
- Low functioning
  - sedentary, pain prevents activity
- Persistent Mood symptoms, PHQ9/GAD>9
- Presence drugs/conditions that increase risk overdose
  - benzodiazepines, sedatives/alcohol, chronic lung disease, sleep apnea, obesity, prior overdose, kidney/liver disease, advanced age
- Social withdrawal/isolation
  - family member's history useful
- Central/Visceral Pain syndrome that opioids may worsen
  - Fibromyalgia, headaches, some neuropathies
  - IBS, abdominal/pelvic pain

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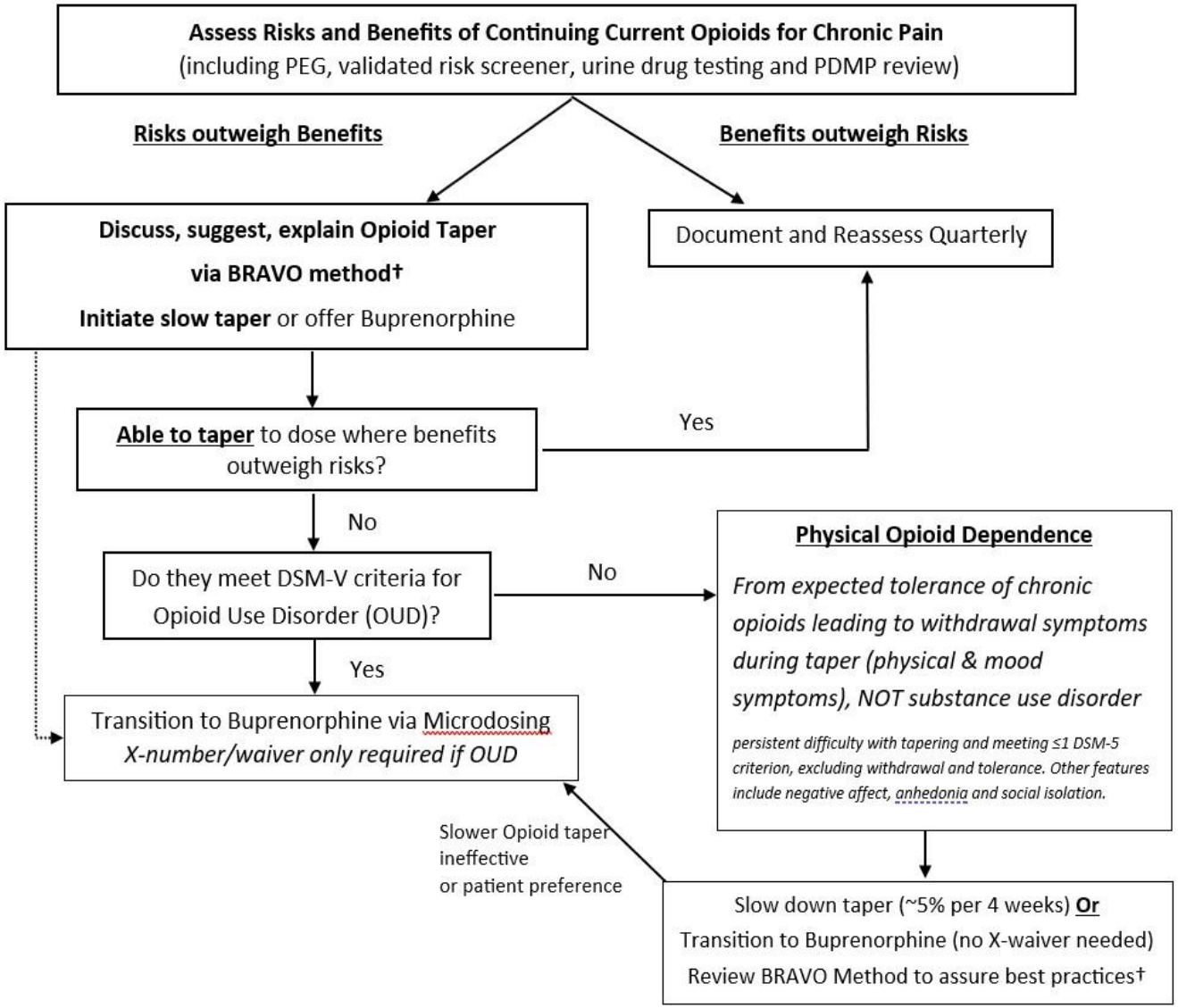

Assess Risks and Benefits of Continuing Current Opioids for Chronic Pain
(including PEG, validated risk screener, urine drug testing and PDMP review)
Risks outweigh Benefits
Benefits outweigh Risks
Discuss, suggest, explain Opioid Taper
via BRAVO method†
Initiate slow taper or offer Buprenorphine
Document and Reassess Quarterly
Able to taper to dose where benefits outweigh risks?
Yes
No
Do they meet DSM-V criteria for Opioid Use Disorder (OUD)?
No
Yes
Physical Opioid Dependence
From expected tolerance of chronic opioids leading to withdrawal symptoms during taper (physical & mood symptoms), NOT substance use disorder
persistent difficulty with tapering and meeting ≤1 DSM-5 criterion, excluding withdrawal and tolerance. Other features include negative affect, anhedonia and social isolation.
Transition to Buprenorphine via Microdosing
X-number/waiver only required if OUD
Slower Opioid taper
ineffective
or patient preference
Slow down taper (~5% per 4 weeks) Or
Transition to Buprenorphine (no X-waiver needed)
Review BRAVO Method to assure best practices†

BRAVO: How to Taper Patients Off Chronic Opioid Therapy

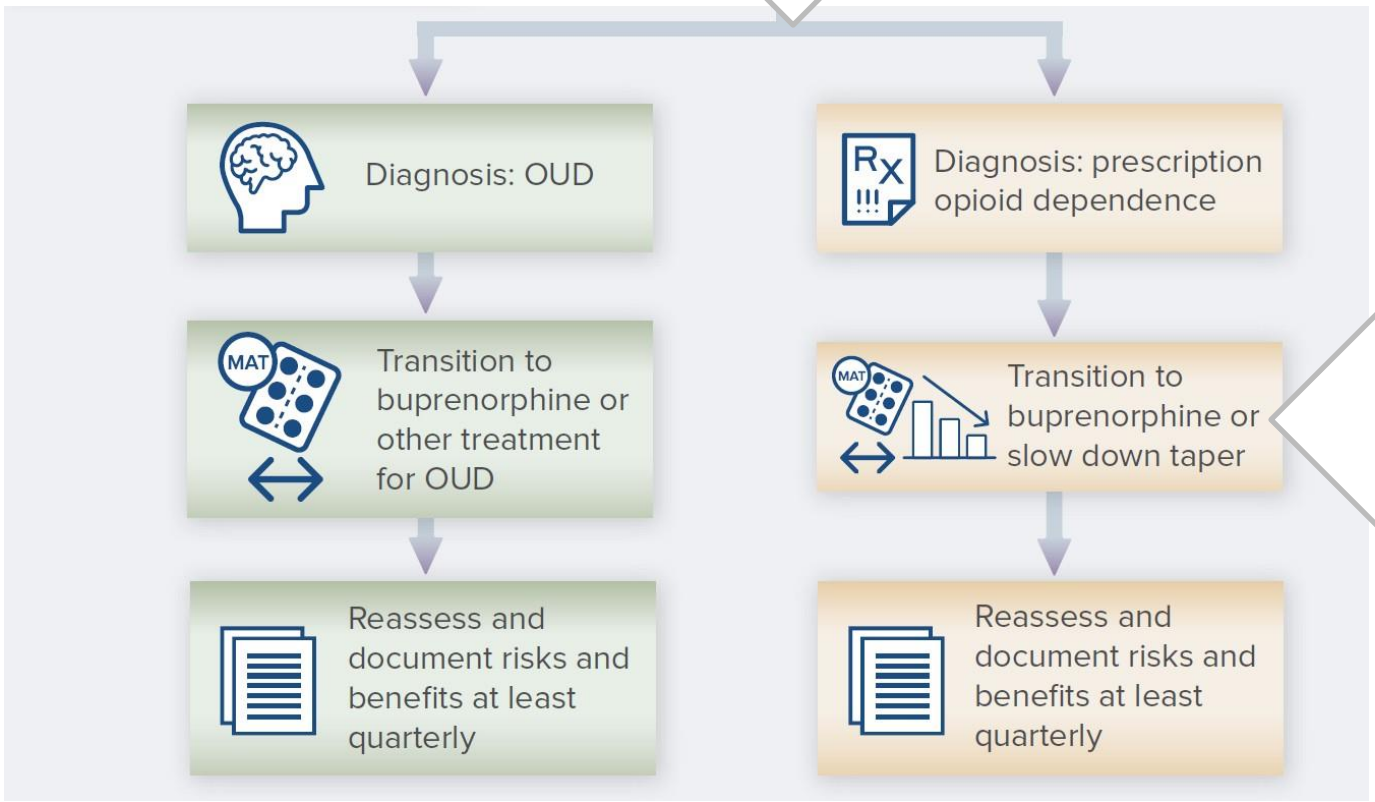
- Broach the subject with empathy
  - acknowledge anxiety and be clear that tapering is not punitive
- Risk–benefit assessment
  - address effects on pain and function, risk for overdose/addiction/adverse events
- Addiction assessment
  - normalize addiction and initiate appropriate management if OUD emerges
- Velocity and Validate
  - do not taper too quickly, slow down if needed, and validate the pain of withdrawal
- Other strategies for coping with pain
  - implement nonopioid alternatives for pain treatment

Highly Recommended

Dr Anna Lembke
Stanford Addiction Psychiatry

Stanford Center for Continuing Medical Education: https://stanford.cloud-cme.com/default.aspx?P=0&EID=20909

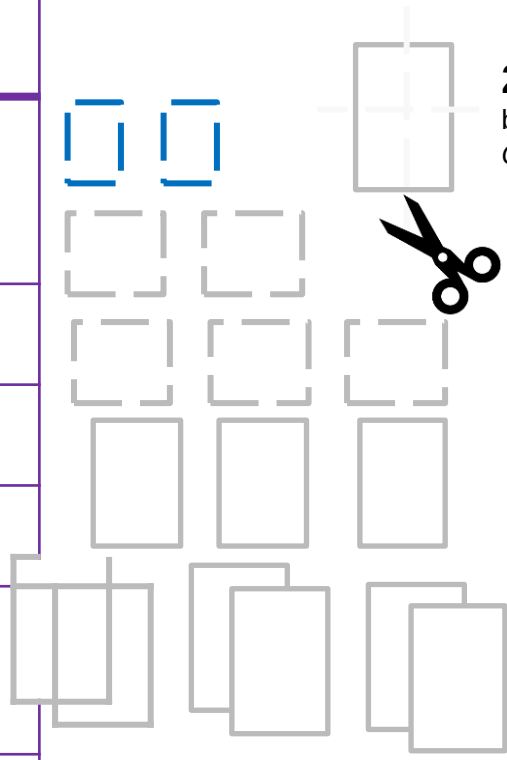
If NOT able to Taper, Assess for OUD



https://www.oregonpainguidance.org/

Bernese Style Microdosing

Day	Continue Opioids?	Bupe Dose	2mg bup films
1	Yes	0.5mg BID	¼ BID
2	Yes	1mg BID	½ BID
3	Yes	1mg TID	½ TID
4	Yes	2mg TID	1 TID
5	**No! Stop them**	4mg TID	2 TID
6	no	(adjust)	



2/0.5mg
bup/nal film
Cut into 1/4

0.5mg bup = (1/4 film)

Hämmig, R. et.al 2016. Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method. Substance abuse and rehabilitation, 7, p.99

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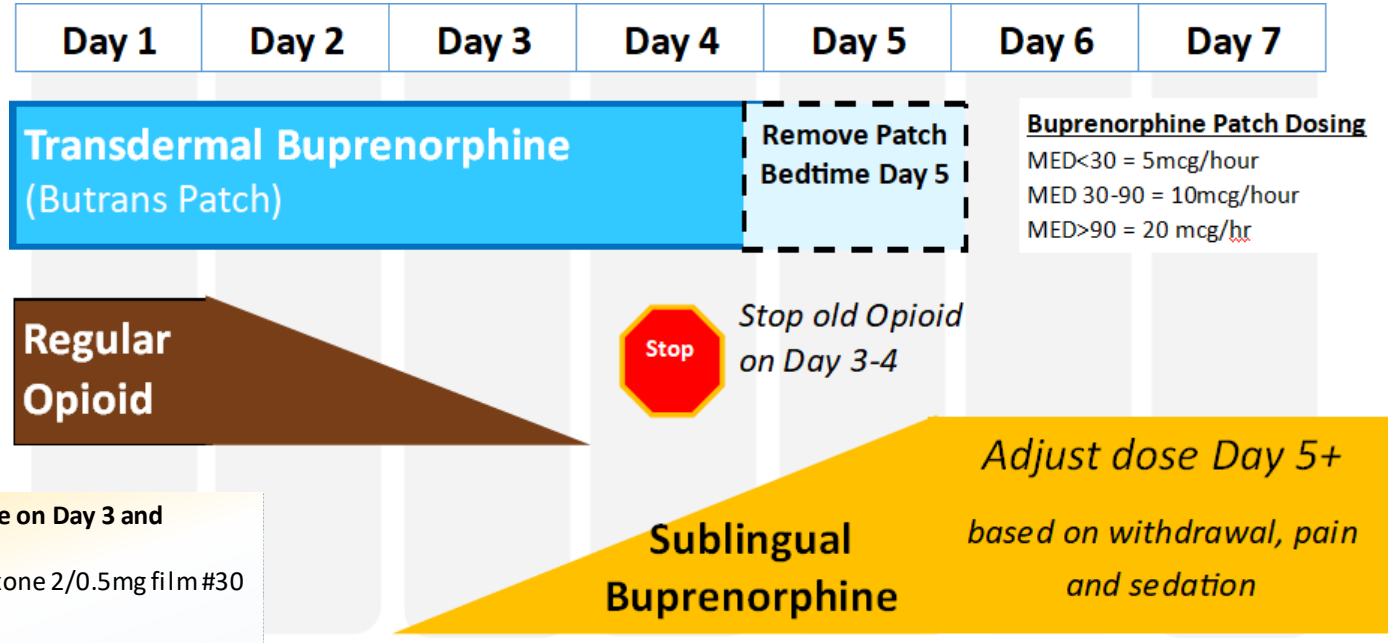
Patch to Sublingual Buprenorphine Details

from opioids like oxycodone, hydrocodone, morphine

Apply Butrans Patch.
Remove bedtime on 5th day

Taper Opioid as tolerated
- Use clonidine as needed
- Reduce by ~50% Day 2
- Stop on Day 3 or 4



Start Sublingual Buprenorphine on Day 3 and gradually increase.
Prescribe buprenorphine/naloxone 2/0.5mg film #30

Adapted from

- Amer Raheemullah, MD; Anna Lembke, MD, JAMA internal medicine. January 2019. Initiating Opioid Agonist Treatment for Opioid Use Disorder in the Inpatient Setting A Teachable Moment
- Saal D, Lee F. Rapid induction therapy for opioid use disorder using buprenorphine transdermal patch: A case series. Perm J 2020;24:19.124. DOI: https://doi.org/10.7812/TPP/19.124
- Webster et al., Understanding Buprenorphine for use in Chronic pain: Expert Opinion. Pain Medicine, 0(0), 2020, 1–10 doi: 10.1093/pm/pnz356

Conversion from full agonist opioid to buprenrophine

≤90 MME	Fentanyl transdermal: ≤25 µg/h Oxycodone: ≤60 mg/d Hydrocodone or morphine: ≤90 mg/d Hydromorphone: ≤16 mg/d Oxymorphone: ≤45 mg/d Tapentadol: Any dose

Either ON label

- Day 1: 4-12h after discontinuation of full mu agonist start:
  - Either 10 ug/h TD Patch or 150ug buccal buprenorphine bid
  - Titrate buprenorphine as needed for pain
- May consider starting adrenergic a2 agonist (clonidine, lofexidine) to reduce risk of withdrawal

Or OFF label

- Day 1: 4-12 hours after last opioid
  - 2-4/0.5-1mg SL, increase every 1-2 hours as needed up to 8/2mg SL
- Days 2-7
- Increase by 2/0.5mg SL every 1-2 hours as needed up to 8 or even 16/4mg per 24 hours
- May consider starting adrenergic a2 agonist (clonidine, lofexidine) to reduce risk of withdrawal

Webster L. et al. Pain Medicine 2020

Conversion from full agonist opioid to buprenrophine

≥90 MME	Fentanyl transdermal: >25 µg/h Oxycodone: >60 mg/d Hydrocodone or morphine: >90 mg/d Hydromorphone: >16 mg/d Oxymorphone: >45 mg/d

Either ON label

- Day 1: 4-12h after discontinuation of full mu agonist start:
  - Either 20 ug/h TD Patch or 300ug buccal buprenorphine bid
  - Titrate buprenorphine as needed for pain
- May consider starting adrenergic a2 agonist (clonidine, lofexidine) to reduce risk of withdrawal

Or OFF label

- Day 1: 4-12 hours after last opioid
  - 2-4/0.5-1mg SL, increase every 1-2 hours as needed up to 8/2mg SL
- Days 2-7
- Increase by 2/0.5mg SL every 1-2 hours as needed up to 16/4mg per 24 hours
- May consider starting adrenergic a2 agonist (clonidine, lofexidine) to reduce risk of withdrawal

Webster L. et al. Pain Medicine 2020

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Prescribers of Sublingual Buprenorphine for Chronic Pain*

	No.(%)/M (SD)
• Buprenorphine Prescriber Characteristics	
• Possess DEA X-waiver (n=44)	27(61.4%)
• Buprenorphine prescribers by formulation (n=44)	
• Buprenorphine/naloxone	23(52.3%)
• Buprenorphine without naloxone	2(4.5%)
• Both	19(43.2%)
• Buprenorphine doseage	
• Typical starting dose (n=44)	
• ≤ 4 mg	24(54.5%)
• 8 mg	12(27.3%)
• 12 mg	1(2.3%)
• 16 mg	6(13.6%)
• 24 mg	1(2.3%)
• Average dose (n=43)	
• ≤ 4 mg	1(2.3%)
• 8 mg	13(30.2%)
• 12 mg	8(18.6%)
• 16 mg	15(34.9%)
• 24 mg	5(11.6%)
• 32 mg	1(2.3%)
• Buprenorphine management challenges (n=40)	
• Switching to	26(65%)
• Switching from	9(22.5%)
• Titrating	5(12.5%)

K Rosen et al "Sublingual buprenorphine for Chronic Pain." Clinical Journal of Pain 2014

QUESTIONS?

TYPE QUESTIONS INTO THE CHAT OR RAISE HAND

Additional questions:

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