Opioid Initiative Wave I – Treating Opioid-Use Disorder in the ED Part 2
Presenter

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BUPRENORPHINE IN THE E.D.: Initiating Medication Assisted Treatment for Opioid Addiction

Expanding the scope of emergency care during an addiction epidemic

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emupdates.com
O.D. is now the #1 cause of death for Americans under age 50

1999-2016: more than 600,000 overdose deaths

Life expectancy for Americans is falling -- two years in a row
MAT: _Medication Assisted Treatment is the MOST EFFECTIVE Treatment for Opioid Addiction_

Opioid addiction does not respond to the same treatments as alcoholism.
Abstinence based therapies generally DO NOT WORK: ~ 95% relapse rate.
Twelve Step programs have a <5% rate of sobriety at one year, when treating Opioid Use Disorder.

MAT:
- Naltrexone
- Methadone
- Buprenorphine ("bupe")
MAT: Medication Assisted Therapy
Depot Naltrexone: **Vivitrol**

Patient must have already completed withdrawal, or completely weaned off mu agonist therapy (or will precipitate withdrawal).

**Increasing use in correctional facilities and residential programs.**

Some patients opt for Vivitrol after “detoxing” or after completion of an abstinence program.

**Overall outpatient numbers are still low.**

**NOT a medication to be initiated in the E.D.**

Monthly Injection for Assisted Abstinence Therapy

Intended to prevent any reward from opioid use, and thus gradually reduce cravings.
MAT: Methadone

Very Effective Medication for Opioid Use Disorder:

• The “gold standard” by which other treatments are measured.
• Long half-life (~ 24 hrs), full mu agonist.
• The dosing is very patient specific.
• Nearly all methadone clinics (addiction treatment) use liquid methadone (to deter diversion).
• Many regard methadone as 2nd line medication – for patients who fail office-based buprenorphine treatment.
MAT: Methadone

HOWEVER:
Requires daily travel to the clinic.
May not be available in suburban & rural areas.
Inconvenient for many occupations -- daily dosing at a clinic.
Dosing at the methadone clinic means congregating with other patients with OUD: Pros & Cons.

The E.D is NOT the place to begin methadone treatment.
PRESCRIBING Methadone – DON’T

PRESCRIPTION FORM – very RISKY!

High risk drug for treating chronic pain by prescription.
24 hr ½ life for dependency, but only ~ 8 hr ½ life for pain relief.
Slow onset ~ 3-4 hours to peak.
24 hr ½ life for potential effects of respiratory depression.
Vast majority of Methadone deaths are from treatment for pain by Rx, or diverted use, rather than in an addiction clinic.
Vast majority of diverted methadone is in the tablet form (the prescription form).
**BUPRENORPHINE (“BUPE”) NUTS & BOLTS:**

- Key properties of bupe:
  - “Partial agonist”
  - Long half-life: ~ 36 hours (treating dependency)
  - Rapidly effective
  - Binds tightly to the Mu receptor (blocking other opioids)
  - Induces less euphoria (particularly after the first dose)
    - Many patients get no euphoria from bupe ever.
  - Very effective analgesic.
“Partial agonist”:

Has a ceiling effect on respiratory depression

“No more respiratory depression at 32mg than at 16mg”

However, may potentiate respiratory depression effects of alcohol, and other sedating medications (e.g. benzos).

- Important consideration if prescribing bupe.

Any Doc can use bupe in the ED to treat opioid withdrawal.
Any Doc can prescribe bupe for pain.
Must have an DEA license “X-waiver” to PRESCRIBE for ADDICTION
Long half-life: ~ 36 hours:

- When dosed daily, at a therapeutic dose, maintains the patient at a therapeutic level – a ‘steady state’
- Thus eliminating withdrawal symptoms and cravings
- Concept Similar to methadone, which has a half-life of ~ 24 hours. However, bupe is:
  - Easier to dose.
  - Safe for office based treatment.

Beginning MAT with bupe in the E.D. does not preclude or complicate transitioning the patient to methadone in an addiction clinic (if that is a better option for that patient).
NUTS & BOLTS OF BUPE TX

Effective within 15 minutes (sublingual), and peak effects at ~ 1 hour.

SL bioavailability ~ 50%

Be sure it goes under the tongue.

Buccal ~ 28%

Oral (swallowed) ~ 15%

• High rate of first pass metabolism
“Suboxone” (others: “Zubsolv” and “Bunavail”)

Combinations of buprenorphine and naloxone (tablets or strips)

“Suboxone,” is a 4:1 ratio of bupe/naloxone.

Naloxone has a very poor sublingual and oral bioavailability (~ <2%).

Included to prevent the dissolution and IV injection of buprenorphine.

In my E.D. we only use the generic mono-product bupe:

-- administered by a nurse

– less expensive.
BUPRENORPHINE ("BUPE")
NUTS & BOLTS:

Addiction CLINIC Dosing initiation:

• Therapeutic dosing can begin on the first day of treatment
  • Older protocols suggested starting at low doses, and observing the patient in clinic for an hour.
• However, most patients with OUD have had experience with buprenorphine.
• Effective dosing is related to the volume/dose of the patient’s habit or tolerance.
• Eric Ketcham’s rule of thumb for INITIAL effective bupe dosing in clinic:
  • <50mg/day of oxycodone or ~<1/2 G/day (or less) of heroin -- ~2-4mg/day
  • ~150-200mg/day of oxy or ~2 G/day of heroin or more -- ~16mg/day
• Adjust dosing on follow up visits.
IN 1996, FRANCE RESPONDED TO ITS HEROIN OVERDOSE EPIDEMIC BY TRAINING/LICENSING GP’S TO PRESCRIBE BUPRENORPHINE

Over 8 years:

• 3x increase methadone treated patients (up to ~15,000 pts)
• 4.5x increase in bupe tx pts (up to ~90,000 pts)
• 90% reduction in heroin overdoses!!
• ~50,000 pts down to ~5,000 pts!

Heroin overdose deaths and opioid agonist treatment: Baltimore, MD, 1995–2009

- Rapid expansion of access to buprenorphine treatment
- Rate of heroin overdose deaths drops in half.
- Despite a substantial increase in local heroin purity.

Opioid Agonist Therapy is Much More Valuable than Drug Abuse Counseling!!

Swedish Study:
- 40 patients randomized
- Daily supervised medication administration for the first 6 months

1-year retention in treatment was 75% in the buprenorphine group
0% in the placebo group

Review specifically studied value added of routine, mandatory counseling sessions in MAT programs

“… adding any psychosocial support to standard maintenance treatments does not add additional benefits.”
EVERYONE NEEDS A THERAPIST, BUT AN OPIOID ADDICT NEEDS AN OPIOID AGONIST
Beginning MAT in the ED: the warm hand-off


• 329 ED patients with OUD, screened, and randomized:
  • ~1/3 to the referral group (patient is handed a pamphlet)
  • ~1/3 to the brief intervention group (meets with a social worker or pt advocate)
  • ~1/3 to the buprenorphine treatment group (and above)

MAIN OUTCOMES AND MEASURES:

• Enrollment in, and receiving, addiction treatment 30 days after randomization was the primary outcome.

Engaged in Treatment at 30-Days

Proportion in Treatment at 30 Days

Referral

Brief Intervention

Buprenorphine

\[ P < 0.001 \]
Needed inpatient addiction treatment services?

• Bupe group: **11%** \( (95\% \text{ CI}, 6\%-19\%, \, P < 0.001) \)

• Referral Group: **37%** \( (95\% \text{ CI}, 27\%-48\%, \, P < 0.001) \)

• Brief Intervention Group: **35%** \( (95\% \text{ CI}, 25\%-37\%, \, P < 0.001) \)
In the outpatient setting:

“According to DEA ... the “three-day rule” allows a practitioner who is not separately registered as a narcotic treatment program or certified as a waiver DATA 2000 physician, to administer (but not prescribe) narcotic drugs to a patient for the purpose of relieving acute withdrawal symptoms while arranging for the patient’s referral for treatment, under the following conditions:

• Not more than one day’s medication may be administered or given to a patient at one time.
• Treatment may not be carried out for more than 72 hours
• The 72-hour period cannot be renewed or extended”

• *Is it necessary to be able to refer a patient to an opioid addiction treatment clinic, to administer bupe in the ED for withdrawal or MAT?*

• Officially, it is required ...

• In practicality ...

• The DEA cares about **DIVERSION** of prescribed, or dispensed, bupe.

• The DEA is far, far less concerned about medications ordered and administered in hospitals.
NUTS & BOLTS OF BUPE TX

Binds tightly to the Mu receptor (blocking other opioids):

• Displaces full agonist opioids (heroin, morphine, methadone, etc.)

• Requires high doses of naloxone to displace bupe.

• Patients must be in withdrawal – (or craving post w/d) -- to benefit from bupe!

• PRECIPITATED WITHDRAWAL CAN BE HORRIBLE.
Avoiding Precipitating Withdrawal with Bupe

• Find out what the patient uses (if possible):
  • Type of opioids used
  • Low dose user, high dose user
  • Last use (how many hours ago).
• Ensure the patient is in adequate withdrawal (or withdrawal completed)
  • Can be in mild withdrawal for short acting opioids,
  • At least moderate for long acting opioids (e.g. methadone)
• Perform a COWS score:
  • A quick 11 element scale, which includes elements such as heart rate, pupil size, rhinorrhea, tremor, and restlessness.
  • COWS ≥ 8 mild, ≥ 13 moderate, ≥ 36 severe.
  • Takes <1 minute to score
Bupe After Naloxone for O.D?

To Avoid Precipitating withdrawal:

• This has not been well studied.
• Shared decision-making with pt.
• If pt only uses short acting opioids (e.g. heroin, oxycodone), may consider initiating bupe:
  • Be prepared to monitor pt until the naloxone would have worn off.
  • Offer non-opioid w/d tx as well.
• After NALOXONE, caution with giving bupe to pts on long half-life opioids, such as methadone, MS Contin, Opana, etc.
Treating Buprenorphine Precipitated Withdrawal

Treating Precipitated Withdrawal:

- Also not well studied. Somewhat controversial.
- Can offer non-opioid Tx.
- Alternatively .. More bupe.
- Titrate additional doses, while the patient is monitored, until withdrawal symptoms have subsided.

CAUTION:

- Nausea is a common adverse effect of buprenorphine.
- Do not assume that all nausea induced by buprenorphine is due to precipitated withdrawal.
PATIENT SELECTION PITFALLS FOR E.D. BUPE INITIATION:

1. The very mild withdrawal patient who states, “I feel like the withdrawals are just starting” is an ideal candidate for counseling and referral (not ED bupe).
   - Check a COWS score! Must be at least 8 -- if no other contraindication.
   - No need to precipitate withdrawal.

2. METHADONE in the last 48 hours (not an absolute contraindication):
   - Unpredictable precipitated withdrawal can occur
   - Unless pt in severe withdrawal, consult an expert first.

3. Intoxicated -- alcohol, benzodiazepines, stimulants, etc...
   - Unpredictable immediate results.
   - At risk for polypharmacy synergistic respiratory depression, with polydrug use after discharge.
   - Do your best to engage and encourage them to consider the ED an “open door” to return when sober.
PATIENT SELECTION PITFALLS FOR E.D. BUPE INITIATION:

4. “Chronic pain patients” taking medically prescribed opioids:
   • Many “chronic pain” patients truly painful conditions, but also have developed opioid dependence, and experience opioid induced hypersensitivity, tachyphylaxis, and withdrawal – reported as pain flares.
     • Although may be excellent candidates for tx with bupe for pain (and OUD) -- very effective analgesic.
     • However, the dosing is different for chronic pain.
     • Better handled in Clinic.

5. Patients with severe medical illnesses: renal failure, advanced liver disease, heart failure, severe COPD:
   • Not an absolute contraindication, may be a good option.
   • HOWEVER, this treatment must be COORDINATED. Requires a team approach.
BASIC E.D. DOSING CONCEPTS:

• Screen out high risk patients (previous slide).

• Base the first dose based on:
  • Patient’s use history (average daily opioid use) – high vs. low
  • Severity of withdrawal
  • Example: ~ lower dose user, mild to moderate withdrawal: consider 4mg of bupe.
  ~ high dose user, in at least mild withdrawal: start at 8mg of bupe.

• Repeat dosing every 30 minutes as necessary to get the patient comfortable:
  • Then the pt can have a meaningful conversation with a social worker/advocate for clinic referral.

• If no contraindications:
  • Consider bupe loading (up to 24-32mg)
  • Or, if you have an X-Waiver: write the patient a short-term bupe RX.
    • Prolongs the return of withdrawal symptoms,
    • Gives the patient more time to get to a clinic, without having to return to the ED.

• Avoid bupe loading in the polypharmacy patient.
BUT IF WE START ADMINISTERING BUPE IN THE E.D...

“The E.D. will be awash with drug seekers, trying to get bupe!”

EDs which have started bupe programs have not seen significant visits increase, opioid-seeking patient visits may decrease.

If more patients did come to the ED hoping to start MAT, would that be a bad thing?

These patients are coming to the ED anyway.

Might not more patients suffering from opioid addiction get into treatment?
ED Management of Pain and Opioid Misuse During an Addiction Epidemic

1. Prevent opioid naive patients from becoming misusers by your prescription
   - Calculate benefit:harm whenever opioid Rx considered
   - If opioid Rx, small number of low dose, lower-risk pills

2. For existing opioid users
   2a. Revealed, willing
       - I’m an addict, I need help
       - Aggressive move to treatment
       - ED-initiated buprenorphine
       - Arranged specialty followup
   2b. Revealed, unwilling
       - I overdosed
       - Harm reduction e.g. naloxone
       - Supportive stance, open door
   2c. Partially revealed
       - I have chronic pain and need meds
       - Avoid opioids in ED or by prescription
       - Express concern for pain
       - Avoid alternatives for pain
       - Risk stratify with red & yellow flags
   2d. Unrevealed
       - I have acute pain and need meds
       - Move positives to willingness
### Emergency Care During an Opioid Addiction Epidemic

<table>
<thead>
<tr>
<th>in withdrawal</th>
<th>does not desire treatment</th>
<th>not in withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>desires treatment for opioid addiction</td>
<td>consider buprenorphine initiation anyway</td>
<td>desires treatment for opioid addiction</td>
</tr>
<tr>
<td>exclusions from ED buprenorphine initiation on methadone</td>
<td>alternative: methadone 10 mg IM can use non-opioid Rx but much less effective clonidine, NSAID, antianxiety, antidiarrheal haloperidol, ketamine</td>
<td>if waiver is present, can prescribe buprenorphine for home initiation</td>
</tr>
<tr>
<td>on high dose (usually prescribed) opioids</td>
<td>refer to ongoing addiction care</td>
<td>alternatives: return to ED when withdrawing hold in ED to await withdrawal</td>
</tr>
<tr>
<td>very intoxicated (with other substances)</td>
<td>harm reduction (see box)</td>
<td>refer to bup-capable provider/clinic</td>
</tr>
<tr>
<td>buprenorphine allergy</td>
<td>not in withdrawal</td>
<td></td>
</tr>
<tr>
<td>verifying adequate withdrawal is crucial</td>
<td>does not desire treatment</td>
<td></td>
</tr>
<tr>
<td>if inadequate withdrawal, buprenorphine will precipitate withdrawal</td>
<td>recommend to refer to ongoing addiction care</td>
<td></td>
</tr>
<tr>
<td>plug COWS into your favorite medical calculator</td>
<td>COWS should be ≥ 8, the higher the better</td>
<td></td>
</tr>
<tr>
<td>you do not need to be referred to treat withdrawal with buprenorphine in the ED</td>
<td></td>
<td></td>
</tr>
<tr>
<td>buprenorphine 4-8 mg sublingual</td>
<td>the higher the COWS, the larger the bup dose</td>
<td></td>
</tr>
<tr>
<td>if unsure of withdrawal symptoms or borderline COWS, dose 2 mg q6h</td>
<td>observe in ED for 30-60 minutes provide sandwich</td>
<td></td>
</tr>
<tr>
<td>optional testing during buprenorphine initiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCG, urine tox, LFTs, Hep C, HIV</td>
<td></td>
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<tr>
<td>if waiver is present, can discharge with prescription</td>
<td></td>
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<tr>
<td>if expected delay in accessing buprenorphine (≥24h), consider high dose initiation in consultation with addiction specialist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>advise on dangers of etoh/benz use while on bup</td>
<td></td>
<td></td>
</tr>
<tr>
<td>refer to bup-capable provider/clinic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>the smaller the ED buprenorphine dose, the tighter the followup has to be, esp if no Rx</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Harm Reduction for all opioid misusers

- All patients at high risk for OD should receive take-home naloxone
- High risk for OD: prior OD, use of illicit opioids, high daily dose (≥50 MME), concurrent use of sedatives, recent period of abstinence, uses alone
- If NTV, encourage safe injection practices and refer to local needle exchange/safe injection site
- Do you know what the needle is?
- Do you cut your heroin with sterile water?
- Do you discard your cotton after every use?
- Do you mix with other people around?
- Do you do a tester shot to make sure a new batch isn’t too strong?
- Open door policy: If unwilling to be treated for addiction now, return anytime, we’re here 24/7

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### Priorities for Emergency Care

- Prevent opioid-naive patients from becoming misusers by your prescription
- Calculate benefit/harm whenever an opioid prescription is considered, and if opioid Rx, prescribe small # of low dose, lower-risk pills
- Immediate Release Morphine Sulfate (MSIR) 15 mg tabs, 1 tab q4-hr p.r.n.
- Willing: “I have a problem, I need help”
  - Aggressive move to treatment
  - ED-initiated buprenorphine
  - Arrange specialty followup
- Revealed, unwilling: “I overdosed”
  - Harm reduction (see box)
  - Supportive stance, open door
- Partially revealed: “I have chronic pain and need meds”
  - Avoid opioids in ED or by prescription
  - Opioid alternatives for pain
  - Express concern that opioids are causing harm
- Unrevealed: “I have acute pain and need meds”
  - Risk stratify with red & yellow flags
  - POMP = move positively to willingness
  - If low risk, treat as opioid-naive
  - If high risk, treat as partially revealed

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**buprenorphineRx**: buprenorphine/naloxone 8/2 mg sublingual tabs; 1 tab 51, bid—can dispense 6 to 14 tabs

If concern for suboxone abuse/diversion, can disp Rx or 1Rx (though suboxone safer than street opioids)
High dose ED bupe MAT induction: No longer just for the addiction specialist. Coming to an ED near you!
Emergency Department Initiation of Buprenorphine for Opioid Use Disorder

- symptomatic treatment with non-opioids
- consider home-initiated buprenorphine
- harm reduction
- outpatient addiction referral

**opioid withdrawal?**

- Yes
- complicating factors?
  - Yes
  - discuss with addiction specialist
  - if inadequately withdrawn, buprenorphine will precipitate withdrawal
  - score on clinical opioid withdrawal scale
  - COWS should be ≥ 8, the higher the better

- No
  - if inadequately withdrawn, buprenorphine will precipitate withdrawal
  - score on clinical opioid withdrawal scale
  - COWS should be ≥ 8, the higher the better
  - severe medical disease or very intoxicated/altered (e.g., acutely ill, liver failure)
  - using methadone or extended-release opioid naloxone precipitated withdrawal
  - taking high dose prescription opioids daily
  - the higher the daily dose of opioids the patient usually uses, and the more severe the withdrawal, the higher the initial dose of bup
  - if borderline/inconsistent withdrawal symptoms, dose 2-4 mg every 12h
  - if vomiting, may use 0.3 mg NTRM every 30-60 min
  - if symptoms not improved with 8 mg bup, patient may be in buprenorphine precipitated withdrawal and effect of higher buprenorphine dose is uncertain
  - bup can cause nausea if primary symptom is nausea, treat with ondansetron 8 mg
  - the bigger the initiation dose of buprenorphine, the longer the patient is protected from withdrawal, cravings, and street opioid overdose
  - high dose (total dose of 16-32 mg in ED) preferred if patient not able to be seen by bup prescriber or fill prescription in next 24 hours
  - do not initiate high dose if patient is heavy user of alcohol or benzodiazepines

- No
  - if minimally improved, may be inadequate dose of bup. If worsened by bup, may be buprenorphine precipitated withdrawal (BPW)
  - treatment of BPW is controversial
  - may respond to higher doses of bup
  - classic management is to switch to non-opioid Rx (benzodiazepines, neuroleptics, anticonvulsants, anti-adrenergics, analgesics, ketamine)

**Harm Reduction** for all opioid misusers
- all patients at high risk for OD should receive take home naloxone
- consider screening for HIV, Hep C
- if NDOL, refer to local needle exchange program
- open door policy: if unwilling to be treated for addiction now, come back anytime, we're here 24/7

- buprenorphine 4-8 mg SL
  - observe 30-60 min
  - if symptoms improved?

- Yes
  - second dose of buprenorphine 8-24 mg SL
    - observe for 1 hour
  - harm reduction

- No
  - buprenorphine prescription
    - if a waivered prescribing available
  - refer to outpatient addiction treatment

72 hour rule: patient may return to ED for up to 3 days after discharge to administer 16 mg SL on days 2 & 3
MAT is a long term program

High rate of failure with short term “detox” approach.

Most opioid addicted patients will need many months, if not years of treatment, for some many years or even lifelong Tx.

This neuroadaptation to opioids is unique to opioid addiction, as opposed to alcohol dependency.

We must think of opioid dependency/addiction as we think of DM, HTN, and other chronic illnesses.

Successfully weaning off opioids for the long term (not just “Detox”) is a slow, gradual process.

Opioid Addiction Treatment is a journey, and a marathon -- not a Sprint
scheduled opioid consumption
freedom from addiction harms
normal life possible
THANK YOU!

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