NALOXONE: HEALTHCARE PROFESSIONALS' TRAINING GUIDE FOR ADMINISTRATION AND DISPENSING

Kaitlyn Bernard, PharmD
PGY-1 Pharmacy Practice Resident
November 18, 2017

Objectives

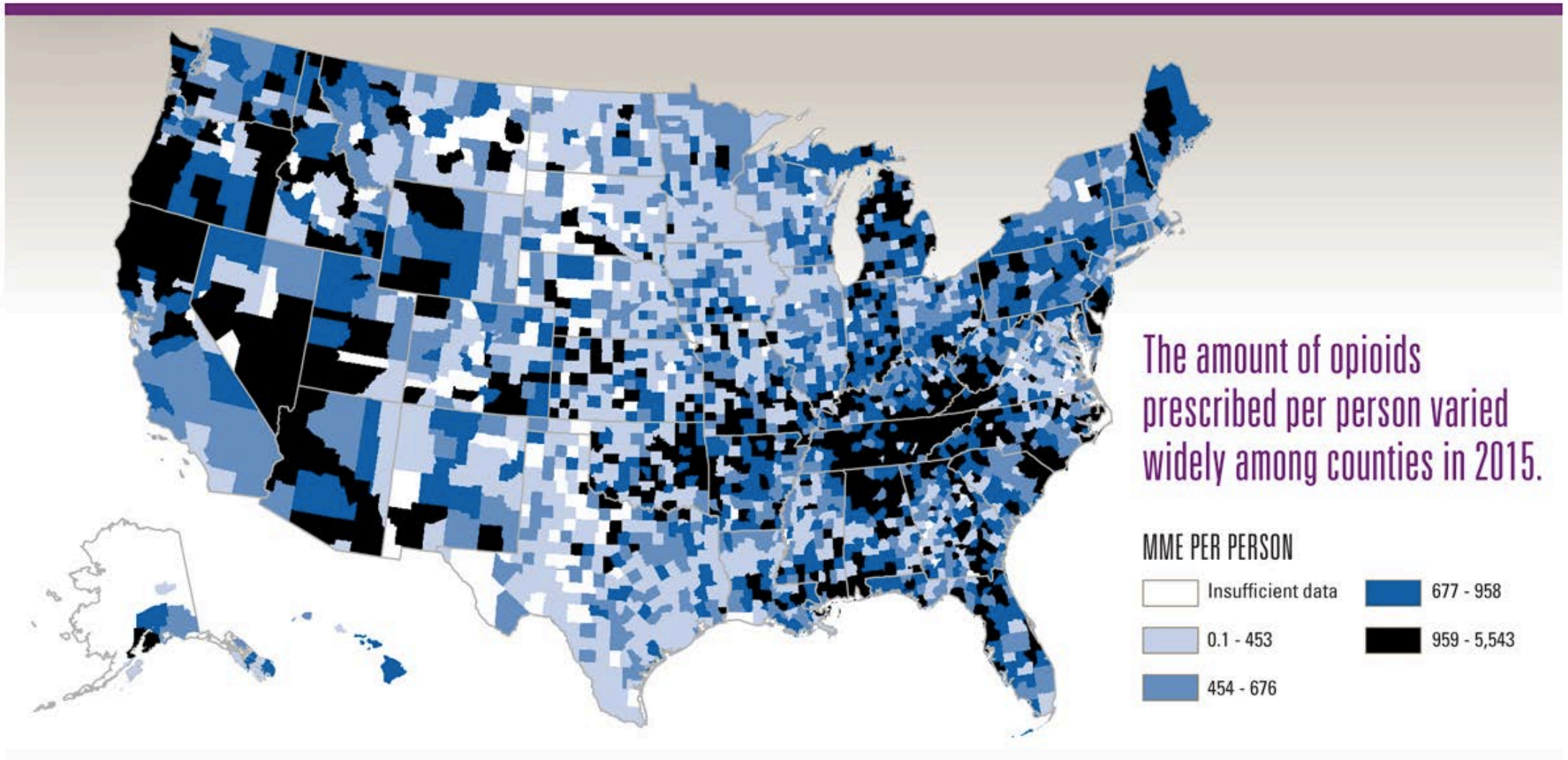
- Explain the impact of the opioid epidemic in Maine
- Identify individuals who are at risk for opioid overdose
- Discuss the pros and cons for each formulation of naloxone
- Explain the *draft* 2017 Maine laws and legal requirements for pharmacies surrounding dispensing naloxone to the public
- Describe proper administration techniques for the dispensed formulation

OPIOID EPIDEMIC

Nationwide Opioid Epidemic

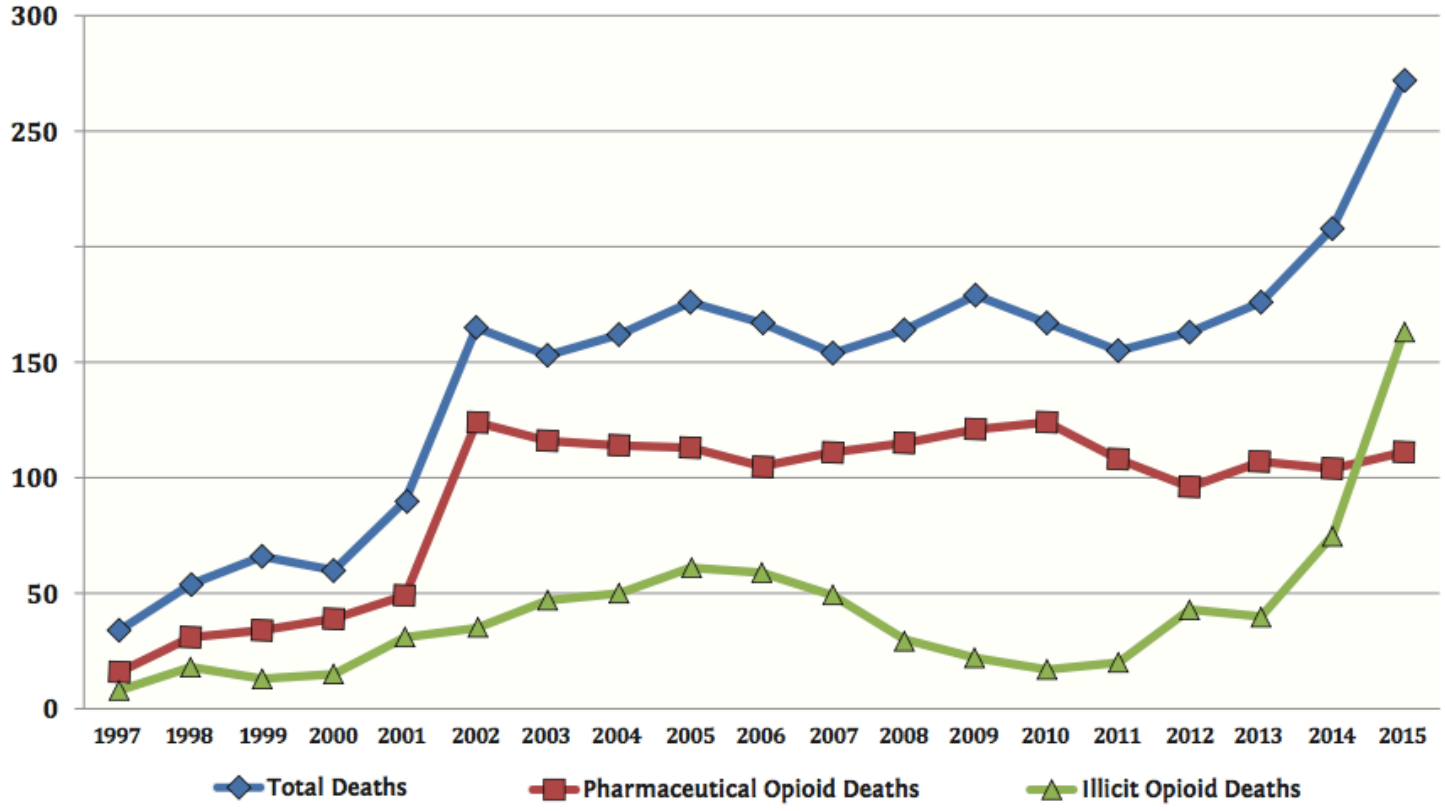
- In 2015, drug overdoses accounted for 52,404 deaths
  - 63.1% of those involved an opioid medication
- Not only are prescription opioids a concern but also heroin and fentanyl-laced drugs (and its derivatives)
- DHHS recognized opioid-related overdose as a major public health concern, addressing 3 priority areas:
  - Opioid prescriber education
  - Community naloxone access
  - Medication-assisted treatment

Rudd et al. Increases in Drug and Opioid-Involved Overdose Deaths – United States, 2010-2015. *MMWR*. 2016. 65(50-51);1445-1452.



https://www.cdc.gov/media/dpk/prescription-drug-overdose/opioid-prescribing/index.html

Maine Overdose Deaths by Drug Type over Time

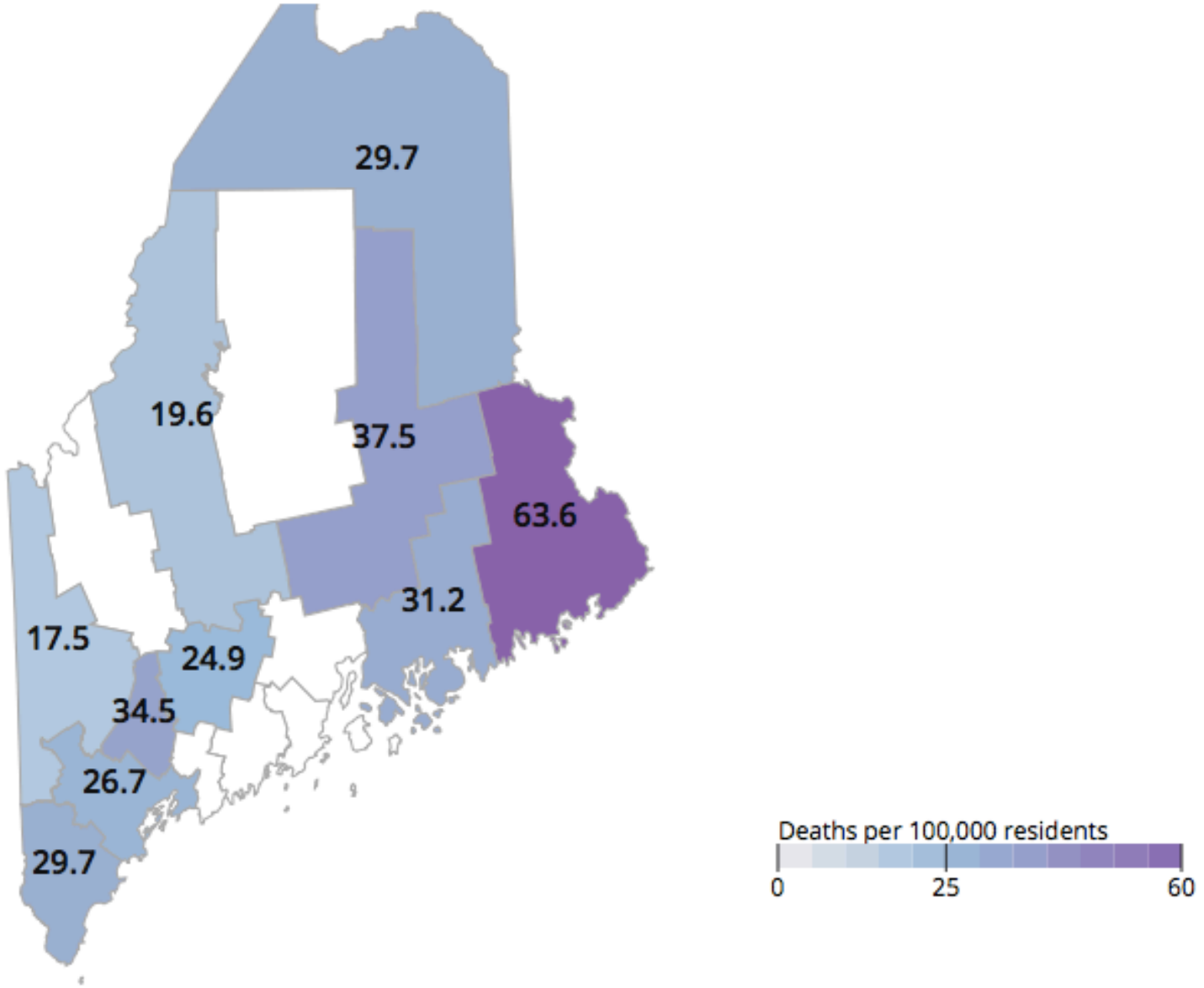


https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_Provider_110316%2002.pdf

"Lost" Findings

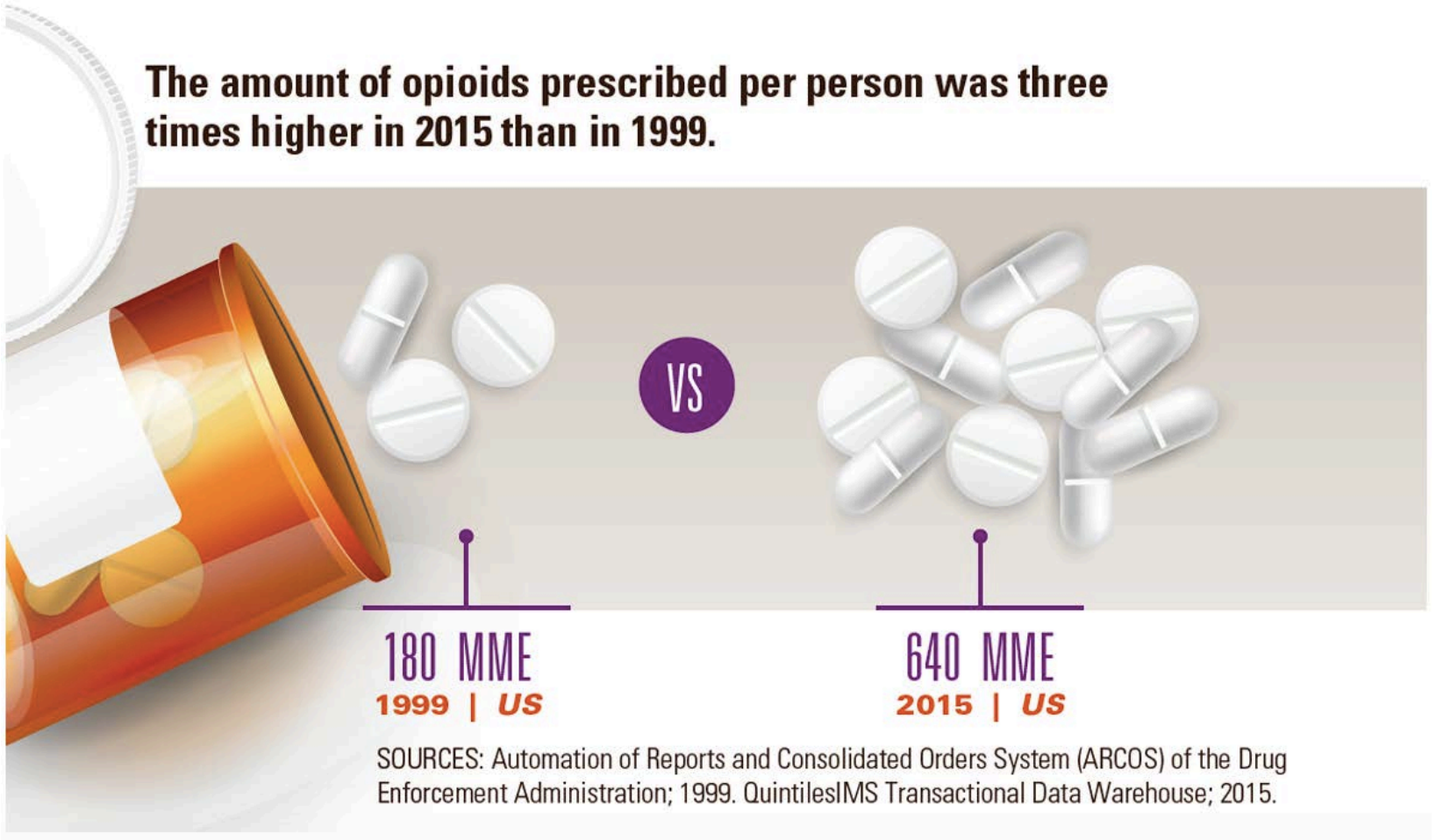
- Death toll has been rising faster in Maine than almost every other state
- Between 2013-2014, Maine had 3rd highest increase in drug-related deaths of any state
- Again, between 2014-2015, Maine was among the top states
- Numbers would be higher without availability of naloxone

Deaths per 100,000 residents in 2016. No data is available for counties with fewer than 10 deaths.



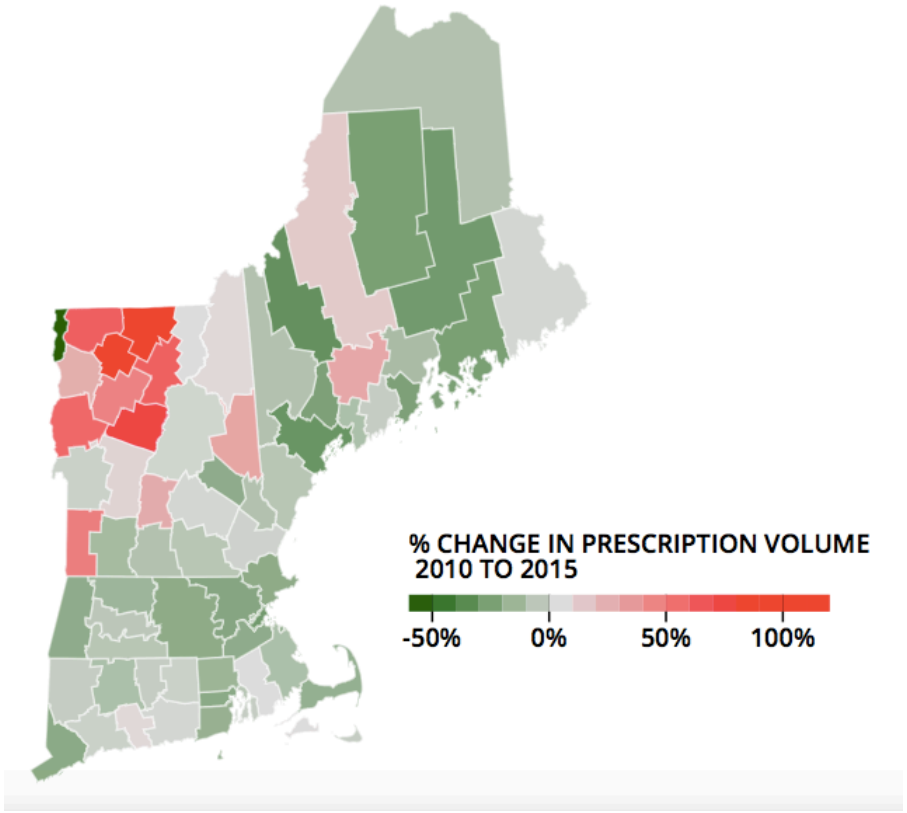
http://www.pressherald.com/2017/04/11/maine-breaks-record-for-drug-overdose-deaths-in-2016/

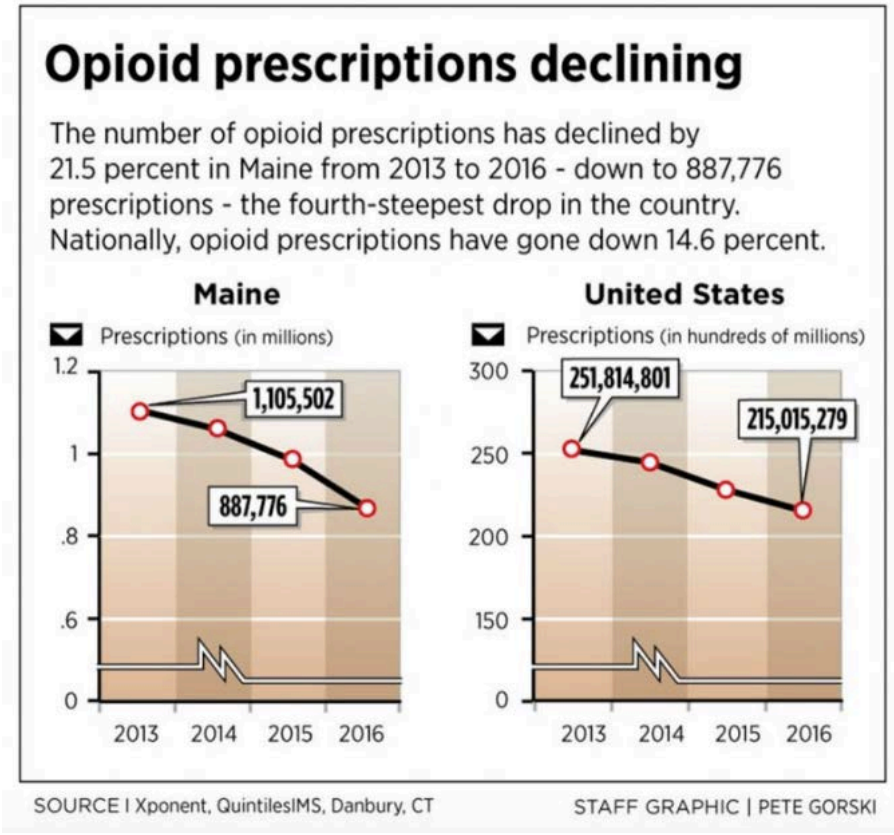
One major contributor… prescribing



https://www.cdc.gov/vitalsigns/opioids/index.html

Opioid Prescribing Data





http://www.pressherald.com/2017/07/14/map-opioid-prescription-rates-across-new-england/http://www.pressherald.com/2017/07/14/maine-doctors-prescribing-far-fewer-opioids-analysis-at-county-level-shows/

In the News

Drug overdose deaths keep steady pace through first six months of 2017 with 185 deaths recorded through the end of June

September 6, 2017

OFFICE OF THE ATTORNEY GENERAL

FOR IMMEDIATE RELEASE CONTACT: Andrew Roth-Wells Date: September 6, 2017 Telephone: (207) 626-8887

Drug overdose deaths keep steady pace through first six months of 2017 with 185 deaths recorded through the end of June

Overdose deaths are slightly less compared to 2016, but fentanyl use continues to rise

AUGUSTA – Maine's rate of drug overdose deaths is keeping pace with last year. Through the first six months of 2017 the Office of the Chief Medical Examiner recorded 185 deaths attributable to drug overdose, according to Dr. Marcella Sorg of the Margaret Chase Smith Policy Center who analyzes overdose deaths for the Office of the Attorney General. Doubled, that would be 370 compared to 376 in 2016, or more than one drug overdose a day.

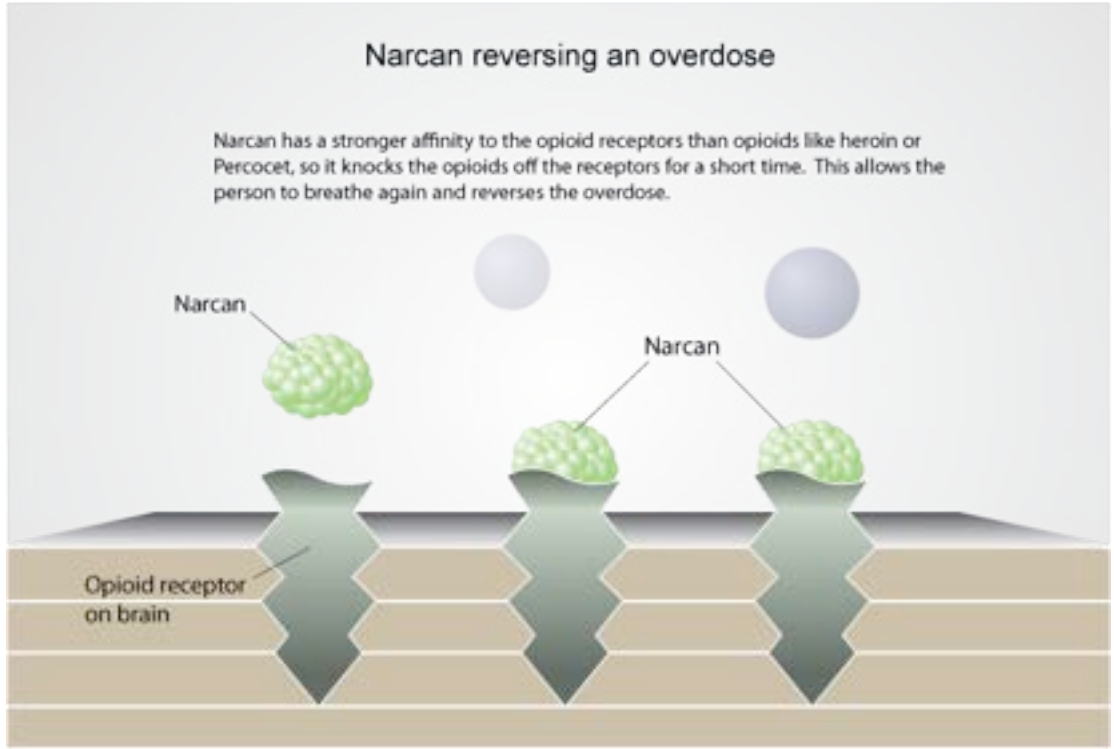
The number of deaths represents a slight decrease from the 193 overdose deaths in the first half of 2016, which represented a 50% increase over the year before. However, the presence of fentanyl and fentanyl analogs continues to grow. Fentanyl is an illicitly manufactured drug that is many times more lethal than morphine; it caused 61% of the deaths between January and June 2017. Fentanyl is often mixed with heroin or presented to the user as heroin.

Fairbairn et al. Naloxone for heroin, prescription opioid, and illicitly made fentanyl overdoses: Challenges and innovations responding to a dynamic epidemic. *International Journal of Drug Policy*. 2017. 46;172-179.

REVERSAL AGENT – NALOXONE

Narcan (naloxone)

- Highly specific, high-affinity opioid antagonist
  - Stronger affinity than other opioids, knocking them off, reversing the overdose
- Naloxone ONLY works if there are opioids involved
  - It does NOT work on other non-opioid based drugs
  - Does NOT harm someone if given when patient has no opioids in system



https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_Provider_110316%2002.pdf

Narcan (naloxone)

- **Onset**: ~2-8 minutes
- **Duration**: 30-90 minutes
- **Bioavailability:**
  - IV – 100%
  - IM – 54%
  - IN – 43.1%
- **Side Effects**: induction of opioid withdrawal – agitation, increased blood pressure, muscle cramping, nausea/vomiting
- No potential for abuse

Micromedex® Healthcare Series, (electronic version). Thomson Micromedex, Greenwood Village, CO. Accessed November 2017.

Naloxone formulations

- **Injectable (and intranasal) generic**
  - Manufacturer: Amphastar & Teleflex (IN adapter)
- **Intranasal branded (Narcan Nasal Spray)**
  - Manufacturer: Adapt Pharma
- **Injectable generic vials**
  - Manufacturers: Hospira, Mylan
- **Auto-injector (Evzio Auto-Injector)**
  - Manufacturer: kaléo

http://mediad.publicbroadcasting.net/p/wshu/files/styles/medium/public/201603/NaloxonePharma_0.jpg

Formulation Comparison Chart

	IJ/IN generic	IN brand	IJ generic[1]	IJ generic[2]	Auto-IJ brand
FDA-approved	X (for IV, IM, SC)	X	X	X	X
Layperson experience	X		X		X
Assembly required	X		X	X	
Titrable	X		X	X	
Strength	1mg/mL	4mg/ 0.1mL	0.4mg/mL OR 4mg/10mL	0.4mg/mL	0.4mg/0.4mL
Total volume	4mg/4mL	8mg/ 0.2mL	0.8mg/2mL OR 4mg/10mL	0.8mg/2mL	0.8mg/0.8mL
Cost/kit	$$	$$$	$	$	$$$$
Storage requirements (all protect from light)	Store at 59-86°F Fragile: glass	Store at 59-77°F	Store at 68-77°F Breakable: glass	Store at 68-77°F Breakable: glass	Store at 59-77°F

Formulation Comparison Chart cont.

	IJ/IN generic	IN brand	IJ generic[1]	IJ generic[2]	Auto-IJ brand
Rx and quantity	#2 2mL Luer-lock needleless syringe plus #2 mucosal atomizer devices	#1 2-pack of 2 0.4mg/ 0.1mL IN devices	#2 single-use 1mL vials OR #1 10mL MDV PLUS #2 3mL syringe w/ 23-25 gauge 1-1.5 inch IM needles	#2 single-use 1mL vials PLUS #2 3mL syringe w/ 23-25 gauge 1-1.5 inch IM needles	#1 2-pack of 2 0.4mg/0.4mL prefilled auto-injector devices
Sig	Spray 1mL (1/2 syringe) into each nostril.	Spray 0.1 mL into one nostril.	Inject 1mL in shoulder or thigh.	Inject 1mL in shoulder or thigh.	Inject into outer thigh as directed by voice-prompt. Place black side firmly on outer thigh and depress and hold for 5 seconds
Repeat dose?	Repeat after 2-3 minutes if no-minimal response				
Manufacturer	Amphastar/ Teleflex (IN adapter)	Adapt Pharma	Hospira	Mylan	kaléo

Knowledge Question #1

Which of the following is NOT a route of administration of naloxone available for dispensing 'over the counter' to patients?

a) Intranasal spray
b) Intravenous injection
c) Intramuscular injection into the thigh
d) Intramuscular injection into the deltoid

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IDENTIFYING AT-RISK INDIVIDUALS

Risk Factors

- History of receiving emergency medical care for acute opioid poisoning/overdose
- Suspected or confirmed history of substance abuse, dependence or non-medical use of prescription or illicit substances
- Recent release from prison or opioid detox program
- In methadone or buprenorphine detox/maintenance for addiction or pain

https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_Provider_110316%2002.pdf

Risk Factors cont.

- Receiving high-dose opioid prescriptions (>100mg morphine equivalence)
- Have difficulty accessing emergency medical services
- Any opioid prescription in combination with:
  - Respiratory diagnoses
  - Renal dysfunction
  - Alcohol, benzodiazepines, or antidepressant use

https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_Provider_110316%2002.pdf

Knowledge Question #2

Which of the following patients would NOT be considered to be at 'high risk' of an opioid overdose?

a) 28 yo male who recently was in the emergency department for an OD
b) 84 yo male who has COPD/emphysema, diagnosed with lung cancer 1 year ago, and has been using benzodiazepines for sleep and high-dose opioids to control his pain (MME > 100)
c) 76 yo frail female who lives in Allagash, ME and has been using fentanyl patches for her chronic lower back pain for years, but the nearest hospital is 1 hour away
d) 45 yo male who uses OxyContin 40mg daily and hydrocodone/APAP 5/325mg TID as needed for breakthrough pain (MME = 75)

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MAINE – AUTHORIZATION TO PRESCRIBE & DISPENSE

Draft Proposal

Authorization to Prescribe & Dispense Naloxone

- May not dispense naloxone without a prescription, standing order, or CDTM agreement unless authorized to prescribe

- Prior to being authorized to prescribe and dispense naloxone – pharmacists must obtain 2 ACPE-approved CE hours of training related to:
  - Writing prescription drug orders for naloxone
  - Safe dispensing of an opioid antagonist
  - Counseling and providing instructions to person receiving prescription
  - Its use as rescue therapy in an opioid overdose

CDTM – Collaborative drug therapy management

Training Requirements for Pharmacists

- Additional requirements for education training must address the following topics:
  1. Risk factors for opioid abuse and overdose
  2. Opioid overdose prevention
  3. Recognizing and responding to opioid overdoses
  4. Indications for use of naloxone as rescue therapy
  5. Contraindications for use of an opioid antagonist
  6. Proper storage and expiration of an opioid antagonist product dispensed
  7. Procedures for administration of an opioid antagonist
  8. Adverse effects associated with an opioid antagonist rescue therapy
  9. Identification of a patient who meets the criteria for provision of an opioid antagonist
  10. Required education to provide to persons receiving an opioid antagonist
  11. Required elements of protocol to initiate dispensing of an opioid antagonist
  12. Required documentation when initiating dispensing of an opioid antagonist
  13. Actions and interventions to be used upon the occurrence of a clinical event

Training Requirements for Pharmacists

- To become an authorized pharmacist:
  - Must submit an application to the Board attesting to:
    1. Holding a valid Maine license
    2. Completion of the training
- "Board-authorized pharmacists may prescribe an oral, injectable, intranasal, or any other form of opiate antagonist AND the necessary medical supplies to administer naloxone to a person that the pharmacist reasonably determines meets the eligible patient criteria"
- "Board-authorized pharmacists may prescribe naloxone emergency rescue kits – must be labeled and include expiration date, patient educational information"

DRAFT

Eligible Recipients Under Maine Protocol

Request from patient, immediate family member, or friend
Hx of emergency medical care for acute opioid poisoning/overdose
Suspected or confirmed Hx of substance abuse, dependence, or non-medical use of prescription/illicit substances
Receiving high-dose opioid prescriptions (>100mg MME)
Recent release from prison or opioid detox program
Starting methadone or buprenorphine detox/maintenance for addiction
Have difficulty accessing emergency medical care ($$, distance)
On opioid prescriptions in combination with: • Smoking, COPD, emphysema, sleep apnea, or other respiratory illness • Renal dysfunction, hepatic disease, or cardiac disease • Known or suspected alcohol use • Anyone who inject opioids, such as heroin or fentanyl • Concurrent benzodiazepines or other sedative prescription • Concurrent antidepressant prescription

DRAFT

Knowledge Question #3

As a Maine pharmacist under the *proposed* naloxone protocol, which of the following patients are you allowed to dispense to?

a) 35 yo female who is picking up a prescription for oxycodone, who also takes sertraline for anxiety/depression, lorazepam for anxiety, prn zolpidem for sleep
b) A mother of a 20 yo male who is concerned that her child may be taking prescription drugs
c) A 18 yo female requests it
d) All of the above patients

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c) A 18 yo female requests it
d) **All of the above patients**

Required Documentation

- Pharmacists MUST document in system each person who receives a naloxone prescription, documentation must include:
  - Name of patient at risk (if known) or name of person requesting
  - Name of person to whom the prescription was dispensed
  - Product name
  - Dose and route of administration and required delivery service
  - Dispense date
  - Name of prescribing pharmacist or practitioner
  - Name of dispensing pharmacist who reviewed and provided patient/caregiver with educational materials appropriate for the dosage form dispensed
- Documentation also applies to prescribing and dispensing emergency kits

Required Notification

- Within 7 days: Pharmacist must provide the patient's physician written notification via fax (or other method) that naloxone was provided to patient under this protocol
    - Notification must include:
        1. Patient's name
        2. Opioid antagonist prescribed or dispensed
        3. Dispensed date
- If the physician is unknown, it must be documented in pharmacy's systems

DRAFT

Required Counseling

- At the time of dispensing opioid antagonist, pharmacist must provide written instructions on proper response, including instructions for seeking medical attention
- Minimum requirements for counseling:
  - Instruct person to call emergency services as soon as practicable either before or after administration of opioid antagonist
  - Personally provide oral counseling with written educational materials for the appropriate dosage form that should include –
    - Risk factors of opioid overdose
    - Strategies to prevent opioid overdose
    - Signs of opioid overdose
    - Steps in responding to an overdose
    - Information on naloxone
    - Procedures for naloxone administration
    - Proper storage and expiration of dispensed product
    - Information on where to get a referral for substance abuse treatment

DRAFT

Ways to Avoid Accidental Overdose

1. Take medicine only if it has been prescribed for you.
2. Do not mix your opioids with alcohol, benzodiazepines, or other sedating medications
3. Store your medicine in a safe place away from children.
4. Learn the signs of overdose and teach your family and friends how to respond.
5. Be extra careful if you miss or change doses, feel ill, or start new medications
6. Dispose of unused medication properly.

https://store.samhsa.gov/shin/content/SMA13-4742/Toolkit_Patients.pdf

WHAT ARE YOUR LIABILITIES?

2017 Maine Naloxone Overdose Prevention Laws

Do **prescribers** have immunity from **criminal prosecution** for prescribing, dispensing, or distributing naloxone to a lay person?	**Yes** Me. Rev. Stat. tit. 22 §2353
Do **prescribers** have immunity from **civil liability** for prescribing, dispensing, or distributing naloxone to a lay person?	**Yes** Me. Rev. Stat. tit. 22 §2353
Do **prescribers** have immunity from **professional sanction** for prescribing, dispensing, or distributing naloxone to a lay person?	**Yes** Me. Rev. Stat. tit. 22 §2353
Do **dispensers** have immunity from **civil liability** for prescribing, dispensing, or distributing naloxone to a lay person?	**Yes** Me. Rev. Stat. tit. 22 §2353
Do **dispensers** have immunity from **professional sanctions** for prescribing, dispensing, or distributing naloxone to a lay person?	**Yes** Me. Rev. Stat. tit. 22 §2353

**** ALL are required to act with reasonable care ****

http://www.pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139

Good Samaritan Law

- You cannot be prosecuted for having a small amount of medication or drugs when you seek help in an overdose
- Overdose victim is also protected
- Law does not protect you or the victim against other crimes or warrants

http://www.drugpolicy.org/sites/default/files/Fact%20Sheet_State%20based%20Overdose%20Prevention%20Legislation%20%28January%202016%29.pdf

REQUIRED PATIENT EDUCATION

Required Patient Education

1. Recognizing signs of an overdose

1. Recognizing the signs of overdose

- Person won't wake up
- Slowed/stopped breathing
- Blue/gray lips and fingernails
- Pale, clammy skin
- Pin-point pupils

https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_PatientFlyer_041416.pdf

http://stopoverdose.org/section/learn-about-overdose/

Required Patient Education

1. ~~Recognizing signs of an overdose~~
2. **Emergency response instructions**

2. Emergency Response Instructions

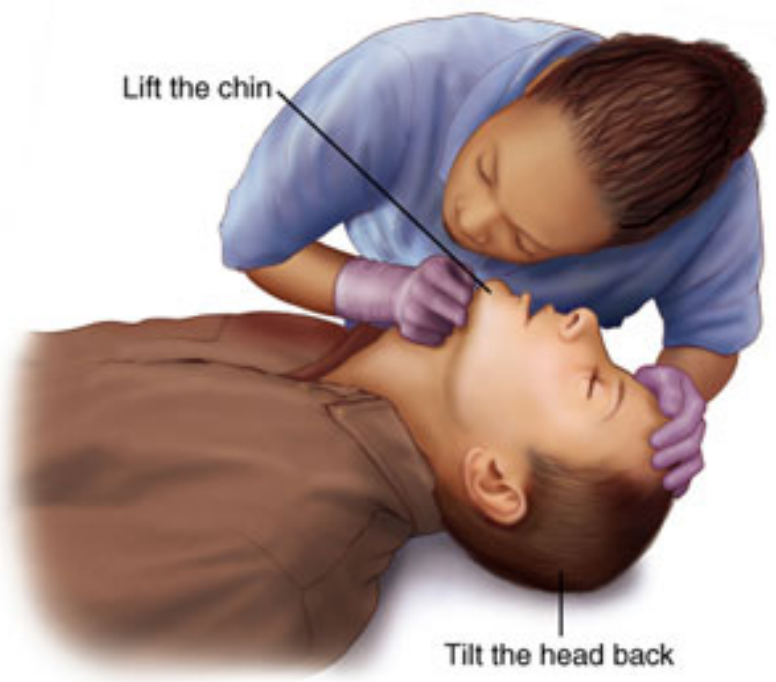
- Call 911
  - Make sure to say the patient is unresponsive and not/struggling to breathe
  - Give a clear address and location
- Administer naloxone (if available)
- Begin CPR or rescue breathing
  - CPR technique should be based on the rescuer's training level
- If alone → give CPR/rescue breaths for ~2 minutes before leaving to get naloxone or AED

https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_PatientFlyer_041416.pdf

http://stopoverdose.org/section/learn-about-overdose/

2. Emergency Response Instructions

- Rescue breathing technique
  - Make sure nothing is in the mouth, blocking their breathing
  - Place one hand on chin & tilt the head back
  - With the other hand pinch the nose closed
  - Administer **2 slow breaths** and look for the chest rising
  - Continue **1 breath every 5 seconds** until the patient starts breathing on own or help arrives



http://highered.mheducation.com/sites/dl/free/0073522007/357519/unapx_01.jpg

Knowledge Question #4

Which of the following is NOT a sign/symptom of an opioid overdose?

a) Respiratory depression
b) Large pupils
c) Unable to be awakened
d) Blue/purple fingernails or lips

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b) **Large pupils**
c) Unable to be awakened
d) Blue/purple fingernails or lips

Required Patient Education

1. ~~Recognizing signs of an overdose~~
2. ~~Emergency response instructions~~
3. **How to administer naloxone**

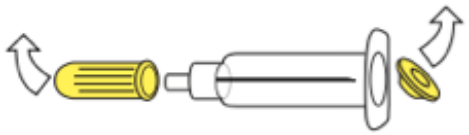
3. How to administer naloxone

- Depends on which formulation is available/on hand:

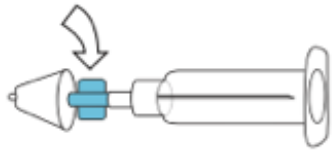
  - Nasal spray naloxone
  - NARCAN® Nasal Spray
  - Auto-injector (Evzio)
  - Injectable naloxone

Nasal spray naloxone

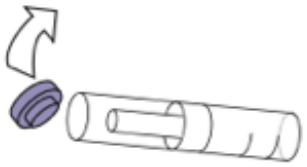
1 Take off yellow caps.



2 Screw on white cone.



3 Take purple cap off capsule of naloxone.



4 Gently screw capsule of naloxone into barrel of syringe.

5 Insert white cone into nostril; **give a short, strong push** on end of capsule to spray naloxone into nose: **ONE HALF OF THE CAPSULE INTO EACH NOSTRIL.**

Push to spray.

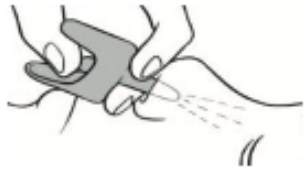
6 If no reaction in 3 minutes, give second dose.

NARCAN® Nasal Spray

1 Peel back the package to remove the device.

2 Place the tip of the nozzle in either nostril until your fingers touch the bottom of the patient's nose.

3 Press the plunger firmly to release the dose into the patient's nose.

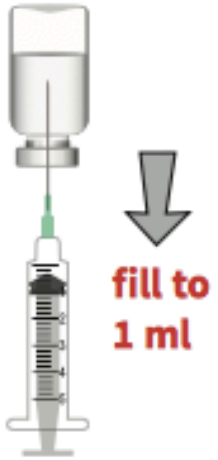


https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_PatientFlyer_041416.pdf

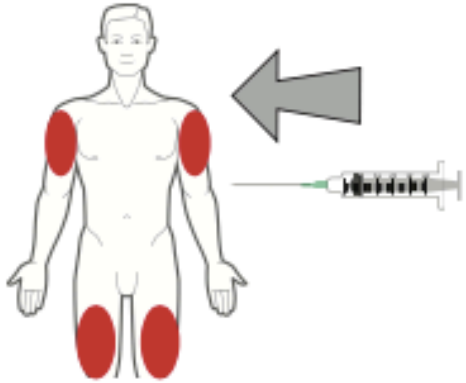
Injectable naloxone

1 Remove cap from naloxone vial and uncover the needle.

2 Insert needle through rubber plug with vial upside down. Pull back on plunger and take up 1 ml.



3 Inject 1 ml of naloxone into an upper arm or thigh muscle.



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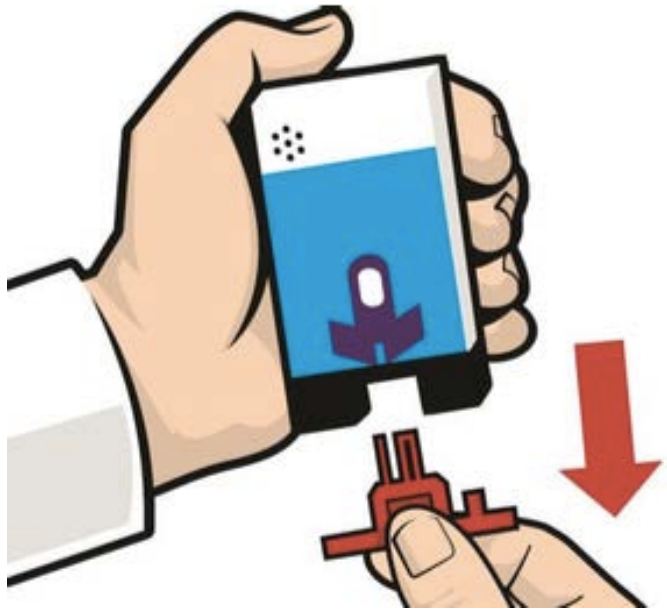
https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_PatientFlyer_041416.pdf

EVZIO Auto-Injector

- Step 1: Pull EVZIO from outer case
  - Do NOT go to Step 2 until you are ready to use EVZIO

- Step 2: Pull off the **Red** safety guard
  - Do NOT touch the **Black** base (where needle comes out)



EVZIO package insert

EVZIO Auto-Injector cont.

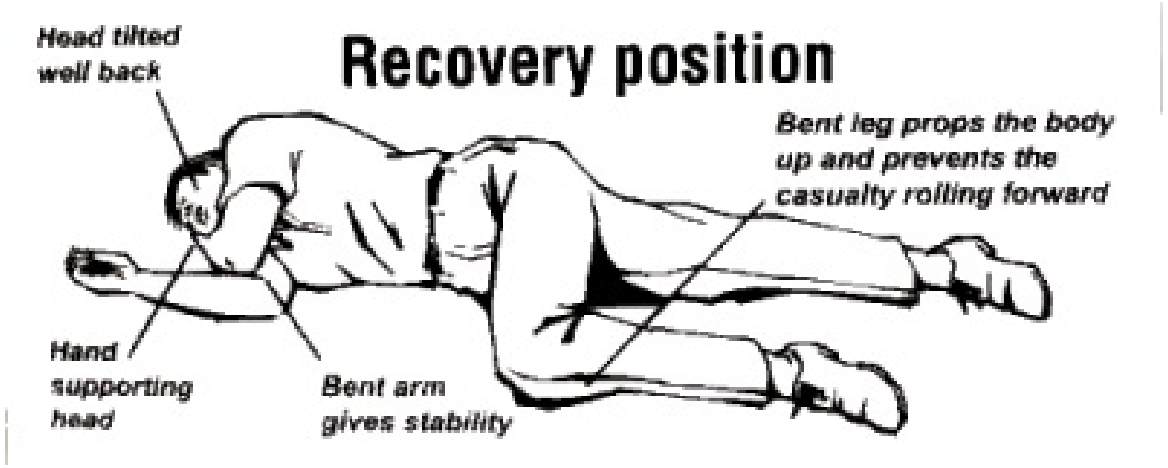
- Step 3: Place the Black end of EVZIO against outer thigh (through clothing if needed)
  - Press firmly and hold in place for 5 seconds

Required Patient Education

1. ~~Recognizing signs of an overdose~~
2. ~~Emergency response instructions~~
3. ~~How to administer naloxone~~
4. **Now what?**

4. Now what?

- Recommended to stay with patient for at least 3 hours or until help arrives
  - If they wake up and start to breathe → STAY WITH THEM!!
- If you MUST leave, put the patient into the recovery position



https://www.lhsfna.org/LHSFNA/assets/File/recovery%20position.jpg

"Opioid Safety Language"

- Remember: Naloxone ONLY works on opioids
- Term "overdose" has negative connotations
  - Study reported that patients prescribed opioids (including those at high-risk with a history of OD) rated their overdose risk as **2 out of 10**
- Consider using other terminology, such as "accidental overdose", "bad reaction", or "opioid safety"
- Other phrases:
  - "Opioids can stop or slow your breathing"
  - "Naloxone is the antidote to opioids – that is sprayed/injected if there is a bad reaction where you can't be woken up"
  - "Naloxone is for opioids as an EpiPen® is for someone with allergies"

https://www.mainemed.com/sites/default/files/content/MICIS_Naloxone_Provider_110316%2002.pdf

Knowledge Question #5

You find an unconscious patient that has slowed breathing and pinpoint pupils. You conclude that the patient is overdosing, so you give them a dose of naloxone. A few minutes later, the patient is breathing normally again and is conscious. Since the patient is acting fine, it is okay for you to leave.

True or False

Knowledge Question #5

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True or **False**


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Resource Websites

- Stopoverdose.org
- Naloxoneinfo.org
- Getnaloxonenow.org
- Naloxonesaves.org
- PrescribetoPrevent.org
- Takeasprescribed.org
- Harmreduction.org/issues/overdose-prevention/overview/overdose-basics/
- https://newsletter.samhsa.gov/2014/01/31/preventing-opioid-overdose-and-accidental-deathdata/

QUESTIONS??

kbernard1@une.edu

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