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

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Disclosures

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The EMBED Team
Evolution of Drivers of Overdose Deaths, All Ages

Analgesics → Heroin → Fentanyl → Stimulants

69,710 from Opioids (Prescription and Illicit)

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). Slide Created by Nora Volkow

2020 Data
93,331 OD Death
↑ 29.4%
MOUD – BUP & Gap in OUD Care

- **Medications for OUD (MOUD)**
  1. Methadone
  2. Buprenorphine
  3. Naltrexone

- Buprenorphine/naloxone (BUP), partial opioid agonist combined with an antagonist
  - Safe, Effective
  - Decreases withdrawal, craving
  - Decreases opioid use and overdose events
  - Increase in retention in treatment

- Only **28.5%** (1.2 million) - receive MOUD - with either buprenorphine, methadone, or naltrexone

(SAMSHA, 2018 National Survey on Drug Use and Health)
Evidence for BUP in the ED

2015 RCT by D’Onofrio. et al. at Yale EM

Engagement in Treatment at 30 days

- BUP – safe to administer in the ED;

- With BUP in ED: 2x More likely to remain engaged in Addiction Treatment at 30 Days (78% vs. 37%) (p < 0.001)
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).

Rhee TG, D’Onofrio G, Fiellin DA. JAMA Network Open. 2020
Barriers & Facilitators to Initiating BUP in the ED

**BARRIERS**
- Stigma – addiction
- Physician readiness
- Concerns – med diversion
- ED too busy
- Patients keep coming back
- Complex protocol
- Knowledge gap
- Poor usability of HIT

**FACILITATORS**
- Physician willingness
- Proper learning tool

When it comes to opioid use disorder (OUD), however, there has been a lot of reluctance among emergency physicians to initiate treatment with buprenorphine....

- Web-based
- EHR Integrated
- Clinical Decision Support System
How EMBED Works
User Centered Design: To Simplify the Process

From a complex, multi-step process

ED-Initiated Buprenorphine

...to a simple, automated application

Simple & automatic 5 min
1) Diagnosing OUD
2) Assessing withdrawal severity (COWS)
3) Motivating patients to accept treatment
4) Automating EHR workflow including –
   - clinical and after visit documentation,
   - order entry
   - prescribing
   - Community referral

Complicated Multi-step workflow
25-30 min
Integrated into EHR workflow
Launch EMBED by clicking on its tab in the Navigation Bar.
Buprenorphine Treatment Options

Does the patient have Opioid Use Disorder?

- No

Is patient ready for treatment?

- No

How severe is patient’s withdrawal?

- <6
- 6-12
- >12

COWS:

- <6
- 6-12
- >12

Optional Decision Support

Care Pathway #1
Does not meet criteria.

Care Pathway #2
Hold in CD

Care Pathway #3
Start with BUP [ ]

Care Pathway #4
Start with BUP

Do you have a waiver to prescribe Buprenorphine?

- Yes
- No
Buprenorphine Treatment Options

Does the patient have Opioid Use Disorder?
- No
- Yes

Is patient ready for treatment?
- No
- Yes

How severe is patient’s withdrawal?
- None
- Mild
- Moderate
- Severe

Optional Decision Support

Evaluation of Opioid Use Disorder based on DSM 5

ODD Evaluation Score:

For each item, select the appropriate description of the patient’s signs of symptoms (points per symptom).

- Have you found that when you started using opioids, you ended up taking more than you intended to?
- Have you wanted to stop or cut down on using opioids?
- Have you spent a lot of time getting or using opioids?
- Have you had a strong desire or urge to use opioids?
- Have you missed work or school or been unable to function at work because you were intoxicated, high, or recovering from the night before?
- Have you used opioids to treat or prevent withdrawal or other physical symptoms?
- Have you had to give up or spend less time working, enjoying hobbies, or being with others because of your drug use?
- Have you ever gotten high before doing something that requires coordination or concentration like driving, climbing a ladder, or operating heavy machinery?
- Have you continued to use even though you knew that opioids caused your problems like making you depressed, anxious, agitated or irritable?
- Have you found you needed to use much more opioids to get the same effect that you did when you first started taking it?
- When you reduced or stopped using opioids, did you have withdrawal symptoms or felt sick when you cut down or stopped using? (sweats, trembling, dizziness, nausea, vomiting, heart palpitations, abdominal pain, muscle pain, or tremors?)
Buprenorphine Treatment Options

Does the patient have Opioid Use Disorder?

- Yes
- No

Is patient ready for treatment?

- No

How severe is patient’s withdrawal?

- 0-12
- 13-24

Evaluation of Opioid Use Disorder based on DSM 5:

- OUD Evaluation Score: 4

For each item, select the appropriate description of the patient's signs of symptoms (points per symptom):

- Have you found that when you started using opioids you ended up taking more than you intended to?
- Have you wanted to stop or cut down on using opioids?
- Have you spent a lot of time getting or using opioids?
- Have you used opioids despite telling family members friends, people at work?
- Have you had to give up or spend less time working, enjoying hobbies, or being with others because of your drug use?
- Have you ever gotten high before doing something that requires coordination or concentration like driving, climbing a ladder, or operating heavy machinery?
- Have you continued to use even though you knew that opioids caused your problems like making you depressed, anxious, agitated or irritable?
- Have you found you needed to use much more opioids to get the same effect that you did when you first started taking it?
- 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 rate increase, or had unexplained weight or dimensional?)

BACK
Buprenorphine Treatment Options

Do you have a waiver to prescribe Buprenorphine?  Yes

Optional Decision Support

Brief Motivation Interview

Use the following techniques to motivate the patient to accept treatment. Treatment should be offered regardless of the patient's current readiness to accept it.

Step 1: Readiness Assessment

Ask the patient to answer the following to determine their readiness to begin treatment with buprenorphine.

On a scale of 1 to 10, with being not ready at all and 10 being totally ready, how ready do you feel about starting treatment with buprenorphine today?

Step 2: Help Motivate

Ask questions that reflect on the patient's previous answers, use reflective listening to help frame your questions and reiterate motivating factors to help encourage starting treatment.

Questions If 1 is Selected

Questions If 2-10 is Selected

Step 3: Encourage Patient

Allow the patient to explain their answers. Ask questions that reflect on the previous answers, and use reflective listening to reiterate motivating topics or factors to help encourage starting treatment.

BACK
Buprenorphine Treatment Options

Do you have a waiver to prescribe Buprenorphine?  

Yes

Brief Motivation Interview

Use the following techniques to motivate the patient to accept treatment. Treatment should be offered regardless of the patient's current readiness to accept it.

Step 1: Readiness Assessment

Ask the patient to answer the following to determine their readiness to begin treatment with buprenorphine.

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Step 3: Encourage Patient

Allow the patient to explain their answers. Ask questions that reflect on the previous answers, and use reflective listening to reframe motivating factors or factors to help encourage starting treatment.
Buprenorphine Treatment Options

Does the patient have Opioid Use Disorder?

Yes

Is patient ready for treatment?

Yes

How severe is patient’s withdrawal?

1-12

Brief Motivation Interview

about starting treatment with buprenorphine today:

Step 2: Help Motivate

Ask questions that reflect on the patient’s previous answers, use reflective listening to help frame your questions and reiterate motivating factors to help encourage starting treatment.

Questions If 1 is Selected

Some questions to consider asking if the patient selected 2-10 on the readiness scale:

- What made you choose that number and not a lower one?
- What would be good about considering buprenorphine treatment?
- What are the benefits you’ve heard other folks about?
- What might make you more motivated once you go home (or in a few days from)
- Have you ever done anything you wish you hadn’t while using drugs?
- How important would it be to prevent that from happening again?

Allow the patient to explain their answers. Ask questions that reflect on the previous answers, and use reflective listening to reiterate motivating topics or factors to help encourage starting treatment.
Buprenorphine Treatment Options

Does the patient have Opioid Use Disorder?
- Yes
- No

Is patient ready for treatment?
- Yes
- No

Optimal Decision Support
- OOD TOOL
- INTERVIEW TOOL

How severe is patient's withdrawal?
- 0-12
- 13-24
- 25-36

Clinical Opiate Withdrawal Scale (COWS)

For each item, select the appropriate description of the patient's signs of symptoms (points per symptom).

- Resting Pulse Rate
  - 80 OR BELOW (3)
  - 81 - 100 (1)
  - 101 - 120 (2)
  - > 120 (4)

- Restlessness
  - ABLE TO SIT STILL (0)
  - SOME DIFFICULTY SITTING STILL (1)
  - FREQUENT SHIFTING OF LIMBS (2)

- Anxiety or Irritability
  - NONE (0)
  - INCREASING AMOUNTS (1)
  - OBVIOUSLY IRITABLE/ANGUISH (2)
  - TOO DIFFICULT (3)

- Yawning
  - NO YAWING (0)
  - 1 OR 2 TIMES/ASSESSMENT (1)
  - 3 OR 4 TIMES/ASSESSMENT (2)
  - SEVER (4)

- Pupil size
  - NORMAL (0)
  - POSSIBLY LARGER (1)
  - MODERATELY DILATED (2)
  - ONLY Rim of Iris Visible (4)

- Runny nose or tearing
  - NOT PRESENT (0)
  - STUFFINESS/MOIST EYES (1)
  - NOSE RUNNING/TEARING (2)
  - CONSTANT (4)

- Tensioner
  - NO TENSION (0)
  - FEEL - NOT OBSERVED (1)
  - SLIGHT TENSION OBSERVABLE (2)
  - GROSS TENSION (4)

- Sweating
  - NO SWEATING (0)
  - NICE SWEATING (1)
  - BOLD SWEATING (2)
  - HEAVY SWEATING (4)

COWS Score: [ ]
Buprenorphine Treatment Options

Do you have a waiver to prescribe Buprenorphine? Yes

Clinical Opiate Withdrawal Scale (COWS)

For each item, select the appropriate description of the patient's signs of symptoms (points per symptom).

- Resting Pulse Rate
  - 80 OR BELOW (0)
  - 81 - 100 (1)
  - 101 - 120 (2)
  - > 120 (4)

- Restlessness
  - ABLE TO SIT STILL (0)
  - SOME DIFFICULTY SITTING STILL (1)
  - FREQUENT SHIFTING OF LIMBS (2)

- Anxiety or irritability
  - NONE (0)
  - INCREASING AMOUNTS (1)
  - OBVIOUSLY IRRITABLE/ANXIOUS (2)
  - TOO DIFFICULT (3)

- yawning
  - NO YAWNING (0)
  - 1 OR 2 TIMES/ASSESSMENT (1)
  - 3 OR 4 TIMES/ASSESSMENT (2)
  - SEVERE (3)

- Pupil size
  - NORMAL (0)
  - POSSIBLY LARGER (1)
  - MODERATELY DILATED (2)
  - ONLY Rim of Iris Visible (3)

- Runny nose or tearing
  - NOT PRESENT (0)
  - STUFFINESS/MOIST EYES (1)
  - NOSE RUNNING/TEARING (2)
  - CONSTANT (3)

- Tremor
  - NO Tremor (0)
  - FELT - NOT OBSERVED (1)
  - SLIGHT TREMOR OBSERVABLE (2)
  - GROSS TREMOR (3)

- Sweating
  - < (0)

COWS Score: 11
Thank you for using the Buprenorphine (BUP) initiation pathway. The following actions will now be completed:

Start 4 mg BUP (2x)

Note (use EMBED SmartPhrase)
I have used the EMBED Buprenorphine initiation decision support app to assess this patient for opioid use disorder, opioid withdrawal, and readiness for treatment.

Using this app, I determined that this patient has:
1. moderate to severe opioid use disorder,
2. a clinical opioid withdrawal scale of 6-10, and
3. has expressed readiness to begin treatment with buprenorphine.

The patient will receive:
- Buprenorphine 4 mg in the ED today, be observed for 45-60 minutes, and given another 4 mg dose if they have no side effects.
- prescriptions for buprenorphine 16 mg b.i.d. daily for 5 days and a prescription for naltrexone (usual dose).

Referral to treatment, and
- education on opioid use disorders and naltrexone use.

Orders (The following orders will be placed now for your signature)
- Buprenorphine 16 mg b.i.d.
- Naltrexone (usual dose)

Prescriptions (The following prescriptions will be placed now for your signature)
- Naloxone Nasal Spray 4 mg
- Buprenorphine-naltrexone 16 mg b.i.d.

AVS/Discharge instructions
- Opioid Use Disorder
- Naloxone (usual dose)
- Buprenorphine b.i.d.

Referral to treatment
- A referral for an addiction specialist appointment will be offered when you exit this window.
Thank you for using the Buprenorphine (BUP) initiation pathway. The following actions will now be completed:

Start 4 mg BUP (2x)

Note (use EMBED Sound/Phrase)
I have used the EMBED Buprenorphine Initiation decision support app to assess this patient for opioid use disorder, opioid withdrawal, and readiness for treatment.

Using this app, I determined that this patient has:
1. moderate OP; severe opioid use disorder,
2. a clinical opioid withdrawal cutoff of 6-15, and
3. has expressed readiness to begin treatment with Buprenorphine.

The patient will receive:
1. buprenorphine 4 mg in the ED today, be observed for 45-60 minutes, and given another 4 mg dose if they have no side effects.
2. prescription for buprenorphine 55 mg sublingual daily for 5 days and a prescription for naloxone nasal spray.
3. referral to treatment, and
4. education on opioid use disorder and naloxone use.

Orders (The following orders will be placed now for your signature)
- Buprenorphine-naloxone 5.6 mg 4 mg
- Admit 4 mg now. Observe patient for 45-60 minutes. If no adverse events, administer second dose

Prescriptions (The following prescriptions will be placed now for your signature)
- Naloxone nasal spray 4 mg
- Buprenorphine-naloxone 5.6 mg 4 mg

AVS/Discharge Instructions
- Oral Use Disorder
- Naloxone (nasal spray)
- Buprenorphine nasal spray

Referral to treatment
- A referral for an addiction specialist appointment will be offered when you exit this window.
After signing the orders, the clinician continues to work in the EHR
## Project Timeline

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<th>YEAR</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

*Note: We are here in Q2 of YEAR 4.*
COVID trend research: leveraging trial infrastructure

*Trends* in ED visits, hospital admissions, and non-fatal opioid overdoses in the first months of the COVID-19 pandemic across 5 health systems in 5 states

Figure:
The EMBED Trial
Methods

- 18-month pragmatic, parallel, group randomized trial
- 18 ED clusters (21 sites) in 5 healthcare systems randomly allocated in 1:1 ratio to intervention versus usual care arm with stratified covariate constrained randomization
- Intervention: CDS to support diagnosis & withdrawal assessment & automate orders, notes, Rx, AVS, referral
- Primary outcome: initiation of BUP in ED at patient level
- Protocol approved by Western IRB (WIRB)

**Intervention Group:** 9 Emergency Departments

**Control Group:** 9 Emergency Departments

Ongoing Data Collection

18-month trial

Nov 2019 to May 2021
Consort Diagram

18 ED Clusters for EMBED Trial

INTERVENTION ARM
9 Clusters
• Total ED Visits Assessed = 775,873

ED visit, not OUD related = 772,430

ED OUD Visits
3,443

Excluded from analysis
• Patient repeat visit = 625
• Missing provider = 21
• Treated by NP or PA = 10

Included in analysis
• OUD ED visits = 2,787
• Attending physicians = 340

CONTROL ARM
9 Clusters
• Total ED Visits Assessed = 637,820

ED visit, not OUD related = 634,000

ED OUD Visits
3,820

Excluded from analysis
• Patient repeat visit = 469
• Missing provider = 0
• Attending physician crossover = 1,043
• Treated by NP or PA = 48

Included in analysis
• OUD ED visits = 2,260
• Attending physicians = 259

*Note that repeat visits do not equate to patients. Therefore, sums of patient numbers may not appear complete across the diagram.
### Patient Characteristics

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<th>Intervention N (%)</th>
<th>Control N (%)</th>
<th>Total N (%)</th>
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<td>2787</td>
<td>2260</td>
<td>5047</td>
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<td><strong>Age</strong></td>
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<td>36.0 (29.0-46.0)</td>
<td>36.0 (29.0-47.0)</td>
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<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Male</td>
<td>1870 (67.1%)</td>
<td>1447 (64.0%)</td>
<td>3317 (65.7%)</td>
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<tr>
<td>Female</td>
<td>917 (32.9%)</td>
<td>813 (36.0%)</td>
<td>1730 (34.3%)</td>
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<tr>
<td><strong>Race</strong></td>
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<tr>
<td>Black</td>
<td>452 (16.2%)</td>
<td>406 (18.0%)</td>
<td>858 (17.0%)</td>
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<td>White</td>
<td>2048 (73.5%)</td>
<td>1565 (69.2%)</td>
<td>3613 (71.6%)</td>
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<td>Other</td>
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<td>219 (9.8%)</td>
<td>415 (8.2%)</td>
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<td><strong>Ethnicity</strong></td>
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<td>701 (13.9%)</td>
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<td>Not Hispanic or Latino</td>
<td>2166 (77.7%)</td>
<td>1934 (85.6%)</td>
<td>4100 (81.2%)</td>
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## Physician Characteristics

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<tr>
<td>Male</td>
<td>210 (66.9%)</td>
<td>141 (67.1%)</td>
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<td>Female</td>
<td>104 (33.1%)</td>
<td>69 (32.9%)</td>
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<td><strong>Age Group, in years</strong></td>
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<td>&lt;35</td>
<td>68 (21.7%)</td>
<td>41 (19.5%)</td>
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<td>124 (39.5%)</td>
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<td>84 (26.8%)</td>
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<td>55-64</td>
<td>29 (9.2%)</td>
<td>24 (11.4%)</td>
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<td>65+</td>
<td>9 (2.9%)</td>
<td>7 (3.3%)</td>
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<td>Intervention</td>
<td>Control</td>
<td>Effect size</td>
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<td>Patient level outcomes</td>
<td>N = 2787 (%)</td>
<td>N = 2260 (%)</td>
<td>OR (95 % CI)</td>
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<tr>
<td>BUP initiated</td>
<td>233 (8.4%)</td>
<td>193 (8.5%)</td>
<td>1.24 (0.57, 2.71)</td>
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<td>Naloxone prescription at discharge</td>
<td>517 (18.6%)</td>
<td>135 (6.0%)</td>
<td>1.62 (0.81, 3.22)</td>
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<td>BUP initiated using EMBED</td>
<td>111/261 (42.5%)</td>
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<td>Unique Physicians who:</td>
<td>N = 340 (%)</td>
<td>N = 259 (%)</td>
<td>OR (95 % CI)</td>
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<tr>
<td>Initiated BUP</td>
<td>135 (39.7%)</td>
<td>78 (30.1%)</td>
<td>1.53 (1.08, 2.15)</td>
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<tr>
<td>Prescribed naloxone at discharge</td>
<td>177 (52.1%)</td>
<td>71 (27.4%)</td>
<td>2.88 (2.03, 4.07)</td>
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<td>Initiated BUP using EMBED</td>
<td>76/129 (58.9%)</td>
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Proportion of OUD patients receiving BUP by study arm

* Bubble size indicating OUD cluster patient volume
Temporal trends of physicians initiating BUP and X-waiver (cumulative)
Subgroup Analyses

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>OR (diamond) with 95% CI (line)</th>
<th>P value</th>
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<td>45-64</td>
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<tr>
<td>Patient Gender</td>
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<tr>
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<td>Patient Ethnicity</td>
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<td>OUD Phenotype</td>
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<td>Algorithm 1</td>
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<td>Algorithm 2</td>
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<tr>
<td>Community</td>
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</table>

In favor of control and intervention
Conclusion

- **Patient level:** no change, limitations of data collection (e.g., methadone not in EHR)

- **Physician level:** Increased number of unique physicians that provided ED-initiated BUP and naloxone prescriptions

- CDS like EMBED can:
  - Bridge provider knowledge gap
  - Streamline and automate EHR workflows
  - Increase provider adoption of complex, unfamiliar evidence-based practices

- **BUT** additional barriers (stigma, physician attitude) remain and must be addressed to increase the rate of ED-initiated BUP among OUD patients.

- Together with strategies addressing these barriers, EMBED can help improve consistency and quality of care for OUD patients in ED.
Conclusion

Unobservable innovations may fail to diffuse or diffuse slowly.

To accelerate adoption of this life-saving practice, we must:

• Embrace treating addiction as part of routine emergency care

• Implement user-centered CDS with automated EHR workflows to facilitate adoption of this complex, unfamiliar practice
<table>
<thead>
<tr>
<th>Date</th>
<th>Journal</th>
<th>Author</th>
<th>Article Title</th>
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</thead>
<tbody>
<tr>
<td>Jun-20</td>
<td>Int J Epidemiol</td>
<td>Li et al.</td>
<td>Commentary: Right truncation in cluster randomized trials can attenuate the power of a marginal analysis.</td>
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<td>Jul-19</td>
<td>J Subst Abuse Treat.</td>
<td>Ahmed et al.</td>
<td>A scalable, automated warm handoff from the emergency department to community sites offering continued medication for opioid use disorder: Lessons learned from the EMBED trial stakeholders.</td>
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<tr>
<td>May-19</td>
<td>BMJ Open</td>
<td>Melnick et al.</td>
<td>User-centred clinical decision support to implement emergency department-initiated buprenorphine for opioid use disorder: protocol for the pragmatic group randomised EMBED trial.</td>
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</table>
Yale - EMBED Resources Page

All EMBED related activities and resources available at: embed.ynhh.org

- Demo video of EMBED

Smartphone app for Bup Initiation
- Android app
- iOS app

EMBED on MDCalc
- Web version
- App version
EMBED dissemination activities

- **Conferences:**
  - ACEP, October 2021, Boston, MA – EMBED Booth & Plenary for trial results
  - Epic UGM meeting, August 2021, WI
  - Southeast Regional ACEP Conference, June 2021, FL
  - SAEM, May 2022, New Orleans, LA – EMBED booths in Exhibit Hall & submitted abstract on Secondary analysis of EMBED data

- **IT**
  - 3rd party apps: MDCalc (app & Epic integration), BUP Initiation (iPhone & Android)
  - EMBED v2.0 web application to interested Epic clients now
  - Being built in native Epic Foundation System for 2022 go live
  - Cerner native build planned

- **Investigative:**
  - Trial manuscript in revision for BMJ
  - Qualitative analysis of barriers to widespread adoption of EMBED tools
  - Tracking BUP use nationally with OptumLabs Data Warehouse
  - Secondary analysis of trial results underway
The EMBED Team
Thank you!

Questions?

nih pragmatic trials collaboratory
rethinking clinical trials®

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@Ted_Melnick            @DonofrioGail