ADDICTION POLICY FORUM

American College of Emergency Physicians
ADVANCING EMERGENCY CARE

E·QUAL | EMERGENCY QUALITY NETWORK

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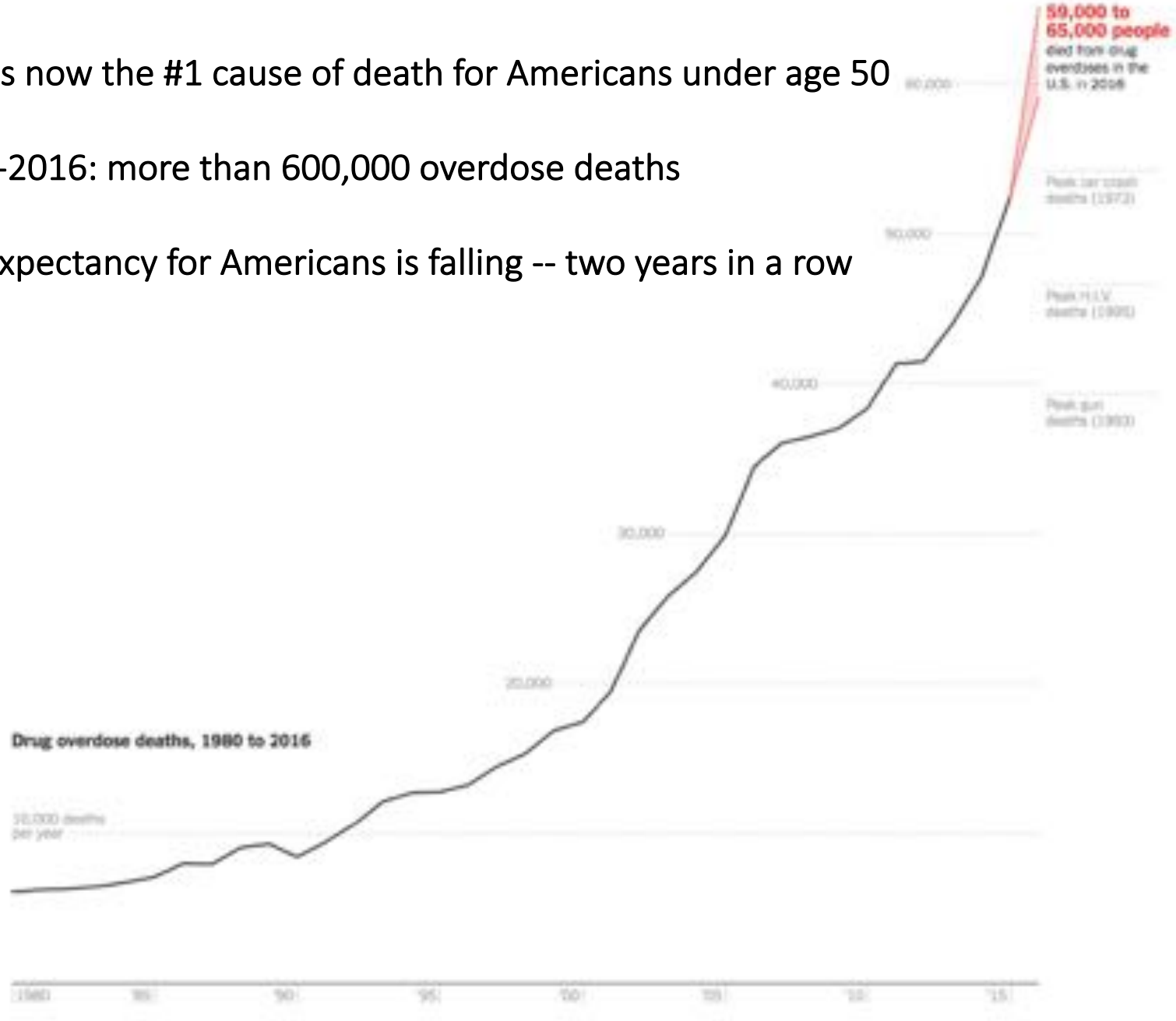
O.D. is now the #1 cause of death for Americans under age 50

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*


Monthly Injection for Assisted Abstinence Therapy

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

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.

# 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.

# NUTS & BOLTS OF BUPE TX

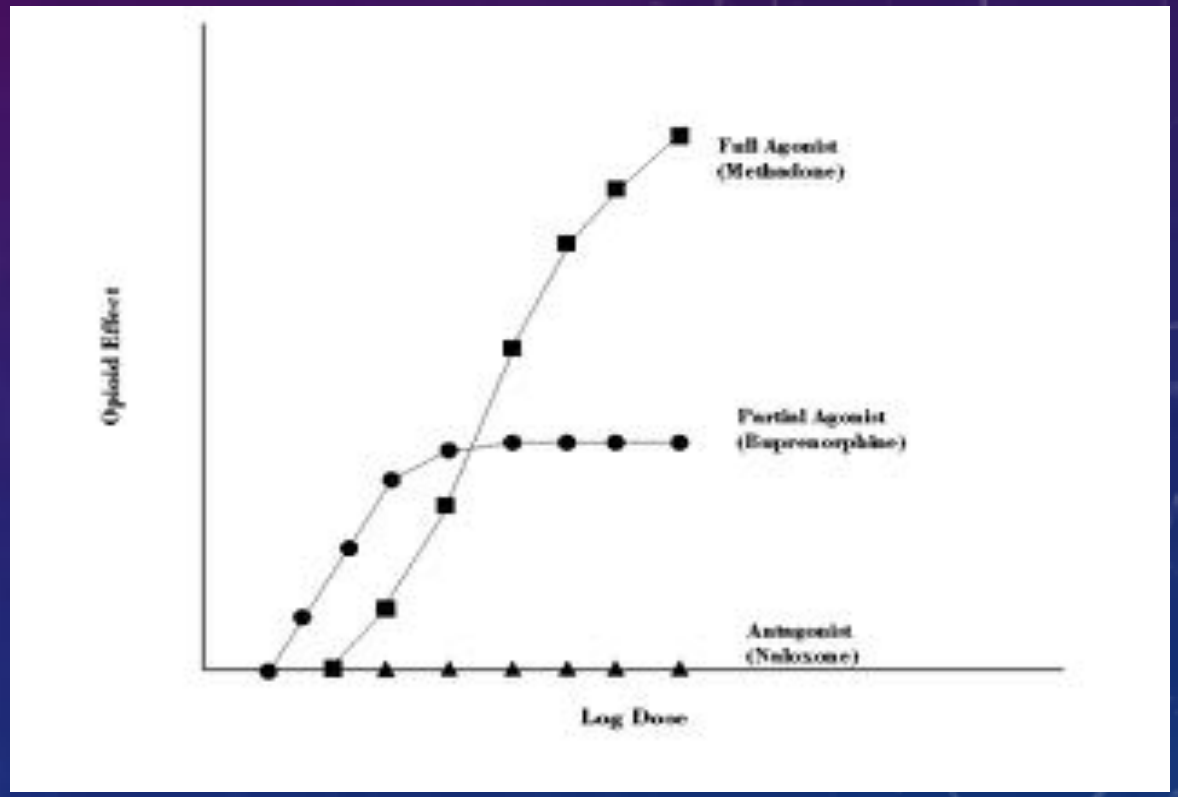
"Partial agonist":

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 <u>prescribing</u> bupe.**




Any Doc can use bupe in the ED to treat opioid withdrawal.

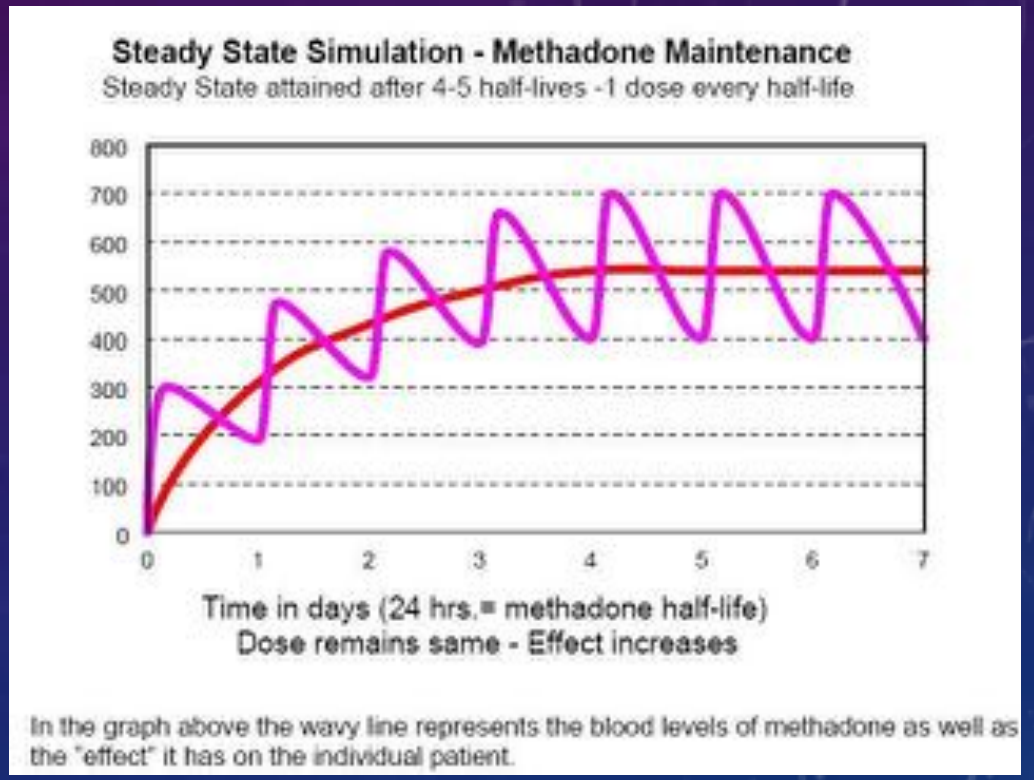
Any Doc can prescribe bupe for pain.

Must have an DEA license "X-waiver" to PRESCRIBE for ADDICTION

# NUTS & BOLTS OF BUPE TX

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



# NUTS & BOLTS OF BUPE TX

"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:

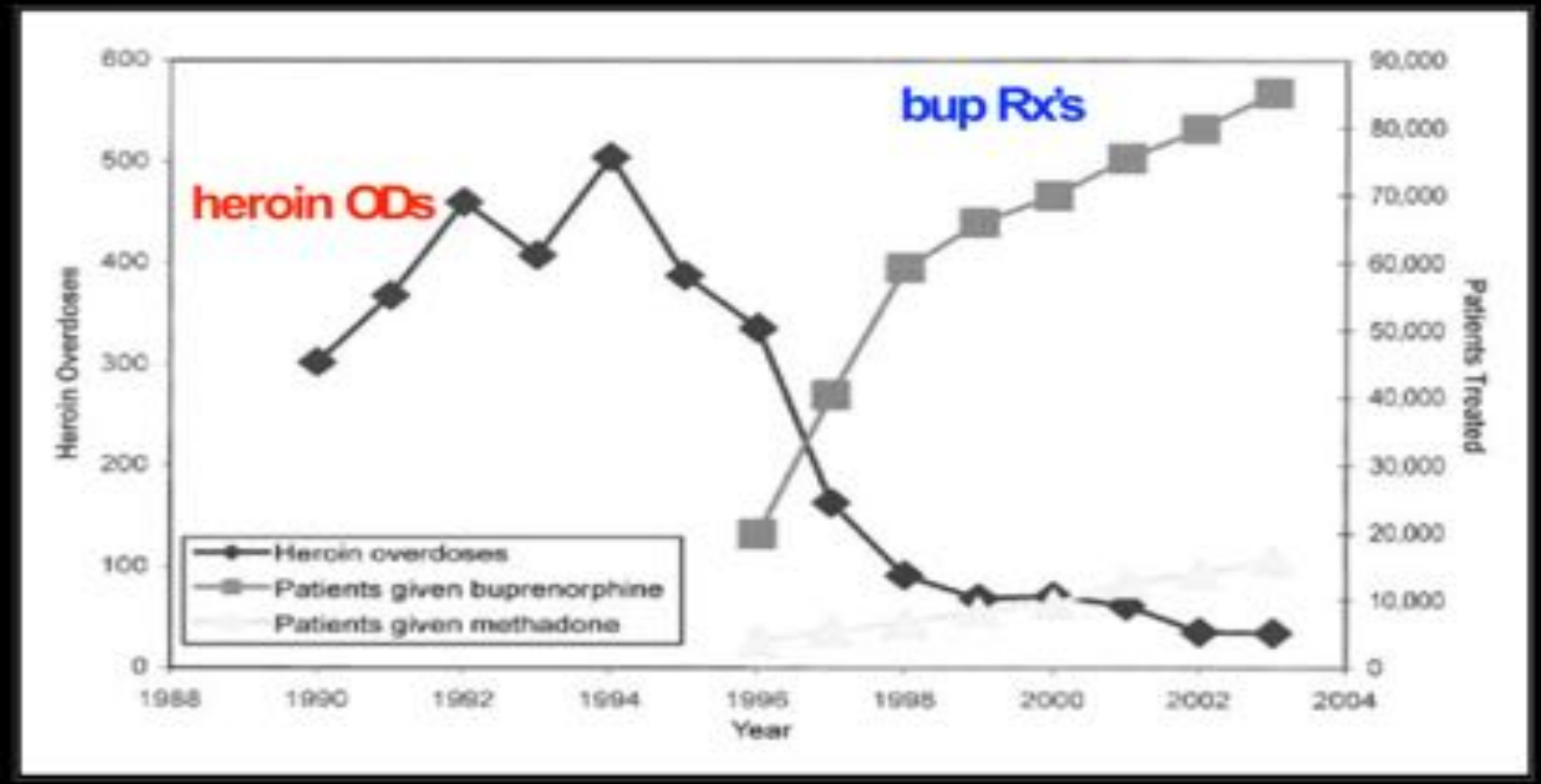
## Addiction CLINIC Dosing initiation:

- 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!

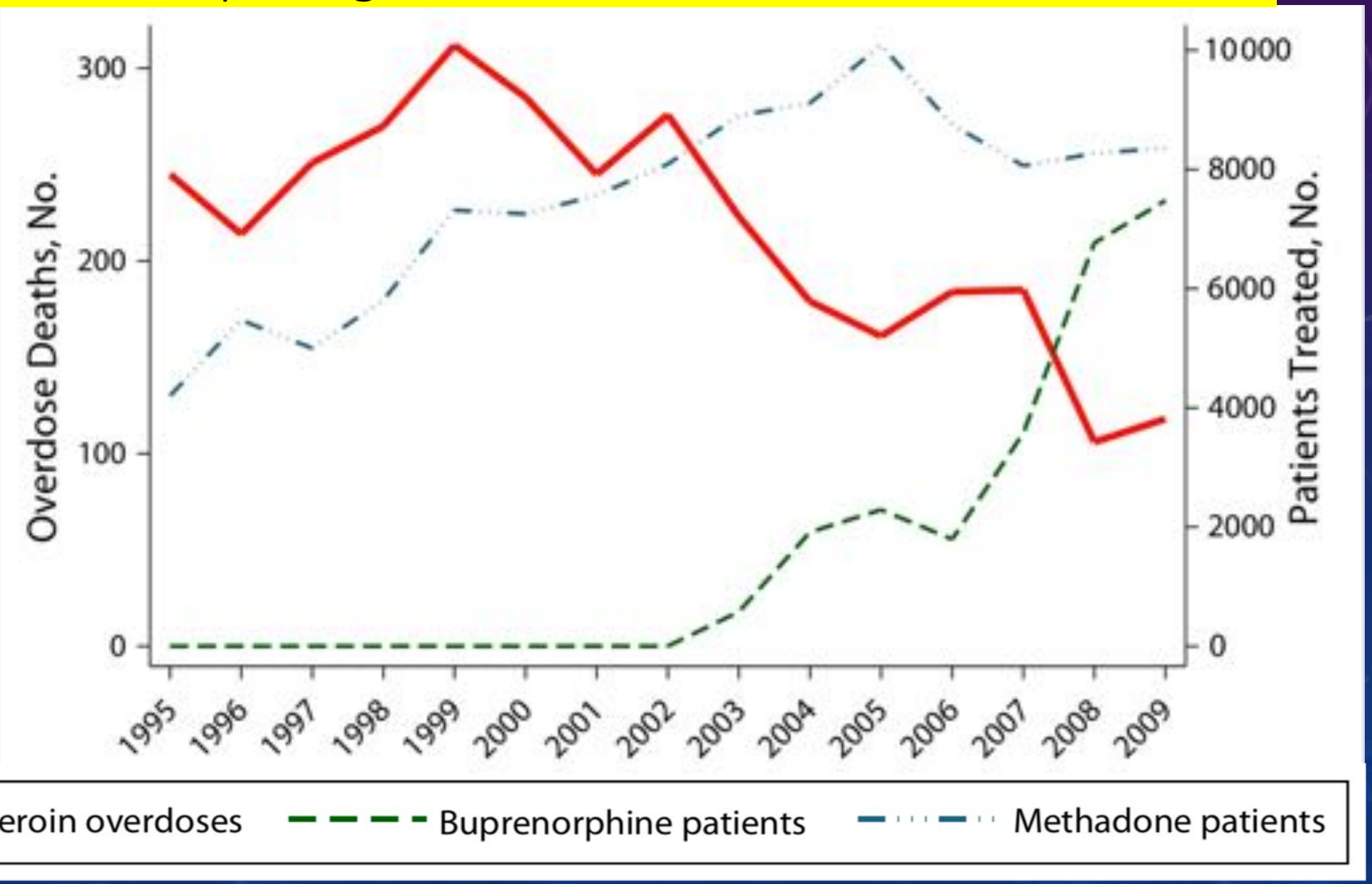



Auriacombe, et al, *Am J Addict*. 2004;13 Suppl 1:S17-28.

# 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.

Schwartz et al, Am J Public Health. 2013 May;103(5):917-22



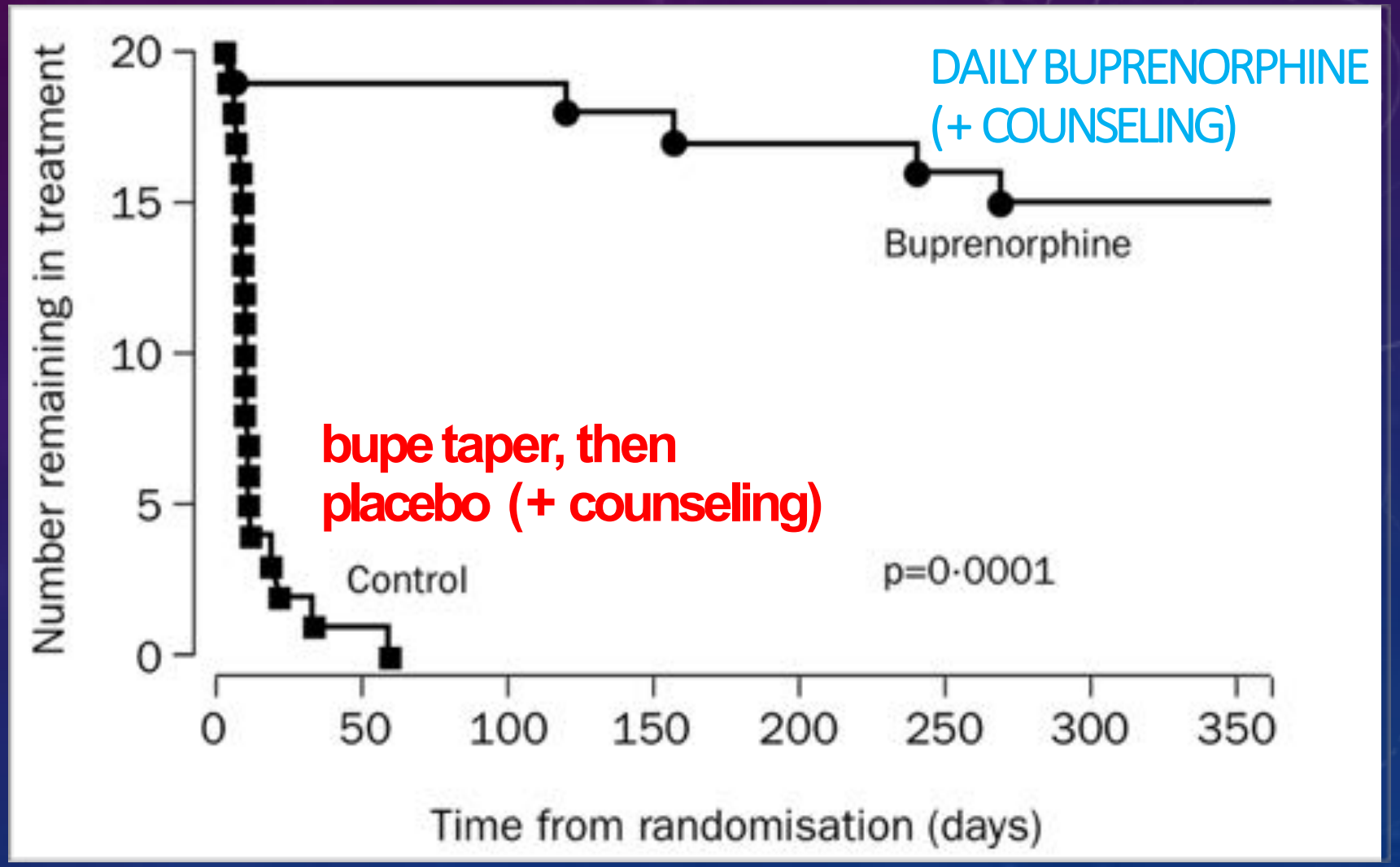
# Opioid Agonist Therapy is Much More Valuable than Drug Abuse Counseling!!

Swedish Study:

- 40 patients randomized
- Daily supervised med administration for the first 6 months

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

0% in the placebo group




Kakko, et al, Lancet. 2003 Feb 22;361(9358):662-8.


Cochrane Database Syst Rev. 2011 Oct 5;(10):CD004147

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

**Yale:  D'Onofrio:**  Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: a randomized clinical trial.

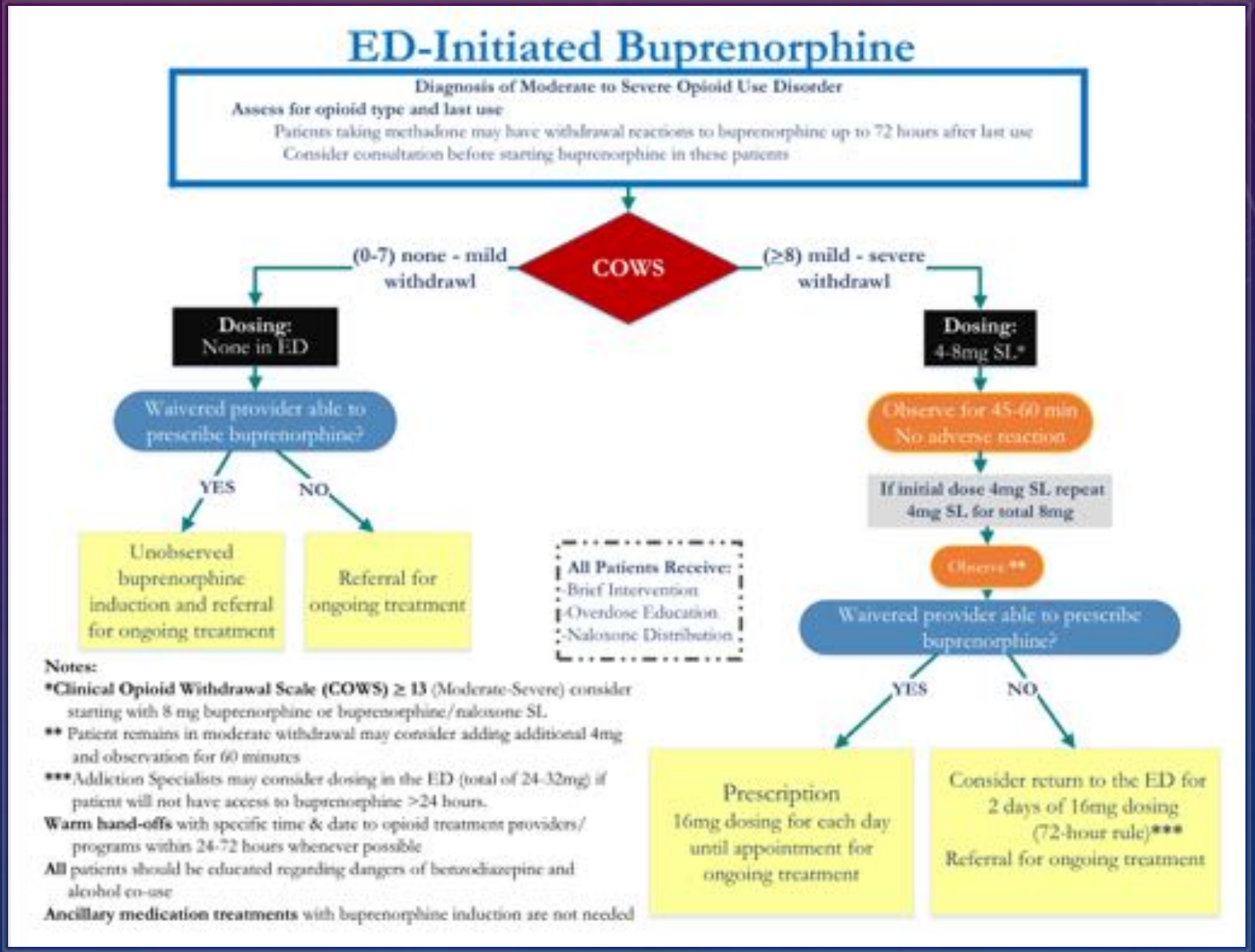
- 329 ED patients with OUD, screened, and randomized:
- ~1/3 to the referral group (patient is handed a pamphlet)
- ~1/3 to the brief intervention group (meets with a social worker or pt advocate)
- ~1/3 to the buprenorphine treatment group (and above)

MAIN OUTCOMES AND MEASURES:

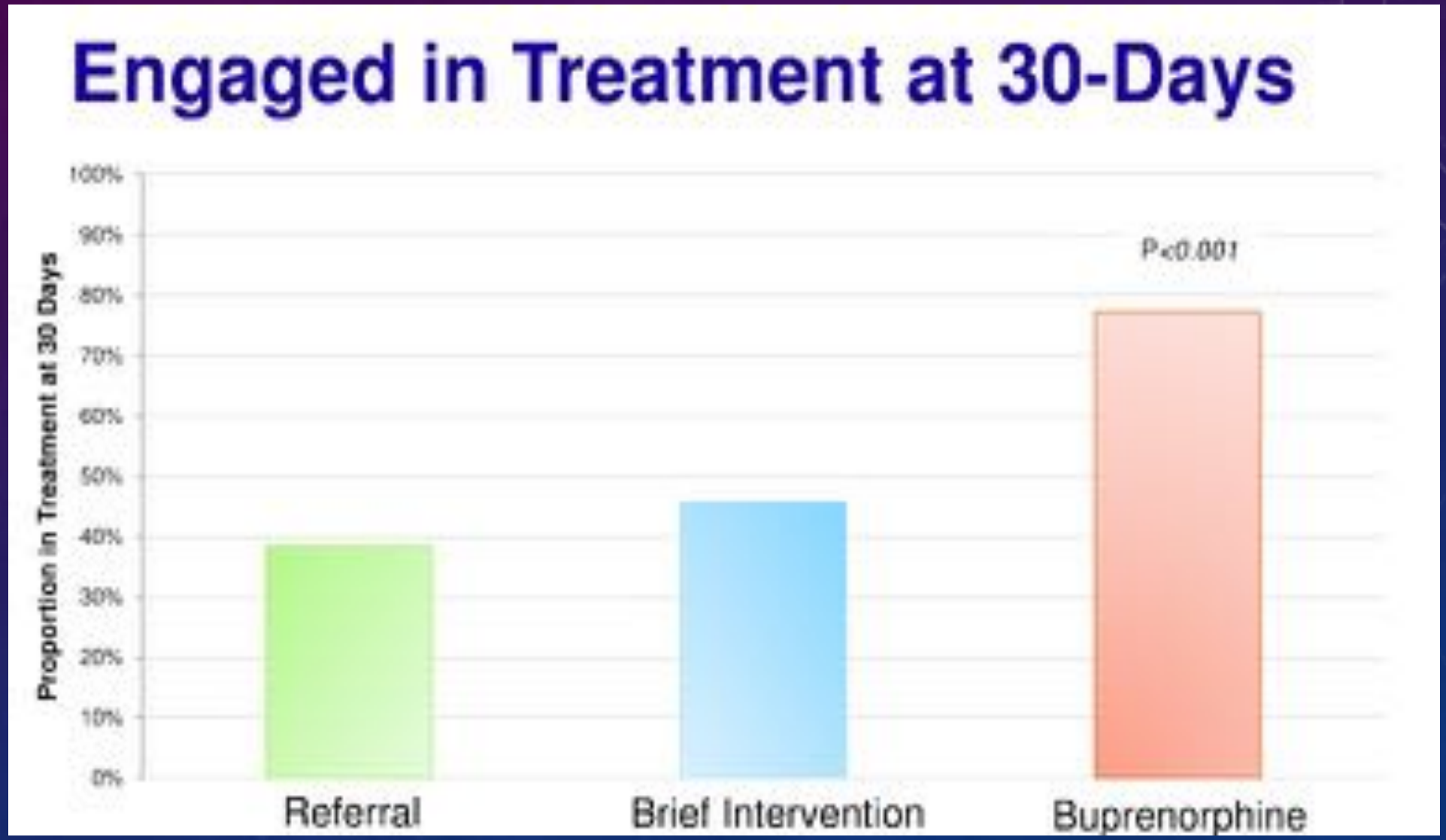
- Enrollment in, and receiving, addiction treatment 30 days after randomization was the primary outcome.

D'Onofrio G, O'Connor PG, Pantalon MV, et al, *JAMA*. 2015 Apr 28;313(16):1636-44

# YALE (D'ONOFRIO) ED-IB PROTOCOL



# YALE (D'Onofrio) ED-IB … continued



# YALE (D'ONOFRIO) ED-IB continued

Needed inpatient addiction treatment services?

- Bupe group: **11%** (95% CI, 6%-19%, P <0.001)
- Referral Group: 37% (95% CI, 27%-48%, P <0.001)
- Brief Intervention Group: 35% (95% CI, 25%-37%, P <0.001)

# "THREE-DAY RULE"

**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 waivered 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"

http://www.samhsa.gov/medication-assisted-treatment/legislation-regulations-guidelines/special-circumstances-providing-buprenorphine

# THREE DAY RULE

- *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.

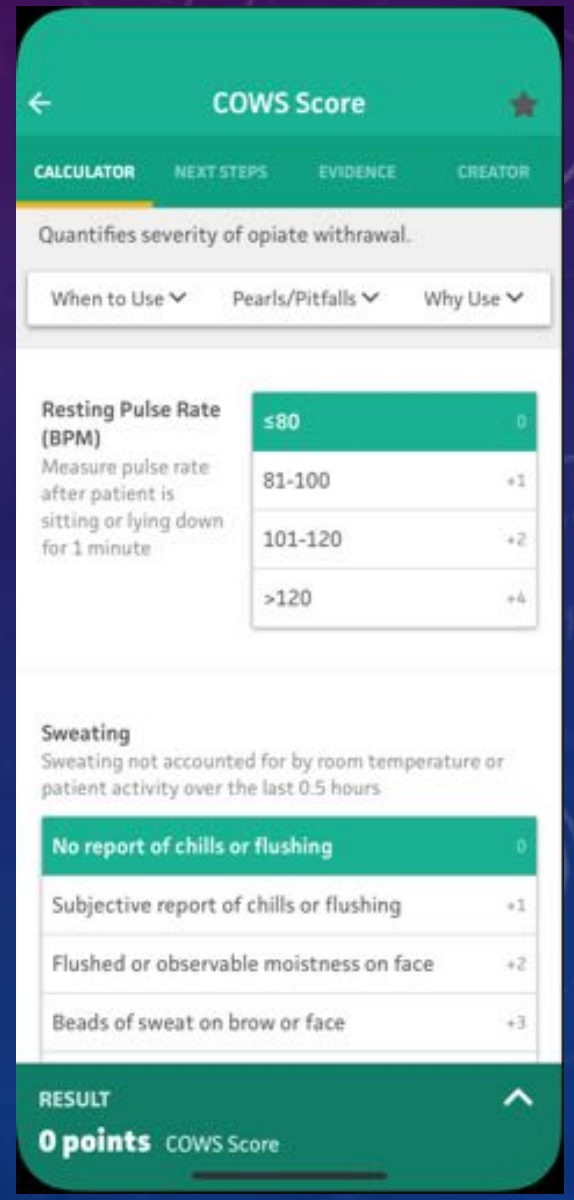
# NUTS & BOLTS OF BUPE TX

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 speciality follow up

### 2b. revealed, unwilling

"I overdosed"
harm reduction e.g. home naloxone
supportive stance, open door

### 2c. 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

### 2d. unrevealed

"I have acute pain and need meds"
risk stratify with red & yellow flags PMDP-
move positives to willingness

# Emergency Care During an Opioid Addiction Epidemic

## in withdrawal
## desires treatment for opioid addiction

exclusions from ED buprenorphine initiation
on methadone
on high dose (usually prescribed) opioids
very intoxicated (with other substances)
buprenorphine allergy

verifying adequate withdrawal is crucial
*if inadequate withdrawal, buprenorphine will precipitate withdrawal*
plug COWS into your favorite medical calculator
COWS should be ≥ 8, the higher the better

you do not need to be x-waivered to treat withdrawal with buprenorphine in the ED

buprenorphine 4-8 mg sublingual
the higher the COWS, the larger the bup dose
if unsure of withdrawal symptoms or borderline COWS, dose 2 mg q2h

observe in ED for 30-60 minutes
provide sandwich

optional testing during buprenorphine initiation
HCG, urine tox, LFTs, Hep C, HIV

if waivered doc present, can d/c with prescription

if expected delay in accessing buprenorphine (≥24h), consider high dose initiation in consultation with addiction specialist

advise on dangers of etoh/benzo use while on bup

**refer to bup-capable provider/clinic**
the smaller the ED buprenorphine dose, the tighter the followup has to be, esp if no Rx

## in withdrawal
## does not desire treatment

consider buprenorphine initiation anyway
alternative: methadone 10 mg IM
can use non-opioid Rx but much less effective
clonidine, NSAID, antiemetic, antidiarrheal
haloperidol, ketamine

refer to ongoing addiction care

harm reduction (see box)

## not in withdrawal
## does not desire treatment

engage, encourage to move to treatment

refer to ongoing addiction care

## not in withdrawal
## desires treatment for opioid addiction

if waivered doc present, can prescribe buprenorphine for home initiation

alternatives:
return to ED when withdrawing
hold in ED to await withdrawal

refer to bup-capable provider/clinic

## **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 IVDU, encourage safe injection practices and refer to local needle exchange/safe injection site
Do you lick your needles?
Do you cut your heroin with sterile water?
Do you discard your cotton after every use?
Do you inject 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

## 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 q4-6h prn pain, disp #9

Willing: **"I have a problem, I need help"**
aggressive move to treatment
ED-initiated buprenorphine
arranged speciality 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
PDMP - move positives to willingness
if low risk, treat as opioid-naive
if high risk, treat as partially revealed

**buprenorphine Rx**

buprenorphine/naloxone 8/2 mg sublingual tabs
1 tab SL bid--can dispense 6 to 14 tabs

if concern for suboxone abuse/diversion, can skip Rx or 1 Rx
(though suboxone safer than street opioids)

alternatively, **patient can return to ED** while awaiting followup: on days 2 and 3 dose 16 mg SL
x-waiver not required to dose in ED on days 2&3
however cannot continue beyond 3 days by law

reuben j. strayer - @emupdates - **emupdates.com/help**

ED-BRIDGE | Emergency Buprenorphine Treatment

HIGHLAND EMERGENCY
DEPARTMENT OF EMERGENCY MEDICINE

# Emergency Department Initiation of Buprenorphine With a Loading Dose

• Andrew A Herring, MD, Eben Clattenburg MD, Mac Chamberlin MD, Mari Nomura MD, Martha Montgomery MD, Cody Schultz MD

**Background:** The opioid crisis has led to calls for emergency departments(EDs) to provide access to medication assisted treatment(MAT) for opioid use disorder(OUD) with buprenorphine(BUP). Most ED providers do not have DEA authority to prescribe BUP for OUD and those that do may be reluctant to prescribe due to concerns for diversion. Because same day access to outpatient treatment is often not available, there is a need to implement strategies to suppress opioid withdrawal for at least 72 hours after ED discharge. The effect of a standard 8mg SL BUP dose may wane after as little as 4 hours. The ceiling effect and long half-life of BUP offer an elegant solution. Previous clinical studies have found a 32mg sublingual (SL) BUP dose is well tolerated and provides 72 hour suppression of opioid withdrawal symptoms. ED BUP loading for OUD has not previously been described. Herein we describe our initial cohort of patients initiated onto BUP with a loading dose of 32mg SL.

**Methods:** We performed a retrospective review of all patients who were administered buprenorphine for the treatment of opioid withdrawal in a single urban emergency department between July 1st and December 15th,2017. Patients treated for the indication of pain were excluded. ED visit characteristics including total buprenorphine dose, patient sex and age, length of stay, chief complaint, vital signs, incidence of adverse events, and administration of rescue medications were described.

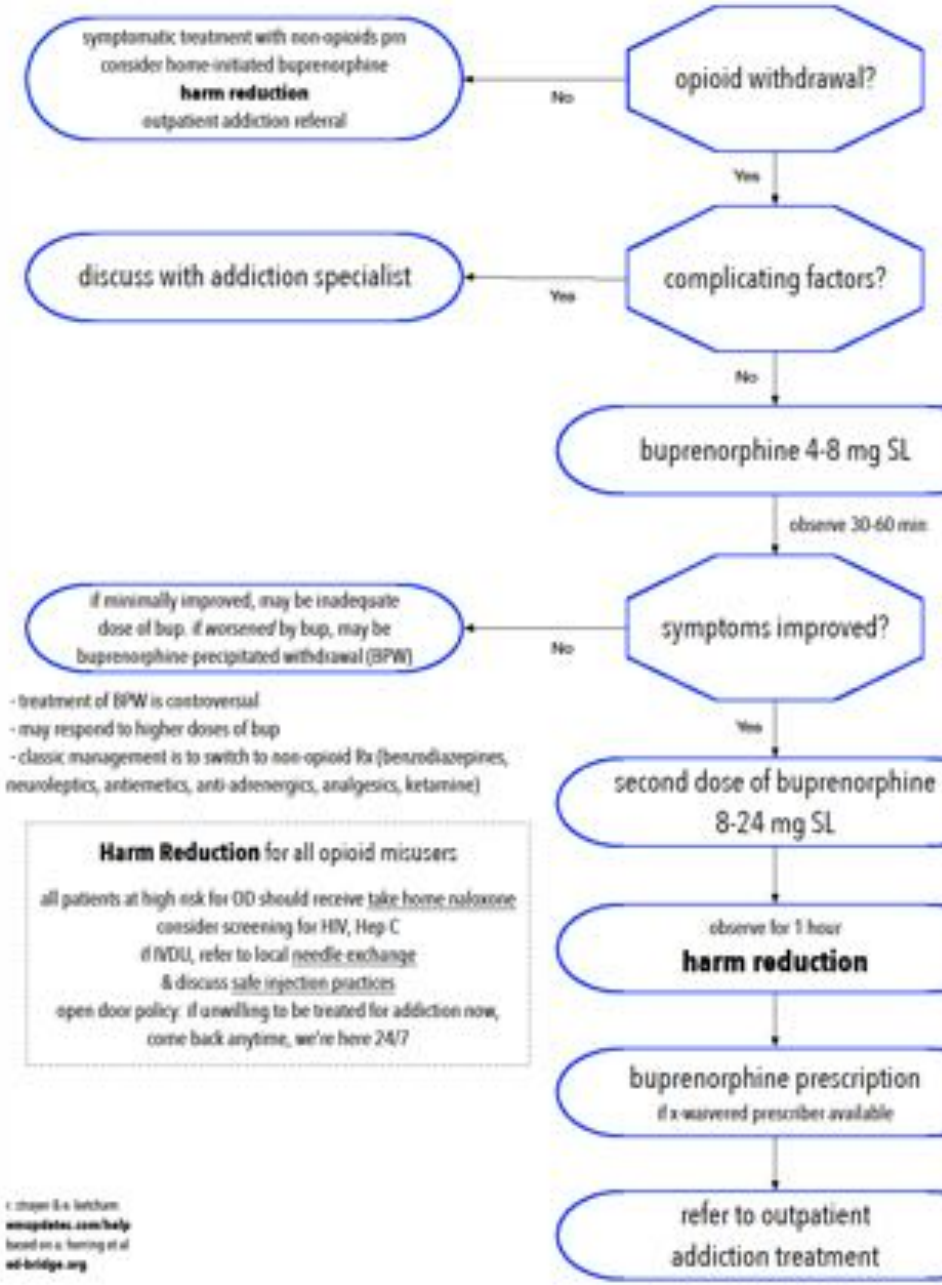
**Results:** A total of 101 ED patients were treated for opioid withdrawal during the study period with an average of 4.8 buprenorphine treatments per week. There were 12 ED patients who were administered at least 32mg SL buprenorphine. All patients were discharged in good condition. No patient showed clinical signs of opioid toxicity, nor was naloxone administered for any patient. Most of these patients (56%) were seen in a "fast track" area. There were no adverse events including: hypoxia, excessive sedation, hypotension, or hypersensitivity. Most patients were male (77 %) and young (average age 31.5 years). The median length of stay was 221 minutes. All patients were enrolled in a linkage program to ensure access to follow up treatment after discharge.

**Conclusion:** a BUP loading dose of 32mg SL is well tolerated. Prolonged suppression of withdrawal symptoms after ED discharge may promote successful linkage to long term treatment of opioid use disorder with buprenorphine. Non-waivered emergency providers can provide several days of relief from withdrawal symptoms without need for a prescription of buprenorphine.

Attending and Associate Director of Research Department of Emergency Medicine, Medical Director of the Highland Hospital System Substance Use Disorder Program, Attending Highland Hospital Pain Medicine and Functional Restoration Clinic, Assistant Clinical Professor of Emergency Medicine UCSF

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




*if inadequate withdrawal, buprenorphine will precipitate withdrawal*
score on clinical opiate 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 1-2h
- if vomiting, may use 0.3 mg IV/IM 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

- treatment of BPW is controversial
- may respond to higher doses of bup
- classic management is to switch to non-opioid Rx (benzodiazepines, neuroleptics, antiemetics, anti-adrenergics, analgesics, ketamine)

- 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 12-24 hours
- do not initiate high dose if patient is heavy user of alcohol or benzodiazepines, medically complex, older age - for risk of respiratory depression

**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 IVDU, refer to local needle exchange
& discuss safe injection practices
open door policy: if unwilling to be treated for addiction now, come back anytime, we're here 24/7

buprenorphine/naloxone 8/2 mg
1 tab/strip BID SL
dispense x 1 week

**72 hour rule** patient may return to ED for up to 3 days
administer 16 mg SL on days 2 & 3


c. chapin & a. ketcham
emcpdatec.com/help
based on a. herring et al
ed-bridge.org

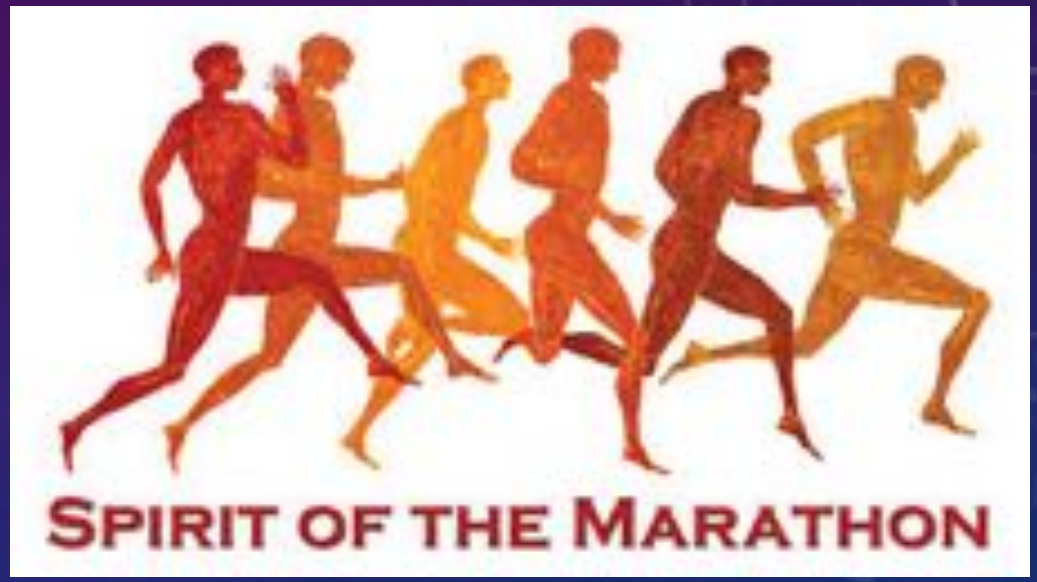
# MAT is a long term program

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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