Buprenorphine
An Effective Partial Agonist Medication for OUD

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Disclosure Information

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Royalties: ASAM / RecoverySearch
Salary, Stock: DynamiCare Health
Options/Stock: Alkermes; Intent Solutions
Consultant Fees: BioCorRx, Indivior, Kaleo, Purdue, RCA IBM Watson/Truven Health Analytics, Rand Corp.
Purpose of the Webinar

• U.S. opioid crisis – epidemic proportions
  Society demands that we use every tool in the toolkit
  – that is not the case, so the burden is on us to change.
• FDA: approved Buprenorphine in addiction treatment (MAT)
  as safe & effective for opioid use disorder (OUD)
• BUP has unique chemistry, brain effects, side effects,
  and impact on behavior.
• We will review BUP’s pharmacology, clinical indication,
  formulations, federal law requirements,
  patient selection issues, practice guidelines,
  counseling recommendations, contraindications, adverse
  effects, abuse risks & considerations in treatment completion.

Objectives:

As a result of this workshop, participants will be able to:

• Describe the brain receptor actions and time-course
  of BUP in addiction treatment (MAT)

• Implement clinically effective use of BUP
  + psychosocial treatment

• Manage initiation, stabilization, maintenance &
  discontinuation of BUP in suitable patient populations
The U.S. Opioid Epidemic

- 4.3 million aged ≥12 used past mo. nonmedical Rx pain meds
- 435,000 used heroin in the past month
- Overdose: leading U.S. cause of personal injury-related death
- Since 1999 opioid overdose deaths quadrupled
- 2014: 1.5 times more US deaths from OD vs. MVA
- 2014: Heroin OD deaths rose 26%; fentanyl doubled
- 2015, 27 million (8% of total population ≥12) met SUD criteria
- <10% of these received any specialized care

Pathophiology

Cortex
Role:
- Decision making
- Thinking
- Reasoning
- Learning

Limbic Region
Role:
- Basic Drives
- Experience of Reward, Euphoria

Interventions
- Psychosocial Therapies
- 12 Step Programs
- Monitoring

Interventions
- Agonist Medications
- Antagonist Medications

Healthy Opioid Receptor Activity

**Endorphins**
- Pain relief
- Stress relief
- Emotional bonding

**Dopamine**
- Eating when hungry
- Drinking when thirsty
- Rewards survival behavior

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Opioid Agonists & Partial Agonists

**Agonists**
- Opioid analgesics
- Illicit opioid (e.g., heroin)
- Methadone
- Activates opioid receptors
- Excess dopamine release

**Partial Agonists**
- Buprenorphine
- Same as agonists, but ceiling effect – about half the reward of full agonists
An agonist has an active site of similar shape to the endogenous ligand binding to the receptor and producing the same effect. An antagonist is close enough in shape to bind to the receptor but not close enough to produce an effect. It also takes up receptor space and so prevents the endogenous ligand from binding.

**Full and Partial Agonists vs. Antagonists**

- **Full Agonist** (Methadone)
- **Partial Agonist** (Buprenorphine)
- **Antagonist** (Naloxone)

### Specific Binding

- **[18F]cycloxy(m ligand)**
  - 30-35% receptor occupancy for methadone > 80 mg/day
  - Kling et al., *JPET* 2000

- **[11C]carfentanil (m ligand)**
  - Bup 2 mg: 27-47% occupancy
  - Bup 16 mg: 85-92% occupancy
  - Bup 32 mg: 94-98% occupancy
  - Greenwald, MK et al., *Neuropsychoph* 2003

**Normal Control**

**Methadone Maintained Patient**
**Neurobiology of Opioid Use Disorder**

- Opioids: at substantia nigra & VTA interneurons, rapidly & briefly bind MOP-r, $\downarrow$ GABAergic inhibition of DA neurons
- $\uparrow$ Dopaminergic Reward: Initial positive reinforcement; later, regulatory changes via mRNA or protein/peptides
- Recurrent withdrawal negatively reinforces recurrent use, via regulatory changes that persist for weeks/months
- Negative Reinforcement: mediated via
  - Upregulation of the KOP-r/dynorphin system (may underlie aversion, dysphoria/anhedonia, and depression-like or anxiety-like states)
  - Stress-responsive brain areas via the hypothalamo-pituitary-adrenal (HPA) axis

(Kreek et al., J Clin Investigation 2012)
Goals of Anti-Opioid Pharmacotherapy

- **Detoxification**: detox without continued meds dominates, but research & experience prove this to be inadequate care
- **Early recovery protection**: period of highest risk for OD
  - Death rates upon prison release = 12-100x general population
  - Harm reduction, e.g., from HIV and HEP C transmission
- **Anti-craving**: stabilize urges/impulses to use long enough to permit counseling effects to take hold
- **Stress Response Normalization**: OUD disrupts ACTH/Cortisol
- **Extinction**: of both positive and negative cue response
- **Biological Stabilization**: Eating, diurnal cycle, sexual function, capacity for self-care / activities of daily living / treatment retention, general healthcare, relationship bonding
- **NOT Recovery**: Disease acceptance, coping skills, rehab

Rationale for Opioid Partial Agonist Treatment

- (Opioid Substitution, or Opioid Maintenance Treatment)
- Stabilizes neuronal circuitry in OUD
  - Mu occupation with potent blockade
  - Cross-tolerant, long-acting, sub-lingual or 6-month implant
- Prevents withdrawal and craving
- Extinguishes compulsive behavior
- Reduces spread of HIV and HCV
- Reduces criminal activity
- Safe for use in pregnant women
- An advance over agonist therapy
  - Less opioid effect than Methadone
  - Longer duration of effect than Methadone
  - Reduced overdose risk vs. Methadone
### History

- Early 1960s: Methadone Maintenance Treatment (MMT) eliminates withdrawal, stabilizes craving, drug & IV use, ID
- Adverse events: physical dependence, long/difficult withdrawal, sedation/respiratory depression, fatal OD
- Regulations control sites, staffing and procedures
- Diversion is problematic, particularly after AIDS epidemic
- 1970s: Buprenorphine proposed (Jasinski 1978)
- 2000: Drug Abuse Treatment Act authorizes Buprenorphine
- 2002: Buprenorphine enters use in U.S.
- 2016: Probuphine implant approved by FDA

### Drug Abuse Treatment Act (DATA) of 2000

- Federal law 21 CFR §1306.07, authorizes BUP via OBOT office-based opioid treatment, weekly or monthly basis
- Allows “Qualified” physicians to treat OUD in non-MMT sites
  1. Addiction certification from approved organization, or
  2. Physician in clinical trial of qualifying medication, or
  3. Complete 8-hour course from approved organization
- DEA issues (free) to qualifying physicians a new DEA number to use medication for opioid dependence
- As of today, only buprenorphine is approved for this use
- NPs/PAs are also eligible to prescribe now, through CARA
Buprenorphine: Who Can Prescribe?

- Federal authorizing laws: DATA 2000, 2016 CARA
- PHYSICIAN WAIVER ELIGIBILITY: Providers must have a state license, a valid registration # from the DEA, 8hrs of an approved course, and:
  - Board certification in addiction psych (ABMS), addiction (ASAM), or addiction medicine (ABAM, Am Ost. Acad of Add’n Med)
  - Or, participation as an investigator in a BUP FDA trial or other Schedule III-V narcotic med used for detox/maintenance in OUD
  - Equivalent training/experience per state Medical Board or HHS
  - NP/PAs also eligible to prescribe now, through CARA
- REFERRALS: Prescribers must be able to refer patients to counseling or psychiatric services.

Buprenorphine: How Many Can Be Treated?

- PATIENT LIMITS: Year 1 of waiver, providers limited to 30 patients at a time; after year 1, limited to 100 patients at any given time. (e.g., if Rx is for 30 days & patient discharged, patient still counts until the end of the 30 day Rx.)
  - To treat ≤100 patients, must obtain CSAT extended waiver.
  - NP/PA ELIGIBILITY: 24 hours of approved training; limited to 30 patients in year 1; then can apply to increase to 100.
  - Eligible physicians may treat up to 275 patients (not other clinicians)
  - Eligible physicians complete a ‘Request for Patient Increase Form’ Physician must have a current waiver to treat ≤100, for ≥1 yr.
## Treatment vs. Addiction

<table>
<thead>
<tr>
<th></th>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Heroin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Route</strong></td>
<td>Oral or SL</td>
<td>IV, IN</td>
<td></td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>30 minutes</td>
<td>Immediate</td>
<td></td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>24-36 hours</td>
<td>3-6 hours</td>
<td></td>
</tr>
<tr>
<td><strong>Euphoria</strong></td>
<td>Absent</td>
<td>Marked</td>
<td></td>
</tr>
</tbody>
</table>

## Buprenorphine: Properties

- Modest $\mu$ agonist activity with ceiling, about ½ of methadone’s
- Strong affinity for the $\mu$-receptor, e.g., greater than naloxone
- Long half life, with up to 36 hours anti-craving effect
- Precipitated withdrawal if taken after full agonist
- Decreased risk of respiratory & CNS depression
- Sublingual route of administration
- “Combo” tablet with naloxone (“Suboxone®” & others) limits abuse by injection in naïve individuals
Buprenorphine

- Start patient in mild withdrawal (avoids provoking withdrawal)
- Slow onset, long-duration: helps reduce reinforcement
- Extensive research shows benefit of treatment initiation
- Prescribed daily, weekly or monthly in outpatient care
- Has greatly expanded access to care, but more is needed
- DEA Schedule C-III, requiring federal waiver, 100 patient limit
- Approved for opioid addiction (2002) as Subutex; now more commonly used as Suboxone (with naloxone in a 4:1 ratio)
- Generics (Zubsolv) & film preparations (Bunavail) approved

Agonists vs. Antagonists: Features

<table>
<thead>
<tr>
<th>Feature</th>
<th>AGONIST</th>
<th>ANTAGONIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>maintain physiological dependence and potential for withdrawal</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>potential for tolerance development</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>euphoric effects/abuse/diversion</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>compatible with ongoing illicit opioid use</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>may alter use of other drugs</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>extinction of heroin-reinforced behaviors/ reversal of underlying neurobiology</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>duration of treatment</td>
<td>indefinite</td>
<td>?</td>
</tr>
<tr>
<td>cultural/ideological barriers to availability</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>professional/public opposition</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Not offering medication after they stop drug use puts patients at increased risk of overdose and death
### Agonists vs. Antagonists: Features

<table>
<thead>
<tr>
<th>FDA Scheduling- Abuse Liability</th>
<th>AGONIST Agents</th>
<th>ANTAGONIST Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone (full)</td>
<td>Buprenorphine (partial)</td>
<td>Oral Naltrexone, VIVITROL</td>
</tr>
<tr>
<td>CII</td>
<td>CIII</td>
<td>none</td>
</tr>
<tr>
<td>Maintenance of physiological opioid dependence</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Potential for tolerance development</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Compatible with ongoing illicit opioid use</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Diversion issues</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Requires Opioid Detoxification</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Risk of Opioid Withdrawal - Initiation</td>
<td>no</td>
<td>✓</td>
</tr>
<tr>
<td>Risk of Opioid Withdrawal - Discontinuation</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Pain Management Issues</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

### Agonists vs. Antagonists: Clinical Considerations

![Motivation vs. Stability Diagram]

- **METHADONE**
  - Strongest drug reward
  - Highest level of accountability

- **SUBOXONE**
  - Moderate drug reward
  - Moderate level of accountability

- **VIVITROL**
  - No drug reward
  - Moderate level of accountability
### Agonists vs. Antagonists: FDA Indications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Type</th>
<th>FDA Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>agonist</td>
<td>For maintenance treatment of opioid addiction.</td>
</tr>
<tr>
<td>Suboxone (buprenorphine/naloxone)</td>
<td>partial agonist</td>
<td>For the maintenance treatment of opioid dependence.</td>
</tr>
<tr>
<td>ReVia (oral naltrexone)</td>
<td>antagonist</td>
<td>In the treatment of detoxified, formerly opioid-dependent individuals.</td>
</tr>
<tr>
<td>Vivitrol (extended-release naltrexone; XR-NTX)</td>
<td>antagonist</td>
<td>For the prevention of relapse to opioid dependence, following opioid detoxification.</td>
</tr>
</tbody>
</table>

All MATs are FDA-approved as in combination with psychosocial therapy

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### Agonists vs. Antagonists: Key Differences

<table>
<thead>
<tr>
<th>Prescribing Considerations</th>
<th>Extended-Release Injectable Naltrexone</th>
<th>Buprenorphine</th>
<th>Methadone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of Administration</td>
<td>Monthly</td>
<td>Daily</td>
<td>Daily</td>
</tr>
<tr>
<td>Route of Administration</td>
<td>Intramuscular injection in the gluteal muscle by healthcare professional</td>
<td>Oral tablet or film is dissolved under the tongue. Can be taken at a physician’s office or at home.</td>
<td>Oral (liquid) consumption usually witnessed at an OTP, until the patient receives take-home doses.</td>
</tr>
<tr>
<td>Restrictions on Prescribing or Dispensing</td>
<td>Any individual who is licensed to prescribe medicine (e.g., physician, physician assistant, nurse practitioner) may prescribe and order administration by qualified staff</td>
<td>Only licensed physicians who are DEA registered and either work at an OTP or have obtained a waiver to prescribe buprenorphine may do so.</td>
<td>Only licensed physicians who are DEA registered and who work at an OTP can order methadone for dispensing at the OTP.</td>
</tr>
<tr>
<td>Abuse and Diversion Potential</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Additional Requirements</td>
<td>None; any pharmacy can fill the prescription.</td>
<td>Physicians must complete limited special training to qualify for the DEA prescribing waiver. Any pharmacy can fill this prescription.</td>
<td>For opioid dependence treatment purposes, methadone can only be purchased by and dispensed at certified OTPs or hospitals.</td>
</tr>
</tbody>
</table>

Substance Abuse and Mental Health Services Administration
Opioid Treatment: Changing Approach

<table>
<thead>
<tr>
<th>Methadone Clinic</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Criteria:</td>
<td>• Criteria:</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>DSM IV or 5</td>
</tr>
<tr>
<td>12 months prior use</td>
<td>No past use time criteria</td>
</tr>
<tr>
<td>• Dose regulated</td>
<td>• MD sets dose</td>
</tr>
<tr>
<td>• Age &gt; 18</td>
<td>• Age &gt; 16</td>
</tr>
<tr>
<td>• Limited take homes</td>
<td>• Take homes (30 days)</td>
</tr>
<tr>
<td>• Tx Services “required”</td>
<td>• Services must be “available”</td>
</tr>
</tbody>
</table>

U.S. Treatment System (2014)

• 1,800,000 Rxed with MMT or OBOT
• Dramatic growth in OBOT since 2004
  Agent 2004 2014
  – MMT: 241,000 336,000
  – BUP: 42,000 1,526,000
• 30,000 US physicians waived for OBOT
• 9,600 US physicians certified for ≤100 pts
• 1,300 MMT programs licensed

(IMS 2015; SAMHSA)
BUP OUD Treatment in Primary Care

At 24 weeks, overall, 59% remained in treatment

FIGURE 1. Program retention time by week 1 opiate test.

Stein, JGIM 2005

BUP/Naloxone Retention in HIV+ (n=303)

Fiellin DA et al., JAIDS 2011; 56(Suppl 1) S33-S38
**Buprenorphine: Reduces Other Drug Use**

![Graph showing urine samples negative for drugs over weeks]  
*Fudala, NEJM 2003*

**Most often heard quotes with Buprenorphine**

"Doc, I feel normal"

"I wake up not sick"

"I have my life back"

- Treatment in normal medical settings:
  - Encourages continuity of medical/specialty care
  - Encourages relationship building with clinicians
  - Legitimize opioid dependence as a normal, treatable, chronic illness
Buprenorphine: For Whom?

- Able to maintain a treatment plan without the daily supportive contacts/structure of a clinic
- Has structure in daily life (e.g., employed)
- Has a strong sober support system
- Has adequate stress management skills
- Pregnant women
- Wants to continue a subjective sense of opioid reinforcement, but less than with methadone
- Does not need ongoing or planned opioid pain medication

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Buprenorphine: For Whom?

- Less likely appropriate candidate for OBOT:
  - Dependence on high doses of benzodiazepines, alcohol, or other CNS depressants
  - Significant psychiatric co-morbidity
  - Multiple previous treatments (methadone) and relapses
Buprenorphine: For Whom?

- Cautions: Active alcohol, sedative/hypnotic/anxiolytic use
- Better if cardiac risk (prolonged QTC) that precludes methadone
- For patient who is able to tolerate a 12-24 hrs without opioids
- Has a daily schedule, routine, & environmental supports
- Can manage week-to-week visits without serious risks
- Is not active with alcohol BZx, or other sedative/hypnotics

Kampman & Jarvis. ASAM National Practice Guideline for Medications in OUD, JAM 2015

- Treatment Matching is key: There is no superior approach
  — except the one that works for the particular patient!
- Segregated care = BAD care; patients need integrated care

Withdrawal Management

- Opioid withdrawal management alone – is not treatment
- Opioid WM w/methadone must be done inpatient or in an OTP
- BUP: To avoid precipitated withdrawal, wait for mild–mod WD
- BUP + low dose NTX-PO (accelerated WD) shows promise
- Clonidine: not FDA-approved; 0.1–0.3mg q6–8 hrs PO to 1.2mg qD
- Clonidine Transdermal: delayed response may require PO on day 1
- Hypotension may limit dose; may combine with other WD Sx meds
- Anxiety - BZs, diarrhea - loperamide, pain – acetaminophen/NSAIDs, nausea – ondansetron
- Ultrarapid opioid detox (UROD) – high mortality

Kampman & Jarvis. ASAM National Practice Guideline for Medications in OUD, JAM 2015
**Buprenorphine: Initiation**

- Patient arrives in MILD opioid withdrawal (e.g., COWS 6-12)
- Sublingual/buccal administration necessitates being kept in the mouth for a long period of time for appropriate absorption
- BUP/naloxone 2-4mg initial dose SL, observed
  BUP/naloxone buccal film: same doses as with SL tabs
- Reassess at 30-60 min; 2-4mg SL PRN, observed
- Next day – morning dose is sum of initial day’s dose(s) with increases, usually up to 8mg SL by end of day
  Provide total day’s dose, for each of the next 2 – 7 days
- Days 2-7, maintain in-person or phone contact each day, titrate up as needed for stability, up to 16mg SL per day
- Home-based induction is recommended only if the patient or prescribing physician is experienced with the use of BUP

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**Buprenorphine: Clinical Opioid Withdrawal Score**

1. Resting pulse rate: _____BPM
   - 0 80 or below
   - 1 81–100
   - 2 101–120
   - 4 >120
2. Sweating: over past half hour
   - 0 None
   - 1 Subjective chills or flushing
   - 2 Flushed or moisture on face
   - 3 Beads of sweat on brow or face
   - 4 Sweat streaming off face
3. Restlessness: during assessment
   - 0 Able to sit still
   - 1 Reports difficulty sitting still
   - 3 Frequent movements
   - 5 Unable to sit still >few seconds
4. Pupil size
   - 0 Pupils pinned or normal size
   - 1 Possibly larger than normal
   - 2 Pupils moderately dilated
   - 5 Dilated; only rim of iris visible
5. Bone or joint aches: (due to WD)
   - 0 None
   - 1 Mild diffuse discomfort
   - 2 Severe diffuse joint/muscle ache
   - 4 Rubbing joints/muscles
6. Runny nose or tearing: not from cold
   - 0 None
   - 1 Stiffness or unusually moist eyes
   - 2 Nose running or tearing
   - 4 Constant nose running or tearing
**Buprenorphine: Clinical Opioid Withdrawal Score**

7. GI upset: over last half hour
   - 0 No GI symptoms
   - 1 Stomach cramps
   - 2 Nausea or loose stool
   - 3 Vomiting or diarrhea
   - 5 Episodes of diarrhea or vomiting

8. Tremor: observe outstretched hands
   - 0 No tremor
   - 1 Tremor felt, but not observed
   - 2 Slight tremor observable
   - 4 Gross tremor or muscle twitching

9. Yawning: during assessment
   - 0 No yawning
   - 1 Yawning 1-2x during assessment
   - 2 Yawning ≥3X during assessment
   - 4 Yawning several times/minute

10. Anxiety or irritability
    - 0 None
    - 1 Fells increasingly irritable/anxious
    - 2 Patient obviously irritable, anxious
    - 4 Difficult participating in assessment

11. Gooseflesh skin
    - 0 Skin is smooth
    - 3 Arm hair standing up
    - 5 Prominent piloerection

**Total:** sum of all 11 items
- 5–12=Mild; 13–24=Moderate; 25–36=Mod. severe; >36=Severe

(Adapted from Wesson et al., 1999)

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**Buprenorphine: Initiation**

- Post OD reversal: Receiving agonist MAT is associated with a 50% reduced risk of a subsequent fatal opioid overdose.
- OD survivors have a short window of opportunity after a nonfatal overdose to reduce their risk of death.
- BUP for high OD risk could significantly lower the death rate.
  (report only included data for agonists; Viv work ongoing)
  (MA DPH Report to the Legislature, 2017)

- Patients previously on methadone or long-acting opioids: with FILM, better to start on BUP monotherapy (e.g., Subutex) because some naloxone can be absorbed & produce withdrawal
### Buprenorphine: Switching from MMT to BUP

Switching from MMT to BUP may be appropriate...
- If patient experiences intolerable side effects
- Or is unsuccessful in attaining /maintaining treatment goals w/MMT
- Should be on low doses of methadone before switching
- Low dose methadone (≤30–40mg per day) generally tolerate transition to BUP with minimal discomfort, whereas higher doses may produce significant discomfort in switching medications

Kampman & Jarvis. ASAM National Practice Guideline for Medications in OUD, JAM 2015

### Buprenorphine: Stabilization

- Weeks 1-6: Target dose is ≤16 mg/day (max = 24mg/day).
- Opioid blockade usually occurs at 16 mg/day.
- The US FDA approves up to 24 mg/day; limited support for more. Higher doses may increase the risk of diversion.
- May be taken in divided doses, especially for chronic pain
- Goal: stabilize craving, drug use & counseling attendance
- Patient should be seen at least x1 every week
- Lost, destroyed, stolen meds: indicative of relapse/diversion; No replacements – except on an individualized basis by team review, only once, & repeat request leads to treatment plan escalation, e.g., more frequent visits or increased LOC
- Store in labeled, child-proof container, locked box/space (w/cotton to prevent broken pills if carried)
**Buprenorphine: Stabilization**

- Counseling should be used in conjunction with BUP
- Counseling may be provided by the Rxer or by a separate therapist
- Clinicians should take steps to reduce diversion, including:
  - Frequent office visits (weekly in early treatment)
  - Drug testing, including BUP & metabolites, pill counts
  - Testing: should be frequent for BUP, other drugs & Rx meds
  - Access the Prescription Drug Monitoring Program (PDMP)

  Kampman & Jarvis. ASAM National Practice Guideline for Medications in OUD, JAM 2015

**Buprenorphine: Maintenance**

- After Weeks 4 - 6: Dose is maintained without change
- Goal: Establish routine, address ASAM Dimensions 2-6
- Patient visits ~every week, no less than every month
- Each decrease in frequency of visits is based on team review
- Clinic visits include drug testing, follow-up labs (e.g., LFTs)
- Include Breathalyzer if any risk of problems with alcohol
- If needed, begin Anti-Alcohol MAT: Acamprosate (Campral), disulfiram (Antabuse), topiramate (Topamax)
  – but NOT naltrexone
**Buprenorphine: Drug Testing**

- Urine sample required at each visit.
- Leave belongings (coats, bags, etc.) outside bathroom
- No handwashing until urine handed off in bio-hazard bag
- No toilet flushing until urine handed off to gloved Assistant
- Questionable urine: automatic repeat, same day
- Random observed urines: Optimal, but only by same sex staff, & rarely routine. Oral swabs are better.
- If chain of custody required, can refer to a lab or higher LOC
- Validity checks: Urine temperature, pH; Oral swab witnessing
- If signs of TAMPERING: Repeat test; counsel, consider higher LOC

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**Buprenorphine: Addressing Relapse**

- Warning Signs:
  - Negative BUP urine test
  - Ongoing BZ/barb/CNS depressants, stimulants, alcohol
  - Impairment, sedation, OD, unsafe med/hazardous behaviors
  - Presenting intoxicated, or hospitalization due to drug use
  - BUP is a harm reduction model — so no automatic discharge
  - Revise treatment plan, increase monitoring & supports
  - If continued use despite intensified treatment plan → ↑LOC
Opioid WD Severity: Untreated vs. Treated
Balancing the Intensity & Duration of Withdrawal

- Warning: Patients who discontinue agonist therapy with MM or BUP and then resume opioid use should be made aware of the risks of opioid overdose, and especially the increased risk of death.
- Weiss et al., AGP 2012 treated BUP patients who were dependent on opioid analgesics for 3 mos., followed by a 1 mo. BUP taper
- 92% relapsed to opioid use again within 8 weeks
- Therefore, BUP taper & discontinuation should be done slowly, is indefinite in duration, & requires close monitoring even after BUP
- BUP taper is generally accomplished over several months
- Patients should remain in treatment for ongoing monitoring past the point of discontinuation

Kampman & Jarvis. ASAM National Practice Guideline for Medications in OUD, JAM 2015
**Alternative: Buprenorphine & Bunavail Film**

- BUP film: Similar dosing - 2 mg/0.5 mg, 4/1, 8/2 and 12/3 strips
- Bunavail: Backing speeds blood absorption, using less
  Film should disappear in 15-30 minutes, has pleasant taste
- Doesn’t disrupt swallowing or speaking while dissolving
  (Speaking is not as easy with Suboxone SL tabs)
- Bunavail 4.2 mg/0.7 mg buccal film ≈ 8 mg/2 mg Suboxone SL tab
  Dosages: 2.1 mg/0.3 mg; 4.2 mg/0.7 mg; or 6.3 mg/1 mg
- Bunavail naloxone levels are ~33% lower than with Suboxone, because naloxone exposure is higher with buccal than SL
- Cost: Bunavail = $8.39 vs. Suboxone = $4.81

---

**Alternative: Probuphine SC Implant**

- Four 1” rods implanted inside the upper arm under the skin (SC)
  - Probuphine Risk Evaluation & Mitigation Strategy (REMS):
    Requires certified live training for surgical insertion/removal
  - 6-mo release; one 2nd implant can be placed in the opposite arm
  - FDA requires postmarketing studies RE safety/feasibility >12 mos.
  - Safety & efficacy RCT: 176 OUD adults stabilized first on BUP SL
  - 84% on Probuphine showed no illicit opioid use over 6 months (vs. 79% on BUP sublingual; non-inferior)
Alternative: Probuphine Implant

- Safety & efficacy not established under age 16 or over age 65
- Side Effects: implant-site pain, itching, redness; headache, depression, constipation, nausea, vomiting, back pain, toothache & oropharyngeal pain
- Boxed warning: Insertion & removal associated with implant migration, protrusion, expulsion & nerve damage
- Risk: Accidental overdose, misuse & abuse if an implant protrudes from skin
- See patient during week 1 after insertion & at least once-monthly for counseling
- Cost: $4,950 for 6-month implant – ~$825 a month

Buprenorphine: Switching from BUP to MMT

- Consider if patient is not stabilizing on BUP despite intensified care
- Consider if patient is unhappy without perceived opioid effects
- When considering a switch from BUP to MMT, there is no required time delay because addition of a full mu-opioid agonist to a partial agonist does not create withdrawal

Kampman & Jarvis. ASAM National Practice Guideline for Medications in OUD, JAM 2015
### Buprenorphine: Switching from BUP to XR-NTX

- When considering a switch from BUP to XR-NTX, 7–14 days should elapse after the last BUP dose to conclude physical dependence.
- It may be useful to conduct a naloxone challenge.
- However, naloxone may NOT displace BUP.
- Therefore an oral naltrexone challenge (25 mg) is wise.

Kampman & Jarvis. ASAM National Practice Guideline for Medications in OUD, JAM 2015

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### Buprenorphine: Pain Management

- Temporary ↑ in BUP dose may be effective for mild acute pain.
- For severe acute pain, switch to high-potency opioid (fentanyl).
- Monitor closely and consider, e.g., regional anesthesia.
- Decision to D/C BUP pre-elective surgery should be made in consultation with the surgeon & anesthesiologist.
- If it is decided that BUP should be discontinued, this should occur 24–36 hrs in advance of surgery and reinduction should restart postop when the need for full opioid agonist analgesia has passed.

Kampman & Jarvis. ASAM National Practice Guideline for Medications in OUD, JAM 2015
Pregnancy

- 0.1% of pregnant women self-report illicit opioid use; but prescription misuse has more than doubled, 1992 – 2008
- Prenatal opioid exposure, with complex environmental conditions, is associated with many adverse outcomes
- Prenatal methadone: usual treatment, BUT...
  − is associated with neonatal abstinence syndrome (NAS)
- NAS requires medical intervention for possible GI, respiratory, CNS, autonomic nervous system, and breastfeeding dysfunction and prolonged hospitalization
- BUP (vs. methadone) NAS: less morphine need & hospitalization
- BUP monotherapy is preferred in pregnancy
- BUP is excreted at low levels in breast milk


Retention in Youth, Ages 15-24
Naturalistic treatment data, Baltimore MD (N=92)

<table>
<thead>
<tr>
<th># of Weeks Retained in Treatment</th>
<th>Any medication</th>
<th>XR-NTX</th>
<th>Buprenorphine</th>
<th>No medication</th>
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</thead>
<tbody>
<tr>
<td>26</td>
<td>15.8</td>
<td>15.3</td>
<td>15.9</td>
<td>10.3</td>
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<td>24</td>
<td>5.5</td>
<td>5.4</td>
<td>4.9</td>
<td>2.8</td>
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<tr>
<td>22</td>
<td>10.3</td>
<td>9.9</td>
<td>11</td>
<td>7.8</td>
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<td>4</td>
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<td>2</td>
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<td>0</td>
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</tr>
</tbody>
</table>

= p < 0.01 vs. no meds

(Fishman et al., SAMHSA-NIDA, 2016)
Buprenorphine: Safety

- No alteration of cognitive functioning
  - Patient feels “normal”
- No organ damage
  - Early concern of hepatic toxicity unconfirmed
  - No evidence of QT prolongation
- Ceiling opioid effect prevents respiratory depression, OD
  (BUT overdose is a risk if combined with alcohol & anxiolytics)
- No clinically significant interactions with other drugs
- Hepatic impairment reduces naloxone clearance more than BUP

Buprenorphine: Concerns

- Can be lethal with benzodiazepines (BZs) & sedative/hypnotics
- >30% of opioid-related deaths involve BZs
- In 231,228 urines from 144,535 patients in health care settings,
  > 25% showed concurrent opioids + BZs
- In 52% with concurrent use, 1 drug was Rxed, the other non-Rxed
  (McClure FL et al., J Addict Med. 2017)
- Fatalities have occurred in children or adults who lack tolerance
- Stigmatized by some in 12 step groups,
  criminal justice system, and other health care providers
  as “just substituting one drug for another”
BUP Limitations & Problems
(Stein et al., Milbank Q 2015; 93:561-83)

- A 2006 law increased waived physician limits from 30 to 100 patients on BUP
- 100-patient-waivered MDs were significantly associated with growth in buprenorphine use, but not 30-patient-waivered MDs
- Policies increasing the patient limits per physician may be more effective in increasing BUP use raising the overall number of waivered physicians.
- But, the greater amounts of BUP also make its misuse more likely.

BUP Limitations & Problems

- BUP is 3rd most diverted prescription opioid (DEA Nat’l Forensic Lab Info System, 2014)
- 50% in opioid treatment (N=10,000) diverted BUP in the month prior to entering treatment “to get high” (Cicero et al., DAD 2014)
- 50-80% of BUP patients still use non-medical opioids (Johnson et al., JAMA 1992; Johnson et al. NEJM 2000; Weiss et al., Arch Gen Psych 2011)

Mean retention on BUP:

- Yser et al., Addiction 2014: 66 days
- Baser et al., AJMC, 2011: 69 days
- Fishman et al., CPDD 2011: 9.6 weeks (adol/young adults)
- 92% of BUP patients relapse within 8 weeks of taper
**BUP Limitations & Problems**

- **French Experience:**
  After initial reduction in opioid deaths, steady increases followed; by 2011, half of opioid deaths were BUP-related (more than heroin). French authorities responded by increasing controls on BUP. (Reitox Nat’l Focal Point, Nat’l EMCDDA Report 2013)

- **Baltimore Experience:**
  BUP reversed the heroin epidemic through 2009, but by 2014 MD DHMH reported an 88% increase in heroin OD deaths, despite on-demand BUP/MMT access (MD DHMH, Drug & Alc-Related Intox Deaths, 2013)

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**BUP vs. MMT: Mortality**

*(Kimber et al., Lancet Psychiatry 2015; 2:901-8)*

- Retrospective cohort study (n=32,033) in Australia

- BUP had less all-cause & drug-related mortality than MMT in the 1st 4 weeks (adjusted all-cause MRR 2·17, 95% CI 1·29-3·67)

- After 4 weeks, mortality risk did not differ

- In the 4 weeks after treatment cessation, all-cause mortality did not differ, but drug-related mortality was lower for methadone (adjusted all-cause MRR 1·12, 0·79-1·59; adjusted drug-related MRR 0·50, 0·29-0·86).

- In the initial high risk of death period (1st 4 weeks of opioid substitution therapy, BUP seemed to reduce mortality

- Little difference between BUP vs. MMT was noted thereafter
BUP vs. MMT: Cognitive Function

During Month 1 of Treatment:
- Delayed reaction time & verbal memory deficits:
  Methadone > BUP > CTLRs (Rapeli P et al. ISAM 2006)

After Maintenance is Established:
- \( \equiv \) Reaction time: MMT 100 mg vs. CTLRs
  (Gordon, Psychopharm 1970)
- ▼ Working memory: MMT 70 mg (Mintzer & Stitzer. DAD 2002)
- ▼ Verbal memory: MMT 35 vs. 17.5 mg
  (Curran et al. Psychopharm 2001)
- ▼ Visual memory vs. CTLRs: MMT 66 mg & BUP 9 mg
  (Pirastu et al. DAD 2006)
- Driving reaction time delay: MMT > BUP

BUP vs. MMT: Treatment Retention

Mean retention on BUP:
- Yser, Addiction 2014: 66 days
- Baser, AJMC, 2011: 69 days
- Fishman, CPDD 2011: 9.6 wks (adol/young adults)

92% relapse within 8 wks of taper (Weiss et al., 2011)
**BUP vs. MMT: Retention**

- 31 RCTs (N=5,430); evidence: mod to high
- Flexible dose MMT: better retention vs. BUP doses <16 mg
- BUP: when high dose MMT isn’t tolerated
- BUP advantages: relative safety, alternate-day administration, convenience & access
- No need for more MMT vs. BUP RCTs

(Mattick et al., Cochrane 2014)

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**BUP vs. MMT: Retention ( Flexible Dosing)**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Buprenorphine Events</th>
<th>Methadone Events</th>
<th>Total Events</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Double-blind flexible dose studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Johnson 2000</td>
<td>32</td>
<td>55</td>
<td>87</td>
<td>0.80 (0.61, 1.05)</td>
<td></td>
</tr>
<tr>
<td>Mattick 2003</td>
<td>96</td>
<td>200</td>
<td>296</td>
<td>0.82 (0.68, 0.99)</td>
<td></td>
</tr>
<tr>
<td>Potthoorn 2001</td>
<td>15</td>
<td>27</td>
<td>42</td>
<td>0.62 (0.43, 0.88)</td>
<td></td>
</tr>
<tr>
<td>Strain 1994a</td>
<td>47</td>
<td>84</td>
<td>131</td>
<td>0.99 (0.76, 1.30)</td>
<td></td>
</tr>
<tr>
<td>Strain 1994b</td>
<td>13</td>
<td>24</td>
<td>37</td>
<td>0.97 (0.79, 1.21)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>390</td>
<td>398</td>
<td>788</td>
<td>0.83 (0.72, 0.95)</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>203</td>
<td>248</td>
<td>451</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau^2 = 0.00; Ch^2 = 1.24; df = 3; P = 0.97; I^2 = 0%
Test for overall effect Z = 0.29 (P = 0.77)

| 1.2 Open-label flexible dose studies |
| Fischer 1999          | 11                   | 22               | 33           | 0.53 (0.32, 0.90)              |                                |
| Kristensen 2005       | 9                    | 21               | 30           | 0.43 (0.25, 0.74)              |                                |
| Linbergl 2004         | 38                   | 81               | 119          | 0.86 (0.63, 1.17)              |                                |
| Magura 2009           | 49                   | 77               | 126          | 0.95 (0.78, 1.16)              |                                |
| Neri 2005             | 29                   | 31               | 60           | 1.04 (0.89, 1.22)              |                                |
| Soos 2008a            | 28                   | 64               | 92           | 0.88 (0.67, 1.14)              |                                |
| Subtotal (95% CI)     | 307                  | 296              | 593          | 0.80 (0.63, 1.02)              |                                |
| Total events          | 164                  | 189              | 353          |                                |                                |

Heterogeneity: Tau^2 = 0.08; Ch^2 = 18.72; df = 5; P = 0.002; I^2 = 73%
Test for overall effect Z = 1.81 (P = 0.07)

| Total (95% CI)        | 697                  | 694              | 1391         | 0.83 (0.73, 0.94)              |                                |
| Total events          | 367                  | 437              | 804          |                                |                                |

(Mattick et al., Cochrane 2014)
**BUP vs. MMT: Retention**

- 31 RCTs (N=5,430); evidence: mod to high
- Flexible dose MMT: better retention vs. BUP doses <16 mg
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- No need for more MMT vs. BUP RCTs

(Mattick et al., Cochrane 2014)

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**Buprenorphine: Diversion**

![Graph showing average number of cases of abuse of buprenorphine, methadone, tramadol, and oxycodone per drug abuse expert, showing a rising trend for oxycodone and buprenorphine.](image)

*Cicero, NEJM 2005*
“We find that all of us, as a society, are to blame, but only the defendant is guilty.”

Buprenorphine: Abuse/diversion
Lavonas et al., JSAT 2014; 47:27-34
Buprenorphine: Abuse/diversion

Lavonas et al., JSAT 2014; 47:27-34

**Poison Center Program**
Intentional Abuse Cases

**Drug Diversion Program**
Illicit Diversion Investigations

**Treatment Programs**
Abuse in the Past Month

**College Survey Program**
Abuse in the Past Semester

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Shading denotes the formulation with the highest abuse, diversion, or non-medicinal use rate in that state

- Buprenorphine tablets
- Buprenorphine / naloxone tablets
- Buprenorphine / naloxone film
- No sublingual buprenorphine cases in program during time period
- No program coverage during time period
Buprenorphine: Reducing Diversion via Urine Tests

- Conduct periodic, random urine tox screens for BUP
- “5-panel” tests detect methadone, oxycodone, heroin, etc., but test for a different metabolite than that found with BUP -- these will NOT be positive in BUP (only)-maintained patients
- BUP: detected in a 12-panel test or if specifically requested
- BUP plasma half-life = 24-42 hours (2-12 hours for naloxone)
- Typical BUP doses are detectable in the urine for 3 days

Buprenorphine: Other Ways to Reduce Diversion

- Limit the prescription quantity & # of refills
- Write prescriptions in pen
  No pre-printed DEA numbers on scripts!
- If diversion suspected: Perform random callbacks, pill counts, & observed dosing
- Outline these policies in the patient contract
- Use Rx forms with preprinted numbers for refills quantities
  Circle the desired number, & strike through others
- Use the PDMP to detect forgery, improper Rxing, & doctor-shopping patients
MMT vs. BUP Conclusions

- MMT flex-dose: better retention
- BUP: preferred when high dose MMT cannot be administered or tolerated
- BUP advantages: relative safety, alternate-day administration, convenience & access
- “There does not appear to be any need for further randomized control trials of the relative efficacy of methadone compared with buprenorphine.”

(Mattick et al., Cochrane 2014)

Healthcare Costs in Opioid Dependence: Comparison of Four Agents

O Baser1, M Chalk2, DA Fiellin3, DR Gastfriend4

1 STATInMED Research, Inc. & U of Michigan, Ann Arbor, MI
2 Treatment Research Institute, Philadelphia, PA
3 Yale University Medical School, New Haven, CT
4 Alkermes, Inc., Waltham, MA

Funding: through a contract from Alkermes Inc. to Ingenix Pharmaceutical Services Inc. and STATInMED Research, Inc.

Objective: 6-month retrospective insurance claims study (N=10,413) using instrumental variable analysis to control for baseline group differences to determine total healthcare costs (all meds + inpt + outpt)
6-Mo TOTAL Healthcare Costs
(Inpatient + Outpatient + Pharmacy)

Cost per patient

P-value vs. XR-NTX: †P<0.001

Inpatient Admission Rates
Real-World 6 Month Outcomes After Treatment Initiation

Baser et al., Am J Manag Care 2011b
Opportunities: Agents & Formulations

- LAAM – full mu agonist; no longer used clinically
- XR morphine sulphate; Heroin-assisted treatment
- Heroin vaccine
- Probuphine 6 mo. BUP implant; FDA approved

![6-mo BUP Implant: Retention](chart)

Attitudes: Harmful & Helpful

- Attitudes that do a disservice to patients:
  - “If you’re using drugs, you’re not really sober; I did it the hard way”
  - “If you just work the program, you won’t need any drugs”
  - “You can’t treat a drug problem with a drug”
  - “If you are on drugs, you can’t speak at a meeting”

- Attitudes that are justified by the science:
  - We don’t withhold medication from heart disease patients, saying: “You have to stop smoking & lose weight on your own, like I did”!
  - Chronic diseases, like hypertension & asthma have meds. If we want addiction to be treated as equal to other medical illnesses, we need to accept the role of medicine in addiction treatment, too.
  - Opioid patient on XR-NTX: “I never understood it before... but now I know how it is that non-addicts can just ignore drugs. And suddenly I see what it means that I really do have an addiction.”
Is OST a Necessity for OUD Recovery?
(Merlo et al., JSAT 2016, 64:47-54)

- A 5-year, retrospective review of 702 physicians in 16 programs (N=702; 85.5% male; age=24-75). Alcohol Only (n=204), Any Opioid with or w/o alcohol use (n=339), 3) Non-Opioid drug use with or w/o alcohol (n=159)
- Of 22.1% of physicians who had a positive test, 2/3rds had just 1 + test, and only 1/3rd had >1 + test. Results were similar in all 3 groups.

CONCLUSIONS:
- MDs with OUD in PHPs have long-term abstinence from opioids, alcohol, and other drugs
- Without OST via abstinence-based psychosocial treatment with extended, intensive management after discharge

Q&A

- How to determine necessary BUP dose?
  - Difficult: patient subjective self-report
  - Balanced by objective function (incl. collaterals) and drug testing

- Are there head-to-head trials of BUP vs. XR-NTX?
  - Insurance claims retrospective analysis
  - Norwegian head-to-head RCT
  - Awaited: NIDA CTN Prospective RCT
Conclusions: Opioid Dependence

- Opioid dependence is a chronic disease requiring long-term rehabilitation with both meds AND counseling.
- The goals of treatment/rehabilitation are: saving lives, stabilizing behavior and establishing social functioning.
- Agonists & antagonists are superior to counseling alone.
- All FDA-approved agents are appropriate 1st-line approaches.
- Therefore, programs should provide ALL options, so that patients can be informed of and offered ALL options.
- Low initial costs can become high costs longer-term, and high initial costs can result in lower costs longer-term, therefore, cost should NOT be a consideration in clinical care.
- Patient choice may be the BEST basis for drug selection.
- If one agent is unsuccessful, other options should be tried.

Case 1 (Part I)

Johnny is a 34 yo male; hurt back working in the coal mines and was Rxed opioids; use escalated and he began using multiple oxycodone with APAP 30/500 mg tabs IV daily. Met criteria for Opioid Dependence, LFTs less than 3x normal.

Tried BUP from a doctor and received a prescription: “It didn’t work for me. I just stopped taking it and used, and took it some more and then stopped and used. It was too easy to game it. I need more. I don’t want that medicine”.

84
Case 1 (Part II)

Johnny did extremely well with methadone at a maximum dose of 85 mg per day and began a gradual dose reduction.

At 3 years he on 70 mg and has been eligible for 27 take homes per 28 days, but opts to get 13 in 14 days ("I don’t trust myself with more. I need to come here to keep myself honest").

He has an opportunity to change jobs from underground mining to hauling coal locally, which requires a commercial driver’s license. He is willing to change to BUP, recognizing he is now doing well presenting every 2 weeks to clinic.

Case 1 (Part III)

Johnny made the change from methadone to BUP, stabilized at 12 mg qd for a year and gradually tapered to 4 mg qd. Attempts to lower the dose have failed.

Continues to choose present q 2 weeks to clinic, although eligible for monthly visits and has been encouraged to find support outside of clinic.

Local mines have closed, and he has the option for work in another state. Plans to come home once monthly. Will have insurance with new job, and has saved substantial money since he stopped using street opioids and began treatment 6 years ago.
Case 2

"I was on Suboxone for about 5 years when I became pregnant. During my pregnancy my Doc had me on Subutex and then after my pregnancy it was time to go back to Suboxone. My Doc gave me Bunavail instead.

It said it was 4.2 mg instead of 8 and my addict brain immediately did not like that. And when I first started it, I HATED it. I would take a whole piece in my right cheek and it BARELY touched my withdraws. I had to wait for it to melt, which takes FOREVER, and then take another one.

BUT, one day I put it in my left cheek just to mix it up, and I was SHOCKED that it worked!

Ever since I've been using my left cheek and have had no problems, besides the time it takes to melt."

Q&A

- Why is it that when you transport something by car, it's called a shipment, but when you transport something by ship, it's called cargo?
- If nothing ever sticks to TEFLON, how do they make TEFLON stick to the pan?
- Why are there Braille dots on keypads of drive-up ATMs?
- Why do we drive on parkways and park on driveways?
- You know that little indestructible black box that is used on planes – why can't they make the whole plane out of the same substance?
Jordyn  Ashland, KY  @Jenna..:

- I'll be 10 months clean tomorrow. I still struggle with the lack of energy. It takes months to gain back your strength, energy, and stamina.
- I know that energy drinks aren't necessarily the best option... best crutch that I found through the days that I felt drained was Redbull. I now may drink one Redbull every two weeks... so it is getting MUCH better. I can say that as you get farther into being completely clean & sober, you gain a lot of muscle mass back. Where as, while you're still taking the Suboxone, you continue to lose muscle mass and natural body strength daily. You can do it.
- My recommendation would be that if you're only taking the small amount that you stated, I would quit completely cold turkey.

Q&A: MAT in Opioid Use Disorders

The following are all TRUE, EXCEPT (choose one):

- A. Methadone’s structured care may help patients with chaotic lifestyles.
- B. Oral naltrexone has shown little benefit vs. placebo for most patients.
- C. XR-NTX can be used in patients with severe disease or criminal justice involvement.
- D. Buprenorphine can be started immediately without detox or withdrawal.
- E. Patients may choose meds based on their job, desire for an opioid effect, concerns of treatment cessation difficulty and convenience.
Q&A: MAT in Opioid Use Disorders

Which of the following is FALSE about Buprenorphine treatment? (choose one):

- A. Partial agonists have low overdose risk, unless sedatives are present.
- B. With a partial agonist, acute pain can be managed with non-opioids, or anesthesia-trained staff can override the blockade with opioids.
- C. A one-month taper after 3 months of BUP treatment for prescription opioid analgesic dependence yields >90% success.
- D. Buprenorphine may be used to treat OUD during pregnancy.
- E. Federal law allows Nurse Practitioners and Physician Assistants to obtain waivers to prescribe BUP.

Q&A: MAT in Opioid Use Disorders

The following are all TRUE, EXCEPT (choose one):

- A. BUP has withdrawal symptoms, so it should be used long-term.
- B. BUP is safe in Hep C+ & HIV+ patients.
- C. Buprenorphine is available for office practices, in tablet, film or extended-release implant versions.
- D. Programs can and should offer all FDA-approved medications, either directly or via active affiliation agreements.
- E. In a head-to-head random control study, BUP was superior to XR-NTX.
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