Candidates for Naloxone: What the Data Tell Us

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Senior Advisor and Director of Strategy and Innovation
National Center for Injury Prevention and Control
U.S. Centers for Disease Control and Prevention
High Risk Groups

Individuals Prescribed Opioids for Pain

- Opioid doses 50 MME/day or higher
- Co-prescribed benzodiazepines (regardless of opioid dose)
- Respiratory conditions such as COPD or obstructive sleep apnea (regardless of opioid dose)
- Substance use disorder, excessive alcohol use, mental disorder (regardless of opioid dose)

Individuals at High-Risk for Opioid Overdose

- Using heroin or synthetic opioids or misusing Rx opioids
- Using methamphetamine, cocaine, other drugs potentially contaminated with illicit synthetic opioids
- Receiving treatment for OUD, including medication-assisted treatment
- Released from incarceration or other controlled setting and history of opioid misuse
High Risk Groups

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- Substance use disorder, excessive alcohol use, mental disorder (regardless of opioid dose)
Patients Receiving Opioid Doses of 50 MME or Higher

**Risk for Non-Fatal Opioid Dose**

Adjusted Hazard Ratio

- No use: 0.4
- 1 to <20 MME: 1.0
- 20 to 50 MME: 2.5
- 50 to <100 MME: 4.1
- ≥100 MME: 6.2

Source: Campbell et al., Preventive Medicine, 2018; Baumblatt et al., JAMA IM. 2014.

**Figure 3. Association of Mean Daily Dosage of Opioid Analgesics With Risk of Unintentional Opioid-Related Overdose Death**

Reference was patients receiving a mean of less than 20 morphine milligram equivalents (MMEs) per year. Error bars indicate 95% CIs.
Patients Receiving Opioid Doses of 50 MME or Higher

Overdose death rate per 1,000 person-months

Maximum prescribed daily opioid dose, mg/day

- 0
- 1 to < 20
- 20 to < 50
- 50 to < 100
- ≥ 100

Source: Bohnert et al, JAMA, 2011
Patients Receiving Opioids and Benzodiazepines

Source: Dasgupta et al., Pain Med, 2015
Patients Receiving Opioids with Other Co-Morbidities

Overdose Risk

<table>
<thead>
<tr>
<th>Mental Disorders</th>
<th>aOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>1.5</td>
</tr>
<tr>
<td>Substance use disorder</td>
<td>10.2</td>
</tr>
<tr>
<td>Depression</td>
<td>3.1</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>2.2</td>
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<tr>
<td>Schizophrenia</td>
<td>2.1</td>
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<tr>
<td>Anxiety disorder</td>
<td>1.6</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Source: Nadpara et al., Pain Med, 2018; Campbell et al., Preventive Medicine, 2018
High Risk Groups

Individuals at High-Risk for Opioid Overdose

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- Receiving treatment for OUD, including medication-assisted treatment
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Fentanyl Contamination of the Illicit Drug Supply Expanding Population At-Risk for Opioid Overdose

Counterfeit Norco Poisoning Outbreak — San Francisco Bay Area, California, March 25–April 5, 2016

Kathy T. Vo, MD¹,²; Xander M.R. van Wijk, PhD³; Kara L. Lynch, PhD³; Alan H.B. Wu, PhD³; Craig G. Smollin, MD¹,²

HEALTH ALERT:

FENTANYL IS KILLING NEW YORKERS

Fentanyl is a dangerous opioid that’s showing up in heroin, cocaine, street pills marked as Norco® and other drugs. Its involved in more overdose deaths than ever before. Anyone using drugs, even casually, is at risk.

SAFETY TIPS:

1. USE YOUR OWN NARCOTIC KIT: If you overdose, it’s important to have someone around to help.
2. TAKE TIME OUT: Be prepared with naloxone and have a phone on hand in case you need to call 911.
3. TEST YOUR DRUGS: Use a small amount first to see how strong your drugs are.
4. ENSURE MEDICATION: Show others where it is and how to use it. More than one dose may be needed.
5. AVOID MIXING DRUGS: Mixing drugs—including alcohol—increases your risk of overdose.

AVOIDING DRUG USE IS THE BEST WAY TO PROTECT YOURSELF AGAINST FENTANYL.
Find out where to get naloxone: call 311 or visit nyc.gov/health/naloxone.

Fentanyl-Fentanyl Overdose Events Caused by Smoking Contaminated Crack Cocaine — British Columbia, Canada, July 15–18, 2016

Salman A. Klar, MPH¹; Elizabeth Brodkin, MD¹; Erin Gibson¹; Shovita Padhi, MD¹; Christine Paredy²; Corey Green, MHSc¹; Victoria Lee, MD¹
People Using Other Illicit Drugs

Percentage of Deaths Involving Synthetic Opioids

- Percentage

Cocaine
- 2012: 4.1%
- 2013: 5.0%
- 2014: 11.6%
- 2015: 22.7%
- 2016: 40.3%

Psychostimulants
- 2012: 3.5%
- 2013: 3.9%
- 2014: 6.4%
- 2015: 8.6%
- 2016: 13.8%

Benzodiazepines
- 2012: 10%
- 2013: 11.5%
- 2014: 15.4%
- 2015: 20.5%
- 2016: 31.0%

NFLIS Reports

- Fentanyl alone: 22,278
- Fentanyl and heroin: 8,017
- Fentanyl and opioids: 1,341
- Fentanyl and cocaine: 496
- Fentanyl, heroin, and cocaine: 577
- Fentanyl and other substances: 492

Source: Jones et al., JAMA, 2018; DEA National Drug Threat Assessment, 2018
Proliferation of Fentanyl Analogs and Other Illicit Synthetic Opioids

Figure 29. Identifications of Fentanyl, Fentanyl Related Substances, Fentanyl Precursors, and Other Synthetic Opioids, CY 2017.

Source: DEA National Drug Threat Assessment, 2018
Released from incarceration or other controlled setting

Figure. Mortality rate, by week since release, for overdose and all other (nonoverdose) causes of death.

Source: Binswanger et al., AIM, 2013
THANKS!
& Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Opioid Overdose Education and Naloxone Distribution (OEND) Within the Veterans Health Administration

Elizabeth Oliva, PhD
VA National OEND Coordinator
VA Program Evaluation and Resource Center
VA Office of Mental Health and Suicide Prevention
Investigator
VA Center for Innovation to Implementation
VA Palo Alto Health Care System
AADPAC/DSARM
December 2018
ACKNOWLEDGMENTS

• Veterans Health Administration
  – Staff across the country getting lifesaving OEND to Veterans!
  – VA OEND National Support & Development Workgroup; VA OEND Spanish Translation Workgroup
  – Pharmacy Benefits Management Services (PBM); PBM Academic Detailing Services
  – Office of Mental Health and Suicide Prevention
  – Homeless Programs
  – Office of Nursing Services
  – Specialty Care Services (Pain Management; Emergency Medicine; Enterprise Opioid Strategy team)
  – Patient Care Services (Primary Care, Social Work)
  – Employee Education System
  – Diffusion of Excellence, National Center for Patient Safety, Office of Security & Law Enforcement
  – Health Services Research & Development (IIR 16-078); Quality Enhancement Research Initiative (RRP 13-446)

• Community
  – Eliza Wheeler and Sharon Stancliff
  – Alexander Walley
  – Phillip Coffin
  – Maya Doe-Simkins
  – Corey Davis
  – Traci Green
  – Jeffrey Bratberg
  – Robert Childs
  – Andrew McAuley
WHAT IS OEND?

- Risk mitigation initiative that aims to prevent opioid-related overdose deaths
  - *One of many risk mitigation strategies* employed by VA to minimize risk of opioid-related adverse events
  - *Target patient populations*:
    - Patients with opioid use disorder
    - Patients prescribed opioids

- **Opioid Overdose Education (OE)**
  - Provide patient education on how to *prevent, recognize, and respond* to an opioid overdose

- **Naloxone Distribution (ND)**
  - Provide patient with *naloxone*
    - Train patient and potential bystanders on how to use naloxone

*VA Clinical Guidance: *Offer naloxone rescue to Veterans prescribed or using opioids who are at increased risk for opioid overdose or whose provider deems, based on their clinical judgment, that the Veteran has an indication for ready naloxone availability*"
Addressing the Opioid Epidemic in the United States
Lessons From the Department of Veterans Affairs

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Center for Health Equity Research and Promotion, Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, Pennsylvania; and Center for Pharmaceutical Policy and Prescribing, University of Pittsburgh, Pittsburgh, Pennsylvania.

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David J. Shulkin, MD
Office of the Under Secretary for Health, US Department of Veterans Affairs, Washington, DC.

Over the past 15 years, more than 165,000 people in the United States have died from overdoses related to prescription opioids, and millions more have suffered adverse consequences. The misuse and abuse of prescription opioids have contributed to a precipitous increase in heroin and fentanyl overdoses.

Patients treated in the health care system of the Department of Veterans Affairs (VA) are part of this epidemic and chronic pain impacts half of veterans using the VA, often in the presence of psychiatric comorbidities stemming from traumatic stress disorder. VA efforts to streamline prescriber knowledge and refine opioid stewardship have many components, but today we focus on implementation of four broad strategies to address the opioid epidemic: education, pain management, risk mitigation, and addiction treatment.

Strategies to Address the Opioid Epidemic

The VA has employed 4 broad strategies to address the opioid epidemic: education, pain management, risk mitigation, and addiction treatment (eTable in the Supplement).

The VA’s data capabilities have improved the safety of opioid prescribing, while expanding alternative pain therapies (Figure). By mid-2016 compared with mid-2012, the number of veterans dispensed an opioid each quarter had decreased by 172,000, or about 25%. Moreover, there were 57,000 (47%) fewer patients receiving concomitant opioids and benzodiazepines and 22,000 (36%) fewer patients receiving daily opioid dosages of more than 100 morphine-milligram equivalents, both measures of potentially unsafe opioid use. Between 2010 and 2015, the rate of pharmacists engage directly with opioid prescribers, similar to detailing by pharmaceutical representatives. The VA detailers use sophisticated dashboards with real-time prescriber-level data to engage clinicians in adopting best practices around opioid prescribing. This focus is not simply on reducing opioid medications, but rather on improving the safe use of opioids. Beyond detailing, the VA developed an overdose education and naloxone distribution system that has distributed tens of thousands of naloxone doses and developed standardized patient and provider education to complement broader educational efforts outside of the VA that support prescribing.

Risk Mitigation

The VA implemented several strategies to support and track risk mitigation activities for opioid therapy (eTable in the Supplement). A key component of the Opioid
In 2014, VA established a national OEND program

- Informed by pilot VA OEND programs
- Developed by national, cross-program office workgroup
  - Composed of representatives from pharmacy, mental health, pain management, nursing, primary care, emergency medicine, and employee education
  - National workgroup members facilitated presentations to program offices to garner leadership and staff buy-in

Major innovations
- Policy and clinical guidance
- Educational resources
- Implementation and evaluation resources
- Pharmacy-driven
4. VA providers should consider providing OEND to Veterans who are at significant risk of opioid overdose. Clinical judgment about risk/benefit and patient-centered care involving Veterans and their significant others in shared decision-making should guide decisions on provision of OEND.

- Naloxone layperson formulations added to National Drug File
- “Free-to-Facilities” Naloxone Initiative
  - VA Pharmacy Benefits Management Services (PBM) has provided funding for naloxone to be dispensed to VA patients without the medical center incurring the cost of naloxone
  - To allow the initiative to last as long as possible, funds go to purchasing the nasal spray (the current preferred option when clinically appropriate)

- CARA Section 915. ELIMINATION OF COPAYMENT REQUIREMENT FOR VETERANS RECEIVING OPIOID ANTAGONISTS OR EDUCATION ON USE OF OPIOID ANTAGONISTS
  - Exempts copays for naloxone as well as training on naloxone (when visit is solely for naloxone)
- Recommendations for Issuing Naloxone (July 2017; RFU)
Assess the risk of opioid-related adverse events. Discuss the provision of naloxone rescue as an opioid risk mitigation option with patients and/or family/carers. Offer naloxone rescue to Veterans prescribed or using opioids who are at increased risk for opioid overdose or whose provider deems, based on their clinical judgment, that the Veteran has an indication for ready naloxone availability. Educate patients and carers on the proper use and storage of naloxone rescue medications. Document OEND-related discussions and opioid overdoses in patients’ medical records and through appropriate diagnostic coding, including documenting any reversal events with VA naloxone rescue medications using a nationally recommended and standardized note template (see VA National OEND SharePoint for more information).

- **Assess** risk
- **Discuss** naloxone as an option
- **Offer** naloxone
- **Educate** patients and caregivers
- **Document** OEND-related discussions and opioid poisonings and overdoses (including reversal events)
### VA Intranasal Naloxone Kit
- 2 mucosal atomizer devices
- 2 Luer-lock prefilled syringe naloxone 1 mg/mL (2 mL)
- 1 Laerdal face shield
- 1 pair nitrile gloves
- 1 opioid safety brochure
- 1 intranasal naloxone kit brochure
- 1 blue zippered pouch

### VA Intramuscular Naloxone Kit
- Two 3 mL 25g, 1-inch syringes
- 2 vials naloxone 0.4 mg/mL (1 mL) injection
- 1 Laerdal face shield
- 1 pair nitrile gloves
- 2 alcohol pads
- 1 opioid safety brochure
- 1 intramuscular naloxone kit brochure
- 1 black zippered pouch

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### Naloxone Nasal Spray (4 mg)
**Carton/box contains:**
- Two 4 mg naloxone nasal sprays (each spray includes a Quick Start Guide)
- 1 prescribing information and patient instructions for use

### Naloxone Auto-Injector (2 mg)
**Carton/box contains:**
- 1 auto-injector trainer
- 2 naloxone 2 mg auto-injectors
- 1 prescribing info
- 2 instructions for use
• **VA National OEND SharePoint** *(internal VA site)* Step-by-step instructions for implementation; Quick Guide; **TWO** VA Patient Education Brochures (English and Spanish): (1) patients with opioid use disorder and (2) patients prescribed opioids; Posters; “Program Models”

• **VA OEND Videos** *(links to all videos)*
  – Intro for People with Opioid Use Disorders [https://youtu.be/-qYXZDzo3cA](https://youtu.be/-qYXZDzo3cA)
  – Intro for People Taking Prescribed Opioids [https://youtu.be/NFzhz-PCzPc](https://youtu.be/NFzhz-PCzPc)
  – How to Use the VA Naloxone Nasal Spray [https://youtu.be/0w-us7fQE3s](https://youtu.be/0w-us7fQE3s)
  – How to Use the VA Auto-Injector Naloxone Kit [https://youtu.be/-DQBCnrAPBY](https://youtu.be/-DQBCnrAPBY)

• **VA Academic Detailing**
  – Patient education brochures, “Kit” brochures, DVDs for providers and patients (VA staff can order through depot)

• **Panel Management Tools**
  – OEND Patient Risk Dashboard; Stratification Tool for Opioid Risk Mitigation; Opioid Therapy Risk Reduction Report

• **VA Monthly OEND Call**

• **Accredited TMS training:** VA TMS trainings 27440 and 27441
  – Available outside VA on [www.train.org:](https://www.train.org/main/course/1064943)

• **Opioid Safety Initiative (OSI) & Psychotropic Drug Safety Initiative (PDSI)**
**Provider Materials**

- **Quick Reference Guide**
  - [Order](#)
  - [IB#: 18-756]

- **Preventing Rx Overdoses**
  - [Order](#)
  - [Centers for Disease Control](#)

- **Opioid Overdose Toolkit**
  - [SAHM-SA](#)

**Patient Materials**

- **Naloxone Instructions**
  - [Order](#)
  - [IB#: 10-634]

- **Naloxone Auto-injector**
  - [Order](#)
  - [IB#: 10-769]

**Brochures & Handouts**

- **Opioid Safety Brochure (For Patients on Opioids)**
  - [Order](#)
  - [IB#: 18-754]
  - [Spanish: View | IB#: 10-764]

- **Opioid Safety Brochure (For Patients w/SUD)**
  - [Order](#)
  - [IB#: 18-758]
  - [View | IB#: 10-768]

- **Opioid Safety Brochure - A Quick Reference Guide**
  - [Order](#)
  - [IB#: 18-767]

- **Am I At Risk? Brochure**
  - [Order](#)
  - [IB#: 18-821]

**Order DVDs**

- **Patient (IB#: 10-769) | Provider (IB#: 10-770)**
  - Introduction to Naloxone for People with Opioid Use Disorders
  - Introduction to Naloxone for People Taking Prescribed Opioids
  - How to Use the VA Naloxone Nasal Spray
  - How to Use the VA Auto-Injector Naloxone Kit
  - Narcan Saves Lives: I am the evidence - Brian
**Academic Detailing Service Data Resources**

**Available Tools and When to Use Them**

- **Risk Dashboard**
  - Data: VISN/Facility/Provider Scores
  - Target Audience: Admin/Leadership

- **Priority Panel Report**
  - Data: Provider Panel Opportunities
  - Target Audience: Academic Detailers

- **Trend Reports**
  - National VISN Facility Prescriber
  - Target Audience: Admin/Leadership

- **Patient Risk Report**
  - Data: Patient Information
  - Target Audience: Clinicians

- **Detailed Patient Report**
  - Data: Patient Information
  - Target Audience: Clinicians

- **Daily Appointment Report**
  - Data: Clinic & Patient Information
  - Target Audience: Clinicians

- **Implementation Status Report**
  - Data: National/VISN/Facility Summaries
  - Target Audience: Admin/Leadership

- **Naloxone Rx Release Report**
  - Data: Patient Information
  - Target Audience: Supervisors/Clinicians

**Additional Data Resources**

- **Distribution Report**
  - Data: VISN/Facility Summary
  - Target Audience: Admin/Leadership

- **STORM**
  - Data: Summary & Patient Data
  - Target Audience: All Users

- **OTRR**
  - Data: Patient Information
  - Target Audience: PACT & BHIP Teams

*Special Access Required*
Choose Before You Use

If at all possible, do not use. There is no safe dose of opioids. Help is available, contact your local VA. But if you do use—Choose!

1. Go Slow - Not taking drugs for even a few days can drop your tolerance, making your “usual dose” an “overdose,” which can result in death. If you choose to use, cut your dose at least in half.

2. Wait - If you choose to use, wait long enough after you use to feel the effects before you even consider dosing again (regardless if IV, snorting, smoking).

3. Let Someone Know - Always let someone know you’re using opioids so that they can check on you. Many who overdose do so when dosing alone.

Buddies take care of Buddies. Share this brochure with a friend or family member.

www.mentalhealth.va.gov/substanceabuse.asp
(Adapted from the Harm Reduction Coalition, Oakland, CA)

You are at higher risk for opioid overdose or death when

- You’ve not used for even a few days, such as when you are in the hospital, residential treatment, detoxification, domiciliary, or jail/prison.
- You are under the influence of alcohol, other opioids, cocaine, methamphetamine, or other stimulants.
- You have medical problems (liver, heart, lung, advanced AIDS).
- You use long-acting opioids (such as methadone) or powerful opioids (such as fentanyl).
- You use alone, and don’t let someone know you are using opioids.

Ask a VA clinician if naloxone is right for you

Important considerations:

- Naloxone works only for opioid overdose and may temporarily reverse opioid overdose to help a person start breathing again.
- During an overdose the user cannot react, so someone else needs to give naloxone.
- Encourage family and significant others to learn how to use naloxone (see “Overdose Resources” section).
- If you have naloxone, tell family and significant others where you keep it.
- Store naloxone at room temperature (59° to 77° F), away from light. Avoid extremes of heat or cold (e.g., do not freeze).

www.va.gov

Overdose Resources

SAMHSA Opioid Overdose Prevention Toolkit
Contains safety advice for patients and resources for family members

Community-Based Overdose Prevention and Naloxone Distribution Program Locator
Identifies programs outside of the VA that distribute naloxone
- http://hopeandrecovery.org/locations/

Prescribe to Prevent
Patient resources and videos demonstrating overdose recognition and response, including naloxone administration
- http://prescribetoprevent.org/video/

“How To” VA Naloxone Video
VA Naloxone Nasal Spray:
- https://youtu.be/0w-4s7lOE3s
VA Naloxone Auto-Injector Kit:
- https://youtu.be/-DQBCnAPBY
Signs of Overdose

Signs of an Overdose*
Check: Appears sleepy, heavy nodding, deep sleep, hard to arouse, or vomiting
Listen: Slow or shallow breathing (1 breath every 5 seconds); snoring; raspy, gurgling, or choking sounds
Look: Bluish or grayish lips, fingernails, or skin
Touch: Clammy, sweaty skin
  - If the person shows signs of an overdose, see next section “Responding to an Overdose”
* Even if the person responds to an initial safety check, bystanders should continue to monitor any person with these signs constantly to make sure the person does not stop breathing and die.

Resources
Consider seeking long-term help at your local VA substance use disorder treatment program

Help on the Web
  » VA Substance Use Disorder Program Locator: www2.va.gov/directory/guide/SUD.asp
  » Substance Use Disorder Treatment Locator for non-Veterans: https://findtreatment.samhsa.gov/
  » VA PTSD Programs: www.va.gov/directory/guide/PTSD.asp

Help is Available Anytime
  » Local Emergency Services: 911
  » National Poison Hotline: 1-800-222-1222
  » Veterans Crisis Line: 1-800-273-TALK (8255), or text – 838255

Responding to an Overdose

1. Check For A Response
   - Lightly shake person, yell person's name, firmly rub person's sternum (bone in center of chest where ribs connect) with knuckles, hand in a fist
   - If person does not respond—Give Naloxone, Call 911

2. Give Naloxone, Call 911
   - If you have naloxone nasal spray, DO NOT PRIME OR TEST the spray device. Gently insert the tip of the nozzle into one nostril and press the plunger firmly to give the entire dose of naloxone nasal spray.
   - If you have the naloxone auto-Injector, pull device from case and follow voice instructions.
   - When calling 911, give address and say the person is not breathing.

3. Airway Open
   - Rescue Breathing (if overdose is witnessed)
     - Place face shield (optional)
     - Tilt head back, lift chin, pinch nose
     - Give 1 breath every 5 seconds
     - Chest should rise
   - Chest Compressions (if collapse is witnessed)
     - Place heel of one hand over center of person's chest (between nipples)
     - Place other hand on top of first hand, keep elbows straight, shoulders directly above hands
     - Use body weight to push straight down, at least 2 inches, at rate of 100 compressions per minute
     - Place face shield (optional)
     - Give 2 breaths for every 30 compressions

4. Consider Naloxone Again
   - If person doesn’t start breathing in 2-3 minutes, or responds to the first dose of naloxone and then stops breathing again, give second dose of naloxone
   - Because naloxone wears off in 30 to 90 minutes be sure to stay with the person until emergency medical staff take over or for at least 90 minutes in case the person stops breathing again

5. Recovery Position
   - If the person is breathing but unresponsive, put the person on his/her side to prevent choking if person vomits
What are Opioids?

Opioids are a type of drug found in some pain or other prescription medications, and in some illegal drugs of abuse (e.g., heroin). In certain situations, opioids can slow or stop a person’s normal breathing function.

Opioid harms

• Taking too much opioids can make a person pass out, stop breathing and die.
• Opioids can be addicting and abused.
• Tolerance to opioids can develop with daily use. This means that one will need larger doses to get the same effect.
• If a person stops taking opioids, he/she will lose tolerance. This means that a dose one takes when tolerant could cause overdose if it is taken again after being off of opioids.
• An opioid dose a person takes could cause overdose if shared with another person. Another person may not be tolerant.

Safe Use of Opioids

Safe use of opioids prevents opioid harms from happening to not only you, but also to family, friends and the public.

To use opioids safely

• Know what you’re taking (e.g., color/shape/size/name of medication)
• Take your opioid medication exactly as directed
• Review the booklet Taking Opioids Responsibly for Your Safety and the Safety of Others with your provider
• DON’T mix your opioids with:
  » Alcohol
  » Benzodiazepines (Alprazolam/Xanax, Lorazepam/Ativan, Clonazepam/Klonopin, Diazepam/Vallium) unless directed by your provider
  » Medicines that make you sleepy

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Important considerations:

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• During an overdose the user cannot react, so someone else needs to give naloxone.
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• If you have naloxone, tell family and significant others where you keep it.
• Store naloxone at room temperature (59° to 77°F), away from light. Avoid extremes of heat or cold (e.g., do not freeze).

Resources

Local Emergency Services: 911
National Poison Hotline: 1-800-222-1222
Veterans Crisis Line: 1-800-273-TALK (8255), or text – 838255

Taking Opioids Responsibly for Your Safety and the Safety of Others


VA Substance Use Disorder Treatment Locator

• www2.va.gov/directory Locate/SUD.asp

VA Posttraumatic Stress Disorder (PTSD) Treatment Locator

• www.va.gov/directory Locate/PTSD.asp

“How To” VA Naloxone Video

• VA Naloxone Nasal Spray: https://youtu.be/0w-us7QEU3s
• VA Auto-Injector Naloxone Kit: https://youtu.be/-DQ8CnAPBY
Opioid Overdose

Opioid overdose occurs when a person takes more opioids than the body can handle, passes out and has no or very slow breathing (i.e., respiratory depression).

- Overdose can occur seconds to hours after taking opioids and can cause death.

Signs of an Overdose*

Check: Appears sleepy, heavy nodding, deep sleep, hard to arouse, or vomiting

Listen: Slow or shallow breathing (1 breath every 5 seconds); snoring; raspy, gurgling, or choking sounds

Look: Bluish or grayish lips, fingernails, or skin

Touch: Clammy, sweaty skin

- If the person shows signs of an overdose, see next section “Responding to an Overdose”

* Even if the person responds to an initial safety check, bystanders should continue to monitor any person with these signs constantly to make sure the person does not stop breathing and die.

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Responding to an Overdose

1. **Check For A Response**
   - Lightly shake person, yell person’s name, firmly rub person’s sternum (bone in center of chest where ribs connect) with knuckles, hand in a fist
   - If person does not respond—**Give Naloxone, Call 911**

2. **Give Naloxone, Call 911**
   - If you have naloxone nasal spray, DO NOT PRIME OR TEST the spray device. Gently insert the tip of the nozzle into one nostril and press the plunger firmly to give the entire dose of naloxone nasal spray.
   - If you have the naloxone auto-injector, pull device from case and follow voice instructions.
   - When calling 911, give address and say the person is not breathing.

3. **Airway Open**
   - **Rescue Breathing (if overdose is witnessed)**
     - Place face shield (optional)
     - Tilt head back, lift chin, pinch nose
     - Give 1 breath every 5 seconds
     - Chest should rise
   - **Chest Compressions (if collapse is unwitnessed)**
     - Place heel of one hand over center of person’s chest (between nipples)
     - Place other hand on top of first hand, keep elbows straight, shoulders directly above hands
     - Use body weight to push straight down, at least 2 inches, at rate of 100 compressions per minute
     - Place face shield (optional)
     - Give 2 breaths for every 30 compressions

4. **Consider Naloxone Again**
   - If person doesn’t start breathing in 2-3 minutes, or responds to the first dose of naloxone and then stops breathing again, give second dose of naloxone.
   - Because naloxone wears off in 30 to 90 minutes be sure to stay with the person until emergency medical staff take over or for at least 90 minutes in case the person stops breathing again.

5. **Recovery Position**
   - If the person is breathing but unresponsive, put the person on his/her side to prevent choking if person vomits
General Information / Trends

# Patients w/ Naloxone Fill by Quarter

% Opioid + Benzo Patients w/ a Naloxone Fill in the Previous Year

# Naloxone Prescribers by Quarter

% OUD Patients w/ a Naloxone Fill in the Previous Year
• Provider Education

• Patient Identification

• Patient Education

• Post-Overdose Care
• In-person training
  – Academic Detailing

• Web-based training
  – Available outside VA on www.train.org: https://www.train.org/main/course/1064943

• Monthly national call

• Address stigma and misperceptions (e.g., risk compensation)

---

From October 2014 to Sept 2016, detailed providers had prescribing rate of naloxone >3 times higher than non detailed providers 1 year after first OEND-related AD visit, and >7 times greater at 2 years.

Moreover, the average rate of increase in naloxone prescribing was 7.1% greater in the AD-exposed versus the AD-unexposed providers (95% CI: 2.0%, 12.5%)
• Provider Education

• Patient Identification

• Patient Education

• Post-Overdose Care
## OEND Dashboard

<table>
<thead>
<tr>
<th>Location/Prescriber</th>
<th># Naloxone Fills</th>
<th>% Nasal Fills (90d)</th>
<th>% Auto-Inj. Fills (90d)</th>
<th>% IM Fills (90d)</th>
<th># Naloxone Patients</th>
<th># Naloxone Prescribers</th>
<th># Naloxone Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>National</td>
<td>224,757</td>
<td>100.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>158,545</td>
<td>17,159</td>
<td>286</td>
</tr>
</tbody>
</table>

### Naloxone Rx Released to Patient (1 year) / Total Patient Cohort

<table>
<thead>
<tr>
<th>Location / Prescriber</th>
<th>Potential Risk Factor</th>
<th>Patient Cohort</th>
<th>Score</th>
<th>National Score</th>
<th>Patients w/ No Fill</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD)</strong></td>
<td><strong>RIOSORD Risk Class (View Publication)</strong></td>
<td><strong>RIOSORD Cohort Inclusive of All Opioid, OUD, and OAT Risk Group Patients</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National</td>
<td></td>
<td>All Patients</td>
<td>36.0%</td>
<td>36.0%</td>
<td>281,888</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk Class ≥ 8</td>
<td>54.4%</td>
<td>54.4%</td>
<td>2,684</td>
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<tr>
<td></td>
<td></td>
<td>Risk Class 5-7</td>
<td>43.3%</td>
<td>43.3%</td>
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<tr>
<td></td>
<td></td>
<td>Risk Class ≤ 4</td>
<td>22.7%</td>
<td>22.7%</td>
<td>269,692</td>
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<tr>
<td><strong>Opioid Pharmacotherapy</strong></td>
<td></td>
<td>All Patients</td>
<td>31.8%</td>
<td>31.8%</td>
<td>12,552</td>
</tr>
<tr>
<td>National</td>
<td>Opioid + Benzodiazepine</td>
<td>All Patients</td>
<td>38.1%</td>
<td>38.1%</td>
<td>31,096</td>
</tr>
<tr>
<td></td>
<td>MEDD ≥ 50 (Last 30 days)</td>
<td>All Patients</td>
<td>17.8%</td>
<td>17.8%</td>
<td>8,011</td>
</tr>
<tr>
<td></td>
<td>MEDD ≥ 90 in Past Year w/ No Fill in the Past 90 Days</td>
<td>All Patients</td>
<td>30.6%</td>
<td>30.6%</td>
<td>11,824</td>
</tr>
<tr>
<td><strong>OUD &amp; OAT Pharmacotherapy</strong></td>
<td></td>
<td>All Patients</td>
<td>23.0%</td>
<td>23.0%</td>
<td>72,464</td>
</tr>
<tr>
<td>National</td>
<td>OUD Diagnosis</td>
<td>All Patients</td>
<td>35.3%</td>
<td>35.3%</td>
<td>6,366</td>
</tr>
<tr>
<td></td>
<td>Possible Overdose (3 Years)</td>
<td>All Patients</td>
<td>41.6%</td>
<td>41.6%</td>
<td>9,115</td>
</tr>
<tr>
<td></td>
<td>Buprenorphine SL (Outpatient Rx or Active Non-VA Medication)</td>
<td>All Patients</td>
<td>38.8%</td>
<td>38.8%</td>
<td>1,804</td>
</tr>
<tr>
<td></td>
<td>Naltrexone (Outpatient Rx, Active Non-VA, or Recent Clinic Order)</td>
<td>OUD Patients</td>
<td>34.1%</td>
<td>34.1%</td>
<td>2,250</td>
</tr>
<tr>
<td></td>
<td>OUD-Related Fee Basis</td>
<td>All Patients</td>
<td>34.1%</td>
<td>34.1%</td>
<td>2,250</td>
</tr>
</tbody>
</table>
Main Page

STORM: Patient Detail Dashboard
Stratification Tool for Opioid Risk Mitigation

What factors contribute to my patient’s risk?

- Substance use disorder
- Alcohol
- Tobacco
- Narcotic
- Antidepressant
- Mental Health
- Depression
- Psychosis
- Medical
- Congestive heart failure
- Hypertension
- Weight loss
- Opioid

Risk Mitigation Strategies

- MEPPS
- 24 Hour
- Opioid strategy
- Timely follow-up
- Pain clinic
- Physical therapy
- Occupational therapy
- Special therapy

Care team & Follow-up

- DOP TEAM
- DRP TEAM
- MTX TEAM
- MTX TEAM
- PACT TEAM
- Primary Care Provider
- Mental Health
- Pain Management
- Pain Management

Contributing Risk Factors

Patient Information and Risk of Suicide/Overdose

Risk Mitigation Management

Care team & Follow-up
→ Create Panels by **Provider, Prescriber, & Teams**

→ Choose Opioid Group(s)

**Any Opioid in Past Year**

**Long-Term Opioid Therapy**

**Active Rx**

---

**Naloxone Dispense Date**

**Veteran-Focused  Actionable**
Opioid Therapy Risk Report (OTRR)

Veteran Details

- All data refreshed daily
- Naloxone Dispense Date
- Naloxone Product Dispensed
- Quickly determine which patients require proactive clinical action
- Check recent interactions w/other VA health providers
- Latest information from across the VA regardless of location
- One Year history of Prescribed Opioids, Benzos, & Pain Scores

★ Veteran-Focused ★ Actionable
Clinic Huddle Patient Appointments Planning Tool

- **Actionable, Time-Sensitive, Cross-functional**
  - Address issues essential to veteran health & well-being
  - Efficient, Consistent
  - Pulls data from across the VA into one place
  - Select specific clinics by Name & Date Range
  - Links directly to full details
Among patients prescribed opioids, those at greatest risk for overdose tend to be complex patients with multiple comorbidities in addition to pain.

- Comorbidities account for more risk compared to opioids across multiple predictive risk models (Glanz et al., 2018; Oliva et al., 2017; Zedler et al., 2015, 2018).
- Patient-centered risk mitigation addressing comorbidities is important for all patients, regardless of MEDD threshold, naloxone prescribing, or if opioids are no longer part of the patient’s treatment plan.
• Almost 4 out of every 5 patients who died from overdose/suicide were prescribed doses < 90 MEDD
• Almost 3 out of every 4 overdose/suicide deaths were among patients with MH/SUD diagnoses
• More than 1 out of every 2 deaths were among patients with MH/SUD diagnoses prescribed < 90 MEDD
MH/SUD AND NON-OPIOID RELATED FACTORS HAVE HIGHER ODDS RATIOS THAN OPIOID-RELATED FACTORS IN PREDICTIVE MODEL

Risk increased slightly with increasing MEDD
- e.g., 120 MEDD would increase modeled risk by about as much as a PTSD or AUD diagnosis

Odds Ratios for Overdose/Suicide-Related Events
KEY IMPLEMENTATION CONSIDERATIONS

- Provider Education
- Patient Identification
- Patient Education
- Post-Overdose Care
**Targeted Outreach**

- Patients prescribed opioids
  - Various efforts using MEDD (<50 or 100); Co-Rx benzodiazepines; Intrathecal pump patients
  - Primary care, Pain clinics, Pharmacy
- Patients with opioid use disorder
  - Substance Use Disorder Treatment programs (including Medication Assisted Treatment; Residential treatment); detoxification; inpatient; emergency department

**Increasing Awareness**

- “Am I At Risk?” brochure
- E-board
- Buttons

**Educational Efforts**

- Individual and group visits in primary care and pain clinics
  - Schedules “scrubbed” daily for same-day education opportunities
  - Phone-outreach by care team with educational materials mailed and discussed via phone and/or in a group visit
- Residential treatment
  - Initial assessment/evaluation; Upon admission and at discharge; classes for all residents; ensure naloxone can be kept on person and taken on passes
- Medication Assisted Treatment Programs
  - Offered upon enrollment; during medication management visits
- Pharmacy
  - Window dispensing; Consult Service; Residency projects
- Electronic Medical Record
  - Standardized notes for OEND
  - Health factor added to opioid refill note
  - Included in order sets
- Letter-based

Images from Mendes, 2/22/17 presentation
KEY IMPLEMENTATION CONSIDERATIONS

• Provider Education

• Patient Identification

• Patient Education

• Post-Overdose Care
• Improve care post-overdose
• Cover sheet reminder component if patient’s treatment provider does not complete sections of the note specified for patient’s treatment provider
HEALTHCARE SYSTEM CONSIDERATIONS

- One tool in clinical armamentarium—not a panacea, not just about naloxone!
- Numerous levers—policy, funding, technical assistance
  - Coordination across program offices
  - Academic Detailing can help support implementation

- Patient Identification
  - Patients prescribed opioids
  - Patients with opioid use disorder

- Provider and Patient Education
  - Provide patient education on how to prevent, recognize, and respond to an opioid overdose
    - A few minutes of training that could save a life!
• Medication Assisted Treatment (MAT) for Opioid Use Disorder (OUD)
  – OEND lifesaving; MAT lifesaving and life-transforming

• Post-overdose care
  – Non-fatal overdose—critical juncture
    • OEND and MAT
    • Standardize response (e.g., national note templates)

• Consider comorbidities and ANY history of opioid use
  – Even if opioids are no longer being taken (prescribed or illicit)
    high risk patients are still at-risk; naloxone is still needed + risk
    mitigation targeting comorbidities
    • Patients with OUD, even if in treatment
    • Patients with past chronic opioid therapy; even if opioids are no longer
      prescribed; also need to address pain and other risk factors!!
RELEVANT CONSIDERATIONS

• Patient refusal of naloxone
  – More effective methods for explaining risk
  – Recommendations for patients who live alone
    • Emphasize OE part of OEND
  – Recommendations for patients in recovery
  – Strategies to decrease stigma

• Letter-Based approaches
  – Involvement of provider/treatment team (do not want to undermine patient-provider relationship)
  – Opt-in versus Opt-out
    • “Why you may be denied life insurance for carrying naloxone”
      (WBUR)
  – Training considerations

“I feel that whether or not you say that it isn't held against us, it still feels that way”
The program increases the availability of naloxone in the following ways:

**VA Police Naloxone**
- Equips VA police with naloxone and trains them in its use

**Naloxone-stocked in AED cabinets**
- Stocked in areas such as cafeterias, substance use disorder treatment programs, and primary care clinics

**Opioid Overdose Education and Naloxone Distribution (OEND)**
- Educates at-risk patients and their families in how to prevent, recognize, and respond to an overdose, including how to respond with naloxone

**The Impact**
Making naloxone more readily available will increase the likelihood of successful overdose reversal, potentially saving hundreds of Veteran lives. VA Boston Healthcare System implementation of all three elements resulted in 132 opioid overdose reversals.

- **Implementation to date**
  - OEND in all VA facilities
  - VA Police Naloxone (109 facilities implementing)
  - AED Cabinet Naloxone (95 facilities implementing)

- **Media**
  - Diffusion of Excellence Gold Status Practice ([medium.com; VAntage Point](medium.com; VAntage Point))
  - [Ted-style Talk on VA gold status practice that inspired this initiative](https://medium.com; VAntage Point)
  - [NPR feature](https://medium.com; VAntage Point)

- **Questions about the initiative can be sent to** [VHARapidNaloxoneNaloxone@va.gov](mailto:VHARapidNaloxoneNaloxone@va.gov)
• Effectiveness of a Rescue Medication in Preventing Opioid Overdose in Veterans (PI: Oliva; VA HSR&D Grant; Beginning this winter)
  – Aim 1: Characterize naloxone distribution within VA and patient-, prescriber-, and setting-related factors associated with distribution.
  – Aim 2: Assess whether naloxone distribution to at-risk Veterans compared to similar at-risk Veterans who did not receive naloxone is associated with reduced fatal and non-fatal opioid overdose.

• VHA Rapid Naloxone Initiative Partnered Evaluation: Improving Implementation to Save Lives and Transform Post-Overdose Care (PIs: Bounthavong & Oliva; submitted grant)
  – Aim 1: Identify barriers and facilitators of VHA Rapid Naloxone Initiative adoption to inform the development of an enhanced implementation strategy.
  – Aim 2: Test the effectiveness of the enhanced implementation strategy using a cluster randomized stepped wedge trial and identify effective elements of the enhanced implementation strategy.
  – Aim 3: Characterize opioid overdose across VHA reporting systems and ways to improve post-overdose care via interviews with VHA staff who have reported an opioid overdose, VHA patients who have experienced a non-fatal opioid overdose, and concerned others of VHA patients who have experienced a non-fatal opioid overdose.
THANK YOU!!!
• Identifying high risk patients for OEND
• OEND Research
• Using Motivational Interviewing in OEND
• Strategies for managing patients after non-fatal overdose
• Innovative approaches to OEND expansion (VA Police, AED Cabinets)
• Models of OEND Implementation in Primary Care
• Getting OEND to Patients with OUD and Patients Prescribed Opioids: Strategies and Lessons Learned from VA’s High Performing Facilities
• Letter-Based Approaches to OEND: Comparing and Contrasting Different Strategies
• VA Pharmacy Resident OEND Innovations—Increasing access to OEND, Improving Veterans’ comfort with OEND, and Understanding why Veterans refuse naloxone
• VA National Naloxone Use Note and Emergency Department Model of OEND
THIS SECTION TO BE COMPLETED BY PATIENT’S TREATMENT PROVIDER, CLICK BOX TO CONTINUE

What risk factors are present that could increase the risk of overdose? (NOTE: VA has developed automated clinical decision support tools that can help identify some of these risk factors from VA administrative data, e.g., Stratification Tool for Opioid Risk Mitigation (STORM) and Opioid Therapy Risk Report (OTRR))

- Previous overdose
  - Comment:
    - Discuss circumstances surrounding current and previous overdoses to identify potential patterns and ways to mitigate risk and improve patient safety

- Periods of abstinence from opioids (e.g., detoxification, inpatient or residential treatment, incarceration)
  - Discuss how periods of abstinence can decrease tolerance and increase risk for overdose as well as strategies to decrease risk

- Opioid tapering
  - Discuss how opioid tapering can decrease tolerance and increase risk for overdose as well as strategies to decrease risk (e.g., slow taper, 5-20% reduction every 4 weeks; see Opioid Taper Decision Tool)

- Substance use disorder (SUD, including opioid use disorder and alcohol use disorder)
  - Plan: Consider SUD treatment, including medication and counseling for opioid use disorder and alcohol use disorder
    - SUD being addressed in treatment plan
    - Referral for SUD treatment
    - Discussed with the patient and the patient declined SUD treatment/referral

- Mental health (e.g., PTSD, depression, anxiety, schizophrenia, bipolar disorder)
  - Comment:
    - Mental health being addressed in treatment plan
    - Referral for mental health treatment
    - Discussed with the patient and the patient declined mental health treatment/referral
Use of sedatives (e.g., benzodiazepines) Comment: 

- Discuss risks associated with use of sedatives
- Discuss alternative treatments
- Discuss tapering/discontinuation

Use of non-prescribed opioids Comment: 

- Discuss risks associated with use of non-prescribed opioids and ways to mitigate risk and improve patient safety

Use of prescribed opioids

- Opioids prescribed only from the VA
  - Discuss how there is no safe dose of opioids and that risk increases with increased dose and other co-morbidities
  - Ask the patient to consider strategies to improve opioid safety, including alternative pain management approaches

  Treatment Considerations (Check each treatment that will be recommended)
  - Consider non-opioid treatments for pain
  - Change in opioid treatment plan
    - Slow taper (e.g., 5-20% reduction every 4 weeks; see Opioid Taper Decision Tool)
    - Other:
    - No change in opioid treatment plan

- Opioids prescribed only from non-VA sources
  - Discuss how there is no safe dose of opioids and that risk increases with increased dose and other co-morbidities
  - Ask the patient to consider strategies to improve opioid safety, including alternative pain management approaches

  Treatment Considerations (Check each treatment that will be recommended)
  - Discuss overdose with outside provider and ways to improve patient safety
  - Consider non-opioid treatments for pain
• **90 Veterans receiving opioids for ≥ 3 months**
  – 52 Opioid Substitution Clinic (OSC); 38 Pain Management Clinic (PMC)
  – High risk→Average risk factors for opioid overdose—6 PMC, 8 OSC

• **Perception of risk**
  – ~70% believed their overdose risk was BELOW that of the average American adult

• **Opioid overdose experience**
  – 52% of OSC and 21% PMC Veterans had **experienced** an opioid overdose
  – 83% of OSC and 50% PMC Veterans had **witnessed** an opioid overdose

• **Knowledge about and interest in naloxone**
  – ~1/3 had heard of naloxone (46% OSC, 18% PMC); none had a kit
  – **After a brief explanation, 73% of OSC and 55% of PMC Veterans wanted a kit**
  – NOTE: Among patients NOT interested in naloxone kits—23% were using benzos and 23% were using additional opioids NOT prescribed by the VA (**other risk mitigation strategies are also needed**)
Saving Veterans Lives through Implementation of Opioid Overdose Education and Naloxone Distribution (OEND)

Elizabeth M. Oliva, PhD
VA National Opioid Overdose Education and Naloxone Distribution (OEND) Coordinator
VA Program Evaluation and Resource Center
Office of Mental Health Operations
Investigator
VA Center for Innovation to Implementation
VA Palo Alto Health Care System
July 1, 2015
Opioid overdose epidemic
- Veterans twice as likely to die from accidental overdose compared to non-Veterans (Bohnert et al., 2011)

Successful VA pilots
- In fall 2013 Cleveland VA was first to implement OEND; inspired VISN 10 to implement OEND in every facility in FY14 as part of a phased roll-out
- Overwhelmingly positive response

OEND SAVES LIVES!
- 5400+ kits dispensed from 115 VA facilities with 79 reported opioid overdose reversals (as of 6/23/15)
VA OEND Implementation: Zeitgeist

- Holidays 2011—Concern surrounding OEF/OIF overdoses; Blue ribbon panel
- February 2012—CDC MMWR article (Wheeler et al.)
- April 2012—FDA, Office of the Assistant Secretary for Health, NIDA, and CDC public workshop: “Role of Naloxone in Opioid Overdose Fatality Prevention”
- January 2013—Mortality and cost-effectiveness (Walley et al.; Coffin & Sullivan)
- April 2013—Cleveland VA champions OEND
- May-July 2013—Other VAs interested; VA/DoD CPG for patients at risk for suicide
- August 2013—Cleveland VA dispenses 1st VA naloxone kit; SAMHSA toolkit release
- November 2013—PBM endorses request for National OEND program
- December 2013—Establish VA OEND National Support & Development Workgroup
- February 2014—VA Leadership support for OEND implementation
- March-May 2014—develop standard VA naloxone rescue kits; add to National Drug File; centralize distribution through CMOP; dispense 1st VA national kit May 2014

Oliva, July 2015, Exploring Naloxone Uptake and Use, Interagency Scientific Workshop
Moving Beyond MEDD and Opioids to Address the Opioid Crisis*

Elizabeth M. Oliva, PhD
VA National Opioid Overdose Education and Naloxone Distribution (OEND) Coordinator
VA Program Evaluation and Resource Center
VA Office of Mental Health and Suicide Prevention

UCSF-Gladstone Center for AIDS Research (CFAR) Symposium on Opioids and HIV
May 11, 2018

*This is an abbreviated version of a 2018 National Rx Drug Abuse & Heroin Summit presentation (Kertesz, Manhapra, Oliva, & Sandbrink)
Clinical Considerations in Addressing Overdose and Suicide Among Patients Prescribed Opioids

- Moving beyond Morphine Equivalent Daily Dose (MEDD) and opioids
  - Based on previous observational research, many assume that overdose is mostly an opioid dose-related event
  - Re-examining data from these studies suggests that:
    • Most patients who die are below commonly recommended MEDD thresholds
    • MH/SUD diagnoses and other comorbidities play just as critical a role, and in some cases an even more critical role than opioids, in overdose and/or suicide outcomes
Review of Risk Factors for Overdose and OUD

Risk factors are related to:

- Opioid prescribing
- Interaction with other medication/drugs
- Medical comorbidities
- Mental health comorbidities

“Opioid dosage was the factor most consistently analyzed and also associated with increased risk of overdose. Other risk factors include concurrent use of sedative hypnotics, use of extended-release/long-acting opioids, and the presence of substance use and other mental health disorder comorbidities.”

Park et al., J Addict Med 2016

Review of 15 articles published between 2007 and 2015 that examined risk factors for fatal and nonfatal overdose in patients receiving opioid analgesics
Higher Dosage Associated with Increased Risks from Opioids

Hazard Ratios (HR):
Mortality (all causes):
HR 1.64 for LA opioids

Overdose deaths (unintentional)
HR 7.18-8.9 for MME > 100 mg/d

Opioid use disorder on long-term opioids (> 90 d)
HR 15 for 1-36 mg/d MME
HR 29 for 36-120 mg/d MME
HR 122 for > 120 mg/d MME

Edlund et al., 2014
Most Opioid Overdoses In Patients with No or Lower Dose Opioids (Bohnert et al, JAMA 2011)

<table>
<thead>
<tr>
<th>Table 2. Unadjusted Rate of Prescription Opioid Overdose Death by Opioid Dose and Fill Type</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients With Chronic Noncancer Pain Diagnoses</strong></td>
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<tr>
<td>Maximum prescribed daily opioid dose, mg/d</td>
</tr>
<tr>
<td>Overdose Deaths, No.</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1-&lt;20</td>
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<tr>
<td>20-&lt;50</td>
</tr>
<tr>
<td>50-&lt;100</td>
</tr>
<tr>
<td>≥100</td>
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</table>

- **79%**

<table>
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<tr>
<th><strong>Patients With Acute Pain Diagnoses</strong></th>
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<tbody>
<tr>
<td>Maximum prescribed daily opioid dose, mg/d</td>
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<tr>
<td>Overdose Deaths, No.</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1-&lt;20</td>
</tr>
<tr>
<td>20-&lt;50</td>
</tr>
<tr>
<td>50-&lt;100</td>
</tr>
<tr>
<td>≥100</td>
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</table>

- **81%**

<table>
<thead>
<tr>
<th><strong>Patients With Substance Use Disorder Diagnoses</strong></th>
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<tr>
<td>Maximum prescribed daily opioid dose, mg/d</td>
</tr>
<tr>
<td>Overdose Deaths, No.</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1-&lt;20</td>
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<tr>
<td>20-&lt;50</td>
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<tr>
<td>50-&lt;100</td>
</tr>
<tr>
<td>≥100</td>
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</table>

- **85%**
Most Overdose/Serious Opioid-Induced Respiratory Depression In Patients with No or Lower Dose Opioids

**Table 1 Continued**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cases (n = 817) n (%)</th>
<th>Controls (n = 8,170) n (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAXIMUM PRESCRIBED DAILY MED (mg), Mean (SD)</td>
<td>98.7 (122.1)</td>
<td>24.2 (48.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum Prescribed Daily MED Group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1—&lt;20</td>
<td>35 (4.3)</td>
<td>1,331 (16.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>20—&lt;50</td>
<td>227 (27.8)</td>
<td>2,614 (32)</td>
<td></td>
</tr>
<tr>
<td>50—&lt;100</td>
<td>163 (20)</td>
<td>718 (8.8)</td>
<td></td>
</tr>
<tr>
<td>≥100</td>
<td>268 (32.8)</td>
<td>273 (3.3)</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>693 (84.9%)</td>
<td>4,936 (60.4%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>124 (15.1%)</td>
<td>3,234 (39.6%)</td>
<td></td>
</tr>
</tbody>
</table>

Zedler et al., Pain Med 2015

67%
No Clear Cut-Point to Distinguish Opioid Overdose Cases; Majority of Opioid Overdose Deaths Among Patients Below 100 MEDD

- Median dosage for patients with opioid overdose was 60 MEDD; i.e., vast majority below 100 MEDD

Average opioid dosages
Cases (overdose deaths):
98.1 MEDD (SD 112.7)

Controls:
47.7 MEDD (SD 65.2)
MH/SUD-related Factors Account for Similar OSORD Risk as Opioid-related Factors in VHA Sample

- MH/SUD-related factors 29% of index
  - Model ORs: Opioid dep=4.5
  - Bipolar/SZ=1.9
  - Benzo=1.5
  - Antidep=2.0

- Opioid-related factors 32% of index
  - Model ORs: ER/LA=2.5
  - Methadone=2.4
  - ≥100 MEDD=5.0

Zedler et al., Pain Med 2015
VETERANS HEALTH ADMINISTRATION

MH/SUD-related Factors Account for Similar OSORD Risk as Opioid-related Factors in US Commercial Health Plan Sample

Table 3  CIP-based risk index for serious opioid-induced respiratory depression (RIOSORD)

<table>
<thead>
<tr>
<th>Question</th>
<th>Points for “yes” response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the patient have any of the following health conditions?</td>
<td>25</td>
</tr>
<tr>
<td>Substance use disorder (abuse or dependence)?</td>
<td>10</td>
</tr>
<tr>
<td>Bipolar disorder or schizophrenia?</td>
<td>9</td>
</tr>
<tr>
<td>Stroke or other cerebrovascular disease?</td>
<td>8</td>
</tr>
<tr>
<td>Kidney disease with clinically significant renal impairment?</td>
<td>7</td>
</tr>
<tr>
<td>Heart failure?</td>
<td>7</td>
</tr>
<tr>
<td>Nonmalignant pancreatic disease (e.g., acute or chronic pancreatitis)?</td>
<td>7</td>
</tr>
<tr>
<td>Chronic pulmonary disease (e.g., emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)?</td>
<td>5</td>
</tr>
<tr>
<td>Recurrent headache (e.g., migraine)?</td>
<td>5</td>
</tr>
<tr>
<td>Does the patient consume:</td>
<td></td>
</tr>
<tr>
<td>Fentanyl?</td>
<td>13</td>
</tr>
<tr>
<td>Morphine?</td>
<td>11</td>
</tr>
<tr>
<td>Methadone?</td>
<td>10</td>
</tr>
<tr>
<td>Hydromorphone?</td>
<td>7</td>
</tr>
<tr>
<td>An extended-release or long-acting formulation of any prescription opioid?</td>
<td>5</td>
</tr>
<tr>
<td>A prescription benzodiazepine?</td>
<td>9</td>
</tr>
<tr>
<td>A prescription antidepressant?</td>
<td>8</td>
</tr>
<tr>
<td>Is the patient’s current maximum prescribed opioid dose $\geq 100$mg morphine equivalents per day? (Include all prescription opioids consumed on a regular basis)</td>
<td>7</td>
</tr>
</tbody>
</table>

Total point score (maximum = 146)

• MH/SUD-related factors 36% of index
  - Model ORs:
    - SUD=12.7
    - Bipolar/SZ=2.8
    - Benzo=2.3
    - Antidep=2.2

• Opioid-related factors 36% of index
  - Model ORs:
    - Fentanyl=3.7
    - Methadone=2.8
    - ER/LA=1.7
    - $\geq 100$ MED=2.0

Zedler et al., Pain Med 2018
MH and SUD Diagnoses Were Largest Predictors of Opioid Overdose in Kaiser Predictive Model

Table 3 Unadjusted and Adjusted (final) Cox Regression Models for Predicting 2-Year Overdose Risk for Patients Prescribed Chronic Opioid Therapy at the Derivation Site

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unadjusted model</th>
<th>Adjusted model*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio (95 CI†)</td>
<td>β coefficient</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.93 (0.88–0.98)‡</td>
<td>−0.06915</td>
</tr>
<tr>
<td>Age-squared</td>
<td>1.00 (1.00–1.00)‡</td>
<td>0.0005626</td>
</tr>
<tr>
<td>Mental health diagnosis§</td>
<td>4.18 (2.88–6.07)‡</td>
<td>1.22076</td>
</tr>
<tr>
<td>Psychotropic prescription</td>
<td>2.82 (1.88–4.25)‡</td>
<td>1.24387</td>
</tr>
<tr>
<td>Substance abuse/dependence diagnosis‖</td>
<td>6.01 (4.03–8.96)‡</td>
<td>0.42788</td>
</tr>
<tr>
<td>Tobacco use or tobacco abuse/dependence diagnosis‖</td>
<td>2.31 (1.60–3.32)‡</td>
<td>1.43 (1.00–2.05)</td>
</tr>
<tr>
<td>History of opioid prescriptions in the year prior to initiating chronic opioid therapy</td>
<td>1.43 (1.00–2.05)‡</td>
<td></td>
</tr>
<tr>
<td>Long-acting or extended-release opioid formulation</td>
<td>2.47 (1.25–4.87)‡</td>
<td>0.68552</td>
</tr>
<tr>
<td>Daily opioid dose (per 10 mg morphine equivalents)**</td>
<td>1.01 (0.99–1.03)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C diagnosis†</td>
<td>2.82 (1.04–7.63)†</td>
<td></td>
</tr>
</tbody>
</table>
MH and SUD Diagnoses Account for More Opioid Overdose Risk than Opioids

Table 5: Point-Based System* to Calculate 2-Year Risk of Opioid Overdose Based on Model Coefficients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number of points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>18–25</td>
<td>98</td>
</tr>
<tr>
<td>26–30</td>
<td>94</td>
</tr>
<tr>
<td>31–35</td>
<td>91</td>
</tr>
<tr>
<td>36–40</td>
<td>88</td>
</tr>
<tr>
<td>41–45</td>
<td>85</td>
</tr>
<tr>
<td>46–50</td>
<td>84</td>
</tr>
<tr>
<td>51–55</td>
<td>83</td>
</tr>
<tr>
<td>56–60</td>
<td>82</td>
</tr>
<tr>
<td>61–65</td>
<td>83</td>
</tr>
<tr>
<td>66–70</td>
<td>84</td>
</tr>
<tr>
<td>71–75</td>
<td>84</td>
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<tr>
<td>76–80</td>
<td>86</td>
</tr>
<tr>
<td>81–85</td>
<td>87</td>
</tr>
<tr>
<td>86–90</td>
<td>89</td>
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<tr>
<td>91–95</td>
<td>92</td>
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<tr>
<td>96–100</td>
<td>96</td>
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<tr>
<td>Mental health diagnosis</td>
<td>22</td>
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<tr>
<td>Substance abuse/dependence diagnosis</td>
<td>22</td>
</tr>
<tr>
<td>Tobacco use or tobacco abuse/dependence diagnosis</td>
<td>8</td>
</tr>
<tr>
<td>Long-acting or extended-release opioid formulation</td>
<td>12</td>
</tr>
</tbody>
</table>

*Scores of summed points, based on patient characteristics, indicate low (≤ 85), medium (86–103) or high risk (≥104)

- MH/SUD diagnoses 27% of max points; 69% of non-age related points
- Opioid-related factor 7% of max points; 19% of non-age related points

Glanz et al., JGIM 2018
MH/SUD and Non-Opioid Related Factors Have Higher Odds Ratios than Opioid-Related Factors in VHA Predictive Model

### Odds Ratios for Overdose/Suicide-Related Events

<table>
<thead>
<tr>
<th>Medical comorbidity</th>
<th>Psychiatric comorbidity</th>
<th>Substance use Disorder</th>
<th>Healthcare utilization</th>
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</thead>
<tbody>
<tr>
<td>Benzo+</td>
<td>PTSD</td>
<td>AUD</td>
<td>IP MH Tx</td>
</tr>
<tr>
<td>HIV</td>
<td>Depression</td>
<td>Stimulant</td>
<td>Detox</td>
</tr>
<tr>
<td>Elec. Dis.</td>
<td>Bipolar</td>
<td>OUD</td>
<td>OD/suicide</td>
</tr>
<tr>
<td>Liver dis</td>
<td>Other MH</td>
<td>Sedative UD</td>
<td></td>
</tr>
<tr>
<td>Other Neuro</td>
<td></td>
<td>IP MH Tx</td>
<td></td>
</tr>
</tbody>
</table>

Risk increased slightly with increasing MEDD
- e.g., 120 MEDD would increase modeled risk by about as much as a PTSD or AUD diagnosis

Oliva et al., Psychol Serv 2017
High Odds Ratios for Other Evidence-Based Sedating Pain Medications

**Odds Ratios for Overdose/Suicide-Related Events**

- Having TCAs, SNRIs and Anti-convulsants is associated with increased risk
  - Association could be related to unmanaged pain, cumulative sedation, depressive symptoms, etc.

![Odds Ratios Graph]

Oliva et al., Psychol Serv 2017
Healthcare System-Based Implementation of Opioid Overdose Education and Naloxone Distribution (OEND) in the Veterans Health Administration: Strategies and Lessons Learned from the First Nationwide Program in the United States

Elizabeth M. Oliva, PhD and Julianne Himstreet, PharmD, BCPS

1VA National OEND Coordinator, VA Program Evaluation and Resource Center, VA Office of Mental Health Operations
2National Program Manager, VA Academic Detailing Services, VA Pharmacy Benefits Management Services

National Rx Drug Abuse & Heroin Summit
April 19, 2017
• April 2013—VA facility interest in OEND
• August 2013—Cleveland VA implements first OEND program
• January 2014—VA National OEND workgroup’s first meeting
• May 2014—VA national program launched, first kit dispensed
• November 2015—OEND implemented in every VA facility
• As of March 16, 2017—68,141 naloxone prescriptions dispensed
  – 172 spontaneously reported opioid overdose reversals with VA naloxone (2/2/16)
Reversal of overdose on fentanyl being illicitly sold as heroin with naloxone nasal spray: A case report (Fareed et al., 2015)

- Atlanta VA—One of the early adopters of OEND
- Describes reversal of fentanyl overdose with naloxone nasal spray
  - Patient was unaware that fentanyl was being sold as heroin
  - Required 2 doses
- Implemented OEND in Evaluation, Stabilization and Placement (ESP) substance abuse outpatient assessment clinic
  - Provided educational sessions for 63 Veterans and their families
  - Prescribed 41 naloxone kits
  - 3 reports of opioid overdose reversals
- Strongly advocate for dissemination of OEND
  - Easily implemented and low cost
Cincinnati VA studies
(Tiffany et al., 2015; Wilder et al., 2015)

• 90 Veterans receiving opioids for ≥ 3 months
  – 52 Opioid Substitution Clinic (OSC); 38 Pain Management Clinic (PMC)
  – High risk→Average risk factors for opioid overdose—6 PMC, 8 OSC

• Perception of risk
  – ~70% believed their overdose risk was BELOW that of the average American adult

• Opioid overdose experience
  – 52% of OSC and 21% PMC Veterans had experienced an opioid overdose
  – 83% of OSC and 50% PMC Veterans had witnessed an opioid overdose

• Knowledge about and interest in naloxone
  – ~1/3 had heard of naloxone (46% OSC, 18% PMC); none had a kit
  – After a brief explanation, 73% of OSC and 55% of PMC Veterans wanted a kit
  – NOTE: Among patients NOT interested in naloxone kits—23% were using benzos and 23% were using additional opioids NOT prescribed by the VA (other risk mitigation strategies are also needed)
Patient perspectives on VA OEND
( Oliva et al., 2016)

Method
• 4 focus groups conducted with 21 patients in VA residential tx
  – 6 month program for Homeless Veterans, 3 month substance use disorder tx program

Results
• Benefits
  – Training is interesting, novel, and empowering; **Kits will save lives**
• Concerns
  – Legal and liability issues; Challenges of involving family in training; Kits may contribute to relapse (among non-opioid users NOT opioid users; opioid users—kits not a relapse trigger)
    • “Whether it increases, decreases or triggers someone to go out and use it, at least we have a means to save a life”
• Suggestions for improvement
  – **Increasing OEND awareness and access to OEND**
  – Active learning (hands-on practice)
Legal Regimes: Naloxone Access

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CLINICAL PHARMACY SPECIALIST, MENTAL HEALTH VETERANS AFFAIRS NORTH TEXAS HEALTH CARE SYSTEM
DALLAS, TEXAS
Disclaimer

The content and views expressed in this presentation belong solely to the author and do not reflect official policy or position of The United States Department of Veterans Affairs.
Legal Concerns

Prescriber

- Criminal prosecution
  - “Aiding and abetting” unauthorized practice of medicine*
  - Absent practitioner-patient relationship*
- Civil prosecution
  - Damages from prescribing/dispensing
  - Injury/death/loss from act or omission

Patient/Bystander/Lay Administrator

- Criminal prosecution
  - Unlawful possession of a legend drug
  - Controlled substance/paraphernalia possession
  - Violation of probation/parole/restraining order
- Civil prosecution
  - Injury/death/loss from act or omission

*Cause for professional sanctions by licensing board
Aims of Legislation: Naloxone Access Laws$^{1-3}$

- **Expand Access**
  - Third-party prescribing
  - Distribution
    - Standing order
    - Protocol order
    - Collaborative practice agreement
    - Direct authorization by legislature
  - Pharmacist prescriptive authority
- **Promote Education/Training**
- **Provide Legal Immunity**
  - Prescriber
  - Dispenser
  - Patient/Lay administrator
Aims of Legislation: Good Samaritan Laws\textsuperscript{1,2}

- Promote Use of Emergency Services
- Provide Legal Immunity
  - Possession of controlled substance
  - Possession of drug paraphernalia
  - Other violations\textsuperscript{a}
- Other protections\textsuperscript{b}

\textsuperscript{a} Violation of protective/restraining order; pretrial, probation, or parole conditions; other controlled-substance crimes
\textsuperscript{b} Reporting mitigating factor; civil forfeiture
Statewide Legislation

Adoption of legislation by states over time
## Comparison of Legislation

<table>
<thead>
<tr>
<th>State</th>
<th>NAL</th>
<th>CRIM (PRESC)</th>
<th>CIV (PRESC)</th>
<th>THIRD PARTY</th>
<th>DISTR</th>
<th>CRIM/CIV (ADMIN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama</td>
<td>X(^a)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>Alaska</td>
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<td>X</td>
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<td>X</td>
<td>CIV ONLY</td>
</tr>
<tr>
<td>Arizona</td>
<td>X(^a,b)</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>X</td>
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<tr>
<td>Arkansas</td>
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<td>California</td>
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<td>Colorado</td>
<td>X(^a)</td>
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<tr>
<td>Connecticut</td>
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<td>Delaware</td>
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<td>X</td>
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<td>X</td>
</tr>
<tr>
<td>District of Columbia</td>
<td>X(^c)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

\(^a\) Includes pharmacist protections  
\(^b\) Includes professional/disciplinary immunity  
\(^c\) Includes pharmacist prescriptive authority  

NAL = naloxone access law; CRIM (PRESC) = criminal immunity for prescriber; CIV (PRESC) = civil immunity for prescriber; DISTR = naloxone distribution; CRIM/CIV (ADMIN) = criminal/civil immunity for administrator
## Comparison of Legislation 15-25

<table>
<thead>
<tr>
<th>State</th>
<th>NAL</th>
<th>CRIM (PRESC)</th>
<th>CIV (PRESC)</th>
<th>THIRD PARTY</th>
<th>DISTR</th>
<th>CRIM/CIV (ADMIN)</th>
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<td>GEORGIA</td>
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<td>IDAHO</td>
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<td>X</td>
<td>X</td>
<td>X</td>
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<td>X</td>
</tr>
</tbody>
</table>

\(a\) Includes pharmacist protections  
\(b\) Includes professional/disciplinary immunity  
\(c\) Includes pharmacist prescriptive authority  

NAL = naloxone access law; CRIM (PRESC) = criminal immunity for prescriber; CIV (PRESC) = civil immunity for prescriber; DISTR = naloxone distribution; CRIM/CIV (ADMIN) = criminal/civil immunity for administrator.
Comparison of Legislation 26-34

<table>
<thead>
<tr>
<th></th>
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<th>CRIM (PRESC)</th>
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<td>(\chi^a,\chi^b)</td>
<td>(\times)</td>
<td>(\times)</td>
<td>(\times)</td>
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</tr>
<tr>
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<td>(\times)</td>
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<td>(\times)</td>
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<tr>
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<td>(\times)</td>
<td>(\times)</td>
<td>(\times)</td>
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<td>(\times)</td>
</tr>
</tbody>
</table>

\(\chi\) includes pharmacist protections
\(\chi^a\) includes professional/disciplinary immunity
\(\chi^b\) includes pharmacist prescriptive authority

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# Comparison of Legislation\(^{35-44}\)

<table>
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<th>THIRD PARTY</th>
<th>DISTR</th>
<th>CRIM/CIV (ADMIN)</th>
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<tr>
<td>NEBRASKA</td>
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<td>NEVADA</td>
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<tr>
<td>NEW HAMPSHIRE</td>
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<td>X</td>
<td></td>
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<td>NEW JERSEY</td>
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<td></td>
<td>X</td>
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</tr>
<tr>
<td>NEW MEXICO</td>
<td>X(^{a,b})</td>
<td>X</td>
<td></td>
<td>X</td>
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\(^{a}\) Includes pharmacist protections  
\(^{b}\) Includes professional/disciplinary immunity  
\(^{c}\) Includes pharmacist prescriptive authority

NAL = naloxone access law; CRIM (PRESC) = criminal immunity for prescriber; CIV (PRESC) = civil immunity for prescriber; DISTR = naloxone distribution; CRIM/CIV (ADMIN) = criminal/civil immunity for administrator
## Comparison of Legislation 45-56

<table>
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<tr>
<th>State</th>
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Nuances of Legislation

- Civil/Criminal Protections
  - Conditions for immunity
    - Education/training program participation
    - Acting with reasonable care

- Third Party Prescribing
  - Definition (family, caregiver, “any” person)
  - Education/training program participation

- Distribution
  - Standing order/protocol/collaborative practice agreement
  - Developed by physician/public health department/board of pharmacy/board of medicine
  - Distributed by/to first responders, community-based overdose prevention programs, opioid treatment facilities, correctional facilities, school districts, laypersons
  - Training requirements for patient/distributor
Nuances of Legislation\textsuperscript{19,64-68}

- California
  - Grant program for at-risk populations
    - Overdose education and naloxone provision
- Connecticut
  - Prior authorization not required
- Hawaii
  - Covered drug under Medicaid
- Illinois
  - Covered drug by insurance and state medication assistance program
  - Grants and drug overdose prevention program
Nuances of Legislation

- **Indiana**
  - Requires syringe exchange programs to provide overdose response/naloxone education

- **Maryland**
  - Establishment of guidelines for co-prescribing

- **Massachusetts**
  - Municipal Naloxone Bulk Purchase Trust Fund
  - Pharmacies in high risk areas to maintain stock

- **Minnesota**
  - Naloxone education by state-operated opioid treatment programs
Nuances of Legislation\(^{38,40,41,74}\)

- **Nevada**
  - Grants per Department of Health and Human Services
  - Opioid informed consent to include naloxone

- **New Jersey**
  - Grants per Commissioner of Human Services

- **New York**
  - Pharmacy with $\geq$20 locations to have dispensing protocol or register as opioid overdose prevention program
  - Detailed requirements for operation of opioid overdose prevention programs
Nuances of Legislation \(^{51,75-78}\)

- **North Carolina**
  - Syringe exchange programs shall provide access to naloxone

- **Oklahoma**
  - Naloxone dispensed/sold by pharmacist without prescription or protocol

- **Oregon**
  - Prescription monitoring program for dispensed naloxone

- **Rhode Island**
  - Collection of electronic dispensing data for naloxone
  - Establishment of best practices for co-prescribing
  - Covered drug by insurance
Nuances of Legislation$^{56,57,79}$

- **Utah**
  - Opiate Overdose Outreach Pilot Program Grants
  - Establishment of co-prescribing guidelines by physician licensing boards
- **Vermont**
  - Statewide opioid antagonist pilot program
- **West Virginia**
  - Community Overdose Response Demonstration Pilot Project
  - Data collection for naloxone prescription/dispensing/administration
Summary of Legislation 2,4-79

**Naloxone Access Law** a
- 51 states
- Criminal Protections (Prescriber)
  - 37 states
- Civil Protections (Prescriber)
  - 43 states
- Third Party Prescribing
  - 50 states
- Distribution
  - 48 states

**Criminal/Civil Protections (Layperson)**
- 47 states

**Pharmacist Prescriptive Authority**
- 8 states

**“Any” Person To Possess**
- 7 states

**Good Samaritan Law** b
- 41 states

---
aAs of November 2018
bAs of July 2017
Impact of Legislation

- Naloxone dispensing
- Opioid Overdose Education and Naloxone Distribution (OEND) program implementation
- Layperson emergency response
- Opioid misuse
- Opioid-related mortality
Impact of Legislation

Xu J, et al.

**Purpose**
To examine the effect of naloxone laws (namely third-party prescribing and standing order provisions) on pharmacy naloxone dispensing.

**Methods**
- Prescription Drug Abuse Policy System (PDAPS) for naloxone laws enacted as of June 1, 2016
- Symphony Health Solutions’ PHAST Prescription data from 2007 to 2016 for naloxone dispensed

**Result**
Naloxone access laws were associated with average increase of 78 prescriptions dispensed per state per quarter
Average 79% increase in naloxone dispensed from U.S. retail pharmacies, compared to states without such laws

**Conclusion**
Naloxone access laws can increase the availability and accessibility of naloxone.
Impact of Legislation

Gertner AK, et al.

**Purpose**
To determine whether implementation of naloxone access laws led to increased naloxone dispensing via Medicaid

**Methods**
- Reviewed naloxone legislation passed between 2007 and 2016
- Examined Medicaid State Drug Utilization dataset from 2007 to 2016 for naloxone prescription reimbursement

**Result**
- Presence of any naloxone law was associated with increases in naloxone reimbursed by Medicaid
- Laws with standing order provisions were most robustly associated with increases in naloxone dispensing

**Conclusion**
Naloxone access laws, especially with standing order provisions, may effectively increase naloxone access among Medicaid beneficiaries
Impact of Legislation
Lambdin BH, et al.

**Purpose**
To assess whether state-level naloxone laws and provisions stimulated the implementation of OEND programs.

**Methods**

**Result**
By end of 2014, 259 (8%) counties had OEND programs. Counties within states that had a naloxone law had 28-fold increased odds of OEND program implementation.

**Conclusion**
Naloxone laws facilitated OEND implementation, but future studies should investigate strategies to improve OEND implementation.
Impact of Legislation

Watson DP, et al.

Purpose
To examine attitudes and knowledge among lay responders who received naloxone kits from 20 local health departments across Indiana

Methods
- Postcard surveys distributed inside naloxone kits in 20 Indiana counties
- Collected demographic information, overdose experiences, use of 911, knowledge of Good Samaritan laws

Result
- 77.4% of 217 respondents indicated knowledge of Indiana’s Good Samaritan protections
- Those with knowledge of protections were more likely to have called 911 (84.7 vs. 15.3%; p = .048)

Conclusion
- Strengthening Good Samaritan laws, educating lay persons about protections, and improving police interactions at an overdose scene are likely to improve outcomes of naloxone distribution
Impact of Legislation
McClellan C, et al.

Purpose
To assess the relationship of naloxone access and Good Samaritan laws with opioid overdose mortality and non-medical opioid use.

Methods
Reviewed National Vital Statistics System data, National Survey on Drug Use and Health data, and primary datasets of naloxone access and Good Samaritan laws.

Result
Data from 2000-2014 indicate states with naloxone access or Good Samaritan laws had a 14% (p=0.033) and 15% (p=0.050) lower incidence of opioid overdose mortality, respectively.

Conclusion
Laws were associated with reduced opioid overdose mortality, without increases in non-medical opioid use. Universal adoption of naloxone access and Good Samaritan laws could save an additional 981 and 1,896 lives, respectively.
Impact of Legislation
McClellan C, et al.

**Opioid Overdose Deaths**

- Naloxone access law*
- Third party*
- Standing order*
- Possession*
- Prescriber immunity*
- Dispenser immunity*
- Good Samaritan law*
- Good Samaritan law possession*
- Good Samaritan law probation*

**Percentage Change (95% CI)**

-40 -30 -20 -10 0 10 20 30 40
Impact of Legislation

Erfanian E, et al.

**Purpose**
To investigate the effect of naloxone access laws on opioid overdose death rates

**Methods**
Reviewed mortality data from CDC Wonder and legislative data from Prescription Drug Abuse Policy System, 1999-2014

**Result**
- Three legal provisions decreased overdose death rates
- Three legal provisions increased overdose death rates

**Conclusion**
Overall, no statistical evidence that naloxone access laws reduce opioid death rates
Impact of Legislation

Rees DI, et al.

Purpose
To examine the effect of naloxone access and Good Samaritan laws on opioid-related deaths

Methods

Result
Adoption of a naloxone access law was associated with 9-11% reduction in opioid-related deaths

Comments
Effect was stronger >2 years after law adoption and for non-heroin-related deaths; Removing criminal liability for naloxone possession was associated with 13% reduction in deaths; Laws did not increase recreational use of prescription opioids
Summary

- Legal Concerns
  - Prescriber/Dispenser/Patient/Bystander/Administrator
- Statewide Legislation
  - Not comprehensive in every state
  - Very nuanced
  - Unique/creative provisions
- Impact of Legislation
  - Increase pharmacy dispensing of naloxone
  - Increase distribution to Medicaid-eligible patients
  - Facilitate OEND implementation
  - Improve layperson activation of emergency response
  - ?? Reduce opioid-related mortality ??
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5. Alaska Stat. §§ 08.80.030, 09.65.340, 17.20.085


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8. Cal Civ Code § 1714.22

9. Cal Bus & Prof Code § 4052.01
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11. C.R.S.A. §§ 12-36-117.7, 12-38-125.5, 12-42.5-120, 13-21-108.7, 18-1-712
13. 16 Del.C. §§ 138, 3001G
14. D.C. CODE § 7-401-404
15. Fla. Stat. § 381.887
16. O.C.G.A. §§ 26-4-116.2, 31-1-10
17. HRS §§ 329E-2, 461-11.8
18. Idaho Code § 54-1733B
19. 20 ILCS 301/5-23
20. 225 ILCS 85/19.1
21. 745 ILCS 49/36
23. Iowa Code § 147A.18
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25. KRS § 217-186
26. LA R.S. 40:978.2
27. 22 M.R.S.A. § 2353
29. ALM GL ch. 94C, §§ 19, 19B
30. MCLS §§ 333.17744b, 333.17744c 333.17744e, 691.1503
31. Minn. Stat. § 245G.08, § 604A.04
32. Miss. Code Ann. § 41-29-319
33. § 195.206 R.S.Mo.
34. 50-32-601 – 50-32-611, MCA
35. R.R.S. Neb. §28-470
37. RSA 318-B:15
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41. 10 NYCRR 80.138
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44. OH ST §§ 2925.61, 4723.488, 4729.44, 4730.431, 4731.941
45. ORC Ann. 3707.561
46. 76 Okl. St. § 5
47. 63 Okl. St. § 1-2506.2
48. 63 Okl. St. § 1-2506.2, 2-312.2
49. ORS §§ 689.681, 689.682
50. 35 P.S. § 780-113.8
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54. Tenn. Code Ann. §§ 63-1-152, 63-1-157
57. 18 V.S.A. § 4240
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60. Rev. Code Wash. § 69.41.095
62. Wis. Stat. §§ 441.18, 448.037, 450.11
63. Wyo. Stat. § 35-4-901 - 35-4-906
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Legal Regimes: Naloxone Access

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