# Buprenorphine Induction, Taper, Diversion

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I have nothing to disclose

# Overview

- Induction
  - In clinic
  - Home induction
  - Hospital/Emergency Department (ED) Induction
- Tapering
- Urine Testing
- Diversion
- DEA

# Induction Basics

- Medically monitored startup of buprenorphine therapy
- Administered:
  - When individual has abstained from using opioids for 12–24 hours
  - Use COWS to measure withdrawal severity
  - Start while in mild-moderate withdrawal
- If the patient is not in the early stages of withdrawal (i.e., if he or she has other opioids in the bloodstream), then the buprenorphine dose could **precipitate acute withdrawal**

## Clinical Opiate Withdrawal Scale (COWS)

**TABLE 7**
**COWS**

| *Symptoms* | *Scores* | *Examples* |
|---|---|---|
| Resting pulse rate | 0-4 | 0=80 or less; 1= 81-100; 2=101-120; 4=120 or greater |
| Sweating | 0-4 | 0=none; 4=sweat streaming from face |
| Restlessness | 0-5 | 0=sits still; 5=unable to sit still (even for a few seconds) |
| Pupil size | 0-5 | 0=normal; 5=dilated (only iris rim visible) |
| Bone or joint aches | 0-4 | 0=none; 4=severe discomfort |
| Runny nose or tearing | 0-4 | 0=none; 4=constant |
| GI upset | 0-5 | 0=none; 5=multiple episodes of vomiting or diarrhea |
| Tremor | 0-4 | 0=none; 4=gross tremor |
| Yawning | 0-4 | 0=none; 4=yawning several times/minute |
| Anxiety & Irritibility | 0-4 | 0=none; 4=severe, precluding participation |
| Gooseflesh skin | 0-5 | 0=smooth; 5=prominent piloerection |

COWS=Clinical Opiate Withdrawal Scale; GI=gastrointestinal.

Score: 5-12 mild; 13-24=moderate; 25-36=severe.

Baron D, Garbely J, Boyd RL. *Primary Psychiatry.* Vol 16, No 9. 2009.

## Models of Induction

- Induction and treatment at Opioid Treatment Clinic (OTP)
- Induction Clinics
- At home induction
- Preliminary Data
  - In Emergency Department
  - In hospital induction
- Induction dose too high or too low

# SAMHSA Recommendation

**Center for Substance Abuse Guidelines** (TIP 40):

- Administer the first dose of 2-4 mg under observation in the office or inpatient setting
- Keep the patient in the office for at least an hour to determine the effect of the first dose, and

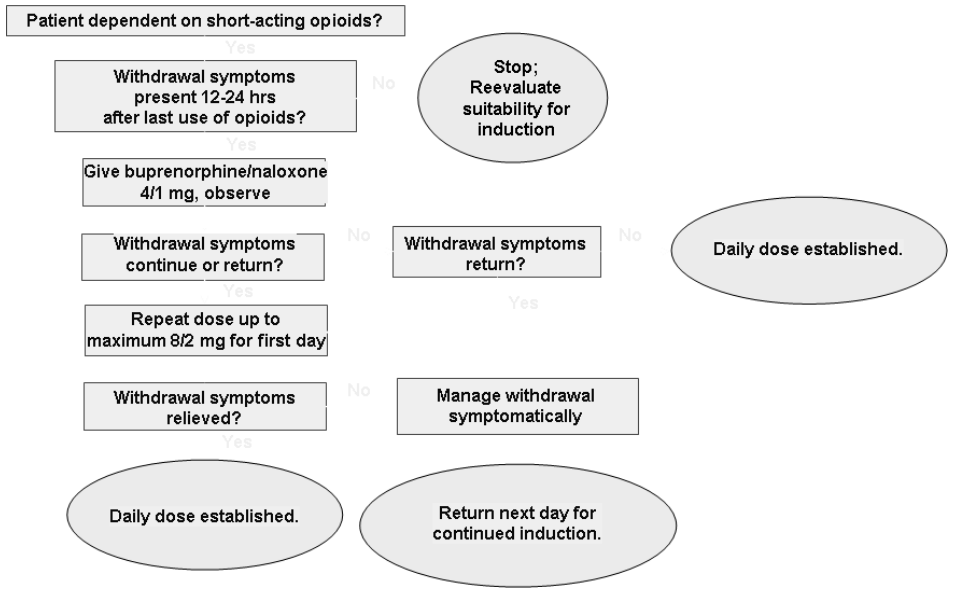
  then document the effect of the first doses
  - Depending on the amount and type of opioid use, the first day's dose may range from 2 to 16 mgs
  - If withdrawal occurs after the patient leaves the office, request that the patient return for

    withdrawal assessment

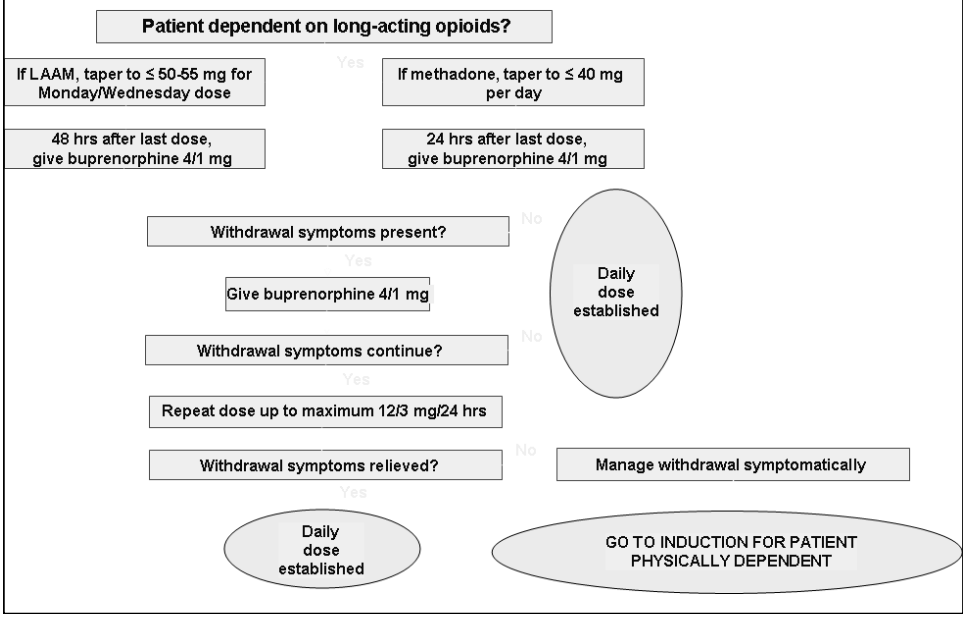
# Observed Buprenorphine Induction

| PRE-INDUCTION | INDUCTION | STABILIZATION | STABILIZATION |
|---|---|---|---|
| Day-2 | Day 1 | Day 2 | DAY 3 |
| Alcohol and Drug Screening and Assessment | Withdrawal Assessment | Assessment for Dose increase | |
| Medical History<br>Medications<br>LABS<br>Pregnancy Test<br>UDS | Observe sublingual administration 1 tablet | Observe sublingual administration 1 tablet | Observe sublingual administration 1 tablet |
| Education<br>Withdrawal Specifics | RX: 1 tab home | RX: 1 tab home | RX: 1 week supply |
| | Daily Counseling | Daily Counseling | Daily Counseling |

# Day 1 Induction: Short Acting Opioids




# Day 1 Induction: Long Acting Opioids



# Home Inductions: Safe, Feasible?

- (Patterson et al, 2014) (n=485)
  - Patients who were prescribed buprenorphine from January 2006 to June 2013
  - Patients received an instructional handout, a 1-week written prescription for buprenorphine, and then sent home and followed with telephone support
  - ***Results****:*
    - Buprenorphine induction was **feasible and safe**
    - **No serious adverse effects**

**Table 1**

Home-based buprenorphine induction kit

| Contents | Purpose |
|---|---|
| *Instruction sheet* | |
| What's in the kit? | Guide to medications |
| When to start Suboxone | Guide to timing of treatment initiation |
| Things not to do | Guide to appropriate behaviors/treatment |
| How to take Suboxone | Facilitate correct dosing |
| Plan | Provide schedules and facilitate follow-up |
| What was taken? | Manage/Track medications taken |

Patterson et al, 2014

*Medications*

| No. of pills | Medication | Dose (mg) | |
|---|---|---|---|
| 10 | Buprenorphine/ Naloxone | 2/0.5 | Initiate buprenorphine treatment (Day 1) |
| 4 | Buprenorphine/ Naloxone | 8/2.0 | Continue buprenorphine treatment (Days 2–3) |
| 6 | Ibuprofen | 200 | Manage withdrawal symptoms: pain |
| 6 | Clonidine | 0.1 | Manage withdrawal symptoms: anxiety |

Patterson et al, 2014

# Retention Rates of Office-based Inductions vs. Home-based Inductions

**Sohler et al, 2009**

- Two year program where all patients were given office-based inductions and in the following two years gave patients the opportunity to choose to have buprenorphine inductions at home or the physician's office
- 51 patients (58.6%) had home-based inductions and 36 (41.4%) had office-based inductions
- Results:
  - Did not indicate superiority of either induction type
  - No indication that of superiority of either induction type on experiencing difficulties with the induction process

## Comparison of Induction Experiences

- Nielsen et al, 2014
  - Multi-site randomized clinical trial (n=69)
    - Examines induction of participants who self-reported primary PO use of methadone, ER-oxychodone, IR-oxychodone, and hydrocodone
  - Results:
    - Type of prescription opioid does not predict induction outcomes
    - Having a COWS score too low at baseline more often led to increased COWS score after the 1st dose (precipitated withdrawal)
      - Demonstrated the importance of not starting induction prior to the presence of at least moderate withdrawal symptoms

# Comparison of Induction Experiences

| Participant characteristics | ER Oxycodone n = 219 | IR Oxycodone n = 107 | Methadone n = 41 | Hydrocodone n = 202 | $\chi^2$/F | p-value |
|---|---|---|---|---|---|---|
| Mean pre-dose COWS Score | 12.7 (SD3.5) | 12.4 (SD3.5) | 13.0 (SD3.6) | 12.7 (SD3.5) | 0.301 | .825 |
| Mean post-dose COWS Score | 5.3 (SD3.9) | 5.8 (SD3.9) | 5.6 (SD4.8) | 5.9 (SD4.1) | 0.833 | .476 |
| Mean reduction in COWS post dose | 7.37 (SD4.7) | 6.6 (SD5.4) | 7.4 (SD5.7) | 6.8 (SD5.1) | 0.845 | .470 |
| Increase COWS post dose | 8 (3.7%) | 11 (10.3%) | 3 (7.3%) | 10 (5%) | 6.368 | .095 |

*Only completed for participants who reported pain at screening

†n = 497

††n = 495

‡n = 529

‡‡n = 543, $\chi^2$ not reported as >25% of cells had <5 or one cell had value of 0

Nielsen et al, 2014, *American Journal on Addictions*

# Low vs High Induction Dose

- A recent systematic review found that in fixed dose studies, **low doses of BUP were less effective than higher doses** (n=740)
  - BUP decreases opioid use by eliminating craving and withdrawal symptoms and blocking the reinforcing effects of opioids
  - low dose (≤8), moderate dose (>8≤24), high dose (<24)

Jacobs (2014) *The American Journal on Addictions*

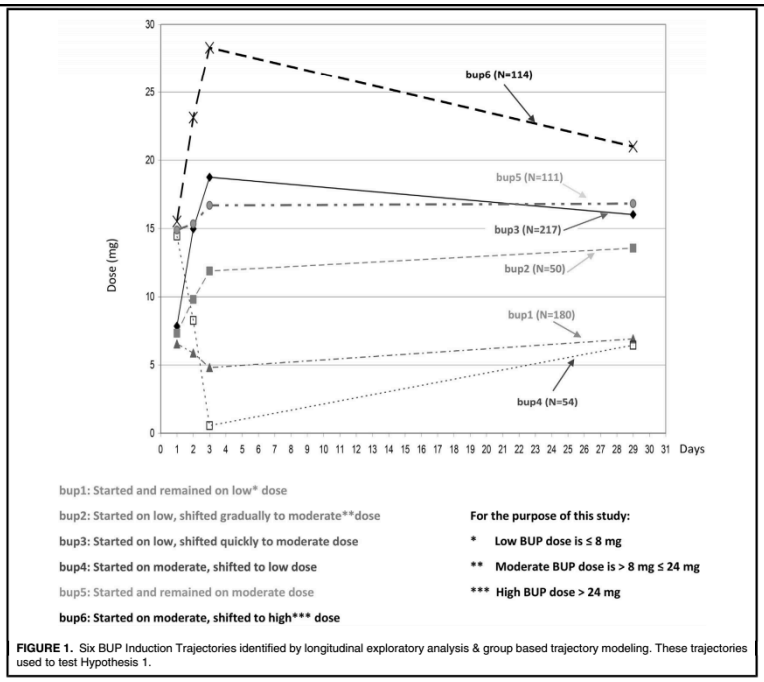



**FIGURE 1.** Six BUP Induction Trajectories identified by longitudinal exploratory analysis & group based trajectory modeling. These trajectories used to test Hypothesis 1.

Jacobs (2014) *The American Journal on Addictions*

# Hospital/Emergency-Department Initiated Buprenorphine Induction

JAMA (D'Onofrio, 2015)

- A randomized clinical trial (n=329) examined the efficacy of different opioid treatment interventions:
  - referral
  - brief intervention
  - screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone
- Results:
  - ED-initiated buprenorphine treatment vs brief intervention and referral significantly:
    - increased engagement in addiction treatment
    - reduced self-reported illicit opioid use
    - decreased use of inpatient addiction treatment services
  - but did not:
    - significantly decrease the rates of urine samples that tested positive for opioids or of HIV risk

## Buprenorphine treatment for hospitalized, opioid-dependent patients: a randomized clinical trial

JAMA Intern Med. 2014 Liebschutz JM et al

- OBJECTIVE: To determine whether buprenorphine administration during hospitalization and linkage to OAT increase entry and engagement in OAT, and decrease illicit opioid use at 6 months
- DESIGN, SETTING, AND PARTICIPANTS: 663 hospitalized, opioid-dependent patients. 139 were assigned to the detoxification (n = 67) or linkage (n = 72) INTERVENTIONS: 5 day buprenorphine detoxification protocol or buprenorphine induction, and postdischarge transition to OAT

RESULTS: Linkage participants were more likely to enter buprenorphine OAT than detoxification group (52 [72.2%] vs 8 [11.9%], P < .001).

At 6 months, 12 linkage participants (16.7%) and 2 detoxification participants (3.0%) were receiving buprenorphine OAT (P = .007).

Participants randomized to the linkage group reported less illicit opioid use in the 30 days before the 6-month interview.

Linkage to OAT is an effective for engaging medically hospitalized patients who are not seeking addiction treatment

## Buprenorphine Tapering

- Review studies
- Discuss pro's and con's of tapering
- Clinical approaches to tapering
  - –Taper to low dose or taper to 0
  - –Fast or Slow

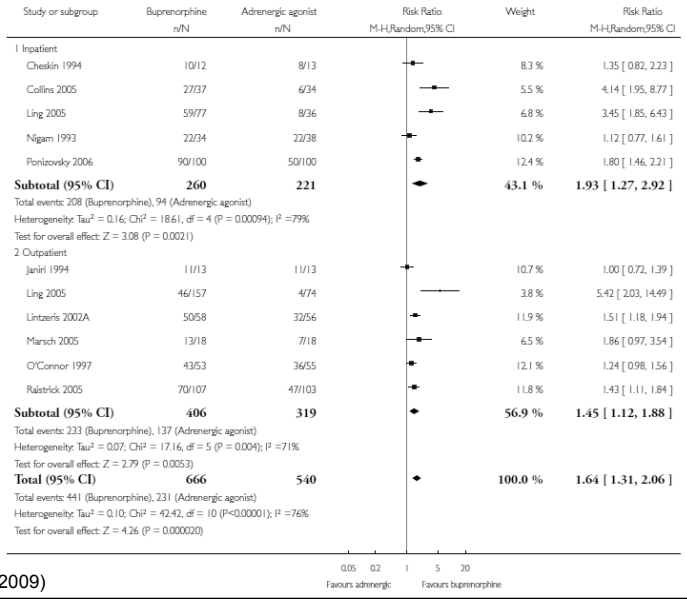
## Why Taper Buprenorphine?

- Patient non-compliance
- Reduce side effects
- Financial issues
- Entering a controlled environment (e.g. incarceration)
- Patient desire to be off medication

# Tapering Buprenorphine: Finding

- Most research studies to date indicate that tapering buprenorphine to zero usually leads to relapse
- Better outcomes typically occur with ongoing medication assisted treatment
- Have a solid justification and support for recovery if you plan to taper a patient completely off medication

# Cochrane Meta-analysis: Bup vs Clonidine Treatment Completion




(Gowing et.al, 2009)

# Buprenorphine Tapering

- JAMA (Fiellin et al, 2014)
  - 14-week randomized clinical trial (n=113 prescription opioid dependent subjects)
  - 2-mg decrease every 3 days for 3 weeks
  - Tapering was less efficacious than ongoing maintenance treatment in patients
    - Had fewer maximum consecutive weeks of opioid abstinence and were less likely to complete trial
    - Taper schedule? Opioids?

# Buprenorphine Taper Strategies

- Compare the relative advantage of two taper schedules (7 vs. 28 days) of Suboxone following four weeks of stabilization
- Purpose was not to advocate detoxification or short-term treatment… whether or not a patient *should go off* is another matter!
- A prior study (Amass et al., 1994) compared a 36 to a 12 day taper in a small sample and found advantage for the longer tapering schedule.

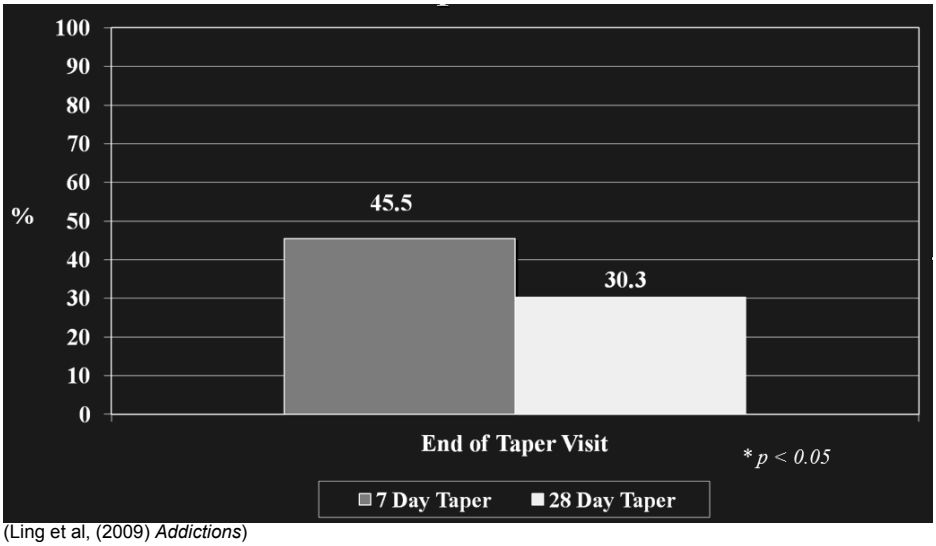
(Ling et al, (2009) *Addictions*)

# Group Assignment

| | | Taper Group | | Total |
|---|---|---|---|---|
| | | 7 day taper | 28 day taper | |
| Stabilization Dose | 8 mg | 22 | 26 | 48 (9.3%) |
| | 16 mg | 68 | 73 | 141 (27.3%) |
| | 24 mg | 165 | 162 | 327 (63.4%) |
| Total | | 255 (49.4%) | 261 (50.6%) | 516 (100%) |

(Ling et al, (2009) *Addictions*)

# Percent "Successful" Present and Abstient at 1 Month




(Ling et al, (2009) *Addictions*)

Arch Gen Psychiatry. 2011 Dec;68(12):1238-46. Epub 2011 Nov 7. ( 1 )

## Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid dependence: a 2-phase randomized controlled trial.

Weiss RD, Potter JS, Fiellin DA,.

**OBJECTIVE:**

To evaluate the efficacy of brief and extended buprenorphine hydrochloride-naloxone hydrochloride treatment, with different counseling intensities, for patients dependent on prescription opioids. N= 653

**DESIGN:**

Multisite, randomized clinical trial using a 2-phase adaptive treatment research design. **phase 1: included 2-week buprenorphine-naloxone stabilization, 2-week taper, and 8-week postmedication follow-up**. Patients with successful opioid use outcomes exited the study; unsuccessful patients entered

**phase 2: extended (12-week) buprenorphine-naloxone treatment, 4-week taper, and 8-week postmedication follow-up.**

**INTERVENTIONS:**

In both phases, patients were randomized to standard medical management (SMM) or SMM plus opioid dependence counseling; all received buprenorphine-naloxone.

Arch Gen Psychiatry. 2011 Dec;68(12):1238-46. Epub 2011 Nov 7.

## Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid dependence: a 2-phase randomized controlled trial.

Weiss RD, Potter JS, Fiellin DA,.

**RESULTS:**

Phase 1 ( 2 week detox)**, 6.6%** (43 of 653) had successful outcomes

Phase 2 (12 week detox) **49.2%** (177 of 360) successful (week 12),

with no difference between counseling conditions.

Success rates 8 weeks after completing the buprenorphine-naloxone taper (phase 2, week 24**) dropped to 8.6% (31 of 360),** again with no counseling difference.

## Taper Recommendations

- Low Dose or Taper to 0?
  - Tapering down and stabilizing on a low dose of 2 mg or 4 mg per day is a perfectly acceptable outcome
- Fast or Slow?
  - The data we have indicate a possible slight advantage and certainly no disadvantage of the fast taper (e.g. 7 days) if goal is to get to zero
  - No harm in slow taper if patient prefers

## Tapering Buprenorphine: Summary

- Taper with strong indication to do so
- Taper stable patients
- Buprenorphine superior to clonidine for withdrawal
- If goal is to get off buprenorphine, fast taper has slight advantage
- Observe carefully for stability during taper
- Have plan to resume buprenorphine promptly if relapse occurs

## Federally Regulated Testing Opioid Cut Off

Table 2. Initial and confirmatory cutoff concentrations used for federally regulated testing (proposed [effective May 1, 2010])[20]

| Initial test analyte | Initial test cutoff (ng/mL) | Confirmatory test analyte | Confirmatory test cutoff (ng/mL) |
|---|---|---|---|
| Marijuana metabolites | 50 | THCA | 15 |
| Cocaine metabolites | 300 | Benzoylecgonine | 150 |
| Opiate metabolites | | Codeine | 2000 |
| • Codeine/morphine[a] | 2000 | Morphine | 2000 |
| • 6-MAM | 10 | 6-MAM | 10 |
| Phencyclidine | 25 | Phencyclidine | 25 |
| Amphetamines | | Amphetamine | 250 |
| • Amphetamine/methamphetamine[b] | 500 | Methamphetamine[c] | 250 |
| • MDMA | 500 | MDMA | 250 |
| | | MDA | 250 |
| | | MDEA | 250 |

## Buprenorphine Urine Testing

- Gas chromatography-mass spectrometry (GS/MS) done at a lab but more expensive
- Will NOT show as morphine positive (or any other opiates)
- Mean elimination half-life = 37 hours
- In-office tests made specifically for buprenorphine
  - Cutoff: 10 ng/ml of Buprenorphine-3-β-dglucoronide
  - Purchase on the internet

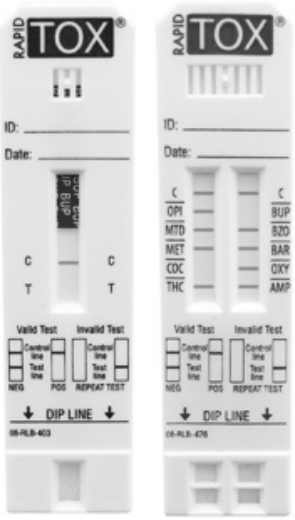


**Table 8. Examples of potential false positives due to cross-reacting compounds for certain immunoassays**

| Immunoassay affected[a] | Cross-reacting drug[b] |
|---|---|
| Opiates | Quinolone antibiotics (eg, levofloxacin, ofloxacin)[96;97] |
| Buprenorphine | Tramadol (analgesic)[114] |

Urine Drug Testing in Clinical Practice (2015) Edition 6

# Diversion

- Definition: unauthorized rerouting or appropriation of a substance
- Buprenorphine diversion: should be assessed clinically and responded to therapeutically
- Tools Diversion Safeguards:
- Prescription monitoring program (CURES)
- Drug testing
- Medication call backs

## Risks for Diversion: Discussing the Harms with Patients

- Diversion may lead to harmful medical consequences, including fatal overdose
- Diversion lead to harmful social consequences (e.g., arrest, jail)
- Diversion can jeopardize treatment participation and treatment availability

## Risks for Diversion

- Pseudopatients ("double-dippers") seeking to divert drug
- Under-prescribing
  - Inadequate withdrawal suppression
  - Inadequate opioid blockad
- Over-prescribing
- Failure to address the disorder beyond medication

# What can physicians do to decrease risk of diversion?

- Comprehensive Evaluation at Intake
  - Checking state prescription monitoring programs to ensure patient is receiving treatment from only you
  - Confirm diagnosis
    - Positive urine test for opioids at admission
    - Positive random test for buprenorphine during treatment
    - Collateral information
    - In clinic dosing
    - Random medication call back

# DEA Overview and Audit

The U.S. Drug Enforcement Administration (DEA) and state DEA oversee office-based buprenorphine treatment and have the right to inspect physicians' buprenorphine practices at any time In case of a DEA audit (random and unscheduled), you may be asked to present the following information:

- documentation of your waiver to prescribe buprenorphine
- treatment logs, including information on how many patients are currently in treatment
- documentation of prescriptions given
- dispensing practices, for physicians who are dispensing buprenorphine tablets from their offices
- DEA license address must match practice location

# Conclusion

- Induction – multiple models discussed
- Tapering – monitor carefully
- Urine Testing – regular drug panel and test for buprenorphine
- Diversion safeguards
- DEA – keep your patient list