Buprenorphine Initiation after Reversal of Opioid Overdose
A New Standard Of Care

Andrew Herring, MD
None of the presenters today have any financial disclosures.
Objectives

1. Discuss the pharmacology of buprenorphine relevant to treatment of overdose after naloxone reversal of opioid overdose.

1. Determine appropriate candidates for buprenorphine after naloxone reversal of opioid overdose.
Goal: 24-7 access to high quality treatment of substance use disorders (SUD) in all California hospitals by 2025.

Status: 50+ hospitals are currently access points for patients with SUD.
Changing Lives, Changing Health Care

9834 patients identified with OUD

6312 Patients provided with treatment

4486 Patients given a prescription for MAT

3930 Patients linked to follow-up MAT care

OUD Opioid Use Disorder
MAT Medication for Addiction Treatment

Cumulative totals across all reporting CA Bridge sites (n = 41) as of April 30, 2020
48 of 52 EDs report offering Buprenorphine after Opioid Overdose.
Patient arrived via Ambulance due to nausea and vomiting with associated pain tonight. Narcan was given on scene by the EMS. Patient has smoked heroin before. Denies falls. Denies chest pain, obt, SOB, headache.

- Resting comfortably and stable vitals
- Plan to observe until 1600
- Following the bridge protocol, pt KD does not meet any exclusion criteria and qualifies for bup after the reversal of overdose with narcan.
Bup After Overdose

Nikita Kaushik Joshi, MD

Also - I am starting bup on a pt who came in OD on heroin!! WIN!
Wed 1:41 AM

Nikita Kaushik Joshi, MD

yes, very stable right now, awake and alert.
Wed 1:44 AM

Nikita Kaushik Joshi, MD

yes, about 30 minutes ago

Nikita Kaushik Joshi, MD

I gave him 8 mg Sl
Wed 2:06 AM

Nikita Kaushik Joshi, MD

will do! thanks... I feel like this is amazing... my own Bup coach...
Wed 2:08 AM

bup after naloxone?
Wed 1:43 AM

has he gotten bup yet?
Wed 2:01 AM

sweet! consider another dose
Wed 2:07 AM

go get 'em tiger
Wed 9:08 AM
Bup Induction after Overdose

Heroin or Fentanyl overdose reversed with naloxone or other short-acting opioid

Are any patient exclusion criteria present?
- Benzodiazepine, other sedative or intoxicant suspected
- Altered mental status, depressed level of consciousness, or delirium
- Unable to comprehend potential risks and benefits for any reason
- Severe medical illness such as sepsis, respiratory distress, organ failure present or suspected
- Report of methadone use
- Not a candidate for buprenorphine maintenance treatment for any reason

NO TO ALL

Is the patient awake with signs of opioid withdrawal? (i.e. COWS >4)

YES

Is the patient agreeable to treatment with buprenorphine?

NO

YES

Provide supportive care, observe and reevaluate

16mg SL Buprenorphine
Administered as a single dose or in divided doses over 1-2 hours.
(Start with 0.3mg IV if unable to tolerate SL.)

Observe in ED until patient shows no clinical signs of excessive sedation or withdrawal (typically 2 hours).
OK to administer additional doses of Bup up to 32mg.
Engage, use motivational interviewing, and link to ongoing care.
“No Shit Science”
CA Bridge Delivers Addiction Treatments When it Matters Most

- Study of patients treated in Massachusetts EDs for opioid overdose 2011-2015
- Illustrates the short-term increase in mortality risk post-ED discharge
  - Of patients that died, 20% died in the first month
  - Of those that died in the first month, 22% died within the first 2 days

Case #1: “By the Book”

- Screen and Diagnose OUD
- Assessment of Withdrawal
- Lab Testing

Treat with Buprenorphine

4mg

Wait 2 hours

4mg

Total 8mg
**Screen and Diagnose OUD**

**DSM-5 Criteria for Diagnosis of Opioid Use Disorder**

1. Take more/longer than intended
2. Desire/unsuccesful efforts to quit opioid use
3. A great deal of time taken by activities involved in use
4. Craving, or a strong desire to use opioids
5. Recurrent opioid use resulting in failure to fulfill major role obligations
6. Continued use despite having persistent social problems
7. Important activities are given up because of use.
8. Recurrent opioid use in situations in which it is physically hazardous (e.g. driving)
9. Use despite knowledge of problems
10. Tolerance
11. Withdrawal

At least 2 criteria must be met within a 12 month period

<table>
<thead>
<tr>
<th>Severity</th>
<th>Presence of Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild:</td>
<td>2-3</td>
</tr>
<tr>
<td>Moderate:</td>
<td>4-5</td>
</tr>
<tr>
<td>Severe:</td>
<td>≥6</td>
</tr>
</tbody>
</table>

“Why are you asking me these questions?”

“I told you I feel sick”

“Where is the dot phrase”

“I am waiting for psychiatry to call me back”

“We have not been trained on DSM 5”
Assessment of Withdrawal

Clinical Opioid Withdrawal Scale (COWS)

Score:
5-12= Mild
13-24= Moderate
25-36= Moderately Severe

“Why are you asking me these questions?”

“I told you I feel sick”

“Where is the dot phrase”

“I am waiting for psychiatry to call me back”

“We have not been trained on COWS”
Lab Testing

- Pregnancy testing for women in reproductive years
  - NOT an exclusion but will guide referral process

- Consider urine toxicology testing if
  - Concerns about accuracy of opioid use history
  - Long acting opioid use (i.e. methadone)
  - Note: Fentanyl will not show up in many hospital urine drug screens

- Consider blood testing
  - LFTs if clinical suspicion of liver failure (Buprenorphine contraindicated if LFTs >5 x normal)
  - HIV, Hepatitis B and C if not otherwise available at referral site

“I just pee’d”

“I hate needles”

“Are you going to tell my parole officer”

“The lab lost the sample”
Treat with Buprenorphine

- 4 mg
  - Wait 2 hours
  - 4 mg
  - Total 8 mg

“Why are you only giving me 4mg?”
- “I still feel terrible”
- “It’s not working”
- “The patient left”
- “The ED is not the right place to start MAT”
M & M Analysis

Failure of care delivery
Failure of care coordination
Overtreatment or low value care
Pricing failure
Fraud and abuse
Administrative complexity

- It didn’t work
- The patient didn’t like it
- It was expensive
- It took to long
- It was complicated
# Starting Buprenorphine (Bup), "Subs", Suboxone

## Step 1: Wait
- **Last use**: 0
- **6 hours**
- **12 hours**

## Step 2: Withdrawal
- **Feel fine**: 0
- **5**
- **10**
- **Very Sick**

## Step 3: First Dose
- **Light user**: 4mg
- **Medium heroin**: 8mg
- **Heavy heroin**: 16mg
Ceiling Effect: Sharon Walsh

- 16 healthy non-opioid dependent volunteers

"How Much Do You Feel the Drug?"

Clinical pharmacology of Buprenorphine: Ceiling effects at high dose
Ceiling Effect

Pharmacokinetics and Pharmacodynamics of Multiple Sublingual Buprenorphine Tablets in Dose-Escalation Trials

Domenic A. Ciraulo, MD, Robert J. Hitzemann, PhD, Eugene Somosza, MD, Clifford M. Knapp, PhD, John Rotrosen, MD, Ofra Sarid-Segal, MD, Ann Marie Ciraulo, RN, David J. Greenblatt, MD, and C. Nora Chiang, PhD

38 subjects
Proportionate agonism: Andy Saxon

Withdrawal intensity

24mg x 1 vs 8mg daily x 3 days SL BUP

Mean VAS Score

Day 2         Day 3         Day 4         Day 5

Study time point

Single Dose of 24 Milligrams of Buprenorphine for Heroin Detoxification: An Open-label Study of Five Inpatients

Kathleen Ang-Lee, Michael R. Oreskovich, Andrew J. Saxon, Craig Jaffe, Charles Meredith, Mei Ling K. Ellis, Carol A. Malte & Patricia C. Knox
<table>
<thead>
<tr>
<th>Mu Opioid Receptor Range of Ki Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Buprenorphine</strong></td>
</tr>
<tr>
<td><strong>Fentanyl</strong></td>
</tr>
<tr>
<td><strong>Methadone</strong></td>
</tr>
<tr>
<td><strong>Naloxone</strong></td>
</tr>
<tr>
<td><strong>Morphine</strong></td>
</tr>
<tr>
<td><strong>Codeine</strong></td>
</tr>
</tbody>
</table>

PDSP Ki Database: [https://pdsp.unc.edu/databases/pdsp.php](https://pdsp.unc.edu/databases/pdsp.php)

Buprenorphine antagonism of ventilatory depression following fentanyl anaesthesia

K. Boyesen, S. Hertel, B. Chræmmer-Jørgensen, A. Risbo and N. J. Poulsen
Department of Anaesthesia, University of Copenhagen, Glostrup Hospital, Glostrup, Denmark

0.6 mg bup vs 0.2 mg naloxone

Table 2
Respiratory rate – median (range).

<table>
<thead>
<tr>
<th>Time: min</th>
<th>Preinduction</th>
<th>0</th>
<th>15</th>
<th>30</th>
<th>60</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>13</td>
<td>0</td>
<td>10</td>
<td>12</td>
<td>11.5</td>
<td>11</td>
</tr>
<tr>
<td>n = 10</td>
<td>(12–14)</td>
<td>(0–4)</td>
<td>(8–12)</td>
<td>(8–16)</td>
<td>(8–16)</td>
<td>(8–12)</td>
</tr>
<tr>
<td>Naloxone</td>
<td>12</td>
<td>0</td>
<td>14.5*</td>
<td>14</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>n = 10</td>
<td>(11–15)</td>
<td>(0–2)</td>
<td>(9–20)</td>
<td>(10–20)</td>
<td>(9–16)</td>
<td>(6–16)</td>
</tr>
</tbody>
</table>

Time = min from beginning treatment with either B or N. *P < 0.05 between groups.
Naloxone.
2 mg RR <6; 0.04 mg RR of 6-12

Buprenorphine:  
10 μg/kg or 15 μg/kg of IV over 6 and 9 min, respectively.
Groups B and C were given 10 μg/kg and 15 μg/kg of IV buprenorphine (slowly administered over 6 and 9 min, respectively).

Table 3 Per-protocol comparison of outcomes in three arms of the study (n = 81)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Naloxone (n = 27)</th>
<th>Buprenorphine 10 μg/kg (n = 27)</th>
<th>Buprenorphine 15 μg/kg (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to bolus antidote doses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>13 (48%)</td>
<td>Complete 23 (85%)</td>
<td>Complete 27 (100%)</td>
</tr>
<tr>
<td>Partial</td>
<td>13 (48%)</td>
<td>Relative 3 (11%)</td>
<td>Partial 0</td>
</tr>
<tr>
<td>No response</td>
<td>1 (4%)</td>
<td>No response 1 (4%)</td>
<td>No response 0</td>
</tr>
<tr>
<td>Opioid withdrawal</td>
<td>15 (56%)</td>
<td>0</td>
<td>6 (22%)</td>
</tr>
<tr>
<td>Further apnea</td>
<td>6 (22%)</td>
<td>4 (15%)</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>1 (4%)</td>
<td>5 (18%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Intubation</td>
<td>8 (30%)</td>
<td>4 (15%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Continuing sedation</td>
<td>9 (33%)</td>
<td>0</td>
<td>3 (11%)</td>
</tr>
</tbody>
</table>
TOXICOLOGY/CASE REPORT

Elective Naloxone-Induced Opioid Withdrawal for Rapid Initiation of Medication-Assisted Treatment of Opioid Use Disorder

Reid H. Phillips, MD*; Matthew Salzman, MD; Rachel Haroz, MD; Rachel Rafeq, PharmD; Anthony J. Mazzarelli, MD, JD; Alexis Pelletier-Bui, MD

*Corresponding Author. E-mail: phillips-reid@cooperhealth.edu.
Sacred COWS

Concurrent validation of the Clinical Opiate Withdrawal Scale (COWS) and single-item indices against the Clinical Institute Narcotic Assessment (CINA) opioid withdrawal instrument

D. Andrew Tompkins, a,b, George E. Bigelow, a Joseph A. Harrison, b, Rolley E. Johnson, a,b, Paul J. Fudala a, Eric C. Strain a

a Yale University School of Medicine, Department of Psychiatry and Behavioral Science, Behavioral Pharmacology Research Unit, New Haven, CT 06520, USA
b Purdue Frederick Pharmaceuticals Inc., Richmond, IN 47374, USA

![Graph showing VAS Score over Time for Placebo and Naloxone treatments.](image)
“Single Big Dose“
Discussion “Goldilocks” Dose

- Just a tad...they don’t even notice
- Displaces but doesn’t replace
- Displaces and Overcomes
“Do I have to feel sick”: Single Big Dose

Displacement

\[ H + H + H + H = \text{Pain} \]
“Do I have to feel sick”: Single Big Dose

100mcg Heroin

4 mg Bup

16mg
“Do I have to feel sick“: Single Big Dose

Agonism

Displacement

Blockade
Heroin

Bup Agonism

“Feel good”

Bup Displacement

Abstinence & dependency

“Feel bad”
Bup After Overdose
Bup After Overdose

Nikita Kaushik Joshi, MD

Also - I am starting bup on a pt who came in OD on heroin!! WIN!

Wed 1:41 AM

bup after naloxone?

Wed 1:43 AM

Nikita Kaushik Joshi, MD

yes, very stable right now, awake and alert.

Wed 1:44 AM

has he gotten bup yet?

Wed 2:01 AM

Nikita Kaushik Joshi, MD

yes, about 30 minutes ago

Wed 2:06 AM

I gave him 8 mg sl

Wed 2:06 AM

sweet! consider another dose

Wed 2:07 AM

Nikita Kaushik Joshi, MD

will do! thanks... I feel like this is amazing... my own Bup coach...

Wed 2:08 AM

good get 'em tiger
Bup After Overdose

D via Ambulance due to nausea and vomiting with associated diaphoresis. Narcan was given on scene by the EMS. Patient has smoked heroin before. Denies falls. Denies chest pain, palpitations, SOB, headache.

- Resting comfortably and stable vitals
- Plan to observe until 1600
- Following the bridge protocol, pt KD does not meet any exclusion criteria and qualifies for bup after the reversal of overdose with narcan
New Jersey first state to authorize paramedics to provide addiction-treatment drug to overdose victims
**BUPRENORPHINE FIELD INITIATION OF RESCUE TREATMENT BY EMERGENCY MEDICAL SERVICES (BUPE FIRST EMS): A CASE SERIES**

Gerard G. Carroll, MD FAAEM EMT-P, Deena D. Wasserman, MD FAWM, Aman A. Shah, MD, Matthew S. Salzman, MD, Kaitlan E. Baston, MD MSc DFASAM, Rick A. Rohrbach, BSN CFRN CCRN-K MICP, Iris L. Jones, MA LPC, LCADC, Rachel Haroz, MD, FAACT

**TABLE 1. Patient Characteristics and Treatment**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Naloxone given</th>
<th>Initial COWS</th>
<th>Buprenorphine given</th>
<th>Repeat COWS</th>
<th>1st visit</th>
<th>30 day retention</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2 mg IM</td>
<td>13</td>
<td>16 mg</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>B</td>
<td>2 mg IM</td>
<td>15</td>
<td>16-32 mg</td>
<td>3</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>C</td>
<td>4 mg IN</td>
<td>12</td>
<td>16 mg</td>
<td>4</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Bup Induction after Overdose

**Flowchart: Bup Induction after Overdose**

1. **Heroin or Fentanyl overdose reversed with naloxone**
   - or other short-acting opioid

2. **Are any patient exclusion criteria present?**
   - Benzodiazepine, other sedative or intoxicant suspected
   - Altered mental status, depressed level of consciousness, or delirium
   - Unable to comprehend potential risks and benefits for any reason
   - Severe medical illness such as sepsis, respiratory distress, organ failure present or suspected
   - Report of methadone use
   - Not a candidate for buprenorphine maintenance treatment for any reason

   **Decision Point:**
   - **NO TO ALL**
   - **YES TO ANY**

3. **Is the patient awake with signs of opioid withdrawal?** *(i.e. COWS >4)*
   - **NO**
   - **YES**

4. **Is the patient agreeable to treatment with buprenorphine?**
   - **NO**
   - **YES**

5. **16mg SL Buprenorphine**
   - Administered as a single dose or in divided doses over 1-2 hours.
   - *(Start with 0.3mg IV if unable to tolerate SL.)*

6. **Observe in ED until patient shows no clinical signs of excessive sedation or withdrawal (typically 2 hours).**
   - OK to administer additional doses of Bup up to 32mg.
   - Engage, use motivational interviewing, and link to ongoing care.
Need help with pain pills or heroin?

We want to help you get off opioids and started on Suboxone (Buprenorphine).

Ask for more information here.
Andrew Herring, MD
Highland Hospital
Andrew@BridgeToTreatment.org
MORE RESOURCES AVAILABLE: BridgeToTreatment.org/resources