EMBED: A Pragmatic Trial of User Centered Clinical Decision Support for <u>EM</u>ergency Department Initiated <u>B</u>uprenorphin<u>E</u> for Opioid Use <u>D</u>isorder

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NIH Collaboratory Grand Rounds January 28, 2022



Disclosures

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The EMBED Team



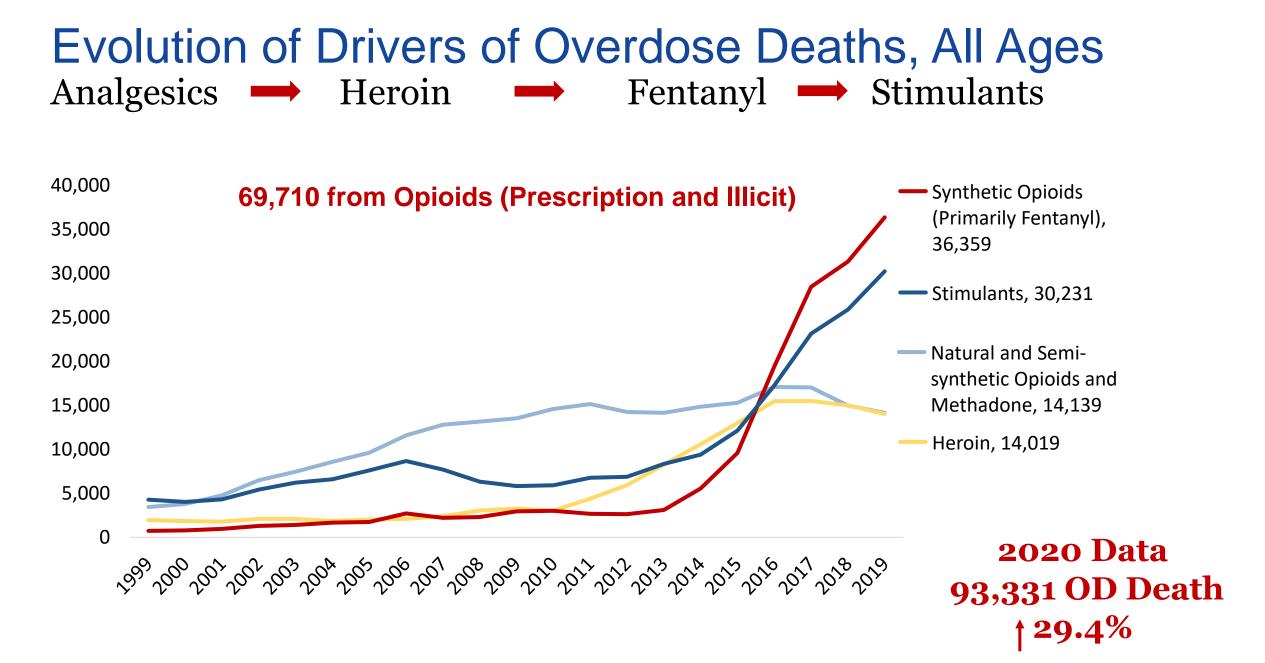


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Background





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

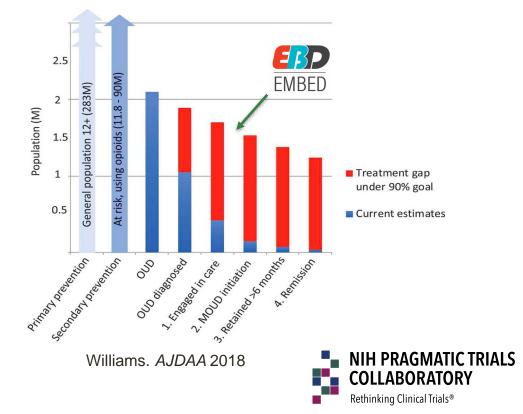
MOUD – BUP & Gap in OUD Care

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

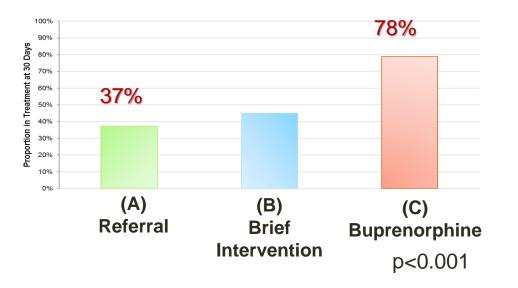
 Only 28.5% (1.2 million) - receive MOUD - with either buprenorphine, methadone, or naltrexone

> (SAMSHA, 2018 National Survey on Drug Use and Health)



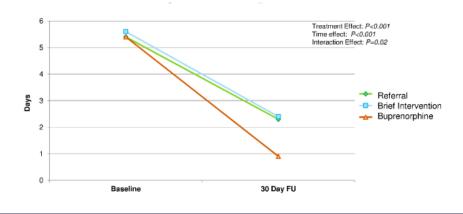
Evidence for BUP in the ED

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)





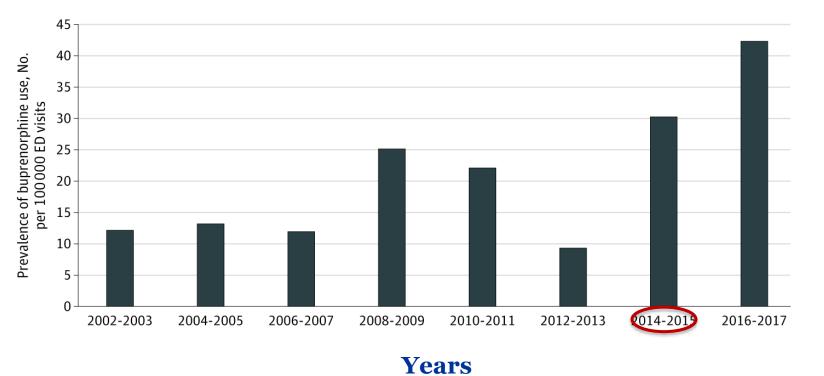




Research Letter | Emergency Medicine Trends in the Use of Buprenorphine in US Emergency Departments, 2002-2017

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).

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

The NEW ENGLAND JOURNAL of MEDICINE

Emergency Departments — A 24/7/365 Option for Combating the Opioid Crisis

Gail D'Onofrio, M.D., Ryan P. McCormack, M.D., and Kathryn Hawk, M.D., M.H.S.

When it comes to opioid use					
disorder (OUD), however, there has					
been a lot of <mark>reluctance</mark> among	ou re: pc flu				
emergency physicians to initiate	se				
treatment with buprenorphine	d +				

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JAMA Network Open...

Original Investigation | Substance Use and Addiction

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

Kathryn F. Hawk, MD; Gail D'Onofrio, MD; Marek C. Chawarski, PhD; Patrick G. O'Connor, MD; Ethan Cowan, MD; Michael S. Lyons, MD; Lynne Richardson, MD; Richard E. Rothman, MD; Lauren K. Whiteside, MD; Patricia H. Owens, MS; Shara H. Martel, MPH; Edouard Coupet Jr, MD; Michael Pantalon, PhD; Leslie Curry, PhD; David A. Fiellin, MD; E. Jennifer Edelman, MD

- Web-based
- EHR Integrated
- Clinical Decision Support System



How EMBED Works



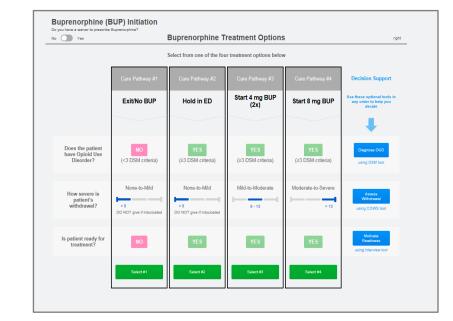
User Centered Design: To Simplify the Process

ED-Initiated Buprenorphine Diagnosis of Moderate to Severe Onioid Use Dise 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 (0-7) none - mild (≥ 8) mild - severe COWS withdrawl withdrawl Dosing 4-8mg SL YES initial dose 4mg SL repea 4mg SL for total 8mg All Patients Receive: buprenorphine Referral for -Brief Intervention induction and referral. ongoing treatment d provider able to prese -Overdose Education for ongoing treatment -Naloxone Distributio *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 Consider return to the ED for Prescription ***Consider high dosing in consultation with an Addiction Medicine Specialist 2 days of 16mg dosing 16mg dosing for each day Warm hand-offs with specific time & date to opioid treatment providers/ (72-hour mle)*** programs within 24-72 hours whenever possible until appointment for Referral for ongoing treatment All patients should be educated regarding dangers of benzodiazepine and ongoing treatment alcohol co-use Ancillary medication treatments with buprenorphine induction are not needed

From a complex, multi-step process

Complicated Multi-step workflow **25-30 min**

...to a simple, automated application



Simple & automatic 5 min

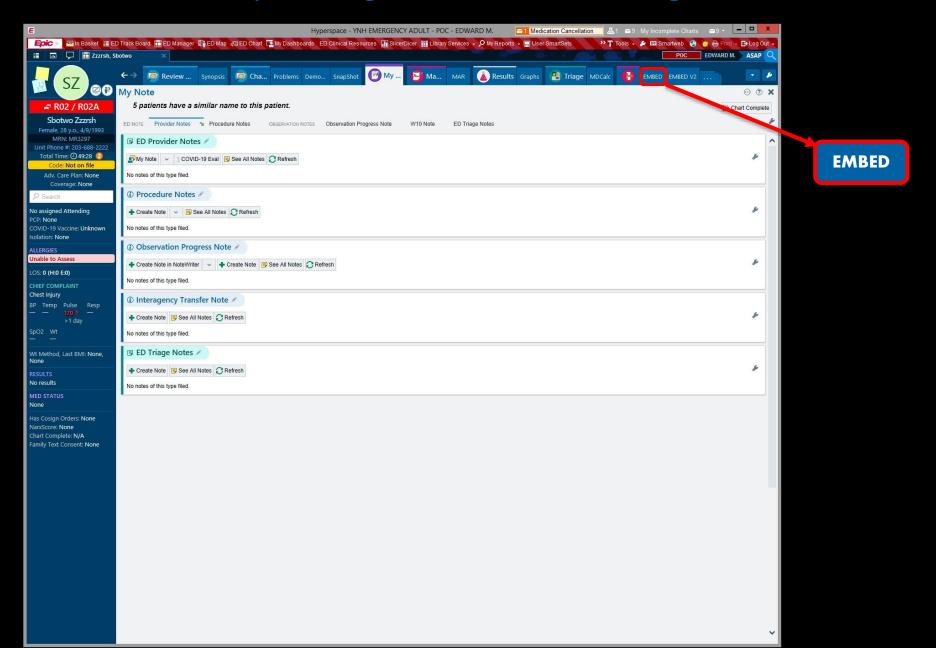
- 1) Diagnosing OUD
- 2) Assessing withdrawal severity (COWS)
- 3) Motivating patients to accept treatment
- 4) Automating EHR workflow including -
 - clinical and after visit documentation,
 - order entry
 - prescribing
 - Community referral

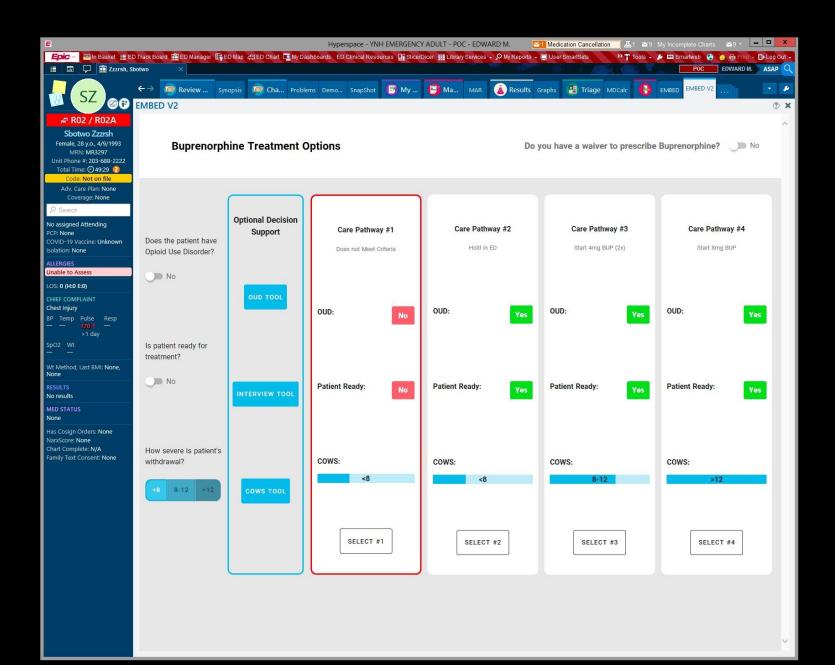
Integrated into EHR workflow

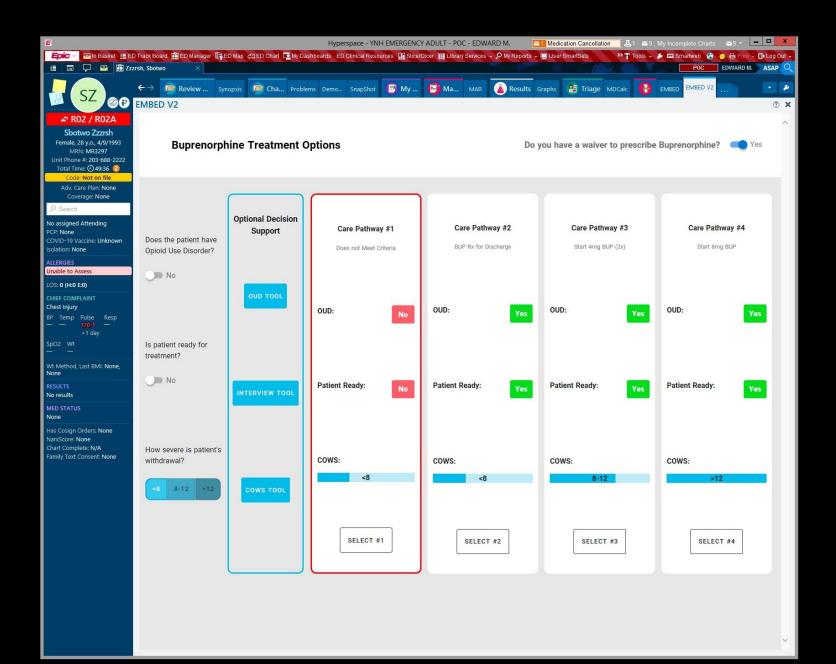


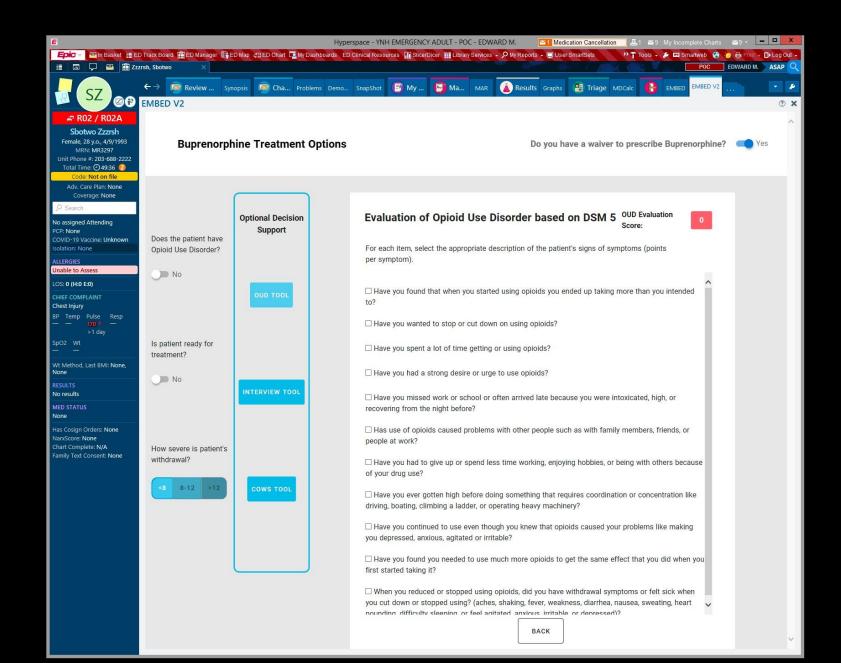


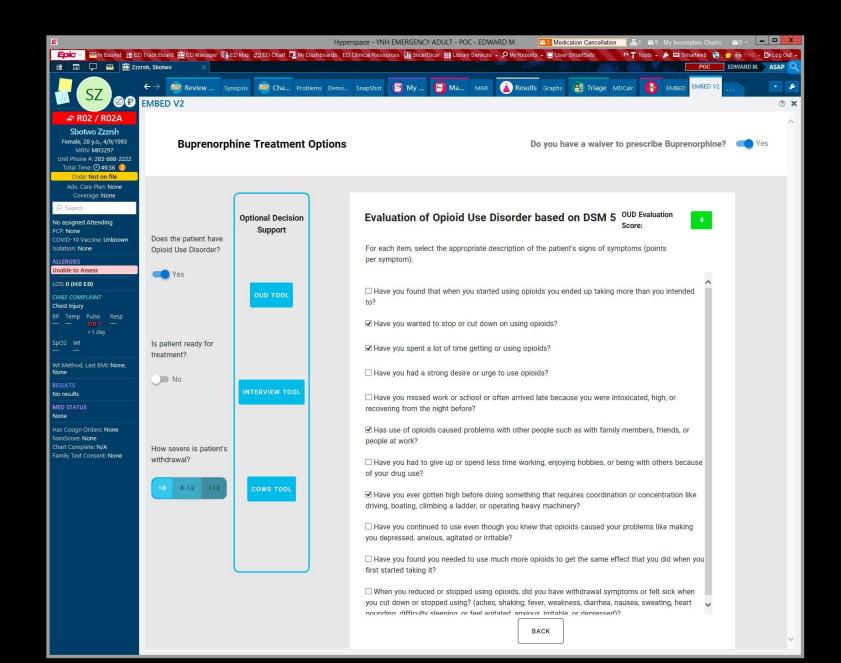
Launch EMBED by clicking on its tab in the Navigation Bar

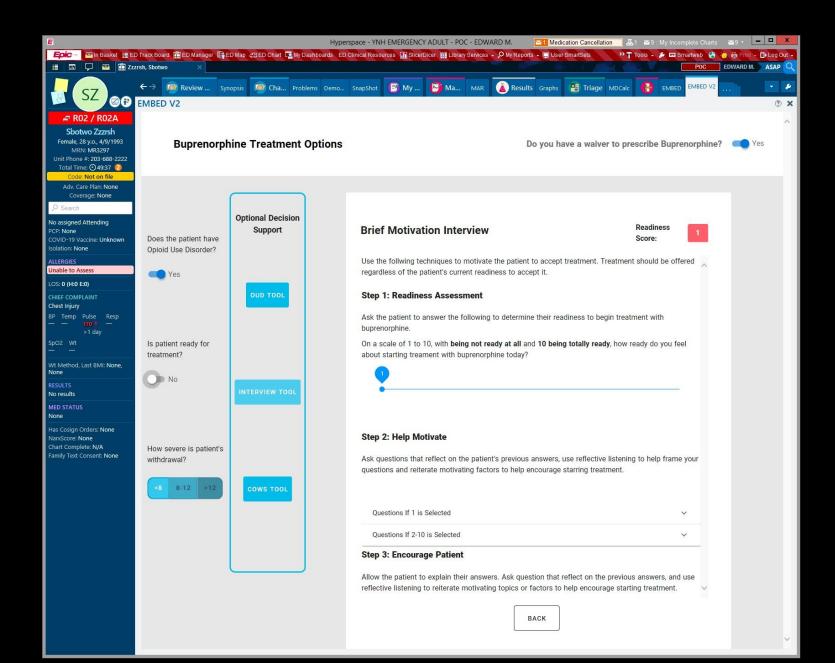


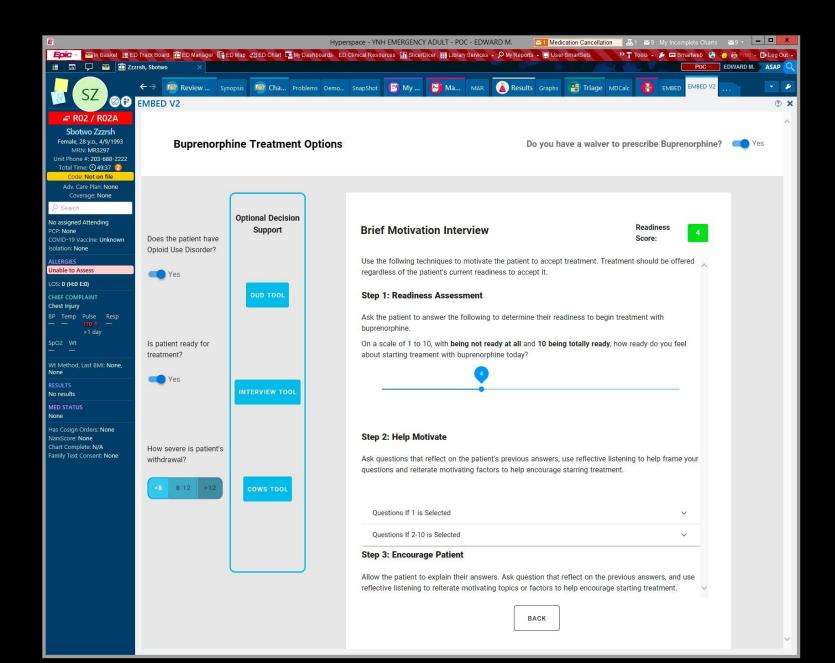


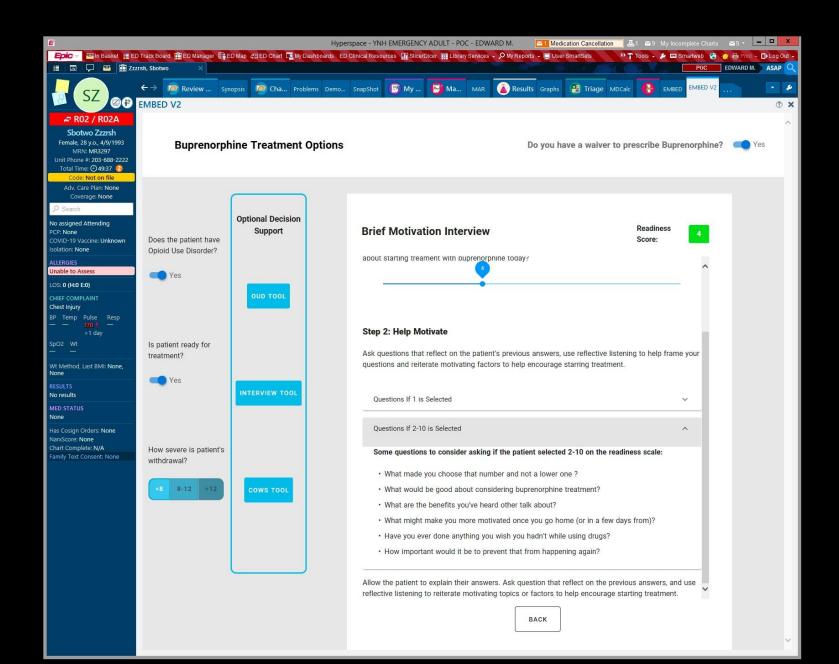


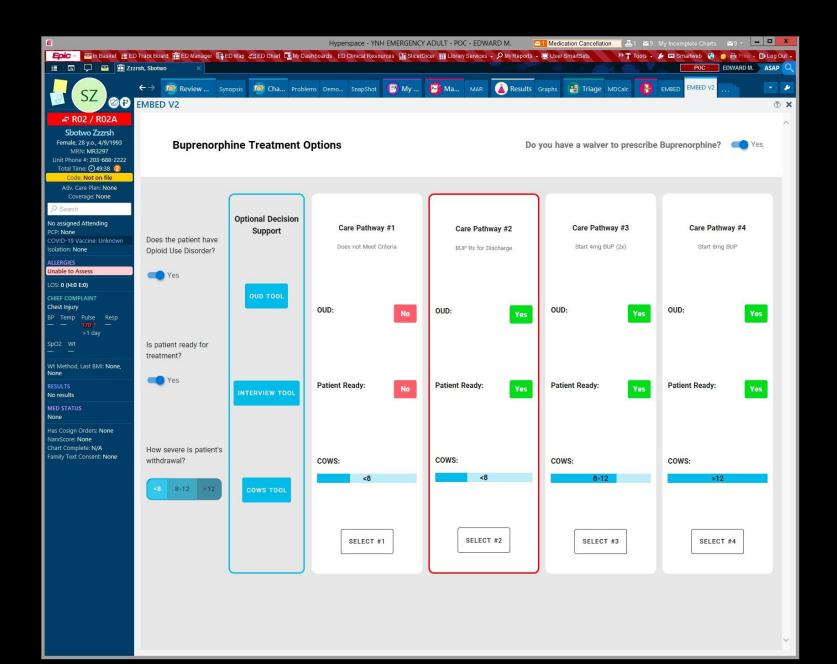


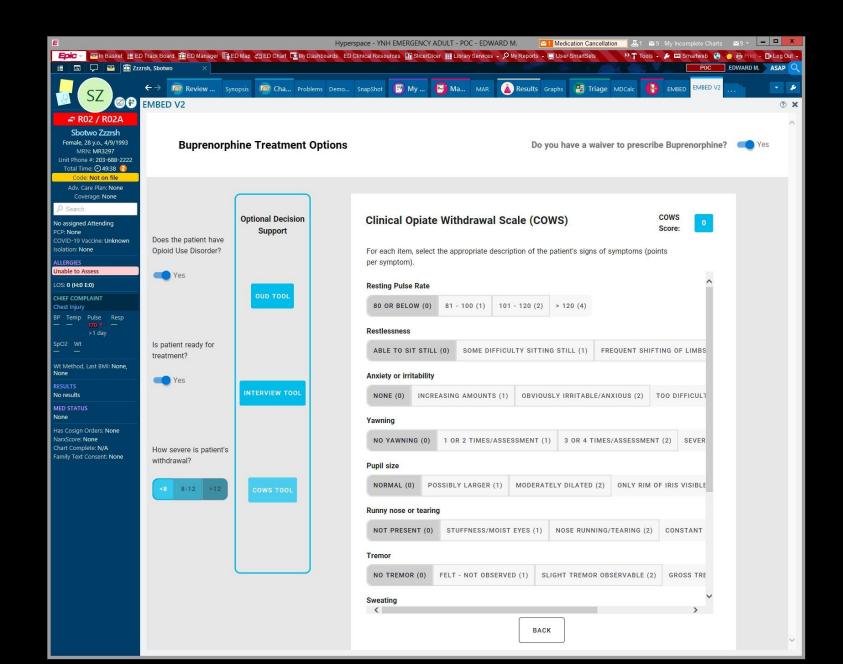


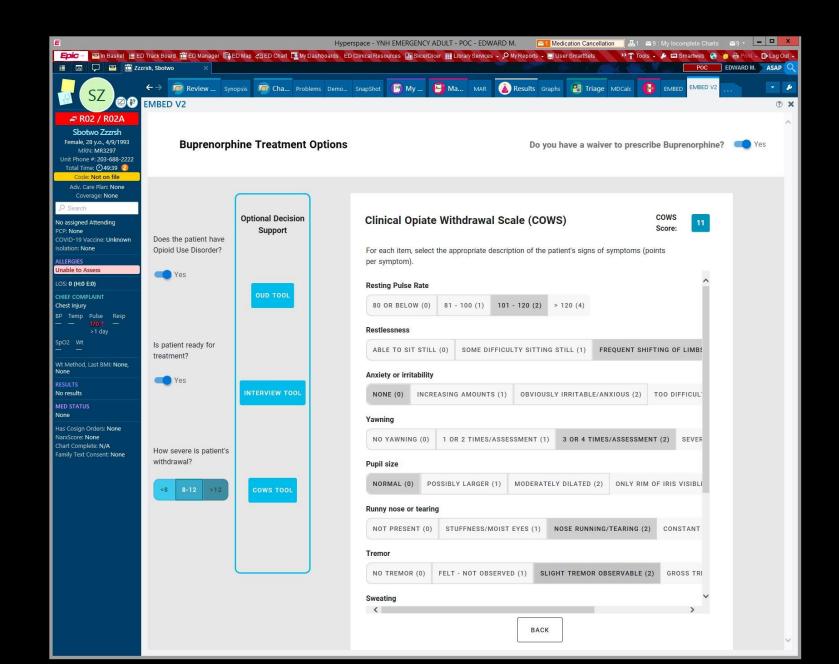


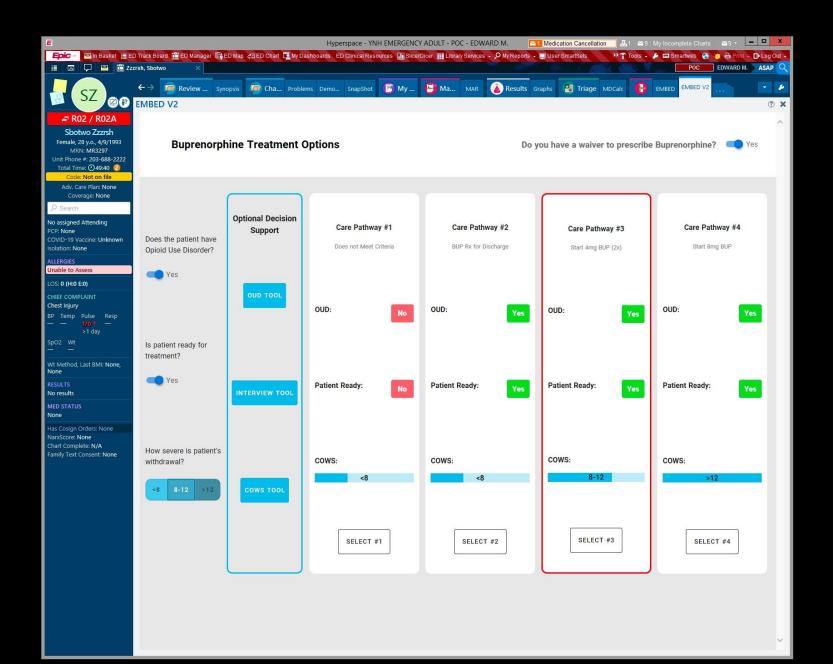


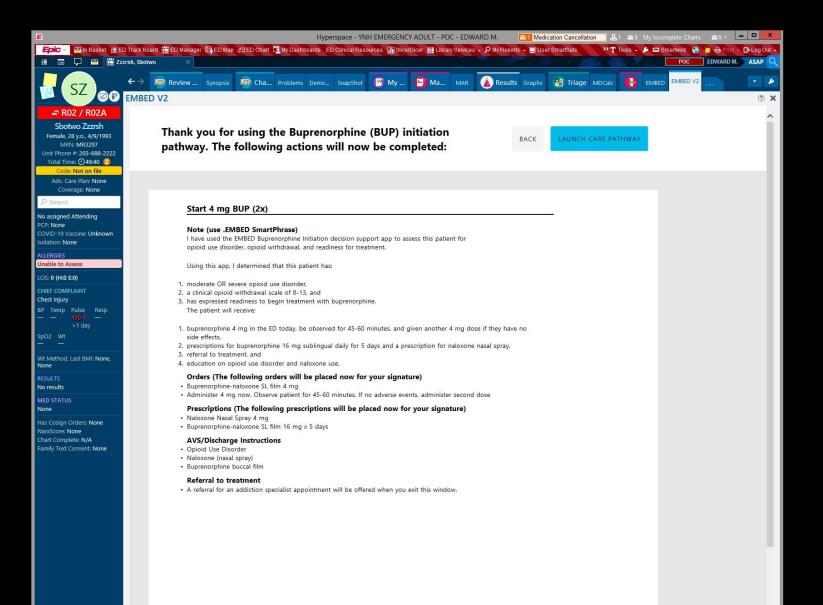


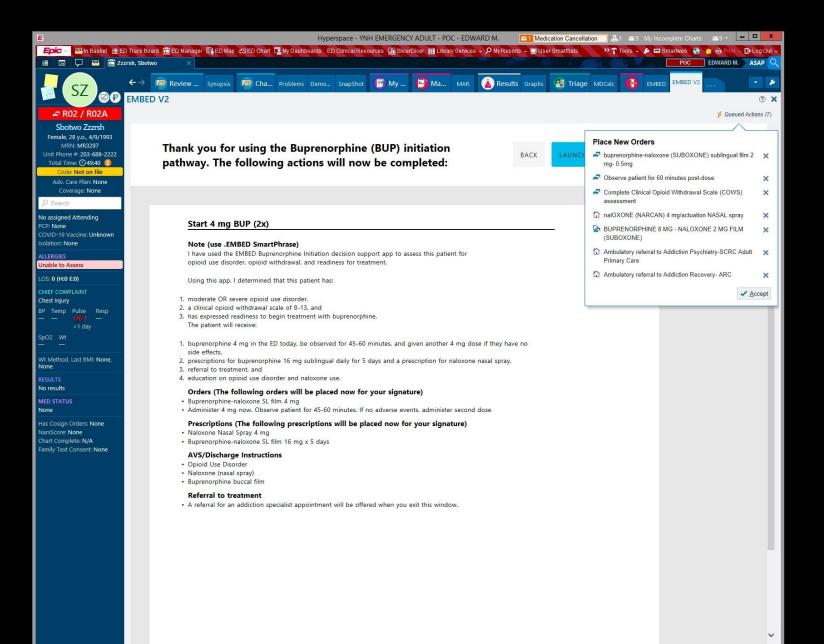


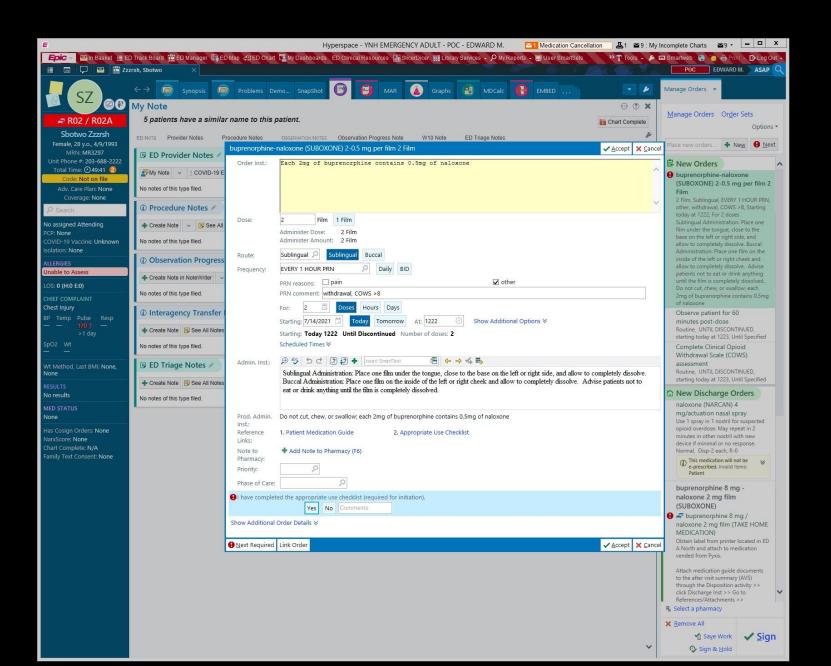










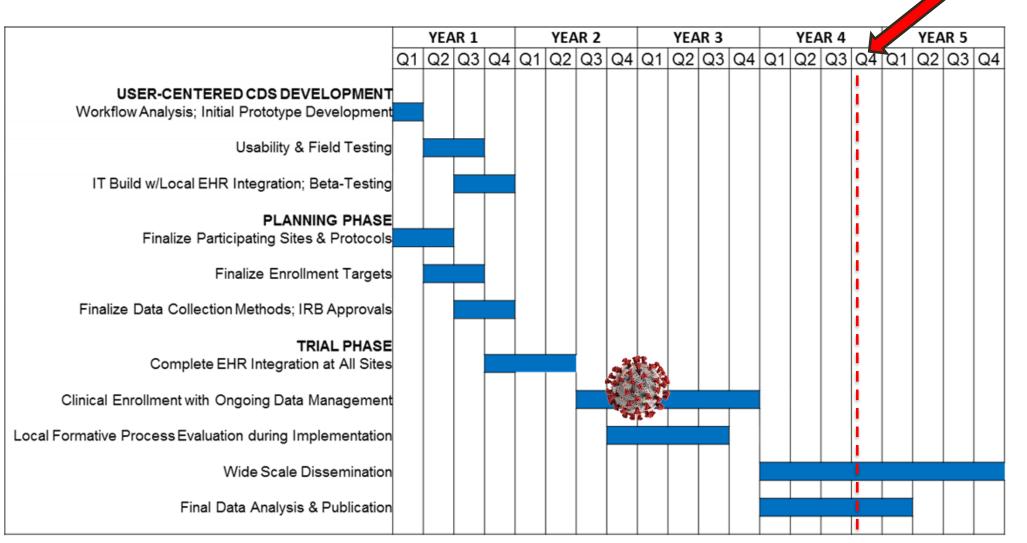


After signing the orders, the clinician continues to work in the EHR





Project Timeline





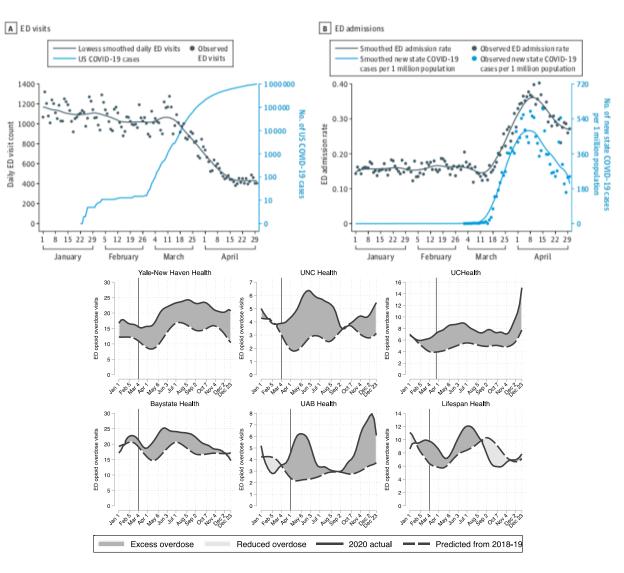
We are here

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:

Jeffery et al. JAMA Intern Med 2020;180(10): 1328-33. Soares et al. Ann Emerg Med 2021 Mar 19; online ahead of print.

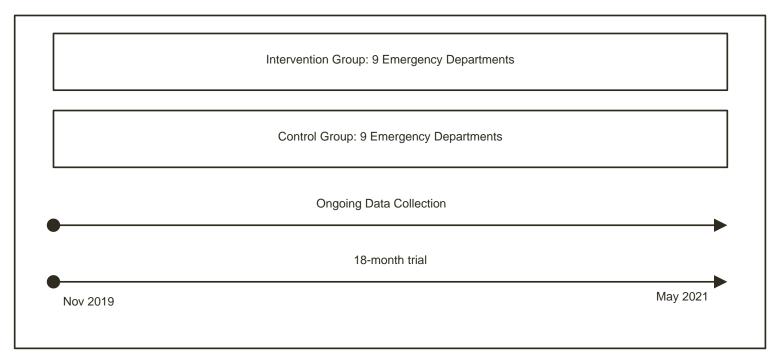


The EMBED Trial



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)

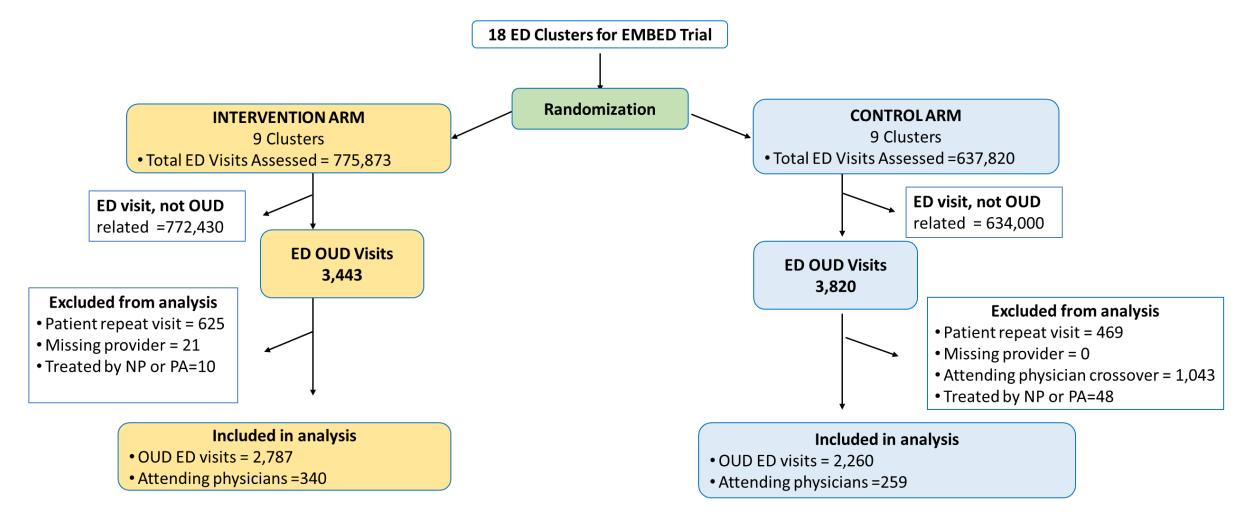


EMBED Trial Protocol. BMJ Open, 2019





Consort Diagram



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



Patient Characteristics

	Intervention	Control	Total
	N (%)	N (%)	
Total, N	2787	2260	5047
Age	36.0 (29.0-48.0)	36.0 (29.0-46.0)	36.0 (29.0-47.0)
Gender			
Male	1870 (67.1%)	1447 (64.0%)	3317 (65.7%)
Female	917 (32.9%)	813 (36.0%)	1730 (34.3%)
Race			
Black	452 (16.2%)	406 (18.0%)	858 (17.0%)
White	2048 (73.5%)	1565 (69.2%)	3613 (71.6%)
Other	196(7.1%)	219 (9.8%)	415 (8.2%)
Ethnicity			
Hispanic or Latino	505 (18.1%)	196 (8.7%)	701 (13.9%)
Not Hispanic or Latino	2166 (77.7%)	1934 (85.6%)	4100 (81.2%)



Physician Characteristics

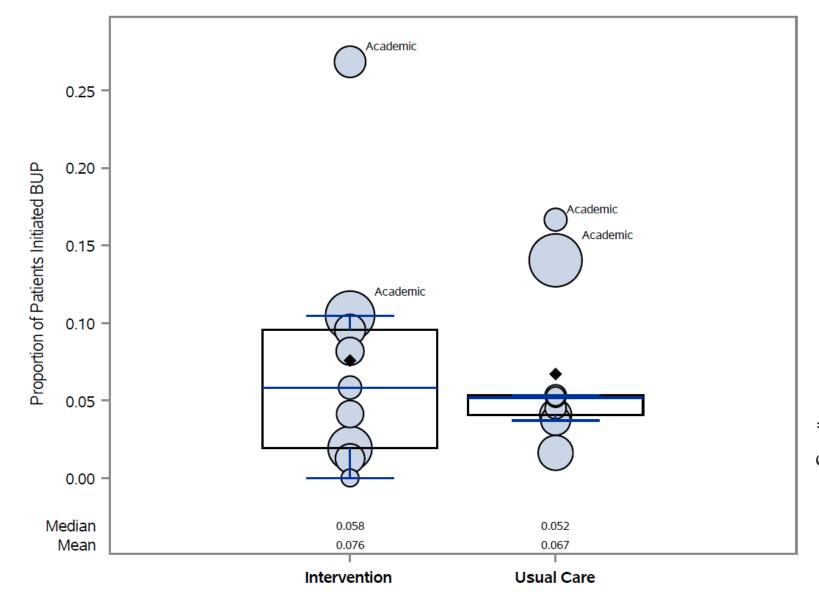
Physicians	Intervention N (%)	Control N (%)	Total
Total, N	340	259	599
Gender			
Male	210 (66.9%)	141 (67.1%)	351 (67.0%)
Female	104 (33.1%)	69 (32.9%)	173 (33.0%)
Age Group, in years			
<35	68 (21.7%)	41 (19.5%)	109 (20.8%)
35-44	124 (39.5%)	82 (39.0%)	206 (39.3%)
45-54	84 (26.8%)	56 (26.7%)	140 (26.7%)
55-64	29 (9.2%)	24 (11.4%)	53 (10.1%)
65+	9 (2.9%)	7 (3.3%)	16 (3.1%)



Outcomes

	Cou	nts	Unadjust	ed	Adjusted**	
	Intervention	Control	Effect size	p-value	Effect size	p-value
Patient level outcomes	N = 2787 (%)	N = 2260 (%)	OR (95 % CI)		OR (95 % CI)	
BUP initiated	233 (8.4%)	193 (8.5%)	1.24(0.57, 2.71)	0.59	1.17 (0.64, 2.14)	0.60
Naloxone prescription at discharge	517 (18.6%)	135 (6.0%)	1.62 (0.81, 3.22)	0.17	1.17 (0.45, 3.09)	0.75
BUP initiated using EMBED	111/261 (42.5%)					
Unique Physicians who:	N = 340 (%)	N = 259 (%)	OR (95 % CI)		OR (95 % CI)	
Initiated BUP	135 (39.7%)	78 (30.1%)	1.53 (1.08, 2.15)	0.02	1.76 (1.12, 2.76)	0.02
Prescribed naloxone at discharge	177 (52.1%)	71 (27.4%)	2.88 (2.03, 4.07)	<0.0001	5.30 (3.33, 8.44)	<0.0001
Initiated BUP using EMBED	76/129 (58.9%)					

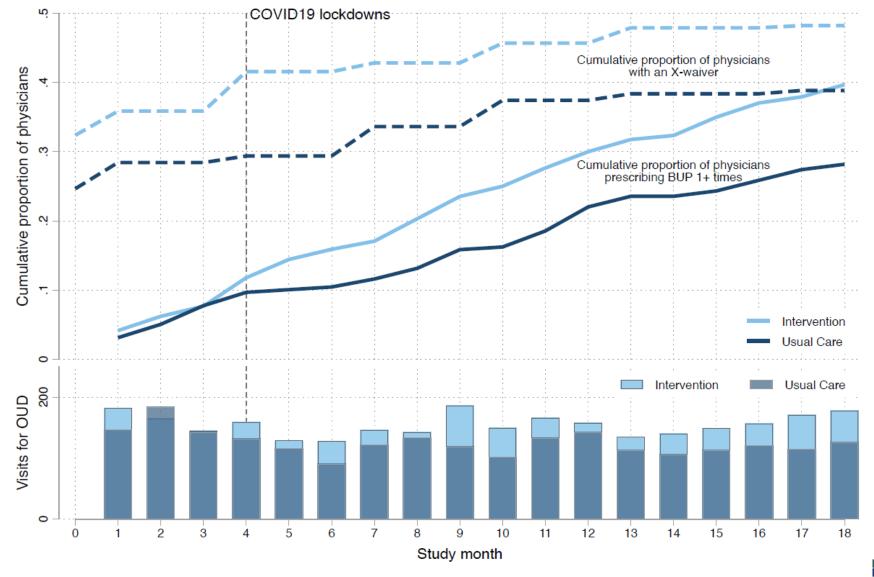
Proportion of OUD patients receiving BUP by study arm



* Bubble size indicating OUD cluster patient volume



Temporal trends of physicians initiating BUP and X-waiver (cumulative)





Subgroup Analyses

Subgroup										P value
Cubgroup			OR(dia	amond) v	with 95	5% CI(I	ine)			Value
Patient Age				1						0.28
18-44						-				
45-64										
65+ Patient Gender										0.30
Male						_				0.50
Female										
Patient Race				1						0.38
Black					+					
White			_							
Other race										0.00
Patient Ethnicity Hispanic or Latino				1						0.06
Non-Hispanic			· · · ·							
Unknown						•				
Patient Insurance										0.37
Medicare										
Medicaid					•	_				
Private/HMO				- 1						
Self-pay Other										
OUD Phenotype										0.87
Algorithm 1			-							0.07
Algorithm 2										
Practice Setting										0.62
Academic		_			•				-	
Community										
	In favor o	of control					In fa	vor of i	nterventio	n
	· · · · · · · · · · · · · · · · · · ·				1	1	-			_
	0.1	0.3	0.5 0.7	1	2	3	5	10	15 20	30

NIH PRAGMATIC TRIALS COLLABORATORY Rethinking Clinical Trials®

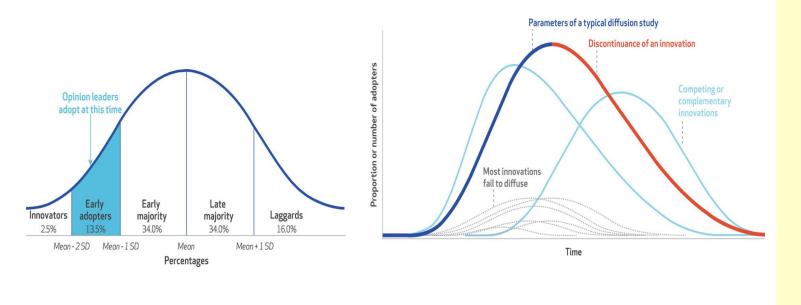
Conclusion

- **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
- <u>BUT</u> 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.



Health Affairs, 2018

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



EMBED related publications

Date	Journal	Author	Article Title
Mar-21	Ann Emerg Med	Soares et al.	Emergency Department Visits for Nonfatal Opioid Overdose During the COVID-19 Pandemic Across Six US Health Care Systems.
Feb-21	Stat Methods Med Res	Li et al.	Mixed-effects models for the design and analysis of stepped wedge cluster randomized trials: An overview.
Oct-20	JAMA Intern Med.	Jeffery et al.	Trends in Emergency Department Visits and Hospital Admissions in Health Care Systems in 5 States in the First Months of the COVID-19 Pandemic in the US.
Aug-20	Acad Emerg Med	Holland et al.	Interrupted Time Series of User-centered Clinical Decision Support Implementation for Emergency Department-initiated Buprenorphine for Opioid Use Disorder.
Jun-20	Int J Epidemiol	Li et al.	Commentary: Right truncation in cluster randomized trials can attenuate the power of a marginal analysis.
Feb-20	J Psychiatr Brain So	ciMelnick et al.	Progress Report on EMBED: A Pragmatic Trial of User-Centered Clinical Decision Support to Implement EMergency Department-Initiated BuprenorphinE for Opioid Use Disorder.
Oct-19	JMIR Med Inform	Chartash et al.	Identifying Opioid Use Disorder in the Emergency Department: Multi-System Electronic Health Record-Based Computable Phenotype Derivation and Validation Study.
Oct-19	JAMIA Open.	Melnick et al.	An integrated web application for decision support and automation of EHR workflow: a case study of current challenges to standards-based messaging and scalability from the EMBED trial.
Jul-19	J Subst Abuse Treat.	Ahmed et al.	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.
May-19	BMJ Open	Melnick et al.	User-centred clinical decision support to implement emergency department-initiated buprenorphine for opioid use disorder: protocol for the pragmatic group randomised EMBED trial.
Feb-19	JMIR Hum Factors	Ray et al.	Computerized Clinical Decision Support System for Emergency Department-Initiated Buprenorphine for Opioid Use Disorder: User-Centered Design.

Yale - EMBED Resources Page

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





EMBED Demo Video for ACEP '21 Conference



Smartphone app for Bup Initiation

- Android app
- iOS app •

MD CALC

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





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Thank you! Questions?

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