DDAP EMERGING DRUGS SYMPOSIUM

PA Groundhogs and the Clinical Importance of Quantitative Drug Checking

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DISCLOSURES

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- No disclosures or conflicts of interest

Outline

1. Clinically, it matters how much of each drug is in the unregulated drug supply, not just whether it's present or not
2. We are trying to adapt our opioid withdrawal management to the fentanyl era
3. We are also adapting buprenorphine & methadone initiations to the fentanyl era

PATIENTS ARE DISSATISFIED WITH CARE

- Untreated withdrawal is common:

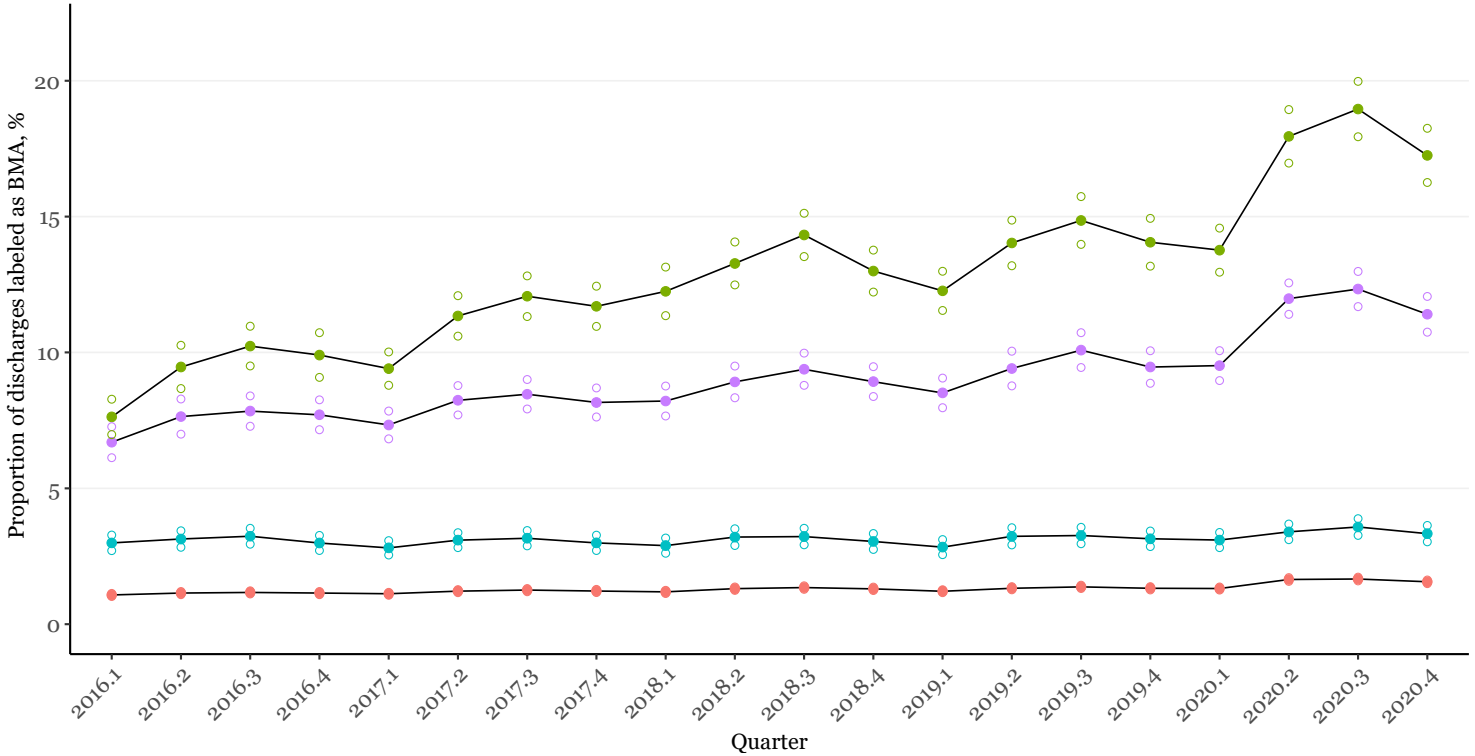
sufficient. One patient described, "They [health care staff] just tell you sorry … They'll give you some clonidine and some bentyl and send you on your way. So that doesn't

- Patients avoid hospitalizations:

I was on my way down here [drug treatment service] and it [my groin] haemorrhaged, it was like I'd been shot. Blood everywhere. Blood everywhere, you know? *(Ryan)*

He turned up in a car and just as he turned up it burst … he was like, what the fuck man, what's going on! And I said, oh nothing-nothing. He was like, come on, get in, I'm taking you to hospital and that. Even the dealer was like worried about it. But I was like, no-no.

VOTING WITH THEIR FEET, 2016-2020



- Admissions with opioid use disorder and an injection–related infection (95% CI)
- Opioid–related admissions (95% CI)
- Non–opioid mental health or substance use admissions (95% CI)
- All non–opioid admissions (95% CI)

Thakrar, *JAMA* (in press)

EVIDENCE-BASED STANDARD (~2020)

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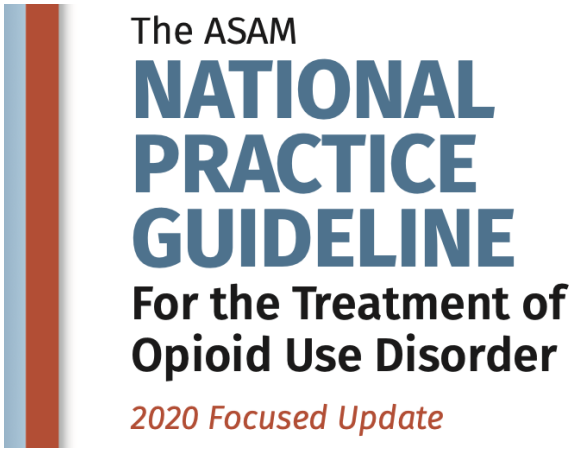
ASAM American Society of Addiction Medicine



- Treat opioid withdrawal: methadone or buprenorphine; +/- clonidine, adjuvants
- Treat pain: for mild or moderate pain, use non-opioids; for severe acute pain, consider adequate doses of short-acting opioids alongside methadone/bup
- Offer to start OUD treatment: methadone, buprenorphine, or XR-NTX

EVIDENCE-BASED WITHDRAWAL TX

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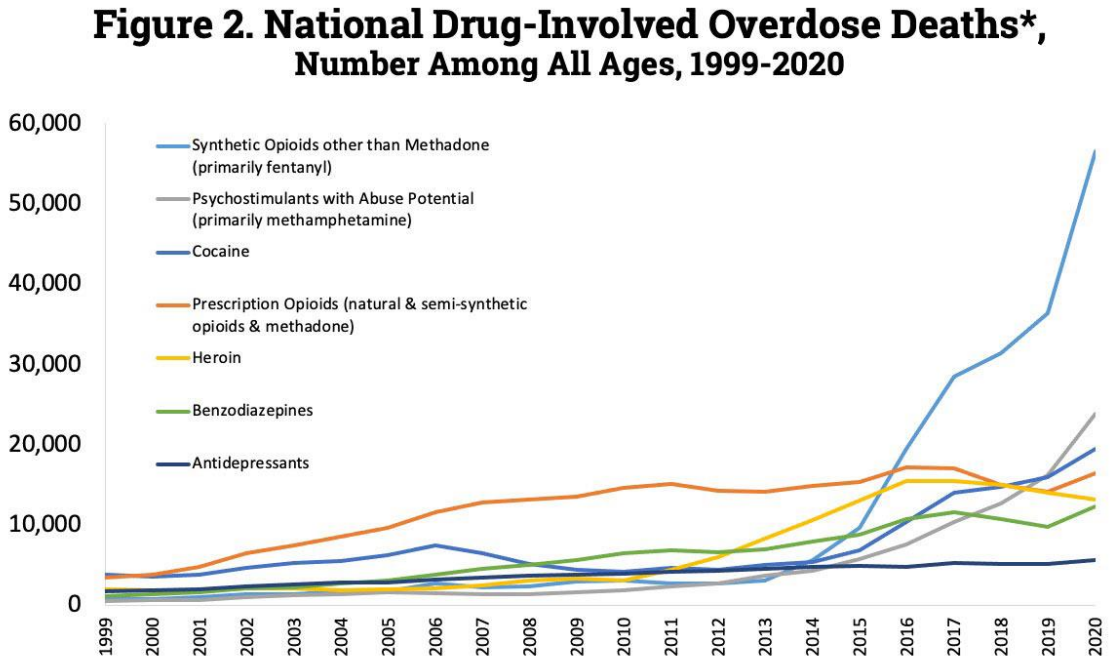
- The alpha$_2$-agonists (eg. clonidine) reduce opioid withdrawal symptoms. [3 RCTs, n=148]
  - Dosing: clonidine 0.1-0.2mg q6-8 hours
- Buprenorphine is better than clonidine alone [7 RCTs, n=902]
  - Dosing: 2-8mg once COWS $\geq$8
- Methadone as effective as buprenorphine, but symptoms resolve more quickly with buprenorphine. [2 RCTs, n=82]
  - Dosing: 30mg + 10mg usually sufficient for withdrawal

The problem: all this evidence is from people using heroin or oxycodone!

Gowing, Cochrane Review (2016)
Gowing, Cochrane Review (2017)
ASAM Guidelines 2020 Focused Update (2020)

WHAT HAS CHANGED?



Overdoses involving fentanyl & fentanyl analogues

Fentanyl ≠ Heroin

- 25-50x as potent
- 30+ analogues

CDC, Vital Statistics, 2021

TREATING WITHDRAWAL

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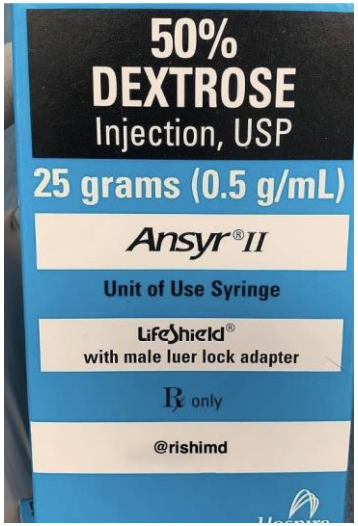
Compare to insulin doses for:

vs.



CFSRE & Philadelphia Dept of Public Health (2023)

RATIONALE FOR SHORT-ACTING OPIOIDS

- Old doses of methadone (30mg) and buprenorphine (2-4mg) may be insufficient for withdrawal
- Some patients are declining or delaying buprenorphine → Fear of precipitated withdrawal within 72h of last fentanyl use
- Xylazine wounds → many patients have acute pain

In this context: Some are now using short-acting opioids as adjuvants to evidence-based medications for withdrawal, craving, and pain

- Emerging evidence: 3 case series [n=25] & two perspectives

Thakrar, *JAMA IM* (2022)
Kleinman & Wakeman, *Annals of IM* (2021)
Thakrar, *ASCP* (2023)

PENN APPROACH TO WITHDRAWAL & PAIN

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Addiction Science & Clinical Practice

Safety and preliminary outcomes of short-acting opioid agonist treatment (sOAT) for hospitalized patients with opioid use disorder

Ashish P. Thakrar[1,2*], Tanya J. Uritsky[2,3], Cara Christopher[3], Anna Winston[4], Kaitlin Ronning[5], Anna Lee Sigueza[5], Anne Caputo[5], Rachel McFadden[2,7], Jennifer M. Olenik[4], Jeanmarie Perrone[2,6], M. Kit Delgado[2,6], Margaret Lowenstein[2,4] and Peggy Compton[2,7]

Annals of Internal Medicine — IDEAS AND OPINIONS

Treating Opioid Withdrawal in the Hospital: A Role for Short-Acting Opioids

Robert A. Kleinman, MD; and Sarah E. Wakeman, MD

DOI: 10.1111/add.15893

LETTER TO THE EDITOR — ADDICTION SSA

Opioid withdrawal management in the fentanyl era

VIEWPOINT

JAMA Internal Medicine

Short-Acting Opioids for Hospitalized Patients With Opioid Use Disorder

Ashish P. Thakrar, MD[1,2,3]

PENN APPROACH TO WITHDRAWAL & PAIN

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Center for Addiction Medicine and Policy

Initial Management of Withdrawal and Pain in Hospitalized Patients with Opioid Use Disorder (OUD) Using Fentanyl

1. Assess & Diagnose OUD

2. Stabilize & Engage

- Start methadone/buprenorphine & clonidine for withdrawal (and as maintenance in those seeking treatment)
- Consider short-acting opioids (oxy 20 q4, titrate) for withdrawal
- When needed, use short-acting opioids (SAOs) for pain

3. Transition to Maintenance OUD Treatment & Plan for Discharge

- By 72h, SAOs for withdrawal should be transitioned to OUD tx
- In general, avoid discharge rx of SAOs for patients with OUD

FENTANYL POTENCY: ONE ESTIMATE…

One back-of-the-envelope estimate from Dr. Joe D'Orazio (Cooper) & Tanya Uritsky (Penn):

1 bag fentanyl in Philly = ~**300 mg oxycodone** *or* ~**500 mg PO morphine**

2023 estimate from pharmacists, toxicologist & addiction specialists at Penn & Temple

VARIATION IN THE DRUG SUPPLY

cfsre NPS DISCOVERY

Department of Public Health CITY OF PHILADELPHIA

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"Heroin" / Dope
(Powder in Glassine Bag)

Date	Suspected	Drugs Identified
9/13/2022	Dope	Fentanyl (18.4%),
9/21/2022	Dope	Fentanyl (6.6%), X
9/21/2022	Dope	Fentanyl (7.7%), Xyl
9/21/2022	Dope	Fentanyl (7.8%), X
9/21/2022	Dope	Fentanyl (8.2%), X

Average fentanyl purity
11.7%, but as high as 35%

How similar is the supply in Eerie, Pittsburgh, Harrisburg, or Allentown?

Should those clinicians use the same doses we're using in Philadelphia?

CFSRE & Philadelphia Dept of Public Health (2023)

Challenges with Starting Buprenorphine

- Increased reports of buprenorphine precipitated withdrawal (PW)
  - Patients report PW despite 12-48h abstinence from fentanyl.[1]
  - Case reports: PW despite initial COWS ≥13.[2,3]
  - In Philadelphia: most are declining traditional/high dose initiation due to fear of buprenorphine PW
- Yet recent studies found 1% incidence of PW (D'Onofrio 2023)
  - Could it be due to variations in how much fentanyl is in the drug supply?
  - Could these challenges in Philadelphia be because of xylazine? Other opioids?

1.Varshneya (2021); 2.Shearer (2021);
3.Spadaro (2023); 4.Weimer (2023);
5.Thakrar (2023)

Challenges with Starting Methadone

- Traditional outpatient induction, developed decades ago:
  - 30mg + 10mg first day, add 5-10mg every 3-7 days
  - Takes weeks & prioritized safety in outpatient settings
- What's missing?
  - How to titrate while inpatient? Can we go faster?
- Rapid inpatient titration: 3 retrospective case series
  - 30mg+10mg q4h PRN for withdrawal up to 40-80mg Days 1-3
  - Low rates of sedation. Penn study ongoing (HUP data).

Summary

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We need to stay alert to what's next – xylazine, nitazines, etc

1.Varshneya (2021); 2.Shearer (2021);
3.Spadaro (2023); 4.Weimer (2023);
5.Thakrar (2023)