


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

Andrew Herring, MD



**None of the presenters today have any
financial disclosures.**

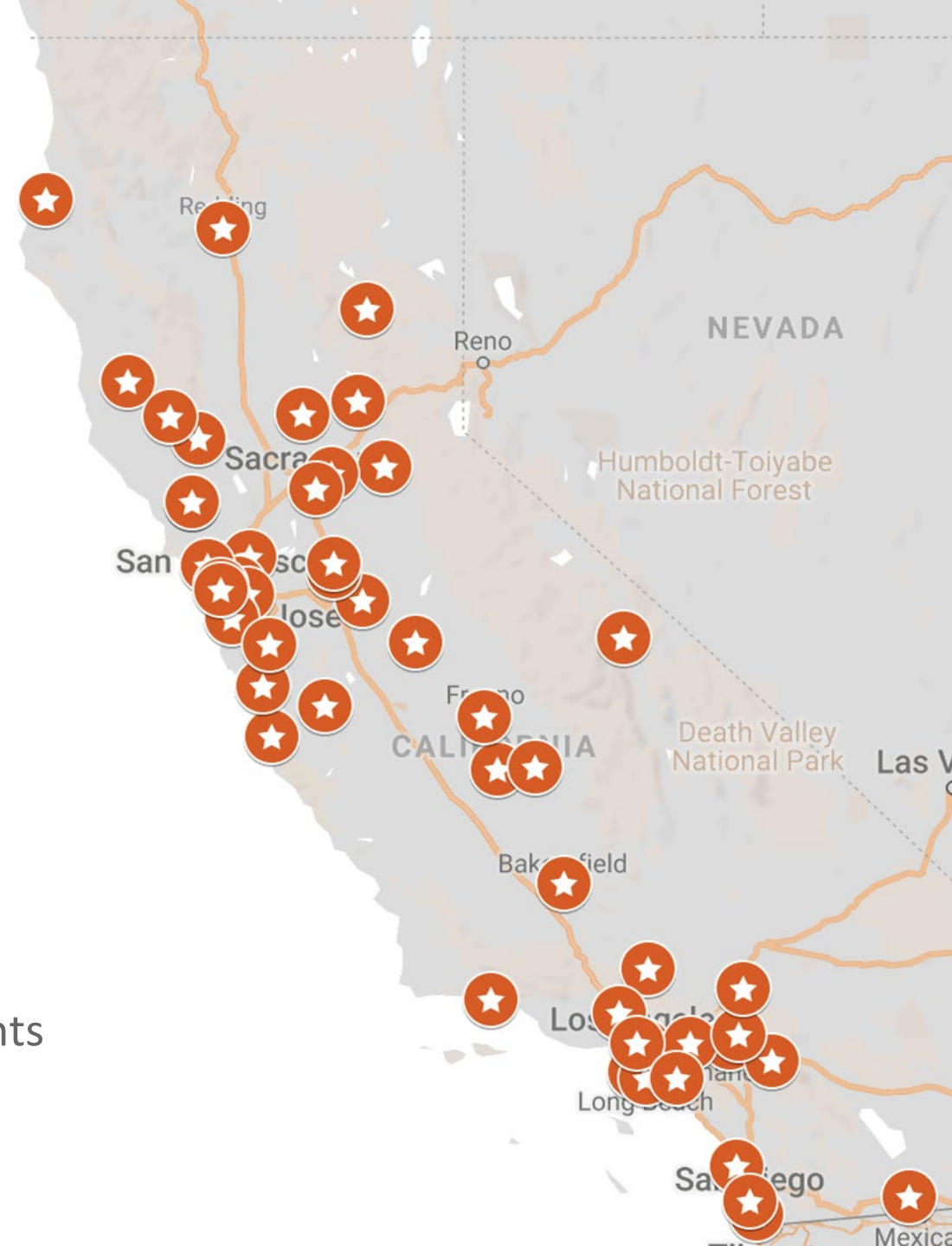
Objectives

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



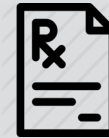
9834

patients identified
with OUD



6312

Patients provided
with treatment



4486

Patients given a
prescription for MAT



3930

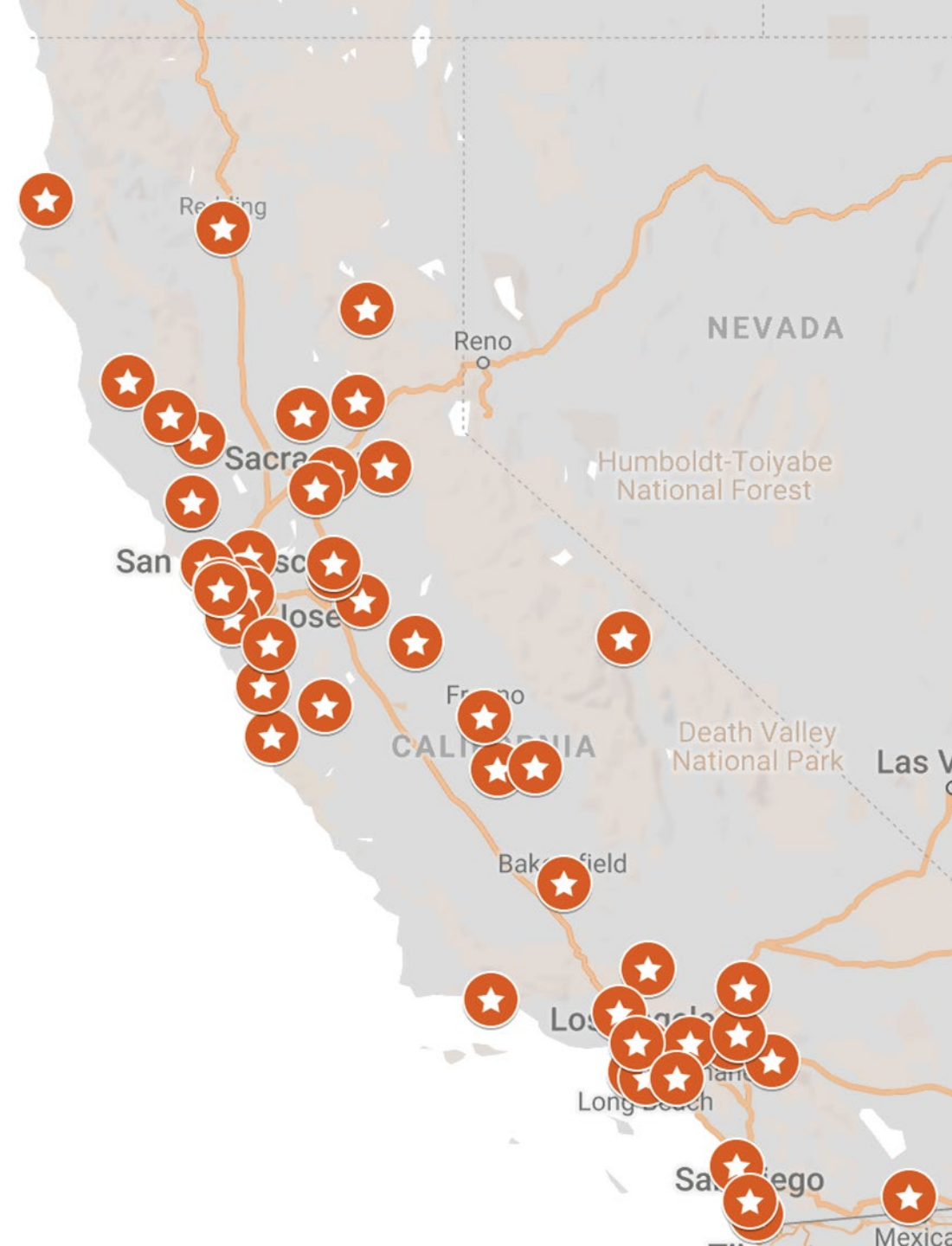
Patients linked to follow-
up MAT care

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.**



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

-  Resting comfortably and stable KD 0207
vitals
-   Plan to observe until 1600 NJ 0205 
-  following the bridge protocol , pt KD 0146
does not meet any exclusion
criteria and qualifies for bup after
the reversal of overdose with
narcan

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

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

go get 'em tiger

Wed 2:09 AM

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

YES TO ANY

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

NO

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.

Bup Induction after Overdose

“No Shit Science”



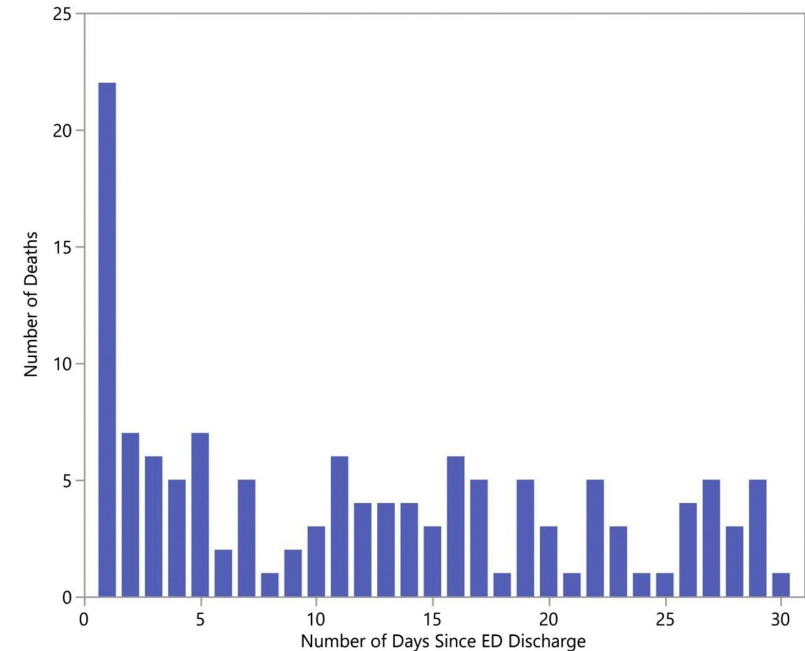
CA Bridge Delivers Addiction Treatments When it Matters Most

One-Year Mortality of Patients After Emergency Department Treatment for Nonfatal Opioid Overdose

[Scott G. Weiner, MD, MPH^{a,b}](#), [Olesya Baker, PhD^a](#), [Dana Bernson, MPH^a](#), [Jeremiah D. Schuur, MD, MHS^c](#)

- 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

Number of deaths after ED treatment for nonfatal overdose by number of days after discharge in the first month (n=130)

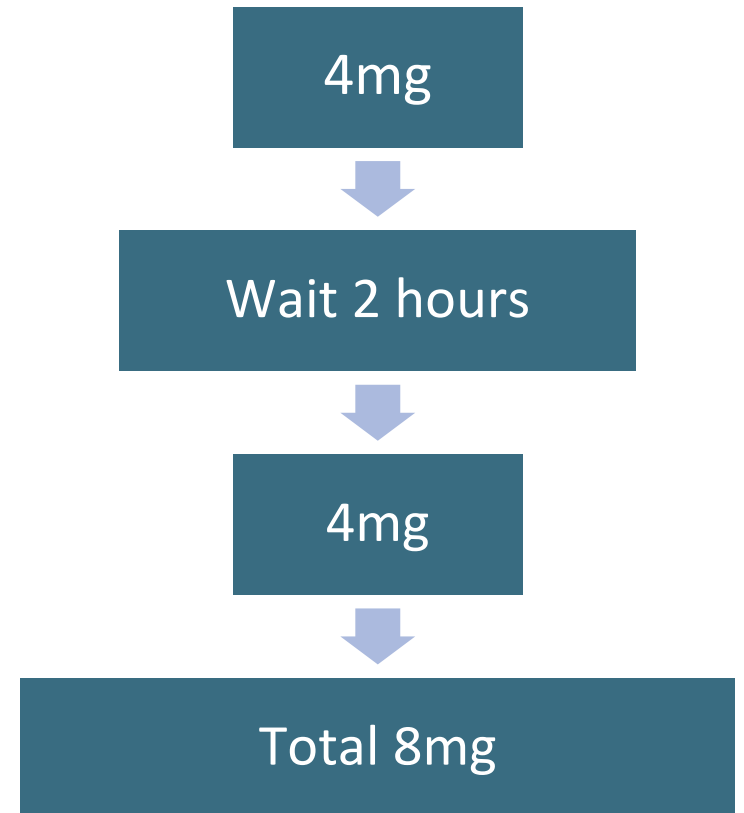


Source: Weiner, Scott, et al.. One-Year Mortality of Patients After Emergency Department Treatment for Nonfatal Opioid Overdose. *Annals of Emergency Medicine*. April 2, 2019.

Case #1: “By the Book”

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

Treat with Buprenorphine



Screen and Diagnose OUD

DSM-5 Criteria for Diagnosis of Opioid Use Disorder

1. Take more/longer than intended
2. Desire/unsuccessful 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

<u>Severity</u>	
	Presence of Symptoms
Mild:	2-3
Moderate:	4-5
Severe:	≥6

“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

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”

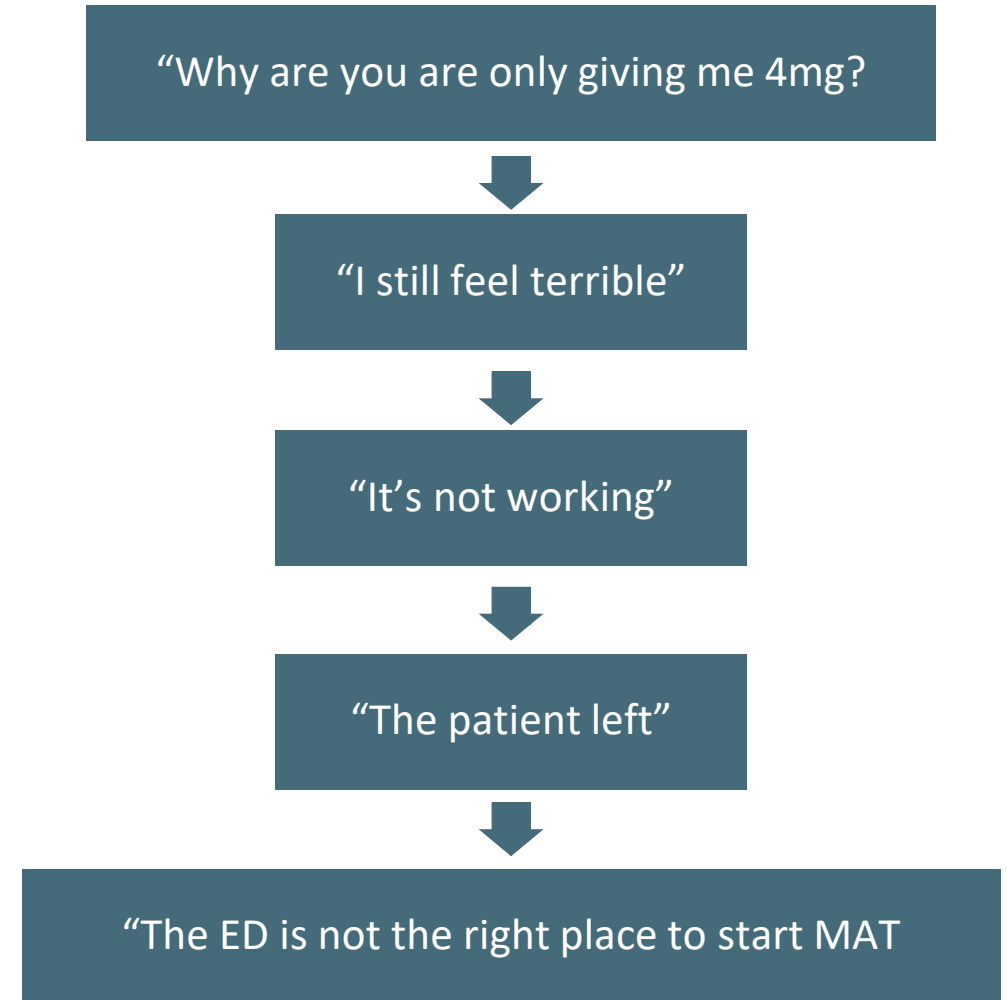
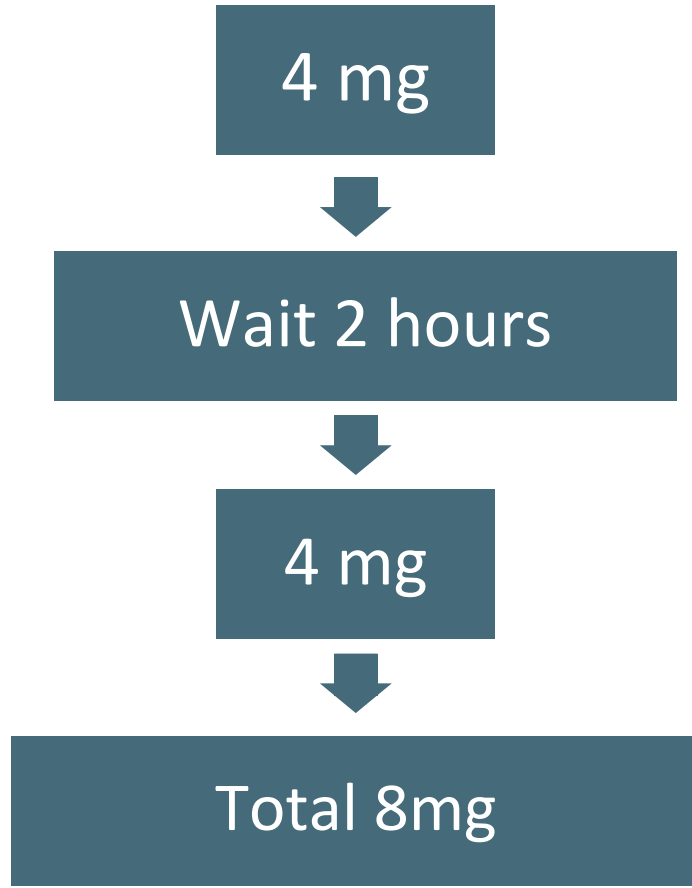


“Are you going to tell my parole officer”



“The lab lost the sample”

Treat with Buprenorphine



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 too long

It was complicated

Starting Buprenorphine (Bup), "Subs", Suboxone

Step 1

Wait

0-----6 hours ----- **12 hours**

Last use

Step 2

Withdrawal (start when you feel sick)

0-----5 -----10

Feel fine

Very Sick

Step 3

First Dose



4mg

Light user



8mg

Medium heroin

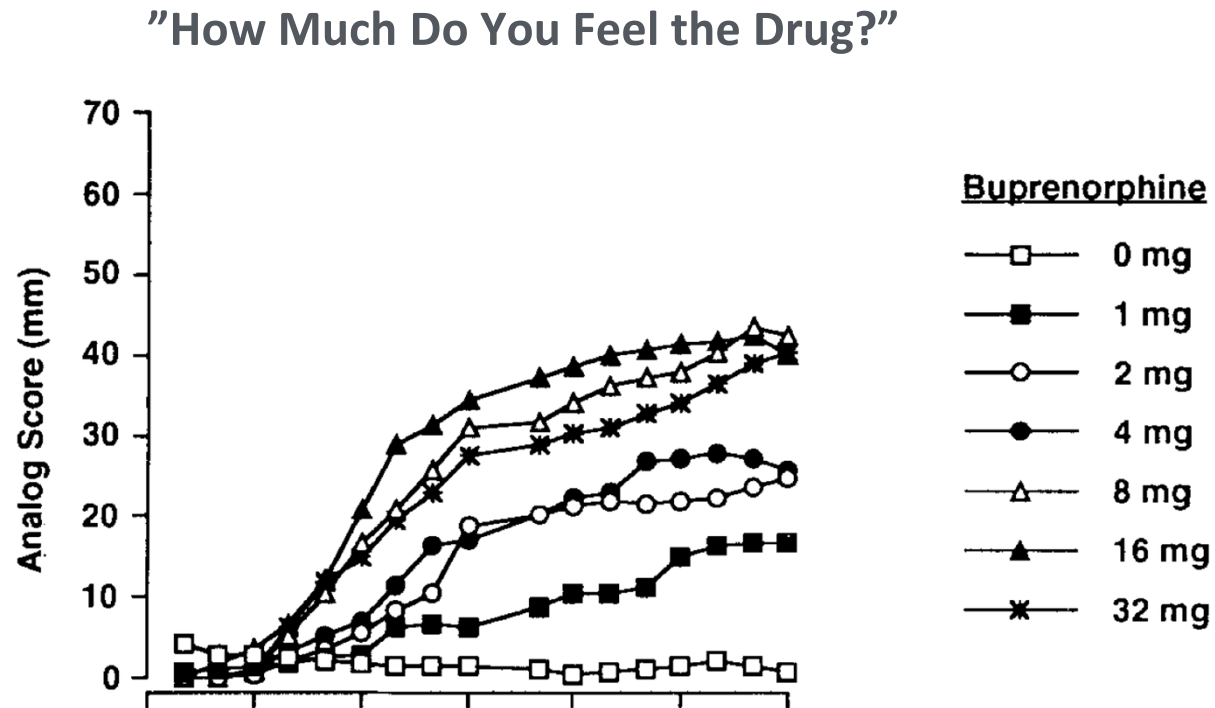


16mg

Heavy heroin

Ceiling Effect: Sharon Walsh

16 healthy non-opioid dependent volunteers



Clinical pharmacology of Buprenorphine: Ceiling effects at high dose

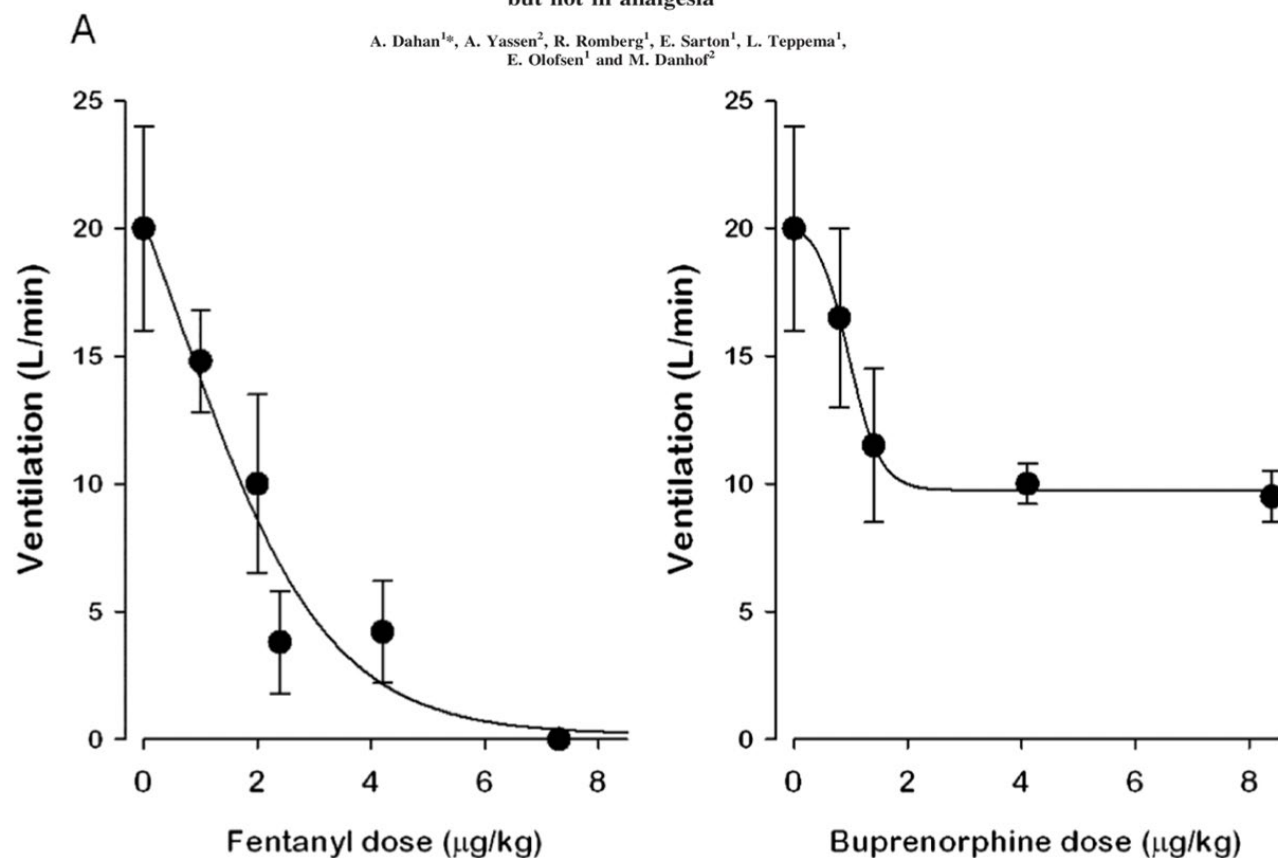
Ceiling Effect

British Journal of Anaesthesia 96 (5): 627-32 (2006)
doi:10.1093/bja/ae051 Advance Access publication March 17, 2006

BJA

Buprenorphine induces ceiling in respiratory depression but not in analgesia

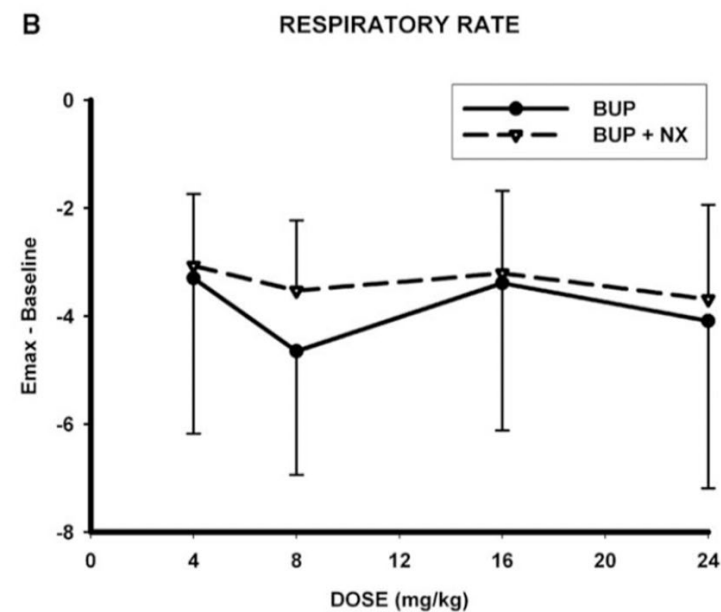
A. Dahan^{1*}, A. Yassen², R. Romberg¹, E. Sarton¹, L. Teppema¹,
E. Olofson¹ and M. Danhof²



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

Domenic A. Ciraulo, MD, Robert J. Hitzemann, PhD, Eugene Somoza, 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

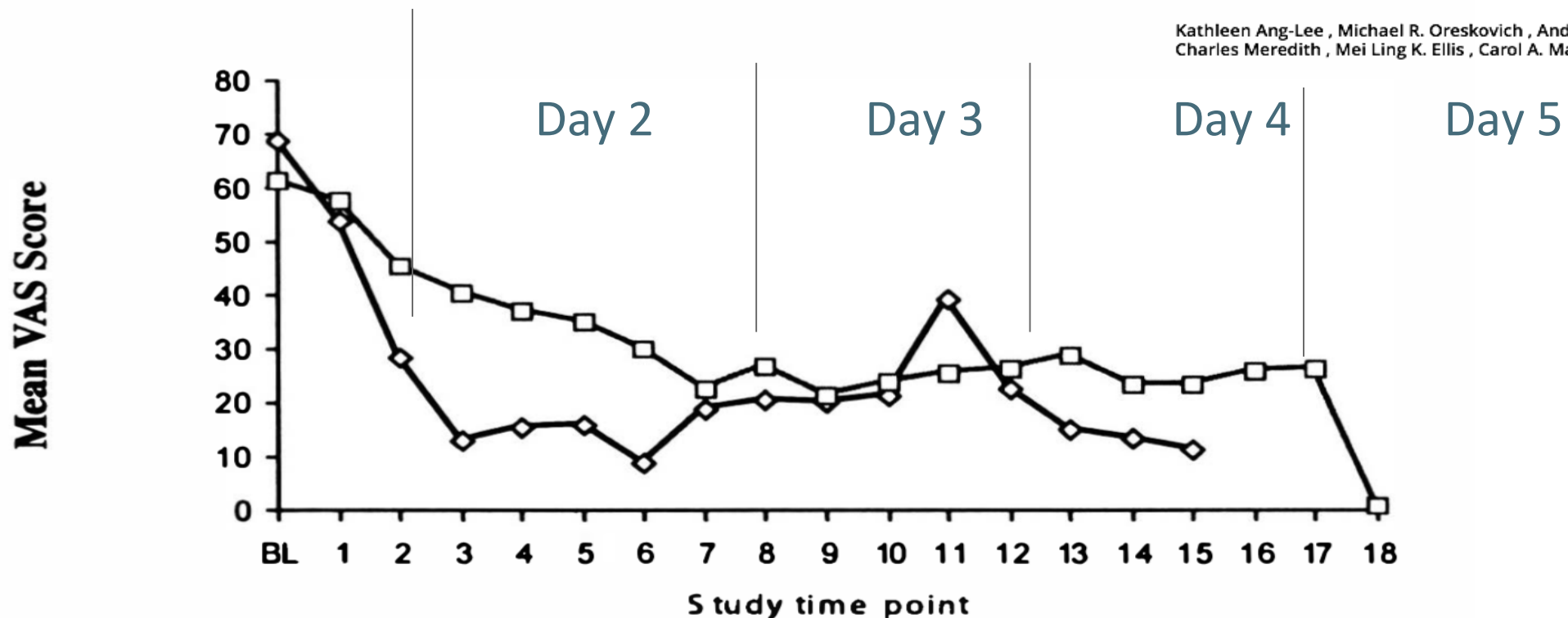


Journal of Psychoactive Drugs

ISSN: 0279-1072 (Print) 2159-9777 (Online) Journal homepage: <http://www.tandfonline.com/loi/ujpd20>

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



High Affinity binding

Mu Opioid Receptor Range of **Ki Value**

<u>Buprenorphine</u>	<u>0.21 to 1.5</u>
Fentanyl	0.7 to 1.9
Methadone	0.72 to 5.6
<u>Naloxone</u>	<u>1 to 3 (antagonist effects)</u>
Morphine	1.02 to 4
Codeine	65 to 135

Buprenorphine antagonism of ventilatory depression following fentanyl anaesthesia

K. BOYSEN, 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).

Time: min	Preinduction	0	15	30	60	120
Buprenorphine n = 10	13 (12–14)	0 (0–4)	10 (8–12)	12 (8–16)	11.5 (8–16)	11 (8–12)
Naloxone n = 10	12 (11–15)	0 (0–2)	14.5* (9–20)	14 (10–20)	12 (9–16)	14 (6–16)

Time = min from beginning treatment with either B or N. * $P < 0.05$ between groups.

RESEARCH

Open Access

Buprenorphine to reverse respiratory depression from methadone overdose in opioid-dependent patients: a prospective randomized trial

Nasim Zamani^{1,2,3}, Nicholas A. Buckley⁴ and Hossein Hassanian-Moghaddam^{1,2*}

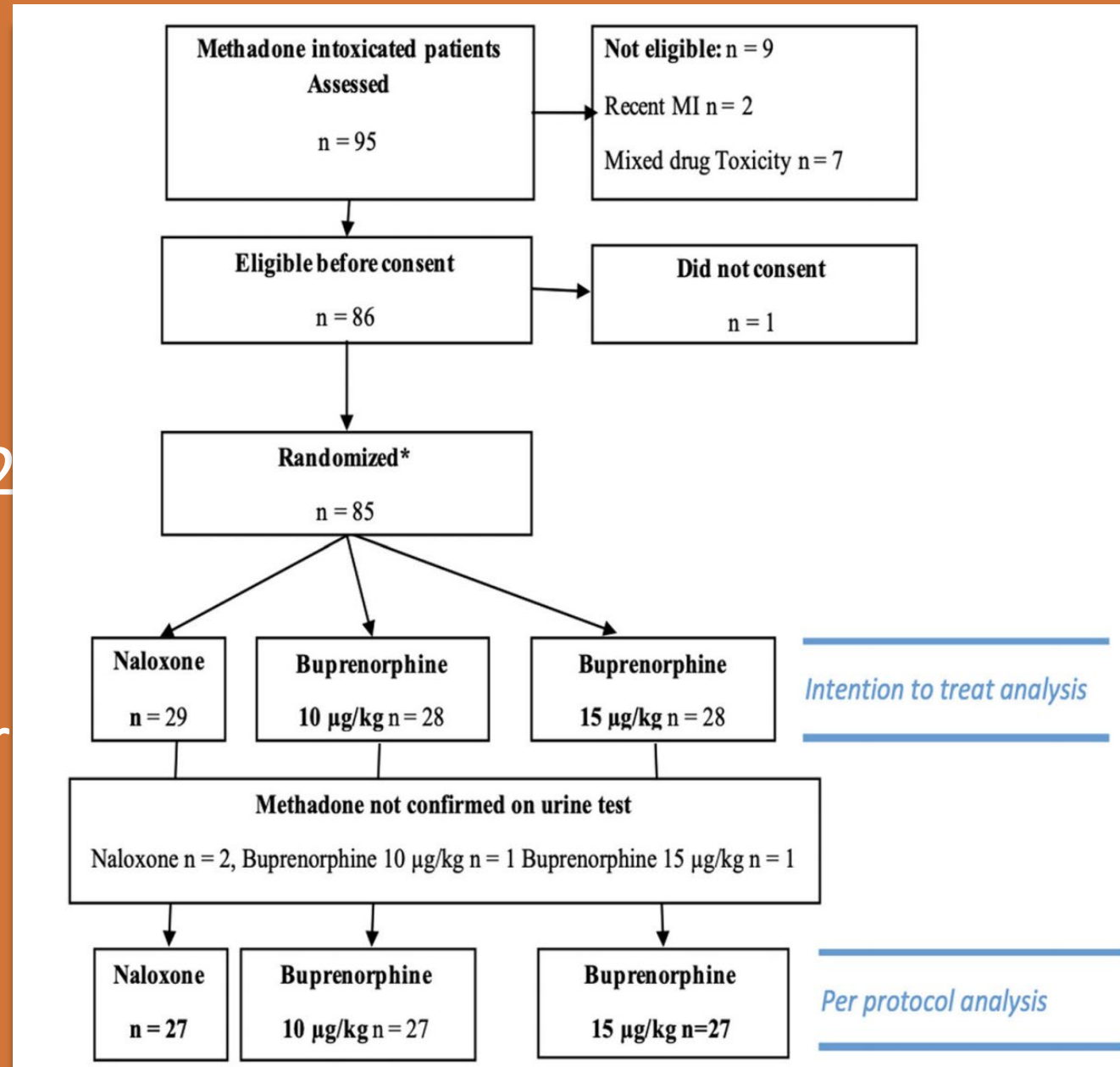


Naloxone.

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.



RESEARCH

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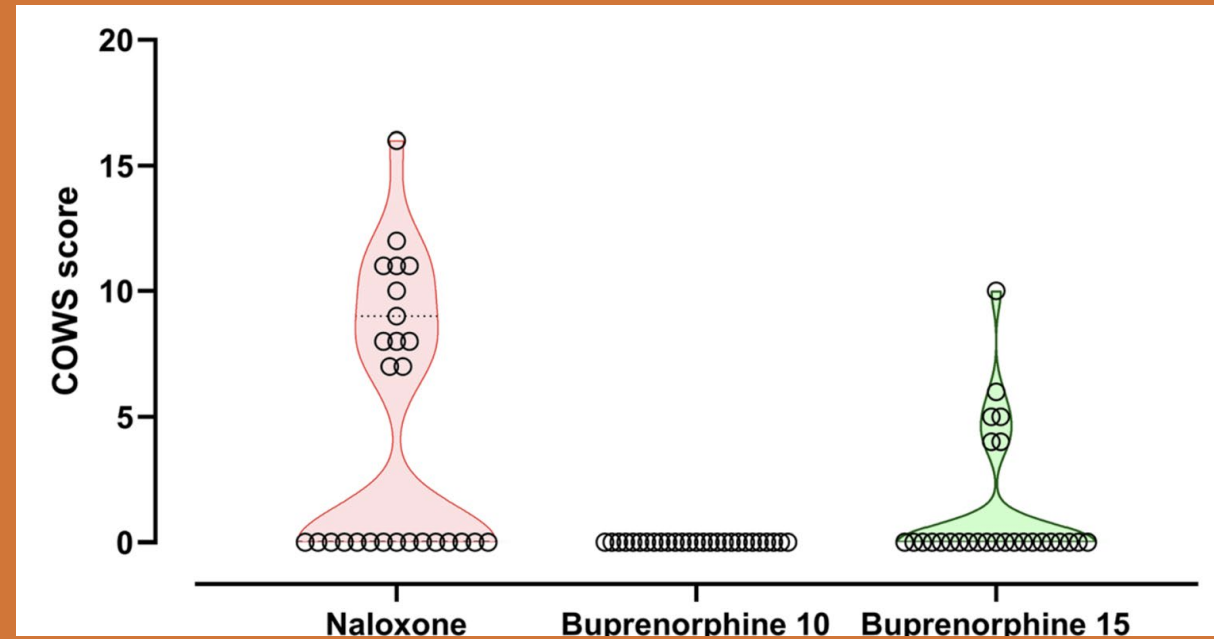


Table 3 Per-protocol comparison of outcomes in three arms of the study ($n = 81$)

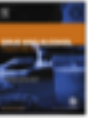
Outcome	Naloxone ($n = 27$)	Buprenorphine 10 $\mu\text{g}/\text{kg}$ ($n = 27$)	Buprenorphine 15 $\mu\text{g}/\text{kg}$ ($n = 27$)
Response to bolus antidote doses	Complete 13 (48%) Partial 13 (48%) No response 1 (4%)	Complete 23 (85%) Relative 3 (11%) No response 1 (4%)	Complete 27 (100%) Partial 0 No response 0
Opioid withdrawal	15 (56%)	0	6 (22%)
Further apnea	6 (22%)	4 (15%)	3 (11%)
Aspiration	1 (4%)	5 (18%)	1 (4%)
Intubation	8 (30%)	4 (15%)	1 (4%)
Continuing sedation	9 (33%)	0	3 (11%)

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. Mazzairelli, MD, JD; Alexis Pelletier-Bui, MD

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



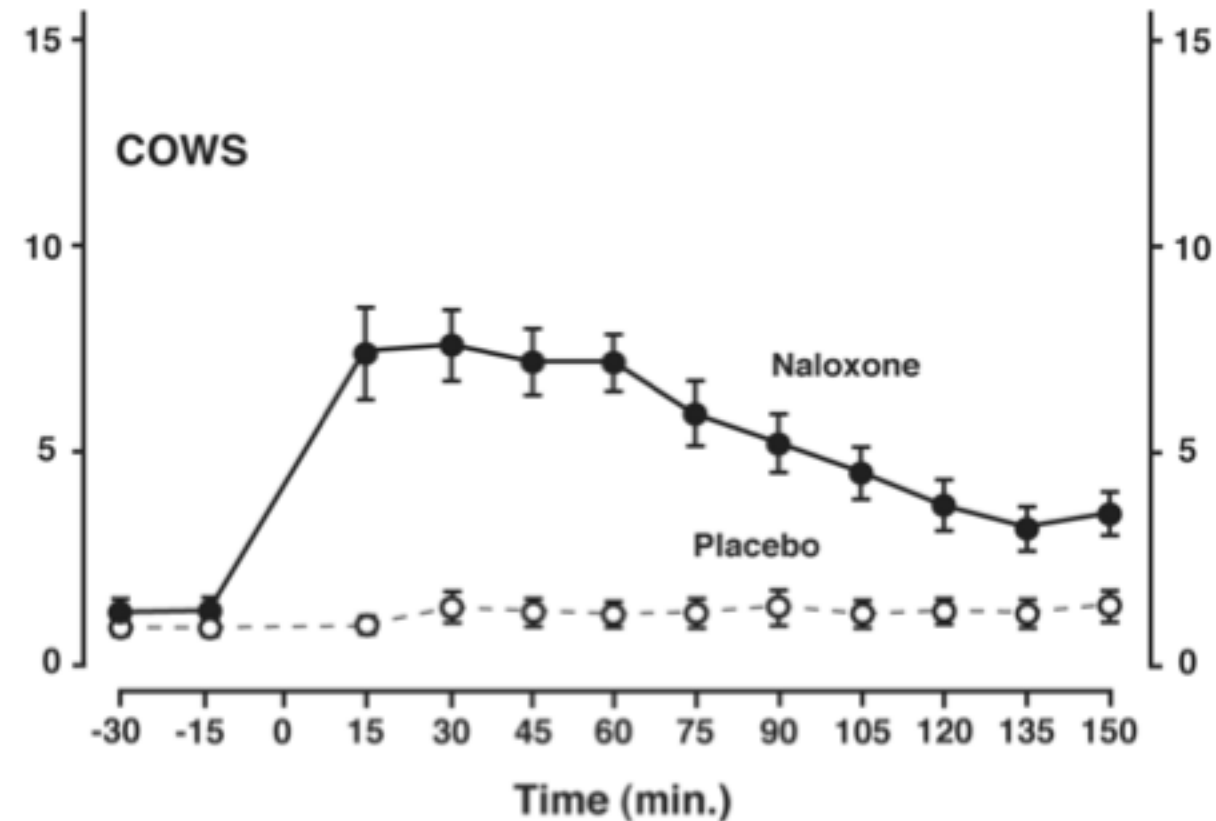
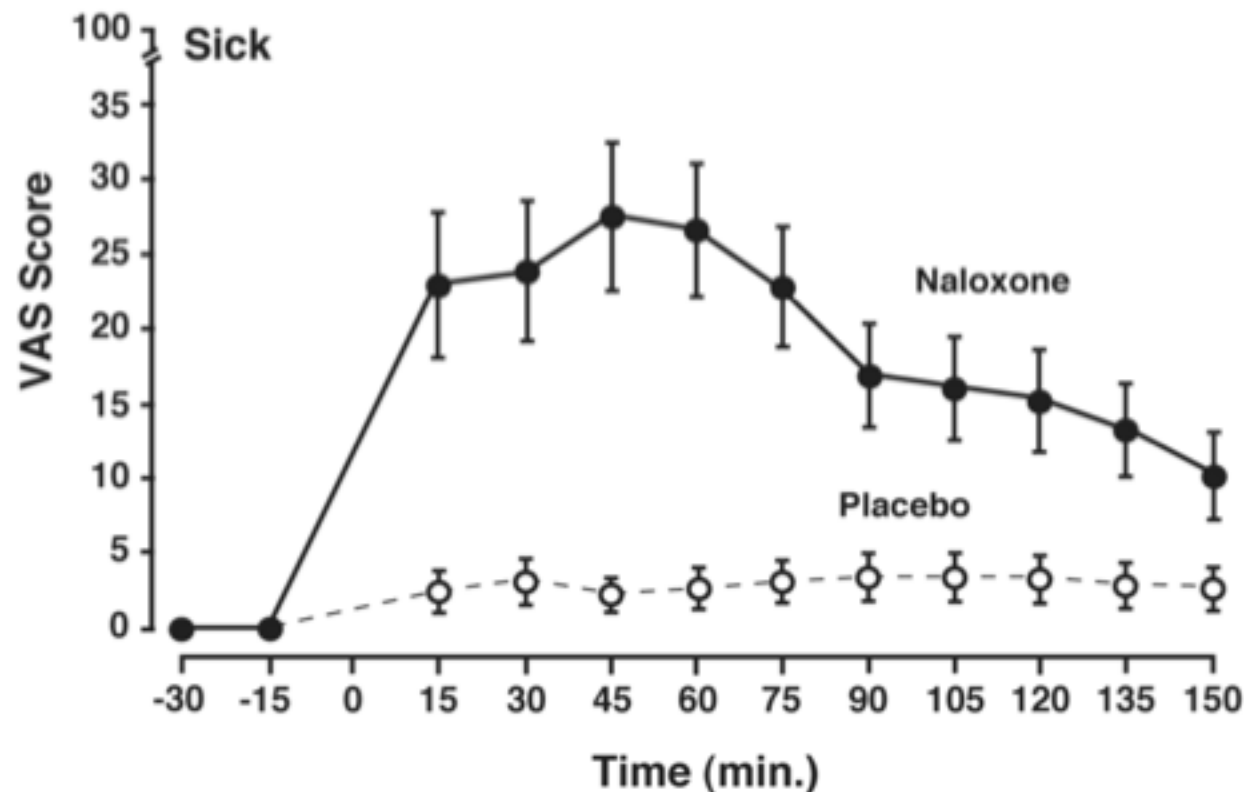
Concurrent validation of the Clinical Opiate Withdrawal Scale (COWS) and single-item indices against the Clinical Institute Narcotic Assessment (CINA) opioid withdrawal instrument

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

^aJohns Hopkins University School of Medicine, Department of Psychiatry and Behavioral Sciences, Behavioral Pharmacology Research Unit, 725 North Wolfe Drive, Baltimore, MD 21224, USA

^bBeckton Dickinson Pharmaceuticals Inc., Richmond, VA 23235, USA

Sacred COWS



“Single Big Dose”



Discussion “Goldilocks” Dose

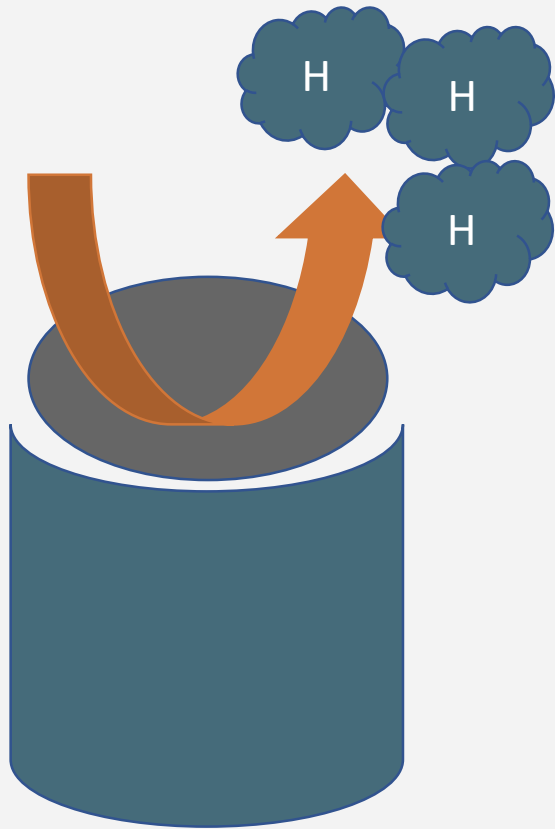
Just a tad...they don't even notice

Displaces but doesn't replace

Displaces and Overcomes

“Do I have to feel sick”: Single Big Dose

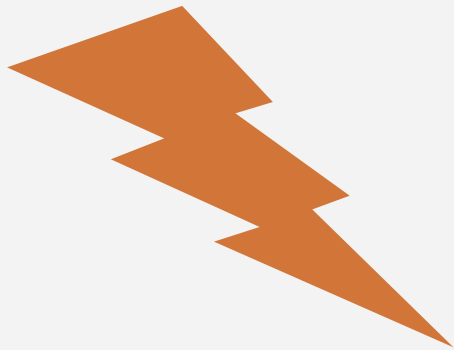
Displacement



= Pain

“Do I have to feel sick”: Single Big Dose

100mcg
Heroin



4 mg
Bup



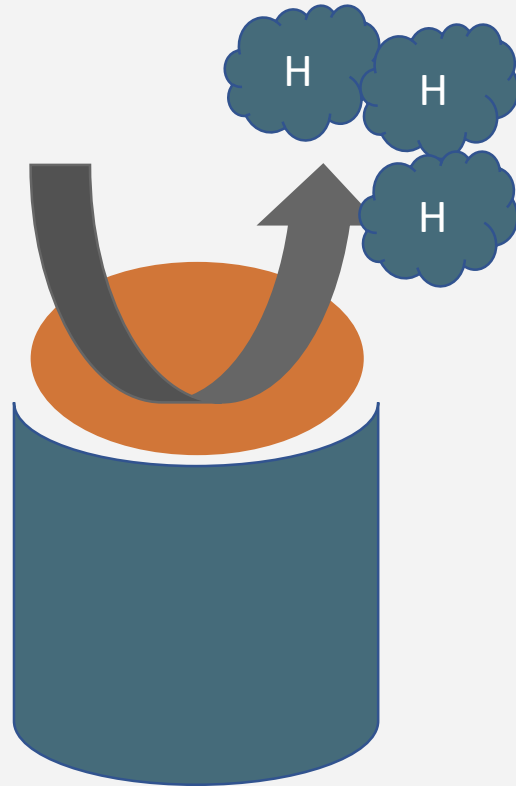
16mg



“Do I have to feel sick”: Single Big Dose

Displacement

Agonism



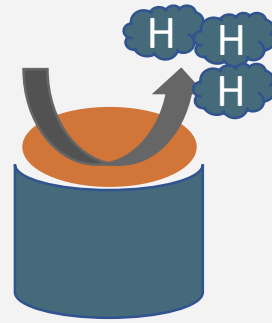
Blockade



Heroin



Bup
Agonism



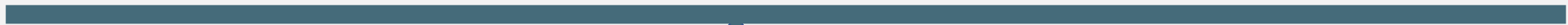
Bup
Displacement



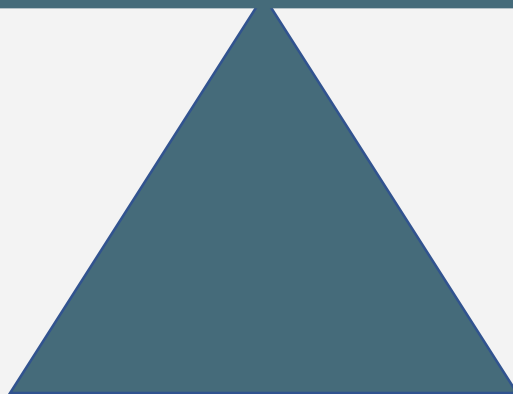
Blockade



Abstinence x
dependency



“Feel good”



“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

I gave him 8 mg sl

Wed 2:06 AM

sweet! consider another dose

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

Wed 2:08 AM

go get 'em tiger

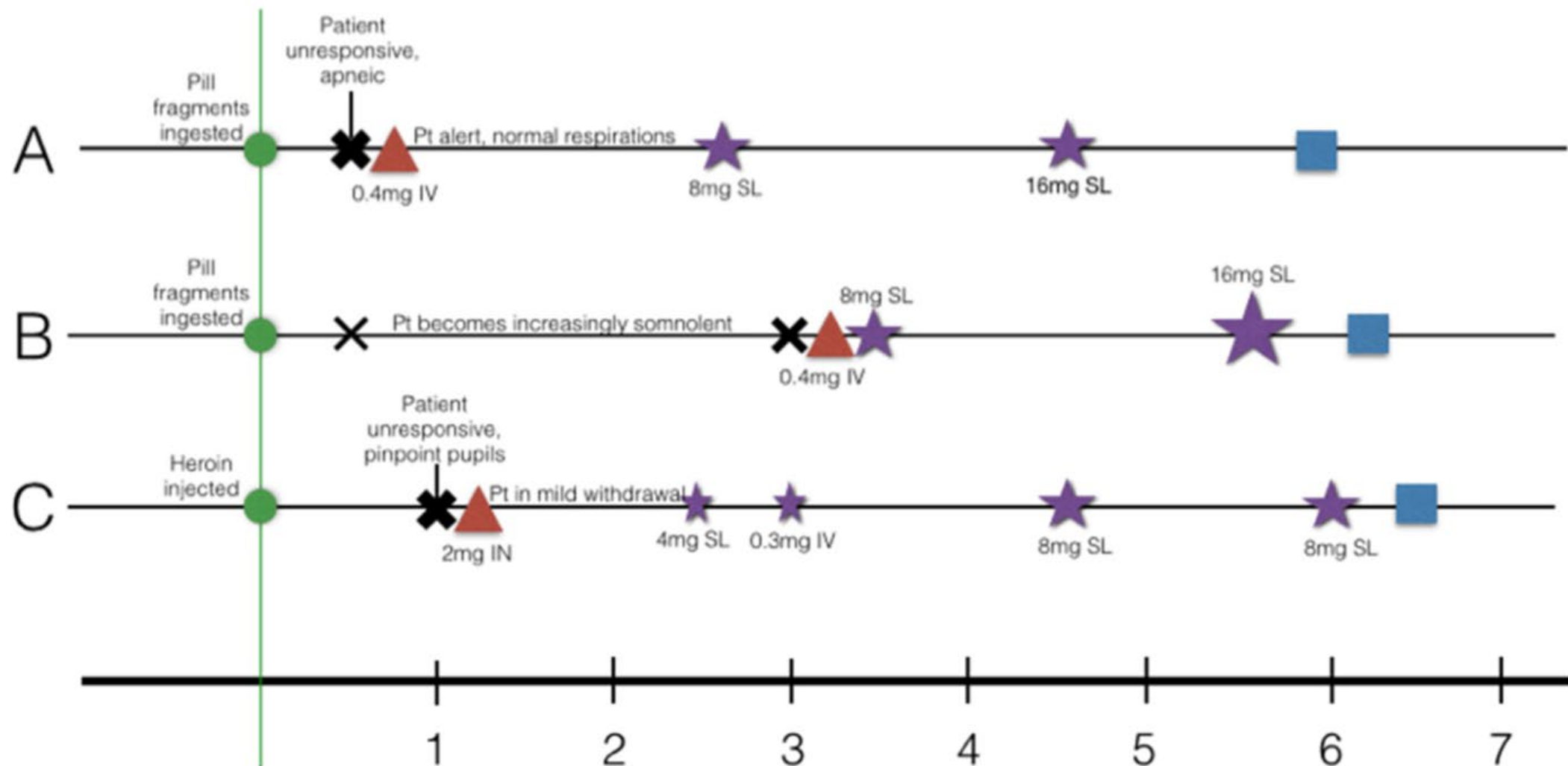
Wed 2:08 AM

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

- Resting comfortably and stable KD 0207
vitals
- Plan to observe until 1600 NJ 0205
- following the bridge protocol , pt KD 0146
does not meet any exclusion
criteria and qualifies for bup after
the reversal of overdose with
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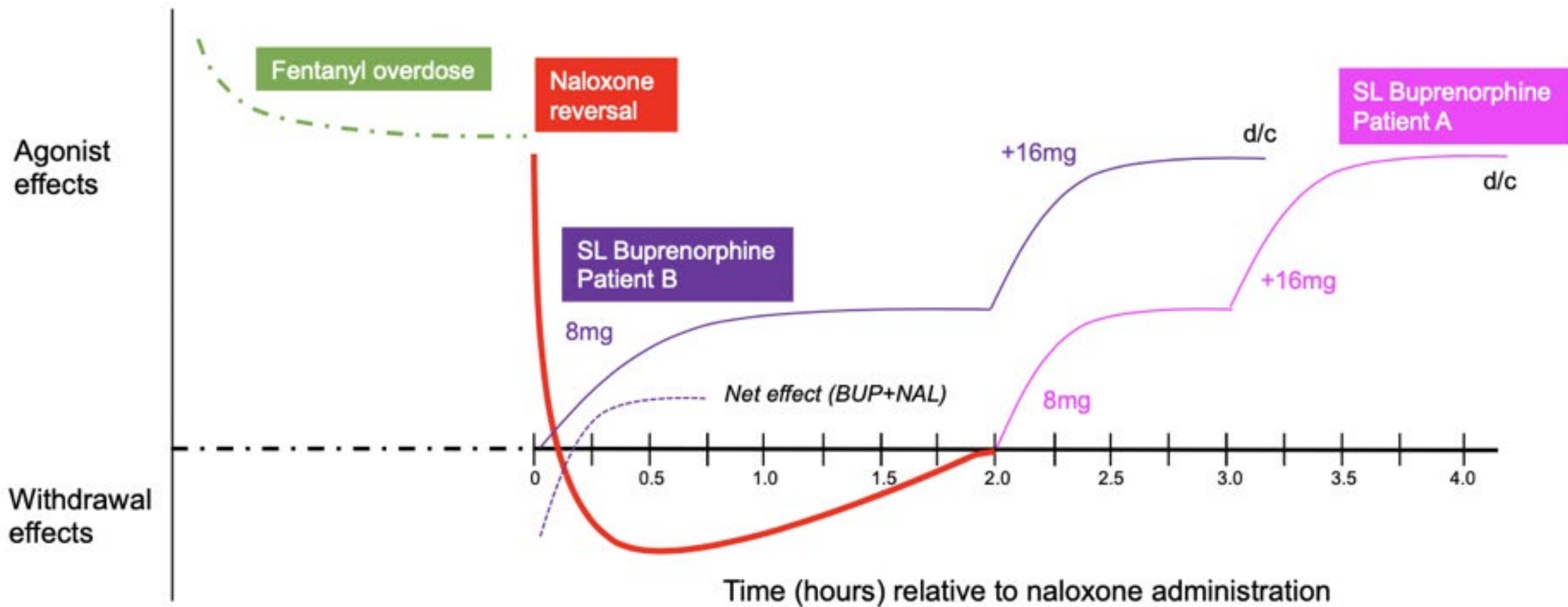
Bup After Overdose

Patient



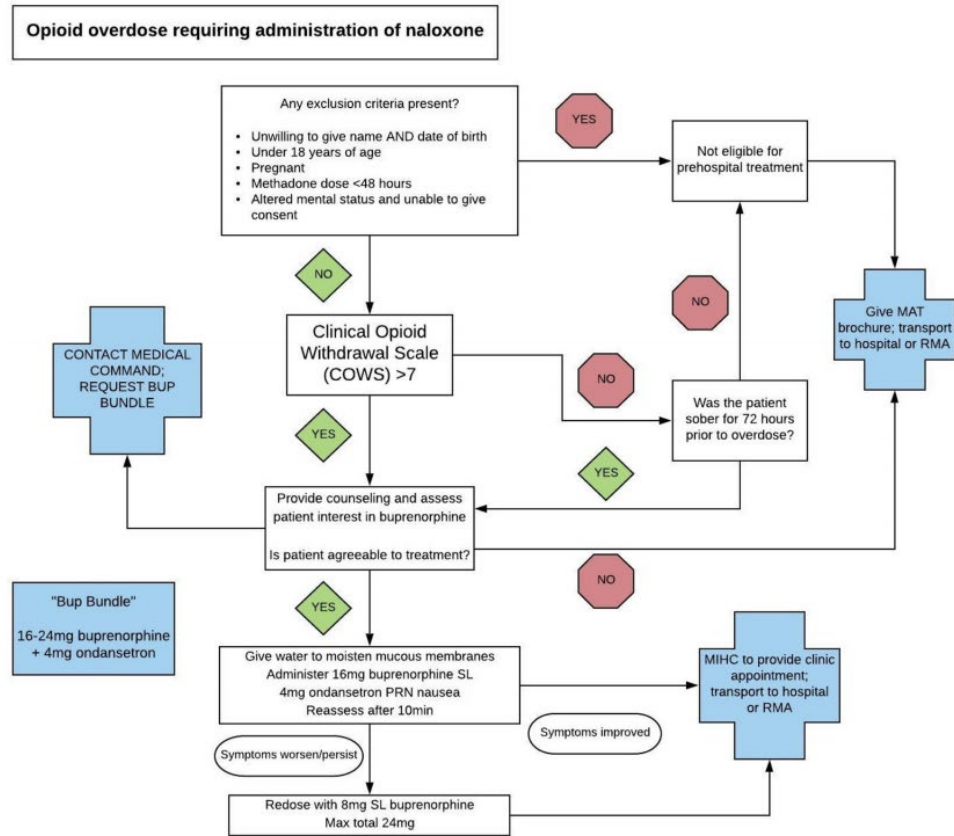
Time after exposure (hrs)

- ✕ = patient deterioration
- ▲ = naloxone administered
- ★ = buprenorphine administered
- = discharge from ED in good condition



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, FAAC

TABLE 1. Patient Characteristics and Treatment

Patient	Naloxone given	Initial COWS	Buprenorphine given	Repeat COWS	1 st visit	30 day retention
A	2 mg IM	13	16 mg	3	Yes	Yes
B	2mg IM	15	16-32 mg	3	Yes	No
C	4 mg IN	12	16 mg	4	Yes	Yes

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

YES TO ANY

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

NO

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.

Bup Induction after Overdose

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](https://www.BridgeToTreatment.org/resources)