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

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Bethesda, MD
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Yale SCHOOL OF MEDICINE

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Teams and People

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  - Molly Jeffery, PhD (Mayo)
- **Project Coordinator**
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- **External collaborators**
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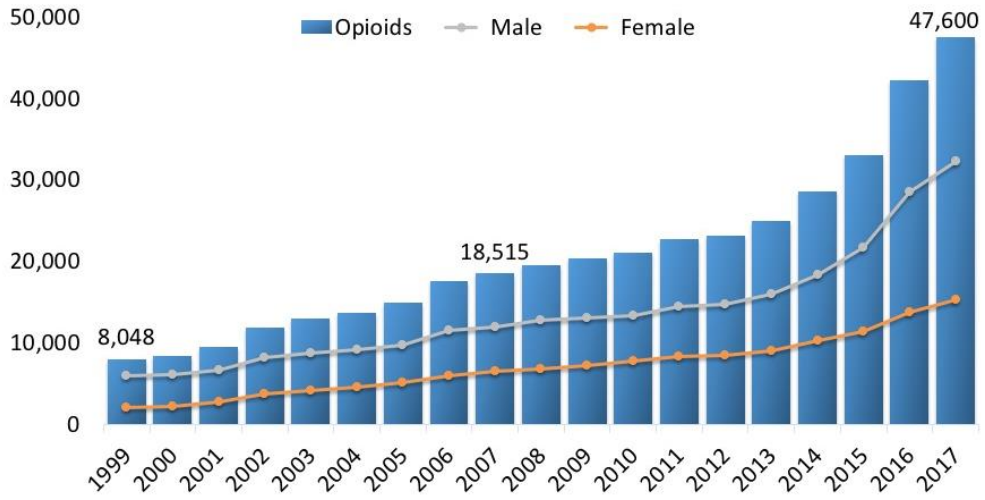
  - **Baystate**: William Soares, MD, MS, Christian Lagier Haiping Li
  - **Colorado**: Jason Hoppe, DO, Sean Michael, MD
  - Each site within each system
    - Medical director
    - Clinical champions
    - MOUD referral sites
- **Summer medical students**
  - Osama Ahmed
  - Jodi Mao
  - Wesley Holland

Background: OUD

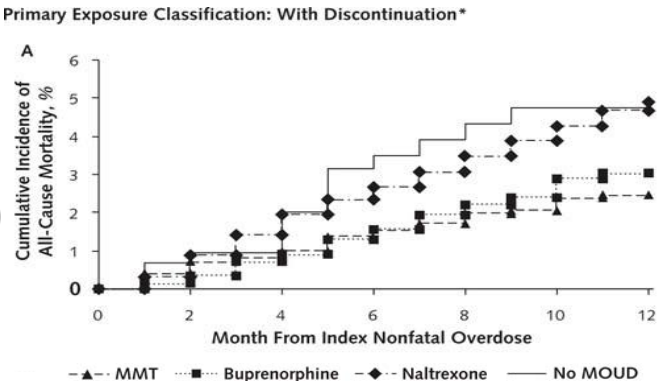
- Opioid use disorder (OUD): Dependence on opioids or heroin
- Major public health problem: 3 million Americans have or have had OUD
- Deaths 5.9 x higher than 1999 (47,000 in 2017)



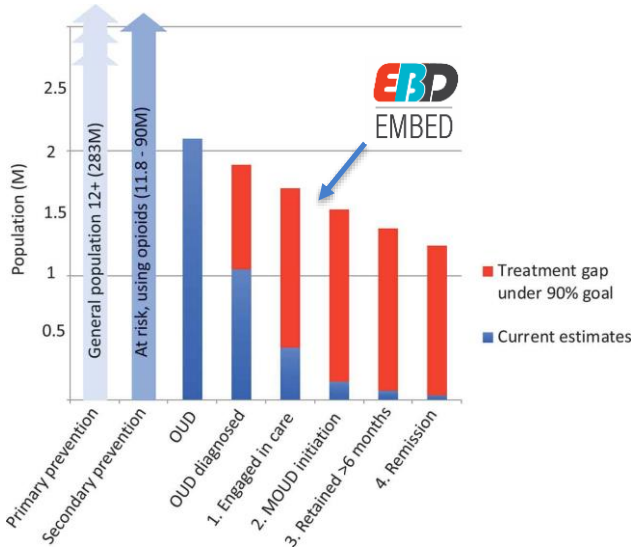
Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018

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?



LaRochelle. *Annals of IM* 2018



Williams. *AJDAA* 2018

Background: Intervention & Outcomes

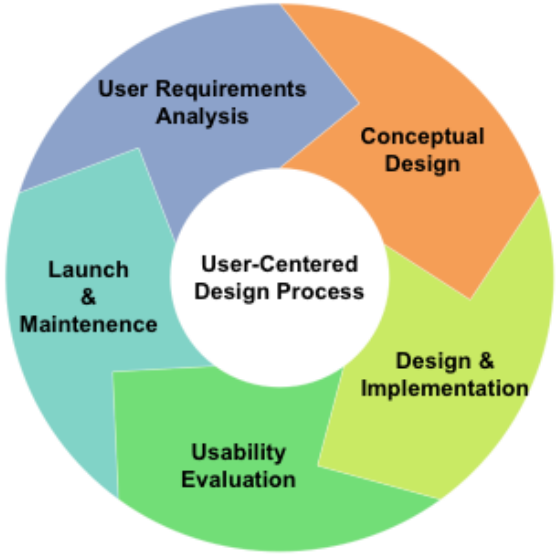
- **Setting**: 20 Emergency Departments (EDs) across 5 healthcare systems

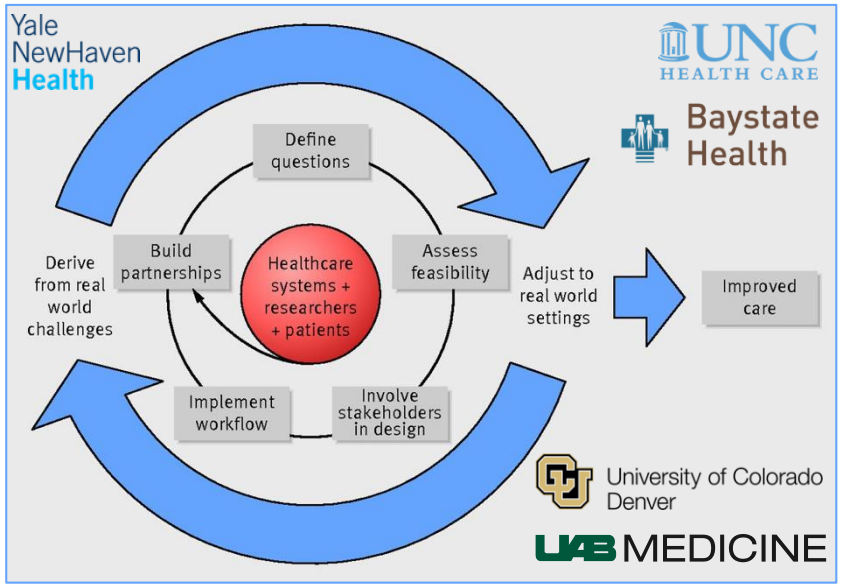
- **Intervention**: The intervention consists of a user-friendly, integrated IT intervention to support:
  1. Evaluation for OUD
  2. Assessment of withdrawal severity
  3. Motivation of patient willingness to start treatment
  4. Initiating buprenorphine
  5. Documentation of the care process
  6. Referral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

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

Background: UG3 Aims

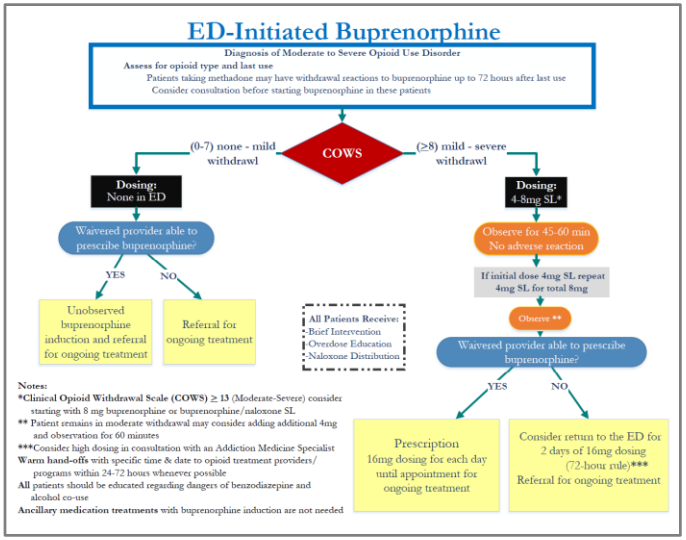
- **UG3 Aim 1.** Develop a pragmatic, user-centered CDS for ED-initiated BUP and referral for MOUD in ED patients with OUD which will automatically identify and facilitate management of potentially eligible patients.
- **UG3 Aim 2.** Establish the infrastructure for the proposed trial.



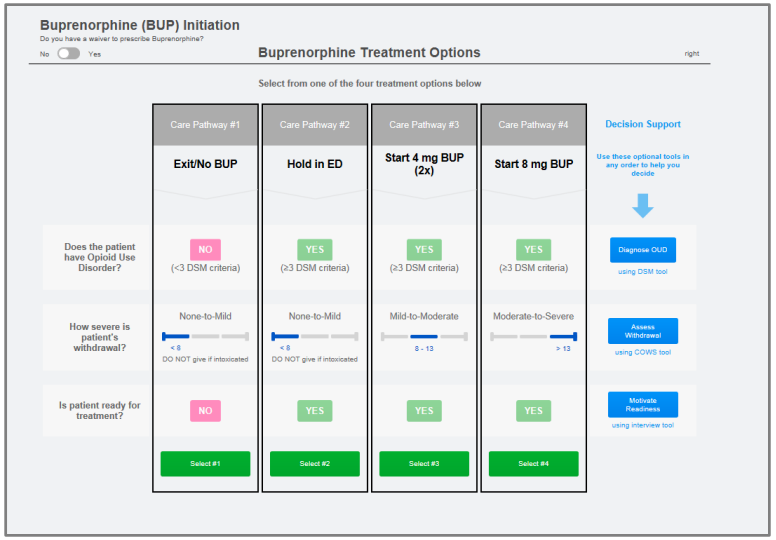


User Centered Design:
To simplify the process of initiating BUP in the ED

From a complicated algorithm …



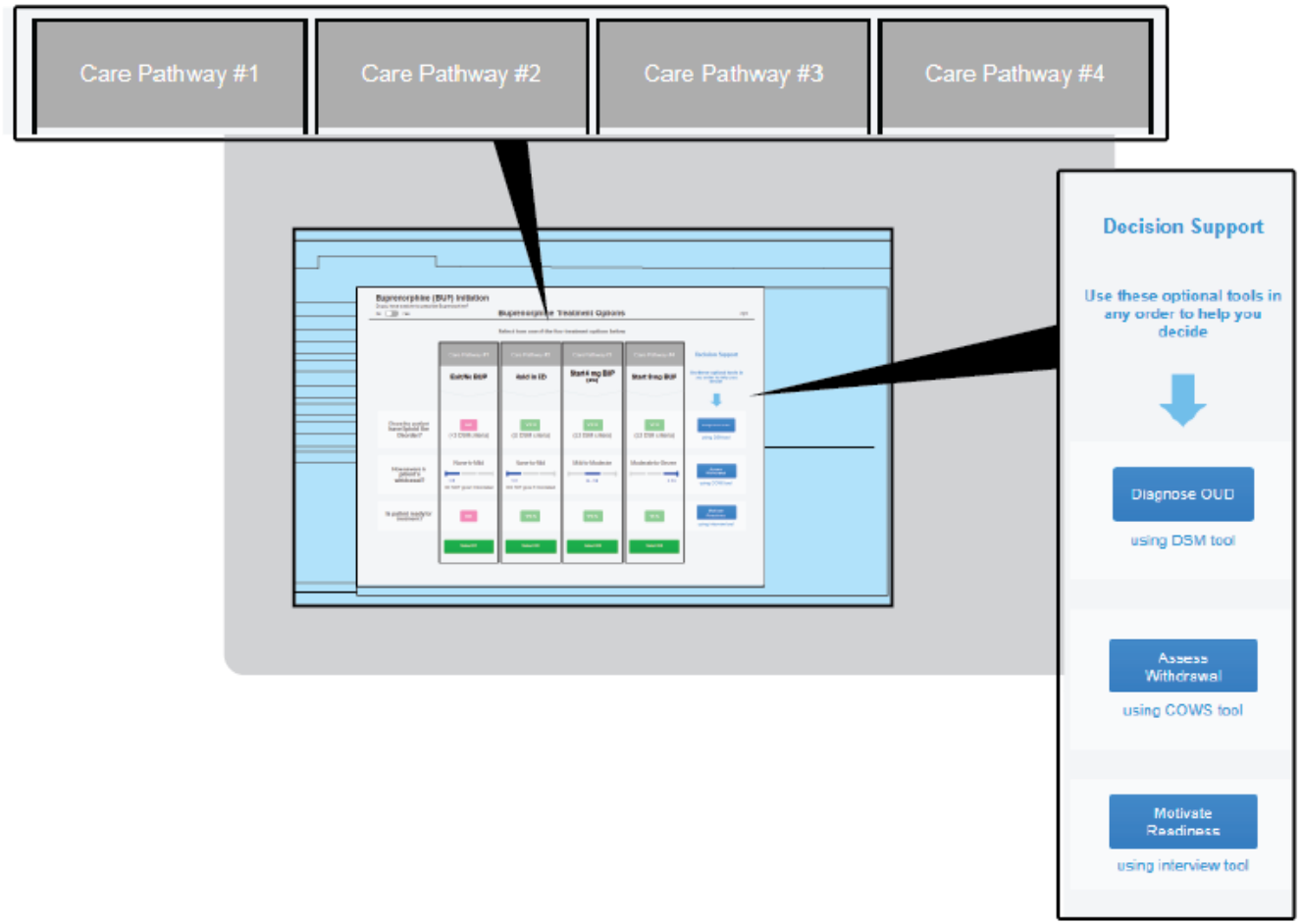
. . . to a simple, automated application



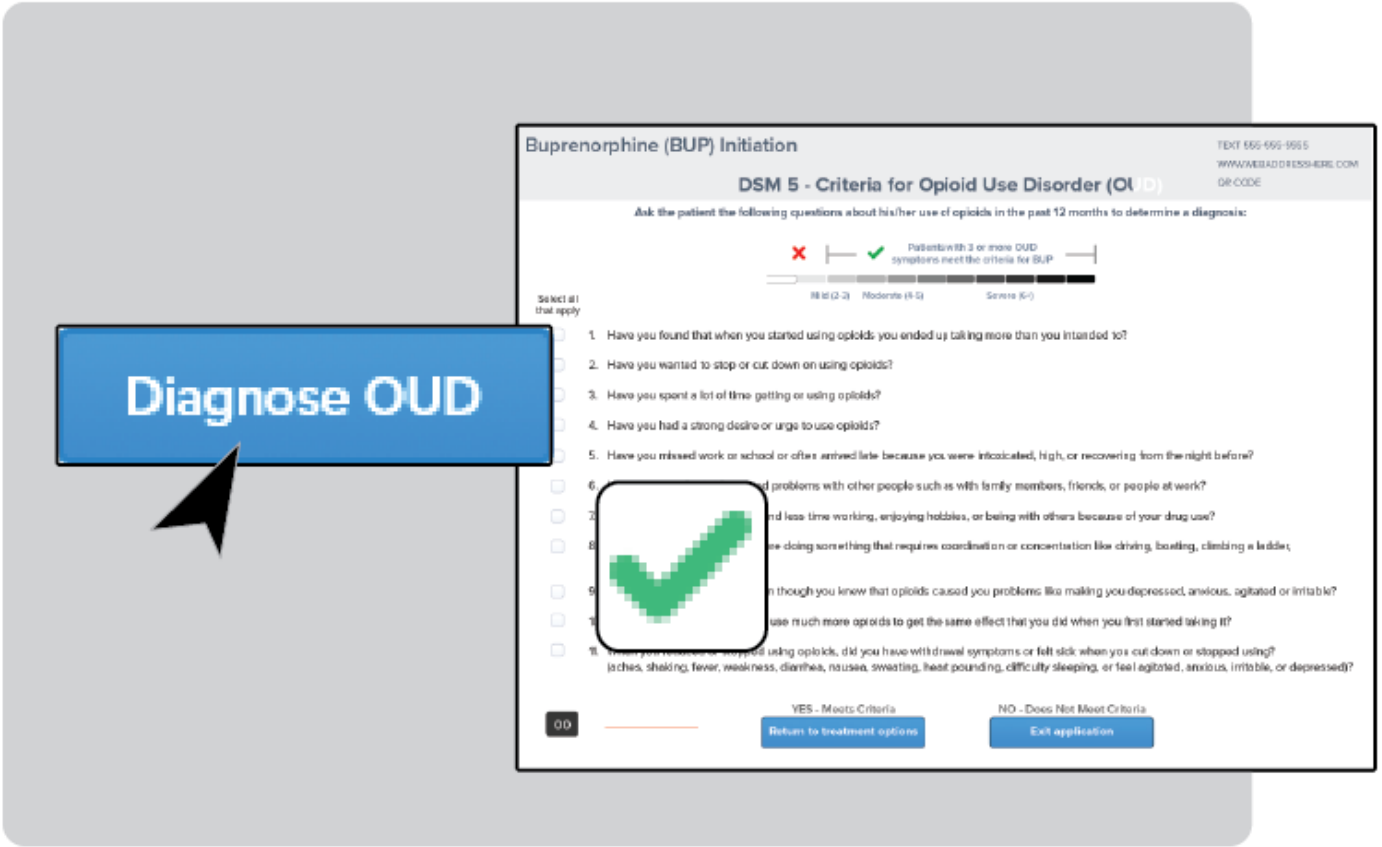
1 Clinicians continue in their current Epic workflow

2 Click the ‘EMBED’ button in the patient’s chart to launch the app

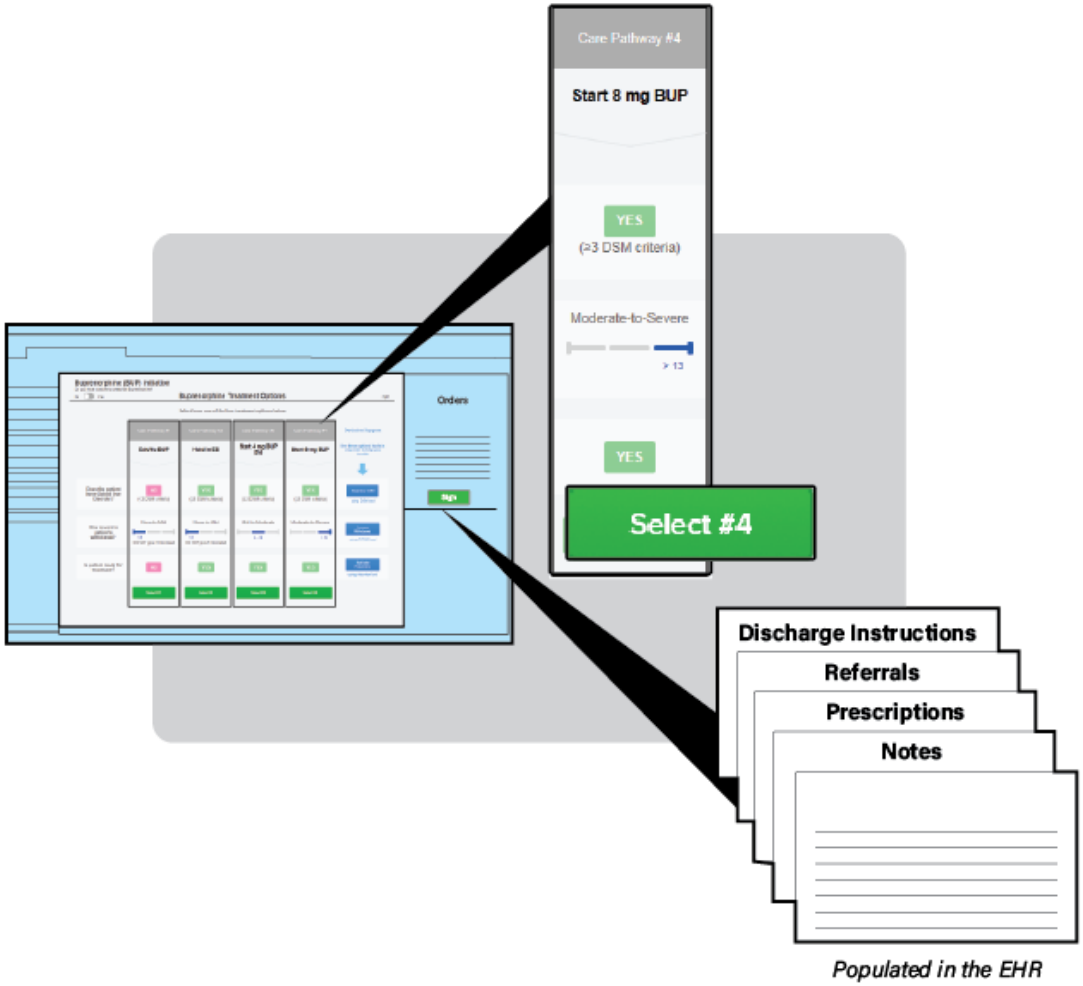
3 App offers care pathways & patient assessment tools with the flexibility to use just the parts you need



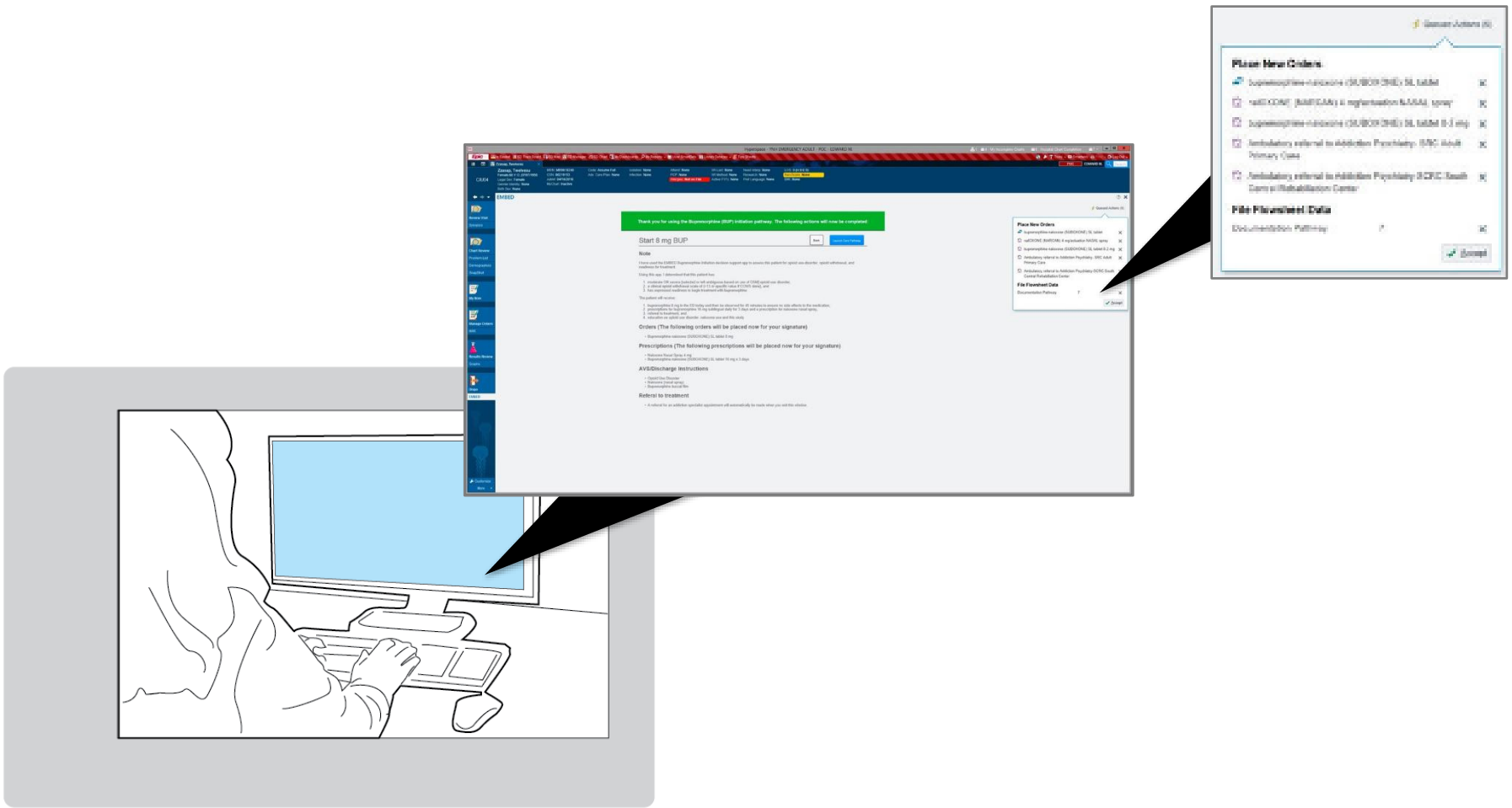
4 Other members of the care team can also complete patient assessments



5 Launching a care pathway automatically generates the appropriate documentation, orders, and referral in Epic



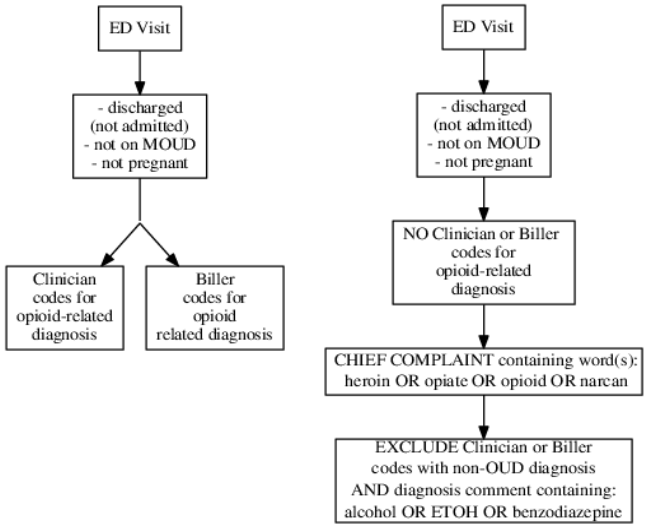
6 Orders appear in an Epic ‘Shopping Cart’ that allows for easy de/selection



7 After signing the orders, you can continue to use Epic

EHR Phenotyping

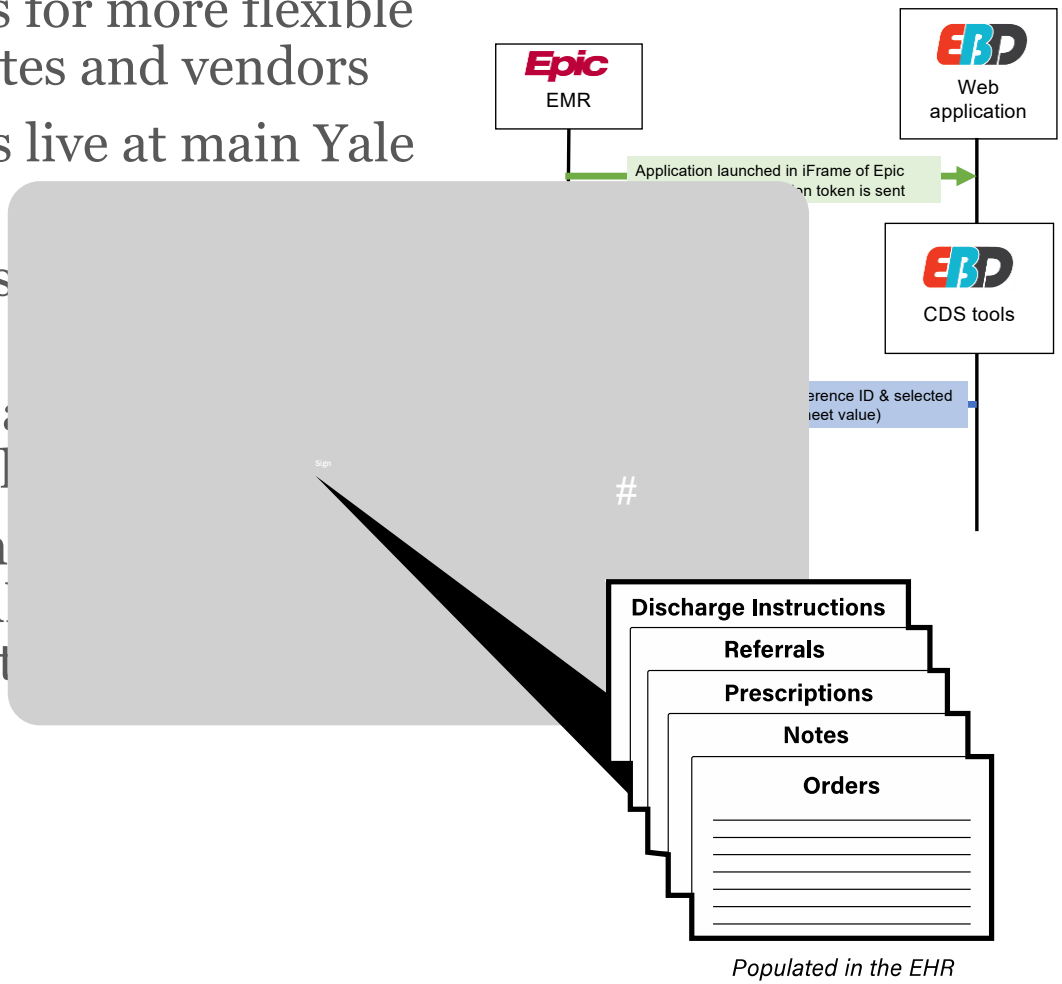
Derived and validated an electronic health record (EHR)-based computable phenotype to identify ED patients with OUD using physician chart review as a reference standard.



	Disease Present: Reference Standard			
Test Result		Reviewers +	Reviewers -	Predictive Value (95% CI)
	Algorithm 1 (internal validation)			
	Phenotype +	48	2	PPV 0.96 (0.863-0.995)
	Phenotype -	1	49	NPV 0.98 (0.893-0.999)
	Algorithm 2 (internal validation)			
	Phenotype +	20	5	PPV 0.8 (0.593-0.932)
	Phenotype -	0	25	NPV 1.0 (0.863-1)
	Combined Phenotype (external validation)			
	Phenotype +	53	3	PPV 0.95 (0.851-0.989)
	Phenotype -	4	46	NPV 0.92

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 hos
  allow future scaling
- Due to security issues,
  system preferred local
- Standards for commun
  web application not ful
  (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.

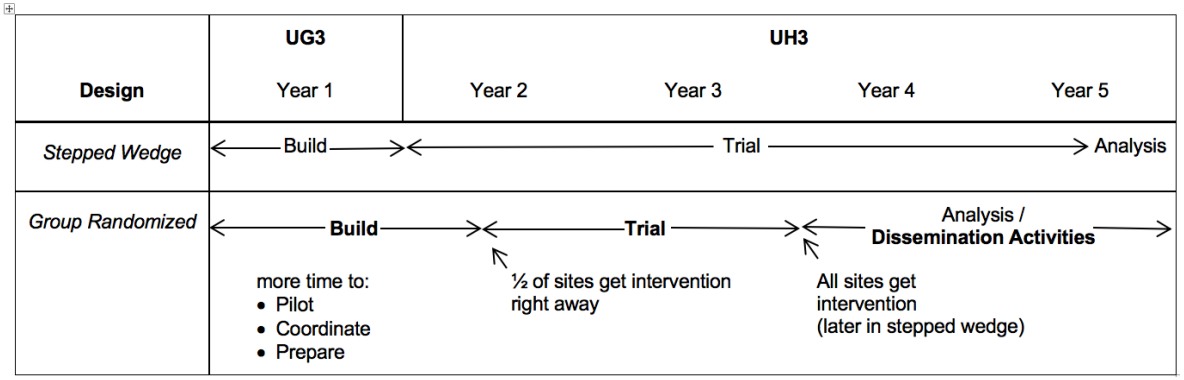
Role	Needs	Solutions
EMERGENCY DEPARTMENT CLINICIANS AND STAFF		
Attending physicians	Automate referral	Referral automated and implemented into EMBED CDS
Resident physicians	Minimize disruption to workflow	
ED addiction counselors	Best match of MOUD site to patient's needs	Include more than one option for referral site selection
CLINICIANS AND STAFF AT THE COMMUNITY MOUD SITES		
Attending physician	Minimize disruption to workflow	Set a limit on how many patients can be overbooked per week by our referral system to ensure a balance between quick referral and manageable workload
Front desk staff	Efficiency	Create a standardized flow of how patients will be referred and booked for every case in order to minimize variability in the process
Scheduling staff	Minimize disruption to workflow	Work with IT staff to ensure the system has multiple modes of sending out referrals and tailor each MOUD site to its specific preference
INVESTIGATIVE TEAM		
Principal Investigator	Scalability	Referral can be sent out via multiple channels, e.g., e-mail, EHR message, or fax. Collect survey data from MOUD sites to determine their preferences.
	Quality Assurance	Build referral network with the capability to collect aggregate data on % of referrals who were scheduled at MOUD sites, those who attended and those who were started on medication
Biostatistician	Collect information on referral effectiveness	For MOUD sites with EHR linkage, we created an automated data pull that can extract referral usage metrics. For non-EHR linked sites, agree with administrative staff to send us usage data
HEALTH SYSTEM IT STAFF		
Local EHR programmers	Specificity of the automation process	Acquire an exact list of patient information that MOUD sites need in order to make a very specific request to IT to generate an automated referral message
MEDICAL ETHICS EXPERTS		
Our institution's IRB	Ensuring patient privacy	Worked with IT to encrypt automated email referrals sent to MOUD sites Fax is considered HIPAA compliant
NIH Ethics Core	Patient consent and collecting data	Since collecting patient consent for measuring referral efficiency would be too cumbersome, we collected data from MOUD sites as aggregate, de-identified data for QA/QI purposes, which does not require consent.

Study Design Change

Feature	Stepped Wedge	Group Randomized
Length of trial	Longer trial period due to baseline and post-implementation phases	Shorter trial period
Control for temporal trends	Weaker, more vulnerable due to longer trial period	Stronger, due to shorter trial period
Control of heterogeneity by site	Yes, sites serve as their own control	Not as good, compensate for this weakness by employing constrained randomization
All sites get intervention	Yes	No, but can offer at end of shorter trial
Number of clusters (ED sites)	Fewer	More (necessitating this supplement request)
Go-live of IT intervention	Staggered, later implementations can learn for issues in earlier ones	Synchronized, requires more lead time and coordination
Additional time for IT build, pilot testing, and dissemination	No, due to longer trial period	Yes, shorter trial period permits additional time for IT build and dissemination in later UH3 years

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

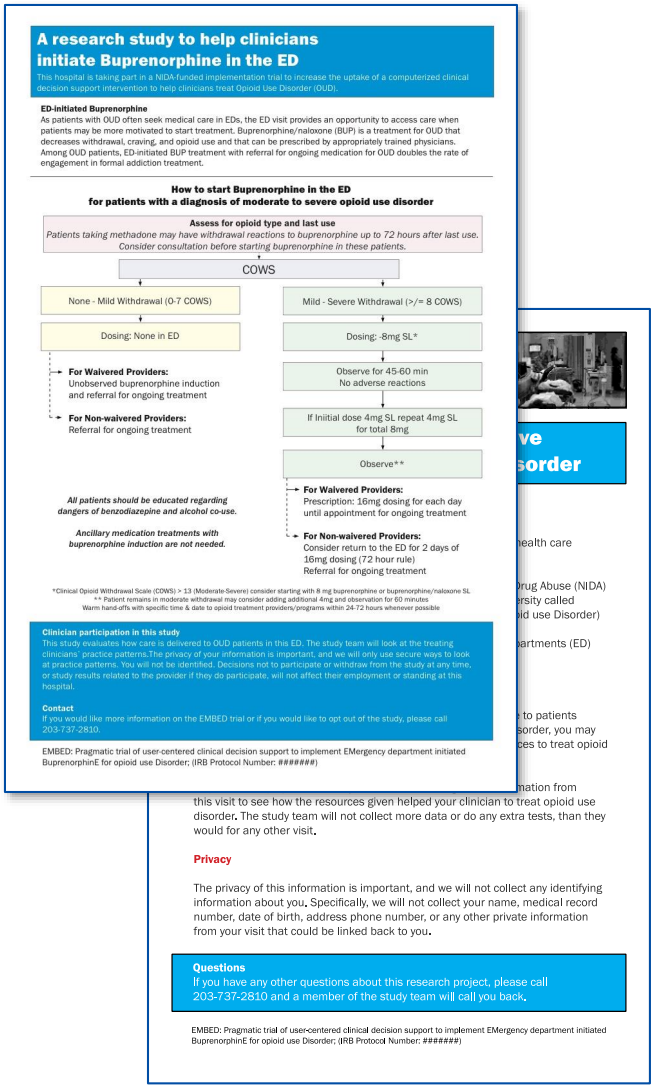
- Multiple sites in same system on same EHR build
  - No two EHR builds are the same
  - Each separate EHR integration requires additive costs
  - Recruiting multiple sites in the same system is more cost-effective
- Serve a population with a high rate of OUD
- Robust referral network in surrounding 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


University of Colorado Denver


Baystate Health

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



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**

For Waivered Providers: Prescription: 16mg dosing for each day until appointment for ongoing treatment

For Non-waivered Providers: Consider return to the ED for 2 days of 16mg dosing (72 hour rule) Referral for ongoing treatment

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

Ancillary medication treatments with buprenorphine induction are not needed.

*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

Clinician participation in this study

This study evaluates how care is delivered to OUD patients in this ED. The study team will look at the treating clinicians' practice patterns.The privacy of your information is important, and we will only use secure ways to look at practice patterns. You will not be identified. Decisions not to participate or withdraw from the study at any time, or study results related to the provider if they do participate, will not affect their employment or standing at this hospital.

Contact

If you would like more information on the EMBED trial or if you would like to opt out of the study, please call 203-737-2810.

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

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

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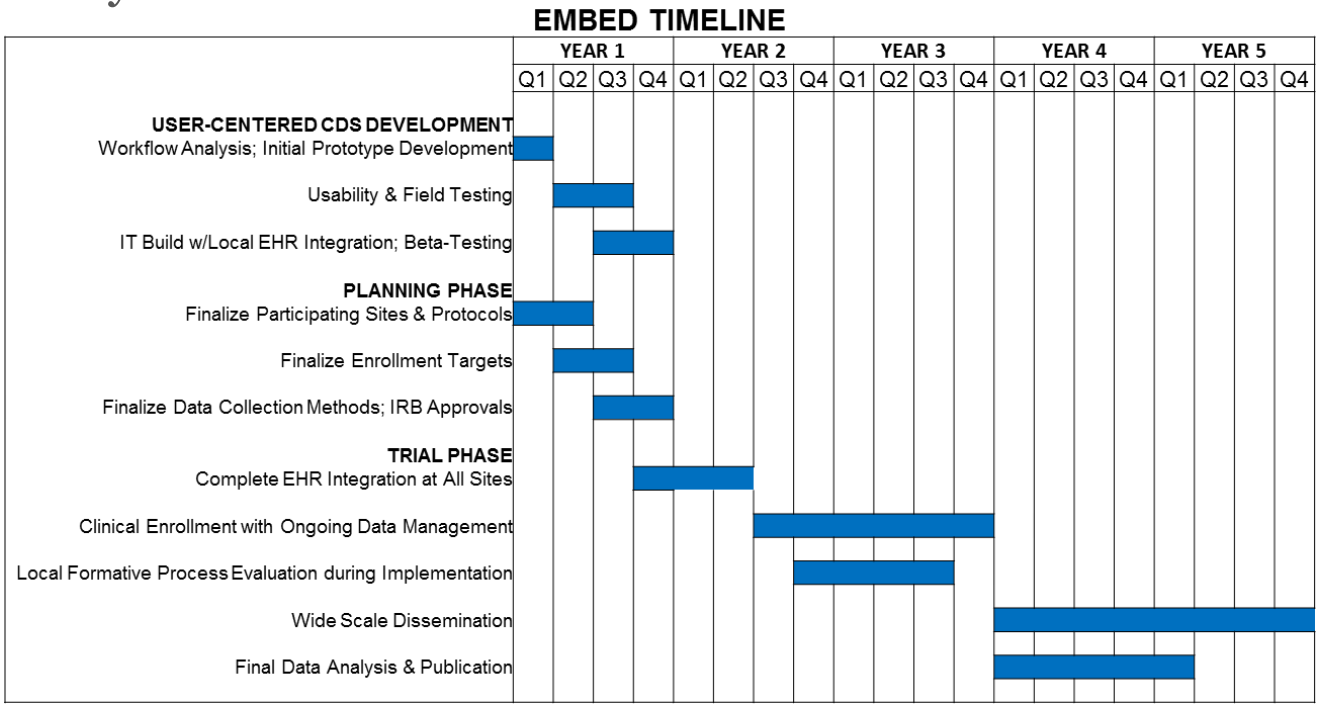
UH3 Aims

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

- **<u>NEW</u> UH3 Aim 2.** Disseminate the EMBED intervention nationally.



Barriers Scorecard

Barrier	Level of Difficulty*				
	1	2	3	4	5
Enrollment and engagement of patients/subjects			x		
Engagement of clinicians and health systems			x		
Data collection and merging datasets				x	
Regulatory issues (IRBs and consent)			x		
Stability of control intervention			x		
Implementing/delivering intervention across healthcare organizations					x

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

*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?

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Posters

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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.

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