Buprenorphine for Opioid Use Disorder and Chronic Pain

Greg Rudolf, MD
Lisa B Voltarelli, MD
7.21.2022

Before We Begin

Questions

You can submit a question at any time through the question module.

Tech Issues

Look for the 'Help' button at the top of the webinar control panel.

Presentation

The slide deck and presentation recording will be available on our website within the next few days.

Stay Connected

Follow us @WAMedCommission and use #WMC to share what you learn.

Continuing Medical Education

- CME is available for attending the webinar or watching the recording.
- If you are watching in a group setting, please make sure you register for the webinar and complete the evaluation as an individual to receive CME credit.
- Accreditation Statement - This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Federation of State Medical Boards and the Washington Medical Commission. The Federation of State Medical Boards is accredited by the ACCME to provide continuing medical education for physicians.
- Credit Designation Statement - The Federation of State Medical Boards designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Faculty and Staff Disclosures

- This webinar is not funded by any commercial entity.
- As an organization accredited by the ACCME, the Federation of State Medical Boards (FSMB) requires that the content of CME activities and related materials provide balance, independence, objectivity, and scientific rigor. All faculty, planners, and others in a position to control continuing medical education content participating in an accredited continuing education activity are required to disclose all financial relationships with ineligible companies. Ineligible companies are organizations whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients. Faculty (authors, presenters, speakers) are encouraged to provide a balanced view of therapeutic options by utilizing either generic names or other options available when utilizing trade names to ensure impartiality.
- All faculty members are asked to disclose all financial relationships they have had in the past 24 months with ineligible companies regardless of the potential relevance of each relationship to the education and of the amount. The FSMB has implemented a mechanism to identify and resolve all conflicts of interest prior to the activity. The intent of this policy is to identify potential conflicts of interest so participants can form their own judgments with full disclosure of the facts. Participants will be asked to evaluate whether the speaker's outside interests reflect a possible bias in the planning or presentation of the activity.
- The speakers, course director, authors, and planners have no relevant financial relationships with ineligible companies to disclose.

Faculty and Staff Disclosures

- The speakers, course director, authors and planners at the Federation of State Medical Boards and Washington Medical Commission have no relevant financial relationships with ineligible companies to disclose.
- This educational activity may contain discussion of published and/or investigational uses of agents that are not approved by the U.S. Food and Drug Administration. For additional information about approved uses, including approved indications, contraindications, and warnings, please refer to the prescribing information for each product, or consult the Physicians' Desk Reference.

Learning Objectives

- Review pharmacology and effectiveness of buprenorphine in Opioid Use Disorder (OUD) and pain.
- Review the legalities of prescribing buprenorphine for OUD and perceived obstacles.
- Empathize with patients taking buprenorphine for OUD.
- Motivate providers on your team to prescribe buprenorphine for the treatment of OUD.

Opioid Use Disorder

A chronic health condition, with high risk for mortality and morbidity, amenable to effective pharmacologic treatment with demonstrated life-saving benefit.

The concept of provider expertise in medication management of chronic conditions is entirely applicable to treatment of OUD.

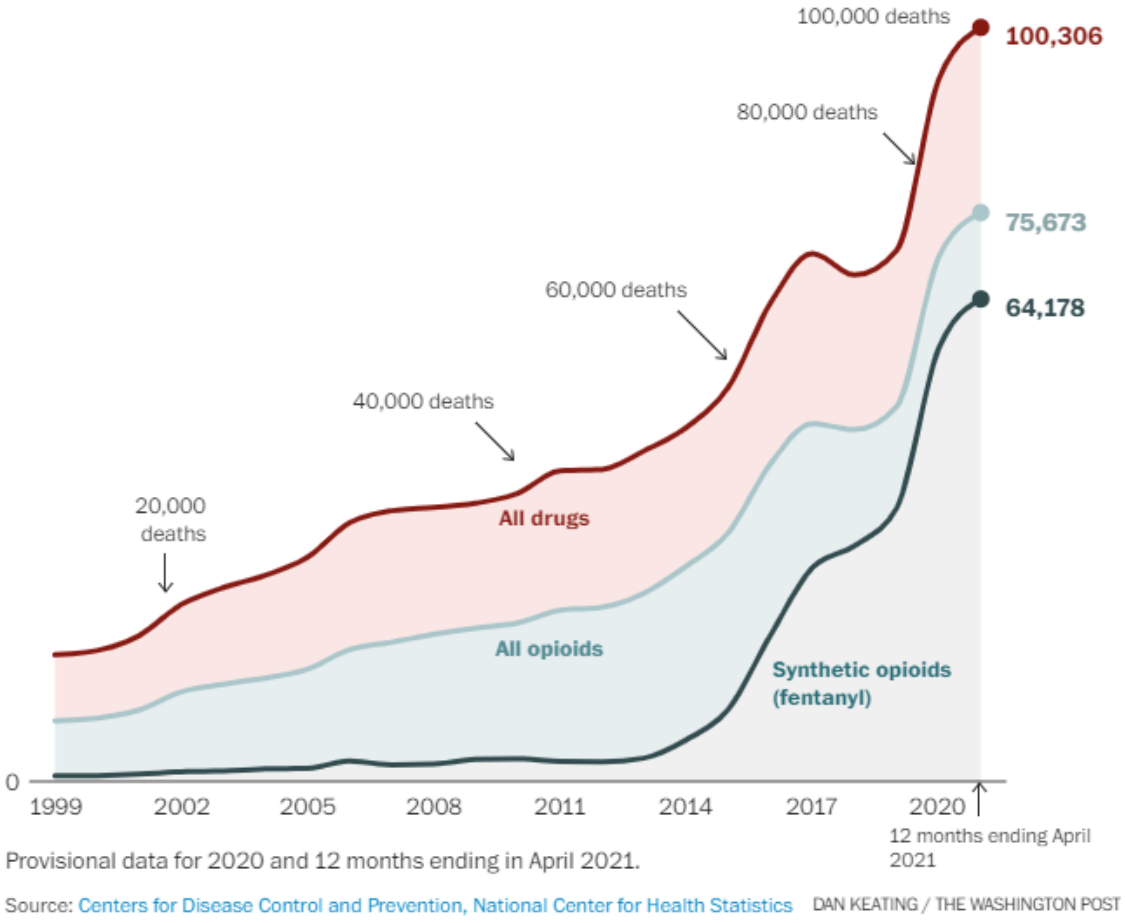
Rising Overdose Deaths in the US

107,000 drug overdose deaths in 2021

Overdose deaths rose:

15% from 2020 to 2021

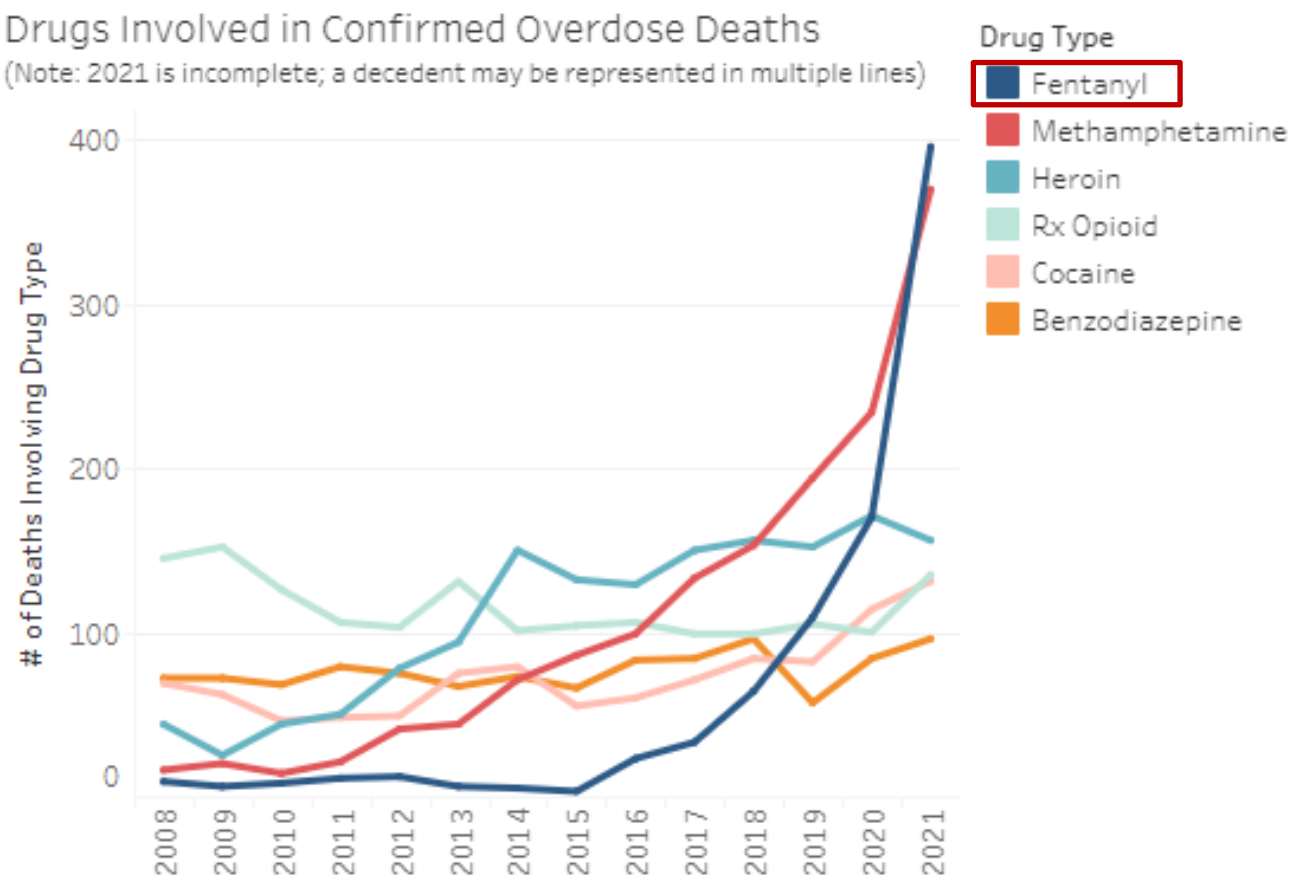
30% from 2019 to 2020



https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm

https://www.washingtonpost.com/health/2021/11/17/overdose-deaths-pandemic-fentanyl/

King County: Overdose Deaths from Fentanyl



We Have Effective Medication for Opioid Use Disorder (MOUD)

- Buprenorphine

  Office-based, reduces mortality

- Methadone

  daily observed dosing, reduces mortality

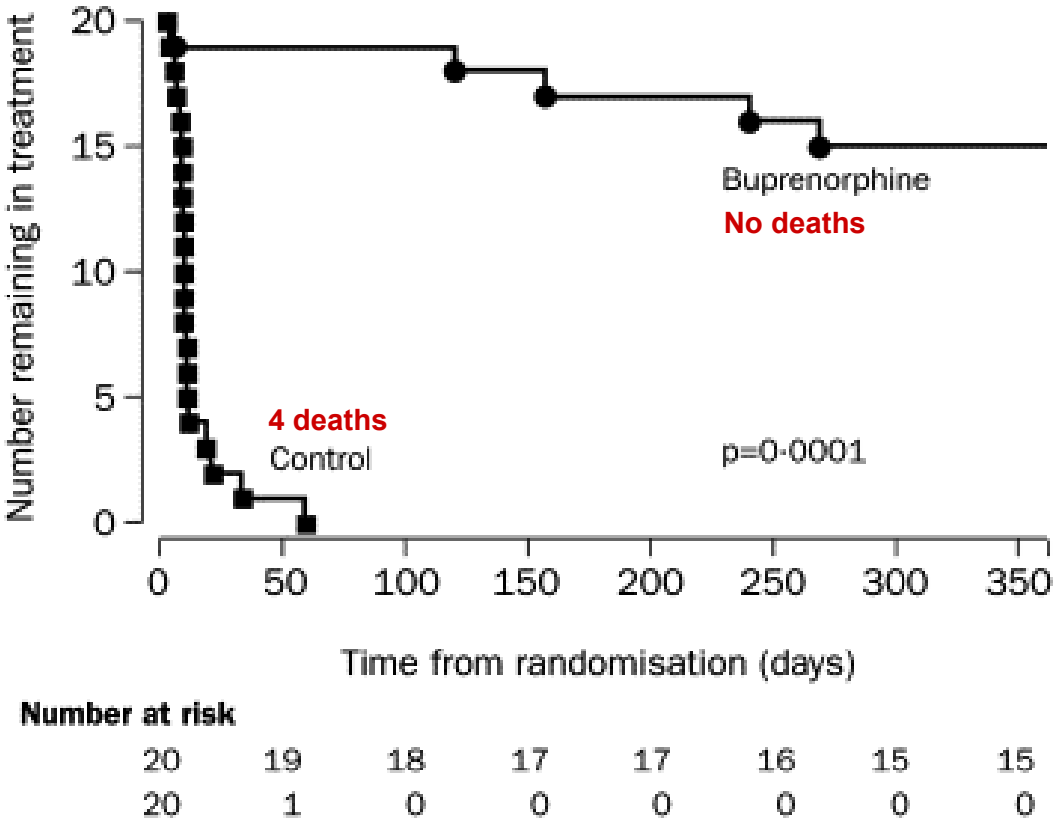
- Naltrexone

  Injectable depot Vivitrol

"Abstinence-based" residential or psychological treatment without medication is associated with 2-fold increase in overdose deaths compared to MOUD

Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England. Pierce M, et al. Addiction. 2016 Feb;111(2):298-308.

Buprenorphine: Life Saving Medication



40 participants

Buprenorphine

Supervised daily administration

Weekly CBT group and individual therapy

Randomized

Maintenance (6+ mos)

6 day taper → placebo

1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. Kakko J Lancet. 2003 Feb 22;361(9358):662-8.

Reduced Risk of Overdose

- Reduced risk of opioid related overdose compared to no medication treatment

  Buprenorphine: AHR 0.40 [0.35-0.46] (1)

  Buprenorphine or Methadone: AHR 0.24 [0.14-0.41] (2)

- No effect of behavioral health, inpatient or residential treatment on overdose outcome (2)

- Reduced Acute Care Visits: AHR 0.68 [0.47-0.99] (2)

1. Morgan, Jake R., et al. "Overdose following initiation of naltrexone and buprenorphine medication treatment for opioid use disorder in a United States commercially insured cohort." Drug and alcohol dependence 200 (2019): 34-39.

2. Wakeman, Sarah E., et al. "Comparative effectiveness of different treatment pathways for opioid use disorder." *JAMA Network Open* 3.2 (2020): e1920622-e1920622.

Buprenorphine Maintenance: Increase in Treatment Retention

RCT

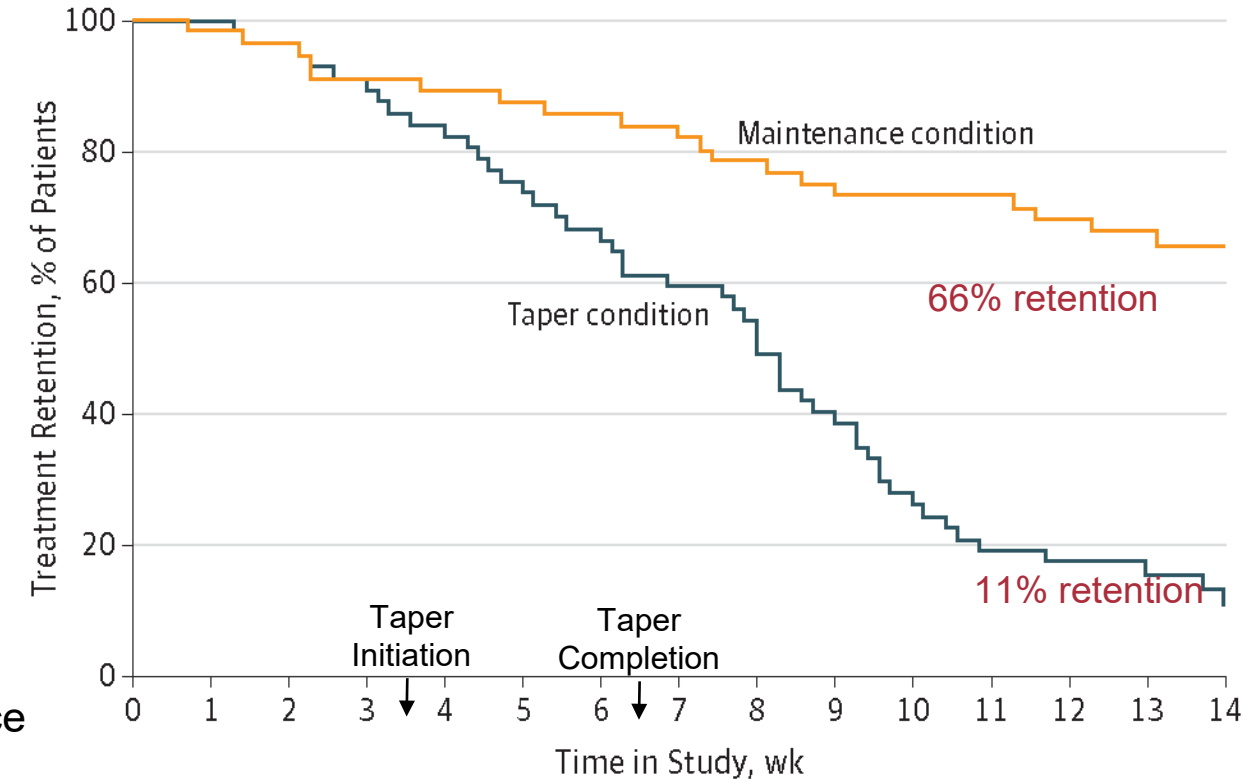
N=113

Primary Care Setting

Prescription Opioid Use Disorder

Maintenance

- Improved retention
- Reduced illicit opioid use
- Longer continuous abstinence



Mean buprenorphine dosage, mg/d															
Maintenance condition	14.9	15.1	15.2	15.3	15.3	16.0	15.9	16.2	16.2	16.6	16.8	16.2	16.1	15.8	14.6
Taper condition	15.6	15.6	15.4	15.3	14.2	9.7	5.7	3.1	0.6	0.2	0	0	0	0	0

Fiellin DA, Schottenfeld RS, Cutter CJ, Moore BA, Barry DT, O'Connor PG. Primary Care–Based Buprenorphine Taper vs Maintenance Therapy for Prescription Opioid Dependence: A Randomized Clinical Trial. JAMA Intern Med. 2014;174(12):1947–1954. doi:10.1001/jamainternmed.2014.5302

Buprenorphine: No Longer a Specialty Medication

All prescribers

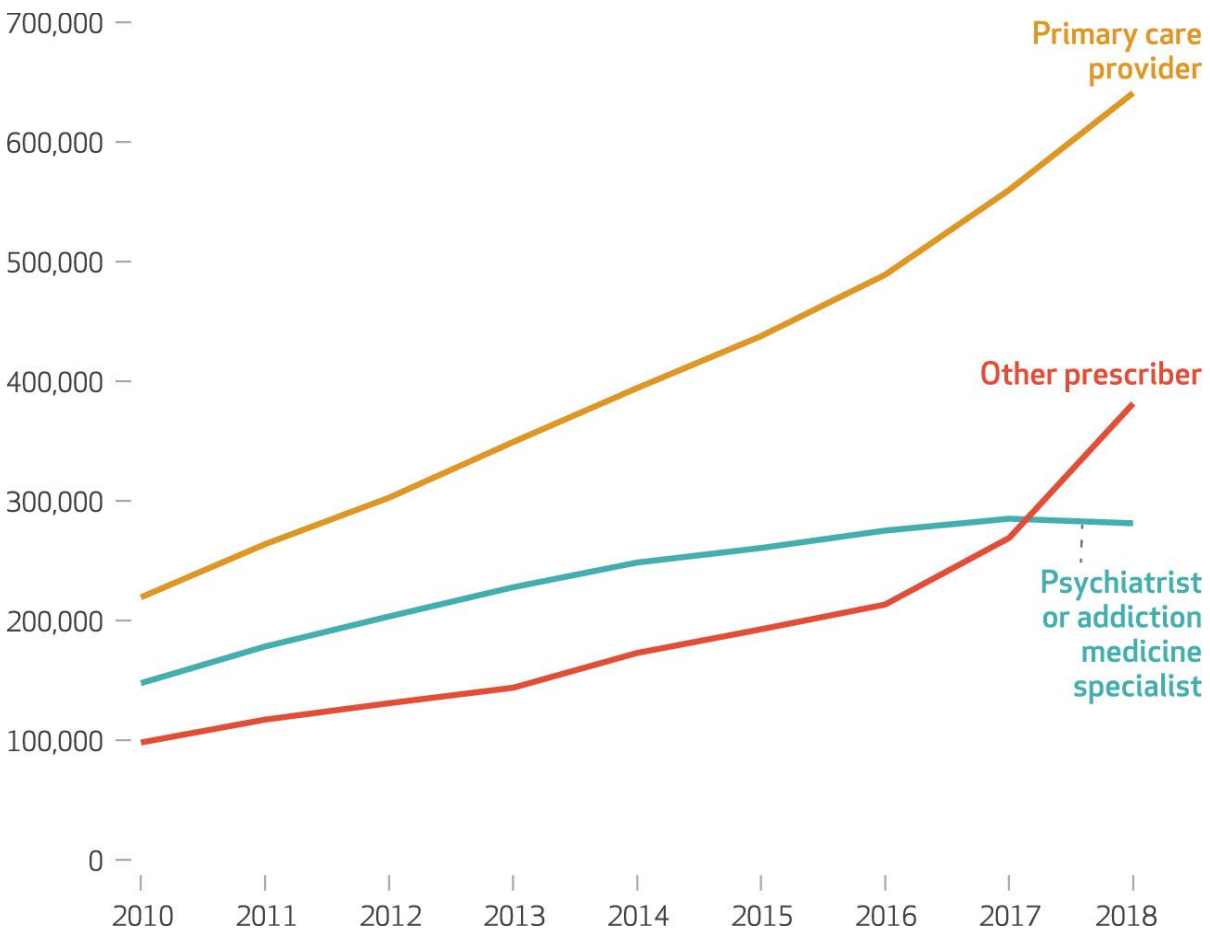
US population

Ages 15-80

Prescription database

Treating more people

23.6 → 44.3 per 10,000



Olfson, M., Zhang, V., Schoenbaum, M., & King, M. (2020). Buprenorphine Treatment By Primary Care Providers, Psychiatrists, Addiction Specialists, And Others: Trends in buprenorphine treatment by prescriber specialty-primary care providers, psychiatrists, and addiction medicine specialists. *Health Affairs*, *39*(6), 984-992.

New Waiver Rules!!!

- As of 4/28/21, you can receive a buprenorphine waiver without having to do any required education.
- This waiver allows up to 30 patients actively treated with buprenorphine at any one time.
- Future legislation: End the X-waiver → increase patient access to life-saving medication

New Waiver Rules!!!

- Information needed to sign up
- Your NPI number
- Your DEA number
- If you are a PA, you need your supervising physician's DEA number

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

Buprenorphine Formulations for OUD

- Suboxone™
  - Sublingual buprenorphine –naloxone (bup/nx)
  - Long available in generic, both film and tablet
- Subutex™
  - Generic sublingual buprenorphine, *no naloxone*
  - Some patients tolerate better, try if pt having trouble staying with bup/nx
  - Usually cheaper out of pocket if bup/nx too $$ or inaccessible through insurance
- Sublocade™
  - Monthly Long-Acting Injectable Buprenorphine

How to take the medication

- Sublingual tablets and films must be held under the tongue several minutes to dissolve
- Start with a moist mouth
- Avoid using nicotine products prior to administration
- Avoid speaking with the sublingual medication
- Keep dissolving medicine under tongue until completely dissolved

https://www.rxlist.com/suboxone-drug.htm

Traditional Buprenorphine Initiation

- First dose typically given:
  - 12-24 hours after last short acting opioid (heroin, oxycodone, morphine)
  - 24-48 hours after longer acting opioids
    - Extended release oxycodone/morphine
    - Methadone
    - Fentanyl *(highly variable)*

Managing Opioid Withdrawal

Early/mild

- Anxiety
- Muscle aches
- Increased tearing
- Runny nose
- Sweating
- Yawning
- Insomnia

Later/severe

- Restlessness
- Agitation
- Abdominal cramping
- Diarrhea
- Dilated pupils
- Gooseflesh
- Nausea
- Vomiting

→ *It feels a lot worse than it looks, but is not life-threatening!*

Other Meds for Opioid Withdrawal

- Tizanidine 4 mg QID for restlessness/myalgias
  - Or Clonidine 0.1 mg QID
  - Hold if dizzy when standing
- Hydroxyzine 50 mg QID for anxiety
- Gabapentin 300 mg TID & 600 mg QHS for anxiety

- Trazodone 50 mg PRN QHS for sleep
- Loperamide 2 mg Q4 PRN diarrhea
- Dicyclomine 10-20 mg Q4 PRN stomach cramps

→ All help with jerking, sweating, cramping, vomiting, diarrhea and insomnia. Patients still have fatigue, dysphoria, deep aching & hyperalgesia.

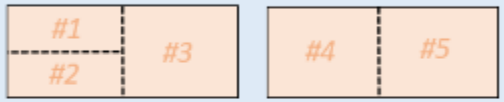
Traditional Buprenorphine Initiation

Traditional Way

Day 1

- Wait 12-24 hours if using heroin and oxycodone
- Wait 48-72 hours if using fentanyl, M30's or methadone

Cut the films or tabs



First dose: put ¼ film under your tongue for 5 min

Second dose: Wait 2 hours and take ¼ film

If you are still sick: take ½ film every 2 hours until out of withdrawal. *Max dose 2 films per day*

Day 2

Add up all you took on day 1 and take that dose at the same time

If you are still sick: take ½ film every 2 hours if you are still sick. *Max dose 2 films per day*

Day 3-7

Add up all you took on day 2 and take that dose every day until your follow up appointment. *Max dose 2 films per day*

.BUPRENORPHINESTARTPATIENTHANDOUT
Borrowed from Dr. Luke Peterson, Banner Health - Pheonix Arizona

Buprenorphine Low Dose Initiation

- Gradual initiation of buprenorphine starting at low doses given *concurrently* with full opioid agonists.
- Initial very low dose (0.5 mg) with slow titration upward over 5-10 days.
- Full opioid agonists tapered once a therapeutic dose of buprenorphine is reached.

Buprenorphine Low Dose Initiation

- Bup/nx 2/0.5 mg film
  - Day 1: ¼ film = 0.5 mg SL qD x 1 day, then
  - Day 2: ¼ film = 0.5 mg SL BID x 1 day, then
  - Day 3: ½ film = 1 mg SL BID x 1 day, then
  - Day 4: 1 film = 2 mg SL BID x 1 day, then
  - Day 5: 2 films = 4 mg SL BID x 1 day, then
  - Day 6: 2 films = 4 mg SL TID x 1 day, then
- → Bup/nx 8/2 mg film
  - Day 7: 1 film SL BID or TID (16-24mg)
- *Some pts do better on lower doses; others up to 32mg*

Transitioning Hospitalized Patients with Opioid Use Disorder from Methadone to Buprenorphine without a Period of Opioid Abstinence Using a Microdosing Protocol. Terasaki D et al Pharmacotherapy. 2019 Oct;39(10):1023-1029
Case report: Successful induction of buprenorphine/naloxone using a microdosing schedule and assertive outreach. Rozylo J et al. Addict Sci Clin Pract. 2020 Jan 15;15(1):2

Opioid Use Disorder

- A chronic health condition,
  with high risk for mortality and morbidity,
  amenable to effective pharmacologic
  treatment with demonstrated life saving
  benefit.

- Provider expertise in medication
  management of chronic condition is entirely
  applicable to treatment of OUD.

Buprenorphine: An Indispensable Part of Your Pain Management Tool Kit

Greg Rudolf, MD
Swedish Pain Services, Seattle
President, WSAM
Chair, ASAM Pain and Addiction Committee

Objectives for Today

- Appreciate the clear evidence for MUCH better outcomes in treatment of opioid use disorder (OUD) with use of medications for opioid use disorder (MOUD)
- Understand the basics of buprenorphine pharmacology and be able to explain to patients its advantages for chronic pain
- Recognize the potential of buprenorphine as a safer, more sustainable, and more effective treatment option for patients with chronic pain who require a long-acting opioid

Medication for OUD Works Better Than Abstinence-based Treatment

Review > Am J Health Syst Pharm. 2019 Jul 18;76(15):1097-1103. doi: 10.1093/ajhp/zxz105.

Medications for management of opioid use disorder

Jennifer L Koehl [1], David E Zimmerman [2], Patrick J Bridgeman [3]

- **Buprenorphine**– DEA X-waiver soon to go away, unclear if other training will be added (MAT Act vs MATE Act now being considered by Congress)
  - ANY licensed provider can use it for pain
- **Methadone**– only available for OUD in separate licensed opioid treatment clinic
- **Naltrexone**– monthly injectable opioid antagonist just as effective as buprenorphine but harder to initiate

Forces Are Mobilizing and Gaining Traction for Removal of the "X-waiver" for treatment of OUD

- www.endsud.org
  - Campaign to push through federal legislation to fully remove restrictions from Rx'ing buprenorphine for all licensed independent practitioners to treat OUD

- *"Talking Points" for benefits of removing X-waiver:*
  - https://drive.google.com/file/d/19AarJB_MSy6NAnhTWkXxTP_aiRyaoonF/view

- Contrary to some providers' beliefs, *there has never been a training or licensing requirement to prescribe buprenorphine for pain* other than regular DEA license

The Opioid Prescribing Dilemma

- **Opioids can be safe and effective for some patients and chronic pain conditions** as part of a multimodal strategy *when other interventions have failed*…
  - ***…but which patients, and for how long?***

- **How to handle patients on long term high dose opioids who do NOT have OUD?**
  - *Opioids are still most prescribed class of medication in the US, though prescribing rates have decreased 40-60% since 2012*
    - Krebs SPACE trial 2018: opioids more harmful than helpful after 1 year for patients started on them de novo
    - Nadeau 2021 Frontiers of Pain Research analytic review: restrictions on prescribing opioids for legitimate pain treatment has been a failed strategy
    - Coffin and Barreveld 2022 NEJM: array of serious harms have come from forced opioid tapering and discontinuation

Managing Chronic Pain with Opioids: Engaging the Patient to Make Safe, Effective Choices

- For patients already on opioids and deriving unclear benefit→ non-judgmental discussion of concerns about role of current opioids in the care plan
  - **focus not only on any aberrant behaviors but also on potential unintended consequences on pain symptoms and overall functioning**
    - **tolerance/opioid-induced hyperalgesia (OIH)**
    - withdrawal symptoms between doses
    - unstable mood/energy level
    - poor sleep (esp. common with short-acting)
    - *These are all **PATIENT-CENTERED ISSUES***
  - discussion should happen after detailed pain history, medication/substance use history, physical exam, review of data/records→ may not work well on first visit as new PCP

Buprenorphine pharmacology: addresses pain, OIH, *and* OUD

- "Partial" mu opioid receptor agonist
  - Ceiling effect for respiratory depression: **SAFER OPIOID**
  - Active metabolite norbuprenorphine does not cross the BBB→targets mostly **spinal-level and peripheral** opioid receptors
  - ***Strong analgesic potency*** (**25-100x morphine**), **no ceiling effect!**
  - helpful in any/all pain requiring long-acting opioid, incl cancer
- High affinity, slow dissociation-->**long half-life (36+ hrs SL)**
  - Pts appreciate **stable opioid levels**
  - High affinity has implications on INDUCTION process for SL
- Kappa opioid receptor antagonist and sodium channel blocker (Leffler, 2012)→ **anti-hyperalgesic effect**

Buprenorphine Pharmacology: Deeper Dive

- Kappa Opioid receptor antagonist
  - blocks activity of **dynorphin**→ less tolerance/hyperalgesia, less "negative reinforcement loop" from opioid use
- Sodium channel blockade (Leffler 2012)
  - blocks voltage-gated sodium channels via the local anesthetic binding site→ systemic antihyperalgesic effect
- ORL-1 (nociceptin) receptor agonist
  - unclear analgesic potency, some antihyperalgesia; no opioid side effects such as resp depression, itch
  - **known antagonist of dopamine transport**→ useful in SUD tx? (Zaveri, 2016)
- Delta opioid receptor agonist
  - contributes to analgesia
  - improves negative emotional states (Pradhan, 2011)

Formulations of Buprenorphine for Pain

- **Transdermal (Butrans™)**: weekly transdermal patch
  - Better tolerated than SL in RCT
    - Skin irritation most common adverse effect
  - Effective for chronic pain of all causes including cancer
  - Lower dose of buprenorphine vs sublingual or buccal
  - Available in generic (approved 2010)
- **Buccal (Belbuca™):** buccal film approved 2015 for chronic daily pain, dosed q12h;
  - lower dose than SL, higher than patch (range 75mcg BID-900mcg BID)
- **Solution (Buprenex™)**: used IV for acute pain in inpatient setting; useful for hospital low-dose initiation (Jablonski 2022)
- **OK to use sublingual off-label, write "for pain" on Rx and use regular DEA number**

Is the patient on board with your recommendations?

- **If pt expresses resistance to buprenorphine, explore why…**
  - **Misconceptions are pervasive about this medication**
  - gently challenge any inaccuracies in understanding of potential benefits and appropriateness for chronic pain
    - *Emphasize pharmacology*
    - *Explain some of the history of use of buprenorphine, first as analgesic then later OUD*
    - *Articles to assist buprenorphine myth-busting:* Gudin 2020, Rudolf 2020, Davis 2012
  - **Where is "cognitive dissonance" about buprenorphine coming from?**
    - Internet, friend/family/acquaintance, fear of withdrawal, or just plain fear of change?
    - If the patient tried it before and reports intolerability/failure, ask further: which formulation? How was it initiated and dosed? How long was the trial?

Thank you for your attention!

Gregory.Rudolf@providence.org
cell 206-890-8039

Questions or comments?

Bonus Slides: How to Apply for X-Waiver

Steps to apply for Waiver

Google “SAMHSA buprenorphine”

Select “Become a Buprenorphine Waivered Practitioner”

Scroll down to “Apply for a patient waiver”

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

Steps to Apply for Waiver

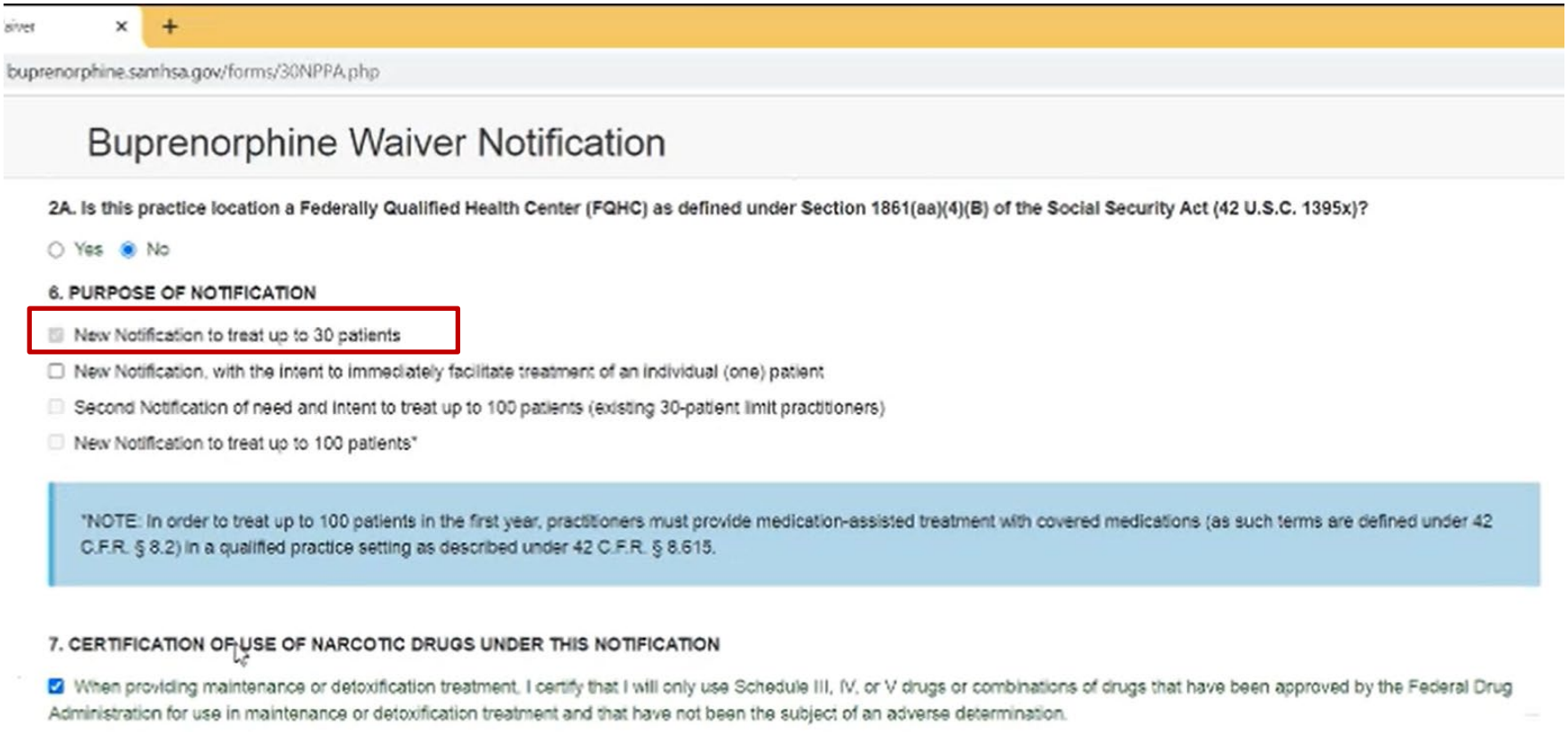
If asked about training date:

APCs check ☑ SAMHSA's Providers Clinical Support System (PCSS) in "CERTIFICATION OF QUALIFYING CRITERIA," then enter "***practice guidelines***" in the text box for the date.

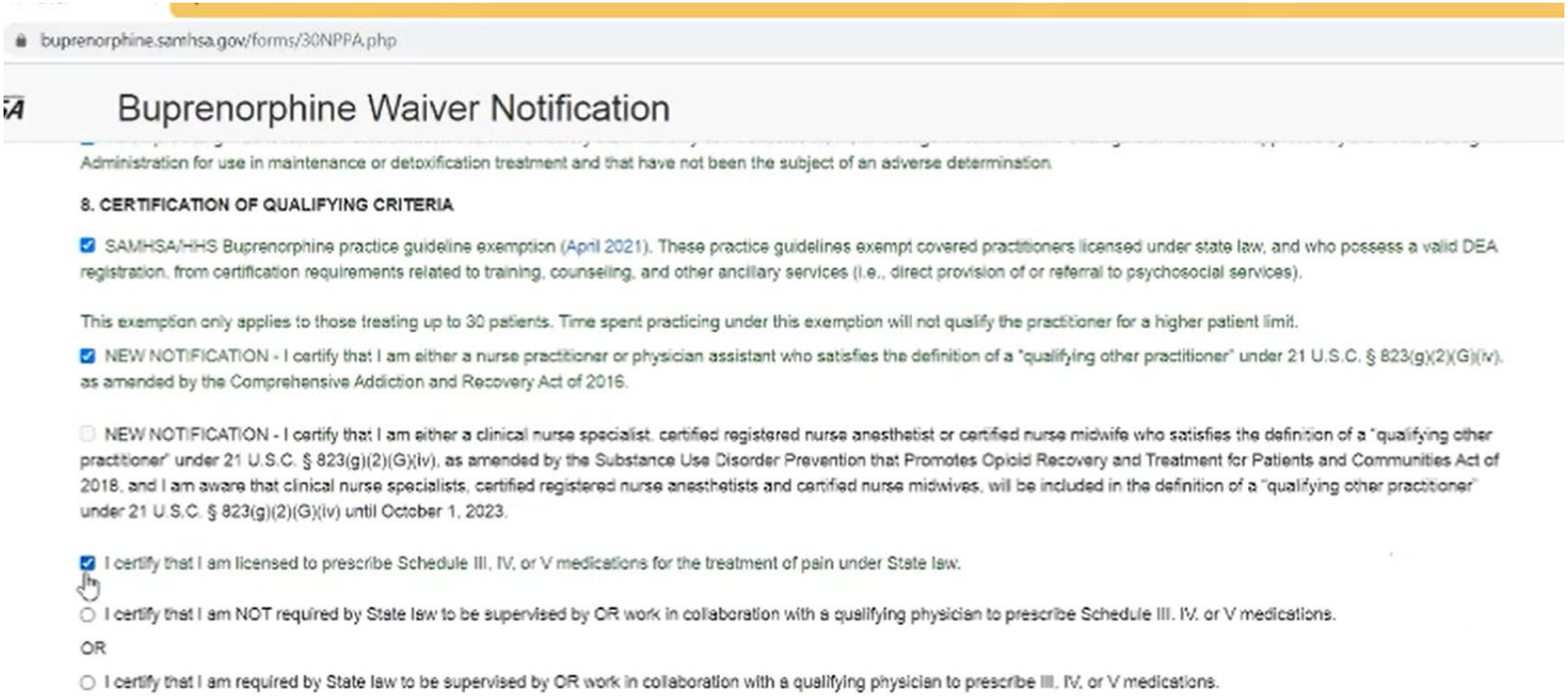
Physicians select "Other" in "CERTIFICATION OF QUALIFYING CRITERIA," then enter "***practice guidelines***" in the text box for the city of the training. The training date should be the application date.

Steps to Apply for Waiver

Steps to Apply for Waiver



Steps to Apply for Waiver



buprenorphine.samhsa.gov/forms/30NPPA.php

Buprenorphine Waiver Notification

Administration for use in maintenance or detoxification treatment and that have not been the subject of an adverse determination.

8. CERTIFICATION OF QUALIFYING CRITERIA

☑ SAMHSA/HHS Buprenorphine practice guideline exemption (April 2021). These practice guidelines exempt covered practitioners licensed under state law, and who possess a valid DEA registration, from certification requirements related to training, counseling, and other ancillary services (i.e., direct provision of or referral to psychosocial services).

This exemption only applies to those treating up to 30 patients. Time spent practicing under this exemption will not qualify the practitioner for a higher patient limit.

☑ NEW NOTIFICATION - I certify that I am either a nurse practitioner or physician assistant who satisfies the definition of a "qualifying other practitioner" under 21 U.S.C. § 823(g)(2)(G)(iv), as amended by the Comprehensive Addiction and Recovery Act of 2016.

☐ NEW NOTIFICATION - I certify that I am either a clinical nurse specialist, certified registered nurse anesthetist or certified nurse midwife who satisfies the definition of a "qualifying other practitioner" under 21 U.S.C. § 823(g)(2)(G)(iv), as amended by the Substance Use Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act of 2018, and I am aware that clinical nurse specialists, certified registered nurse anesthetists and certified nurse midwives, will be included in the definition of a "qualifying other practitioner" under 21 U.S.C. § 823(g)(2)(G)(iv) until October 1, 2023.

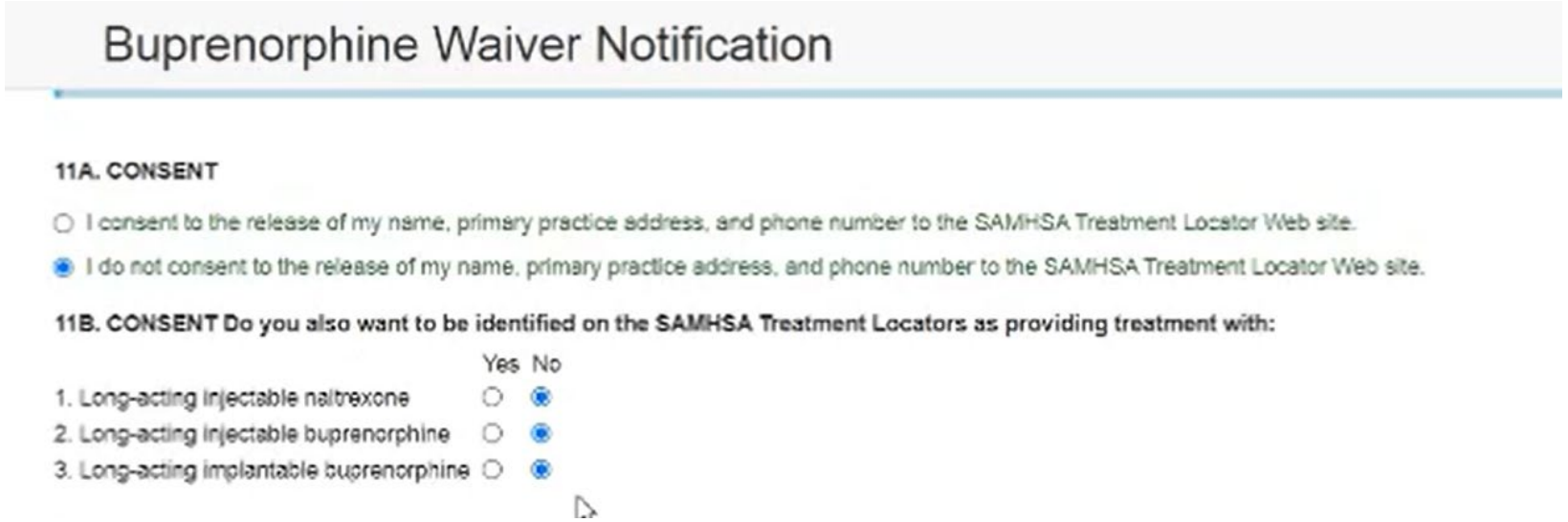
☑ I certify that I am licensed to prescribe Schedule III, IV, or V medications for the treatment of pain under State law.

○ I certify that I am NOT required by State law to be supervised by OR work in collaboration with a qualifying physician to prescribe Schedule III, IV, or V medications.

OR

○ I certify that I am required by State law to be supervised by OR work in collaboration with a qualifying physician to prescribe III, IV, or V medications.

Steps to Apply for Waiver



Buprenorphine Waiver Notification

11A. CONSENT

○ I consent to the release of my name, primary practice address, and phone number to the SAMHSA Treatment Locator Web site.

◉ I do not consent to the release of my name, primary practice address, and phone number to the SAMHSA Treatment Locator Web site.

11B. CONSENT Do you also want to be identified on the SAMHSA Treatment Locators as providing treatment with:

	Yes	No
1. Long-acting injectable naltrexone	○	◉
2. Long-acting injectable buprenorphine	○	◉
3. Long-acting implantable buprenorphine	○	◉

Steps to Apply for Waiver

Success!

Notification of Intent to Use Schedule III, IV, or V Opioid Drugs for the Maintenance and Detoxification Treatment of Opiate Addiction by a "Qualifying Other Practitioner" under 21 USC § 823(g)(2)(G)(iv)

Form Approved: 0930-0234

Date: 01/31/2023

See OMB Statement Below

Note: Notification is required by § 303(g)(2), Controlled Substances Act (21 USC § 823(g)(2)). See instructions below.

Back

Your Waiver Notification has been successfully submitted. Please check your spam/junk folders. If you do not see an email attachment in your inbox within 45 days, please contact the Buprenorphine Center at 866-BUP-CSAT (866-287-2728). If you submitted an increase waiver DO NOT send your training certificate. If this is your first time applying and you did not upload your training, please forward via email to CSATBUPinfo@dsgonline.com.