Methadone Initiation for Opioid Use Disorder in the Emergency Department

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Ensure that your presentation meets the following requirements:

- Includes a disclosure for every presenter
- Includes references and/or citations for all research
- Is free from commercial bias (uses generic rather than trade names, no logos, balanced discussion of therapeutic options)
- Uses language that is inclusive of all members of the health care team and is non-stigmatizing
- Uses 20-point font or higher for all content (except for references)
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◆ Rachel Haroz, MD – Cooper Medical School of Rowan University

- No Disclosures
- Joseph D'Orazio, MD Cooper Medical School of Rowan University
 - No Disclosures
- Matthew Salzman, MD, MPH Cooper Medical School of Rowan University
 - No disclosures
- ◆ William E. Soares, III, MD, MS UMASS Chan Medical School Baystate
 - No Disclosures
- ◆ Ryan P. McCormack, MD, MS NYU Grossman School of Medicine
 - No Disclosures
- ♦ Jessica Heil, MPH Cooper University Health Care
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Learning Objectives

- Describe the pharmacologic properties, risks, and benefits of methadone treatment in OUD treatment.
- Understand the regulatory and geographic considerations of OTPs and their impact on ED-based methadone initiation.
- Apply ASAM Clinical Practice Guidelines to establish safe methadone dosing protocols for ED settings.
- Describe approaches reflective of different geographic, regulatory restrictions



Poll

What is your primary occupation?

- Physician
- Psychologist
- Other Practitioners
- Counselors
- Peer Navigators
- Researchers or Academics
- Residents, Fellows, and Students
- Others

How would you describe the primary location where you currently practice medicine?

• Academic



- Community
- Federal



Purpose

Translating OUD treatment initiation to the ED setting

Transformational Events:

1) The Opioid Epidemic

2) 2015: Landmark study of ED-initiated buprenorphine

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



D' Onofrio et al JAMA. 2015;313(16):1636-1644; Bush et al.



Why focus on the ED?

- ... because that's where the patient's are!
- Logical point of intervention to narrow the treatment gap
- Resources now exist to support implementation, but local champions are essential





Why Methadone??

We have buprenorphine, why do we also need methadone?

Growing reluctance to transition to buprenorphine

- Evolving concerns and approaches in the fentanyl era
- Complicated buprenorphine invitations, including precipitated withdrawal
- Dose adequacy
- Choice and engagement



The Gameplan

- History of regulations
- Commons misconceptions
- Methadone initiation
- Processes, infrastructure and leadership for the ED
- Cases and panel discussion





History of Methadone Treatment

Vincent P. Dole, Jr., MD; Marie Nyswander, MD; and Mary Jeanne Kreek, MD



First research paper describing methadone maintenance treatment research Dole, V.P., Nyswander, M.E. and Kreek, M.J.: Narcotic blockade: a medical technique for stopping heroin use by addicts. <u>Transactions of the Association of</u> <u>American Physicians</u> (May 1966), <u>79</u>:122-136, 1966. *(including discussion)*



Opioid Treatment Programs

•Methadone Clinic

•Federally regulated with state and county regulations superimposed – 5 tiers + 2 federal statutes

•Structure is rigid

•Expectations: daily attendance, participation in counseling, programming

•Little consideration for employment, childcare, illness



19 States and the District of Columbia Impose Barriers on Opening New OTPs

Restrictions on new OTPs as of June 1, 2021

4SAV



Certificate of need Certificate of need and moratorium Certificate of need and cap on number of facilities
No restrictions
No data

8 States Require a Government ID to Access OTP Treatment Rules as of June 1, 2021



Some State Differences

State Stability Requirements Make It Harder to Obtain Take-Home Medication

States with a definition of stability beyond what is described in federal rules as of June 1, 2021



Terminating Care Because of Continued Drug Use Is Common, Despite Being Against Federal Guidelines Regulations allowing for administrative discharge as of June 1, 2021



Overview of Opioid Treatment Program Regulations by State | The Pew Charitable Trusts (pewtrusts.org)

History of Regulations

Harrison narcotic Act 1914

Federal Regulations of 1972 - Title 42 of the Code of Federal Regulations (42 CFR) part 8

Oversight moved to SAMHSA 2001

COVID impact

New Federal Regulations 2024



PRESS RELEASES

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Reps. Norcross, Bacon Lead Introduction of the Modernizing Opioid Treatment Access Act

-March 6, 2023-

WASHINGTON, DC – Today, U.S. Congressmen Donald Norcross (D-NJ-01) and Don Bacon (R-NE-02) unveiled the Modernizing Opioid Treatment Access (MOTA) Act (H.R. 1359). This evidence-based legislation would increase access to care for people experiencing opioid use disorder (OUD) by reforming the outdated regulations governing the prescription and dispensing of methadone. Methadone is one of the most effective medicines used for the treatment of OUD and is considered an "essential medicine" by the World Health Organization. U.S. Representatives Annie Kuster (D-NH-02), David Trone (D-MD-06), Brain Fitzpatrick (R-PA-01), Paul Tonko (D-NY-20), Brittany Pettersen (D-CO-07), and Andy Kim (D-NJ-03) are original cosponsors of the bill.



"Improving access to treatment saves lives, period," **said Congressman Norcross**. "This legislation lowers barriers to care at a time when we are still suffering staggering losses due to the ongoing opioid epidemic. We must end the monopoly on this life-saving medicine that only serves to enrich a **Misconceptions**





Misconceptions

Poll questions:

- 1. Emergency Departments are not allowed to administer more than 30 mg of methadone (T/F) for an initial dose.
- 2. An ECG must be obtained prior to methadone administration (T/F).
- 3. Short-acting opioid analgesics will have no benefit to patients on methadone maintenance (T/F).
- 4. A patient can be dosed in the Emergency Department for a maximum of three consecutive days (T/F).
- 5. Patients presenting to the Emergency Department for a missed methadone dose may only be given 40 mg regardless as to their clinic dose.
- 6. Patients who miss more than 3 days of methadone and present to the Emergency Department should be treated as new start and administered 30 mg of methadone.
- 7. A urine drug screen should be obtained prior to methadone administration in the Emergency Department.





West J Emerg Med. 2022 Apr 4;23(3):386–395. doi: <u>10.5811/westjem.2022.2.54681</u>

Attitudes on Methadone Utilization in the Emergency Department: A Physician Cross-sectional Study

Jessica Heil^{**, So}, Valerie S Ganetsky^{*}, Matthew S Salzman^{**}, Krystal Hunter^{*}, Kaitlan E Baston^{*}, Gerard Carroll^{*}, Eric Ketcham^{\$}, Rachel Haroz^{**}

Initiating patients on ____ is not within the scope of an ED physician's practice.



EM providers should offer _____to help control the symptoms of opioid withdrawal and craving.







The American Journal of Emergency Medicine Volume 89, March 2025, Pages 209-215

Emergency department utilization of the methadone "72-hour rule" to bridge or initiate and link to outpatient treatment

Samantha Huo MD, MPH, MS^{ob} A ⊠, Jessica Heil MS^o, Matthew S. Salzman MD, MPH^{ocd}, Alice Ely PhD^o, Samuel Snyder^c, Dante Terracciano^c, Rachel Rafeq PharmD^d, Valerie Ganetsky PharmD^o, Gerard Carroll MD^{de}, Rachel Haroz MD^{ocd} "At 30 days, 75 % of patients linked to our partner OTP were retained in treatment."



Methadone vs Buprenorphine or Naltrexone

Full opioid agonist: Effective for high-dependency cases.

- No ceiling effect (unlike buprenorphine).
- Beneficial for patients with severe dependence, severe withdrawal intolerance, history of difficult buprenorphine inductions.

Limitations:

- Requires daily visits to an OTP (opioid treatment program).
- QTc prolongation risks.
- Others



Murphy, 2024, American Journal of Drug & Alcohol Abuse Englander et al., 2024, JAMA Internal Medicine

Standard Methadone Initiation Strategies

Traditional Titration:

- Start 10-30 mg PO daily
- Reassess in 2-4 hours, may give 5-10 mg additional dose if needed.
- ◆ Target stabilization in 5-7 days with gradual 5-10 mg daily increases.



Alternate Initiation Strategies

- Methadone 40mg (day 1), 50mg (day 2), 60mg (day 3-5) titrating up for continued withdrawal
- Methadone 40mg daily followed by methadone 10 mg Q6 PRN withdrawal
 - Day 2: TDD from previous day, plus 10 mg PRN
 - Day 3: TDD from previous day, plus 10 mg PRN
- Low-Threshold/Harm-Reduction Model
 - Smaller initial doses with fewer restrictions on takehome options.





Alternative Dosing Routes

- Oral Standard and preferred route
- Intramuscular (IM) or Intravenous (IV) Use
 - May be considered in inpatient settings when unable to use oral route
 - 2:1 ratio dosing (Methadone 40mg PO ~ 20mg IV)
- Take-Home Doses:
 - Policy changes post-COVID increased accessibility.
 - Short-term take-home doses allowed in emergency settings in some states



Hazekamp & Sacco, 2024, Emergency Medicine Practice

Methadone Initiation in the Fentanyl Era

- The dose of fentanyl in the community far exceeds the dose of opioid (50x or greater)
- The affinity to the mu receptor fentanyl > methadone
- A single bag of fentanyl in the Northeast often contains >5mg (600 MME)
- A single fentanyl pressed tablets commonly contains >2mg (240 MME)
- Methadone 30mg PO daily ~ 265 MME





Composition of Glassine Contents

- "Lady Gaga" glassine contained 44 milligrams of white powder
 - 19% Fentanyl (total dose of Fentanyl = 8.4 milligrams)

19.36%

79.40%

Fentanyl 4-ANPP Othe

1.23%





Credit: Ken Hand, MS. Laboratory Director, Cape May County Prosecutor's Office

Methadone & QTc Prolongation

• Risk Factors:

- Doses >100 mg/day.
- Hypokalemia, hypomagnesemia.
- Other QTc-prolonging meds (e.g., fluoroquinolones, SSRIs).

Management Strategies:

- ♦ If QTc >450 ms, monitor more closely.
- If QTc >500 ms, consider dose reduction under 100mg or switch to buprenorphine

CYP3A4 & CYP2B6 Metabolism:

- ◆ Inducers ↓ methadone levels: Rifampin, carbamazepine, phenytoin.
- Sedative Interaction Risks:
 - Benzodiazepines & alcohol $\rightarrow \uparrow$ overdose risk.
 - Gabapentinoids $\rightarrow \uparrow$ respiratory depression



Managing Missed Doses in the ED

Problems to consider: Loss of tolerance QTc prolongation

Variability in practice: <3 days missed: Resume last stable dose* Stretch to 5 days? ≥3 but <14 days missed: Restart at half dose, titrate up* Is the 5-14 day range too long? Alternate approaches? ≥14 days missed: Restart as a new initiation*



ED Take-Home Doses

Policy Changes Post-COVID:

- EDs can now provide 3-day take-home methadone to bridge patients until OTP follow-up in certain states
- Typical Dosing for ED
 - Initial PO once dose in the setting of opioid withdrawal
 - followed by 10mg PRN dose for persistent withdrawal symptoms



Brown University Public Health Journal, 2024







ED Methadone Protocol







-The Patient Face Sheet - A signed last dose letter (see template in protocol) Give to the Patient to bring to the clinic -Methadone Discharge Instructions (see template in protocol) -Completed Last Dose letter in a sealed envelope, with signature over the seal. -Take Home Narcan from Pxvis

Complete the following:

DOCUMENT in the Clinical Chart

1) History of Opioid Use

What drugs does patient use? How much? How do they use? How long have they used? When was last use?

2) Any Prior Methadone Use

Which Clinic? What was their stable dose? When was their last dose?



ED Methadone Protocol









ED - Methadone Protocol (Initiated Pending)					
		٩	This PowerPlan is to be used in conjunction with the ED Methadone Protocol (Guid	elines) Information packet.	$\hat{}$
	Ð	7	Methadone Reference Document	Right click for Methadone reference do	cur
		2	Opioid Overdose (ED Only)		
		٩	Consult Orders		\bigcirc
		3	To assist with patient follow up, place the following order to notify the Buprenorpl	hine Coordinator	0
		2	Buprenorphine Coordinator (ED Only)		
		٩	For patients being ADMITTED to BMC, place the following order to notify the Addiction Medicine service		
	P	2	Addiction Consult	Consultation	
		٩	For patients being ADMITTED to BFMC, place the following order to notify the Addiction Medicine service		$\hat{}$
		٩	Narcan (Naloxone) Narcan Kit for Home Use		$\hat{\mathbf{x}}$
		3	To order a Narcan Kit for the patient to take home, select the following order:		\$
	P	ീ	naIOXONE (Naloxone Take Home Rescue Kit)	1 sprays, Nasal Spray, Nares, Both, Onco	e, S'
		<u> (</u>	Laboratory		$\hat{\mathbf{x}}$
	1	7	Fentanyl Screen, Urine	Stat, T;N	
	Ę		Methadone Urine	Stat, T;N	
	Ð		Opiate Screen Urine	Stat, T;N	
		٩	Nursing Orders		\bigcirc
	Ę	7	ECG 12 Lead	Stat, Reason: Cardiac Arrythmia Unspec	cifie
		3	Methadone Orders		0
		<u>⁄&</u>	Refer to the Methedone Reference Document for docing guidence		1.1



WE DON'T TALK ABOUT.... METHADONE

BILL SOARES MD, MS DIRECTOR OF HARM REDUCTION SERVICES ASSISTANT PROFESSOR OF EMERGENCY MEDICINE UNIVERSITY OF MASSACHUSETTS CHAN MEDICAL SCHOOL -BAYSTATE



Case Presentations/Panel Discussion

We welcome your questions and comments!

- **1**. New initiation of methadone
 - Simple start; high opioid requirements; not yet in withdrawal
- Missed methadone dose (i.e., already engaged in an OTP)
 Dose confirmed vs. unconfirmed
- **1.** Engaging patients with MOUD reluctance
- 1. The "frequent flyer" on methadone
- **1.** Acute pain in a patient on methadone maintenance



Final Takeaways/Summary

Methadone plays a unique role in the fentanyl era

Methadone initiation and referral to an OTP from the ED is feasible from a regulatory and practical standpoint

Patient pathway differences may arise from geographic constraints and local regulatory impact



QR Code for Clinical Toolkit

Referral algorithms

Dosing strategies and risk stratification

Literature/references

Guide to stakeholder recruitment and relationships

Tips of the Trade





References (Required)

•Harrison_Narcotics_Tax_Act_1914.pdf (naabt.org)

•Strang J, Volkow ND, Degenhardt L, Hickman M, Johnson K, Koob GF, Marshall BDL, Tyndall M, Walsh SL. Opioid use disorder. Nat Rev Dis Primers. 2020 Jan 9;6(1):3. doi: 10.1038/s41572-019-0137-5. PMID: 31919349.

•Koehl JL, Zimmerman DE, Bridgeman PJ. Medications for management of opioid use disorder. Am J Health Syst Pharm. 2019 Jul 18;76(15):1097-1103. doi: 10.1093/ajhp/zxz105. PMID: 31361869.

•Ma J, Bao YP, Wang RJ, Su MF, Liu MX, Li JQ, Degenhardt L, Farrell M, Blow FC, Ilgen M, Shi J, Lu L. Effects of medication-assisted treatment on mortality among opioids users: a systematic review and meta-analysis. Mol Psychiatry. 2019 Dec;24(12):1868-1883. doi: 10.1038/s41380-018-0094-5. Epub 2018 Jun 22. PMID: 29934549.

•Clinical Guidelines for Withdrawal Management and Treatment of Drug Dependence in Closed Settings. Geneva: World Health Organization; 2009. 6, Methadone maintenance treatment. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK310658/</u>

•Huo S, Heil J, Salzman MS, Carroll G, Haroz R. METHADONE INITIATION IN THE EMERGENCY DEPARTMENT FOR OPIOID USE DISORDER: A CASE SERIES. J Emerg Med. 2023 Mar;64(3):391-396. doi: 10.1016/j.jemermed.2023.01.012. PMID: 37019500.

•Overview of Opioid Treatment Program Regulations by State | The Pew Charitable Trusts (pewtrusts.org)

