

ED-Initiated Buprenorphine for Opioid Use Disorder



*Gail D'Onofrio MD
Professor and Chair
Department of Emergency Medicine*

Disclosure Statement

Current grant funding:



We Know...

The Extent of the Problem

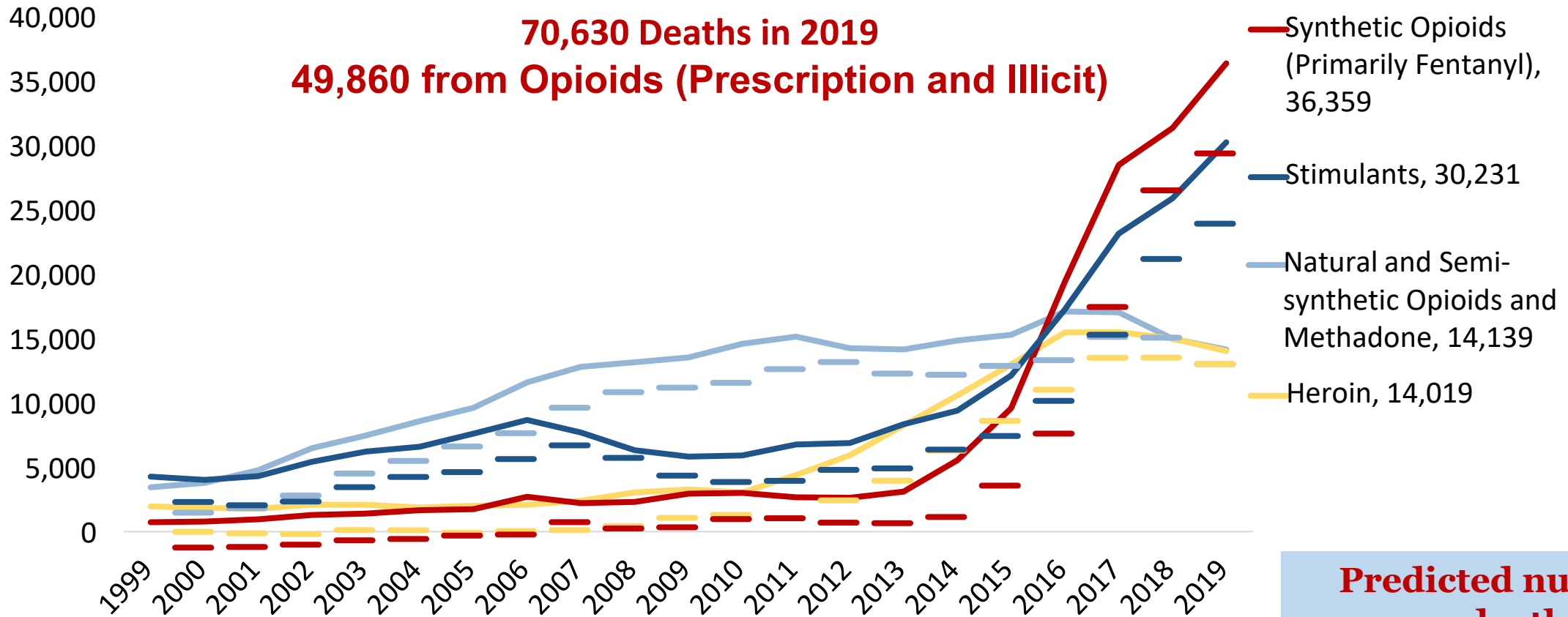
20.4 million Americans >12 years of age have a substance use disorder

1.6 million have a opioid use disorder

9.7 million report non medical use of pain relievers in the past year

Evolution of Drivers of Overdose Deaths, All Ages

Analgesics → Heroin → Fentanyl → Stimulants



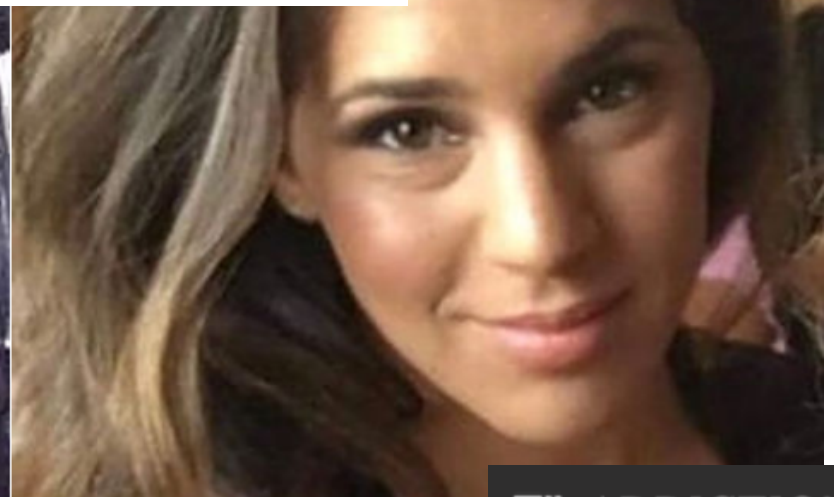
Predicted number of deaths
 (12 month ending Aug 2020)
88,295 ↑ 26%

Source: The Multiple Cause of Death data are produced by the Division of Vital Statistics, National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), United States Department of Health and Human Services (US DHHS).



Recent CDC data for the 12-month period ending in May 2020
81,230 people in a single year

223 people lost in a single day



<https://www.stop-overdose.org/>

223 people die in our country each day from a drug overdose.
Sons, daughters, moms, dads, siblings and friends.

 ADDICTION
POLICY FORUM

We Know...

Treatment Works

The National Academies of
SCIENCES · ENGINEERING · MEDICINE

CONSENSUS STUDY REPORT

MEDICATIONS FOR OPIOID USE DISORDER SAVE LIVES

- ✓ OUD is a treatable chronic brain disease
- ✓ FDA-approved medications to treat OUD are effective and save lives
- ✓ Long-term retention on MOUD is associated with improved outcomes
- ✓ A lack of availability of behavioral interventions is not justification to withhold MOUD
- ✓ Most people who could benefit from MOUD do not receive it, and access is inequitable
- ✓ Withholding or failing to have available all classes of FDA-approved MOUD in any care or justice setting is denying appropriate medical treatment
- ✓ Confronting the major barriers to use of MOUD is critical to addressing the opioid crisis

Sponsors: National Institute on Drug Abuse (NIDA)
Substance Abuse and Mental Health Services Administration (SAMHSA)

We Know...

**The ED Offers the 24/7/365 Option
to Combat the Opioid Crisis**

Why focus on the ED?

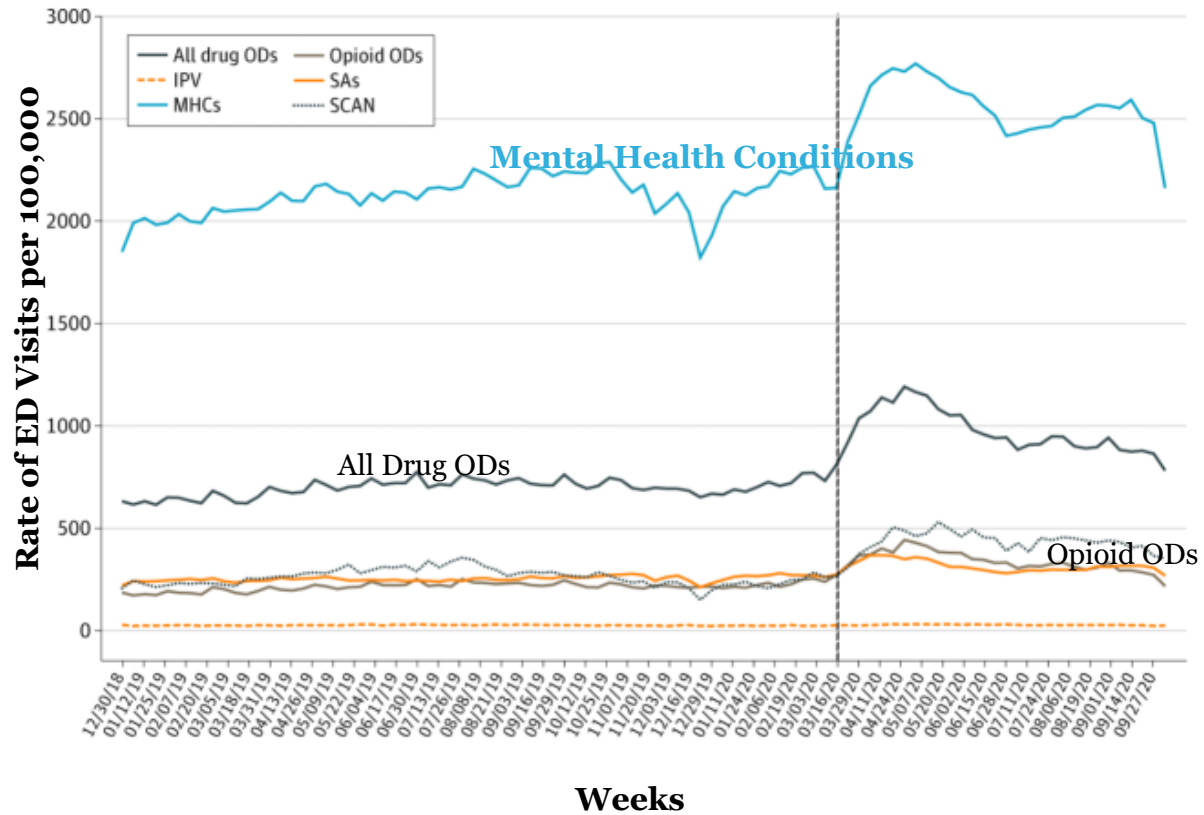


Because that's where the patients are!



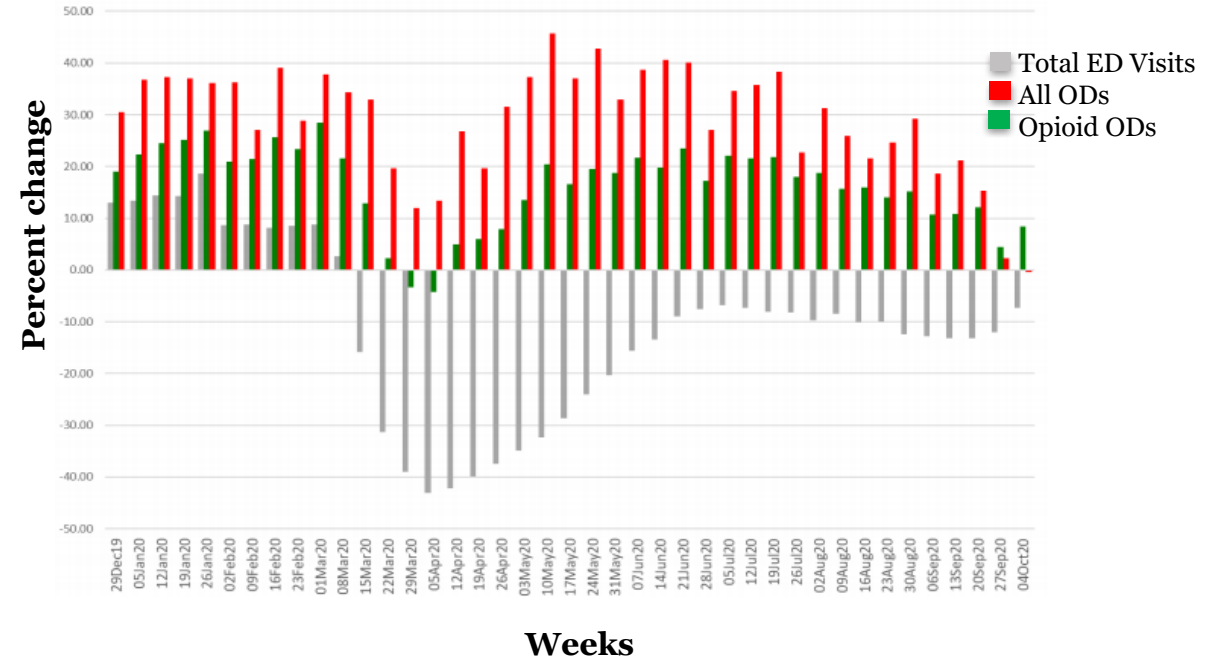
Approximately one of every 80 visits to the ED are opioid-related (costing 5 billion per year)

COVID 19 Collides with the Opioid Epidemic



Count of ED Visits for All Drug and Opioid Overdoses (ODs), Intimate Partner Violence (IPV), Suicide Attempts (SAs), Mental Health Conditions (MHCs), and Suspected Child Abuse and Neglect (SCAN) in the US, December 30, 2018, to October 10, 2020

Weekly % Δ in Total ED visits, all drug OD, and opioid OD in 2020 compared to 2019





EMBED:
PRAGMATIC TRIAL OF USER-CENTERED CLINICAL DECISION
SUPPORT TO IMPLEMENT EMERGENCY DEPARTMENT-INITIATED
BUPRENORPHINE FOR OPIOID USE DISORDER

January-September 2018-2020

Non-fatal OD among adult visits to 25 EDs in 6 States

OD visit counts and rates per 100 all-cause ED visits during COVID compared to levels predicted based on 2018-19 visits by modeling the rate of ED per all cause ED visits accounting seasonal effects

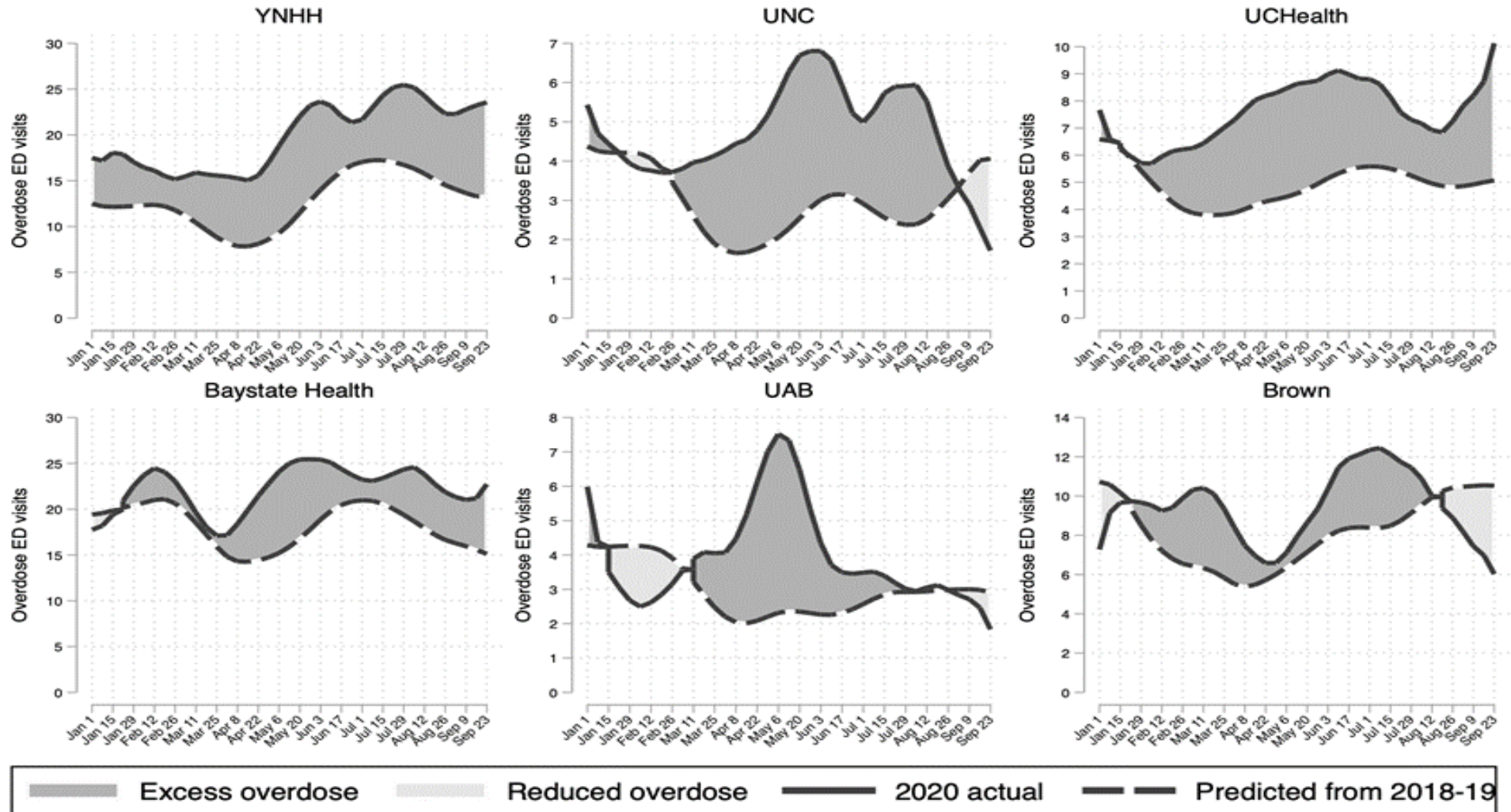
11.3% increase in OD visit counts (N=2639) (95%CI: 3.52%-19.1%; p=0.004)
Compared with 2018 (2302) and 2019 (2439) [**despite 14% decline in all ED visit**]

30.1% increase in OD rates (95% CI: 24%-36.42%); p<.001)

0.25 per 100 visits in 2018-19 to 0.33 per 100 ED visits in 2020



Non-fatal Overdose Trends During COVID



Excess Emergency Department visits for opioid overdose in 6 healthcare systems (25 EDs) January 1 to September 30, 2020; 2018 and 2019 data and 2020 all-cause ED visit counts were used to predict OUD positive visit counts for 2020.

We Know...

The Consequences of Inaction

Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality

A Cohort Study

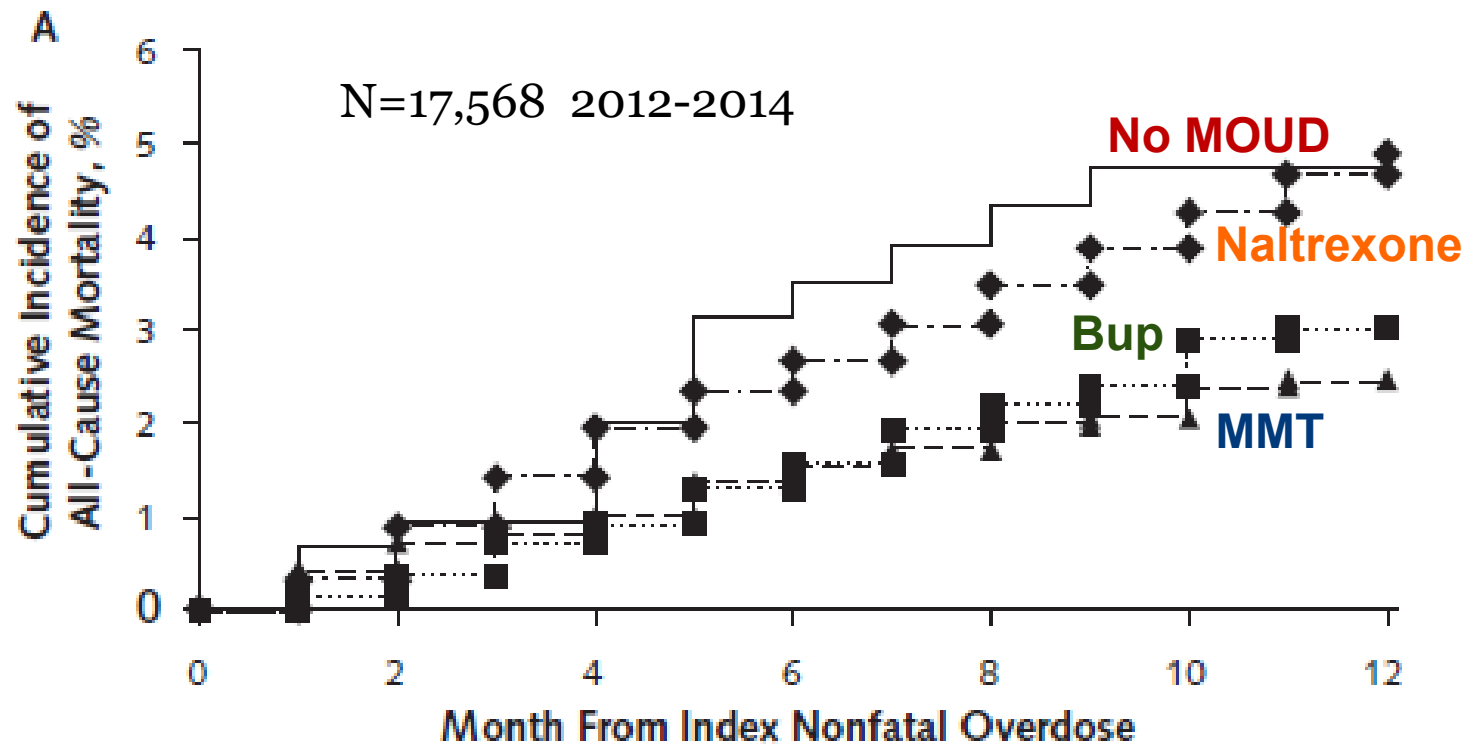
Marc R. Larochelle, MD, MPH; Dana Bernson, MPH; Thomas Land, PhD; Ziming Xuan, ScD, SM; Sarah M. Bagley, MD, MSc; Jane M. Liebsch...

... PhD, MHS; Na Wang, MA;

Primary Exposure Classification: With Discontinuation*

12 months post non-fatal OD

- 30% received MOUD
- 4.7% all-cause mortality
2.2% opioid-related
- BUP and MMT decreased in mortality



We Know...

The Evidence

A Randomized Trial of ED-Initiated Interventions for Opioid Dependence

Research

Original Investigation

Emergency Department-Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence

A Randomized Clinical Trial

Gail D'Onofrio, MD, MS; Patrick G. O'Connor, MD, MPH; Michael V. Pantalon, PhD; Marek C. Chawarski, PhD; Susan H. Busch, PhD; Patricia H. Owens, MS; Steven L. Bernstein, MD; David A. Fiellin, MD

IMPORTANCE Opioid-dependent patients often use the emergency department (ED) for medical care.

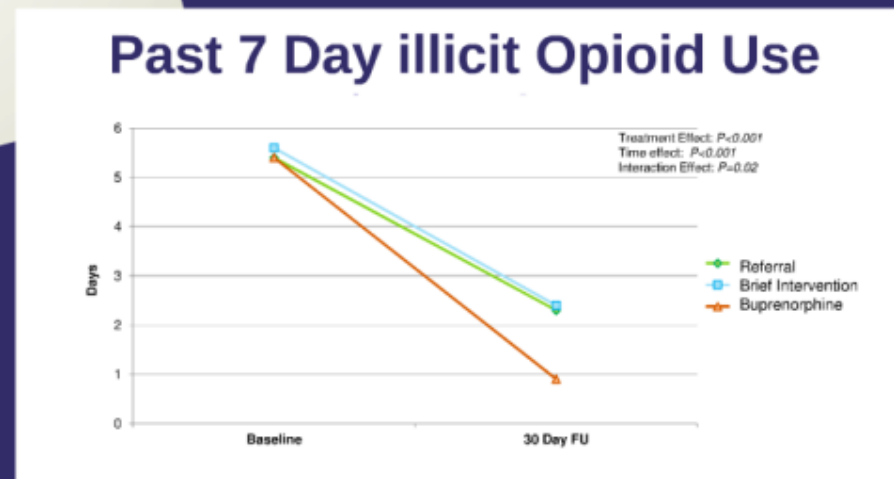
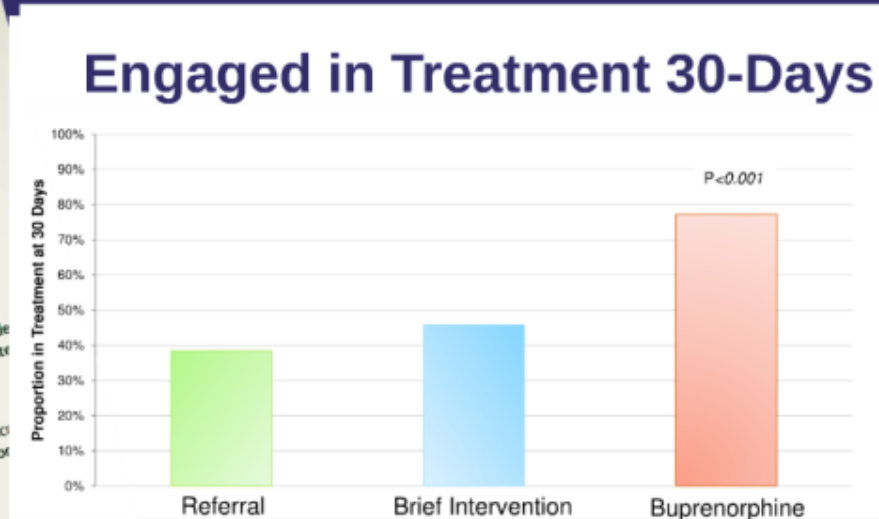
OBJECTIVE To test the efficacy of 3 interventions for opioid dependence: (1) screening and referral to treatment (referral); (2) screening, brief intervention, and facilitated referral to community-based treatment services (brief intervention); and (3) screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral to primary care for 10-week follow-up (buprenorphine).

DESIGN, SETTING, AND PARTICIPANTS A randomized clinical trial involving 329 opioid-dependent patients who were treated at an urban teaching hospital ED from April 7, 2009, through June 25, 2013.

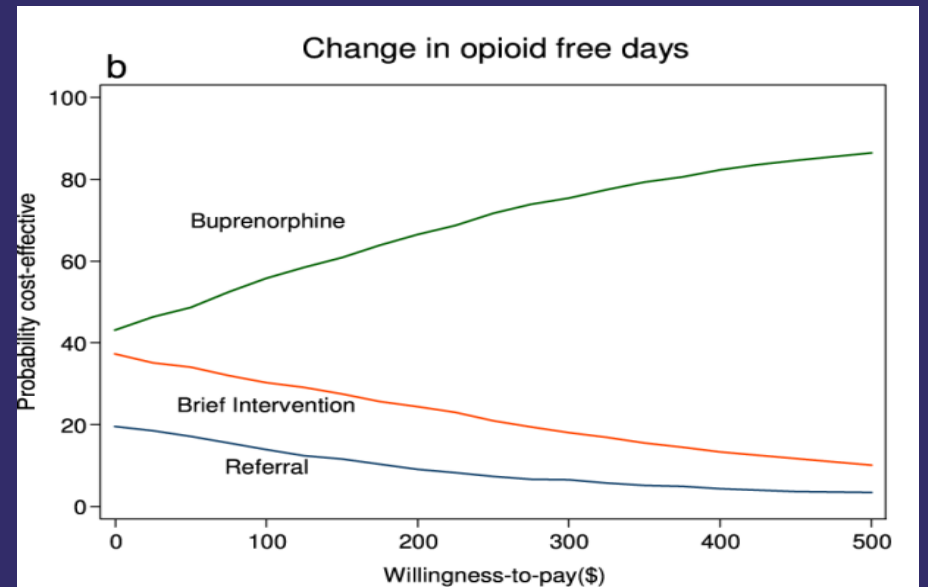
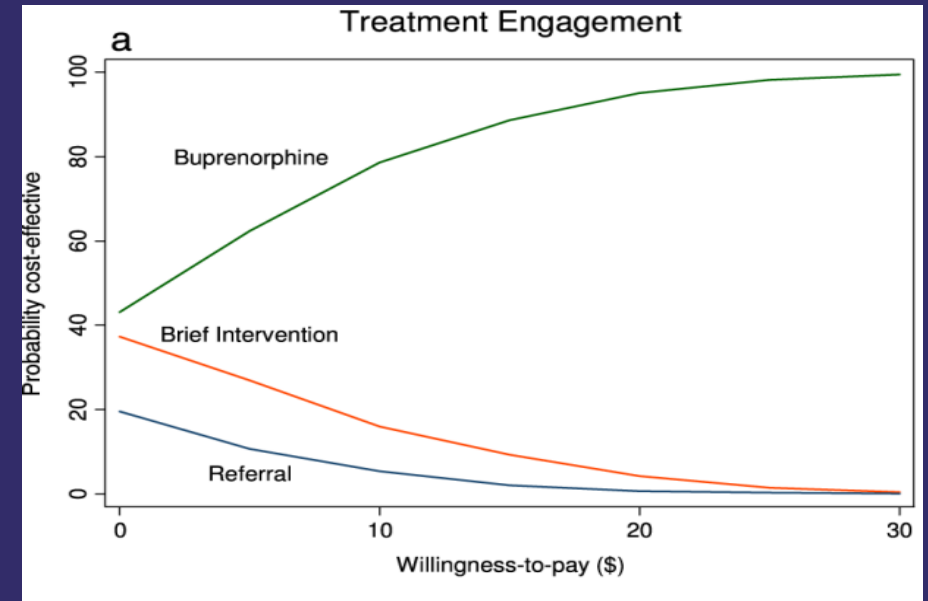
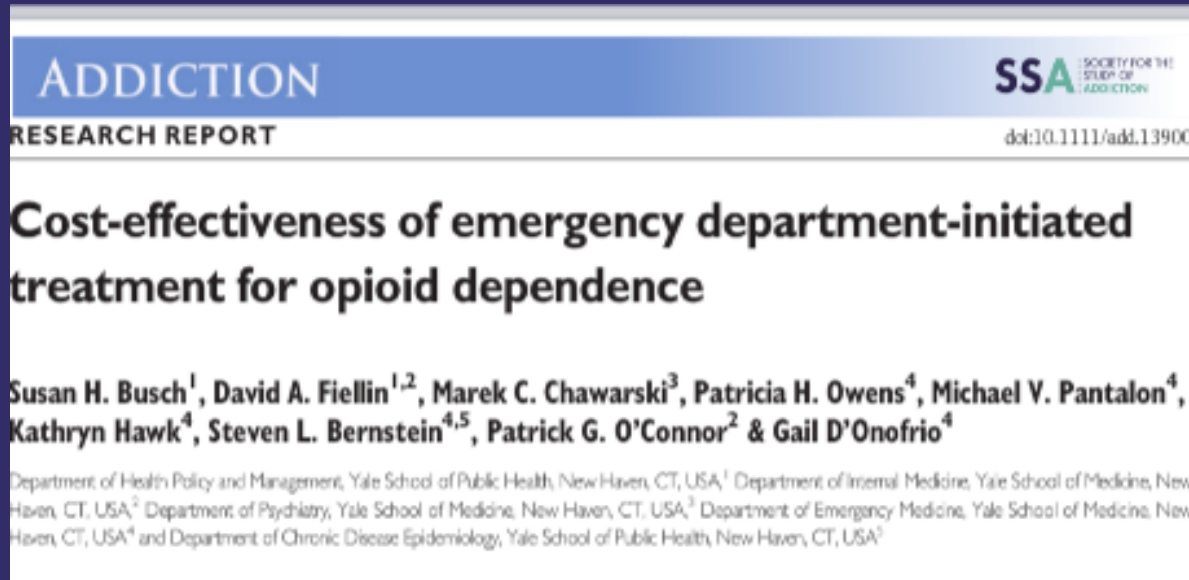
INTERVENTIONS After screening, 104 patients were randomized to the referral group, 111 to

+ JAMA Report Video
Author Video Int
jama.com

+ CME Quiz at
jamanetwork.com
CME Question



Cost - effectiveness of ED - initiated Treatment for Opioid Dependence



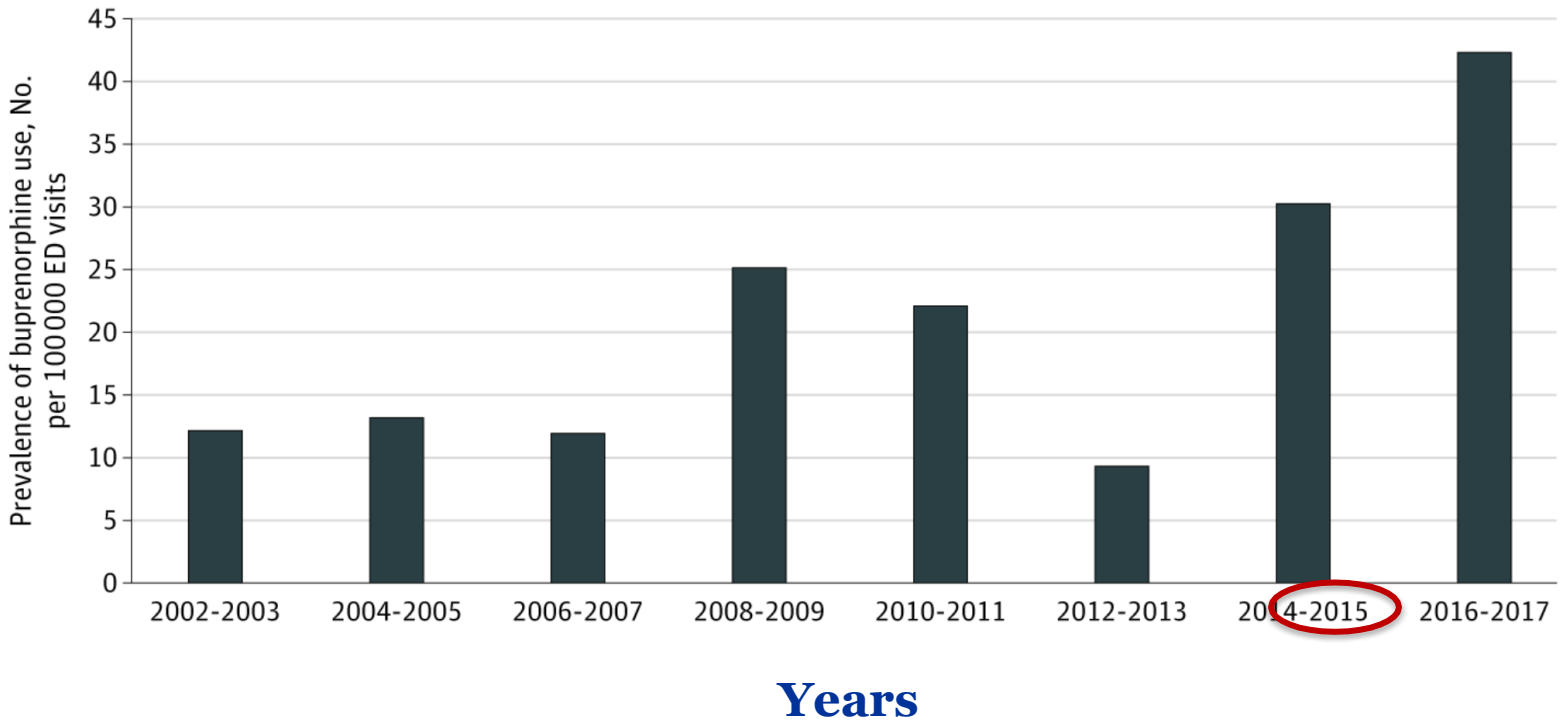
Cost-effective acceptability curve: base case analysis

- Willingness-to-pay for a 1 percentage point increase in the probability a patient is engaged in treatment 30-days post-enrollment.
- Willingness-to-pay for 1 additional opioid-free day in the past 7-days

Trends in the Use of Buprenorphine in US Emergency Departments, 2002-2017

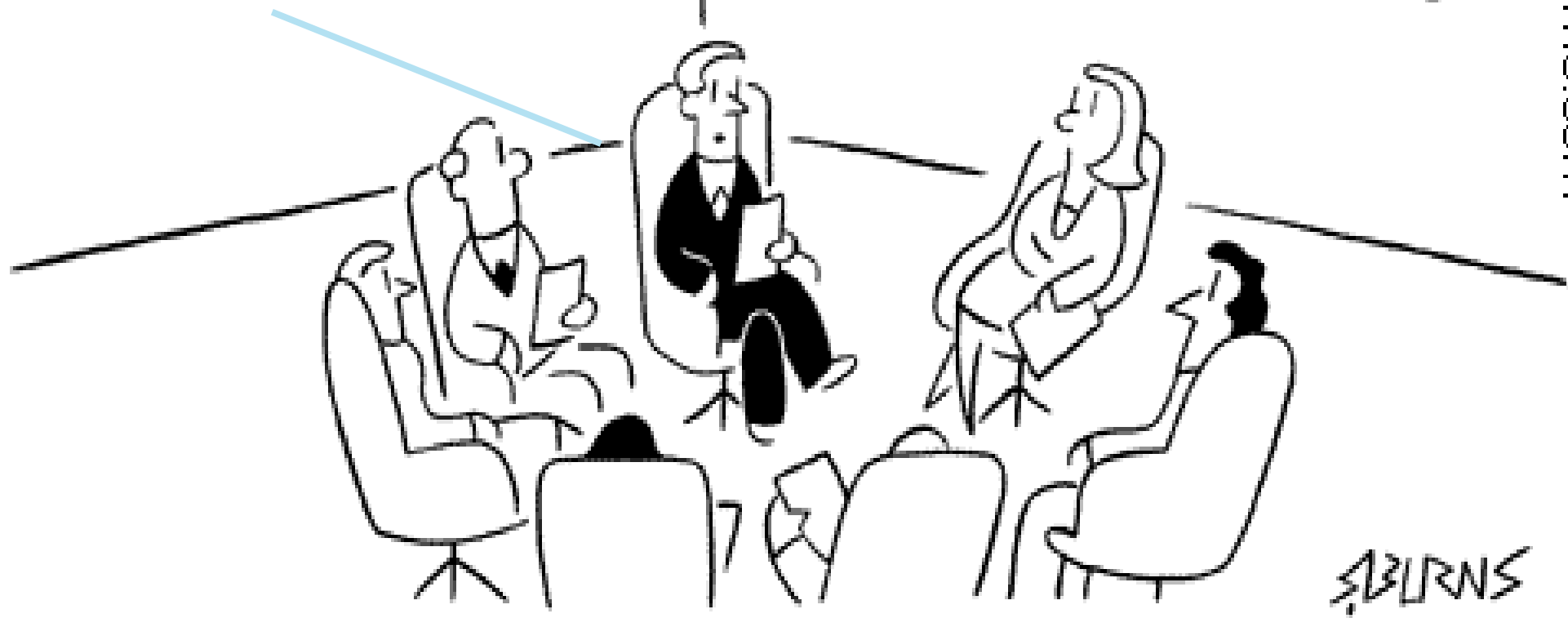
Taeho Greg Rhee, PhD, MSW; Gail D'Onofrio, MD, MS; David A. Fiellin, MD

Prevalence of buprenorphine use, #/100,000 ED visits



Buprenorphine Use increased significantly from 2002-2003 to 2016-2017 (odds ratio for linear trend, 3.31; 95% CI, 1.04-10.50; P = .04).

The latest research shows that we really should do something with all this research



BURNS

We Learned...



CTN-0069 Project ED Health

Opioid Use Disorder in the Emergency Department

Gail D'Onofrio MD, MS

David Fiellin MD



**Yale University
School of Medicine**

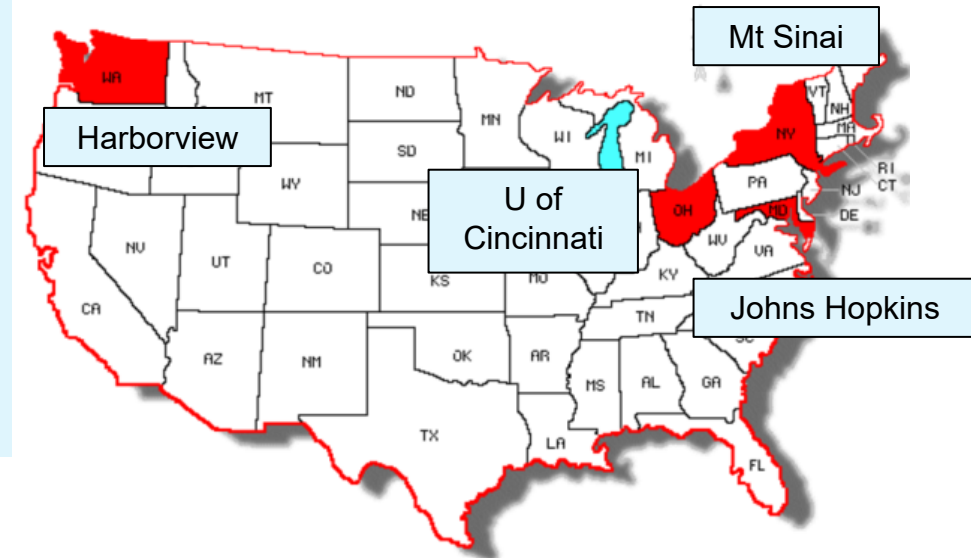
CTN 0069: Opioid Use Disorder in the ED

Design: Hybrid Type 3 Effectiveness-Implementation Study

Using a multisite stepped wedge design allowing for:

- Dual testing of effects & implementation interventions
- Testing of an implementation strategy while observing and gathering information on the intervention's impact on clinical outcomes
- Emphasizing implementation over effectiveness

4 Sites



Components of Implementation Facilitation

Component	Description
External Facilitator	Outside content expert who assists site
Formative evaluation	Quantitative and qualitative determination of impact
Local Champion	Local site stakeholder who promotes change
Stakeholder Engagement	Aligning goals of implementation and those impacted
Tailor Program to Site	Addressing site-specific needs based on formative assessment
Provider Education and Academic Detailing	Provision of unbiased peer education
Performance Monitoring and Feedback	Assess implementation of treatment efforts and inform site of results
Learning Collaborative	Shared learning opportunities tailored to stakeholders
Problem-Solving	Discussions on issues regarding ED, organizational, and community barriers with site champions
Program Marketing	Efforts designed to increase attention to availability of ED-initiated BUP

NIDA CTN-0079 ED-CONNECT

Implementation of ED-BUP programs in rural and urban settings with high need and limited resources



McCormack



Hawk

6-month evaluation

- 112 of 134 (83.6%) unique ED-BUP candidates received BUP
- Approx. 50 unique ED providers



Catholic Medical Center Manchester NH

Among the 40 BUP-recipient enrolled:

Successfully linked to OUD treatment

50% engaged at 30 days; 70% had ≥ 1 visit

Decreased Opioid Use

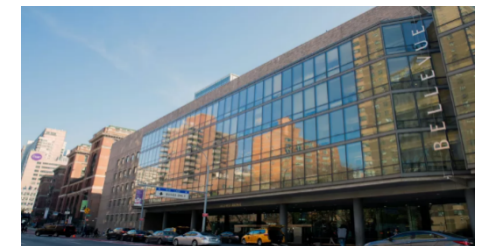
-2.9 days/week ($p < 0.001$); 51.4% negative toxicology

Fewer opioid overdoses

Odds of overdose was **4x** higher at baseline (95% CI: 1.3-12.8; $p = 0.019$)



Valley Regional Hospital, Claremont NH



Bellevue Hospital, NY

Original Investigation | Substance Use and Addiction

Barriers and Facilitators to Clinician Readiness to Provide Emergency Department-Initiated Buprenorphine

Barriers to implementation:

- Requirement for a X-waiver
- Lack of experience in treating OUD with buprenorphine
- Ability to link to treatment
- Competing priorities for ED time and resources,
- Misunderstanding and stigma toward patients with OUD

Solutions:

- Training
- Protocols integrated within the EHR
- Targeted feedback to ED staff on patient outcomes

Anyone Can Treat Opioid Withdrawal with Buprenorphine

72-hour rule

Title 21, Code of Federal Regulations, Part 1306.07(b)

Allows to administer (but not prescribe) narcotic drugs for the purpose of relieving acute withdrawal symptoms while the patient's condition is stable.

HHS Expands Access to Treatment for Opioid Use Disorder

January 14, 2021

Eliminates X-Waiver Requirement for DEA-Registered Physicians


Today, the U.S. Department of Health and Human Services is announcing it will publish [Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder - PDF*](#), to expand access to medication-assisted treatment (MAT) by exempting physicians from certain certification requirements needed to prescribe buprenorphine for opioid use disorder (OUD) treatment.

“Eliminates the requirement that physicians with a DEA registration number apply for a separate waiver to prescribe buprenorphine.”

patient's medication should be administered or given to a

patient to ED each day hours

- This 72-hour period cannot be renewed or extended.

 **the x-waiver**

Patient Themes (CTN 0069 & 0079)

- **Need for low-barrier access to treatment in the ED, particularly after overdose**
- **Sense that ED staff did not understand addiction or perceive it as a medical disease**
- **Perception that pain and medical issues were minimized or not taken seriously because of history of addiction**
- **History of feeling stigmatized while receiving ED care, with recent variability noted across EDs**
- **Rare positive experiences with clinicians**

Patient Barriers

- **Inability to obtain life-saving medications at the ED touchpoint***
 - Provider does not have an X-waiver to prescribe
 - Patient not in sufficient withdrawal to obtain ED dosing, and unobserved induction not possible without an X-waivered provider
- **Difficulty filling prescription**
 - Lack of proper identification and/or transportation
 - Required insurance preapproval
- **Vulnerable populations with unstable housing and under/non insured**

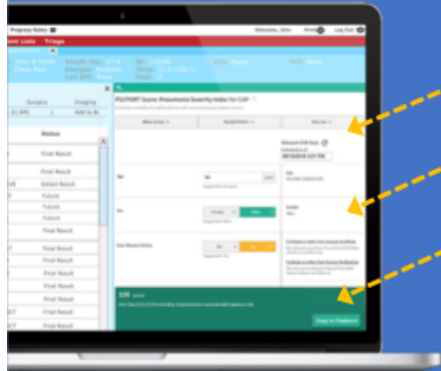
Enhanced Implementation Strategies

Clinical Decision Support



Melnick

MDCalc Connect Early Adopters Program – INVITE ONLY



Embedded in patient chart



Proprietary, next-gen autofills



Dot phrases for easy documentation

Abedin 2020¹ found MDCalc Connect

Among 60 patients, found 57 conditions missed by clinicians

The MDCalc you love, now even better!

Buprenorphine (BUP) Initiation
Do you have a waiver to prescribe Buprenorphine? No Yes

Buprenorphine Treatment Options [ED-initiated Buprenorphine Resources](#)

	Care Pathway #1	Care Pathway #2	Care Pathway #3	Care Pathway #4	Decision Support
	Exit/No BUP	Hold in ED	Start 4 mg BUP (2x)	Start 8 mg BUP	Use these optional tests in any order to help you decide
Does the patient have Opioid Use Disorder?	NO (<4 DSM criteria)	YES (≥4 DSM criteria)	YES (≥4 DSM criteria)	YES (≥4 DSM criteria)	Diagnose OUD using DSM tool
How severe is patient's withdrawal?	None-to-Mild 0-5	None-to-Mild 0-5	Mild-to-Moderate 6-12	Moderate-to-Severe ≥12	Assess Withdrawal using COWS tool
Is patient ready for treatment?	NO	YES	YES	YES	Monitor Readiness using Interview tool
	Select #1	Select #2	Select #3	Select #4	

Don't give buprenorphine if patient is intoxicated or has taken methadone within 72 hours

EMBED App

Buprenorphine Treatment Options

Select from one of the four treatment options below

	Care Pathway #1	Care Pathway #2	Care Pathway #3	Care Pathway #4	Decision Support
	Exit/No BUP	Hold in ED	Start 4 mg BUP (2x)	Start 8 mg BUP	Use these optional tests in any order to help you decide
Does the patient have Opioid Use Disorder?	NO (<3 DSM criteria)	YES (≥3 DSM criteria)	YES (≥3 DSM criteria)	YES (≥3 DSM criteria)	Diagnose OUD using DSM tool
How severe is patient's withdrawal?	None-to-Mild 0-5 DO NOT give buprenorphine	None-to-Mild 0-5 DO NOT give buprenorphine	Mild-to-Moderate 6-12	Moderate-to-Severe ≥12	Assess Withdrawal using COWS tool
Is patient ready for treatment?	NO	YES	YES	YES	Monitor Readiness using Interview tool
	Select #1	Select #2	Select #3	Select #4	

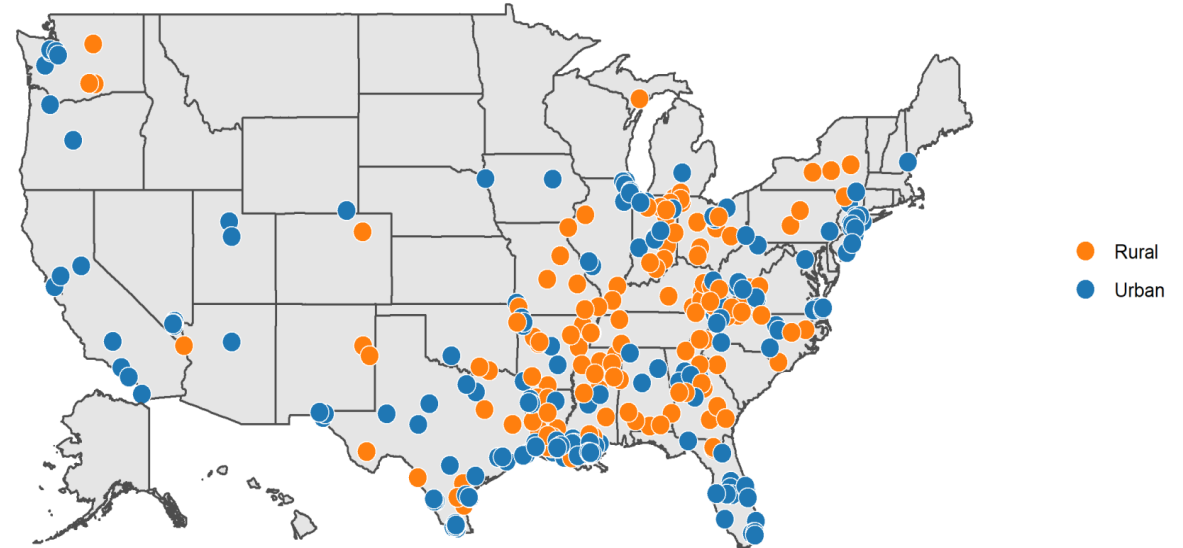
E-QUAL Opioid Initiative:



Mission:

“Engage emergency clinicians and leverage emergency departments to improve clinical outcomes, coordination of care and to reduce costs”

Rapid implementation and assessment of interventions to reduce opioid associated harm through development of a collaborative network that provides structured opioid related quality improvement project, best practices and resources for opioid prescribing and OUD management an multi-component toolkit



Hawk



Venkatesh



Weiner

355 ED sites participated in 2020

380+ ED sites enrolled for 2021

Testing Innovative Treatments

High-dose Buprenorphine Induction for Treatment of Opioid Use Disorder

An accelerated induction procedure achieves therapeutic buprenorphine levels in less 3-4 hours versus the typical 2-3 days; in essence an extended release to potentially increase safety during the crucial gap between ED and follow-up care, particularly in context of COVID limitations



Herring

Retrospective chart review Full 2018 calendar year at single site

- 391 unique patients (579 encounters)
- No cases of respiratory depression or sedation
- 5 cases of precipitated withdrawal had no relation to dose [(4) 8mg]
- Median length of stay was 2.4 hours
- 54 unique providers

High Dose Induction Safe and Effective

CTN 0069-A1

Buprenorphine Formulations and Induction Strategies

ED-Initiated Buprenorphine Validation Network Trial

Hybrid Type 1 Effectiveness-Implementation Design

Implementation

To use implementation facilitation (IF) and training to achieve competence in ED-initiated XR-BUP and SL-BUP inductions in approximately 30 diverse ED sites



Lead Investigators

Effectiveness

To compare the effectiveness of XR-BUP and SL-BUP induction in approximately 2000 patients with untreated OUD in the ED on the primary outcome of engagement in formal addiction treatment at 7 days

Additional Study Components

Ancillary Component

Induction in individuals with minimal to no withdrawal symptoms

(5 sites: UPenn PA , Highland & San Leandro CA, RIH, YNHH CT)

To assess use of XR-BUP in individuals experiencing minimal to no withdrawal (COWS score < 8) in 75 patients

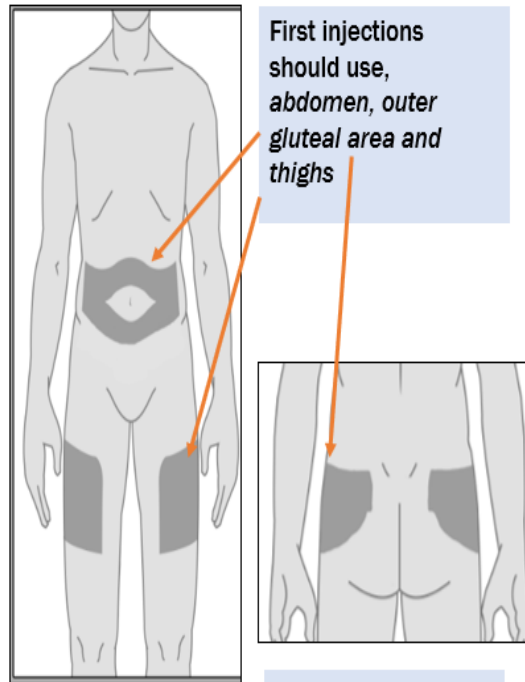
Surveillance techniques –Phenotyping Component

To development and validate EHR opioid-related phenotypes to accurately and automatically characterize opioid-related illnesses

ED INNOVATION

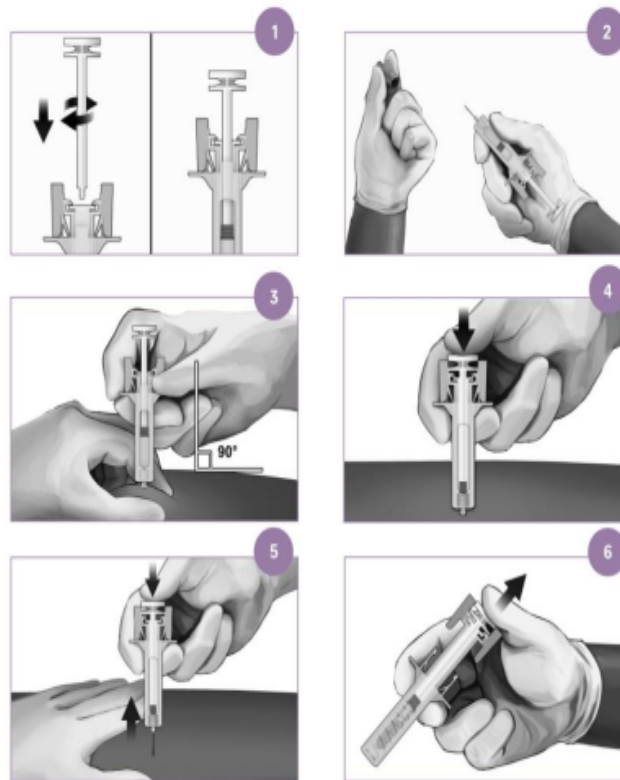
CAM2038 24mg versus 16mg SL-BUP per day

Injection Placement

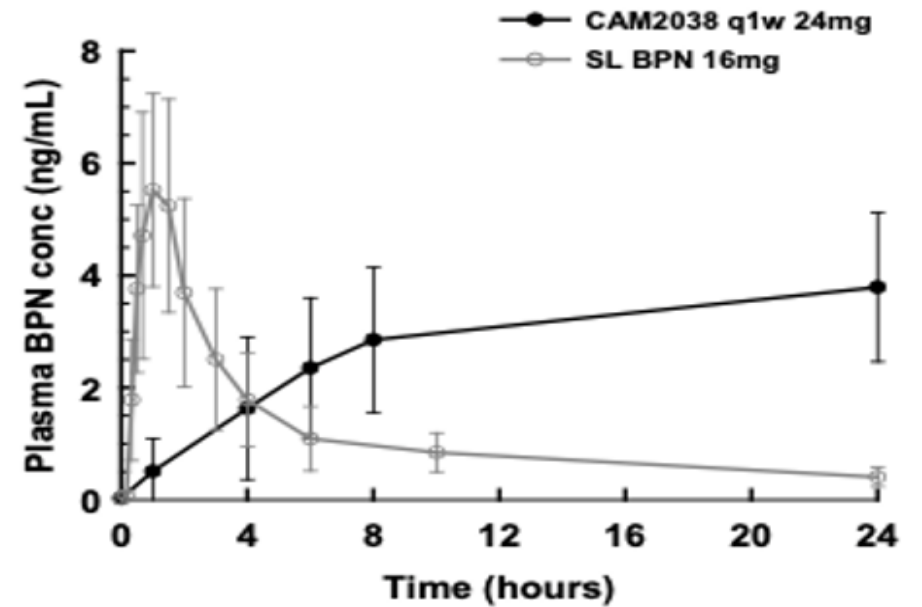


First injections should use, abdomen, outer gluteal area and thighs

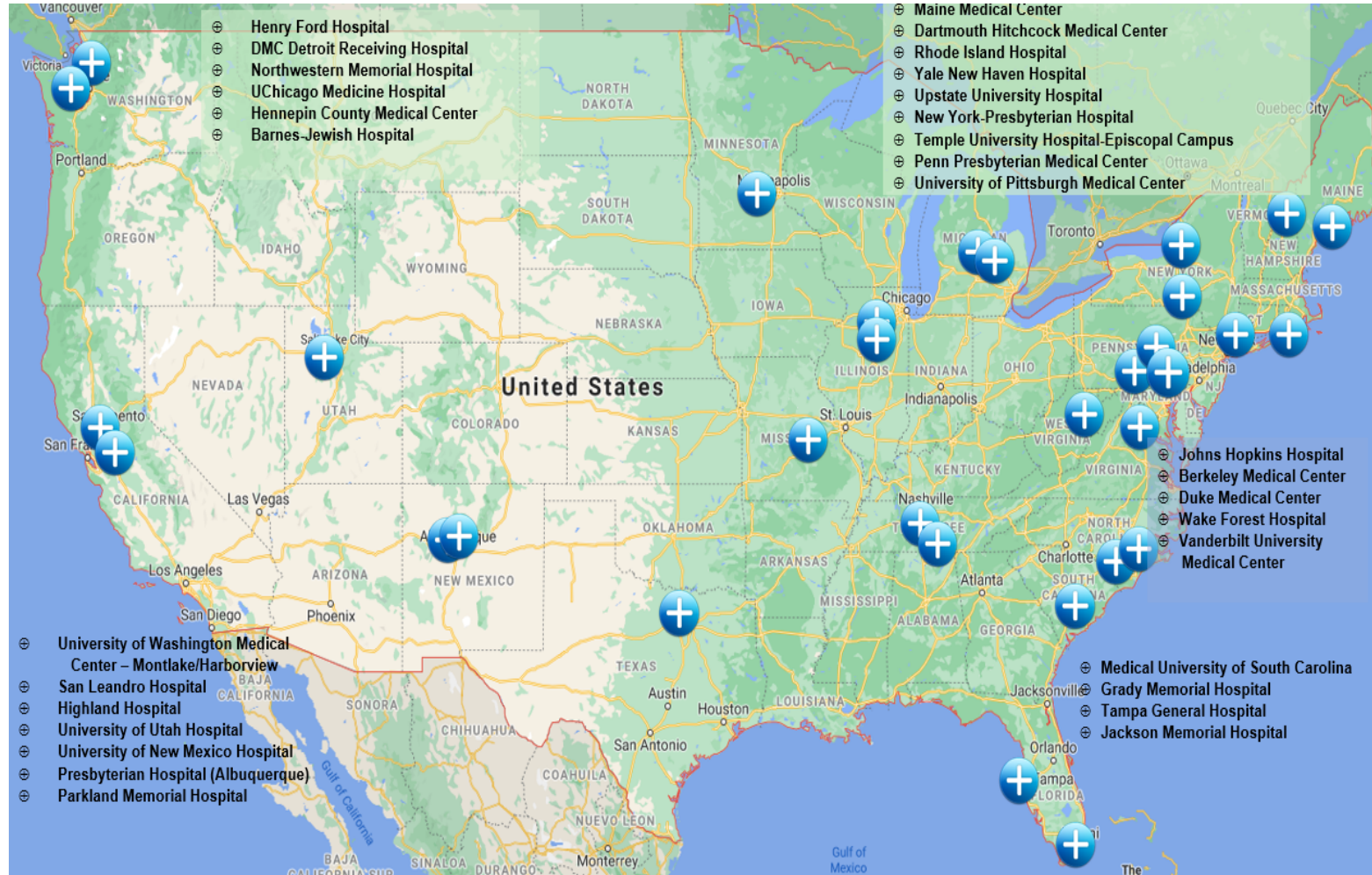
Avoid waistline or within 5 cm of the navel



Pharmacokinetics of XR- & SL- Buprenorphine



ED INNOVATION Sites



RCT
268
enrolled
27 Sites

Ancillary
75
enrolled

Enrollment Complete

We Know...

The Extent of the Problem

Treatment Works

The ED Offers 24/7/365 Day Option to combat the Opioid Crisis

The Consequences of Inaction

The Evidence

We Learned...

How to Break Down Barriers & Increase the Chances Of Success

We Are Investigating...

Implementation strategies, dosing & formulations, surveillance techniques

At the End of the Day.....

Offering ED-initiated buprenorphine
is NOT a choice!!



Need help with pain pills or heroin?

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

Ask here for more information.

Team



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Marek Chawarski PhD	Edward Melnick MD, MHS
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Shara Martel MPH, MS	



...and the ED Health, ED Connect & ED Innovation Investigators

Thank you!!!



Websites:

<https://www.drugabuse.gov/ed-buprenorphine>

<https://medicine.yale.edu/edbup/>