Buprenorphine for Chronic Pain/OUD

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Disclaimer

NOTE:

This presentation was prepared by Dr. Sudheer Potru, DO, with some assistance in slide preparation from Dr. Thomas Hickey. The opinions expressed in this presentation do not reflect the views of the Department of Veterans Affairs or the United States Government.

I have no relevant financial disclosures.

Outline/Objectives

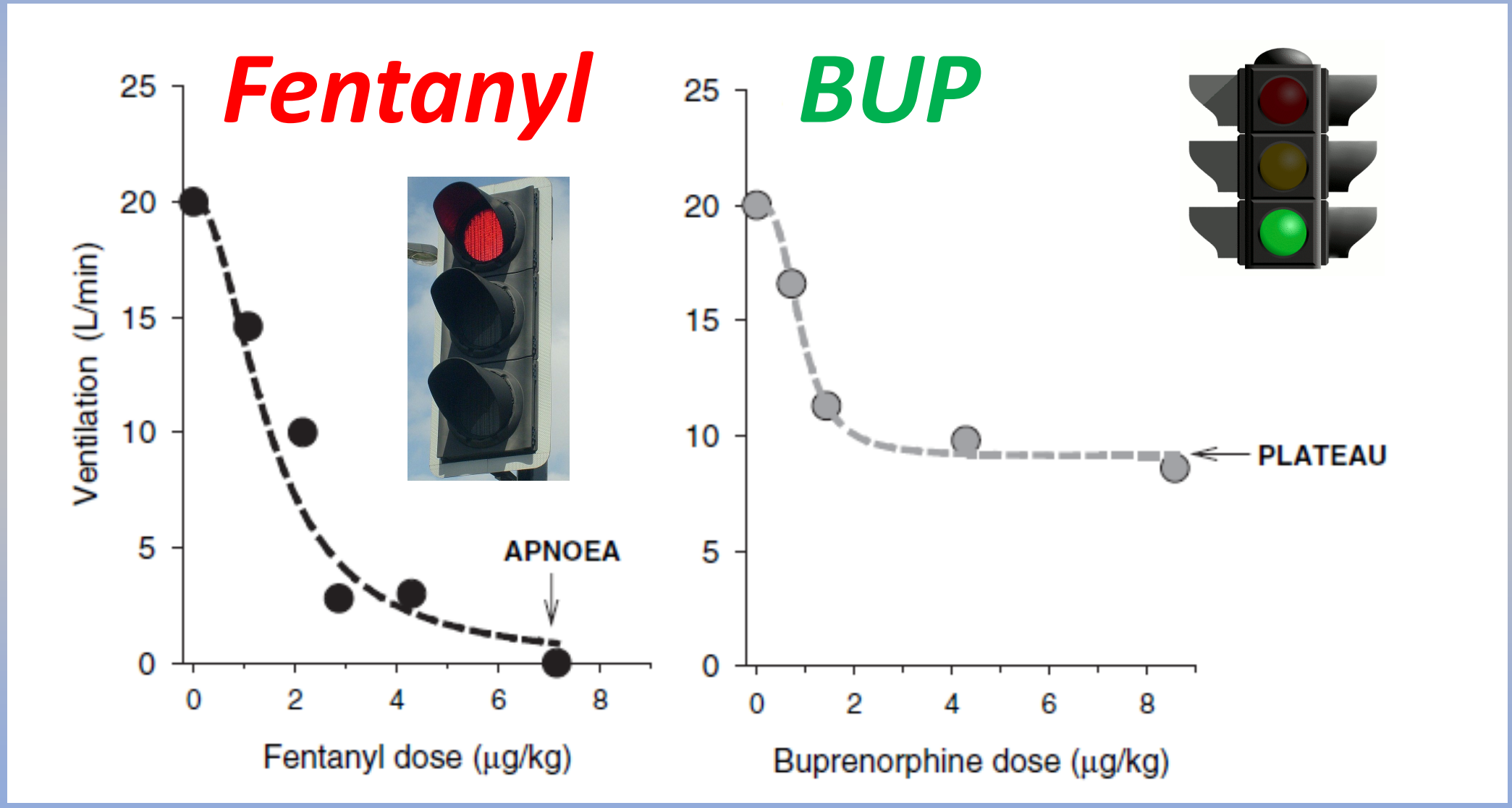
BUP: Key Safety Advantages

Dosing

Data, data, everywhere

Tricky Situations

Respiratory Depression: Fentanyl vs BUP



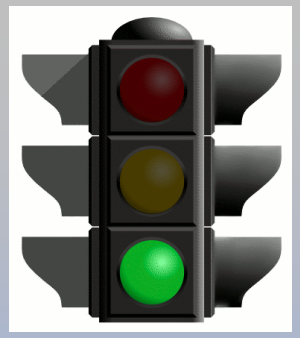
Dahan A. Opioid-induced respiratory effects: new data on buprenorphine. Palliat Med. 2006.

Safety: Respiratory

A Phase I Placebo-Controlled Trial Comparing the Effects of Buprenorphine Buccal Film and Oral Oxycodone Hydrochloride Administration on Respiratory Drive

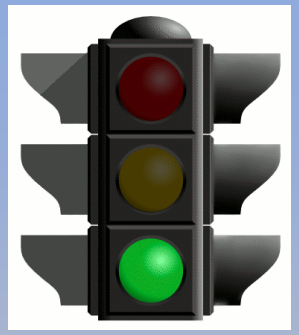
Webster et al. Adv Ther. 2020.

Buprenorphine buccal film did not significantly reduce respiratory drive at any dose compared with placebo



Administration of oxycodone resulted in a significant dose-dependent decrease in respiratory drive

Safety: Respiratory



Clinical pharmacology of buprenorphine: Ceiling effects at high doses

Walsh et al. Clin Pharmacol Ther. 1994

Escalating SL doses up to 32mg

- Caused Max Respiratory Depression…
- …of ***only*** 4 breaths per minute

Safety: Respiratory (Moss 1/2)

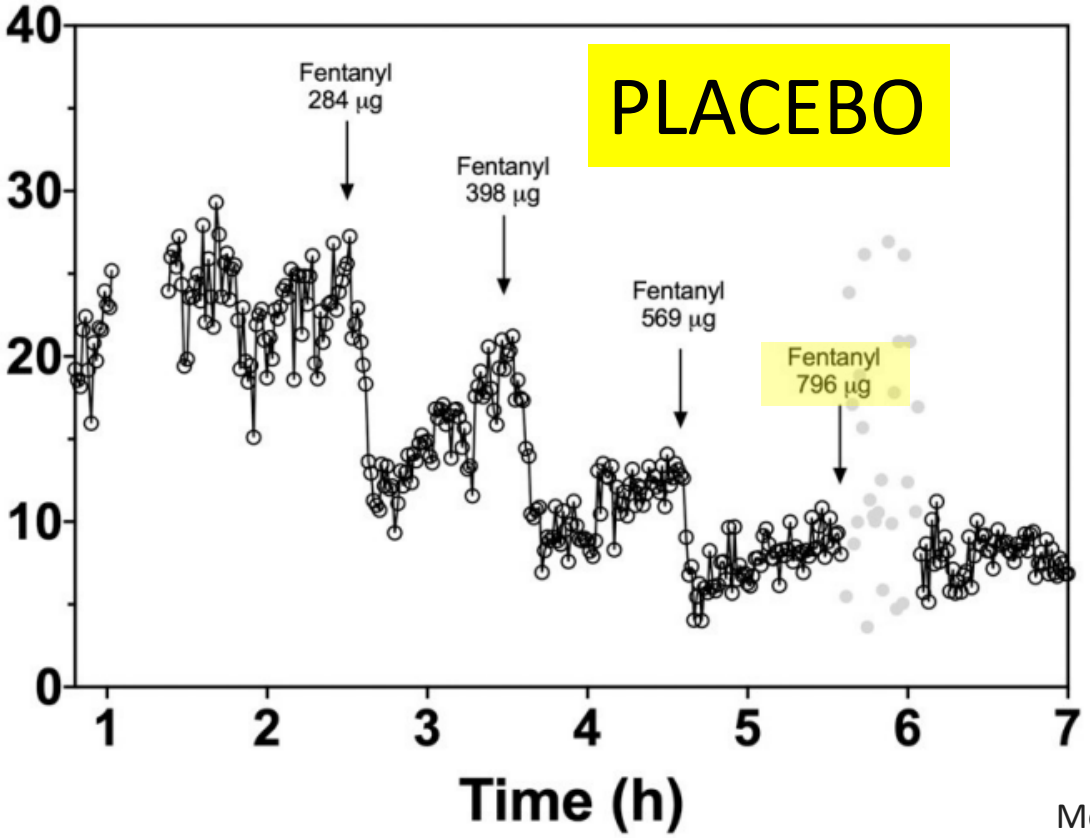
RESEARCH ARTICLE

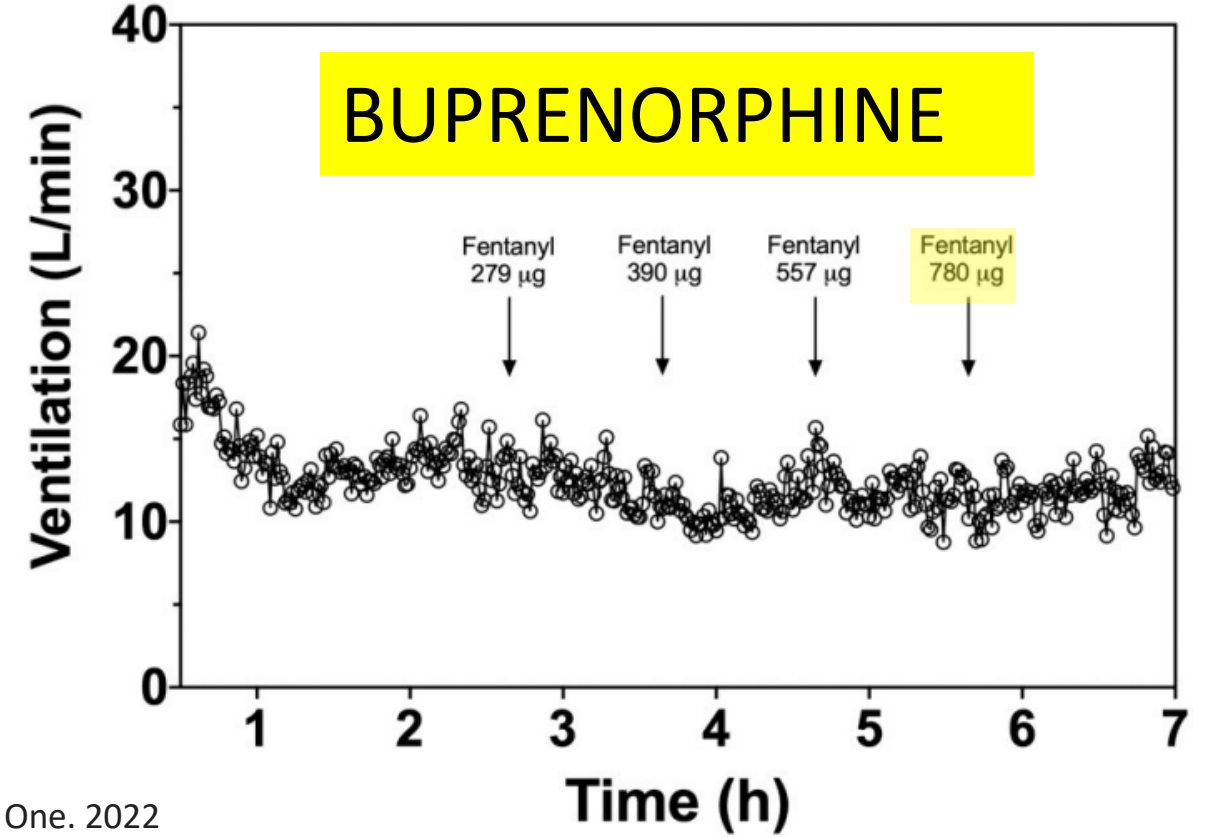
Effect of sustained high buprenorphine plasma concentrations on fentanyl-induced respiratory depression: A placebo-controlled crossover study in healthy volunteers and opioid-tolerant patients

Moss et al. PLoS One. 2022

Safety: Respiratory (Moss 2/2)

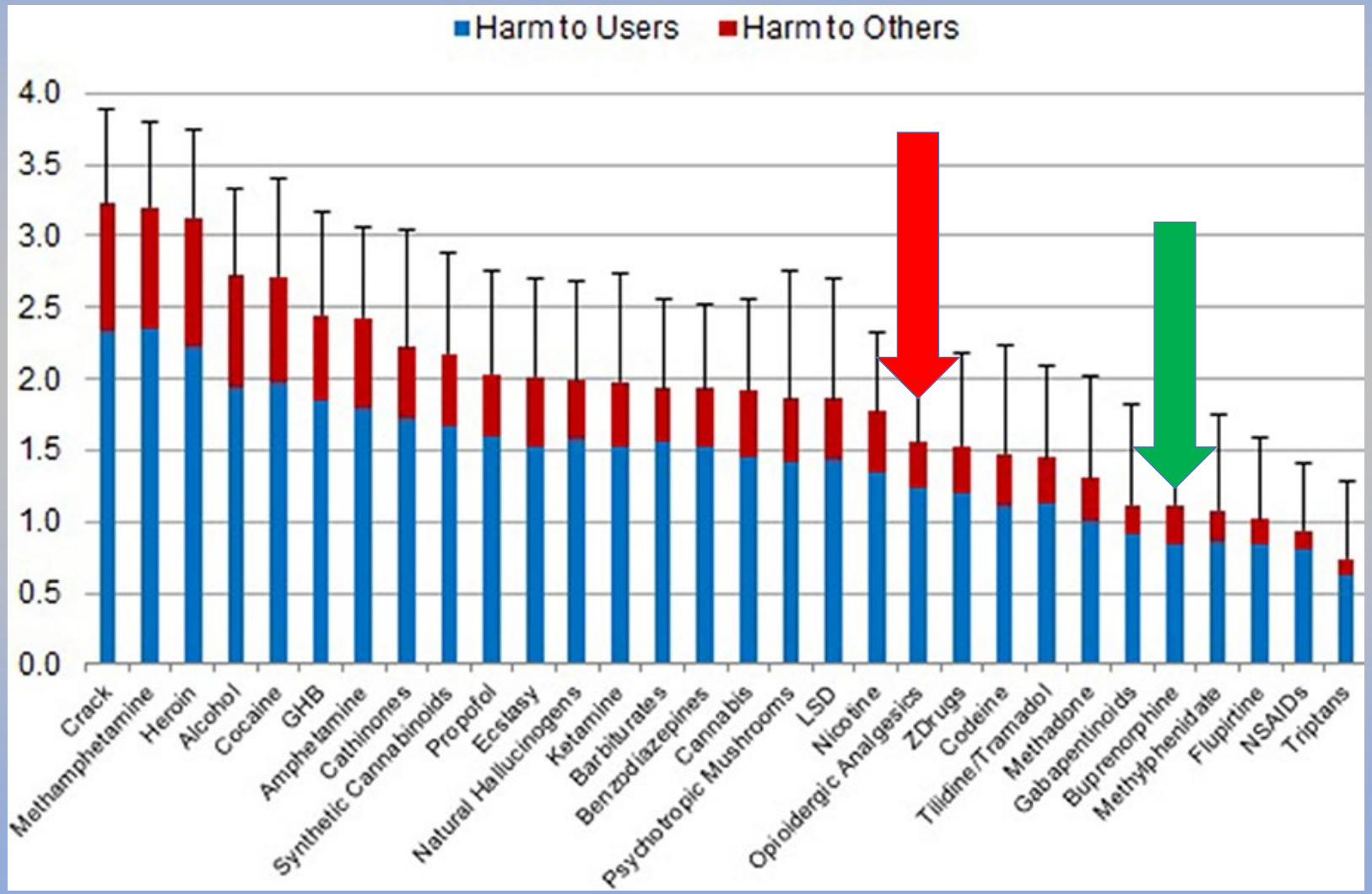
Opioid Tolerant Group





Moss et al. PLoS One. 2022

BUP: Safety Advantages



- Expert Opinion: Rate harms of 33 substances…
- FAO > BUP > NSAIDs

Bonnet U, Ranking the Harm of Psychoactive Drugs Including Prescription Analgesics. Front Psychiatry. 2020 PMID: 33192740.

Lessons from Chronic Pain: Buprenorphine is safer!!

Twelve Reasons for Considering Buprenorphine as a Frontline Analgesic in the Management of Pain

Mellar P. Davis, MD, FCCP, FAAHPM

Davis MP. J Support Oncol. 2012

Treats Multiple Pain Phenotypes: Cancer, neuropathic

Less tolerance

Less constipation

Less cognitive impairment

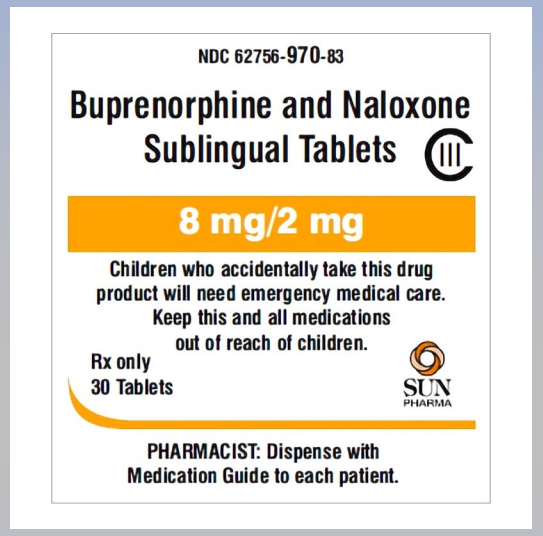
Less immunosuppression

Safety in renal failure, moderate liver disease

Milder withdrawal syndrome

So how do we dose it?

Dosing (SL): OUD >> Analgesia

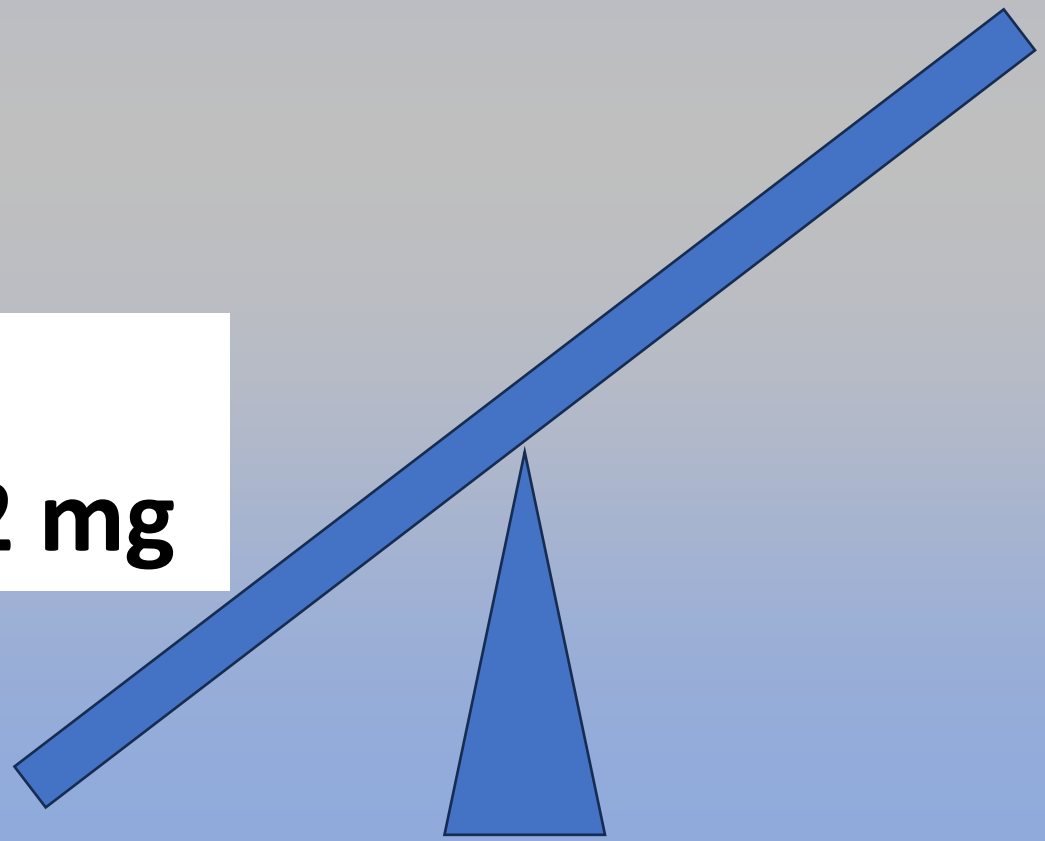


Pain

0.76 mg

OUD

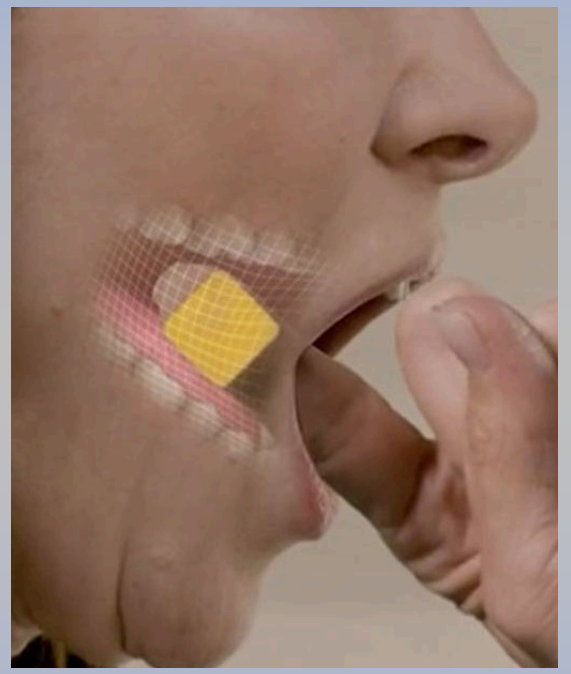
16-32 mg



Chronic Pain Approved

OUD Approved

Chronic Pain Approved



QWeek

QD vs. BID vs. TID

Buccal (BID)

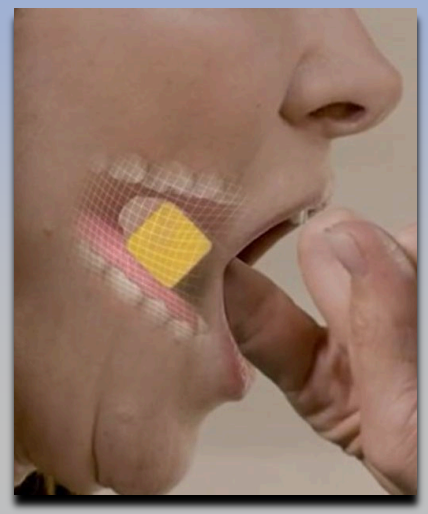
Formulation Pharmacokinetics

- Onset – 18-24 h
- Cmax – 3 days
- Duration – 7 days

Foster B et al. Buprenorphine, *J Pain Symptom Mgmt*, 2013

- Onset – 20min
- Cmax – 1.5h
- Duration – 8-12h

McAleer SD, et al. *Drug Alcohol Depend*. 2003

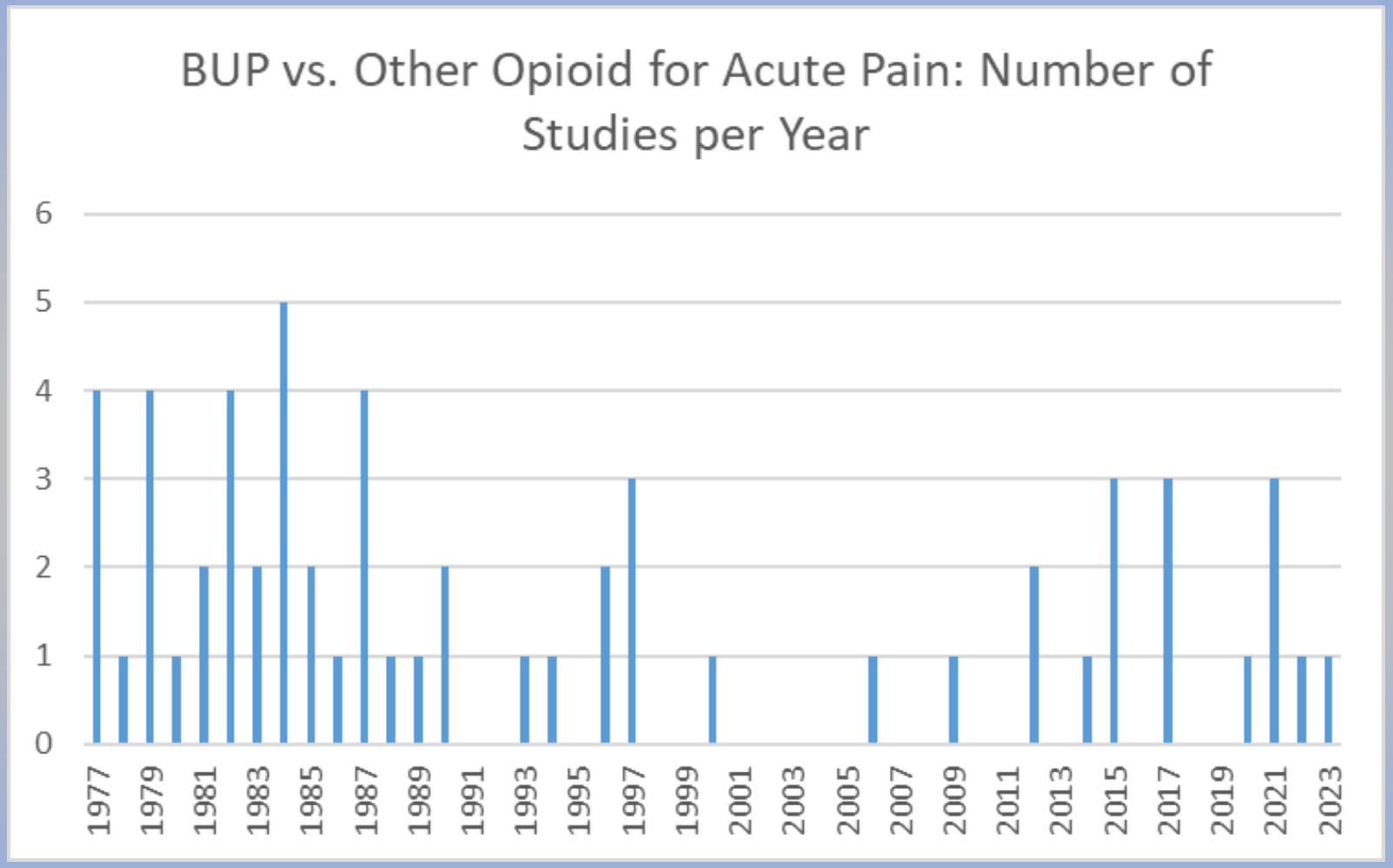


- Onset – 20min
- Cmax – 2h
- Duration – 8-12h

Webster LR, Cater J, Smith T. *Pain Ther*. 2022

So it’s safe…does it work for pain?

BUP for Pain – Discovery, Decline, Rediscovery



1966 Synthesis → 1982 IV (Acute Pain) → 2010 Transdermal (Chronic Pain) → 2015 Buccal (Chronic Pain)

Myth: Partial Analgesia

Randomized Controlled Trial > Clin J Pain. 2012 Sep;28(7):623-7.

doi: 10.1097/AJP.0b013e31823e15cb.

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Randomized Controlled Trial > Pain. 2005 Nov;118(1-2):15-22. doi: 10.1016/j.pain.2005.06.030.

Epub 2005 Sep 9.

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Randomized Controlled Trial > Basic Clin Pharmacol Toxicol. 2011 Apr;108(4):274-84.

doi: 10.1111/j.1742-7843.2010.00649.x. Epub 2010 Dec 8.

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Comparative Study > J Clin Pharm Ther. 2014 Dec;39(6):577-83. doi: 10.1111/jcpt.12196.

Epub 20

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R B Raff
J K Tran,

Review > Reg Anesth Pain Med. 2025 Jan 2:rapm-2024-106014. doi: 10.1136/rapm-2024-106014.

Online ahead of print.

Buprenorphine versus full agonist opioids for acute postoperative pain management: a systematic review and meta-analysis of randomized controlled trials

Thomas R Hickey [1 2], Gabriel P A Costa [3], Debora Oliveira [4], Alexandra Podosek [5], Audrey Abelleira [6], Victor Javier Avila-Quintero [7], Joao P De Aquino [8 9]

Efficacy and adverse effects of buprenorphine in acute pain management: systematic review and meta-analysis of randomised controlled trials

L. D. White[1,2,*], A. Hodge[2], R. Vlok[3,4], G. Hu… Eastern[2] and T. M. Melhuish[3,5]

British Journal … esia, 120 (4): 668–678 (2018)

PAIN: JUST AS EFFECTIVE AS MORPHINE

- Primary Outcome:
  - Pain: …ast as effective
- Secondary O… e:
  - Pruritis: Less with buprenorphine

VAS mean difference pain (−0.29; 95% CI −0.62 to 0.03; **P = 0.07**)

Myth: Ceiling Effect?

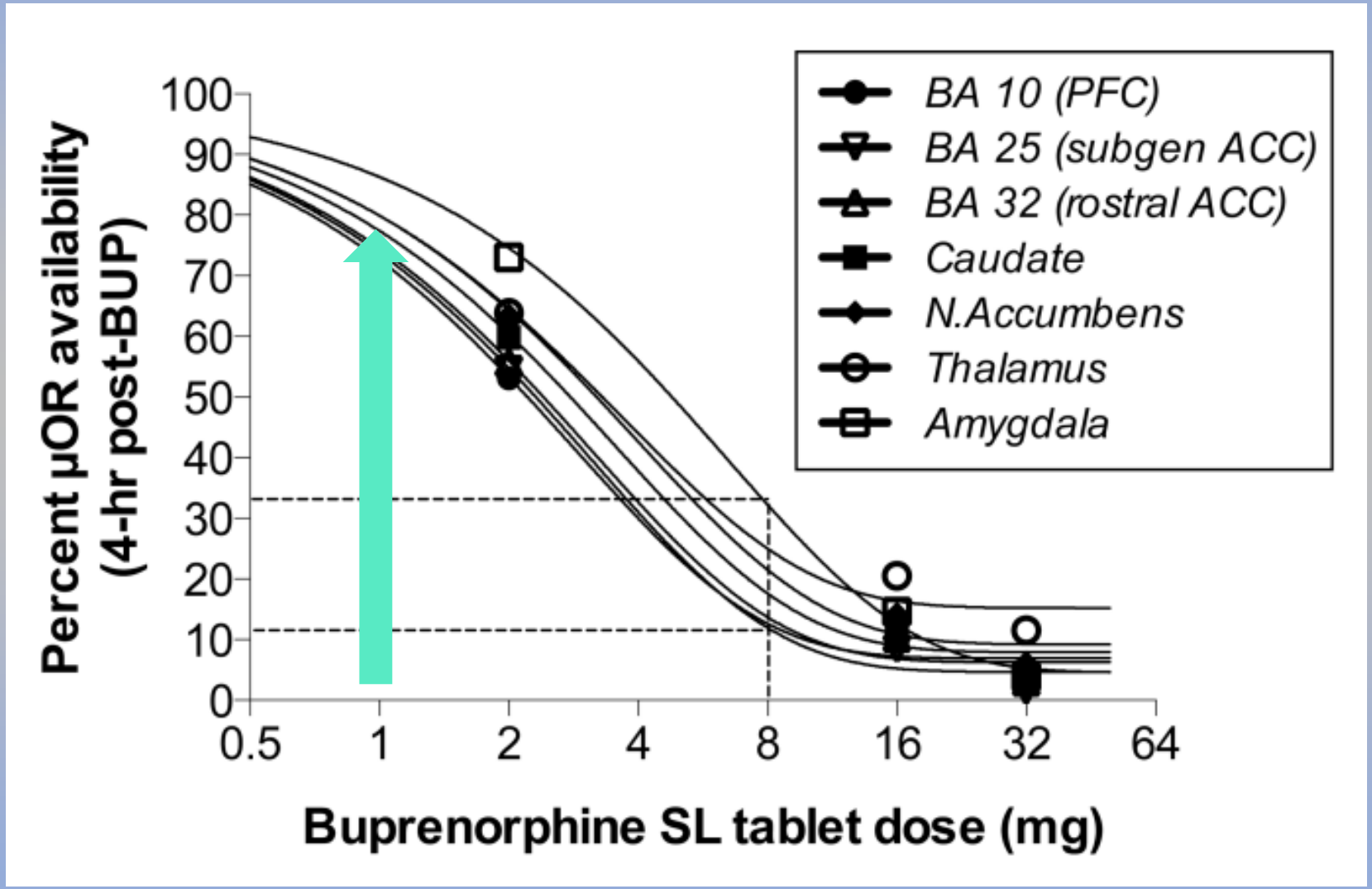
British Journal of Anaesthesia **96** (5): 627–32 (2006)
doi:10.1093/bja/ael051 Advance Access publication March 17, 2006

BJA

Buprenorphine induces ceiling in respiratory depression but not in analgesia

A. Dahan[1]*, A. Yassen[2], R. Romberg[1], E. Sarton[1], L. Teppema[1], E. Olofsen[1] and M. Danhof[2]

Myth: Interfere with Usual Opioids



Adapted from Greenwald MK, Comer SD, Fiellin DA. *Drug Alcohol Depend*. 2014

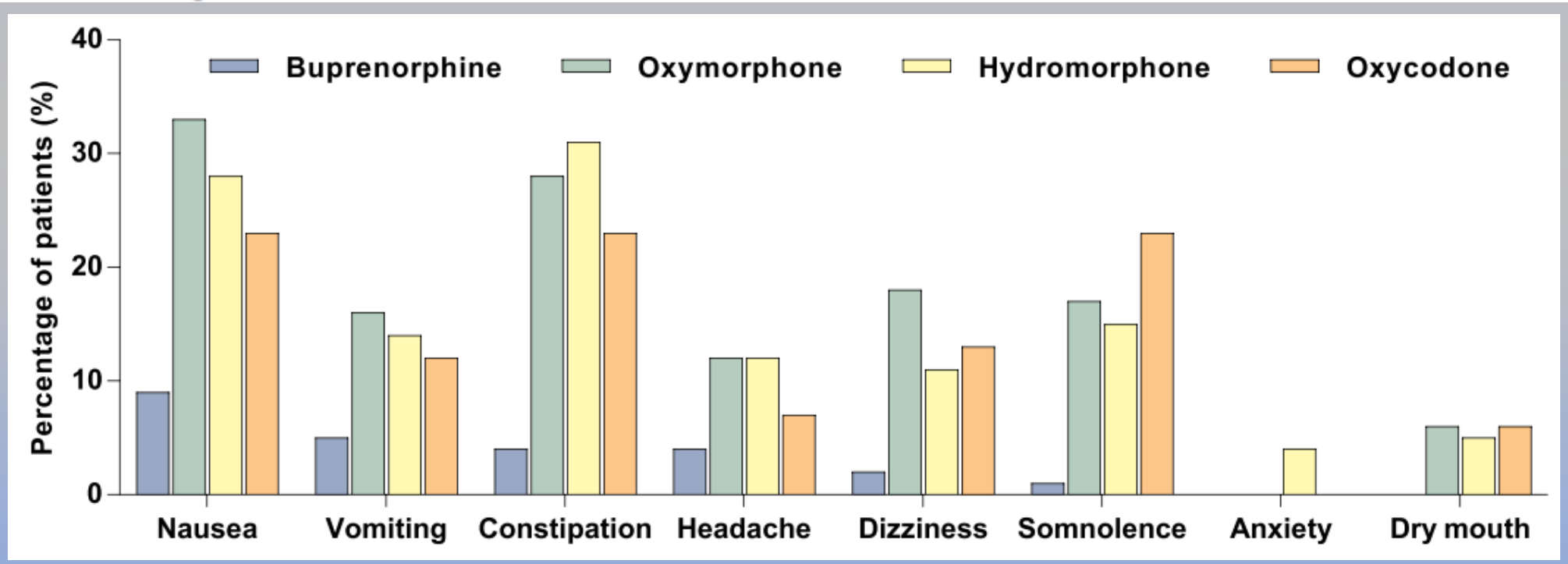
Myth: Interfere with Usual Opioids

Study	Design	Population	Intervention	Outcome
Oifa et al 2009	RCT	120 opioid-naïve patients - major abdominal surgery	Four arms of PCA bolus:infusion - BUP:BUP - BUP:morphine - Morphine:BUP - Morphine:morphine	- Pain **lowest** in BUP:BUP - PCA demand:deliver ratio **lowest** in BUP:BUP - Satisfaction **highest** in BUP:BUP - BUP did not inhibit morphine analgesia

Lessons from Chronic Pain: Buprenorphine works!!

Benefit-Risk Analysis of Buprenorphine for Pain Management

Hale M, Garofoli M, Raffa RB. J Pain Res. 2021 May 24;14:1359-1369.



Original Investigation | Substance Use and Addiction

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

A Systematic Review

Victoria D. Powell, MD; Jack M. Rosenberg, MD; Avani Yaganti, BS; Claire Garpestad, MD; Pooja Lagisetty, MD, MSc; Carol Shannon, MPH; Maria J. Silveira, MD, MA, MPH

FINDINGS A total of 22 studies were analyzed, of which 5 (22.7%) were randomized clinical trials, 7 (31.8%) were case-control or cohort studies, and 10 (45.5%) were uncontrolled pre-post studies, which involved 1616 unique participants (675 female [41.8%] and 941 male [58.2%] individuals). Six of the 22 studies (27.3%) were primary or secondary analyses of a large randomized clinical trial. Participants had diverse pain and opioid use histories. Rationale for buprenorphine rotation included inadequate analgesia, intolerable adverse effects, risky opioid regimens (eg, high dose and/or sedative coprescriptions), and aberrant opioid use. Most protocols were adapted from protocols for initiating treatment in patients with opioid use disorder and used buccal or sublingual buprenorphine. Very low-quality evidence suggested that buprenorphine rotation was associated with maintained or improved analgesia, with a low risk of precipitating opioid withdrawal. Steady-dose buprenorphine was better tolerated than tapered-dose buprenorphine. Adverse effects were manageable, and severe adverse events were rare. Only 2 studies evaluated mental health outcomes, but none evaluated health care use. Limitations included a high risk of bias in most studies.

SPOTLIGHT ON PHARMACY

Is buprenorphine an effective analgesic for treatment of chronic pain in adults?

EVIDENCE-BASED ANSWER

Yes. Buprenorphine effectively reduces chronic pain in adults when compared with placebo (SOR: **A**, meta-analysis of randomized controlled trials [RCTs] and case series, and single RCT). Buprenorphine may be more effective in those without opioid use disorder than those with opioid use disorder (SOR: **A**, meta-analysis of RCTs and case series). If buprenorphine is superior, inferior, or comparable with other analgesics remains uncertain (SOR: **B**, 2 RCTs from meta-analysis).

DOI 10.1097/EBP.0000000000001591

that compared with other analgesics and variability in dosages used.

A 2016 RCT evaluated the effectiveness of transdermal buprenorphine compared with placebo for treatment of diabetic peripheral neuropathic pain (n = 186).[2] Patients had a mean age of 63 years old, 67% were male, 94% were White, and had to have diabetic peripheral neuropathic pain for at least six months with a minimal numeric rating scale score of at least 4 (0 = no pain to 10 = worst pain) at baseline. Patients were excluded if they already were treated with an opioid or if they had a skin condition precluding use of the patch. Treatment consisted of buprenorphine transdermal patch starting at 5 µg/h and titrated to a maximum of 40 µg/h compared with placebo patch, and patients in both

Song, Michael MD; Sliwowska, Anna MD; Amico, Jennifer MD, MPH
Evidence-Based Practice 25(7):p 42-43, July 2022. | *DOI:* 10.1097/EBP.0000000000001591

Analgesic Effect of Buprenorphine for Chronic Noncancer Pain: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Stanley Sau Ching Wong, MD,*† Tak Hon Chan, NA,* Fengfeng Wang, PhD,*† Timmy Chi Wing Chan, MBBS,* Hung Chak Ho, PhD,*† and Chi Wai Cheung, MD*†

KEY POINTS

- **Question:** What is the analgesic efficacy and safety of buprenorphine for chronic noncancer pain?
- **Findings:** Buprenorphine was associated with statistically significant but small reduction in pain scores for chronic noncancer pain when compared to placebo, and subgroup analyses showed positive analgesic effect when given for chronic low back pain, given via the transdermal and buccal routes, and with lengths of follow-up less than and more than 12 weeks.
- **Meaning:** The results suggest that buprenorphine given via the transdermal and buccal routes could reduce chronic noncancer pain compared to placebo, with more evidence supporting its use for low back pain in patients without OUD.

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Lessons from Chronic Pain: Buprenorphine works!!

Annals of Internal Medicine

CLINICAL GUIDELINE

The Use of Opioids in the Management of Chronic Pain: Synopsis of the 2022 Updated U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guideline

Evidence supported a new recommendation for buprenor-
phine in patients receiving a daily opioid for the treatment

phine instead of full μ-opioid receptor agonist opioids
because of a lower risk for overdose and misuse. Although

Sandbrink et al. Ann Intern Med. 2023 Feb 14.

So it’s safe…does it work for OUD?

Umm…yeah.

Lessons from SUD Treatment: Buprenorphine for OUD works!!

- **> 50% reduction in mortality when patients are maintained on bup**
- Buprenorphine treatment improves retention in SUD treatment
- Tapering or discontinuing bup significantly increases risk of losing retention and/or relapse

Published in final edited form as:
Arch Gen Psychiatry. 2011 December ; 68(12): 1238–1246. doi:10.1001/archgenpsychiatry.2011.121.

Adjunctive Counseling During Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence:

A 2-Phase Randomized Controlled Trial

Roger D. Weiss, M.D.[1,2], Jennifer Sharpe Potter, Ph.D.[1,2,3], David A. Fiellin, M.D.[4], Marilyn Byrne, M.S.W.[5], Hilary S. Connery, M.D., Ph.D.[1,2], William Dickinson, D.O.[6], John Gardin, Ph.D.[7], Margaret L. Griffin, Ph.D.[1,2], Marc N. Gourevitch, M.D., M.P.H.[8], Deborah L. Haller, Ph.D.[9], Albert L. Hasson, M.S.W.[10], Zhen Huang, M.S.[11], Petra Jacobs, M.D.[12], Andrzej S.

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research Paper

Availability and use of non-prescribed buprenorphine-naloxone in a Canadian setting, 2014–2020

Paxton Bach [a,b,*], Misha Bawa [a,b], Cameron Grant [b], M.J. Milloy [a,b], Kanna Hayashi [b,c]

? BUP Misuse ?

- **ONLY 1%** reported non-prescription use

...despite widespread availability

Bach P et al. Int J Drug Policy. 2022

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Understanding the use of diverted buprenorphine

Theodore J. Cicero[a], Matthew S. Ellis[a], Howard D. Chilcoat[b,c,*]

? BUP Misuse ?

- Most common non-prescription use is **THERAPEUTIC**

Cicero et al. Drug Alcohol Depend. 2018

Tricky/Sticky Situations

- Running out of medications early repeatedly or UDS discordant?
  - Repeat urine drug screen
  - Check PDMP
  - Utilize DSM-V criteria

- Complex persistent opioid dependence (CPOD)
  - To discuss if there's time

Questions?

sudheer.potru@gmail.com