



**Joint Meeting of the Anesthetic and Analgesic Drug
Products Advisory Committee, and the Drug Safety and
Risk Management Advisory Committee**

17-18 December 2018

Agenda

- **Role of Naloxone in the Opioid Overdose Public Health Crisis**
- **Expanded Access to Naloxone**
 - Risk Factors
 - Universal Precautions
- **Naloxone Implementation**
 - Challenges and Recommendations

➤ Responding to a Dynamic Public Health Crisis

Prescribed opioids

Co-prescribing take-home naloxone to patients on opioid analgesics or medication assisted treatment (MAT)¹⁻³

Opioid Use Disorder (OUD)

Patients who are being treated for OUD and their family members/significant others should be given prescriptions for naloxone and trained in the use of naloxone in overdose³



Heroin

Overdose education and naloxone distribution to opioid users and their families and peers⁴

Synthetic opioids

Illicit fentanyl and fentanyl analogs can trigger rapid onset and progression of overdose: prompt treatment with multiple naloxone doses may be required to reverse overdose⁵

1. Dowell D et al. *MMWR Recomm Rep* 2016;65:1-49. 2. Federation of State Medical Boards. *Guidelines for the Chronic Use of Opioid Analgesics*. 2017. 3. ASAM. *The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use*. 2015. 4. Maxwell S et al. *J Addict Dis* 2006;25:89-96. 5. O'Donnell JK et al. *MMWR Morb Mortal Wkly Rep* 2017;66:1197-202.

➤ Opioids and Chronic Diseases

Chronic Pain

- 5-8 million patients rely on opioids for long term management of pain¹
- 25% decline in total number of opioid prescriptions dispensed 2012-2017²

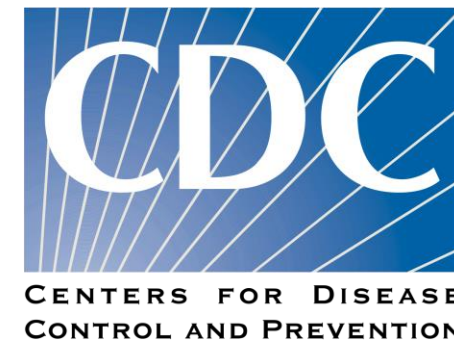
Opioid Use Disorder (OUD)

- 2.1 million people (12 and older) with Opioid Use Disorder in 2017³
- Crucial need to expand access to evidence-based treatments, including medication-assisted therapy (MAT)⁴
- High rates of relapse⁵

1. Reuben DB, et. al. Ann Intern Med. 2015;162 (4):295-300 2. <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html> . Accessed 13 Dec 2018. 3. NSDUH 2017. SAMHSA. 4. <https://www.cdc.gov/drugoverdose/prevention/treatment.html>. Accessed 29 Nov 2018. 5. Hser Y-I, et al. Harv Rev Psychiatry. 2015;23:76-89

➤ Naloxone – Expanded Access is Recommended

Many organizations strongly recommend that naloxone and opioid overdose education be readily accessible to individuals likely to witness a life-threatening opioid overdose (World, Federal, State, Medical)









































➤ Take-Home Naloxone (THN) Considerations for Risk-Based vs Universal Prescribing¹

| PROS | | CONS |
|---|--|------|
| RISK-BASED THN | | |
| Reaches a defined at-risk population Engages patients in conversations about risk | | |
| UNIVERSAL THN | | |
| Reaches a broader population Less targeting/stigma More efficient to HCP office | | |

1. Binswanger I. <https://www.fda.gov/downloads/Drugs/NewsEvents/UCM454769.pdf>. Accessed January 11, 2018.

➤ Opioid Overdose Risk Factors

COMORBIDITIES

| | | Guidelines | | | | | | | Risk Assessment Tools | |
|---|---------------------|---|---|---|---|---|---|---|---|---|
| | | AMA AMERICAN MEDICAL ASSOCIATION | CDC CENTERS FOR DISEASE CONTROL AND PREVENTION | SAMHSA SUBSTANCE USE AND MENTAL HEALTH SERVICES ADMINISTRATION | Academy of Integrative Pain Management | World Health Organization | U.S. DEPARTMENT OF JUSTICE DEPARTMENT OF JUSTICE | Federation of STATE MEDICAL BOARDS | VHA RIOSORD* | CIP RIOSORD* |
|  | Psychiatric |  |  |  |  |  |  |  |  |  |
| | Nervous |  |  | |  | |  |  |  |  |
|  | Respiratory |  | | |  | | |  |  |  |
|  | Hepatobiliary | |  | |  |  | | |  | |
|  | Renal/genitourinary | |  | |  | | |  |  |  |
|  | Gastrointestinal | | | | | | | | |  |
|  | Traumatic injury | | | | | | | |  | |

























VHA = Veterans' Health Administration;

CIP= Commercial Insured health Plan;

RIOSORD = Risk Index for Overdose or Serious Opioid-induced Respiratory Depression;

ER/LA = extended-release/long-acting.

TREATMENT-RELATED

| | | | | | | | | | | |
|---|----------------------------|---|---|---|---|---|---|---|---|---|
|  | ER/LA formulations | |  |  |  | |  |  |  |  |
| | Benzodiazepines |  |  | |  |  |  |  |  |  |
|  | MME/day | HIGH | ≥ 50 | HIGH | HIGH | HIGH | >90 | | ≥20 | ≥100 |
|  | Duration of opioid therapy | | |  | | |  | | | |
| | Prior opioid overdose | |  |  | | |  |  | | |



Two Recent Studies Examined a Universal Precautions Approach to Overdose Education and Naloxone

- **Universal Precautions - Chronic Pain¹**

Prospective, single site, n=164 (18 or older), median morphine equivalent dose of 90 med/day, overdose education and naloxone instruction provided

- Difficulty of predicting which patients on chronic opioid therapy (COT) will experience opioid overdose
- In previous studies, naloxone was given to only high risk patients
- Universal Precautions (all patients receiving COT) may have significant impact on intentional and unintentional overdose deaths

- **Universal Precautions - Opioid Use Disorder²**

Prospective, single site, n=244 (18 or older) in medication assisted treatment; overdose education and naloxone instruction provided

- There is evidence that take home naloxone can help prevent opioid overdose deaths in targeted populations
- Participants with a diagnosis of OUD in an outpatient treatment program (OTP) setting were enrolled
- Study suggests a model for naloxone could be replicated in other OTP settings to reduce opioid overdose deaths

1. Takeda M. et al.. *Subst Abus.* 2016;37:591-596. 2. Katzman, J. et al. *J Addict Med.* 2018;12:113-8

➤ **Treating Chronic Conditions is Challenging**

A Clinician's Perspective

- **Chronic Pain and Opioid Use Disorder (OUD) are chronic conditions**
 - Goals of any long term chronic disease (i.e. diabetes, asthma) are to maximize benefits while managing risk of treatments and progression of disease
 - Individualized treatment for these conditions can drain resources (time, energy, finances)
 - Optimal management of these and other chronic conditions involves other individuals as well (family, friends, other caregivers)
 - Limited data on effective long-term therapies to treat Chronic Pain and OUD
 - With any chronic condition, relapse (of some degree) is expected
 - Return to function vs. symptom reduction
 - Chronic management vs. cure

➤ Recommendations

- **Naloxone should be an integral component of treatment for patients:**
 - On chronic opioid therapy; or
 - With a diagnosis of OUD
- **Health care providers, pharmacists and patients should be educated on naloxone as a life-saving, emergency intervention for opioid overdose**
- **Access to naloxone should be increased for:**
 - People who misuse or abuse opioids, and are not in treatment (harm reduction / naloxone distribution programs)
 - Concerned family members and friends (accidental exposure, potential witness)



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