Dangers of Buprenorphine Dose Limits

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No Financial Disclosures
Will discuss off-label use
May mention brand names in discussion

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Learning Objectives

- Identify five indicators of buprenorphine dose adequacy for each individual patient.
- Develop essential instructions for patients regarding best practices for optimal sublingual buprenorphine administration

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Scope of the Problem

- **Opioid overdose deaths increased >61% from 2019 until 2021**
- **2021 American opioid overdose deaths >80,000**
- **Most street opioids and other drugs contaminated with Fentanyl**
- **Most Fentanyl (*blue pills*) not pharmaceutical grade; content varies**
- **No Fentanyl test strips are FDA approved**
- **Methadone and Buprenorphine have strongest evidence base for opioid replacement therapy**
- **Some providers limit doses to absolute maximum of 16-24 mg**

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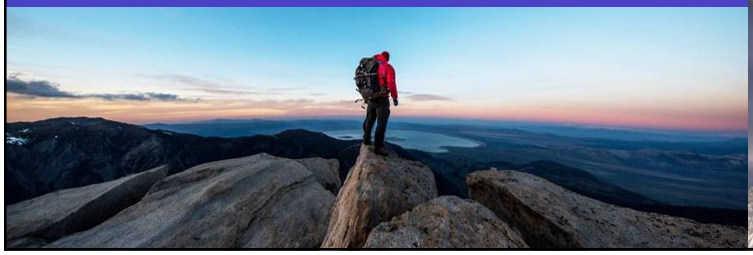
Prior authorizations sometimes required for doses higher than 16/4 mg or 24/6 mg per day

Pharmacy calls: Insurer will not pay for more than 2 of any film dose (may have 8x2=16 + 12 + 4 to get dose of 32 mg)

Many Buprenorphine prescribers refuse to prescribe doses higher than 16 mg per day

Limits referral options for patients discharging from residential treatment, especially those in rural areas!



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Arguments Regarding Dose Limits

For Dose Limits

- FDA package insert
- Receptor occupancy interpretations (2000-2009)
- Concerns about cost
- Concerns about diversion
- *Expert opinion*

Against Dose Limits

- ASAM guidelines
- Individual variability
- Receptor occupancy data (2010-present)
- Improved treatment retention
- Reduced illicit drug Use
- No analgesic ceiling effect
- Kappa receptor role

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FDA Bupe/Naloxone package insert

- **Dosing recommendations are based on data from trials before 2002 at doses equivalent to 6-24 mg/day.**
- **The recommended daily dose for maintenance is 16/4 mg.**
- **The maintenance dose "is generally in the range of 4/1 mg buprenorphine/naloxone to 24/6 mg buprenorphine/naloxone per day depending on the individual patient. Dosages higher than this have not been demonstrated to provide any clinical advantage."**
- https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022410s000lbl.pdf

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Rationale

"In medicine, we are generally concerned about too high a dose being potential poison. However, underdosing (e.g., with oxygen, vasopressors, and antibiotics) can also lead to patient harm. Widespread underdosing of buprenorphine, if responsible for treatment failure, could directly harm many patients whose primary goals are simply to survive and avoid withdrawal." **Grande et. al (2023).**

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Rationale

"Because ongoing use of illicit fentanyl is frequently lethal, the rationale for buprenorphine dose limits must be evaluated carefully and justified using the highest standards of evidence."

Grande, L. A., Cundiff, D., Greenwald, M. K., Murray, M., Wright, T.E., & Martin, S. A. (2023). Evidence on buprenorphine dose limits: A review. In press, Journal of Addiction Medicine. Published online 6/16/2023.

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Case Study: 36-year-old Joe

- **20 years IVDU: heroin**
- **Did not complete high school**
- **Intermittent laborer in local industry**
- **And then: Buprenorphine/Naloxone**
  - **Dose titrated upward from 8/2 Q 12 hours**
  - **At 32/8 able to work intermittently but always felt sick**
  - **At 36/9 worked full time; not sick; primary wage earner**

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Case Study: 28-year-old Jackie

- **SUD counselor doing intake: "You need to see her NOW!"**
- **Cellulitis bilateral forearms, rural ED visit yesterday**
- **Went to different ED on my insistence**
- **Airlifted to population center 2+ hours away**
- **4+ weeks of IV antibiotics; osteomyelitis in knee**
- **Phoned me in panic: "Resident MDs tell me to get off bupe!"**
- **Outcome: stable on 16/4 Q 12 hours; gait resolved in 6 months**
- **Until she talked about bupe/nx at NA meeting…**

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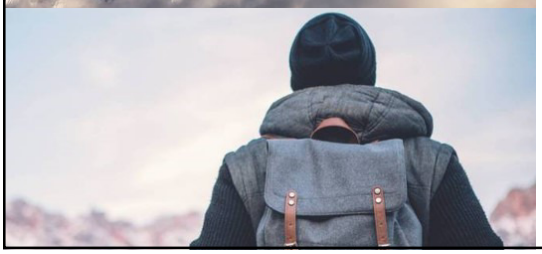
Five Indicators that Bupe Dose is Adequate to Patient's Needs

1. **NO cravings, any time of day or night.**
2. **NO withdrawal symptoms, any time of day or night.**
3. **NO night sweats.**
4. **NO *using dreams*.**
5. **NO use of any opioid that isn't prescribed for the patient and known to the prescriber.**

- These criteria address short-term, buprenorphine-specific issues
- Additional targets depend on relationships and mutual goals
- Test urine/saliva etc. when clinically appropriate/required

Maximize Dose Effectiveness



Stay well hydrated so films or tablets will dissolve easily
No nicotine use (cigarettes, vape, chew) during the 20 to 30 minutes prior to bupe dose
Place film or tablet under tongue; tuck chin to chest
Do not swallow excess saliva! (May precipitate withdrawal symptoms.) Spit out excess saliva!

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Take Aways…

- **Buprenorphine dose is adequate if:**
  - **Patient perceives it as adequate, AND**
  - **Reduced illicit opioid use**
  - **Increased retention**
- **Clinical and preclinical evidence that 32 mg/day or higher can be helpful for some patients, particularly those with pain**
- **Pregnant women need:**
  - **Increased dose of buprenorphine**
  - **Increased frequency of dosing**

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Additional Considerations

Dosing Schedule

- Ideally split doses 12 hours apart
- Adjust as needed according to effects and side effects (e.g., nausea, somnolence, etc.)
- Treating pain requires TID or QID

Avoid Trouble

If taking a few films on person (in wallet) keep pharmacy receipt noting Bupe prescription OR have photo of pharmacy label (so not risking arrest for possession if stopped by police some other reason)

Avoid Confrontation

Don't discuss Bupe in 12-Step meetings: the 12-step fundamentalists will come out of the woodwork!

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Still More Considerations

Privacy

Don't tell friends about Bupe Rx: It's between the patient and provider. Avoid comments, "I wish you'd get off that stuff… It's just switching one addiction for another…"

Harm Reduction

Advise: Don't use alone!

Prescribe Naloxone (Narcan)

Instruct patients and family members on how to administer Narcan

Advise Patient

Treat OUD as a disease as serious as cancer, and just as deadly--only faster ! Analogy of PHP, IOP, support groups like chemo and radiation…

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Summary

Buprenorphine dose is adequate if:

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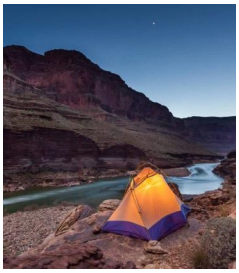
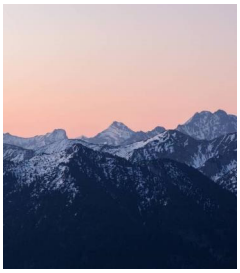

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Buprenorphine dose limits of 16 or 24 mg don't fit in the age of Fentanyl!
Look at the patient and treat to the patient's needs
Educate patients and their families about the value of Medication for Addiction Treatment (MAT)

Bupe can save lives!

Thank you

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References

Ahmad, FB, Rossen LM, Sutton P. Provisional Drug Overdose Death Counts. Hyattsville, MD: National Center for Health Statistics, 2022. Available at https://www.cdc.gov/nchs/nvss/vsn/drug-overdose-data.htm.

Grande LA, Cundiff D, Greenwald MK, Murray M, Wright TE, & Martin SA. Evidence on buprenorphine dose limits: A review. Journal of Addiction Medicine (2023) June (in press). Published online 6/16/2023.