Non-CME Webinar Series
designed with the trainee in mind
first Tuesday of the month

ASRA PAIN MEDICINE

THE ASSOCIATION OF PAIN PROGRAM DIRECTORS
ADVANCING EDUCATION IN MULTIDISCIPLINARY PAIN MEDICINE

Buprenorphine – A Tool in the Toolbox of a Pain Physician

Tuesday, June 7, 2022

7-8:30 pm ET

Buprenorphine

Mohammed A. Issa, MD

Buprenorphine’s analgesic properties

Formulations approved for analgesia: intravenous, transdermal, buccal

Formulations approved for opioid use disorder: sublingual tablet, film, subcutaneous injectable

Original FDA registration study that showed therapeutic efficacy of buprenorphine for pain

Analgesic Efficacy and Tolerability of Transdermal Buprenorphine in Patients with Inadequately Controlled Chronic Pain Related to Cancer and Other Disorders: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

Reinhard Sittl, MD,[1] Norbert Griessinger, MD,[1] and Rudolf Likar, MD[2]

[1]*University of Erlangen, Pain Clinic, Erlangen, Germany, and* [2]*Pain Clinic, General Hospital, Klagenfurt, Austria*

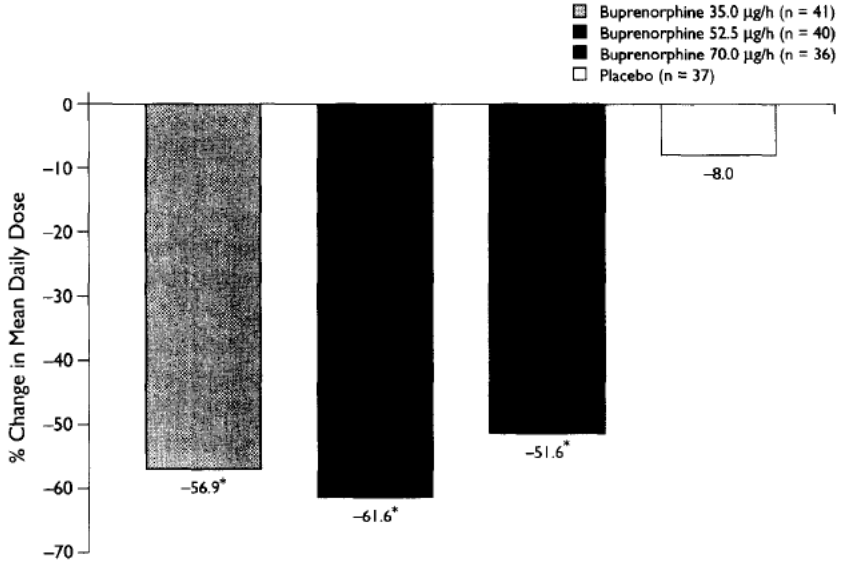


Figure 2. Percentage reduction in consumption of additional oral opioid analgesic medication for breakthrough pain during the study period. *$P < 0.05$ versus placebo group (least significant difference test).

Long term efficacy in chronic pain patients

Clinical Therapeutics/Volume 28, Number 6, 2006

Brief Report

Long-Term Management of Chronic Pain with Transdermal Buprenorphine: A Multicenter, Open-Label, Follow-Up Study in Patients from Three Short-Term Clinical Trials

Rudolf Likar, MD[1]; Hubertus Kayser, MD[2]; and Reinhard Sittl, MD[3]

[1]Pain Clinic, General Hospital Klagenfurt, Klagenfurt, Austria; [2]Practice for Anesthesiology and Special Pain Therapy, Bremen, Germany; and [3]Pain Clinic, University of Erlangen-Nürnberg, Erlangen, Germany

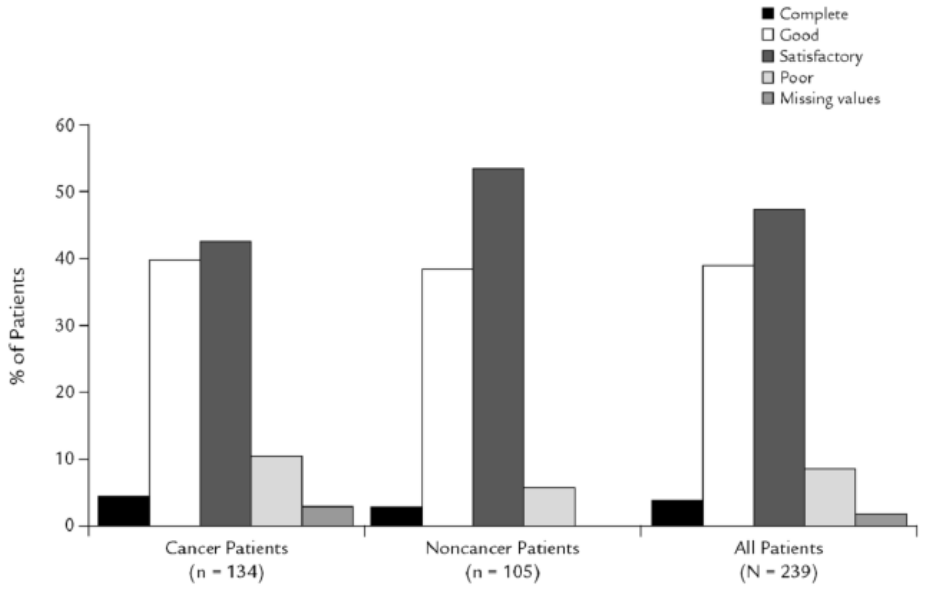
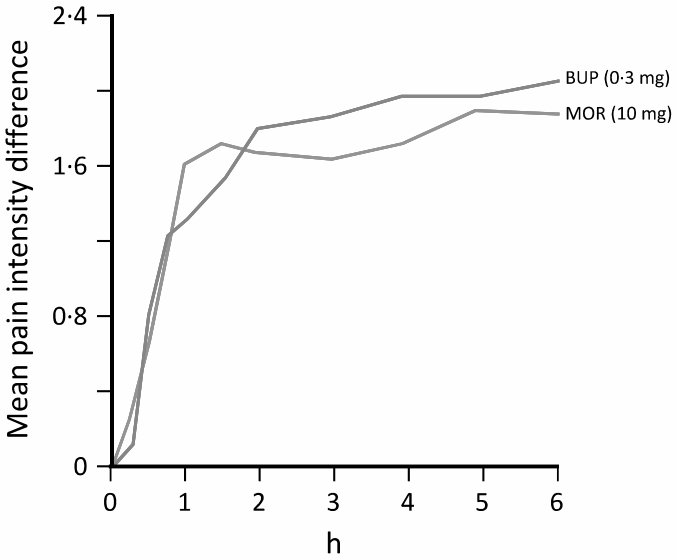


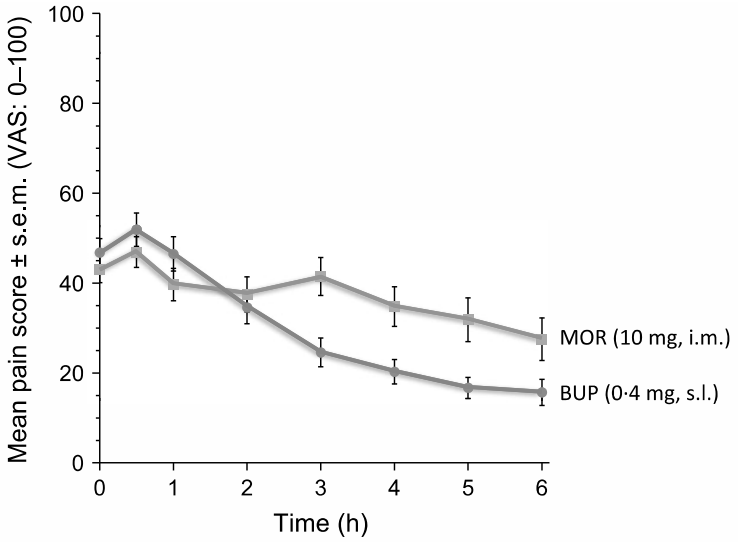
Figure 2. Proportions of patients reporting complete, good, satisfactory, and poor pain relief, as indicated retrospectively on a 4-point verbal rating scale.

Is it as good as other opioids?

60 patients, post op pain relief following upper abdominal surgery. Double blind randomized

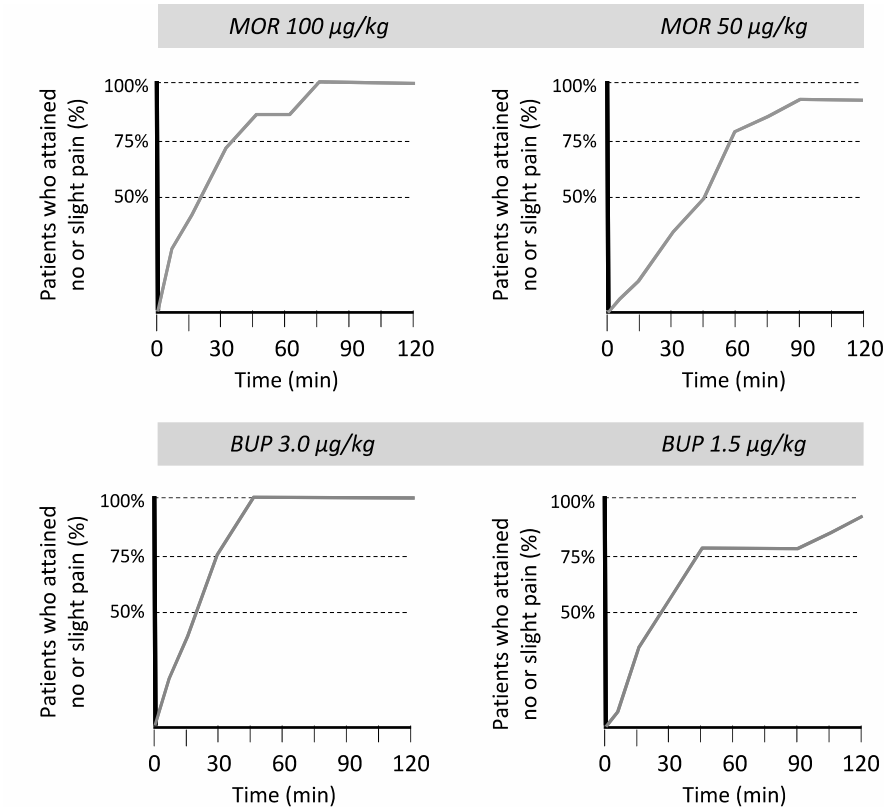


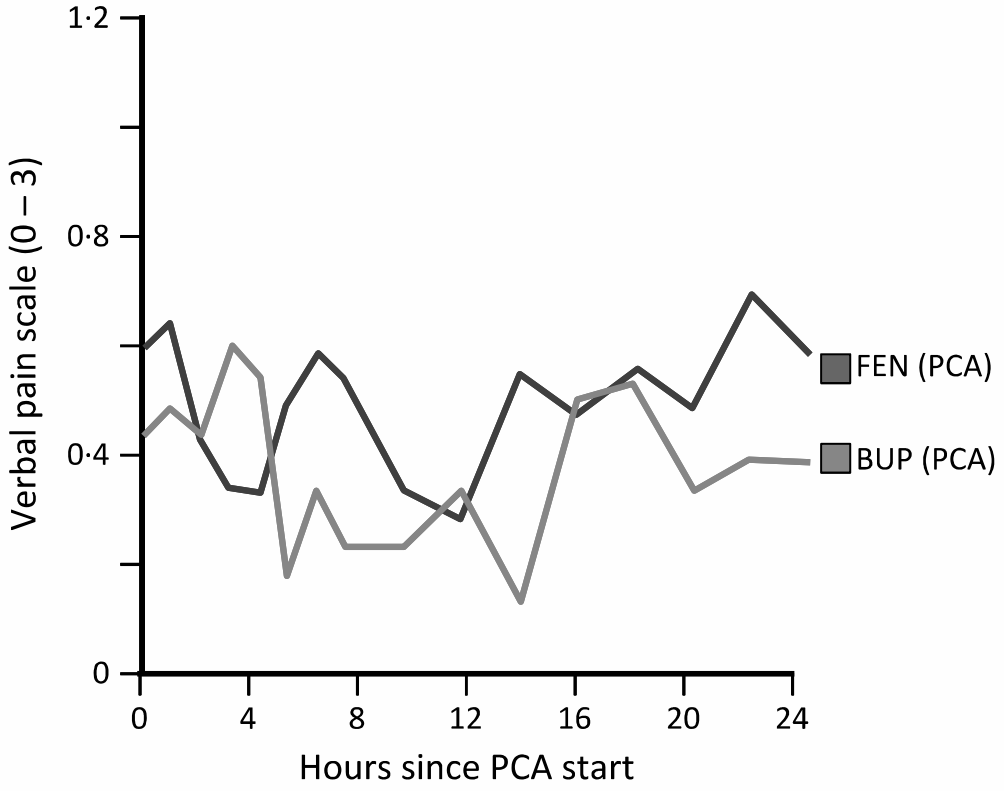
101 patients, post op pain relief, double blind randomized



Really?

Yes, really.


MOR 100 µg/kg
MOR 50 µg/kg
BUP 3.0 µg/kg
BUP 1.5 µg/kg
Patients who attained no or slight pain (%)
100%
75%
50%
0
30
60
90
120
Time (min)


Verbal pain scale (0 – 3)
1·2
0·8
0·4
0
0
4
8
12
16
20
24
Hours since PCA start
FEN (PCA)
BUP (PCA)

The highest dose of transdermal buprenorphine available (20 mcg/hr) is equivalent to which daily dose of sublingual buprenorphine?

A. 0.6 mg/day

B. 1.6 mg/day

C. 5.7 mg/day

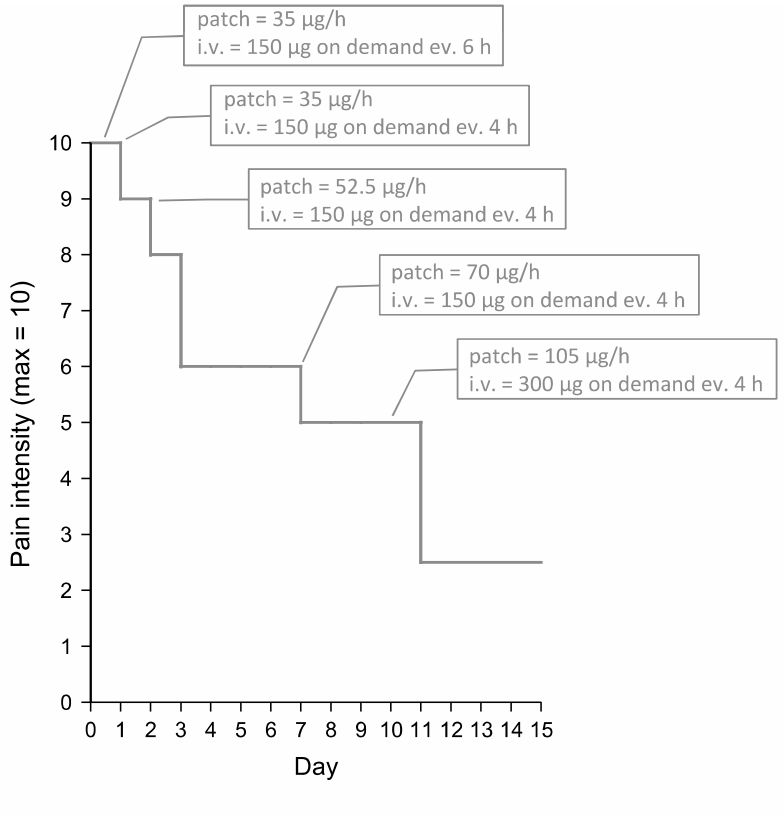
D. 6.3 mg/day

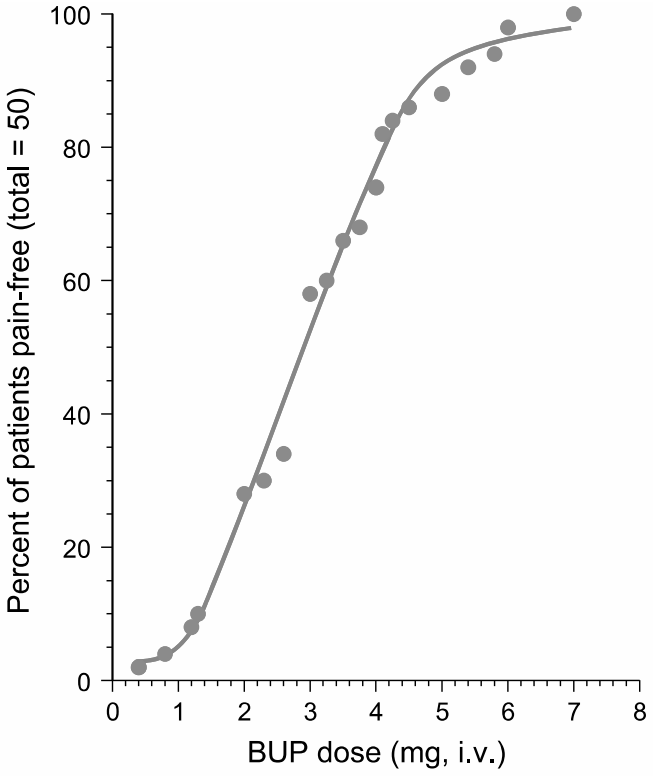
E. 11.4 mg/day

Buprenorphine Dosing for Pain

Table 1 Buprenorphine formulations with an on-label pain indication

Route of admin.	Brand name	Approval date	Indication	Bioavailability	Dosages
Injectable (IV/IM)	Buprenex [10]	1981	Moderate to severe pain	100%	0.3 mg IV 0.3–0.6 mg IM
Buccal film	Belbuca [22]	2015	Pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate	46–65%	BID Dosing 75 mcg 150 mcg 300 mcg 450 mcg 600 mcg, 750 mcg 900 mcg
Transdermal system	Butrans [23]	2010	Moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time	15%	Weekly dosing 5 mcg/h 7.5 mcg/h 10 mcg/h 15 mcg/h 20 mcg/h


patch = 35 µg/h
i.v. = 150 µg on demand ev. 6 h
patch = 35 µg/h
i.v. = 150 µg on demand ev. 4 h
patch = 52.5 µg/h
i.v. = 150 µg on demand ev. 4 h
patch = 70 µg/h
i.v. = 150 µg on demand ev. 4 h
patch = 105 µg/h
i.v. = 300 µg on demand ev. 4 h
Pain intensity (max = 10)
Day


Percent of patients pain-free (total = 50)
BUP dose (mg, i.v.)

Published in final edited form as:
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Treating Chronic Pain: An Overview of Clinical Studies Centered on the Buprenorphine Option

Mellar P. Davis[1], **Gavril Pasternak**[2], **Bertrand Behm**[1]

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Buprenorphine

New Tricks With an Old Molecule for Pain Management

Howard A. Heit, MD, FACP, FASAM and Douglas L. Gourlay, MD, MSc, FRCPC, FASAM†*

Safety of buprenorphine transdermal system in the management of pain in older adults

Joseph V. Pergolizzi, Robert B. Raffa, Zachary Marcum, Salvatore Colucci & Steven R. Ripa

Chronic Pain Medicine

Section Editor: **Honorio T. Benzon**

SYSTEMATIC REVIEW ARTICLE

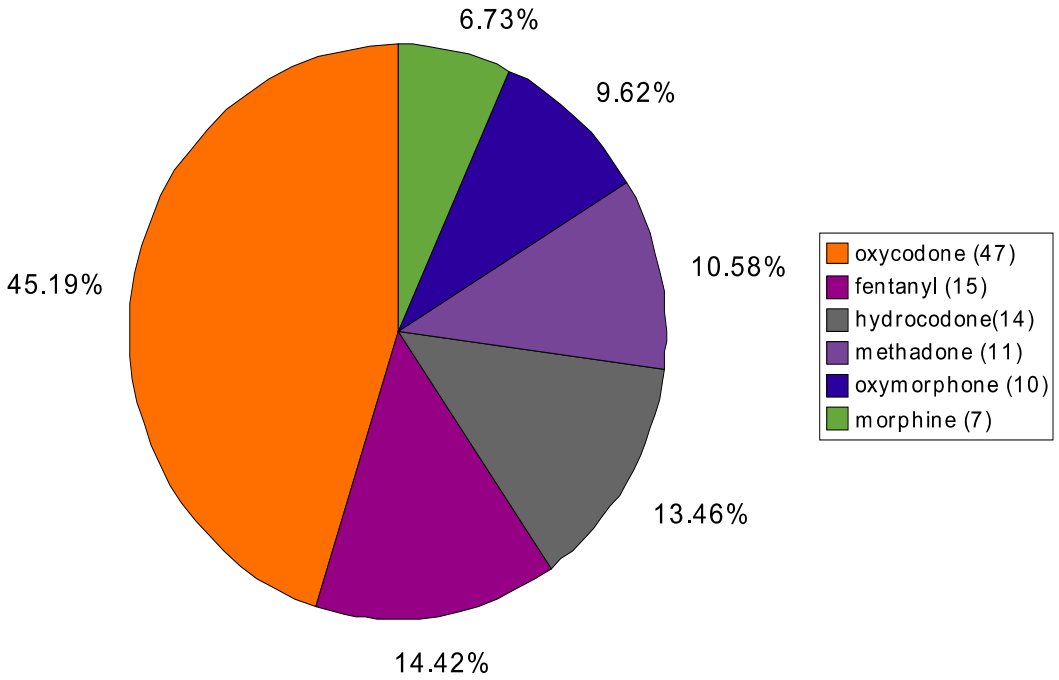
Treatment of Chronic Pain With Various Buprenorphine Formulations: A Systematic Review of Clinical Studies

Rohit Aiyer, MD,* Amitabh Gulati, MD,† Semih Gungor, MD,‡ Anuj Bhatia, MD,§ and Neel Mehta, MD‖

Clinical studies demonstrate that buprenorphine is a pharmacologic agent that can be used for the treatment of various types of painful conditions. This study investigated the efficacy of 5 different types of buprenorphine formulations in the chronic pain population. The literature was reviewed on PubMed/MEDLINE, EMBASE, Cochrane Database, clinicaltrials.gov, and PROSPERO that dated from inception until June 30, 2017. Using the population, intervention, comparator, and outcomes method, 25 randomized controlled trials were reviewed involving 5 buprenorphine formulations in patients with chronic pain: intravenous buprenorphine, sublingual buprenorphine, sublingual buprenorphine/naloxone, buccal buprenorphine, and transdermal buprenorphine, with comparators consisting of opioid analgesics or placebo. Of the 25 studies reviewed, a total of 14 studies demonstrated clinically significant benefit with buprenorphine in the management of chronic pain: 1 study out of 6 sublingual and intravenous buprenorphine, the only sublingual buprenorphine/naloxone study, 2 out of 3 studies of buccal buprenorphine, and 10 out of 15 studies for transdermal buprenorphine showed significant reduction in pain against a comparator. No serious adverse effects were reported in any of the studies. We conclude that a transdermal buprenorphine formulation is an effective analgesic in patients with chronic pain, while buccal buprenorphine is also a promising formulation based on the limited number of studies. (Anesth Analg 2018;127:529–38)

What about patients who are already on opioids and thus, not opioid naive?

Conversion of Chronic Pain Patients from Full Opioid Agonists to Buprenorphine



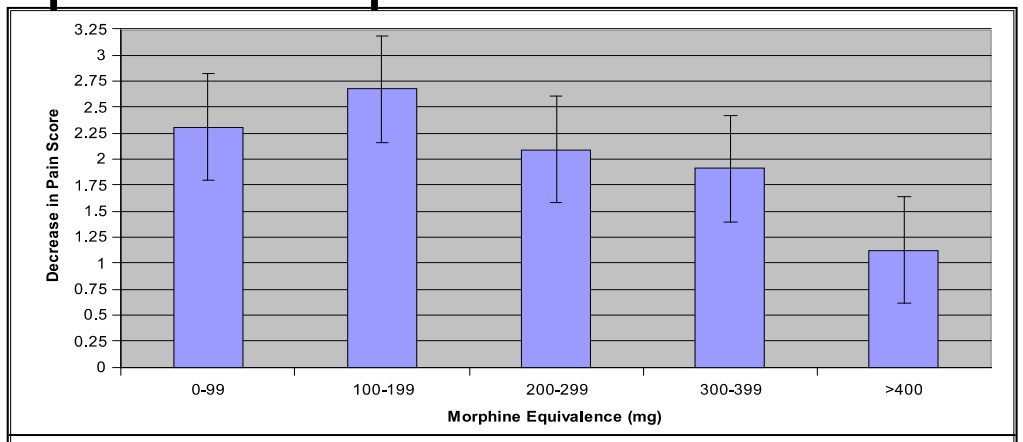


Fig. 3. *Preinduction morphine equivalents versus average decrease in pain.*

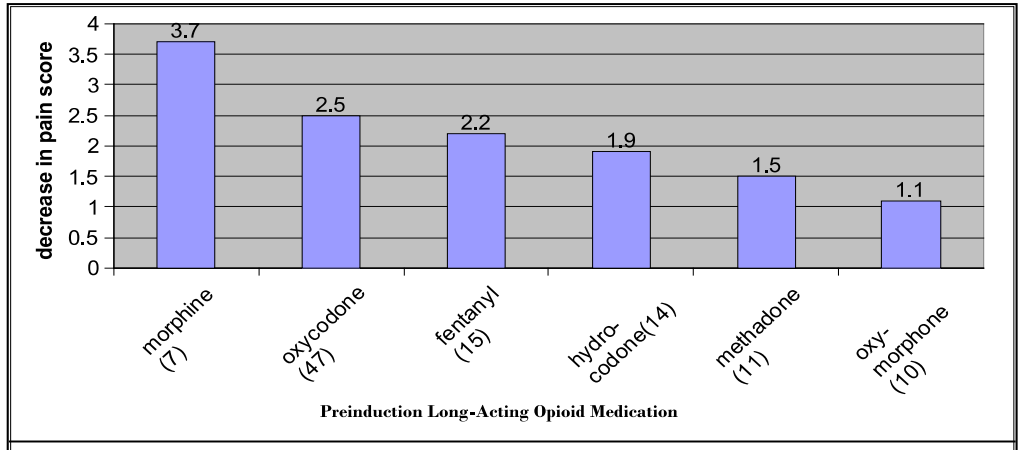
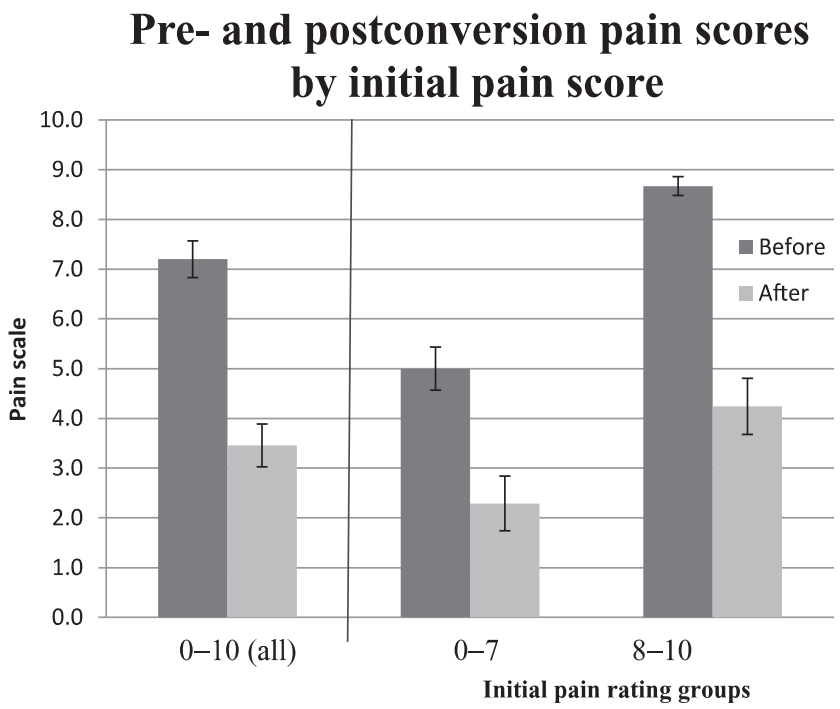
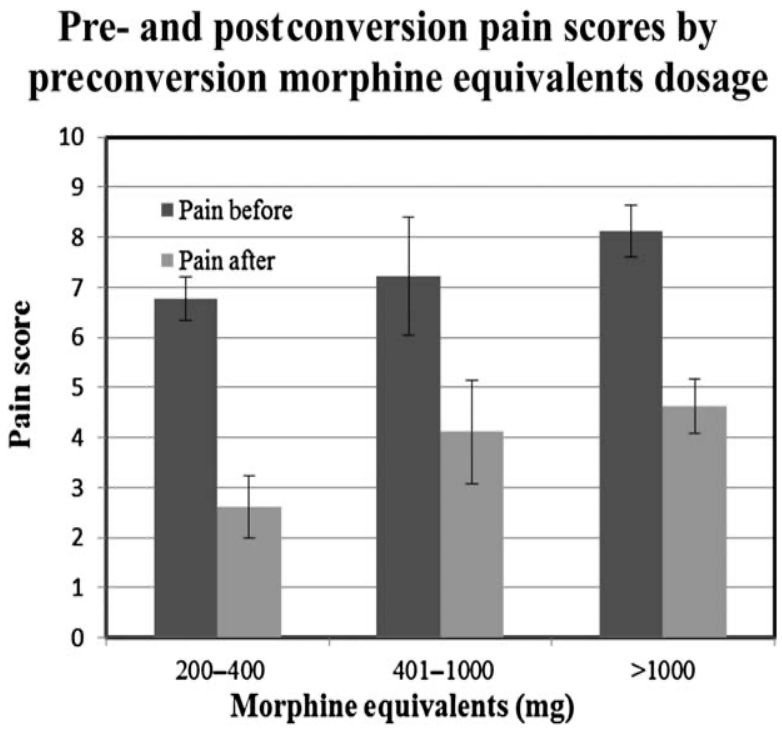


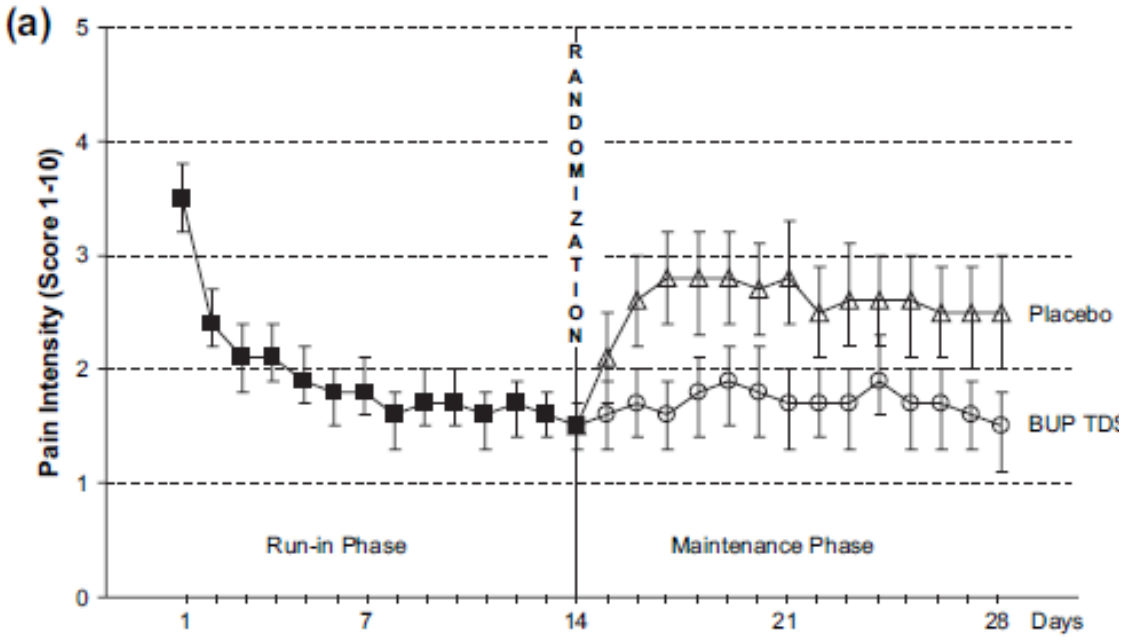
Fig. 4. *Decrease in pain score after conversion from individual opioid drugs to buprenorphine SL.*

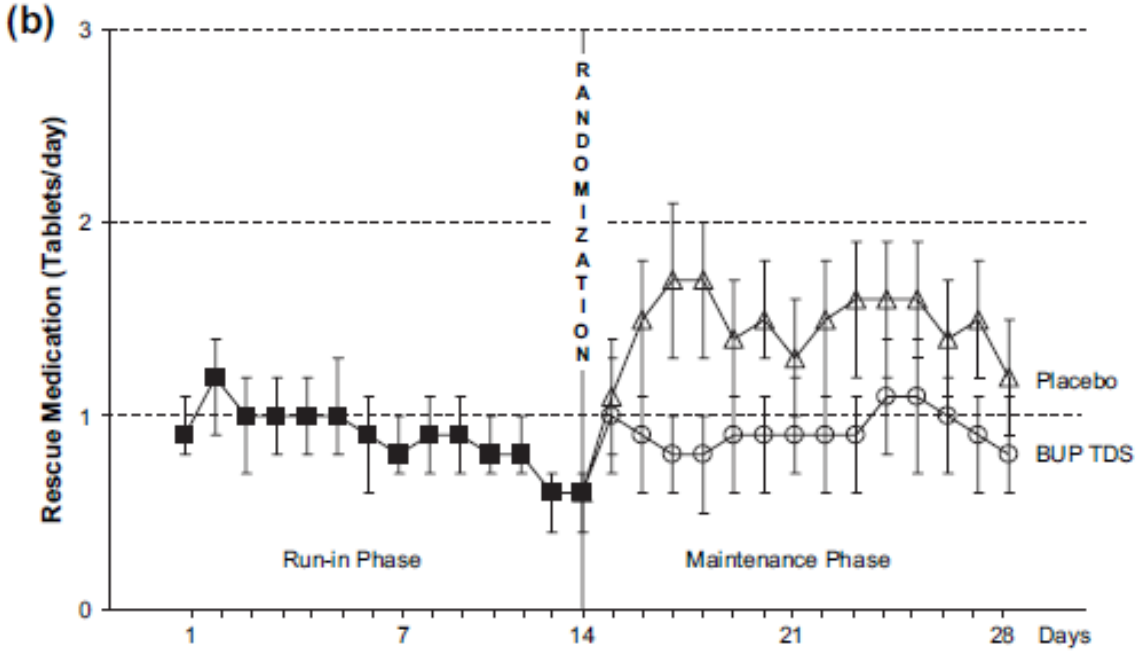
Higher doses of full agonist to Buprenorphine





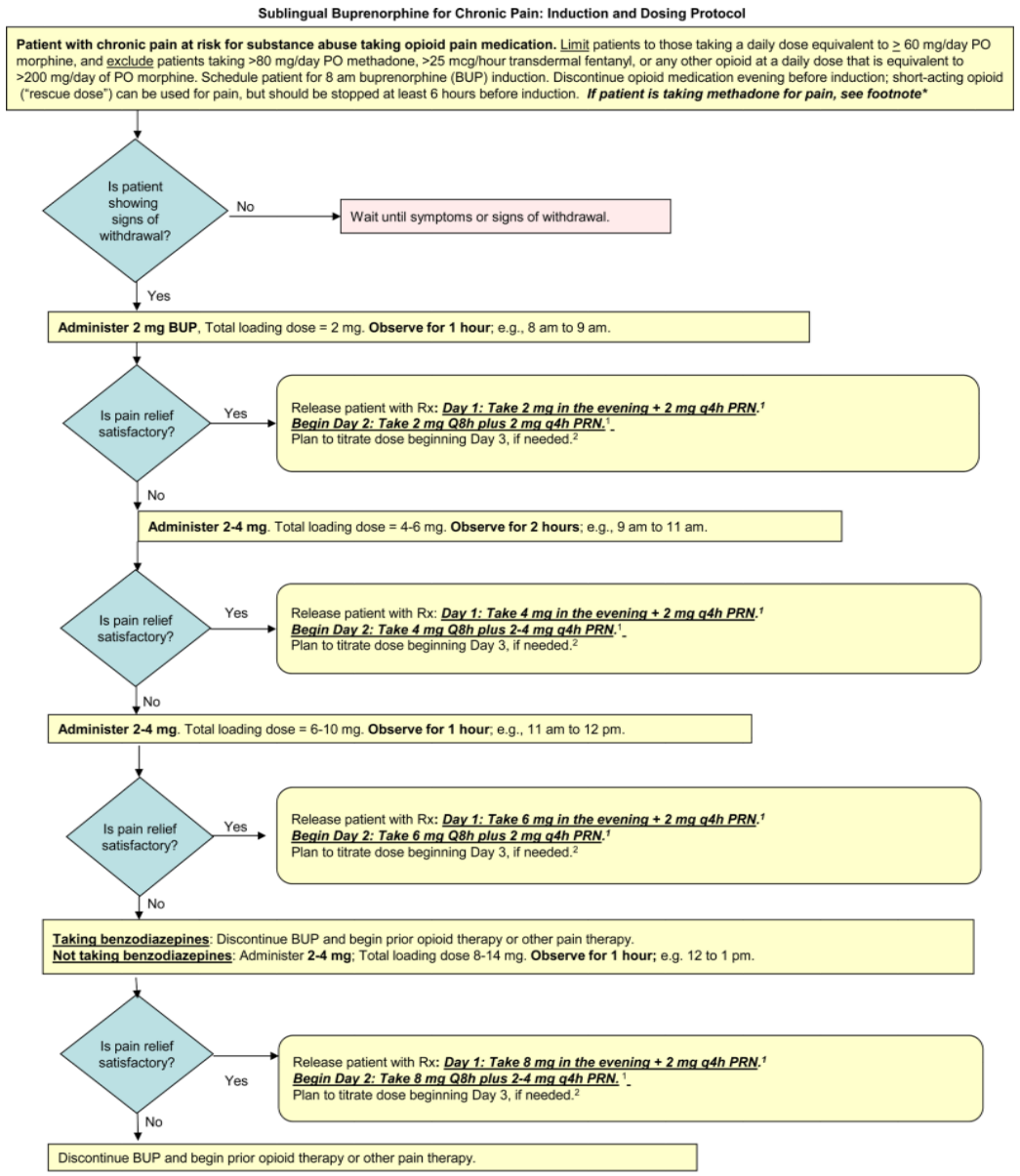
Buprenorphine in patients on 90-150 MME





Oral morphine to transdermal buprenorphine equivalents[a]

Oral morphine (mg/day)	Transdermal buprenorphine (μg/h)
12	5
24	10
48	20
84	35
126	52.5
168	70



1. Limit the number of rescue doses to a maximum of 4/day until induction is complete and the patient is stable. For patients not taking benzodiazepines use the 2 mg PRN rescue dose on Day 1; may increase to a 4 mg rescue dose on Day 2, depending on response .
2. Further increases in the scheduled Q8h dose can begin on Day 3; increase the scheduled dose no more frequently than every other day.
If patient is taking methadone ≥30 mg/day for pain: To reduce the risk of delayed precipitated withdrawal, consider stopping methadone 2 days before induction. Alternatively, consider extending the BUP loading period on Day 1 by using smaller doses at the same intervals to titrate up to the desired level, e.g., 2 mg, 2 mg, 2-4 mg, 2-4 mg, 2-4 mg, 2-4 mg. Maximum in office dose for patients taking benzodiazepine is 10 mg; max. for patients not taking benzodiazepines is 14 mg.

Figure 1.

What makes buprenorphine special?

What most of us already know

Partial agonist at mu receptor

Antagonist at kappa receptor

There is more to buprenorphine than what we have learned.

Ability to increase mu receptor expression on cell membranes

Opioid receptor like 1 agonist

- Mice lacking this protein displayed no buprenorphine analgesia, while showing normal responses to morphine

Does not recruit β-arrestin to the receptor (arrestin associated w adverse effects of typical opioids)

Antinociception (at naloxone insensitive brain site)

Ceiling effect with respiratory depression

No ceiling effect with regards to analgesia

Antihyperalgesic effects (receptor subtype selectivity, G protein binding, kappa antagonism, blockage of Na channels, activates 5HT spinal neurotransmission)

Acts at both level of spinal cord and the brain w action being primarily at spinal cord (not brain like morphine and fentanyl)

Antinociception

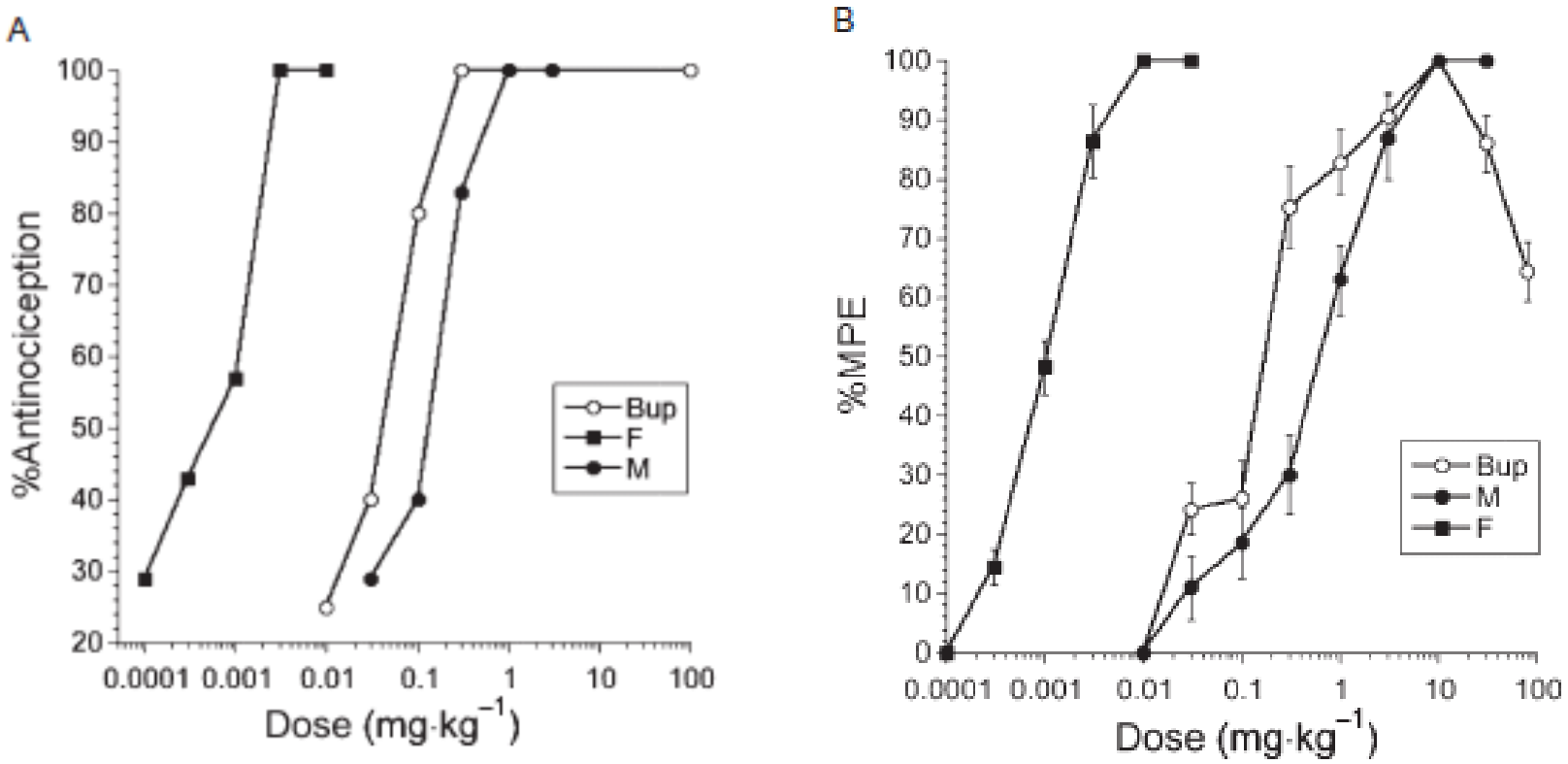


Figure 1 Anti-nociceptive dose–response curves for buprenorphine (Bup), morphine (M) and fentanyl (F) in the (A) abdominal constriction and (B) warm water (48°C) tail-dip/flick test (Raffa and Ding, 2007) in mice (mean ± SEM). Baseline latency = 7.6 ± 0.6 (Bup), 6.7 ± 0.7 (M) and 7.3 ± 0.4 (F) s. n = 4–8 mice per group. MPE, maximum possible effect.

Naloxone sensitive and naloxone insensitive components of action that contribute to pain relief and antinociception

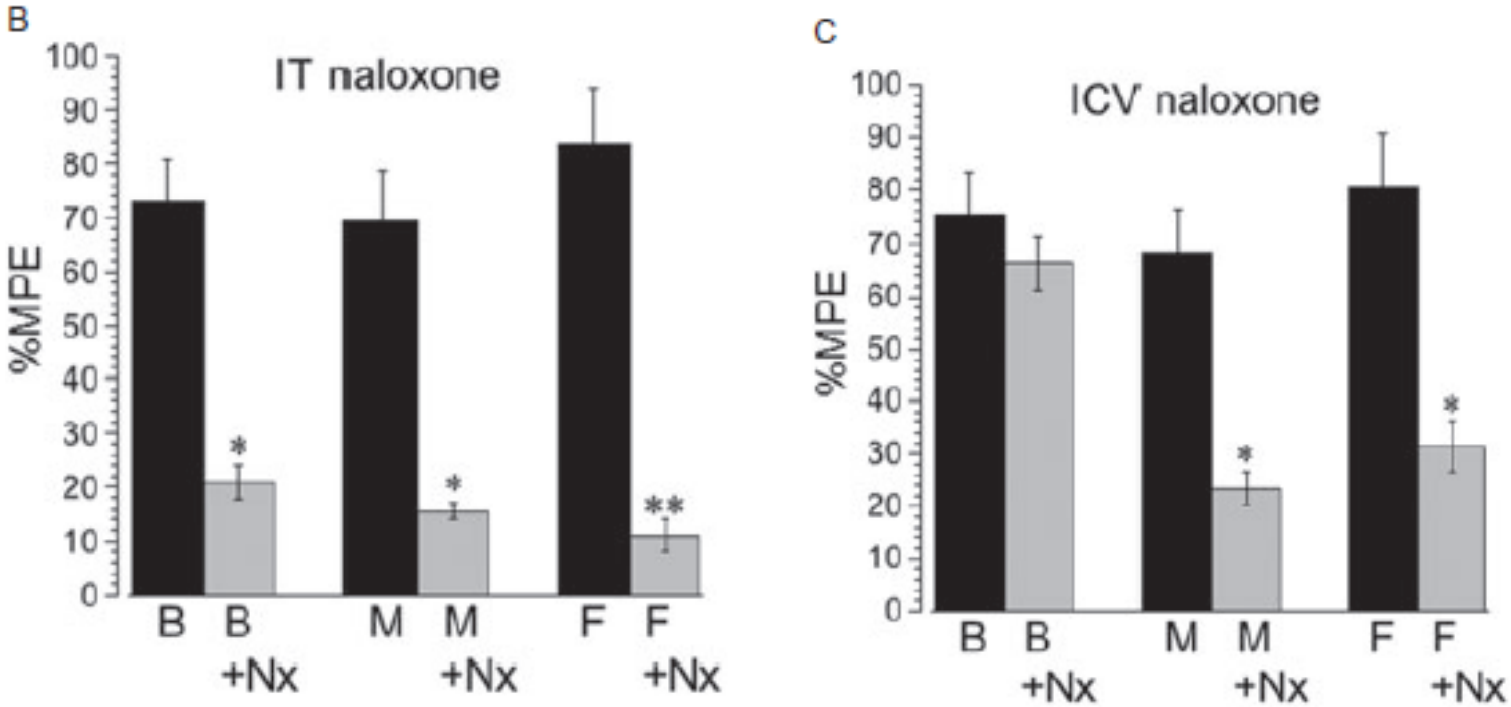


Figure 2 The effect of naloxone (Nx) administered: (A) i.p. (10 mg·kg^{-1}); (B) spinally (IT) (20 μg, 10 min prior); or (C) supraspinally (ICV) (20 μg, 10 min prior) on the anti-nociception induced by s.c. morphine (M) (3 mg·kg^{-1}); fentanyl (F) (0.003 mg·kg^{-1}); or buprenorphine (Bup or B) (1 and 30 mg·kg^{-1} in A; 1 mg·kg^{-1} in B and C). Baseline latencies with/without naloxone: (A) 5.6 ± 0.4 to 7.2 ± 1.1 s/5.9 ± 0.8 to 7.7 ± 0.6 s; (B) 8.3 ± 0.7/7.1 ± 0.6 s (B); 6.2 ± 0.8/7.4 ± 0.7 s (M); 8.1 ± 0.7/8.4 ± 0.3 s (F); (C) 6.2 ± 0.4/6.0 ± 0.8 s (B); 5.6 ± 0.7/5.4 ± 0.5 s (M); 5.4 ± 0.6/6.4 ± 0.6 s (F). Veh = vehicle. n = 6–8 mice per group. Mean ± SEM, *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. ICV, intracerebroventricular; IT, intrathecal.

Which test is classically used in human research to investigate opioid-induced hyperalgesia?

A. Acupuncture

B. FACES Pain Scale

C. Hot plate test

D. Cold pressor test

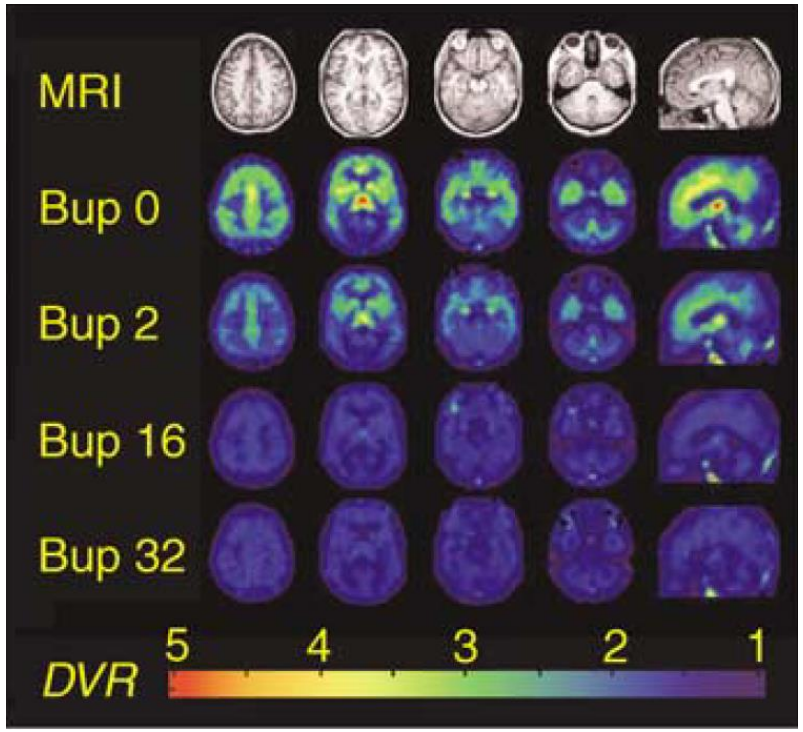
E. Functional magnetic resonance imaging

fMRI and Receptor Occupancy with Buprenorphine

Effects of Buprenorphine Dose on receptor availability in patients with OUD

- Mu Receptor availability by Buprenorphine Dose
  - 2 mg → 60% mu opioid receptors available
  - 16 mg → 8-15% mu opioid receptors available
  - 32 mg → 2-6% mu opioid receptors available

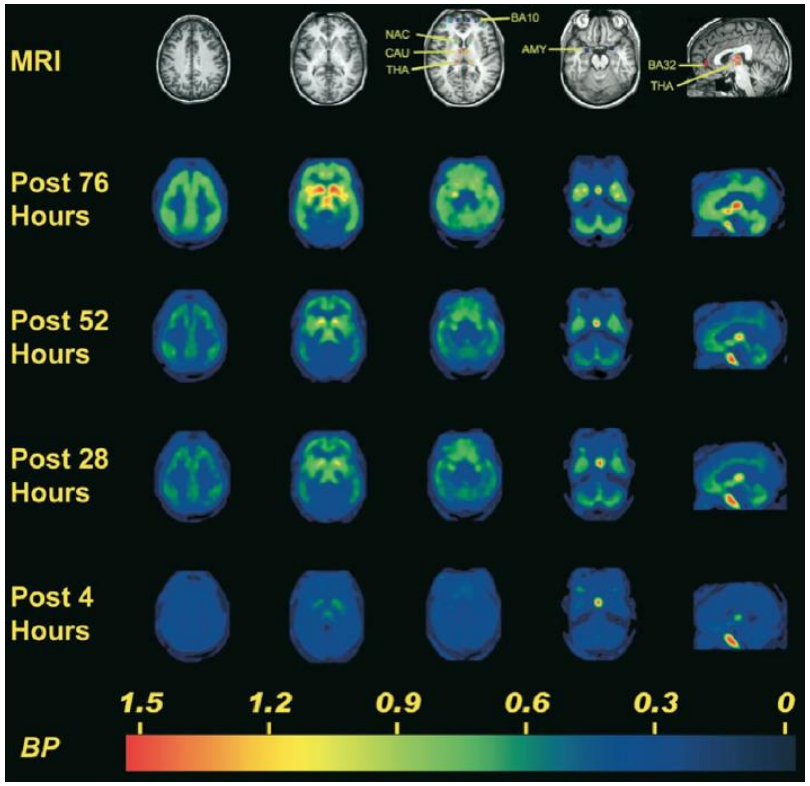
- Similar changes across multiple regions of the brain:
  - Prefrontal cortex
  - Anterior cingulate
  - Thalamus
  - Amygdala
  - Nucleus accumbens
  - Caudate



- Changes in mu opioid occupancy/availability
  - Variable at low doses of 2 mg (prefrontal cortex 47% occupied vs amygdala 27% occupied)
  - Homogenous at higher doses of 32 mg (94-98% at all sites except thalamus)

Opioid receptor occupancy and availability with buprenorphine

- Patients maintained on 16 mg oral buprenorphine had single dose omitted
- Brain mu opioid receptor availability by time:
  - 4 hours → 30% of receptors available
  - 28 hours → 54% of receptors available
  - 52 hours → 67% of receptors available
  - 76 hours → 82% of receptors available
- Additional finding:
  - Approximately 50-60% receptor occupancy is needed to suppress withdrawal



52 yo lady, on LTOT for 20 years

Oxycontin 50mg TID plus Oxycodone IR 5-10 mg q4h prn (295 MME)

Pain is always 7-8/10

Patient asks for opioid dose increases despite high doses

Calls PCP's office 2 days before prescriptions to ensure they are filled

2 occasions in past 2 years: 1-2-day early fills

Urine screens consistent with treatment and absent of concerns for illicit substance use

Steps to Consider

Decrease dose

Decrease Oxycontin/Oxycodone to as close to 200 MME daily as patient can tolerate

- Ok to implement symptomatic regimen during this time

Change to IR

Change all opioids to short acting/immediate release formulation

Consent and Educate

Discuss induction strategy and provide clear, written information for home induction

- In office inductions are also feasible. There is no clear benefit over home induction

Talk about stigma

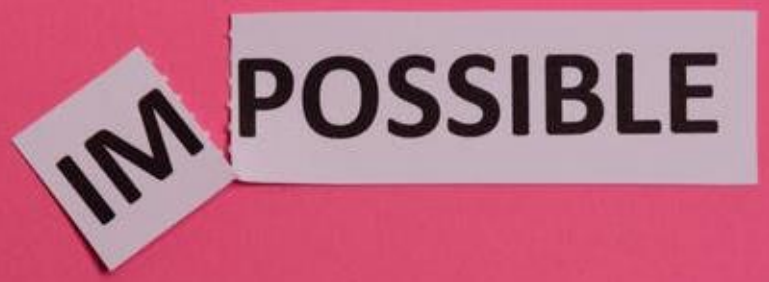
Be transparent about possible pain management options

Start Bup

Start buprenorphine as you would for opioid use disorder

Consider that the dose may be higher on day 1 than usual, and allow for this on your initial prescription

Continue non opioid medications for pain



Barriers for use of SL Buprenorphine for Pain

- Pharmacy requirements for X-waiver
- Limited support and consensus for off label use of buprenorphine for pain
- Stigma suffered by individuals who are on buprenorphine (with or without OUD diagnosis)
- Limited physician education and understanding of acute pain management in people on buprenorphine
- Limited understanding amongst providers about buprenorphine for pain
- ….

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Multi-Society Perioperative Buprenorphine Guidelines

Lynn Kohan M.D

University of Virginia

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Learning Objectives

- Assess the needs for anesthesiologists and pain physicians to manage patients with OUD within the perioperative period
- Discuss the multi-society OUD working group recommendations for patients on buprenorphine for MOUD
- Discuss the multi-society OUD working group recommendation for patients with suspected OUD in need of analgesia

12 ON 7

the IMPACT of OPIOIDS

2018 OPIOID STATISTICS

SOURCE: HHS.GOV.OPIOIDS

130+
PEOPLE DIED EVERY DAY FROM OPIOID-RELATED DRUG OVERDOSES

10.3 MILLION
PEOPLE MISUSED PRESCRIPTIONS

57,600
PEOPLE DIED FROM OVERDOSING ON OPIOIDS

2 MILLION
PEOPLE HAD AN OPIOID USE DISORDER

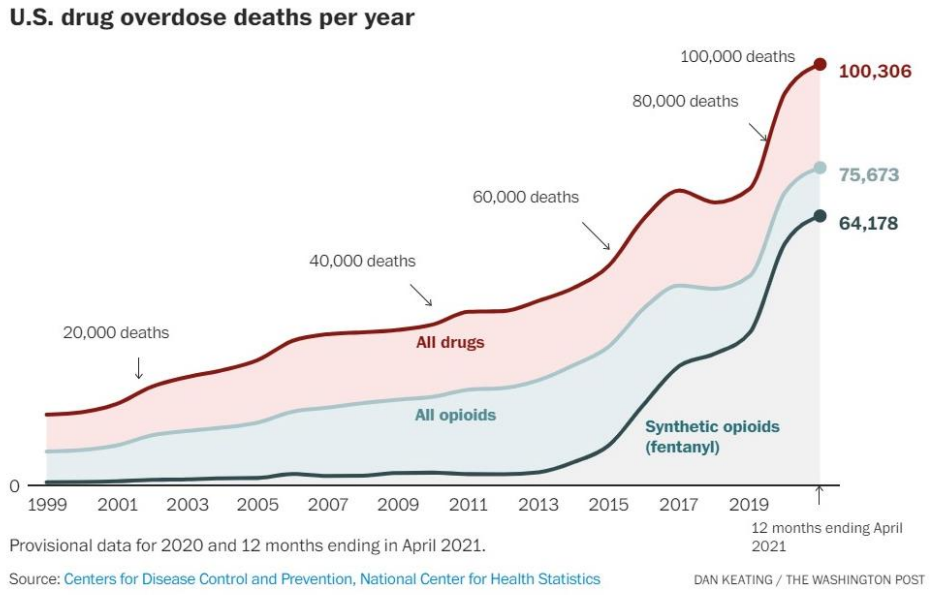
808,000
PEOPLE USED HEROIN

81,000
USED HEROIN FOR THE FIRST TIME

2 MILLION
PEOPLE MISUSED PRESCRIPTION OPIOIDS FOR THE FIRST TIME

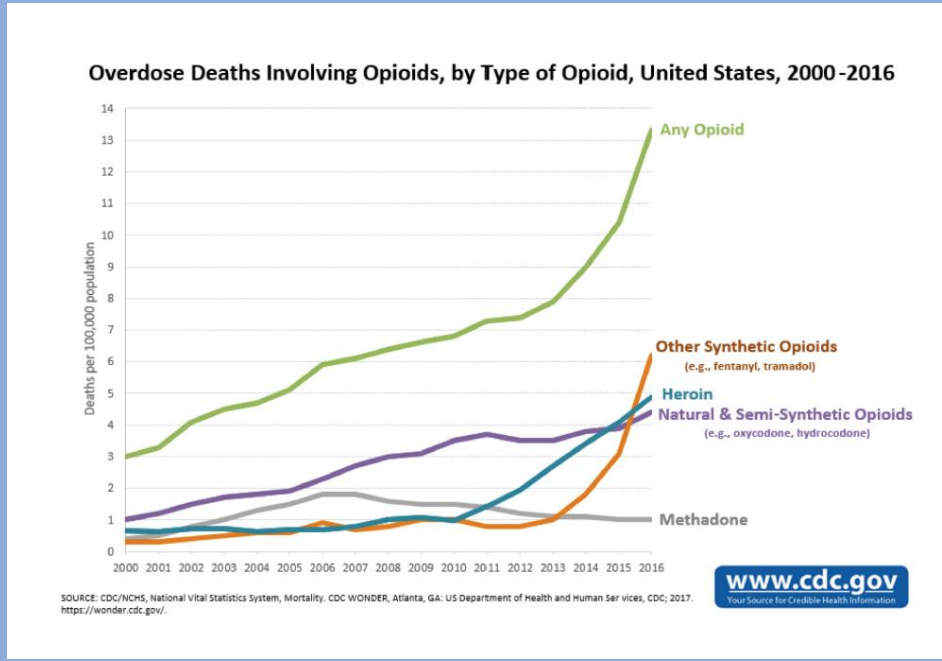
15,349
DEATHS ATTRIBUTED TO OVERDOSING ON HEROIN (DURING 12 MONTH PERIOD)

32,656
DEATHS ATTRIBUTED TO OVERDOSING ON SYNTHETIC OPIOIDS OTHER THAN METHADONE (DURING 12 MONTH PERIOD)



Importance of buprenorphine

- Opioid crisis is ongoing
- Impact
  - Overdose and death
  - Acquired infection
  - Comorbidities
  - Economic loss
  - Family destruction
  - Legal issues



COVID-19 and the opioid crisis: When a pandemic and an epidemic collide

So what is a substance use disorder (SUD)?

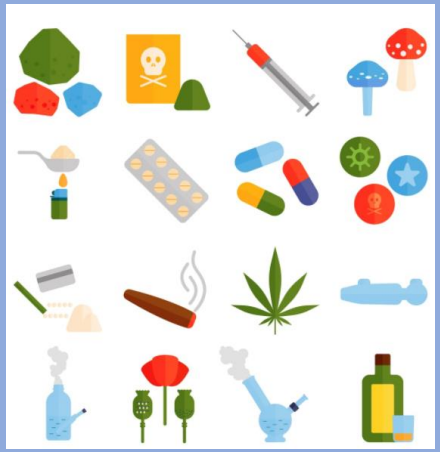
Loss of Control		
1	Substance taken in larger amounts or for a longer time than intended	"I didn't mean to start using so much."
2	Persistent desire or unsuccessful effort to cut down or control use of a substance	**"I've tried to stop a few times before, but I start using this drug again every time."**
3	Great deal of time spent obtaining, using, or recovering from substance use	"Everything I do revolves around using this drug." (In severe cases, most/all of a person's daily activities may revolve around substance use.)
4	Craving (a strong desire or urge) to use opioids	**"I wanted to use so badly, I couldn't think of anything else."**
Social Problems		
5	Continued opioid use that causes failures to fulfill major obligations at work, school, or home	**"I keep having trouble at work/ have lost the trust of friends and family because of using this drug."**
6	Continued opioid use despite causing recurrent social or personal problems	**"I can't stop using, even though it's causing problems with my friends/family/boss/landlord."**
7	Important social, occupational, or recreational activities are reduced because of opioid use	"I've stopped seeing my friends and family, and have given up my favorite hobby because of drugs."
Risky Use		
8	Recurrent opioid use in dangerous situations	"I keep doing things that I know are risky and dangerous to buy or use this drug."
9	Continued opioid use despite related physical or psychological problems	**"I know that using this drug causes me to feel badly/ messes with my mind, but I still use anyway."**
Pharmacological Problems		
10	**Tolerance** (the need to take higher doses of a drug to feel the same effects, or a reduced effect from the same amount)	"I have to take more and more of the drug to feel the same high."
11	**Withdrawal** (the experience of pain or other uncomfortable symptoms in the absence of a drug)	"When I stop using the drug for a while, I'm in a lot of pain."

Source: American Psychiatric Association. (2013). Substance Use Disorders. In *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Slide courtesy of Sudheer Potru

Substance Use Disorder

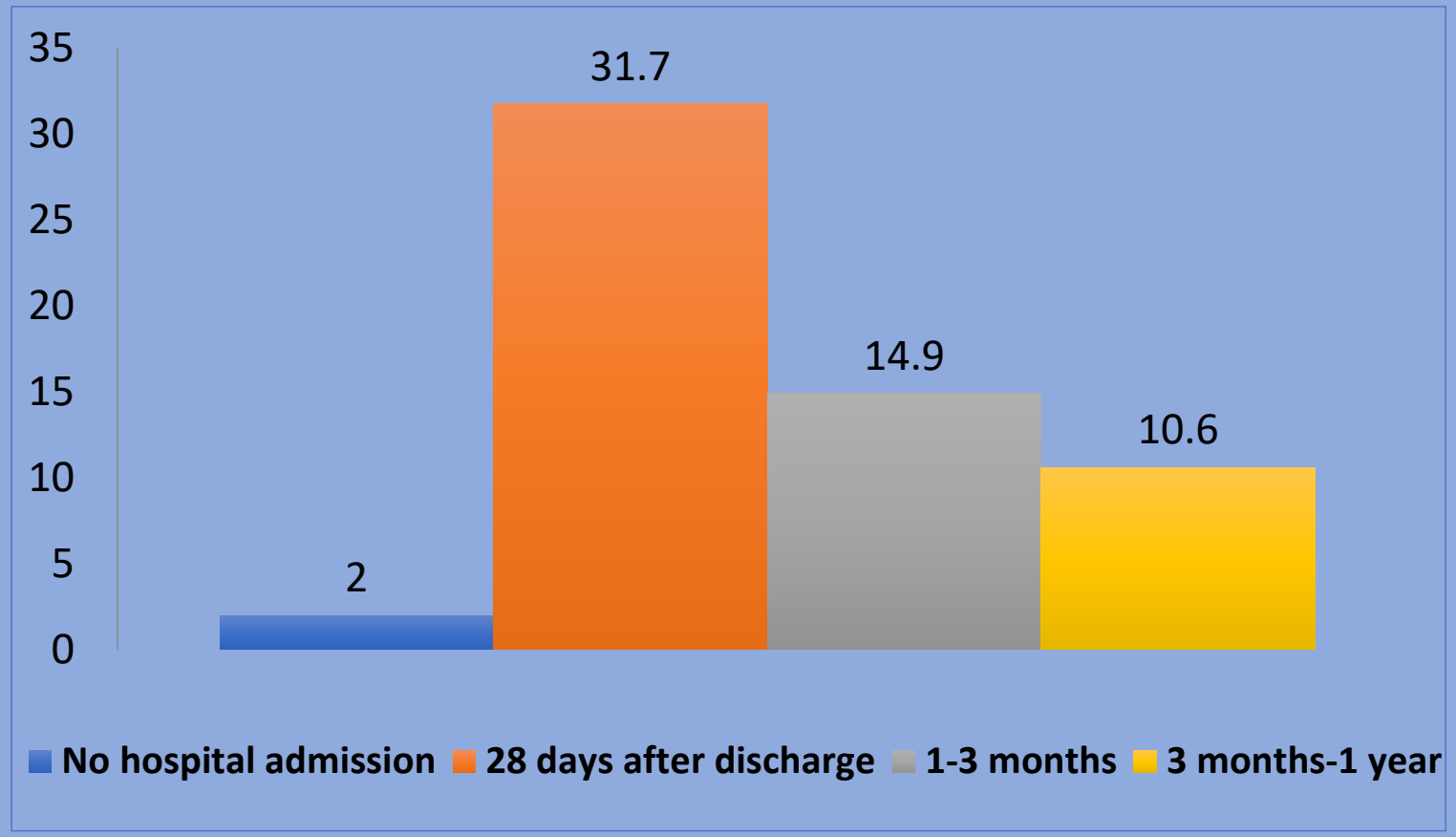
- Approximately 10-30% of hospitalized pt's have a non-alcohol SUD disorder
- Almost 40% are not detected by care team
- Not receiving care anywhere else for the SUD
- Almost 1/3 leave AMA
- Complicates hospital course
  - Poorer adherence to treatment plan
  - Withdrawal
  - Prolonged LOS
- Poor outcomes

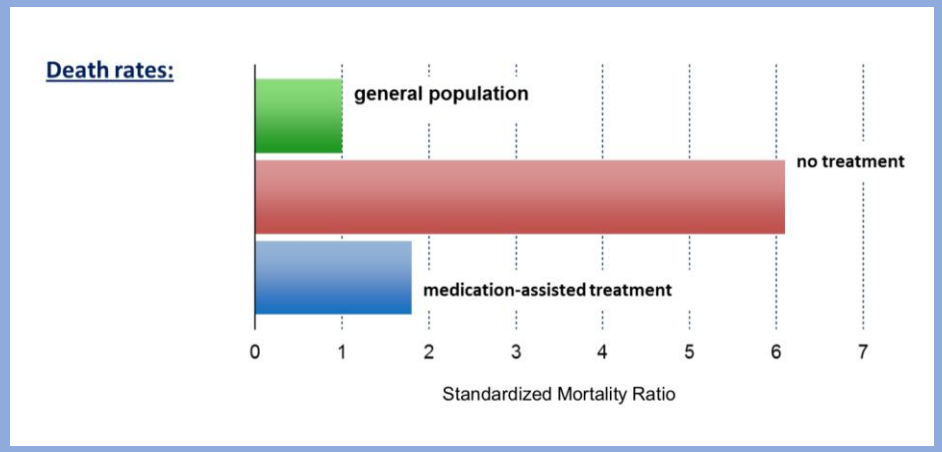


Buprenorphine

- Reduces opioid withdrawal and craving
- High binding affinity for the MOR
  - Will displace other opioid ligands
    - May precipitate withdrawal
  - Once in place prevents additional opioid binding
  - Some receptors may remain unbound and available
- Does not require daily trips to clinic (like methadone)
- Usually ok for use in elderly, and those with hepatic and renal insufficiency (except severe)

Drug Related Death Rate per 1000 Post Discharge





PCSS Providers Clinical Support System

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

White S et al. Drugs-Related Death Soon after Hospital-Discharge among Drug Treatment Clients. PLoS One. 2015; 10(11): e0141073

Buprenorphine is Lifesaving

- The number needed to treat to prevent one death from OUD with buprenorphine is less three.
- Buprenorphine treatment was associated with a 37% reduction in all-cause mortality during the year after a nonfatal overdose.
- **It's rare in medicine to actually be able to save a life.**

Larochelle MR, Bernson D, Land T, et al. Ann Intern Med 2018; 169: 137-45.
Poorman E. NEJM 2021 384;19: 1783-4.

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.

Multi-Society Working Group on SUD

- Initiative
  - Dr. Eugene Visucsi (ASRA President)
  - Dr. Beverly Philip (ASA President)
  - Dr. Jerome Adams (Surgeon General)

- SUD Ad Hoc Committee
  - Chair Lynn Kohan M.D.
  - ASRA reps
    - Sudheer Potru M.D.
    - Olabisi Lane M.D.


  - ASA reps
    - Anuj Aryal M.D.
    - Antje Barreveld M.D.


  - AAPM rep
    - Trent Emerick M.D.
  - ASAM reps
    - Trent Emerick M.D.
    - Michael Sprintz D.O.


  - ASHSP reps
    - Anna Dopp Pharm. D.
    - Sophia Chhay Pharm. D.


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

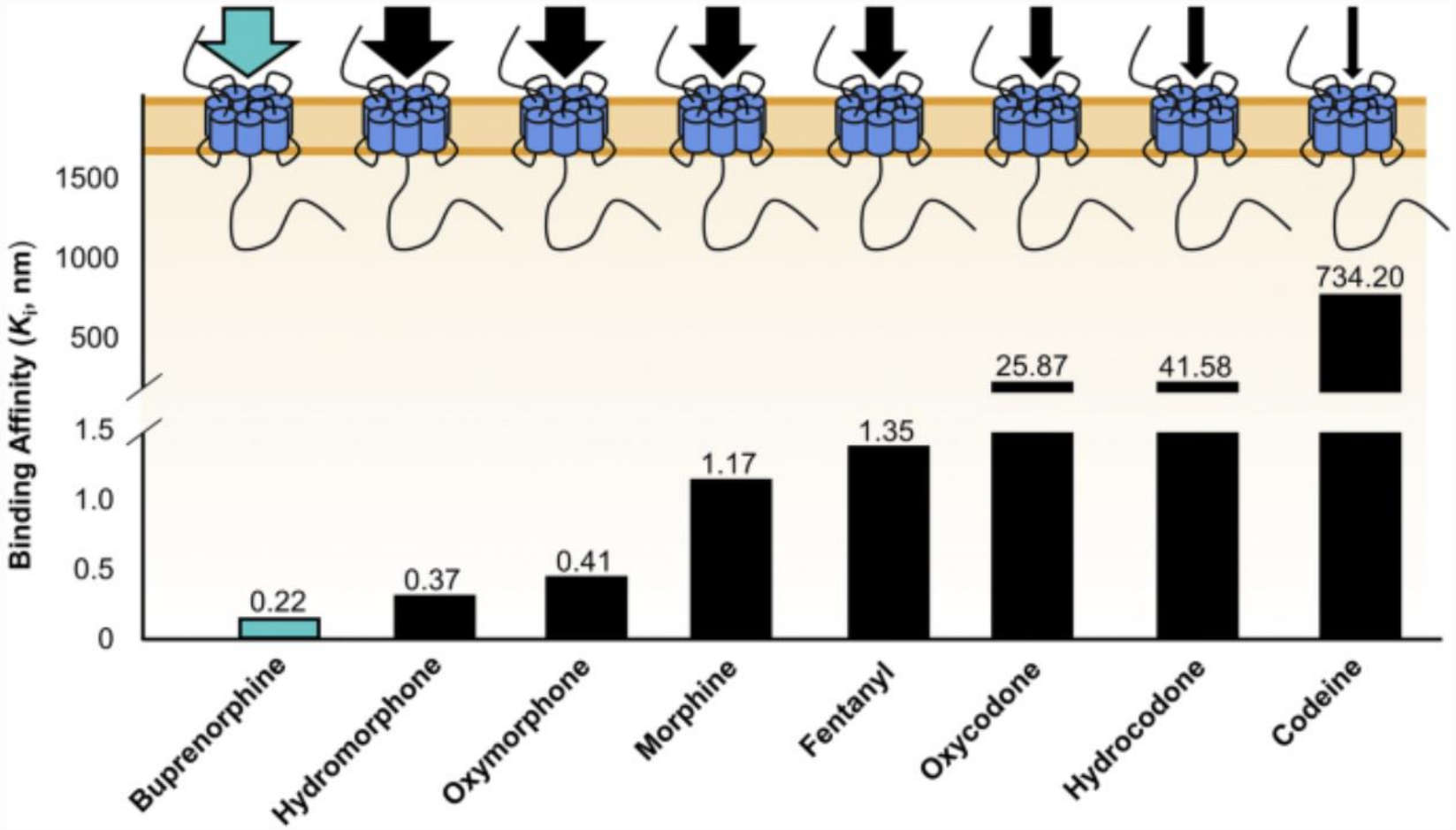
> Br J Anaesth. 2019 Aug;123(2):e333-e342. doi: 10.1016/j.bja.2019.03.044. Epub 2019 May 29.

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]

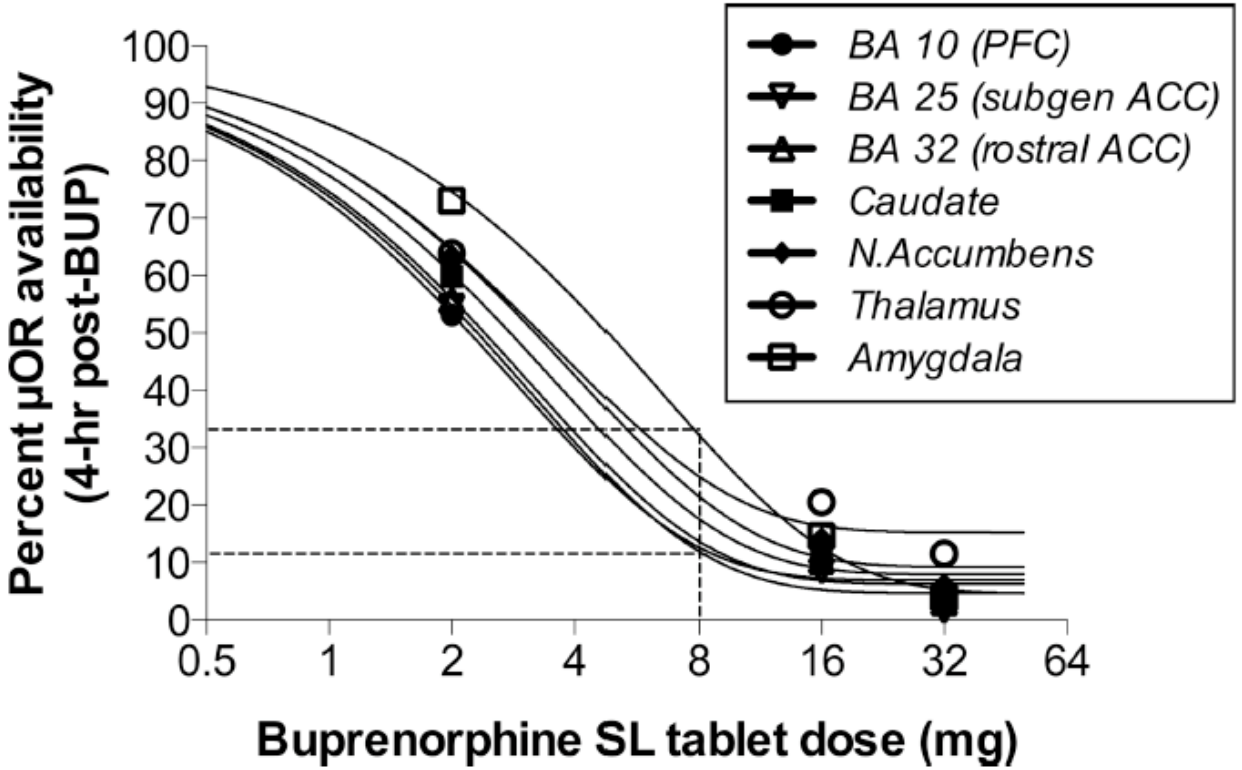
- Continuing buprenorphine occupies the receptors making them unavailable for other opioids
  - Does this provide poorer analgesia?

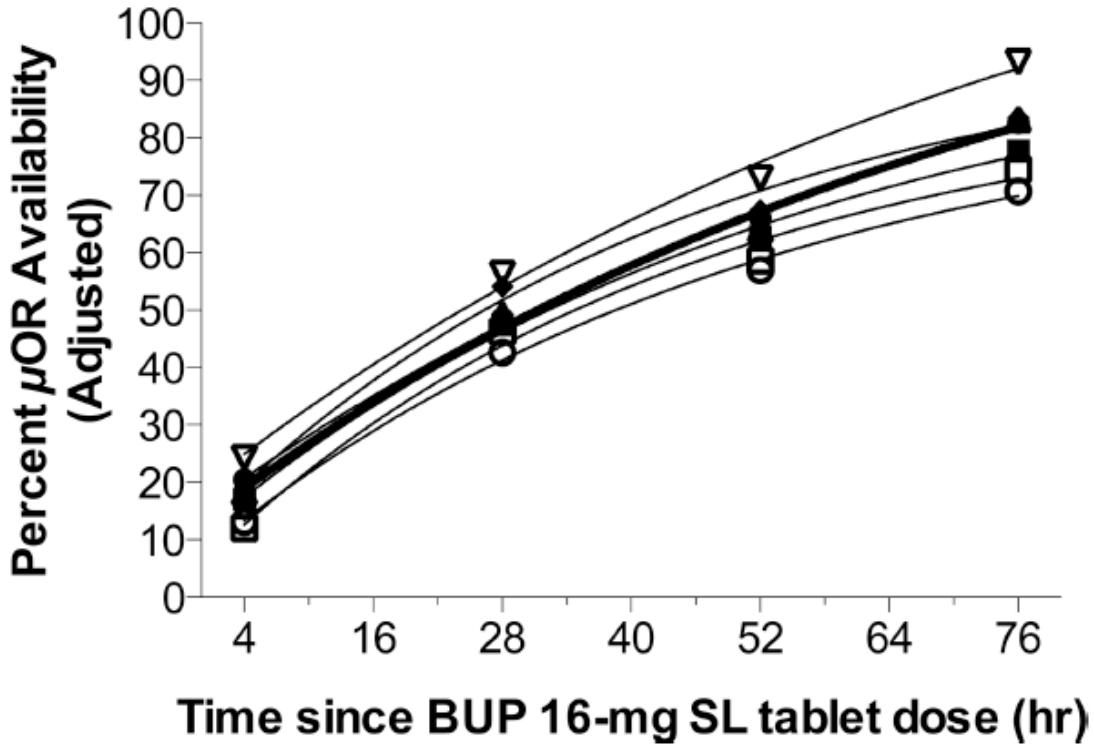
Fig. 1



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





Greenwald MK, Comer SD, Fiellin DA. Buprenorphine maintenance and mu-opioid receptor availability in the treatment of opioid use disorder: implications for clinical use and policy. *Drug Alcohol Depend* 2014;144:1–11

Multi-Society Working Group Recommendations

U.S. Preventive Services
TASK FORCE

Preoperative Pain

Grade B
Moderate Level of Certainty

Buprenorphine **should not** be routinely discontinued

Discontinuing buprenorphine in patients with OUD increases risk of relapse or harm

Home dose of buprenorphine should not be routinely tapered prior to surgery

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

Postoperative Pain

Grade B
Moderate Level of Certainty

Utilize multimodal analgesia in patients receiving buprenorphine for MOUD

Consider administration of short-acting full mu agonists with close monitoring for uncontrolled pain if/when multimodal analgesia is inadequate

Postoperative Pain

Grade C
Low Level of Certainty

Consider increasing and/or dividing doses of buprenorphine with close monitoring for uncontrolled pain if/when multimodal analgesia is inadequate

Discharge Planning

Grade A
Moderate Level of Certainty

Provide post-operative plan to taper off full mu agonists or return to preoperative maintenance dose of buprenorphine

Collaborate and discuss plan with patient's outpatient opioid prescriber

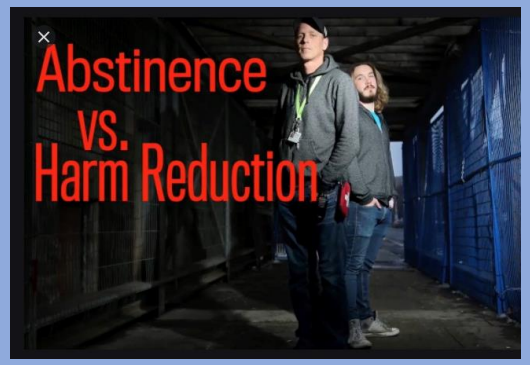
What about the pt not on buprenorphine?

- The patient has pain <u>and</u> an Untreated Opioid Use Disorder (OUD)

- The patient has pain <u>and</u> you suspect the patient has an OUD

Why start buprenorphine in the hospital?

Patients may recognize they have a problem and are ready to change



Forced abstinence may allow time to consider a change

Realization that use disorder is impacting relations with family and friends

Non judgmental care team.

Evidence

- Buprenorphine can safely be initiated in hospitalized pts, promotes engagement in outpt SUD care and increases chances of MOUD
  - Leibschultz et al:
    - Lower rates of illicit opioid use at a 6 month follow up period among hospitalized pts who had been initiated on buprenorphine and linked to buprenorphine treatment upon discharge
    - Hospital Buprenorphine initiation vs detox resulted in greater long term use od MOUD upon discharge

Liebschultz JM et al 2014; Wei J et al 2015]]

Liebschutz JM, Crooks D, Herman D, Anderson B, Tsui J, Meshesha LZ, Dossabhoy S, Stein M . Buprenorphine treatment for hospitalized, opioid-dependent patients: a randomized clinical trial. *JAMA Intern Med. 2014 Aug; 174(8):1369-76;*

Wei J, Defries T, Lozada M, Young N, Huen W, Tulsky J. An inpatient treatment and discharge planning protocol for alcohol dependence: efficacy in reducing 30-day readmissions and emergency department visits. *J Gen Intern Med. 2015 Mar; 30(3):365-70.*

Practice Guideline > Ann Emerg Med. 2020 Sep;76(3):e13-e39.
doi: 10.1016/j.annemergmed.2020.06.049.

Clinical Policy: Critical Issues Related to Opioids in Adult Patients Presenting to the Emergency Department

American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Opioids;
Benjamin W Hatten, Stephen V Cantrill, Jeffrey S Dubin, Eric M Ketcham, Daniel P Runde, Stephen P Wall, Stephen J Wolf

The way many providers handle discussing substance abuse with their patients

https://media.istockphoto.com/photos/head-in-the-sand-picture-id157507641?k=6&m=157507641&s=612x612&w=0&h=gpDPHKmIgXkh5lbJwIQD-kWRoTE0KSNmxsl3cs0-4x8=

ARTICLE IN PRESS

EMERGENCY MEDICAL SERVICES/CONCEPTS

Legal Authority for Emergency Medical Services to Increase Access to Buprenorphine Treatment for Opioid Use Disorder

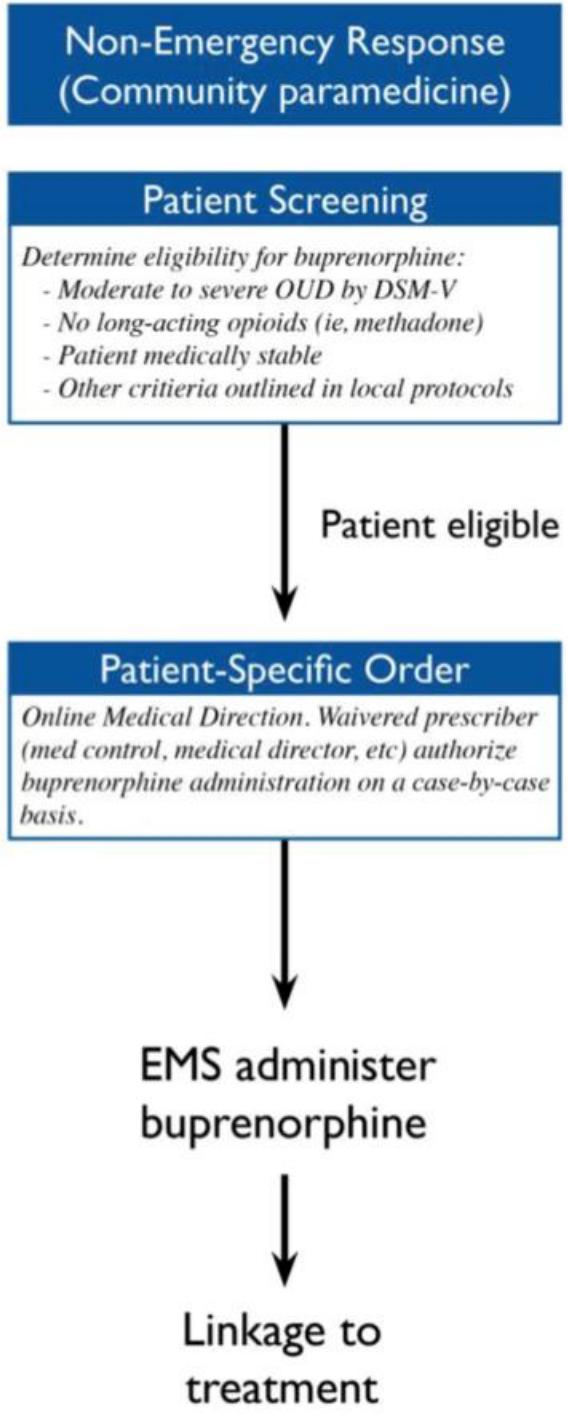
Corey S. Davis, JD, MSPH*; Derek H. Carr, JD; Melody J. Glenn, MD; Elizabeth A. Samuels, MD, MPH

Ann Emerg Med. 2021;.:1-7.

NATIONAL ACADEMY of MEDICINE

Improving Access to Evidence-Based Medical Treatment for Opioid Use Disorder: Strategies to Address Key Barriers Within the Treatment System

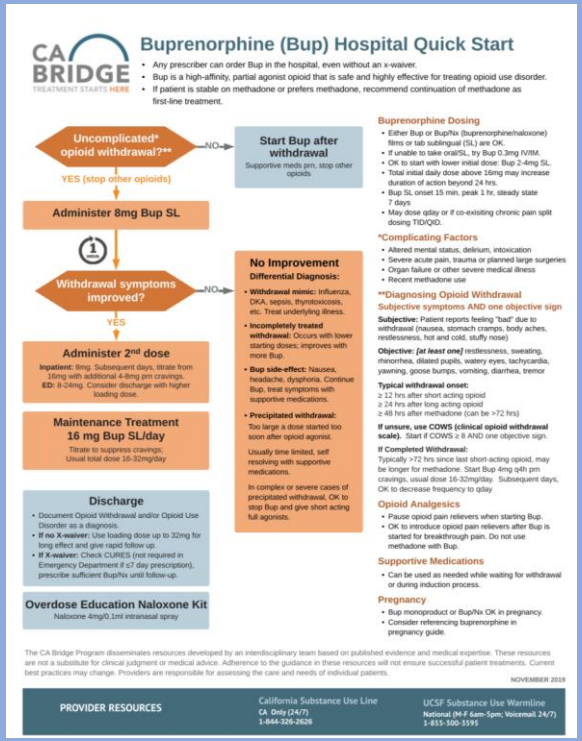
By Bertha K. Madras, N. Jia Ahmad, Jenny Wen, Joshua Sharfstein, and the Prevention, Treatment, and Recovery Working Group of the Action Collaborative on Countering the U.S. Opioid Epidemic



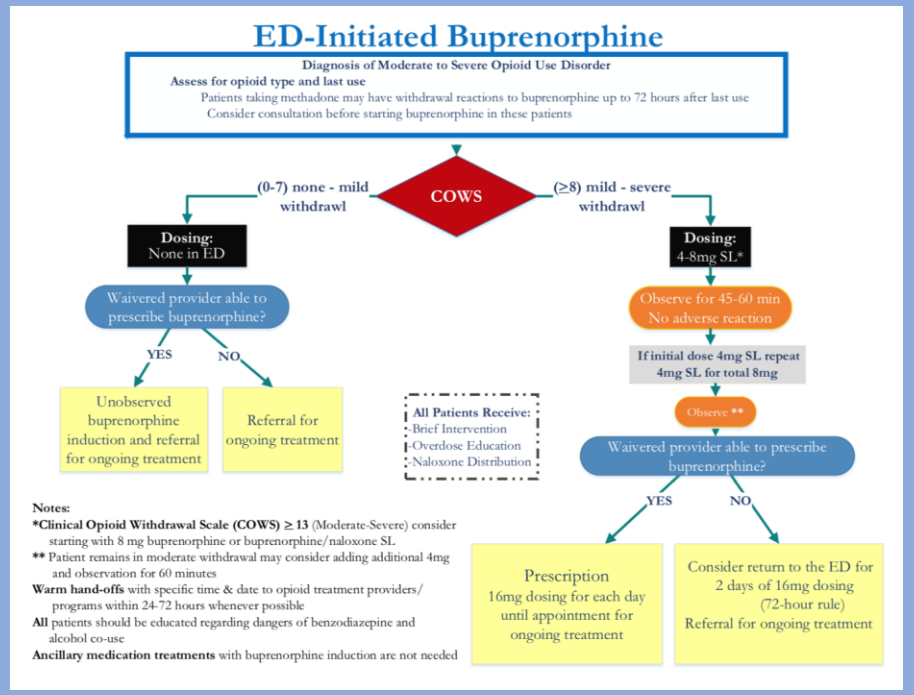
How do I initiate buprenorphine?

Evidence from ER literature

Buprenorphine 4-8 mg safely initiated

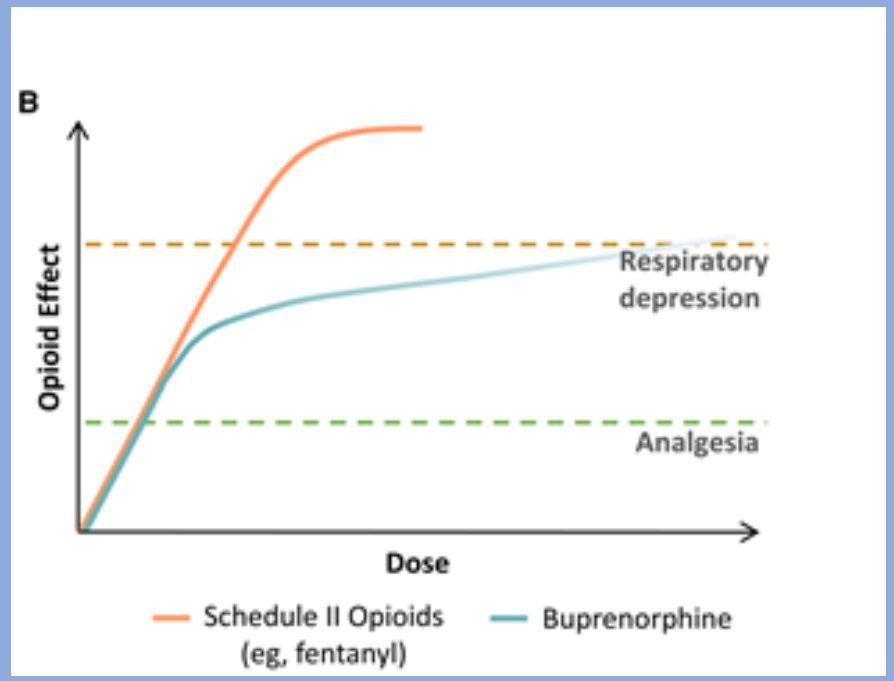


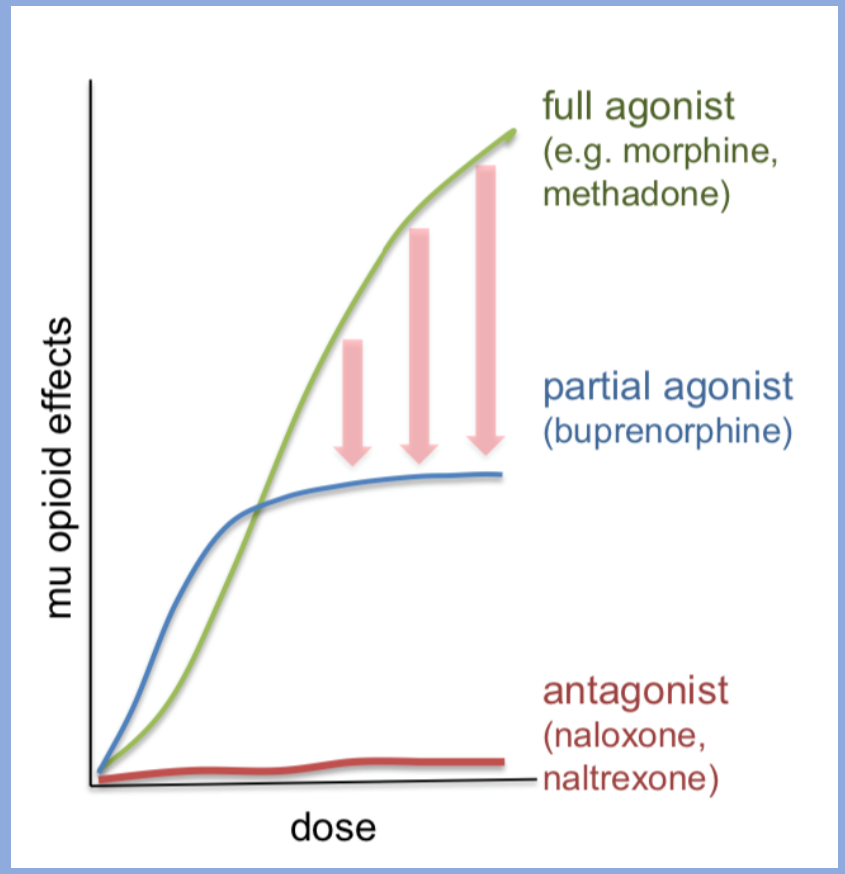
https://static1.squarespace.com/static/5c412ab755b02cec3b4ed998/t/5dc255df2d46c2731a7b366c/1573017059129/CA+Bridge+-+Protocol+-+Bup+Hospital+Quick+Start+-+NOV+2019.pdf



https://www.drugabuse.gov/nidamed-medical-health-professionals/discipline-specific-resources/emergency-physicians-first-responders/initiating-buprenorphine-treatment-in-emergency-department

Buprenorphine





Webster et al. 2020

PCSS Providers Clinical Support System

How to Initiate Inpatient Buprenorphine for a Patient with Suspected Opioid Use Disorder in the Perioperative Period

DAY 1

Patient interest in buprenorphine identified; consult addiction medicine, psych service, and/or acute pain service, if available.

Assess for contraindications.

Contraindications to initiating buprenorphine therapy for opioid use disorder:

1. Hypersensitivity to buprenorphine (or naloxone if combo product) or any listed ingredient
2. Elevated liver function >3x normal
3. Active intoxication/impairment with other CNS depressants (ie, alcohol, sedatives, etc.)
4. Patient refusal

if on IV PCA

Hold IV PCA for 1-3 hrs

if on oral opioids*

Hold full mu agonist 4-6 hours

* If patient taking methadone, do NOT use this algorithm.

Give 2 mg/0.5 mg buprenorphine/naloxone sublingual.

Wait 1 hour, then reassess:

Subjective Opioid Withdrawal Scale/ Clinical Opiate Withdrawal Scale

Give 2 mg/0.5 mg buprenorphine/naloxone sublingual **as tolerated** q 1 hr prn pain or subjective feelings of withdrawal.

Max of16 mg buprenorphine every day.**

**Rarely, 24 mg may be needed. If increasing more than 16 mg/day, we strongly recommend consulting with an addiction specialist.

DAY 2

Schedule post-discharge follow-up visit with addiction medicine specialist or treatment facility.

Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9.

COWS Clinical Opiate Withdrawal Scale

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 Pulse rate 80 or below 1 Pulse rate 81-100 2 Pulse rate 101-120 4 Pulse rate greater than 120	GI Upset: *over last 1/2 hour* 0 No GI symptoms 1 Stomach cramps 2 Nausea or loose stool 3 Vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 No report of chills or flushing 1 Subjective report of chills or flushing 2 Flushed or observable moistness on face 3 Beads of sweat on brow or face 4 Sweat streaming off face	Tremor *observation of outstretched hands* 0 No tremor 1 Tremor can be felt, but not observed 2 Slight tremor observable 4 Gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 Able to sit still 1 Reports difficulty sifting still, but is able to do so 3 Frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	Yawning *Observation during assessment* 0 No yawning 1 Yawning once or twice during assessment 2 Yawning three or more times during assessment 4 Yawning several times/minute
Pupil size 0 Pupils pinned or normal size for room light 1 Pupils possibly larger than normal for room light 2 Pupils moderately dilated 5 Pupils so dilated that only the rim of the iris is visible	Anxiety or irritability 0 None 1 Patient reports increasing irritability or anxiousness 2 Patient obviously irritable anxious 4 Patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 Not present 1 Mild diffuse discomfort 2 Patient reports severe diffuse aching of joints/ muscles 4 Patient is rubbing joints or muscles and is unable to sit still because of discomfort	Gooseflesh skin 0 Skin is smooth 3 Piloerrection of skin can be felt or hairs standing up on arms 5 Prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 Not present 1 Nasal stuffiness or unusually moist eyes 2 Nose running or tearing 4 Nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing Assessment:_____

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

Multi-Society Working Group Recommendations

U.S. Preventive Services
TASK FORCE

Starting Buprenorphine, in the perioperative period, in pt with suspected MOUD

Grade B
Moderate Level of Certainty

When possible Anesthesiologists/pain physicians consider starting buprenorphine for post-operative analgesia in patients with suspected OUD

When possible Anesthesiologists/pain physicians should help facilitate linkage to outpatient buprenorphine prescribers

Starting Buprenorphine, in the perioperative period, in pt with suspected MOUD

Grade C
Low Level of Certainty

Anesthesiologists can still consider initiating buprenorphine even if follow up with an outpatient buprenorphine provider has not been established

It is the group's consensus to advocate for the elimination of barriers to prescribing buprenorphine for patients with OUD.

We also advocate the physicians obtain education in MOUD and x-waiver certification.

Summary

- OUD is a public health crisis
- There is a gap between pt's with OUD and those receiving tx
- We are in a prime position to be able to do something
- Buprenorphine can be safely initiated in the perioperative setting by anesthesia led teams
  - Linkage to outpatient buprenorphine prescriber is recommended

Do I need an X-waiver?

Drug Addiction Treatment Act (DATA) 2000

- Permitted qualified physicians to treat opioid addiction with Schedule III, IV, and V medications (i.e. only bup)
- Requires 8 hours of training for physicians, 24 hours for APPs
- DEA will have an "X" at the beginning when prescribing milligram-dose buprenorphine for OUD
- Apply to SAMHSA (Substance Abuse Mental Health Services Administration) to complete waiver process
- "The practitioner [must have] the capacity to **provide** directly, by referral, [or in another manner] **appropriate counseling and other appropriate ancillary services**."

Slide from Sudheer Potru

Statutes, Regulations, and Guidelines. *SAMHSA.* Accessed September 1, 2021. https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines

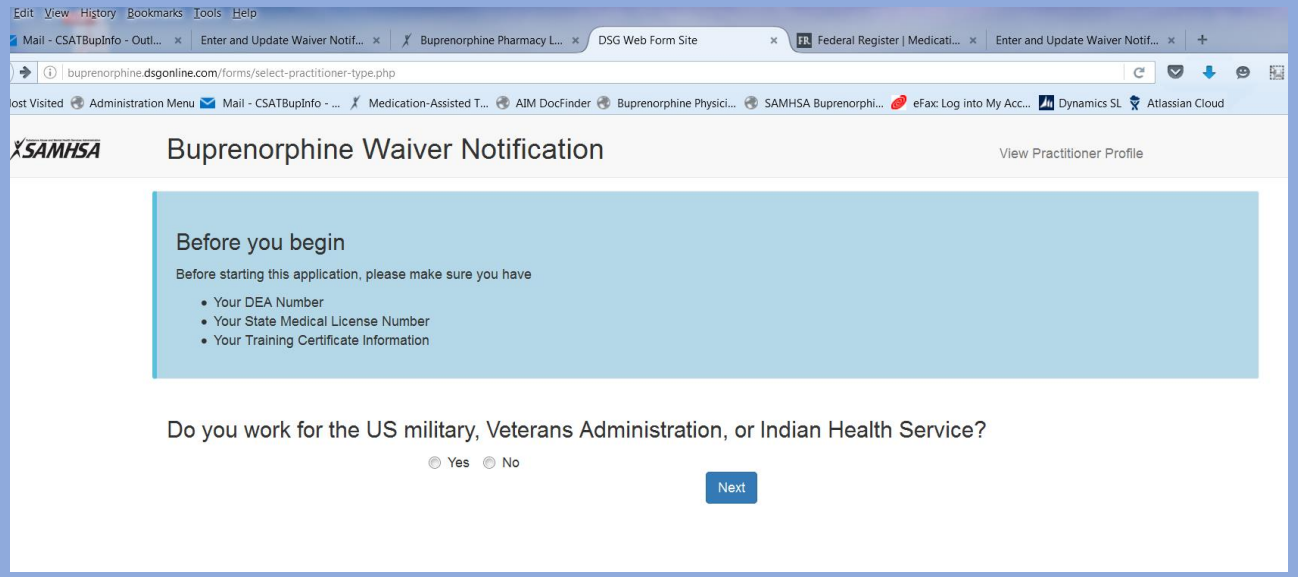
HHS Removes Training Requirement (4/28/21)

Under certain conditions, the attached Practice Guidelines exempt eligible physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, and certified nurse midwives (hereinafter collectively referred to as "practitioners"), from the certification requirements related to training, counseling and other ancillary services (i.e., psychosocial services) under 21 U.S.C. 823(g)(2)(B)(i)-(ii). This action is needed in order to expand access to buprenorphine for opioid use disorder treatment. Specifically, the exemption allows these practitioners to treat up to 30 patients with OUD using buprenorphine without having to make certain training related certifications. This exemption also allows practitioners to treat patients with buprenorphine without certifying as to their capacity to provide counseling and ancillary services. This exemption

Slide from Sudheer Potru

Department of Health and Human Services, Clinical Practice Guidelines for the Use of Buprenorphine for Opioid Use Disorder (4/28/21)

Submit a 30 Patient Notification of Intent (NOI) Form



https://buprenorphine.samhsa.gov/forms/select-practitioner-type.php

SAMHSA Buprenorphine Practitioner Locator

SAMHSA
Substance Abuse and Mental Health Services Administration

Home | Site Map | Contact Us

Search SAMHSA.gov Search

Main menu

- **Medication-Assisted Treatment**
- MAT Medications, Counseling, and Related Conditions
- Find Medication-Assisted Treatment
- Become a Buprenorphine Waivered Practitioner
- Find Buprenorphine Waiver Training
- Buprenorphine Practitioner Resources and Information
- Pharmacist Verification of Buprenorphine Providers
- Become an Accredited and Certified Opioid Treatment Program (OTP)
- OTP Resources and Information
- State Opioid Treatment Authority (SOTA)
- Statutes, Regulations, and Guidelines
- Training Materials and Resources
- About SAMHSA's Division of Pharmacologic Therapies (DPT)

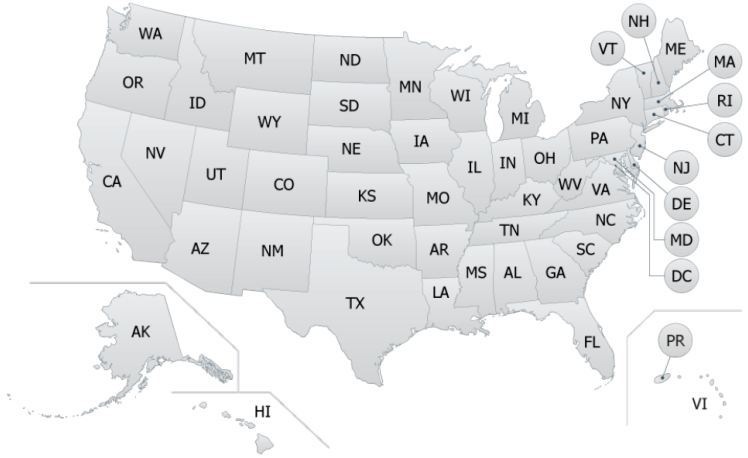
Buprenorphine Practitioner Locator

Find practitioners authorized to treat opioid dependency with buprenorphine by state.

Select a state from the map or use the drop down lists to view all of the practitioners waived to provide buprenorphine for the treatment of OUD in a city, state or zip code.

Please note that this list only contains the contact information from practitioners who consent to release their practice information. Therefore, this list is not inclusive of all waivered practitioners.

Practitioners are responsible for updating their contact information. To update practice information, complete the Update Practitioner Profile form.



ZIP Code: 30324

Distance from ZIP: 25 Miles

City:

State: - Any -

- Any -

Apply | Reset

Slide from Sudheer Potru

https://www.samhsa.gov/medication-assisted-treatment/practitioner-program-data/treatment-practitioner-locator?field_bup_lat_lon_proximity%5Bvalue%5D=25&field_bup_lat_lon_proximity%5Bsource_configuration%5D%5Borigin_address%5D=30324&field_bup_city_value=&field_bup_state_value=All

Should our anesthesia/pain trainees get X-waivers?

Daring discourse

One prescription for the opioid crisis: require buprenorphine waivers for pain medicine fellows

Mark C Bicket ,[1,2] Shravani Durbhakula[1]

Editorial

One prescription for the opioid crisis: require buprenorphine waivers for pain medicine fellows

Lynn Kohan

THE ASSOCIATION OF PAIN PROGRAM DIRECTORS
ADVANCING EDUCATION IN MULTIDISCIPLINARY PAIN MEDICINE

Dear Pain Medicine Fellowship Program Directors,

The APPD is hosting the PCSS 2021 MAT Waiver Eligibility Training for your fellows. The four-hour live session will be split into two, two-hour sessions on:

- **Wednesday, August 18 from 8-10 pm ET**
- **Wednesday, August 25 from 8-10 pm ET**

This virtual course for pain fellows comprises the second half of the relevant training and education to better understand how to prescribe buprenorphine for opioid use disorder. The instructor, Dr. Sudheer Potru, is an assistant professor at the Emory University School of Medicine and a triple-board-certified anesthesiologist, pain physician, and addiction medicine specialist who actively prescribes buprenorphine for both pain and opioid use disorder.

Bicket MC, Durbhakula S. *Reg Anesth Pain Med* December 2019 Vol 44 No 12

Kohan L. *Reg Anesth Pain Med* 2019;**44**:1043–1044. doi:10.1136/rapm-2019-100907