MAT TRAINING

PROVIDERS' CLINICAL SUPPORT SYSTEM
For Medication Assisted Treatment

Buprenorphine Waiver Training: Advanced Review

Faculty Disclosure

Maria Sullivan, M.D., Ph.D receives no financial support from pharmaceutical companies.

Participants will be informed when/if the contents of this activity include discussion of off label or investigative drug uses.

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Frances Levin, MD is a consultant for GW Pharmaceuticals and receives study medication from US Worldmed. This planning committee for this activity has determined that Dr. Levin's disclosure information poses no bias or conflict to this presentation.

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Target Audience

- The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.
- This activity is relevant for providers who have completed waiver trainings and would like to review and refresh their skills and knowledge.

Educational Objectives

At the conclusion of this activity, participants should be able to:

- Characterize the pharmacology of buprenorphine as this relates to its clinical use.
- Describe best practices for buprenorphine/naloxone induction, prescribing and ongoing monitoring.

Accreditation Statement

American Academy of Addiction Psychiatry (AAAP) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation Statement

American Academy of Addiction Psychiatry designates this enduring material educational activity for a maximum of 1 (one) *AMA PRA Category 1 Credit*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

- Date of Release: June 19, 2014
- Date of Expiration: June 19, 2017

Participation in this CME Activity

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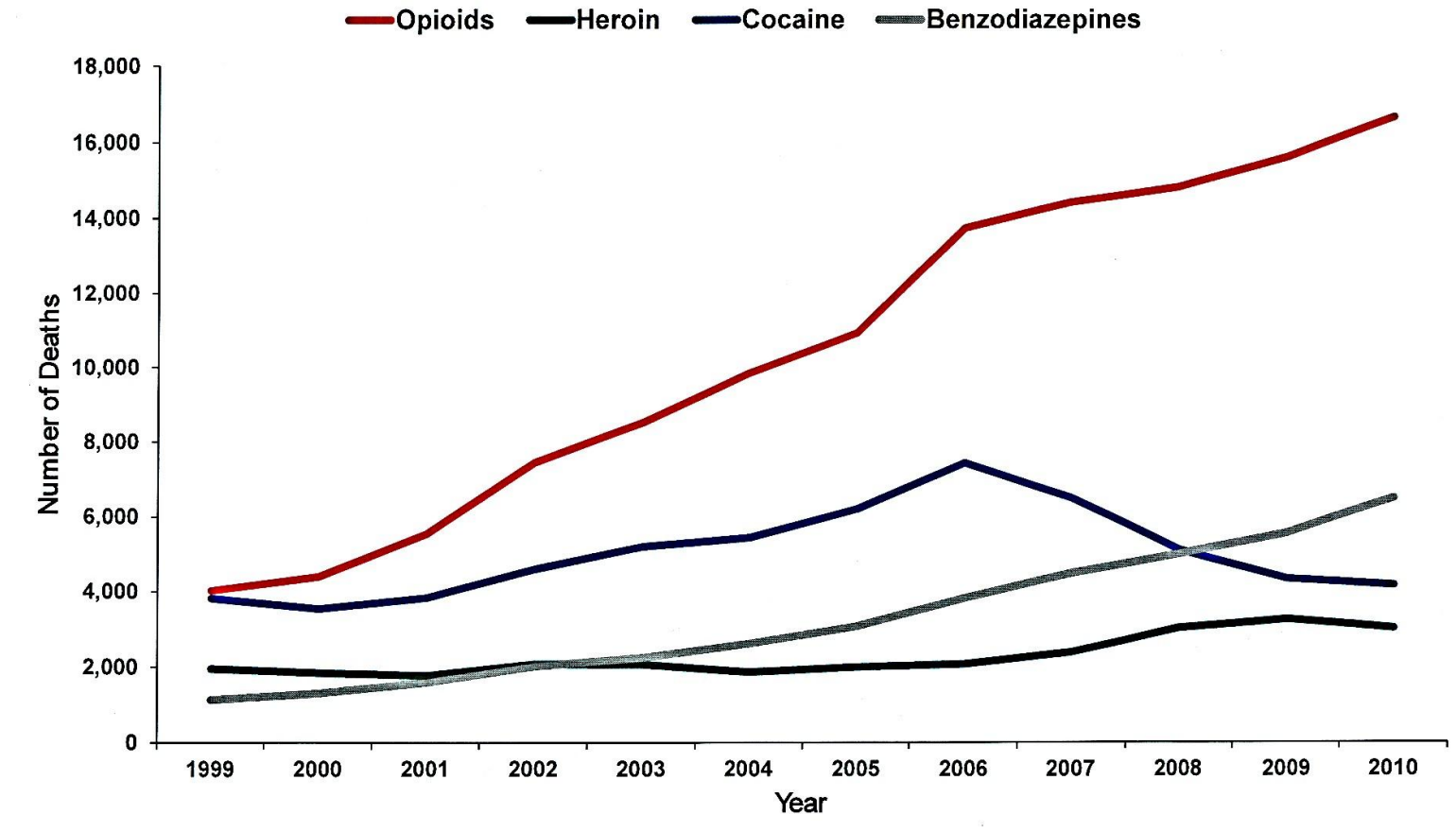
Overview Opioid Dependence Treatment with Buprenorphine/Naloxone: The Growing Epidemic of Opioid Addiction

- Opioid dependence in the U.S.: >2.5 million
- Most people with opioid dependence are not receiving treatment (SAMHSA 2013)
- Nonmedical use of prescription medications (past month, 2010): 7 million, led by opioids (4.4 million)
- Since 1999: 300% increase in the sales of opioid pain medications in the U.S.
- 98% increase in ED visits 2004-2009
- Prescription opioid overdoses increased <300% in the past 20 years: 16,651 deaths in the U.S. in 2010 (Mack et al. 2013).
- CDC: Mixing of drugs was found in half of prescription opioid-related deaths (most frequent: benzodiazepines, heroin, cocaine, and alcohol)

Drug Overdose Deaths by Major Drug Type, U.S. 1999-2010



CDC, National Center for Health Statistics, National Vital Statistics Systems, CDC Wonder. Updated with 2010 mortality data.

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Amended Controlled Substance Act: DATA 2000

- Allows physician to prescribe narcotics (schedules III, IV, V), or combinations, for treatment of opioid dependence
  - **Narcotic drug requirements:**
    - Must be approved by FDA for use in maintenance or detoxification for opioid dependence treatment
    - Schedule III, IV, or V
    - Drugs or combinations of drugs
  - **Practitioner requirements:**
    - "Qualifying Physician" (MD certified in Addiction Medicine by ASAM or AOA or 8-hr training) by must certify capacity to refer patients for counseling and ancillary services
    - ≤ 30 pts. for individual physicians; up to 100 pts. with special waiver post-Year 1
    - Physicians must register with SAMHSA and DEA

Buprenorphine Products are the Only Drugs Currently FDA Approved for Office-Based Treatment of Opioid Dependence

- **Buprenorphine Characteristics:**
  - Mu opioid receptor partial agonist
  - Exhibits ceiling effect on respiratory depression with increasing doses in opioid-experienced individuals (N.B.: not true for opioid-naive persons; buprenorphine can cause adverse events or deaths if ingested by those without opioid tolerance)
  - Buprenorphine is safer in overdose than other opioids
  - Buprenorphine/naloxone formulation is advised to be used for treatment of opioid dependence (naloxone diminishes risk of diversion to injection; precipitates withdrawal)

Buprenorphine: Clinical Use In Practice

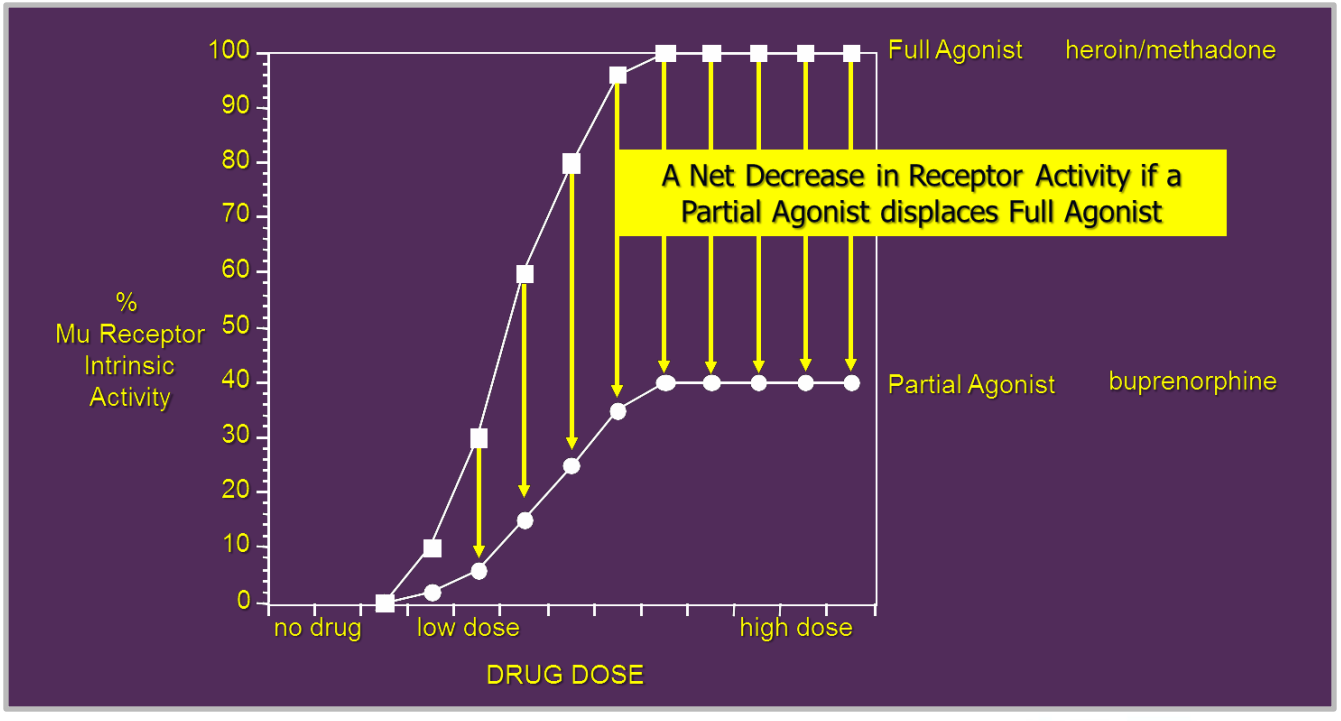
- **Schedule III (vs. methadone: Schedule II)**
  - Note: Methadone can only be dispensed for opioid dependence from specially regulated opioid treatment programs (MMTP), certified and site-visited by SAMHSA/CSAT
  - Treatment modalities for buprenorphine/naloxone:
    - Office-based treatment
      - Primary Care or Specialty Care (e.g.: Infectious Disease, GI, Psychiatry) or Substance abuse Jan. 2013: Revision to federal legislation:
  - Jan. 2013: MMTPs can now dispense buprenorphine using same limits and regulatory requirements that apply to office-based practices

Pharmacology of Full vs. Partial Mu Opioid Receptor Agonists

- Full mu opioid receptor agonists (e.g. morphine):
  - Activate more mu receptors with increasing dose
  - Can result in opioid toxicities at high doses
- Buprenorphine is a mu opioid receptor partial agonist with **stronger affinity** for the mu receptor than full mu agonists, but only **partially activates** the receptors
- When buprenorphine binds to mu receptors in an opioid-person who has full agonist on board, net **decrease** in activation occurs and opiate withdrawal develops
- Therefore, buprenorphine can precipitate opiate withdrawal if it displaces a full agonist from mu receptors

Pharmacology of Full vs. Partial Mu Opioid Receptor Agonists

- Buprenorphine can precipitate opiate withdrawal if it displaces a full agonist from mu receptors



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Clinical Forms of Buprenorphine

- Sublingual (SL) forms for treatment of opioid dependence: "Combo" buprenorphine/naloxone: preferred form
  - Bup 2/0.5 mg/nx film, 4/1 mg, 8/2 mg,12/3 mg film developed to decrease diversion to injected use
  - Newer menthol tablet 5.7/1.4 mg and 1.4/0.36 mg offers higher bioavailability, faster dissolving
- "Mono" sublingual dissolving tablet (Bup 2 or 8 mg)
  - Pregnancy is main use for this formulation
- SL form has relatively lower abuse risk than full agonists
- Human laboratory studies:
  - Injected buprenorphine produces reinforcing "high"
  - Injection of bup/nx precipitates severe withdrawal if opioid-dependent and mu agonist on receptors; naloxone in bup displaces full agonist

Buprenorphine: Abuse Potential

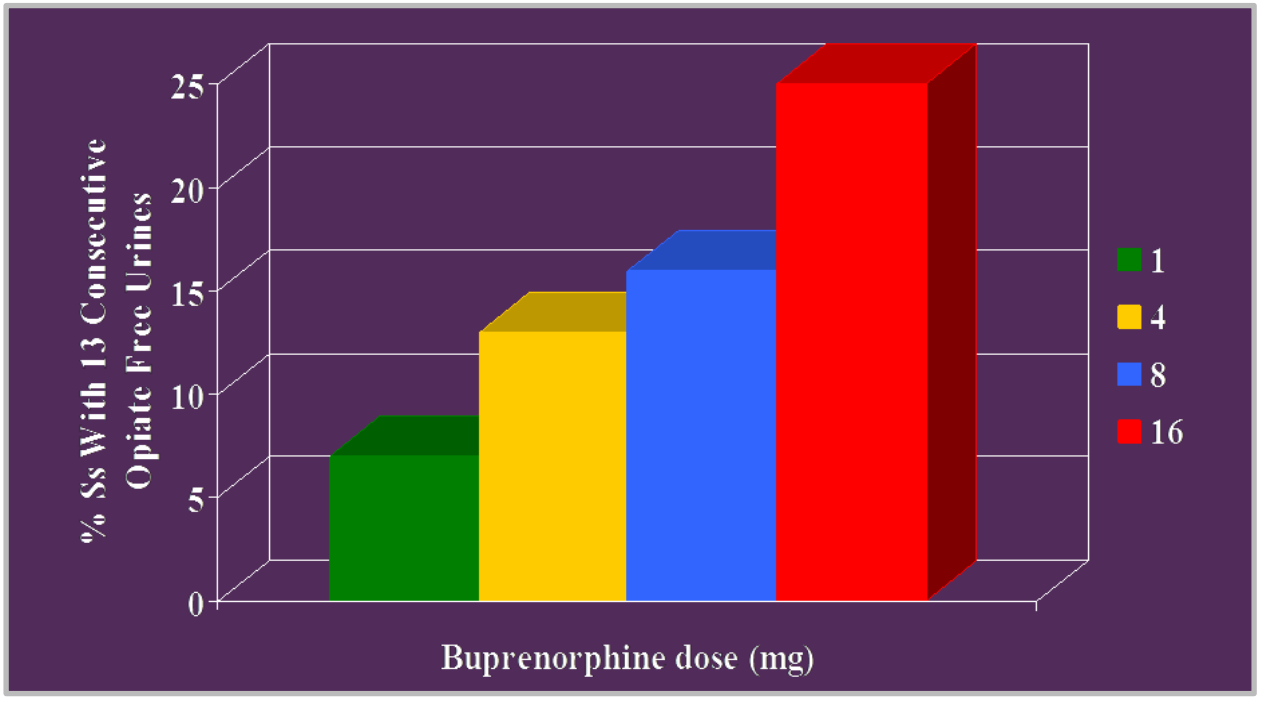
- Abuse potential of buprenorphine varies as function of:
  - Level of physical dependence
    - Lower opioid physical dependence less likely to precipitate withdrawal; more likely to produce an agonist effect
  - Time interval between last dose of opioid agonist and buprenorphine ingestion
    - Longer it has been since last use of opioid, more likely buprenorphine will give opioid effects
  - Two types of treatment: medical withdrawal and maintenance; > 80% undergoing medical withdrawal will relapse in the year following treatment (Dunn et al. 2011)

Buprenorphine Maintenance

- Numerous outpatient clinical trials in people with opioid dependence compared efficacy with:
  - Methadone, placebo or LAAM (a long-acting opioid no longer manufactured in the U.S. but previously used for opioid dependence treatment)
- These trials reliably demonstrated that, in preventing relapse to heroin:
  - Buprenorphine is more effective than placebo
  - Buprenorphine is equally effective as moderate doses of methadone (e.g., 60 mg per day)

Different Doses of Buprenorphine: Opiate Use

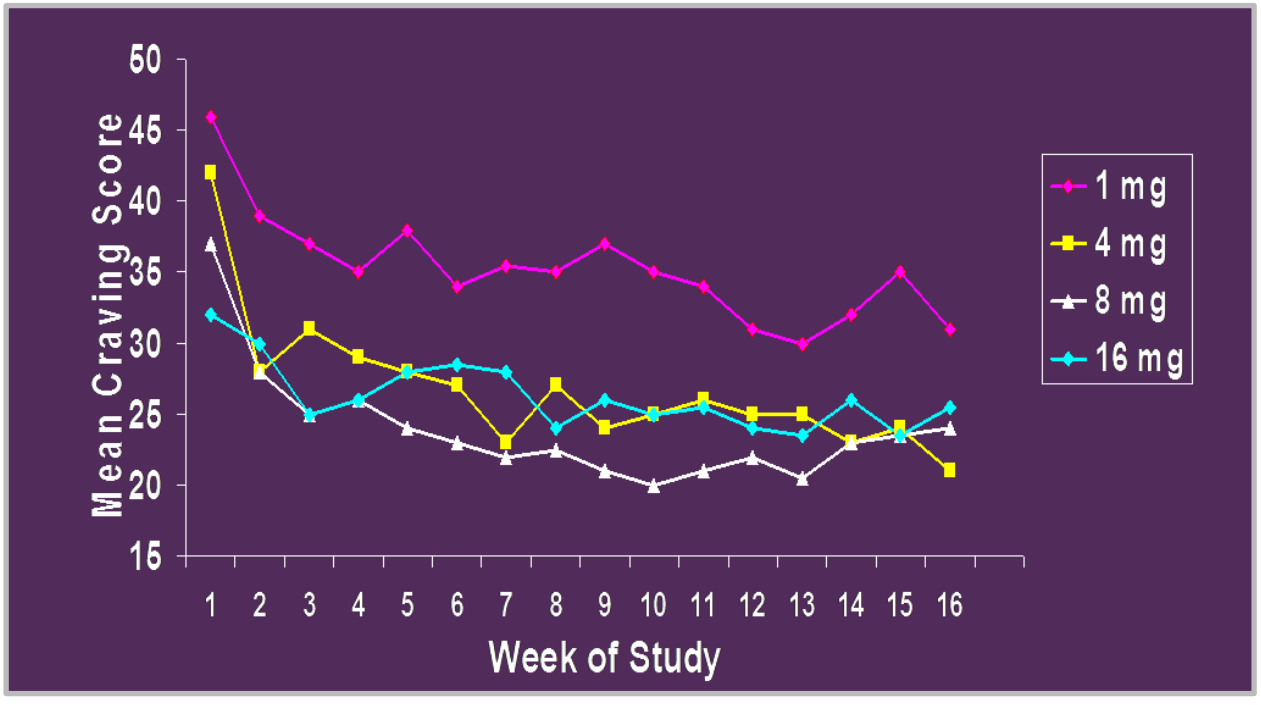
- As dose of buprenorphine increases, opioid use decreases as measured by urine drug screen



Ling et al., 1998

Mean Heroin Craving: 16-Week Completers

- 8- and-16 mg doses of buprenorphine associated with lower opioid craving over time



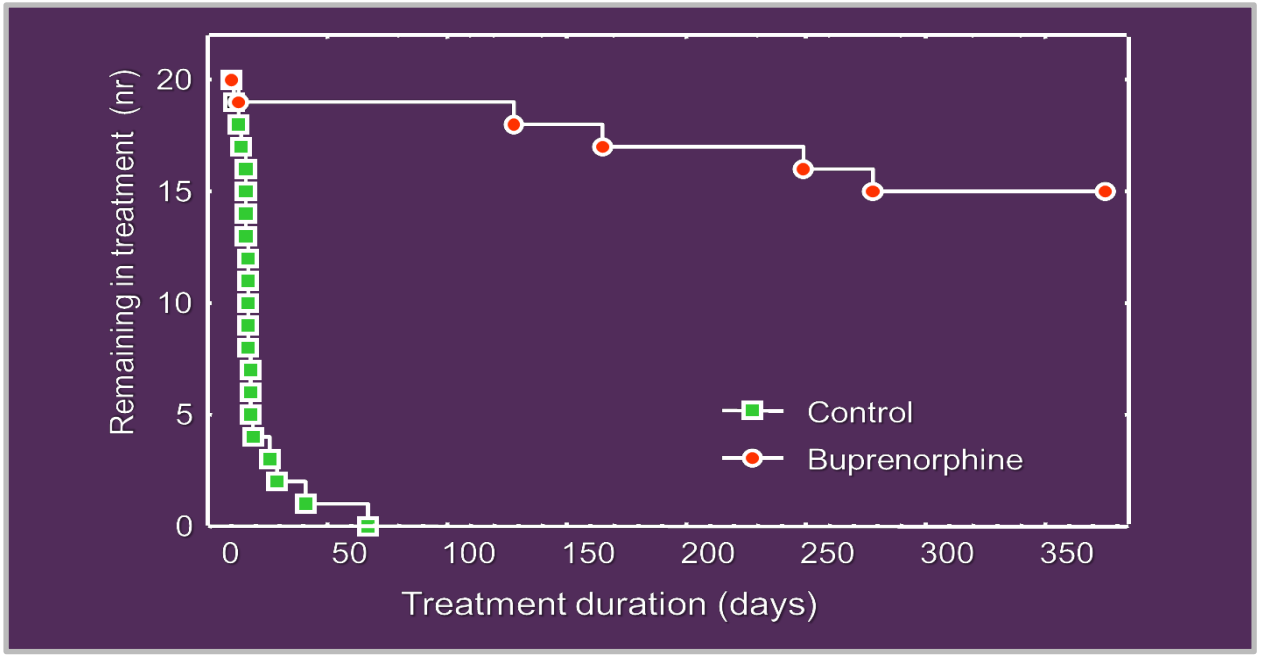
Ling et al., 1998

Buprenorphine vs. Methadone Retention Rates

- Methadone is superior to buprenorphine in retaining patients in treatment using flexible dosing, which is most relevant to patient care (Mattick et al. 2014)
- In a 24-week multi-site randomized trial, methadone produced a treatment completion rate of 74% versus 46% for buprenorphine/naloxone. Bup/nlx participants reached 60% with 30-32 mg, and methadone participants reached 80% when a dose of 60 m/day was reached or exceeded (Hser et al. 2014).

Buprenorphine Maintenance/Withdrawal

- Even with enhanced psychosocial services; those receiving withdrawal treatment (controls) had all left the study by 60 days, while 75% of maintenance patients remained at 1 year



Kakko et al., 2003

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Starting Buprenorphine Treatment: Best Practices

- Confirm that the patient requesting buprenorphine treatment is opioid-dependent
  - History/previous treatment records if available
  - Look for physical signs: withdrawal, track marks
  - Urine drug screen positive for opioids (at least one positive screen).
  - Exception: need not be opioid-positive if documented history of use, currently at high risk after discharge from detox., residential treatment, or jail. If opioid-naïve, start low and assess frequently to avoid potential sedation or relapse.

Starting Buprenorphine Treatment: Best Practices

- Check your state prescription drug monitoring program (PDMP): prior to starting and regularly thereafter
  - Note: Some states have passed legislation requiring state's PDMP be checked before prescribing controlled substances.
  - Once patient is started on buprenorphine you should:
  - Continue random, regular urine screens to confirm that buprenorphine is present and to determine what other drug(s) are being used; can use dipsticks and/or send to clinical lab for analysis
  - Call patient back for random medication counts to decrease diversion risk

Ongoing Buprenorphine Treatment: Best Practices

- Urine Drug Screening:
  - Point-of-Care Testing: 'Dipsticks':
    - Need to order separate dipsticks to detect synthetic opioids
    - Standard "opiates" screen: detects only codeine, morphine, heroin
    - Separate tests needed for:
      - Methadone
      - Buprenorphine
      - Oxycodone
      - Hydrocodone

Ongoing Buprenorphine Treatment: Best Practices

- Every patient with opioid dependence should receive psychosocial treatment in addition to medication
  - Aberrant behaviors of opioid dependence are not addressed by giving medication alone
  - Therapies to be offered should include:
    - Supportive medication monitoring
    - Individual or group counseling
    - Encourage attendance at 12-Step, mutual help groups
  - Physicians must attest (both when apply for waiver and during DEA site visits) that they can refer patients to addiction counseling and other non-pharmacological treatment

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Ongoing Buprenorphine Treatment: Best Practices

- Document all aspects of substance abuse treatment
- Prescribe only FDA-approved medications for office-based treatment of opioid dependence (buprenorphine/naloxone sublingual film, buprenorphine s.l. tablets, or monoproduct s.l. tablet — no other drugs and no other buprenorphine formulations are approved for this use!)
- Advisable not to give large prescriptions for buprenorphine/naloxone early in treatment
- E.g.: No more than a week at a time in first months until patient stabilizes and stops opioid use/other drug use, shows regular treatment attendance, PDMP confirms no other prescribers and without evidence of other controlled substance prescriptions

Ongoing Buprenorphine Treatment: Best Practices

- Prescribe monthly or more frequently; need to assess these patients at least once a month for first 6-12 months. If visit interval is lengthened in stable patients without evidence of substance use for >6 months, prescriber may require patients to submit to random urine testing when called, after first 6 months.
- Regarding medical record keeping: Remember: if it is not documented in the medical record: it didn't happen!
- Make sure patient signs a 42 CFR compliant release of information before any treatment details are released/discussed with another provider

Buprenorphine Dosing

- Sublingual administration
- Medication is held under tongue until fully dissolved which can take several minutes
  - Taste is generally well tolerated; films reported to have better flavor; menthol tablets well tolerated
  - Monitor dissolution after dosing
- Two films/tablets at once is limit to assure adequate absorption
- One film or tablet is placed under tongue on each side
- Therapeutic dose is generally in 12/3-16/4 mg/d but range is 4/1-24/6 mg/d; upper dose limit approved by FDA is 24/6 mg

Buprenorphine: Side Effects

- Nausea/vomiting (consider precipitated withdrawal especially in first 15-20 minutes after dosing)
- Constipation, headache, diaphoresis, vasodilation
- Sedation (generally mild with bup alone, but use of other sedating drugs or use in those not currently dependent, but eligible for buprenorphine treatment by history may have greater sedation)
- Screen for Hep C and monitor for elevations in liver transaminases (as Hep C marker); bup is not hepatotoxic
- Precipitated withdrawal can occur in opioid-dependent patient who has recently used opioid, and is not in withdrawal at the time of buprenorphine ingestion, or if long-acting opioid too recently taken

Induction: Procedure Required to Start Buprenorphine in Opioid-Dependent Patients

- No short-acting opioids for at least 12-18 hours before induction; must wait 24-72 hours after long-acting opioids
- Conversion from methadone: reduce to ≤30 mg, wait at least 24 hours but time elapsed does not suffice; observe withdrawal before first dose using standardized scale, e.g. Clinical Opiate Withdrawal Scale (COWS)
- COWS ≥ 10 (objective signs +/- subjective aspects of withdrawal); ask pt. to wait at office to reach score of 10
- If patient appears not to be in withdrawal remind him/her of risk of precipitated withdrawal if recently used opioids
- Usual Day 1 dose is 4 mg to avoid precipitating w/d
- Important to proceed slowly, using objective signs; consider inpatient induction if necessary

Induction: Procedure Required to Start Buprenorphine in Opioid-Dependent Patients

- **Day 1:** First dose: 2/0.5 mg-4/1 mg SL
- Monitor 1-2 hours before giving a second dose
- If withdrawal symptoms still present after monitoring period; give second dose 2/0.5-4/2 mg
- Generally up to 8/2 mg given on Day 1

- **Day 2:** Assess patient; increase by up to 12/3 mg depending on symptoms from Day 1 dose to present
- Higher initial dose may be needed in short term if patient is coming off long-acting opioid
- Home-based induction is a safe and feasible option associated with outcomes similar to office-based induction (Cunningham et al., 2011; Lee et al., 2009)

Induction: Procedure Required to Start Buprenorphine in Opioid-Dependent Patients

- **Following Day 2**, increase to up to 12/3 mg; do not increase dose for 5-7 days before deciding on a further dose increase. Buprenorphine has a half-life > 24 hrs. It will take 5-7 days to get to steady state, at which time an assessment of medication effectiveness can be completed (has withdrawal discontinued; has craving stopped or abated?)
- Mean maintenance dose: 12/3-16/4 mg/d
- Range of therapeutic dosing: 4/1-24/6 mg/d
- FDA-approved upper dose limit: 24/6 mg/d
- Chronic pain patients may require TID or QID dosing (e.g. 8 mg TID) as analgesic effects last 6-9 hrs

Induction: Possible Complications

- **Precipitated Withdrawal:**
  - Occurs if bup/nx is administered before withdrawal onset in person physically dependent on opioids
  - Can be characterized by severe withdrawal (N/V, cramps, diarrhea, chills, myalgia) within approx. 20-30 minutes of bup/nx dose
  - Check time of last use of opioids if this occurs
- **Options if Precipitated Withdrawal Occurs:**
  - Medications for withdrawal symptoms or
  - Monitor and re-dose with bup/nx after several hours (i.e.: continue induction)

Maintenance Treatment

- What is an “effective dose”?
  - Individual discontinues or substantially reduces opioid use
  - Treatment retention
  - Craving resolves
  - Reduction/cessation of high risk, drug-related activities
- Doses over 16/4 mg/d are not usually required (although patients will sometimes ask for more)
- Two neuroimaging studies have shown 79-95% of mu receptors are occupied at buprenorphine doses of 16 mg/d

Maintenance Treatment

- Repeated administration of bup/nx produces and maintains physical dependence
- Degree of physical dependence is less than that produced by full agonist opioids
- Withdrawal syndrome less severe for bup/nx than for heroin, methadone or other opioids
- Induct onto bup/nx up to 16/4 mg daily; then adjust
- Offer naltrexone (after >7 days free of bup/nx) to help prevent relapse; consider starting with a low (12.5-25 mg) dose (by scoring tablets) and when well tolerated convert to injectable form for adherence

Addressing Problems in Treatment

- Treatment Agreement with every patient recommended:
  - Outlines parameters under which bup will be provided.
  - Describes goals of treatment
  - Informs patient about risks/benefits of the medication
  - Informs patient of other required aspects of treatment: urine drug screens, breath alcohol test if indicated, checking PDMP, medication counts
  - Gives patient notice that you will medically withdraw/refer to higher level of care if noncompliant
  - Informs patient of behaviors that will not be allowed

Addressing Problems in Treatment

- Continued use of opioids
  - Do not medically withdraw for lapse (unless risk outweighs benefit of treatment). If ongoing opioid use is chronic and most tox. screens are positive:
    - More counseling; higher level of care:
    - Increase dose of bup up to 32 mg if necessary
    - Consider referring to MMTP or detox +TC substance treatment program that offers XR-NTX (not associated with ongoing opioid use)
- Benzodiazepines/sedative/ hypnotic drugs can sometimes be used therapeutically in buprenorphine-maintained individuals, but monitoring is required.
- If patient abusing benzodiazepines or drugs/alcohol, consider intensifying frequency of visits or IOP referral

Addressing Problems

- Mental Illness that co-occurs with opioid dependence:
  - Not an absolute contraindication to bup/nx
  - If patient is seeking treatment for co-occurring disorders, then bup/nx can be part of the care plan
- Try to avoid use of drugs likely to have drug interactions with bup/nx: e.g.: fluoxetine and fluvoxamine inhibit CYP 3A4 and could potentially inhibit bup metabolism;
- Benzodiazepines with CNS depressant effects
- While polysubstance abuse is common, drug-drug interactions can be life-threatening (e.g.: benzodiazepines with buprenorphine or other opioids)

Addressing Problems

- Physical Illness:
  - All patients should have a primary care provider who is either the bup/nx prescriber or who provides primary care, and another physician (example: psychiatrist) prescribes bup/nx
  - Primary care and/or specialists (e.g.: Infectious Disease, GI) can treat multiple medical issues in the same patient

Buprenorphine-Methadone Comparison

	Buprenorphine/Naloxone	Methadone
Regulation/Diversion	Partial agonist Combination: buprenorphine/naloxone to be used except in pregnancy Less regulation Office Based Opioid Treatment possible	Full agonist May be diverted- especially when prescribed in pain patients Toxicity risk greater Specialized treatment centers required for opioid dependence
Dose/Side Effects	Preferred is combo: bup/nlx Side effects minor Precipitated withdrawal potential	Relatively high dose required for tolerance induction; continued opiate effects, sedation

Buprenorphine-Methadone Comparison

	Buprenorphine/Naloxone	Methadone
Ease of Use	Induction requires clinical monitoring Available by prescription Withdrawal more easily tolerated One physician for patients with multiple illnesses	Induction and dosing straightforward Withdrawal challenging; patients c/o significant discomfort Need for multiple providers Frequent clinic visits may prevent full time employment
Toxicity	Few medically serious side effects in opioid experienced users except when ingested in combination with other drugs and/or alcohol	Respiratory depression, altered mental status, QT prolongation, Torsades de Pointes
Drug Interactions	Few clinically significant with HIV meds to date; possibly atazanavir/ritonavir, rifampin, BZD use is a concern	Numerous, especially HIV meds, TB meds, anticonvulsants BZD use is a concern

Who Should and Who Should Not Be Treated With Buprenorphine?

- Serious medical illness: some may benefit (e.g.: IDU with HIV or HCV)
- More functional patients may benefit: employment/employable
- Mental illness needs to be considered case by case: no actively suicidal or psychotic individuals; treatment for serious depression or bipolar needs to be with an addiction psychiatrist or psychiatrist with experience treating co-occurring SUDs

Who Should and Who Should Not Be Treated With Buprenorphine?

- No BZD dependence
- Anxiety disorders: best to treat with SSRIs or behavioral therapies, which are treatment of choice for many anxiety disorders
- Polysubstance Dependence: treatment must address all substances—not just opioids

Your Practice in Office-Based Treatment of Opioid Dependence

- Obtain the waiver to offer buprenorphine/naloxone treatment to your opioid-dependent patients
- Make sure all staff understand the confidentiality issues in treating substance use disorders
- Use the PCSS-B clinical tools in your practice:
  - Information for patients and families
  - Screening forms
  - Treatment agreements
  - History and Physical Examination Forms
  - 42 CFR compliant Consent Forms
  - Opiate Withdrawal Rating Scales
  - Example of Progress Notes

What is Happening Now: Cautionary Notes

- Buprenorphine has become one of most prescribed drugs in the United States, as opioid dependence is a chronic, relapsing illness
- Long-term bup/nx maintenance is an accepted course in context of supportive medication monitoring
- If patient seeks to taper off bup/nx, induction onto naltrexone can prevent relapse
- Buprenorphine is being diverted at increasing rates:
  - Need to assess effective dose
  - Test for presence of buprenorphine and other drugs/alcohol with regular urine tox screens
- Call patients back for random medication counts

Summary

- Buprenorphine/naloxone:
  - Opioid partial agonist: fewer opioid effects than heroin or methadone; less potential for toxicity
  - Induction requires clinical observation
  - Withdrawal is better tolerated than for other opioids
- Diversion is an important issue:
  - Should not increase dose without justification
  - Control number of days available by prescription
  - Require regular clinical assessments and assessment of drug/alcohol use as contingency for medication; psychosocial treatment should be encouraged.

References

Center for Disease Control and Prevention. (2010). National Center for Injury Prevention and Control: Unintentional Drug Poisoning in the United States. www.cdc.gov/HomeandRecreationalSafety/Poisoning

Center for Substance Abuse Treatment. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction. Treatment Improvement Protocol (TIP) Series 40. DHHS Publication No. (SMA) 04-3939. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2004. Available online at http://www.ncbi.nlm.nih.gov/books/NBK64245/pdf/TOC.pdf

Centers for Disease Control and Prevention: Injury Prevention and Control Policy Impact: Prescription Painkiller Overdoses. 2011 http://www.cdc.gov/HomeandRecreationalSafety/rxbrief

CSAT Buprenorphine Information Center. Drug Addiction Treatment Act of 2000. Available online at http://buprenorphine.samhsa.gov/data.html

Cunningham CO, Giovanniello A, Li X, Kunins HV, Roose RJ, Sohler NL. (2011). A comparison of buprenorphine induction strategies: patient-centered home-based inductions versus standard-of-care office-based inductions. Journal of Substance Abuse Treatment, 40(4): 349-356.

Dunn KE, Sigmon SC, Strain EC, Heil SH, Higgins ST. (2011). The association between outpatient buprenorphine detoxification duration and duration and clinical treatment outcomes: A Review. Drug and Alcohol Dependence, 119(1-2): 1-9.

References

Hser YI, Saxon AJ, Huang D, Hasson A, Thomas C, Hillhouse M, Jacobs P, Teruya C, McLaughlin P, Wiest K, Cohen A, Ling W. (2014). Treatment retention among patients randomized to buprenorphine/naloxone compared to methadone in a multi-site trial. Addiction 109(1): 79-87.

Kakko J, Svanborg KD, Kreek MJ, Heilig M. (2003). 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: A randomized, placebo-controlled trial. Lancet, 361(9358): 662-668.

Kintz P. (2002). A new series of 13 buprenorphine-related deaths. Clinical Biochemistry, 35: 513-516.

Krupitsky E, Nunes EV, Ling W, Illeperuma A, Gastfriend DR, Silverman BL. (2011). Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomized trial. Lancet 377(9776): 1506-13.

Ling W, Charuvastra C, Collins JF, Batki S, Brown LS Jr, Kintaudi P, Wesson DR, McNicholas L, Tusel DJ, Malkeneker U, Renner JA Jr, Santos E, Casadonte P, Fye C, Stine S, Wang RI, Segal D. (1998). Buprenorphine maintenance treatment of opiate dependence: A multicenter, randomized clinical trial. Addiction, 93(4): 475-486.

McCance-Katz EF. (2004). Office based treatment of opioid dependence with buprenorphine. Harvard Review of Psychiatry, 12: 321-338

Mack KA. (2013). Drug-induced deaths -- United States, 1999-2010. MMWR Surveil Summ 62 Suppl 3: 161-3.

Mattick RP, Breen C, Kimber J, Davoli M. (2014) Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev 2: CD002207.

Maxwell J, McCance-Katz EF. (2010). Indicators of methadone and buprenorphine use and abuse: What do we know? American Journal of Addictions, 19: 73-88.

.

References

Simpson DD, Joe GW, Bracy SA. Six-year follow-up of opioid addicts after admission to treatment. Arch Gen Psychiatry 39(11): 1318-23.

Substance Abuse and Mental Health Services Administration, Office of Applied Studies. Emergency department data from the Drug Abuse Warning Network: Final estimates 1995–2002. (DAWN Series D-24, DHHS Publication Number (SMA) 03-3780). Rockville, MD: SAMHSA OAS, 2003.

Substance Abuse and Mental Health Services Administration (2013). Results from the 2012 National Survey on Drug Use and Health: Mental Health Findings, NSDUH Series H-47, HHS Publication No. (SMA) 13-4805. Rockville, MD: Substance Abuse and Mental Health Services Administration. Available online at http://www.samhsa.gov/data/NSDUH/2k12MH_FindingsandDetTables/2K12MHF/NSDUHmhfr2012.htm

Substance Abuse and Mental Health Services Administration. (2003). Results from the 2002 National Survey on Drug Use and Health: Mental Health Findings, NSDUH Series H-22, DHHS Publication No. (SMA) 03–3836. Rockville, MD: Substance Abuse and Mental Health Services Administration. Available online at http://www.samhsa.gov/data/nhsda/2k2nsduh/results/2k2Results.htm

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MAT TRAINING

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