


Naloxone Education

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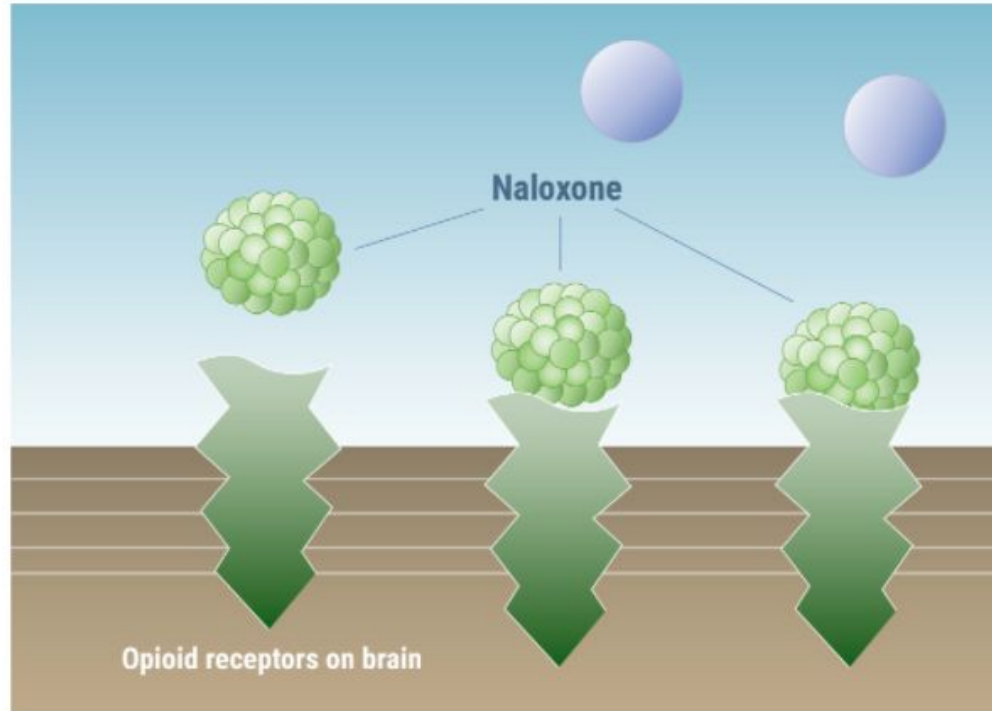
Spring 2022

Objectives

- Review available formulation of naloxone
 - Explain who should have access to naloxone
 - Identify ways to discuss options with patients
 - Provide education points for patients and family members
 - Discuss liability for administration, prescribing and dispensing of naloxone
 - Identify resources to free naloxone
 - Compare and contrast doses of naloxone
 - Determine if benefits outweigh risks when considering high dose naloxone
- 







Overview

FIGURE 4. NALOXONE MECHANISM OF ACTION⁷



Naloxone has a higher affinity to the opioid receptors than opioids like heroin or oxycodone, so it knocks other opioids off the receptors for 30-90 minutes. This reverses the overdose and allows the person to breathe.

Naloxone Product Comparison

	Injectable (and intranasal-IN) generic	Intranasal branded		Injectable generic ¹		Auto-injector branded		
Brand name		Narcan Nasal Spray				Evzio Auto-Injector		
Product comparison								
			(Product not yet released ²)			 (Formulation to be discontinued ³)		
FDA approved Labeling includes instructions for layperson use	X (for IV, IM, SC)	X	X	X	X	X	X	
Assembly required	X				X			
Strength	1 mg/mL	4 mg/0.1 mL	2mg/0.1mL	0.4 mg/mL	4 mg/10 mL	0.4 mg/0.4mL	2 mg/0.4mL	
Storage requirements (All protect from light)	Store at 59-86 °F Fragile: Glass.	Store at 59-77 °F Excursions from 39-104 °F		Store at 68-77 °F Breakable: Glass.		Store at 59-77 °F Excursions from 39-104 °F		
Cost/kit ⁴	\$\$	\$\$		\$		\$\$\$		
Prescription variation								
Refills	Two	Two		Two		Two		
Rx and quantity	#2 2 mL Luer-Jet™ Luer-Lock needleless syringe plus #2 mucosal atomizer devices (MAD-300)	#1 two-pack of two 4 mg/0.1 mL intranasal devices	#1 four-pack of four 2 mg/0.1 mL intranasal devices	#2 single-use 1 mL vials PLUS #2 3 mL syringe w/ 23-25 gauge 1-1.5 inch IM needles	#1 10mL multidose vial PLUS #2 3 mL syringe w/ 23-25 gauge 1-1.5 inch IM needles	#1 two-pack of two 0.4 mg/0.4 mL prefilled auto-injector devices	#1 two-pack of two 2 mg/0.4 mL prefilled auto-injector devices	
Sig. (for suspected opioid overdose)	Spray 1 mL (1/2 of syringe) into each nostril. Repeat after 2-3 minutes if no or minimal response.	Spray 0.1 mL into one nostril. Repeat with second device into other nostril after 2-3 minutes if no or minimal response.		Inject 1 mL in shoulder or thigh. Repeat after 2-3 minutes if no or minimal response.		Inject into outer thigh as directed by English voice-prompt system. Place black side firmly on outer thigh and depress and hold for 5 seconds. Repeat with second device in 2-3 minutes if no or minimal response.		

Who should carry Naloxone?

- Anyone who has or may come in contact with someone who may overdose
- Risk factors:
 - Current med review (benzos, high dose opioids)
 - Substance use history
 - Respiratory disorders (COPD, OSA)
 - PDMP review
 - Overdose history
 - Those who may return to a higher dose and no longer tolerant
 - Currently using illicit substances
 - Misusing prescription opioids



Is naloxone right for me?

- Negative connotation to 'overdose'
 - 'Accidental overdose'
 - 'Bad reaction'
 - 'Opioid safety'
 - 'Severe side effects'
- Frame opioids as 'risk-medications' instead of 'risky patients'
 - Prescribe for all
- Compare to chronic diseases
 - Diabetes and glucagon
 - Asthma and rescue inhalers
- Patient education resources available



What is an opioid overdose?



Opioids can cause bad reactions that make your breathing slow or even stop. This can happen if your body can't handle the opioids that you take that day.

TO AVOID AN ACCIDENTAL OPIOID OVERDOSE:

- Try not to mix your opioids with alcohol, benzodiazepines (Xanax, Ativan, Klonopin, Valium), or medicines that make you sleepy.
- Be extra careful if you miss or change doses, feel ill, or start new medications.

Now that you have naloxone...

Tell someone where it is and how to use it.

Common opioids include:

GENERIC	BRAND NAME
Hydrocodone	Vicodin, Lorcet, Lortab, Norco, Zohydro
Oxycodone	Percocet, OxyContin, Roxicodone, Percodan
Morphine	MSContin, Kadian, Embeda, Avinza
Codeine	Tylenol with Codeine, TyCo, Tylenol #3
Fentanyl	Duragesic, Actiq
Hydromorphone	Dilaudid
Oxymorphone	Opana
Meperidine	Demerol
Methadone	Dolophine, Methadose
Buprenorphine	Suboxone, Subutex, Zubsolv, Bunavail, Butrans

* Heroin is also an opioid.

For patient education, videos and additional materials, please visit www.prescribtoprevent.org



Opioid safety and how to use naloxone



A GUIDE FOR PATIENTS AND CAREGIVERS

In case of overdose:

1 Check responsiveness

Look for any of the following:

- No response even if you shake them or say their name
- Breathing slows or stops
- Lips and fingernails turn blue or gray
- Skin gets pale or clammy

2 Call 911 and give naloxone

If no reaction in 3 minutes, give second naloxone dose

3 Do rescue breathing and/or chest compressions

Follow 911 dispatcher instructions

>> STAY WITH PERSON UNTIL HELP ARRIVES.

How to give naloxone:

There are 4 common naloxone products. Follow the instructions for the type you have.

Nasal spray

This nasal spray needs no assembly and can be sprayed up one nostril by pushing the plunger.



Nasal spray with assembly

This requires assembly. Follow the instructions below.

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

Auto-injector

The naloxone auto-injector needs no assembly and can be injected into the outer thigh, even through clothing. It contains a speaker that provides step-by-step instructions.



Injectable naloxone

This requires assembly. Follow the instructions below.

- 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.
- 4 If no reaction in 3 minutes, give second dose.

Education Points

Is it safe?

- Can be given by lay persons
- Withdrawal risk
 - Higher doses may cause greater withdrawal symptoms
 - Save their life

When to administer:

- Face pale or clammy to touch
- Limp body
- Purple or blue tinge to nails/lips
- Unable to arouse
- Vomiting or gurgling noises
- Breathing or heartbeat slows/stops

Call 911!

Education Points Continued...

- Begin CPR if necessary
- Administer naloxone
 - Provide education and allow for teach-back
- Place in recovery position
- Monitor individual
 - Opioid withdrawal
 - Redose in 2-3 minutes



Prevention of Accidental Overdose

- Take as prescribed
- Never mix with alcohol, sleeping meds, etc
- Store appropriately
- Dispose of unused medication
 - DEA drug take back locator
 - FDA flush list
 - At home trash disposal

Follow these simple steps to dispose of medicines in the household trash

MIX
Mix medicines (do not crush tablets or capsules) with an **unpalatable substance** such as dirt, cat litter, or used coffee grounds;



PLACE
Place the mixture **in a container** such as a sealed plastic bag;



THROW
Throw the container **in your household trash**;



SCRATCH OUT
Scratch out **all personal information** on the prescription label of your empty pill bottle or empty medicine packaging to make it unreadable, then dispose of the container.



Good Samaritan Laws

- Covers naloxone administration

Idaho Statute 54-1733B

- Any licensed or registered health professional may prescribe and dispense naloxone to any person or organization
- Allows organizations and non-medical staff to provide naloxone to people at home

Access to Free Naloxone

- Idaho Harm Reduction Project
 - Request online
 - Postcard program
 - Contact Marjorie Wilson - idahoharmreductionproject@gmail.com
- Idaho Department of Health and Welfare
 - Request online
 - <https://healthandwelfare.idaho.gov/services-programs/behavioral-health/naloxone-information>

High Dose Naloxone - Kloxxado 8 mg NS

Table 1: Mean (CV%) Plasma Pharmacokinetic Parameters of Naloxone Following a Single Dose of Intranasal and Intramuscular/Intravenous Administration in Healthy Subjects

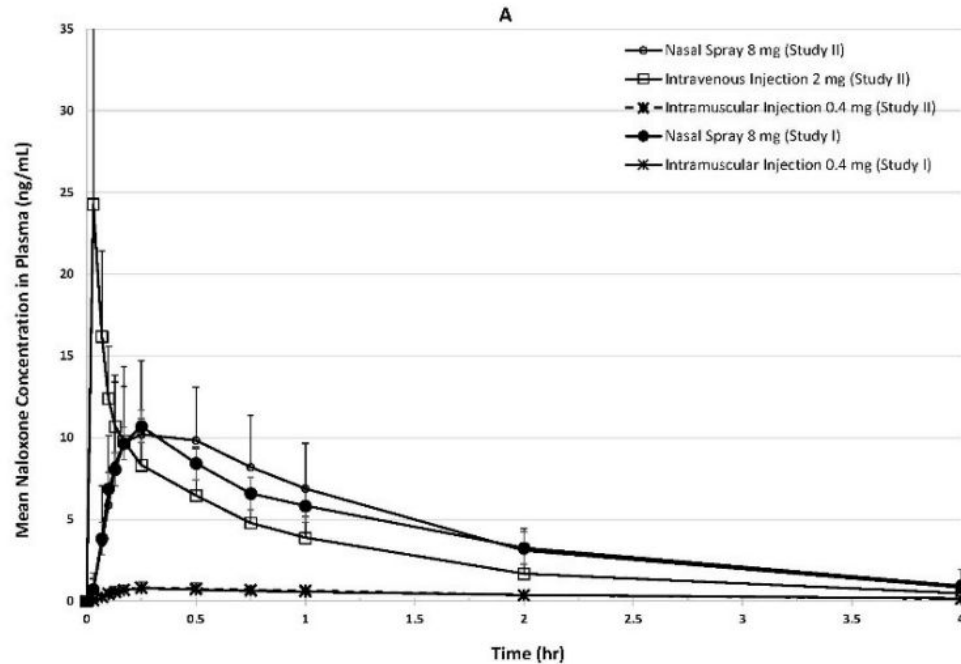
Parameter	KLOXXADO 8 mg		Intramuscular Injection 0.4 mg		Intravenous Injection 2 mg
	Study I	Study II	Study I	Study II	Study II
N	24	23 ¹	24	23 ¹	24
T _{max} (h) ²	0.25 (0.10 – 1.00)	0.25 (0.10 – 1.00)	0.25 (0.13 – 1.00)	0.25 (0.10 – 1.00)	NA
C _{max} (ng/mL)	12.3 (55.4)	12.8 (37.0)	0.876 (36.7)	0.910 (36.8)	26.2 (82.4)
AUC _{last} (ng•h/mL)	18.0 (29.6)	18.4 (33.4)	1.82 (24.0)	1.87 (24.7)	12.7 (27.6)
AUC _{0-inf} (ng•h/mL)	16.7 (31.9) ³	19.0 (32.7) ⁴	1.94 (20.9) ⁵	1.95 (21.9)	12.8 (27.5)
t _{1/2} (h)	2.69 (69.9)	1.76 (39.7) ⁴	1.41 (20.0) ⁵	1.40 (38.9)	1.22 (16.4)
Dose normalized Relative BA (%) vs IM Injection	41.6	47.4	100	100	NA
Dose normalized Absolute BA (%) vs IV Injection	NA	36.6	NA	77.2	100

NA= Not applicable

1. N=23 due to one subject withdrawal.
2. T_{max} reported as median (minimum – maximum).
3. N=15
4. N=19
5. N=22 for AUC_{0-inf} and t_{1/2}
6. C_{max} of Intravenous Injection 2 mg was observed value from the first sampling time of 2 minutes post-dose.

High Dose Naloxone - Kloxxado 8 mg NS

Figure 1: Mean \pm SD Plasma Concentration-Time Profiles of Naloxone Following A Single Dose of Intranasal versus Intramuscular/Intravenous Administration in Healthy Subjects. (A:0-4 h and B: 0-30 min.)



Narcan 4 mg NS

Table 1 Mean Pharmacokinetic Parameters (CV%) for Naloxone Following NARCAN (Naloxone HCl) Nasal Spray and Intramuscular Injection of Naloxone HCl to Healthy Subjects

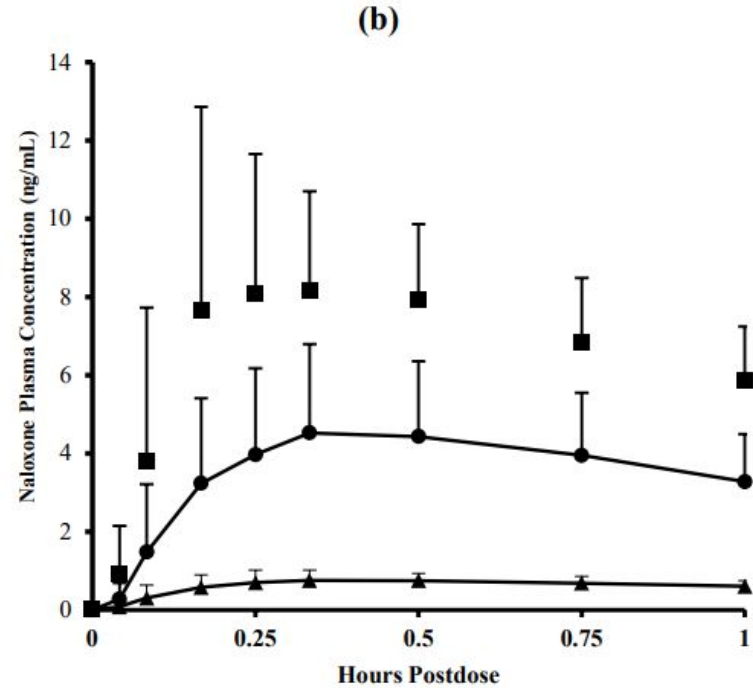
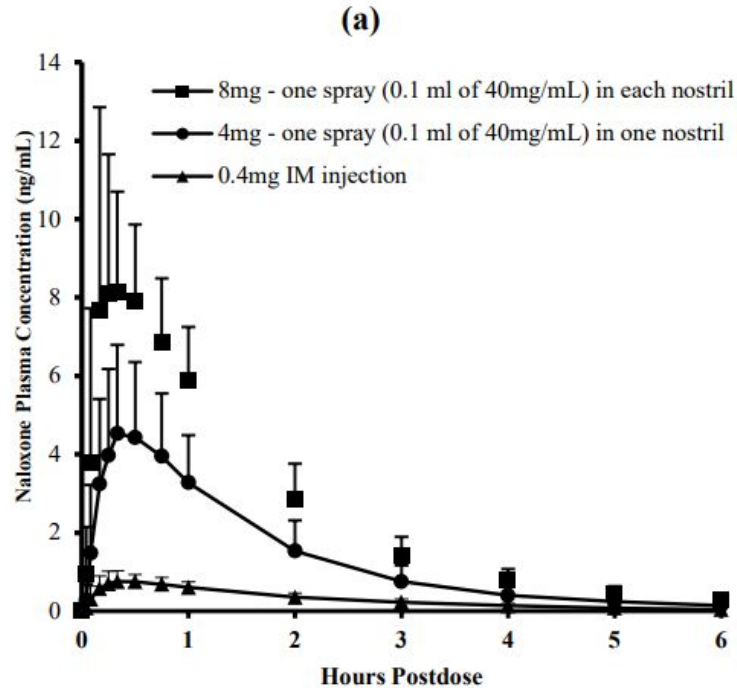
Parameter	4 mg – One Nasal Spray in one nostril	8 mg – Two Nasal Sprays, one in each nostril	0.4 mg Intramuscular Injection
	(N=29)	(N=29)	(N=29)
t_{max} (h) [†]	0.50 (0.17, 1.00)	0.33 (0.17, 1.00)	0.38 (0.08, 2.05)
C_{max} (ng/mL)	4.83 (43.1)	9.70 (36.0)	0.88 (30.5)
AUC _t (hr.ng/mL)	7.87 (37.4)	15.3 (23.0)	1.72 (22.9)
AUC _{0-inf} (h*ng/mL)	7.95 (37.3)	15.5 (22.7)	1.76 (22.6)
$t_{1/2}$ (h)	2.08 (29.5)	2.10 (32.4)	1.24 (25.9)
Dose normalized Relative BA (%) vs. IM	46.7 (31.4) ^{††}	43.9 (23.8)	100

[†] t_{max} reported as median (minimum, maximum)

^{††} N=28 for Relative BA.

Narcan 4 mg NS

Figure 1 Mean \pm SD Plasma Concentration of Naloxone, (a) 0-6 h and (b) 0-1h Following Intranasal Administration and Intramuscular Injection



Risks

- Both have similar risks
 - Redosing may be required
 - Precipitate opioid withdrawal
 - Partial agonists or mixed agonists/antagonist issues
 - CV effects



Is high dose naloxone worth it?

- Difficult to conclude without direct comparisons
- But... Kloxxado may be beneficial in these situations:
 - Patients with access to illicit substances
 - Potentially laced with fentanyl
 - Methadone users
 - Rural communities
- Though greater risk of opioid withdrawal with higher doses
 - Alternative may be death





Questions?

Resources

US Department of HHS

- Office of the Surgeon General Advisory on Naloxone and Opioid Overdose.
<https://www.hhs.gov/surgeongeneral/priorities/opioids-and-addiction/naloxone-advisory/index.html>

SAMHSA

- <https://www.samhsa.gov/medication-assisted-treatment/medications-counseling-related-conditions/naloxone>

National Institute on Drug Abuse

- <https://nida.nih.gov/publications/drugfacts/naloxone>

San Francisco Department of public health

- [CA.Detailing Provider Education final.pdf](#)

California State Board of Pharmacy

- https://www.pharmacy.ca.gov/licensees/naloxone_info.shtml

FDA Package inserts Kloxxado and Narcan

Medscape - Opioid Toxicity Medication Article

- <https://emedicine.medscape.com/article/815784-medication#:~:text=Higher%20doses%20may%20be%20necessary,12%20h%20vs%201%20h>.

Idaho Department of Health and Welfare

- <https://healthandwelfare.idaho.gov/services-programs/behavioral-health/overdose-response>

Idaho Legislature - Idaho Statutes Title 5, Chapter 3

- <https://legislature.idaho.gov/statutesrules/idstat/title5/t5ch3/sect5-330/>

NIH

- Naloxone dosage for opioid reversal: current evidence and clinical implications. Therapeutic Advances in Drug Safety. 2018 Jan; 9(1):63-88. Published online 2017 December 13. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5753997/>. Accessed 3/27/22