

# Medications to address the opioid crisis - methadone, buprenorphine, naltrexone, and naloxone

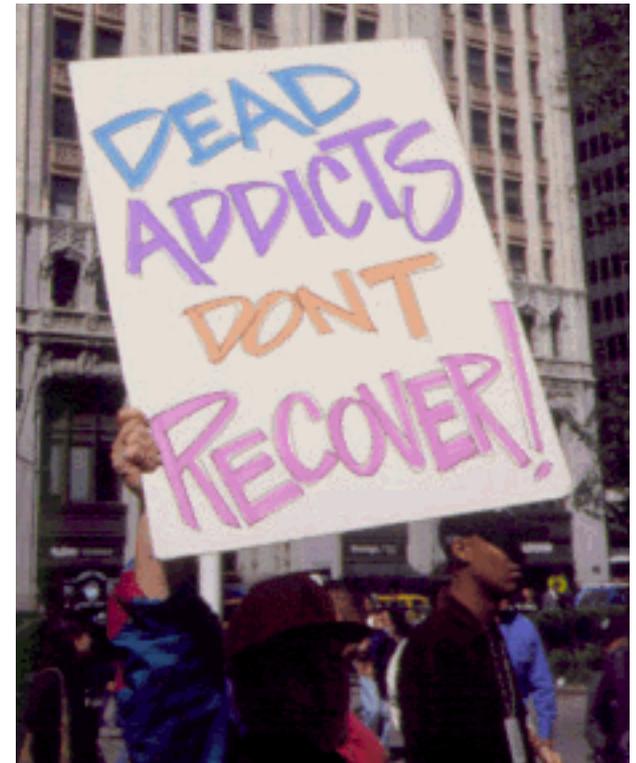
Alexander Y. Walley, MD, MSc  
Director, Addiction Medicine Fellowship and  
Addiction Medicine Consult Service  
Medical Director, MDPH Opioid Overdose Prevention Pilot  
Program

Doc 2 Doc Teleconference  
7:30-8:00am  
Friday, October

# Learning objectives

At the end of this session, you will be able to:

1. Match patients with evidence-based medications (methadone, buprenorphine, and naltrexone) for opioid use disorders
2. Incorporate overdose prevention with naloxone rescue kits into your clinic practice



# The DSM-5 defines a substance use disorder as the presence of at least 2 of 11 criteria, which can be clustered in four groups:

## A. Impaired control:

1. Taking more or for longer than intended
2. Not being able to cut down or stop (repeated failed attempts)
3. Spending a lot of time obtaining, using, or recovering from use
4. Craving for substance

## B. Social impairment:

5. Role failure (interference with home, work, or school obligations)
6. Kept using despite relationship problems caused or exacerbated by use
7. important activities given up or reduced because of substance use

## C. Risky use:

8. Recurrent use in hazardous situations
9. Kept using despite physical or psychological problems

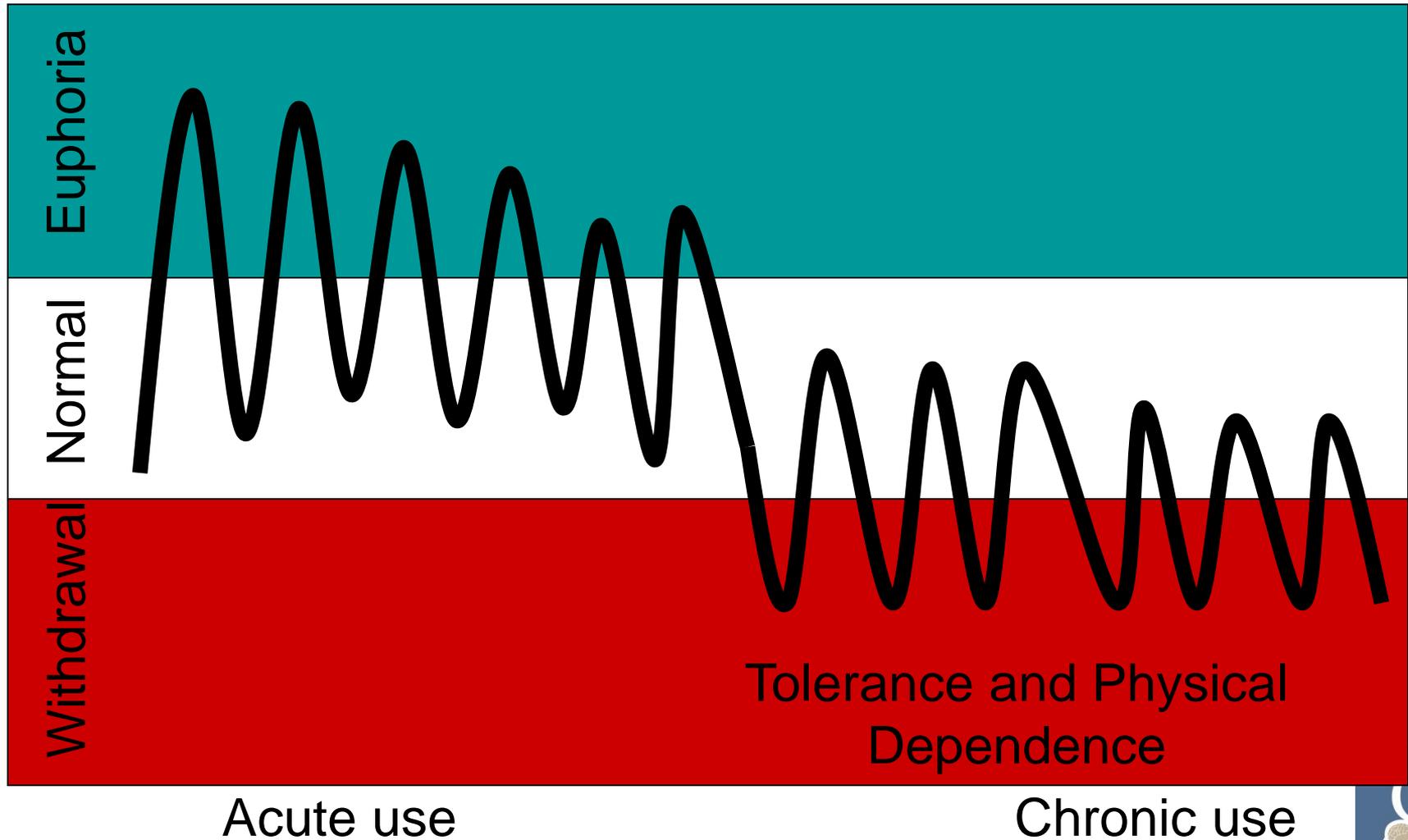
## D. Pharmacologic dependence:

10. Tolerance to effects of the substance\*
11. Withdrawal symptoms when not using or using less\*

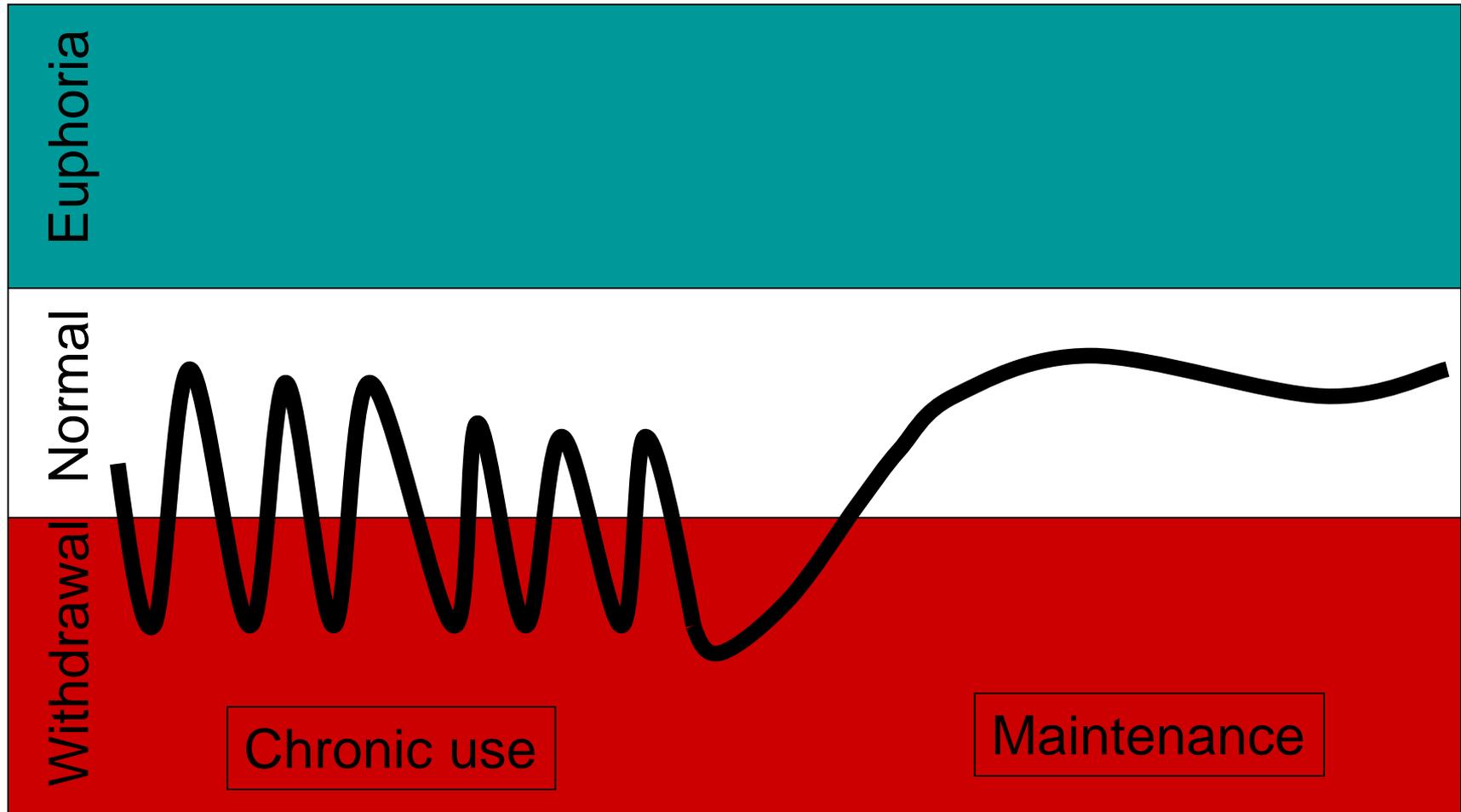
\* Persons who are prescribed medications such as opioids may exhibit these two criteria, but would not necessarily be considered to have a substance use disorder

Mild = 2-3 criteria, Moderate = 4-5 criteria, Severe = 6 or more criteria

# Why do people use opioids?



# Maintenance Treatment for Opioid Dependence



# Goals of maintenance treatment for opioid dependence

1. Relief of withdrawal symptoms
  - Methadone (30-40mg), buprenorphine
2. Opioid blockade
  - Methadone (>60mg), buprenorphine, naltrexone
3. Reduce opioid craving
  - Methadone (>60mg), buprenorphine, naltrexone
4. Restoration of reward pathway
  - Long term (>6 months)
  - Methadone, buprenorphine, naltrexone

# Methadone Maintenance Treatment

## Highly Structured

- Daily nursing assessment
- Weekly individual and/or group counseling
- Random supervised toxicology screens
- Psychiatric services
- Medical services
- Methadone dosing
  - Observed daily ⇒ “Take homes”

# Methadone Maintenance Limitations

- Highly regulated - *Narcotic Addict Treatment Act 1974*
  - Created methadone clinics (Opioid Treatment Programs)
  - Separate system not involving primary care or pharmacists
- Limited access
  - 5 states: 0 clinics, 4 states: < 3 clinics
- Inconvenient and highly punitive
- Mixes stable and unstable patients
- Lack of privacy
- No ability to “graduate”
- Stigma



# Buprenorphine Treatment

- Retention rates comparable to methadone
- Efficacy comparable to methadone (80mg)
- Milder withdrawal syndrome
- Very low risk for overdose
- Decreased risk of abuse
  - Buprenorphine/Naloxone
- Available in primary care settings

# Naltrexone

- Pure opioid antagonist
  - No special training or clinical conditions required
- Oral naltrexone
  - Well tolerated, safe
  - Duration of action 24-48 hours
  - FDA approved 1984
- Injectable naltrexone (Vivitrol<sup>®</sup>)
  - IM injection (w/ customized needle) once/month
  - FDA approved 2010
  - Patients must be opioid free for a minimum of 7-10 days before treatment

# Matching Patients to Maintenance Medications

- The choice between methadone, buprenorphine, or naltrexone depends upon:
  - Patient preference
  - Access to treatment setting
  - Ease of withdrawal
  - Risk of overdose
  - Past experience

How long should maintenance  
treatment last?

Long enough

# Online Training Resources

- Buprenorphine Training and Practice Tools
  - [www.buppractice.com](http://www.buppractice.com)
- Buprenorphine Physician Training Events
  - [buprenorphine.samhsa.gov/training.html](http://buprenorphine.samhsa.gov/training.html)
- Providers Clinical Support System for Medication Assisted Treatment (PCSS-MAT)
  - [pcssmat.org](http://pcssmat.org)

# News

AME  
ASSN

FOR IMMEDIATE RELEASE  
March 26, 2015

Contact: HHS Press Office  
202-690-6343

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## HHS takes strong steps to address opioid-drug related overdose, death and dependence

*Evidence-based, bipartisan efforts focus on prescribing practices and treatment to reduce prescription opioid and heroin use disorders*

U.S. Health and Human Services Secretary Sylvia M. Burwell today announced a targeted initiative aimed at reducing prescription opioid and heroin related overdose, death and dependence. Deaths from drug overdose have risen steadily over the past two decades and currently outnumber deaths from car accidents in the United States. The President’s FY 2016 budget includes critical investments to intensify efforts to reduce opioid misuse and abuse, including \$133 million in new funding to address this critical issue.

www.ama-  
assn.org/ama  
naloxone-pro

The Secretary’s efforts focus on three priority areas that tackle the opioid crisis, significantly impacting those struggling with substance use disorders and helping save lives.

1. **Providing training and educational resources, including updated prescriber guidelines, to assist health professionals in making informed prescribing decisions** and address the over-prescribing of opioids.
2. **Increasing use of naloxone**, as well as continuing to support the development and distribution of the life-saving drug, to help reduce the number of deaths associated with prescription opioid and heroin overdose.
3. **Expanding the use of Medication-Assisted Treatment (MAT)**, a comprehensive way to address the needs of individuals that combines the use of medication with counseling and behavioral therapies to treat substance use disorders.

[www.pharmacist.com/policy/controlled-substances-and-other-medications-potential-abuse-and-use-opioid-reversal-agents-2](http://www.pharmacist.com/policy/controlled-substances-and-other-medications-potential-abuse-and-use-opioid-reversal-agents-2)

initial signs of an opioid overdose reaction.”

[www.asam.org/docs/publicy-policy-statements/1naloxone-1-10.pdf](http://www.asam.org/docs/publicy-policy-statements/1naloxone-1-10.pdf)

management  
oid overdose



# Who is at Risk for Opioid Overdose?



History of alcohol/  
other substance  
abuse



High daily doses of  
opioids



Switching from one  
opioid to another



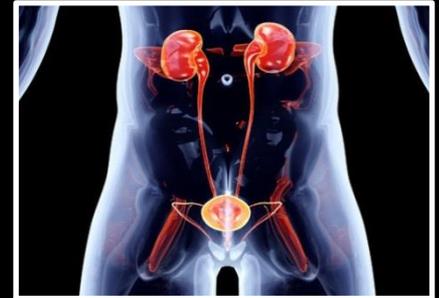
Any opioid for pain +  
benzodiazepine or  
other sedative



Any opioid for pain +  
antidepressant



Any opioid for pain +  
respiratory problems



Any opioid for pain +  
renal/liver disease or  
other conditions

# Overdose Education and Naloxone Rescue

What people need to know:

## 1.Prevention - the risks:

- Mixing substances
- Abstinence- low tolerance
- Using alone
- Unknown source
- Chronic medical disease
- Long acting opioids last longer

## 2.Recognition

- Unresponsive to sternal rub with slowed breathing
- Blue lips, pinpoint pupils

## 3.Response - What to do

- Call for help
- Rescue breathe
- Administer naloxone, continue breathing
- Recovery position
- Stay until help arrives



# How to Respond in an Overdose

1

Recognize the overdose

Call 911 for help



2

Rescue breathe  
Chest compressions  
if no pulse



3



Administer naloxone

- Continue breathing if needed
- Re-administer at 3-5 minutes if no response

4

Stay until help arrives  
Recovery position  
if breathing

5



# Investigate overdose risk

- ✓ Review medications
- ✓ Take a substance use history
- ✓ Check the prescription monitoring program
- ✓ Take an overdose history

*Assess risk by asking your patients whether they:*

- **Feel drowsy or have difficulty breathing when taking opioids or other medications?**
- **Have overdosed?**
- **Witnessed an overdose?**



# Making a risk reduction plan

## *Ask your patients about them*

- What strategies do you use to protect yourself?
- How do you keep your medications safe at home?

## *And their loved ones*

- **What is your plan if you witness an overdose in the future?**
- **Have you received training to prevent, recognize, or respond to an overdose?**



# How to prescribe naloxone

- Three formulations

1. Injectable

- Dispense:
  - 2x Naloxone 0.4mg/ml single dose vial or 1x 0.4mg/ml 10ml vial
  - 2x IM syringe (3ml 25g 1" syringes recommended)
- Directions: For opioid overdose, inject 1ml IM in shoulder or thigh. Repeat after 3 minutes, if no or minimal response



2. Nasal (off-label)

- Dispense:
  - 2x Naloxone 2mg/2ml prefilled luer-lock syringe
  - 2x Mucosal Atomizer Device nasal adapter
- Directions: For opioid overdose, spray 1ml in each nostril. Repeat after 3 minutes, if no or minimal response



3. Evzio Auto-injector - <http://www.evzio.com/hcp/>

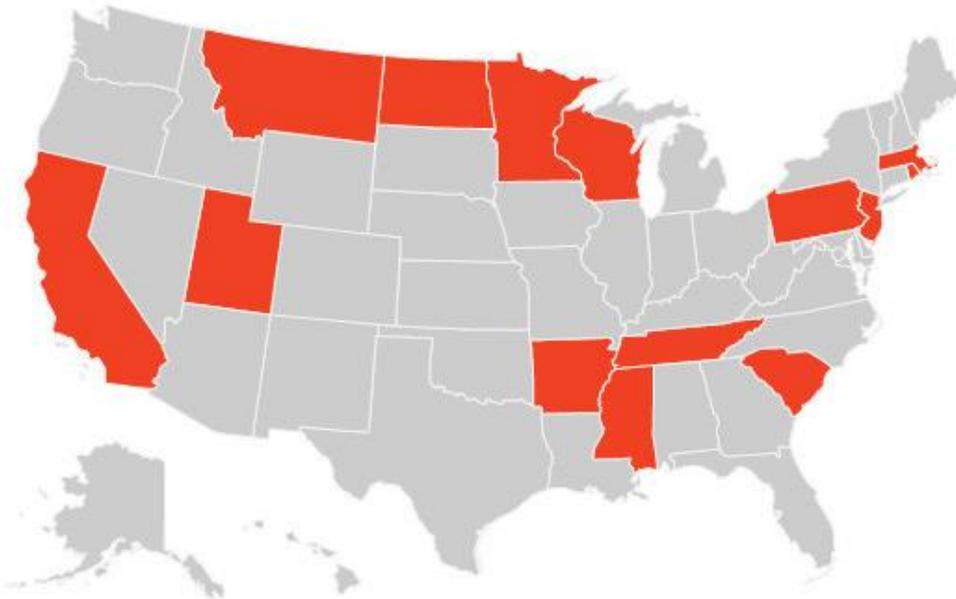




# CVS announcement - Sept 24, 2015

## Naloxone Availability

The life-saving drug is now available without a prescription in **14 states**



# Prescribe to Prevent:

## Overdose Prevention and Naloxone Rescue Kits for Prescribers and Pharmacists

Go to  
[prescribetoprevent.org](http://prescribetoprevent.org)

**Alexander Y. Walley, MD, MSc**  
Boston University School of Medicine

**Jeffrey Bratberg, PharmD, BCPS**  
University of Rhode Island College of Pharmacy

**Corey Davis, JD, MSPH**  
The Network for Public Health Law



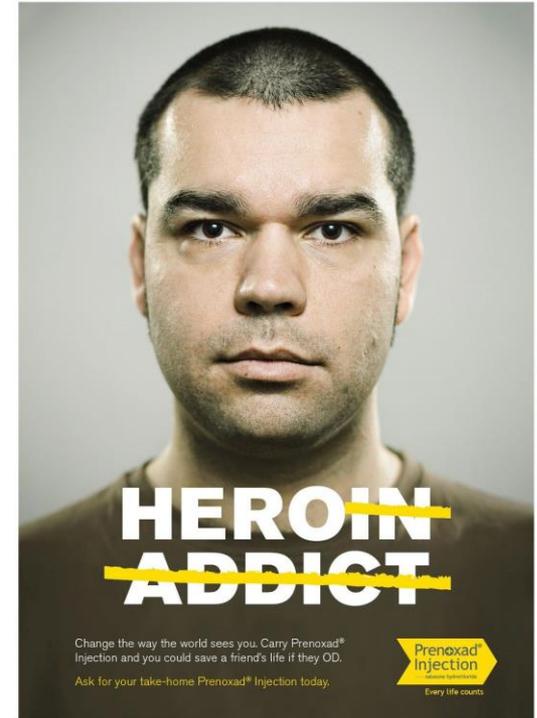
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Thank you!

[awalley@bu.edu](mailto:awalley@bu.edu)



# Models for Prescribing Naloxone

**Prescriber writes prescription  
Patient fills at pharmacy**

**Setting: clinic with insured patients**

**Pharmacies alerted to prescribing plans**

**May need to have atomizers on-site for intranasal formulation**

**Consider providing informational brochure**

**Prescriber writes prescription and dispenses pre-packaged kit**

**Setting: medical care with resources to have and maintain kits on-site**

**Pharmacy provides naloxone directly to customer**

**Without prescriber contact under a collaborative practice agreement (CPA) or standing order**

**Encourage naloxone co-prescribing**

# Massachusetts - Passed in August 2012: An Act Relative to Sentencing and Improving Law Enforcement Tools

## **Good Samaritan provision:**

- Protects people who overdose or seek help for someone overdosing from being charged or prosecuted for drug possession
  - Protection does not extend to trafficking or distribution charges

## **Patient protection:**

- A person acting in good faith may receive a naloxone prescription, possess naloxone and administer naloxone to an individual appearing to experience an opiate-related overdose.

## **Prescriber protection:**

- Naloxone or other opioid antagonist may lawfully be prescribed and dispensed to a person at risk of experiencing an opiate-related overdose or a family member, friend or other person in a position to assist a person at risk of experiencing an opiate-related overdose. For purposes of this chapter and chapter 112, any such prescription shall be regarded as being issued for a legitimate medical purpose in the usual course of professional practice.



# Massachusetts Department of Public Health

## Naloxone

### *Example Standing Order*

### Overview of Pharmacy Naloxone Rescue Kit Access Program

On Thursday March 27, 2014, Governor Patrick declared a State of Public Emergency, providing emergency powers to DPH Commissioner Cheryl Bartlett, RN. At the Governor's direction, Commissioner Bartlett, with the approval of the Public Health Council, issued an Order that authorized pharmacists to dispense naloxone rescue kits to a person at risk of experiencing an opioid-related overdose or a family member, friend or other person in a position to assist a person at risk of experiencing an opioid-related overdose.

The procedures and protocols in this example standing order reflect current medical research and clinical best practice as of April 2014. The standing order can be modified per individual clinical practice and must be signed by a collaborating Massachusetts licensed physician.

#### Requirements:

- A copy of the standing order must be maintained on file and readily retrievable at each participating pharmacy site
- Standing order must be filed with the Board of Registration in Pharmacy (Board) via email: [naloxonestandingorders@Massmail.State.MA.US](mailto:naloxonestandingorders@Massmail.State.MA.US).

Most useful question to determine treatment  
success...

Are you on take homes?  
If not, why not?

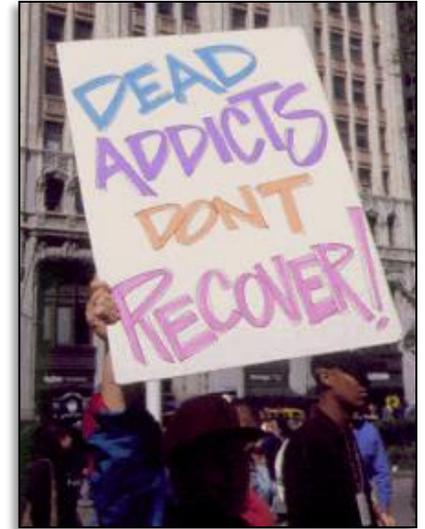
Please communicate with the methadone  
maintenance treatment program

# Opportunities and complications of opioid addiction treatment

- Opportunity - Care Integration
  - Office-based care with agonist treatment
  - Multi-disciplinary – don't forget mental health
- Complications
  - High-risk patients need more
    - Case management services
  - Polysubstance use

# Rationale for Overdose Education and Naloxone Rescue Kits

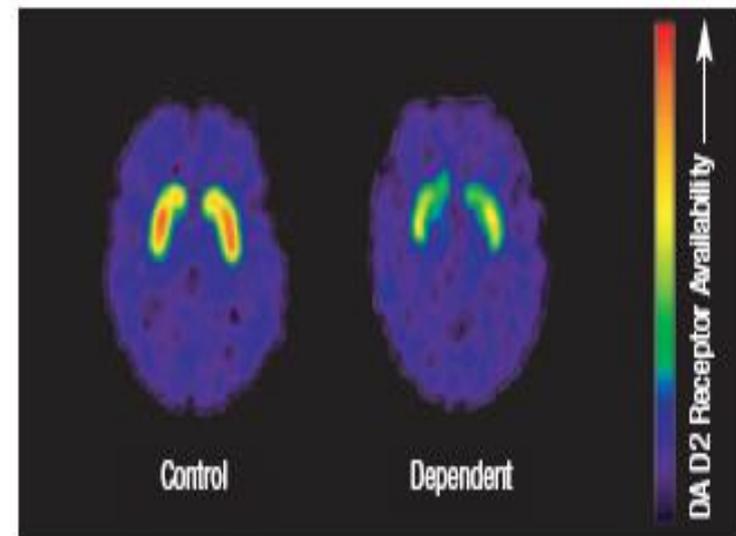
- Most opioid users do not use alone
- Known risk factors:
  - Mixing substances, abstinence, using alone, chronic medical illness
- Opportunity window:
  - Opioid overdoses take minutes to hours
  - Reversible with naloxone
- Bystanders are trainable to recognize and respond to overdoses
- Fear of public safety



# Addiction is a Treatable Brain Disease

- Prolonged substance use causes neurochemical and molecular changes in the brain, which alter<sup>1</sup>:
  - Metabolic brain activity
  - Gene expression
  - Receptor availability
  - Sensitivity to environmental cues

Effects of Heroin Dependence on Brain Dopamine D<sub>2</sub> Receptors<sup>2</sup>



1. Leshner AI. *Science*. 1997;278:45-47.

2. Wang GJ et al. *Neuropsychopharmacology*. 1997;16:174-182.

# Opioid Detox Outcomes

- Low rate of retention in treatment
- Low rate of achieving abstinence
- Low rates of success in maintaining abstinence
  - < 50% at 6 months
  - < 20% at 12 months

# Buprenorphine vs. Methadone

Mattick RP et al. Cochrane Review. 2008

- Review of 24 RCTs found
  - Buprenorphine is effective maintenance treatment, but it is less effective than methadone delivered at adequate doses