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MACS Webinar

Prescribing Buprenorphine for Chronic Pain

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Maryland Addiction Consultation Service (MACS)

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Objectives

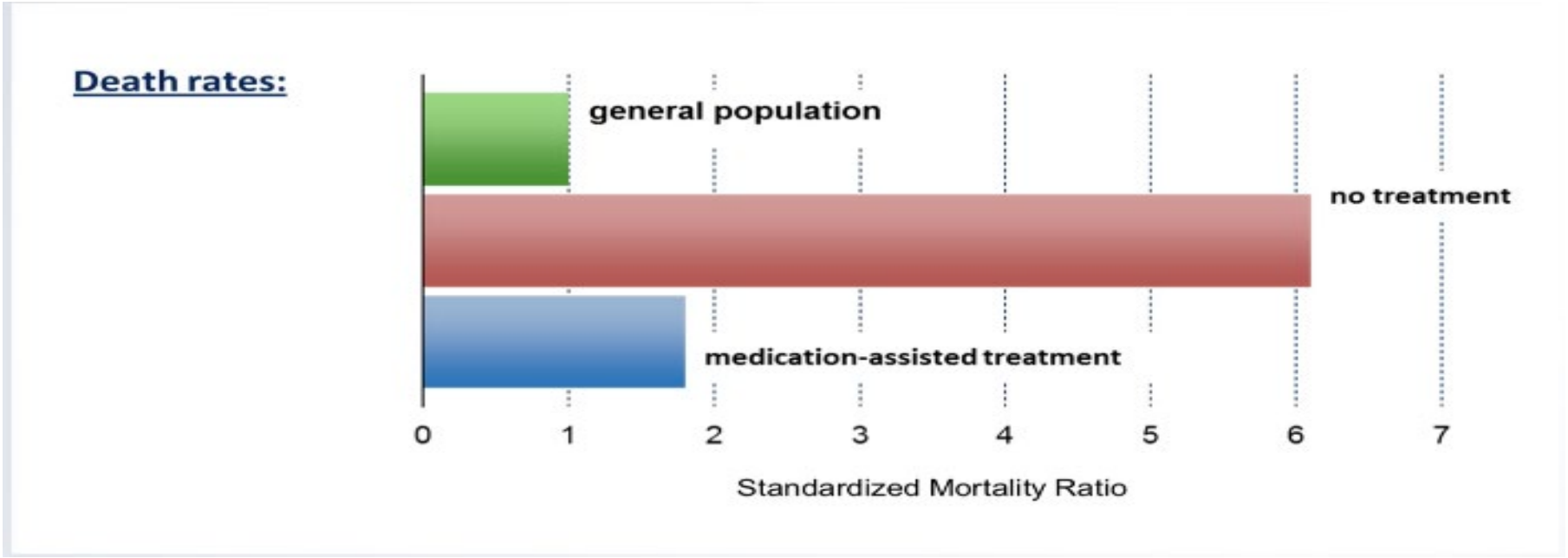
Learners should come to describe:

- The mechanism of action of buprenorphine as distinct form other opioids and how that may help its efficacy for pain
- The clearance of buprenorphine and preference for spinal opioid receptors as factors in its safety profile
- The requirements to write buprenorphine for pain vs writing buprenorphine for opioid use disorder

Buprenorphine is a good option for chronic pain

- But if your patient has OUD, you need to get them treated for OUD

Benefits of MAT



Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017

Buprenorphine is a good option for chronic pain

- But if your patient has OUD, you need to get them treated for OUD

- This talk is “prescribing buprenorphine for chronic pain”
  - NOT “Writing Buprenorphine for Chronic pain when you really think the patient has OUD”

Buprenorphine is an Analgesic

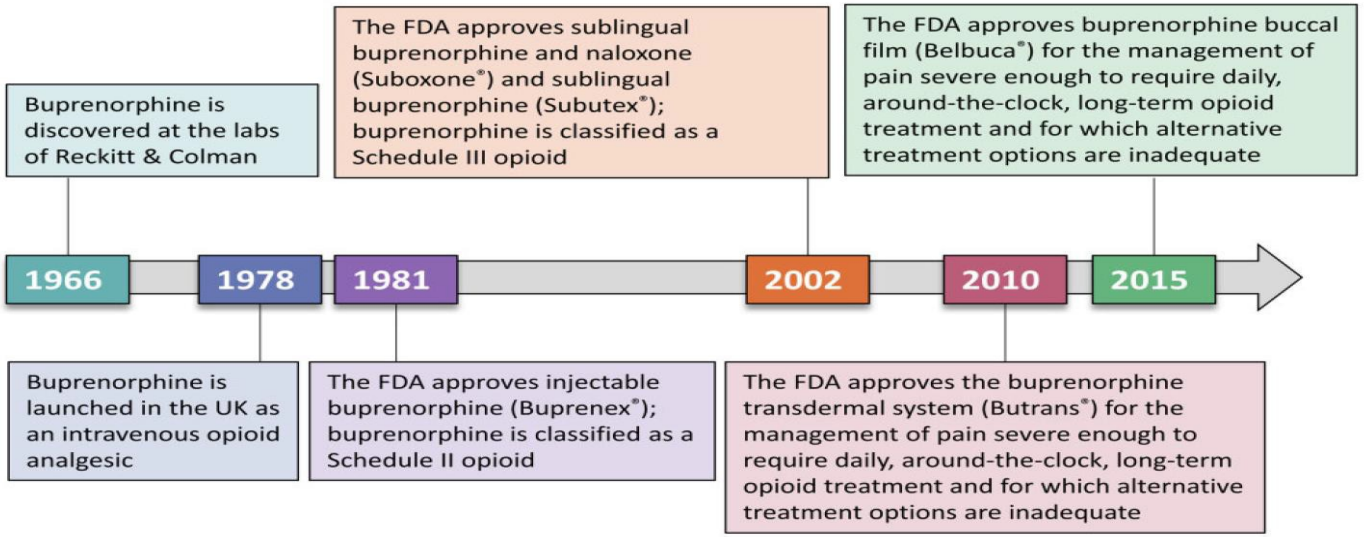


Figure 1. The history of buprenorphine. Buprenorphine was originally developed as an analgesic and was subsequently used for OUD before novel delivery systems allowed for approval in chronic pain management [8,9,12,13]. FDA=Food and Drug Administration; OUD=opioid use disorder.

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

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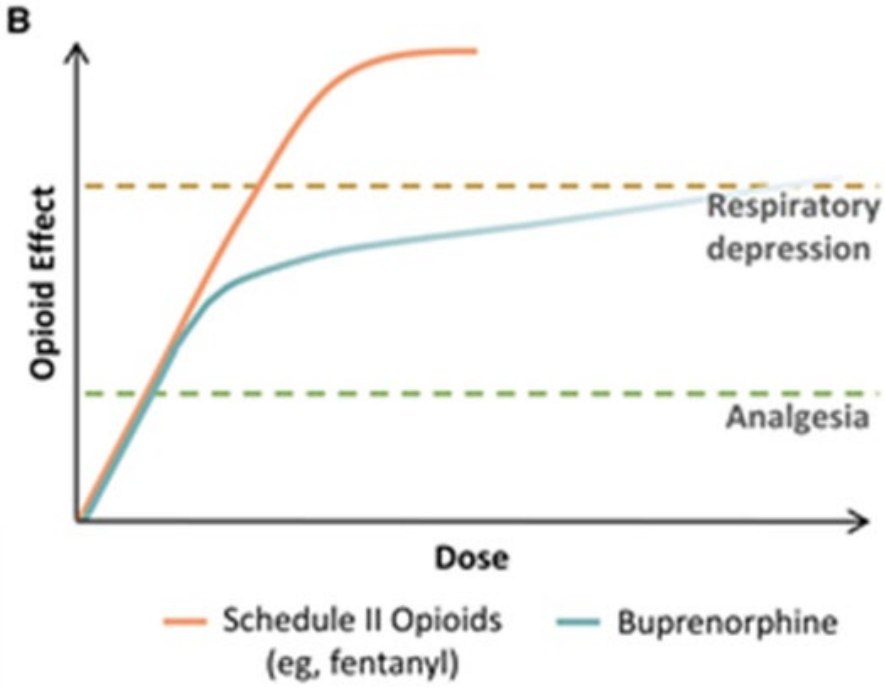
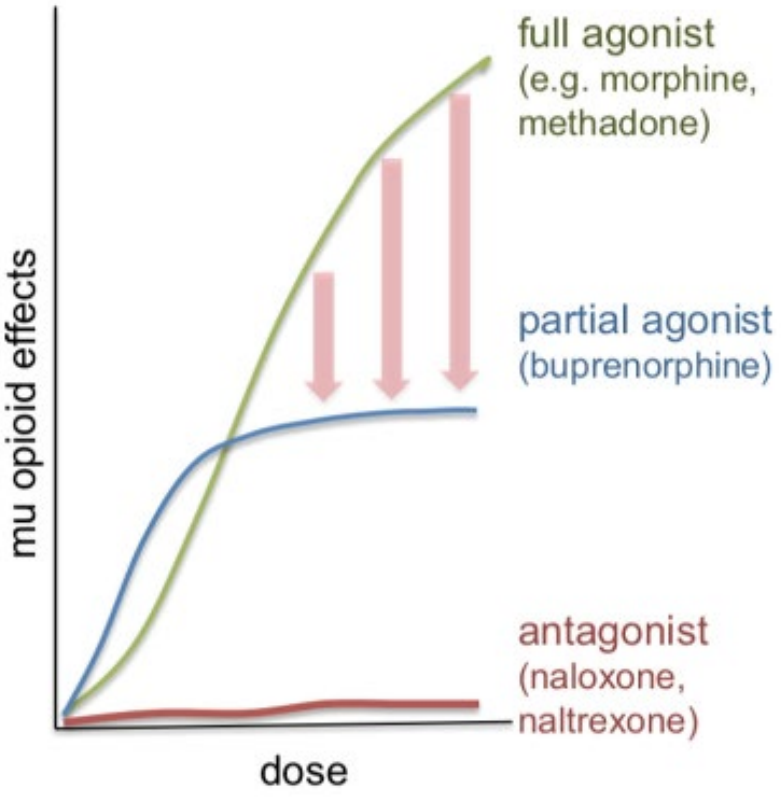
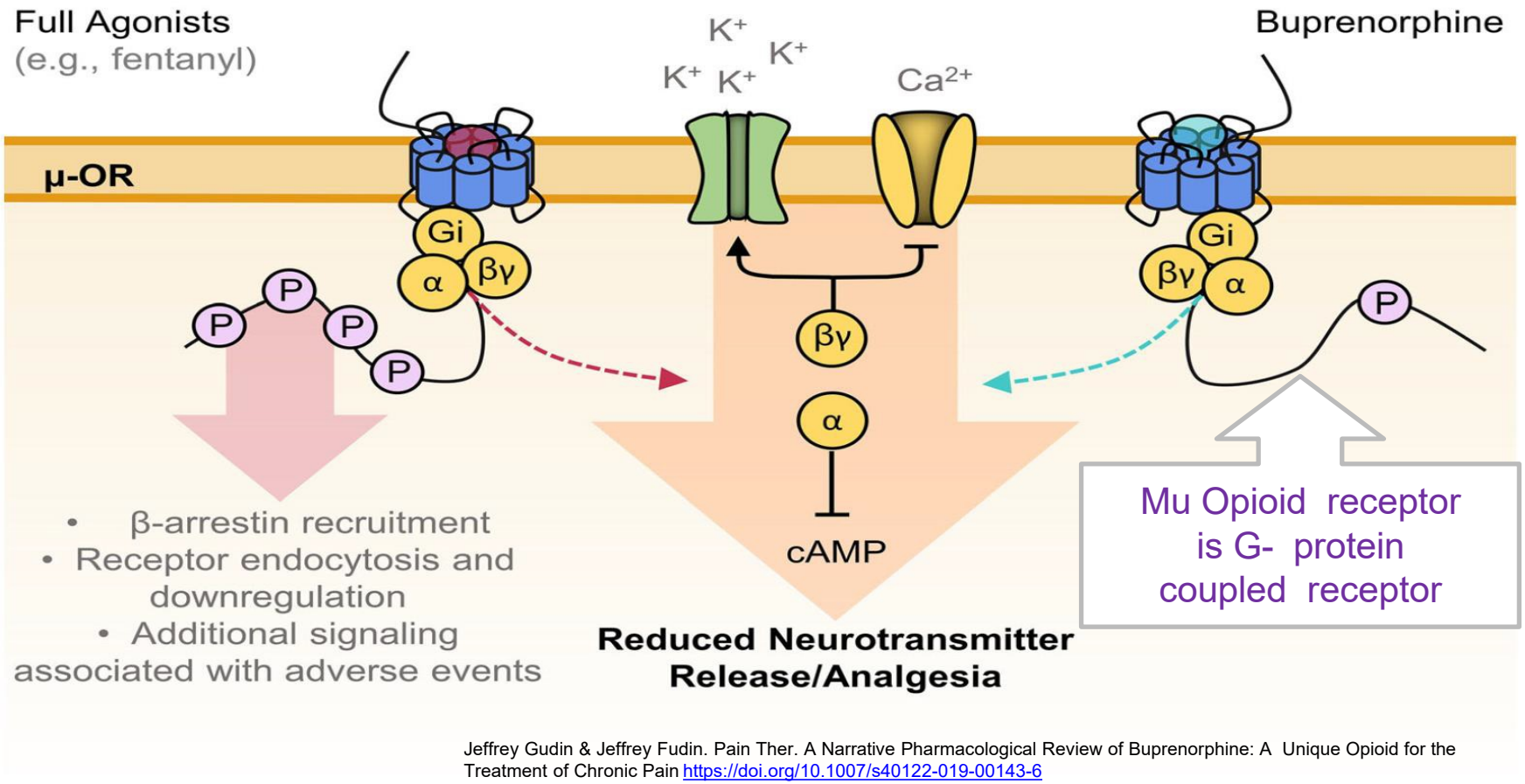
1) Mechanism of Buprenorphine vs other opioids





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

Mechanism 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

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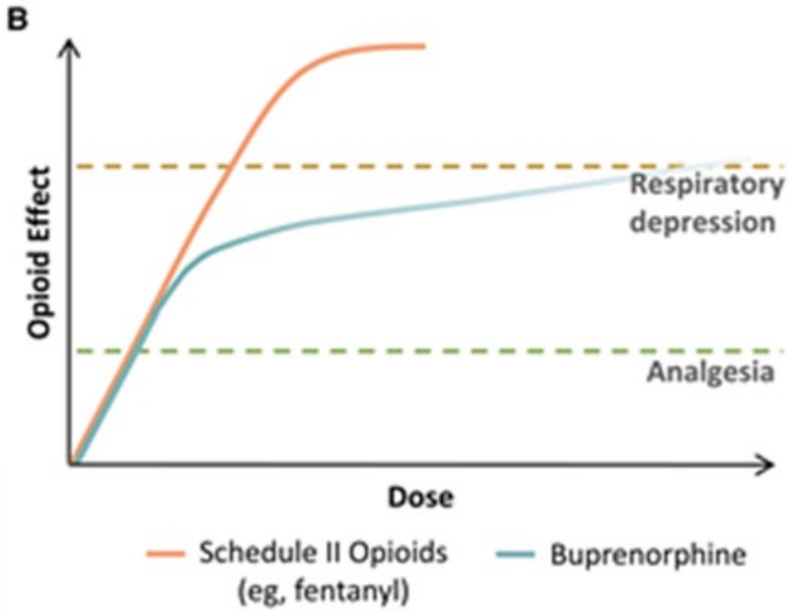
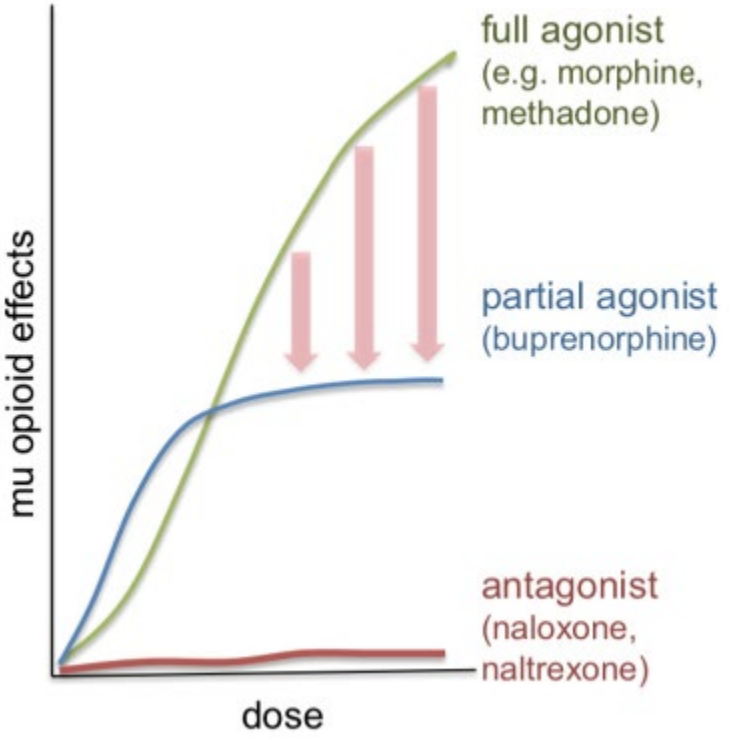
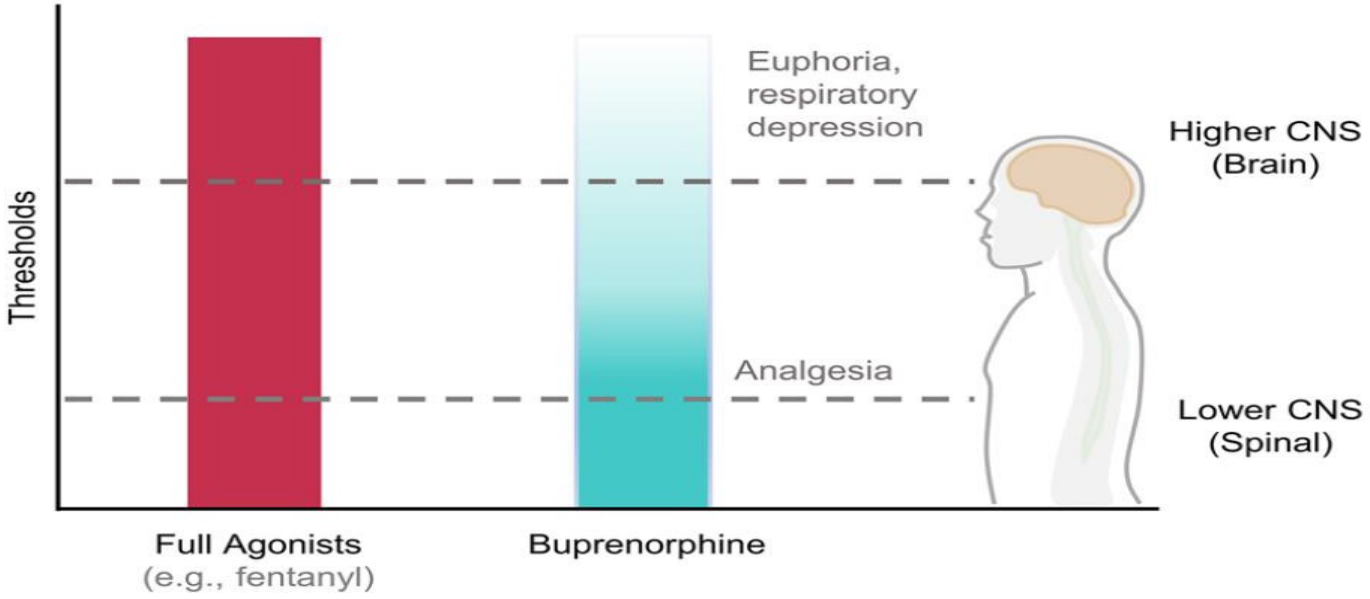
2) Clearance of bup and preference for spinal opioid receptors = safety





Buprenorphine prefers the lower CNS/spinal cord



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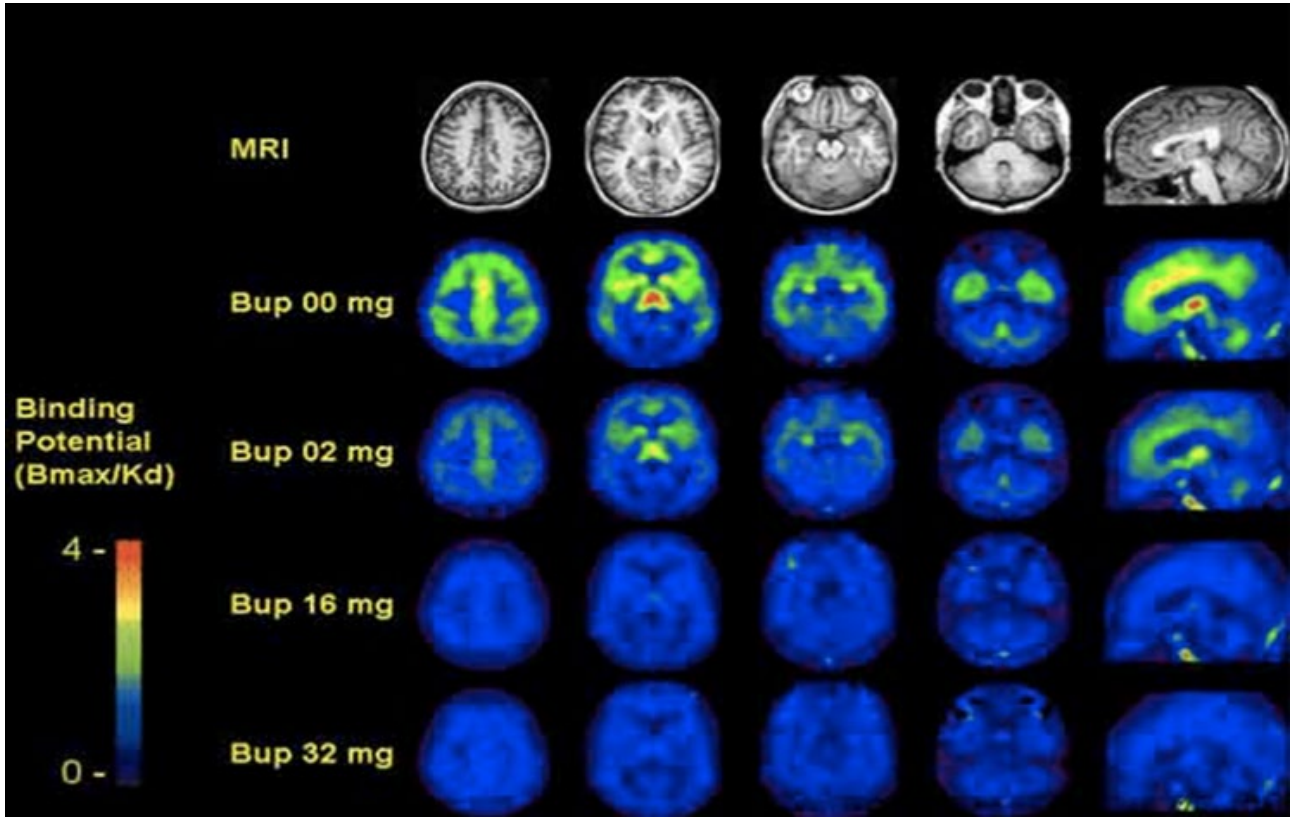
Buprenorphine Receptor Binding



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

Pharmacology

- Duration of action
  - Half-life: 3 hours for intravenous; 24-60 hours for sublingual or buccal formulations
  - Naloxone = very poor oral, sublingual, and buccal bioavailability; absorbed as injection or intranasally
  - Promotes abuse deterrence if crushed/dissolved for nasal/IV misuse
  - Dosed SL/SQ to avoid first pass effect of liver metabolism

Additional Considerations

- Drug-drug interactions (CYP450 3A4 inducers, substrates, and inhibitors)
- Buprenorphine/naloxone products not recommended in moderate hepatic impairment (Child-Pugh 7-9) and do not use in severe hepatic impairment (Child-Pugh 10-15)
- Side effects: headache, dizziness, nausea, vomiting, sweating, constipation, sexual dysfunction; respiratory depression less common than with opioid agonists but still possible
- Schedule III medication; has REMS requirements
  - Long acting opioid REMS apply for pain formulations
  - Separate REMS for OUD formulations

3) 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

Case study #1

- 77 year old male, history of Crohn's disease
- The pt is currently on Oxycontin 10mg 2x/day (for about 7 years) and Oxycodone 2.5mg at 6pm
- 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. The pt's wife also transitioned from pain medications to Suboxone and is doing well. The pt has never been on buprenorphine in the past

Case Approach

- Discussed multiple options:
  - Belbuca is one option - **on label** for chronic 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 study #2

- 50 yo F with h/o GSW, intrathecal pump for pain
- Pt presents with difficulty maintaining pain level on oxycodone 5-10 mg QID
- Offered Butrans 10 mcg/hr patch with oxycodone 10 QID
- Reports pain generally controlled thru the day

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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

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
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- May consider starting adrenergic a2 agonist (clonidine, lofexidine) to reduce risk of withdrawal

Webster L. et al. Pain Medicine 2020

Summary:

1) The mechanism of action of buprenorphine is distinct form other opioids and how that may help its efficacy for pain
2) The clearance of buprenorphine and preference for spinal opioid receptors are factors in its safety profile
3) There are different requirements to write buprenorphine for pain vs writing buprenorphine for opioid use disorder

QUESTIONS?

TYPE QUESTIONS INTO THE CHAT OR RAISE HAND

Additional questions:

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