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

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Informatics Fellowship Director

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Professor
Chair & Physician-in-Chief

NIH Collaboratory Steering Committee
Bethesda, MD
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Overview

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- EHR Phenotyping
- EHR Integration
- MOUD Referral Stakeholder Needs Assessment
- Study Design Change
- Site/System Recruitment
- Ethics/Regulatory
- Barriers
- Data Sharing
Teams and People

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  - Gail D’Onofrio, MD, MS

- **Design**
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  - Jessica Ray, PhD

- **Technology**
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  - Hyung Paek, MD, MSEE
  - Cynthia Brandt, MD, MPH
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- **Data Coordination**
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  - Charles Lu
  - Lilly Katsovich, MBA
  - Haseena Rajeevan, PhD
  - David Chartash, PhD
  - Molly Jeffery, PhD (Mayo)

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

- **External collaborators**
  - **Baystate**: William Soares, MD, MS, Christian Lagier Haiping Li
  - **Colorado**: Jason Hoppe, DO, Sean Michael, MD
  - Each site within each system
    - Medical director
    - Clinical champions
    - MOUD referral sites

- **Summer medical students**
  - Osama Ahmed
  - Jodi Mao
  - Wesley Holland
Background: OUD

- Opioid use disorder (OUD): Dependence on opioids or heroin
- Major public health problem: 3 million Americans have or have had OUD
- Deaths 5.9 x higher than 1999 (47,000 in 2017)

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018
Background: MAT

- Emergency department (ED)
  - may be only access to care for many people with opioid addiction (420,000 visits in 2011)
  - often at vulnerable time: overdose, withdrawal, seeking treatment, comorbid conditions
  - ED-initiated BUP with referral for ongoing MOUD doubles rate of engagement in addiction treatment
- 12 months after ED visit, only 1/3 on opioid agonist treatment; large survival benefit
- How can we EMBED this life-saving treatment into routine emergency care?
Background: Intervention & Outcomes

- **Setting**: 20 Emergency Departments (EDs) across 5 healthcare systems

- **Intervention**: The intervention consists of a user-friendly, integrated IT intervention to support:
  1. Evaluation for OUD
  2. Assessment of withdrawal severity
  3. Motivation of patient willingness to start treatment
  4. Initiating buprenorphine
  5. Documentation of the care process
  6. Referral for ongoing treatment

- **Primary Outcome**: Initiation of BUP in the ED (administered and/or prescribed)
Background: UG3 Aims

- **UG3 Aim 1.** Develop a pragmatic, user-centered CDS for ED-initiated BUP and referral for MOUD 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.
User Centered Design:
To simplify the process of initiating BUP in the ED

From a complicated algorithm ...  

... to a simple, automated application
Clinicians continue in their current Epic workflow
2. Click the ‘EMBED’ button in the patient’s chart to launch the app.
App offers care pathways & patient assessment tools with the flexibility to use just the parts you need.
Other members of the care team can also complete patient assessments.

Diagnose OUD

Buprenorphine (BUP) Initiation

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:

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 other important activities because you were intoxicated, high, or recovering from the night before?

and more...

Select all that apply.

YES - Meets Criteria

NO - Does Not Meet Criteria

Return to treatment options

Exit application
Launching a care pathway automatically generates the appropriate documentation, orders, and referral in Epic.
Orders appear in an Epic ‘Shopping Cart’ that allows for easy de/selection
After signing the orders, you can continue to use Epic.
EHR Phenotyping

Derived and validated an electronic health record (EHR)-based computable phenotype to identify ED patients with OUD using physician chart review as a reference standard.

<table>
<thead>
<tr>
<th>Test Result</th>
<th>Reviewers +</th>
<th>Reviewers -</th>
<th>Predictive Value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Present: Reference Standard</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Algorithm 1 (internal validation)</td>
<td></td>
<td></td>
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<tr>
<td>Phenotype +</td>
<td>48</td>
<td>2</td>
<td>PPV 0.96 (0.863-0.995)</td>
</tr>
<tr>
<td>Phenotype -</td>
<td>1</td>
<td>49</td>
<td>NPV 0.98 (0.893-0.999)</td>
</tr>
<tr>
<td>Algorithm 2 (internal validation)</td>
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</tr>
<tr>
<td>Phenotype +</td>
<td>20</td>
<td>5</td>
<td>PPV 0.8 (0.593-0.932)</td>
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<tr>
<td>Phenotype -</td>
<td>0</td>
<td>25</td>
<td>NPV 1.0 (0.863-1)</td>
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<tr>
<td>Combined Phenotype (external validation)</td>
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<tr>
<td>Phenotype +</td>
<td>53</td>
<td>3</td>
<td>PPV 0.95 (0.851-0.989)</td>
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<tr>
<td>Phenotype -</td>
<td>4</td>
<td>46</td>
<td>NPV 0.92</td>
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</tbody>
</table>
EHR integration: Flexibility and Scalability Challenges

- Web application allows for more flexible user interface across sites and vendors.
- Fully integrated pilot is live at main Yale site.
- Planned for central hosting solution to allow future scaling.
- Due to security issues, all but one health system preferred local hosting.
- Standards for communication between web application not fully mature (SMART on FHIR can’t...
MOUD Referral Stakeholder Needs Assessment

- Performed a needs assessment of stakeholders involved in referral process

- IT solutions must address discordant priorities of ED (rapid and flexible referral process) and community sites offering MOUD (referrals minimize variability and overbooking).

- To prevent drop-out in the referral cascade, need for increased availability and accessibility to MOUD on demand with protected communication channels between EDs and community providers of MOUD.
<table>
<thead>
<tr>
<th>Feature</th>
<th>Stepped Wedge</th>
<th>Group Randomized</th>
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</thead>
<tbody>
<tr>
<td><strong>Length of trial</strong></td>
<td>Longer trial period due to baseline and post-implementation phases</td>
<td>Shorter trial period</td>
</tr>
<tr>
<td><strong>Control for temporal trends</strong></td>
<td>Weaker, more vulnerable due to longer trial period</td>
<td>Stronger, due to shorter trial period</td>
</tr>
<tr>
<td><strong>Control of heterogeneity by site</strong></td>
<td>Yes, sites serve as their own control</td>
<td>Not as good, compensate for this weakness by employing constrained randomization</td>
</tr>
<tr>
<td><strong>All sites get intervention</strong></td>
<td>Yes</td>
<td>No, but can offer at end of shorter trial</td>
</tr>
<tr>
<td><strong>Number of clusters (ED sites)</strong></td>
<td>Fewer</td>
<td>More (necessitating this supplement request)</td>
</tr>
<tr>
<td><strong>Go-live of IT intervention</strong></td>
<td>Staggered, later implementations can learn for issues in earlier ones</td>
<td>Synchronized, requires more lead time and coordination</td>
</tr>
<tr>
<td><strong>Additional time for IT build, pilot testing, and dissemination</strong></td>
<td>No, due to longer trial period</td>
<td>Yes, shorter trial period permits additional time for IT build and dissemination in later UH3 years</td>
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</table>
Study Design Change

- Increasing the CDS build and integration period allowed for the switch to a group randomized CRT
- Better control of temporal trends
- Shorter overall trial period
- Larger number of EDs required to maintain power
- Covariate constrained randomization used for balance across sites/clusters
- Offer intervention to all EDs at end of trial
Site / System Recruitment

- Multiple sites in same system on same EHR build
  - No two EHR builds are the same
  - Each separate EHR integration requires additive costs
  - Recruiting multiple sites in the same system is more cost-effective
- Serve a population with a high rate of OUD
- Robust referral network in surrounding community for ongoing MOUD
- Initial willingness/traction to adopt ED-initiated BUP in routine emergency care
- Investigator at main academic site with expertise in ED opioid research capable of coordinating the trial in their system
Ethics / Regulatory

- Benefited from expert guidance of Collaboratory core
- Protocol approved by Western IRB (WIRB)
- Waiver of informed consent under the Common Rule 45 CFR 46.116
- Patients:
  - Have no identifiers
  - Are not the target of the intervention (minimal risk given life-saving best practices)
  - Do not interact with study directly – retrospective EHR data collection
- Control sites can still follow best practices
  - Patients can request MOUD
  - Physicians retain control over their practice
**UH3 Aims**

- **UH3 Aim 1.** Compare the effectiveness of user-centered CDS for BUP to usual care on outcomes in ED patients with OUD.

- **NEW UH3 Aim 2.** Disseminate the EMBED intervention nationally.

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### EMBED Timeline

<table>
<thead>
<tr>
<th></th>
<th>YEAR 1</th>
<th>YEAR 2</th>
<th>YEAR 3</th>
<th>YEAR 4</th>
<th>YEAR 5</th>
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<tbody>
<tr>
<td><strong>USER-CENTERED CDS DEVELOPMENT</strong></td>
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<tr>
<td>Workflow Analysis; Initial Prototype Development</td>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
<td>Q4</td>
<td>Q1</td>
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<tr>
<td>Usability &amp; Field Testing</td>
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<tr>
<td>IT Build w/Local EHR Integration; Beta-Testing</td>
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<tr>
<td><strong>PLANNING PHASE</strong></td>
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<tr>
<td>Finalize Participating Sites &amp; Protocols</td>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
<td>Q4</td>
<td>Q1</td>
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<tr>
<td>Finalize Enrollment Targets</td>
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<tr>
<td>Finalize Data Collection Methods; IRB Approvals</td>
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<tr>
<td><strong>TRIAL PHASE</strong></td>
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<tr>
<td>Complete EHR Integration at All Sites</td>
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<td>Clinical Enrollment with Ongoing Data Management</td>
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<td>Local Formative Process Evaluation during Implementation</td>
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<tr>
<td>Wide Scale Dissemination</td>
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<tr>
<td>Final Data Analysis &amp; Publication</td>
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</table>
## Barriers Scorecard

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Level of Difficulty*</th>
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<tbody>
<tr>
<td>Enrollment and engagement of patients/subjects</td>
<td>x</td>
</tr>
<tr>
<td>Engagement of clinicians and health systems</td>
<td>x</td>
</tr>
<tr>
<td>Data collection and merging datasets</td>
<td>x</td>
</tr>
<tr>
<td>Regulatory issues (IRBs and consent)</td>
<td>x</td>
</tr>
<tr>
<td>Stability of control intervention</td>
<td>x</td>
</tr>
<tr>
<td>Implementing/delivering intervention across healthcare organizations</td>
<td>x</td>
</tr>
</tbody>
</table>

*Your best guess!  
1 = little difficulty  
5 = extreme difficulty
Date Sharing

- **What is your current data sharing plan and do you foresee any obstacles?**
  - Follow NIH guidelines & HIPAA compliant
  - Studying provider behavior so need to de-identify provider & sites too
  - Mindful of rights and privacy of participants given vulnerability of OUD

- **What information did the IRB require about how the data would be shared beyond the study in order to waive informed consent, if applicable?**
  - No patient identifiers
  - Identifiers confidential, used only for internal data integrity, not shared with Yale, only shared with subject permission or as required by law

- **What data you are planning to share from your project (individual-level data, group-level data, specific variables/outcomes, etc.)?**
  - Primary outcome: rate of BUP use in ED (clinician-level)
  - Secondary outcomes: related to success of referral to MAT
Thank you.

Questions?

Edward.Melnick@yale.edu  Gail.Donofrio@yale.edu
@Ted_Melnick            @DonofrioGail
A research study to help clinicians initiate buprenorphine in the ED

This hospital is taking part in a NIDA-funded implementation trial to increase the uptake of a computerized clinical decision support intervention to help clinicians treat opioid use disorder (OUD).

**ED-initiated Buprenorphine**

As patients with OUD often seek medical care in EDs, the ED visit provides an opportunity to access care when patients may be more motivated to start treatment. Buprenorphine/naloxone (BUP) is a treatment for OUD that decreases withdrawal, craving, and opioid use and that can be prescribed by appropriately trained physicians. Among OUD patients, ED-initiated BUP treatment with referral for ongoing medication for OUD doubles the rate of engagement in formal addiction treatment.

**How to start buprenorphine in the ED for patients with a 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**
  - **None** - Mild Withdrawal (0-7 COWS)
  - **Dosing:** None in ED
  - **For Waivered Providers:** Unobserved buprenorphine induction and referral for ongoing treatment
  - **For Non-waivered Providers:** Referral for ongoing treatment
  - **Mild - Severe Withdrawal (8+ COWS)**
  - **Dosing:** 8mg SL
  - **Observe for 45-60 min**
  - **No adverse reactions**
  - **If initial dose 4mg SL, repeat 4mg SL for total 8mg**
  - **Observe**

- **All patients should be educated regarding dangers of benzodiazepine and alcohol co-use.**
  - **Ancillary medication treatments with buprenorphine induction are not needed.**

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**A research study to improve patient care for opioid use disorder**

**Background**

This hospital is identifying ways to improve care by encouraging health care practitioners in this hospital to follow evidence-based practices.

This Emergency Department is a part of a National Institute for Drug Abuse (NIDA) funded project that is being done in collaboration with Yale University called EMBED (EMergency department-initiated Buprenorphine for opioid use Disorder)

This study will be carried out in approximately 20 emergency departments (ED) across approximately five healthcare systems over 18 months.

**Purpose**

The purpose of this project is to help clinicians give the best care to patients with opioid use disorder. If you meet the criteria for opioid use disorder, you may benefit from the study as additional resources on the best practices to treat opioid use disorder have been made available to your clinician.

As part of this project, the study team will be looking at the information from this visit to see how the resources given helped your clinician to treat opioid use disorder. The study team will not collect more data or do any extra tests, than they would for any other visit.

**Privacy**

The privacy of this information is important, and we will not collect any identifying information about you. Specifically, we will not collect your name, medical record number, date of birth, address phone number, or any other private information from your visit that could be linked back to you.

**Questions**

If you have any other questions about this research project, please call 203-737-2810 and a member of the study team will call you back.

EMBED: Pragmatic trial of user-centered clinical decision support to implement EMergency department initiated Buprenorphine for opioid use Disorder; (IRB Protocol Number: #)