EMBED: Pragmatic Trial of User-Centered Clinical Decision Support to Implement Emergency Department-Initiated Buprenorphine for Opioid Use Disorder

Ted Melnick MD, MHS

Gail D'Onofrio MD, MS
The 24/7/365-day Option
To Fight the Opioid Crisis
US Overdose Deaths

Legend for Drug or Drug Class
- Black: Opioids (T40.0-T40.4, T40.6)
- Blue: Heroin (T40.1)
- Green: Natural & semi-synthetic opioids (T40.2)
- Purple: Methadone (T40.3)
- Brown: Synthetic opioids, excl. methadone (T40.4)
- Pink: Cocaine (T40.5)
- Gray: Psychostimulants with abuse potential (T43.6)

Predicted Value vs. Reported Value

12 Month-ending Period

Number of Deaths
US Overdose Deaths

United States, Mar 2018, Opioids (T40.0-T40.4, T40.6)
- Predicted number of deaths: 48,400
- Reported number of deaths: 46,655
- Percent pending investigation: 0.20
- Percent with drugs specified: 88.6
* Underreported due to incomplete data

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Percent with drugs specified: 88.6
* Underreported due to incomplete data

United States, Mar 2018,
Synthetic opioids, excl. methadone (T40.4)
Predicted number of deaths: 30,051
Reported number of deaths: 28,826
Percent pending investigation: 0.20
Percent with drugs specified: 88.6
* Underreported due to incomplete data
Parishioners Didn’t Suspect Him, Then They Scrolled to Page 631.
A small Catholic church in Pennsylvania reels after its former priest is named in a report on sexual abuse.

He Redefined U.N. in an Era Of Turbulence

An E.R. That Treats Opioid Use as an Emergency

Dr. Andrew Herring giving the withdrawal drug buprenorphine to a homeless patient at Highland Hospital in Oakland, Calif.

Highland, a cluttering big-city hospital where security walls constantly beep as new patients get scanned for weapons, is among a small group of institutions that have started initiating opioid addiction treatment in the E.R. Their aim is to plug a gaping hole in a medical system that consistently fails to provide treatment on demand, or any evidence-based treatment at all, even as more than two million Americans suffer from opioid addiction. According to the latest estimates, overdoses involving opioids killed nearly 50,000 people last year.

By ABBY GOODNOUGH
OAKLAND, Calif. — Every year, thousands of people addicted to opioids show up at hospital emergency rooms in withdrawal so agonizing it leaves them moaning and writhing on the floor.

The Treatment Gap
Help on Demand

Usually, they’re given medicines that help with vomiting or diarrhea and sent on their way, maybe with a few numbers to call about treatment.

When Rhonda Hauswirth arrived at the Highland Hospital E.R. here, retching and shaking violently after a day and a half without heroin, something very different happened. She was offered a dose of buprenorphine on the spot. One of three medications approved in the United States to treat opioid addiction, it works by easing withdrawal symptoms and cravings. The tablet dissolved under her tongue while she slumped in a plastic chair, her long red hair obscuring her ashen face.

Soon, the shakes stopped. “I could focus a little more. I could see straight,” said Ms. Hauswirth, 40. “I’d never heard of anyone going to an emergency room to do that.”

Continued on Page 20
Why Focus on the ED?

Because that’s where the patients are!

July 2016 – September 2017

30% Visits for Opioid Overdose

MMWR, March 9, 2018
EDs and Emergency Physicians can...

- Identify patients with opioid use disorder
- Initiate treatment
  - buprenorphine
  - overdose education & naloxone distribution
- Link to continued opioid agonist treatment & preventive services
What is the Evidence?
A Randomized Trial of ED-Initiated Interventions for Opioid Dependence

D'Onofrio, G., O'Connor, P.G., Pantalon, M.V., Chawarski, M.C., Busch, S.H., Owens, P.H., Bernstein, S.L. and Fiellin, D.A.

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 screening, brief intervention, and facilitated referral, and 114 to screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral to primary care for 10-week follow-up (buprenorphine).

JAMA Report Video and Author Video Interview at jama.com
CME Quiz at jamanetworkme.com/CME Questions
MAT: 2x More Likely to be Engaged in Addiction Treatment at 30 Days

- Referral
- Brief Intervention
- Buprenorphine

P < 0.001
Medication for Opioid Use Disorder


LaRochelle. *Annals of IM* 2018
The latest research shows that we really should do something with all this research
NIDA Clinical Trials Network: Opioid Use Disorder in the ED
Project ED Health (CTN-0069)

**Design:** Hybrid Type 3 Effectiveness-Implementation Study
Clinical Trials Network: Initiating Extended Release Buprenorphine for OUD in Low Resourced, High Intensity EDs

Design: Hybrid Type 3 Effectiveness - Implementation Study
EMBED: Pragmatic trial of user-centered clinical decision support to implement Emergency department-initiated Buprenorphine for opioid use Disorder

UG3 AT009851-01
UG3-UH3
Diffusion of Innovations

- Innovators: 2.5%
- Early adopters: 13.5%
- Early majority: 34.0%
- Late majority: 34.0%
- Laggards: 16.0%

Mean - 2 SD: Opinion leaders adopt at this time
Mean - 1 SD: Early adopters
Mean: Early majority
Mean + 1 SD: Late majority

References:
Rogers. Diffusion of Innovations 1962
Gladwell. Tipping Point 2000
Dearing & Cox. Health Affairs Feb 2018
Diffusion of Innovations

Parameters of a typical diffusion study
Discontinuance of an innovation
Competing or complementary innovations

Most innovations fail to diffuse

Time

Proportion or number of adopters

- Rogers. *Diffusion of Innovations* 1962
- Gladwell. *Tipping Point* 2000
- Dearing & Cox. *Health Affairs* Feb 2018
Background: HIT

- Poor health IT (HIT) usability is major source of frustration with clinicians
- Electronic health record (EHR) usability is a fundamental barrier to implementation of evidence-based medicine
- IT should be designed to meet user needs
- User-centered design
  - streamline workflows
  - address barriers to adoption
  - embed ED-initiated BUP into routine ED care
  - to optimize adoption, dissemination, implementation, and scalability
Aims: UG3

• **UG3 Aim 1.** Develop a pragmatic, user-centered CDS for ED-initiated BUP and referral for MAT in ED patients with OUD which will automatically identify and facilitate management of potentially eligible patients.

• **UG3 Aim 2.** Establish the infrastructure for the proposed trial.
1. Compare the effectiveness of user-centered CDS for BUP to usual care on outcomes in ED patients with OUD.

2. Disseminate the EMBED intervention nationally
Teams and People

**MPI**
- Ted Melnick, MD, MHS
- Gail D’Onofrio, MD, MS

**Design**
- Matt Maleska
- Jessica Ray, PhD

**Technology**
- Allen Hsiao, MD
- Yauheni Solad, MD, MHS
- Hyung Paek, MD, MSEE
- Cynthia Brandt, MD, MPH

**Data coordination**
- Jim Dziura, PhD, MPH
- Lilly Katsovich, MBA
- Charles Lu

**Project Coordinator**
- Shara Martel MPH, MS

**External collaborators**
- UNC
  - Tim Platts-Mills, MD, MSc
  - Mehul Patel, PhD
- Mayo
  - Molly Jeffery, PhD
- UAB
  - Erik Hess, MD, MSc
  - Jim Galbraith, MD
- Also: UC Davis
  - Josh Elder MD, MPH, MHS
- Colorado
  - Jason Hoppe, DO

Within each system
- Medical director
- Clinical champions
- IT leaders
- MAT site contacts
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<th>YEAR 4</th>
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**USER-CENTERED CDS DEVELOPMENT**
- Workflow Analysis; Initial Prototype Development
- Usability & Field Testing
- IT Build w/Local EHR Integration; Beta-Testing

**PLANNING PHASE**
- Finalize Participating Sites & Protocols
- Finalize Enrollment Targets
- Finalize Data Collection Methods; IRB Approvals

**TRIAL PHASE**
- Complete EHR Integration at All Sites
- Clinical Enrollment with Ongoing Data Management
- Local Formative Process Evaluation during Implementation
- Wide Scale Dissemination
- Final Data Analysis & Publication

**NIH Collaboratory**
Rethinking Clinical Trials®
Health Care Systems Research Collaboratory
Sites

- pilot sites
- confirmed trial sites
- potential trial sites

Yale

University of Pennsylvania

UC Davis
University of California

The University of Alabama

Health Care Systems Research Collaborative
User-centered design progress

• Currently 25-30 minute workflow for an addiction counselor
  • Diagnostic criteria
  • Withdrawal assessment
  • Readiness for treatment
  • Treatment initiation
  • Referral (detailed form completed and faxed to referral center)
• Need to embed this in ED clinician busy, dynamic, interruptive workflow
• Goal to identify, treat, and refer in 2-5 minutes while
  • Minimize interruptions & additional cognitive load
  • Allow flexibility for initiation of tool, which parts to use, clinicians training for BUP use, novice-to-expert tool use
  • 30 mouse clicks down to as little as 1
Buprenorphine Integration Pathway

1. **ED presentation**
   - Seeking Treatment
   - Screen Positive
   - Complication of Drug Use
     - Withdrawal
     - Overdose
     - Infection
   - Identified during the course of the visit

2. **Assess**
   - Identification of OUD based on DSM-5
   - Clinical Opioid withdrawal Scale (COWS)

3. **Treat**
   - BNI Buprenorphine algorithm

4. **Discharge & Refer to Treatment**
ED-Initiated Buprenorphine

**Diagnosis of Moderate to Severe Opioid Use Disorder**

Assess for opioid type and last use
- Patients taking methadone may have withdrawal reactions to buprenorphine up to 72 hours after last use
- Consider consultation before starting buprenorphine in these patients

**COWS**

- (0-7) none - mild withdrawal
- (≥8) mild - severe withdrawal

**Dosing:**
- None in ED
- 4-8mg SL

**Waivered provider able to prescribe buprenorphine?**
- Yes
  - Unobserved buprenorphine induction and referral for ongoing treatment
- No
  - Referral for ongoing treatment

**Prescription**
- 16mg dosing for each day until appointment for ongoing treatment

**Consider return to the ED for 2 days of 16mg dosing (72-hour rule)**
- Referral for ongoing treatment

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Notes:

*Clinical Opioid Withdrawal Scale (COWS) ≥ 13 (Moderate Severe) consider starting with 8 mg buprenorphine or buprenorphine/naloxone SL

** Patient remains in moderate withdrawal may consider adding additional 4mg and observation for 60 minutes

Warm hand-offs with specific time & date to opioid treatment providers/programs within 24-72 hours whenever possible

All patients should be educated regarding dangers of benzodiazepine and alcohol co-use

Ancillary medication treatments with buprenorphine induction are not needed
### Buprenorphine Treatment Options

**Buprenorphine (BUP) Initiation**

Do you have a waiver to prescribe Buprenorphine?

- [ ] No
- [ ] Yes

Select from one of the four treatment options below

<table>
<thead>
<tr>
<th>Care Pathway #1</th>
<th>Care Pathway #2</th>
<th>Care Pathway #3</th>
<th>Care Pathway #4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exit / No BUP</strong></td>
<td><strong>Hold in ED</strong></td>
<td><strong>Start 4 mg BUP (2x)</strong></td>
<td><strong>Start 8 mg BUP</strong></td>
</tr>
</tbody>
</table>

#### Decision Support

- **Does the patient have Opioid Use Disorder?**
  - No (≤3 DSM Criteria)
  - Yes (≥3 DSM Criteria)

- **How severe is the patient’s withdrawal?**
  - None-to-Mild
    - < 8
      - DO NOT give if intoxicated
  - Mild-to-Moderate
    - 8 - 13
  - Moderate-to-Severe
    - ≥13

- **Is the patient ready to start treatment?**
  - NO
  - YES

Use these optional tools in any order to help you decide:

- Diagnose OUD using DSM tool
- Assess withdrawal using COWS tool
- Motivate Readiness using interview tool

Health Care Systems Research Collaboratory
DSM 5 - Criteria for Opioid Use Disorder (OUD)

Ask the patient the following questions about his/her use of opioids in the past 12 months to determine a diagnosis:

Select all that apply:

1. Have you found that when you started using opioids you ended up taking more than you intended to?
2. Have you wanted to stop or cut down on using opioids?
3. Have you spent a lot of time getting or using opioids?
4. Have you had a strong desire or urge to use opioids?
5. Have you missed work or school or often arrived late because you were intoxicated, high, or recovering from the night before?
6. Has your use of opioids caused problems with other people such as with family members, friends, or people at work?
7. Have you had to give up or spend less time working, enjoying hobbies, or being with others because of your drug use?
8. Have you ever gotten high before doing something that requires coordination or concentration like driving, boating, climbing a ladder, or operating heavy machinery?
9. Have you continued to use even though you knew that opioids caused you problems like making you depressed, anxious, agitated or irritable?
10. Have you found you needed to use much more opioids to get the same effect that you did when you first started taking it?
11. When you reduced or stopped using opioids, did you have withdrawal symptoms or felt sick when you cut down or stopped using? (aches, shaking, fever, weakness, diarrhea, nausea, sweating, heart pounding, difficulty sleeping, or feel agitated, anxious, irritable, or depressed?)

Patients with 3 or more OUD symptoms meet the criteria for BUP:

Mild (2-3) Moderate (4-5) Severe (6+)

YES - Meets Criteria

NO - Does Not Meet Criteria

Return to treatment options

Exit application
<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Resting Pulse Rate</td>
<td>80 or below (0)</td>
<td>81 - 100 (1)</td>
</tr>
<tr>
<td>2. Restlessness</td>
<td>Able to sit still (0)</td>
<td>Some difficulty sitting still (1)</td>
</tr>
<tr>
<td>3. Anxiety or irritability</td>
<td>None (0)</td>
<td>Increasing amounts (1)</td>
</tr>
<tr>
<td>4. Yawning</td>
<td>No yawning (0)</td>
<td>1 or 2 times/assessment (1)</td>
</tr>
<tr>
<td>5. Pupil Size</td>
<td>Normal (0)</td>
<td>Possibly larger (1)</td>
</tr>
<tr>
<td>6. Runny nose or tearing</td>
<td>Not present (0)</td>
<td>Stiffness/moist eyes (1)</td>
</tr>
<tr>
<td>7. Tremor</td>
<td>No tremor (0)</td>
<td>Felt - not observed (1)</td>
</tr>
<tr>
<td>8. Sweating</td>
<td>No report (0)</td>
<td>Subjective report (1)</td>
</tr>
<tr>
<td>9. Gooseflesh skin</td>
<td>Skin is smooth (0)</td>
<td>Piloerection/hairs standing (3)</td>
</tr>
<tr>
<td>10. Bone or joint pain</td>
<td>Not present (0)</td>
<td>Mild discomfort (1)</td>
</tr>
<tr>
<td>11. GI upset</td>
<td>No symptoms (0)</td>
<td>Stomach cramps (1)</td>
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</tbody>
</table>

Return to treatment options

Score: 25

< 8 Moderate-to-Severe
A Guide for Patients Beginning Buprenorphine Treatment at Home

Before you begin you want to feel very sick from your withdrawal symptoms

It should be at least...
- 12 hours since you used heroin/fentanyl
- 12 hours since snorted pain pills (Oxycontin)
- 16 hours since you swallowed pain pills
- 48-72 hours since you used methadone

You should feel at least three of these symptoms...
- Restlessness
- Heavy yawning
- Enlarged pupils
- Runny nose
- Body aches
- Tremors/twitching
- Chills or sweating
- Anxious or irritable
- Goose pimples
- Stomach cramps, nausea, vomiting or diarrhea

Once you are ready, follow these instructions to start the medication

DAY 1: 8-12mg of buprenorphine
Most people feel better the first day after 8-12mg. (Dosing depends on how early on the first day you started)

Step 1.
Take the first dose
- 4mg
- Wait 45 minutes
- Put the tablet or strip under your tongue
- Keep it there until fully dissolved (about 15 min.)
- Do NOT eat or drink at this time
- Do NOT swallow the medicine

Step 2.
Still feel sick? Take next dose
- 4mg
- Wait 6 hours
- Most people feel better after two doses = 8mg

Step 3.
Still uncomfortable? Take last dose
- Stop
- Stop after this dose
- Do not exceed 12mg on Day 1

DAY 2: 16mg of buprenorphine
Take one 16mg dose
Most people feel better with a 16mg dose

Repeat this dose until your next follow-up appointment

If you develop worsening symptoms while starting buprenorphine before your scheduled outpatient appointment return to the emergency department.
Thank You

Ted Melnick @Ted_Melnick
Gail D’Onofrio @DonofrioGail

Websites
https://drugabuse.gov/ed-buprenorphine
https://medicine.yale.edu/edbup/