# Drug Overdose Epidemic and Naloxone as a Rescue Agent for Overdose

#### Cathy Poirier, BS, PharmD, MBA



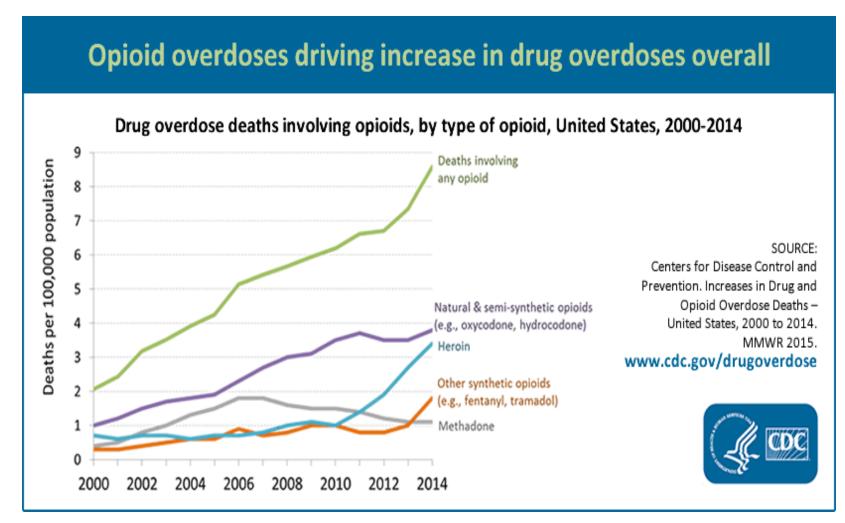




2015: Drug overdoses = 52,000+ U.S. deaths, with 33,000+ deaths (63.1%) involved an opioid.

Rudd, RA, Seth, P, David, F, Scholl, L. Increases in drug and opioid-involved overdose deaths—United States, 2010-2015.*MMWR* 2016;65(50-51)1445-1452.

#### **Drug Overdose Epidemic**







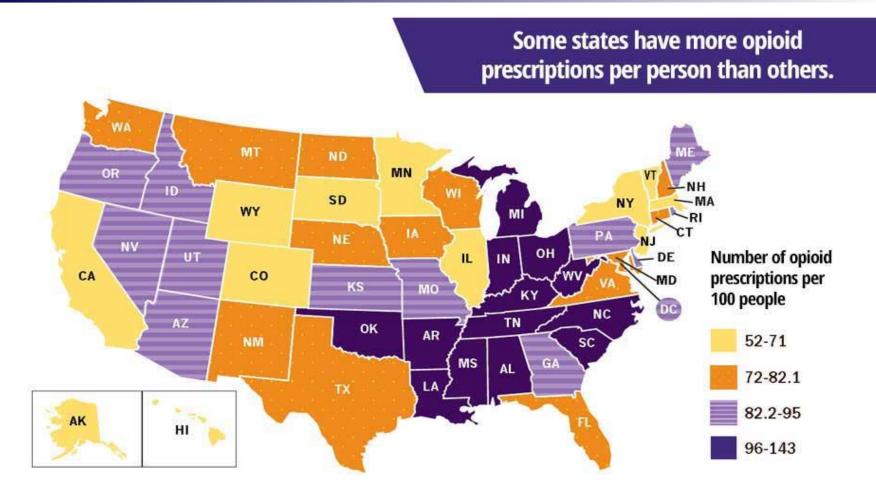
• From 2014 to 2015: Death rate from synthetic opioids other than methadone, but including fentanyl increased by 72.2%.

• Same time period: Heroin death rate increased by 20.6%.

 Significant increases in OD death rates primarily seen in the Northeast and South Census Regions (including Michigan)

### **Michigan's Opioid Epidemic**





SOURCE: IMS, National Prescription Audit (NPA™), 2012.

https://www.cdc.gov/drugoverdose/data/statedeaths.html.





- November 2016 DEA report: Prescription drugs, heroin, and fentanyl are the most significant drugrelated threats to the U.S.
- Methadone death rates decreased by 9.1%.

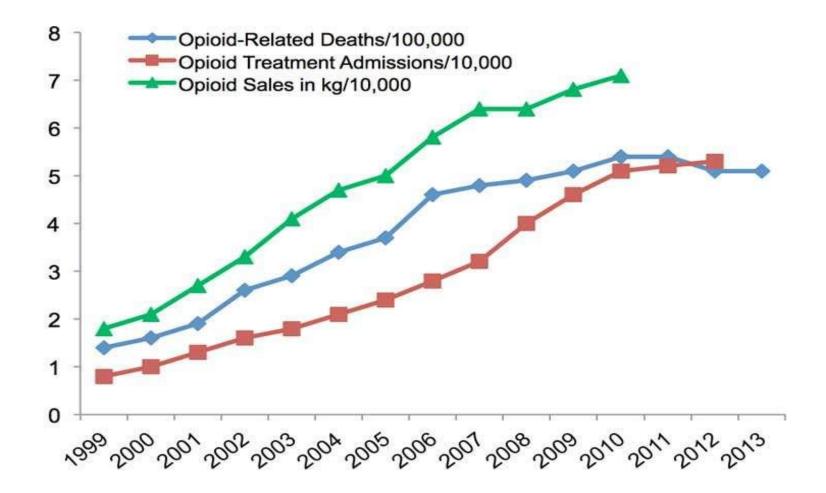
 Overdose death rates are highest among people aged 25 to 54 years old. Also higher among non-Hispanic whites & American Indian or Alaskan Natives (compared to non-Hispanic blacks & Hispanics).



- No change in the amount of pain Americans report (chronic non-cancer adults = 33%) over the past 15+ years, yet sales of rx opioids = nearly 4 x from 1999 to 2014 (see graph).
- 20% of patient with pain are prescribed rx opioids from physicians' offices.
- YET: NO evidence through studies that opioids help with chronic pain, daily functioning, and quality of life.

#### **Opioid Sales, Deaths, Admissions**





National Institute on Drug Abuse, CDC Wonder, 2015; DEA ARCOS, 2015; TEDS, 2015

#### Who Prescribes the Opioid Prescriptions?

Primary Care Providers	OVERALL = nearly 50%
Pain medicine	49%
Surgery	37%
Physical medicine/rehab	36%

MICHIGAN MEDICINE UNIVERSITY OF MICHIGAN

>100% total due to physicians having overlapping specialties.

Daubresse, M, et al. Ambulatory diagnosis and treatment of nonmalignant pain in the United States, 2000-2010. *Medical Care* 2013;51(10):870-878.

# Drug Abuse Warning Network (DAWN)

Each day, more than

1,000

PEOPLE



#### are treated in emergency departments for not using prescription opioids as directed.



The DAWN Report. Highlights of the 2011 Drug Abuse Warning Network (DAWN) findings on drug-related emergency department Visits. 2013.





 Definition: Use of rx opioids <u>"nonmedically"</u>200 or more days a year.

Their own prescriptions	27%
Friends or relatives (free)	26%
Friends or relatives (bought)	23%
Drug dealer	15%

Daubresse, M, et al. Ambulatory diagnosis and treatment of nonmalignant pain in the United States, 2000-2010. *Medical Care* 2013;51(10):870-878.



• 2014: Almost 2 million Americans abused/were dependent on Rx opioids.

• 25% of people who receive Rx opioids for chronic pain from their PCP's struggle with addiction.

• PCP's account for nearly 50% of Rx opioids being dispensed.



- Opioids should NOT be used for first-line or continuous treatment for chronic pain (pain > 3 months past the time of "normal" tissue healing or continuous long-term pain.
- Holding opioid dosages to < 50 oral morphine equivalents per day would MOST LIKELY (professional opinion) reduce the risk of a large percentage of patients who would suffer a fatal OD at higher prescribed dosages of opioids.



- Providers should <u>ALWAYS</u> use caution when prescribing opioids and <u>MONITOR</u> all their patients closely.
- Patients should review forms of pain management that do NOT include the use of opioids, such as the following:
- -Physical exercise
- -Non-opioids medications (APAP, NSAIDS, gabapentin/pregabalin, tri-cyclics, etc.)
- -Physical therapy -Cognitive behavioral therapy (CBT)



# **US Opioid Epidemic**

- Opioid dose titration to pain intensity is the <u>WRONG</u> approach to treating chronic pain!
- Chronic pain treatment experts believe it contributed to our current opioid epidemic.

 <u>Why?</u> Most providers lack sufficient education for managing their patients in pain. Managing intensity = increase in prescriptions for pain medications! Which one of the following risk factors plays a part in the development of an opioid use disorder in patients who take prescribed opioids for legitimate pain complaints?

- a) Younger age
- b) The use of psychotropic medications (anti-psychotics, anti-anxiety agents, etc.)
- c) Major depression
- d) Past history of substance abuse
- e) All of the above



Which one of the following risk factors plays a part in the development of an opioid use disorder in patients who take prescribed opioids for legitimate pain complaints?

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- c) Major depression
- d) Past history of substance abuse
- e) All of the above





- States with law suits against Purdue Pharma and other opioid pain manufacturers:
- > Kentucky
- > New York
- > Washington
- ➤ West Virginia
- 2007: Federal Court in Virginia; pled guilty and paid \$600 million in fees and fines.



- County in WV is also suing 10 wholesale drug distributors.
- Involved are Walgreen's, Walmart, CVS, and Rite Aid.
- WV has the highest rate of fatal opioid overdoses in the country: <u>41.5 deaths per</u> <u>100,000 residents.</u>

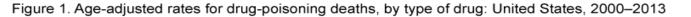
### **Onward: Heroin Use/Abuse**

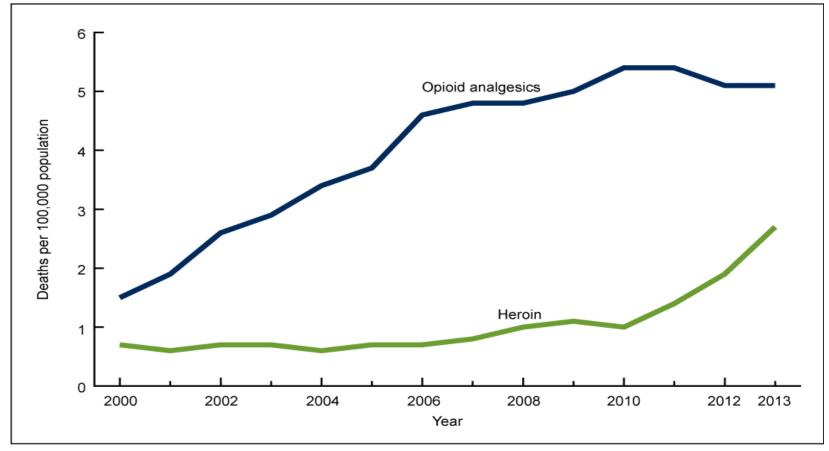


- Heroin is pharmacologically similar to the prescription opioids. "Burst" of dopamine in the reward area of the brain + the subjective "high" from the abused drug.
- Its use has more than doubled during the past 10 years for adults aged 18-25 years old.
- Heroin-related OD deaths have increased 4x since 2010.
  2014-2015: Increased by 20.6% with ~13,000 dead in 2015.

#### **Increased death rates**







NOTES: The number of drug-poisoning deaths in 2013 was 43,982, the number of drug-poisoning deaths involving opioid analgesics was 16,235, and the number of drug-poisoning deaths involving heroin was 8,257. A small subset of 1,342 deaths involved both opioid analgesics and heroin. Deaths involving both opioid analgesics and heroin are included in both the rate of deaths involving opioid analgesics and the rate of deaths involving heroin. Access data table for Figure 1 at: http://www.cdc.gov/nchs/data/databriefs/db190\_table.pdf#1.

SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

### **Risk Factors for Heroin Use**



- Strongest risk factor: Past misuse of rx opioids.
- >90% of people using heroin have used at least 1 other drug.
- New heroin users: 75% have abused rx opioids prior to using heroin.
- Increased availability.
- Relatively low price (compared to rx opioids)
- High purity of U.S. heroin

### Why the Increase in Heroin Use in the US?

• The shift toward heroin use from rx opioid abusers occurred BEFORE increased prescribing restrictions started in various states in the US (NY and FL).

• Rates of heroin abuse continued AFTER the abusedeterrent formulation of Oxycontin® was released.

 Accessibility, reduced price, & high purity = major drivers in increased rates of heroin use.





- a) Increasing restrictions in various states on the prescribing of opioid analgesics
- b) Changing drug formulations (i.e. Oxycontin<sup>®</sup>) so they are not able to be manipulated into another form, such as for injection
- c) Increasing law enforcement strategies to reduce the illicit opioid supply
- d) Growing supply of heroin and illegal counterfeit opioid tablets from countries such as Mexico



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# **Elephant Tranquilizer**

- <u>Carfentanil:</u> Synthesized in 1974, brand name Wildnil® used as a general anesthetic for large animals like elephants.
- 10,000x more potent than morphine. 100x more potent than fentanyl.
- Dose the size of 2, yes 2, salt grains can kill.
- EMT personnel have to double glove and not touch any bodily fluids on a downed patient, including sweat!

#### Carfentanil



- March 11, 2017: DEA has found the drug in a number of states: "Florida, Georgia, Rhode Island, Indiana, Pennsylvania, Kentucky, West Virginia, New Jersey and Illinois."
- Arrives by U.S. Postal Service from a lab in China!
- China has banned sales of carfentanil per the request from the U.S. government.



• March 2016: CDC Guideline for Prescribing Opioids for Chronic Pain recommendations

- Improve access to and use of prescription drug monitoring programs.
- Expand naloxone distribution
- Enhance opioid use disorder treatment capacity and access to treatment



- Implement harm reduction approaches (i.e. syringe services programs, supervised injection sites)
- Law enforcement strategies to reduce illicit opioid supply.



- Huntington, WV, population 49,000---25% or 1 of 4 adults are dependent on opioids!
- August 15, 2016: 28 phone calls to 911 in 5 hours! 2 of them died. Many who survived received NO treatment other than the naloxone to revive them.
- WV: ~150,000 residents, approximately 8% needed substance abuse tx in 2016. Guess what? Only 156 detox beds in the state!



# **Key Takeaway Points**

- More than 40 people from the United States die every day from prescription opioid overdoses.
- Heroin deaths have been on a steep rise since 2010.
- Michigan has one of the greatest number of opioid prescriptions per 100 people compared to other US states.
- 2016 CDC Chronic Pain Treatment Guidelines: "Big" step to try to educate clinicians, give guidance on opioid use, and discuss the benefits and risks of opioid use for both providers and patients.



# **Key Takeaway Points**

- 25% of people who receive Rx opioids for chronic pain from their PCP's struggle with addiction.
- The states hardest hit with opioid overdoses and deaths (many \$\$\$ costs for the states) are suing drug manufacturers and distributors of the opioid medications, especially Oxycontin®.
- Duty to our patients = <u>improve quality of life</u>.
  NOT ALL chronic pain patients NEED opioids to deal with their pain!

# Naloxone/November 2014



#### Naloxone Could Prevent More Than 20,000 U.S. Overdose Deaths, WHO Says

Reuters

Posted: 11/04/2014 8:57 am EST | Updated: 01/04/2015 5:59 am EST





Heroin Overdose: The Case For Take-Home Naloxone: Home Based Supplies Of Naloxone Would Save Lives Author(s): John Strang, Shane Darke, Wayne Hall, Michael Farrell and Robert Ali Source: *BMJ: British Medical Journal*, Vol. 312, No. 7044 (Jun. 8, 1996), pp. 1435-1436 Published by: BMJ Stable URL: http://www.jstor.org/stable/29731877 Accessed: 03-10-2016 15:33 UTC

#### REFERENCES

Linked references are available on JSTOR for this article: http://www.jstor.org/stable/29731877?seq=1&cid=pdf-reference#references\_tab\_contents You may need to log in to JSTOR to access the linked references.



# Does Naloxone Distribution Save \$



#### Annals of Internal Medicine

ORIGINAL RESEARCH

#### Cost-Effectiveness of Distributing Naloxone to Heroin Users for Lay Overdose Reversal

Phillip O. Coffin, MD, and Sean D. Sollivan, PhD

Background: Opicid overdose is a leading cause of accidental death in the United States.

Objective: To estimate the cost-effectiveness of distributing nalosone, an opioid antagonist, to heroin users for use at witnessed overdoses. Desults of Constitution Analysis

Design: Integrated Markov terministic and probabilisti overdoses and a secondary cost to society.

Data Sources: Published III

Target Pupulation: Hypol user and more experienced

Time Horizon: Lifetzme. Pempective: Societal. **Results of Sensitivity Analysis:** Naloxone distribution was costeffective in all deterministic and probabilistic sensitivity and scenario analyses, and it was cost-saving if it resulted in fewer overdoses or emergency medical service activations. In a "worst-case scenario" where overdose was rarely witnessed and naloxone was rarely used, minimally effective, and expensive, the ICER was \$14 000. If national drug-related expenditures were applied to heroin users, the ICER was \$2429.

death was prevented for every 227 nalosone kits distributed (95% Cl, 71 to 716). Nalosone distribution increased costs by \$53 (Cl, \$3 to \$156) and quality-adjusted life-years by 0.119 (Cl, 0.017 to 0.378) for an ICER of \$438 (Cl, \$48 to \$1706).

Nalowone distribution was costrobabilistic sensitivity and scenario f it resulted in fewer overdoses or flors. In a "wont-case scenario" resed and naloxone was rarely pensive, the ICER was \$14 000. If s were applied to heroin users, the

ntrolled data resulted in wide CIs

n to heroin users is likely to reduce tive, even under markedly conser-

Intervention: Neloxone distribution for lay administration.

Outcome Measures: Overdose deaths prevented and incremental cost-effectiveness ratio (ICER).

Results of Base-Case Analysis: In the probabilistic analysis, 6% of overdose deaths were prevented with naloxone distribution; 1 Primary Funding Source: National Institute of Allergy and Infectious Diseases.

Ann intern Aled. 2013;158:1-9. For author affiliators, see end of test.

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ww.unah.org

#### Cost-effectiveness of Distributing Naloxone to <u>Heroin Users for Overdose Reversal</u>



 One heroin overdose death prevented for every 164 kits distributed

- Cost for naloxone distribution would range between:
  - \$438-\$14,000 (best-worst case scenario) for every quality-adjusted life year gained



- Generally accepted cost-savings threshold is \$50,000/year.
  - For dialysis: recently calculated as \$129,000
  - For primary care-based Screening, Brief Intervention, and Referral to Treatment (SBIRT): recently calculated as \$6960



 Best case model assumes baseline survival rate for an OD is 90% without calling 911 or naloxone. ~10% of overdoses are fatal.

 Seeking help from calling 911 or giving naloxone increases survival rate to 98%. 2% are still fatal after calling 911 and/or giving naloxone.

## San Francisco Naloxone Prescribing in Primary Care Clinics

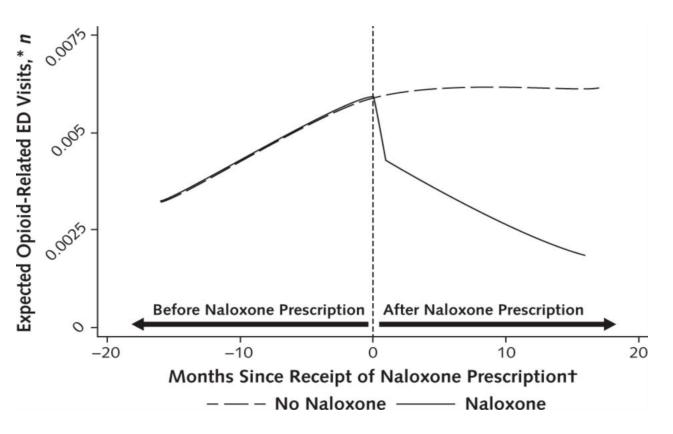


- 2 year study with 6 primary care clinics (2013-2014)
- 1985 adults, number prescribed naloxone, ED visits, and opioids prescribed
- 38% received naloxone
  - Highest in patients with higher doses and more ED visits
- No change in prescribing of increased doses of opioids
- Oxycodone was the most common
- Older patients had a lower odds of getting naloxone prescriptions



### Impact of Naloxone Prescriptions on ED Visits



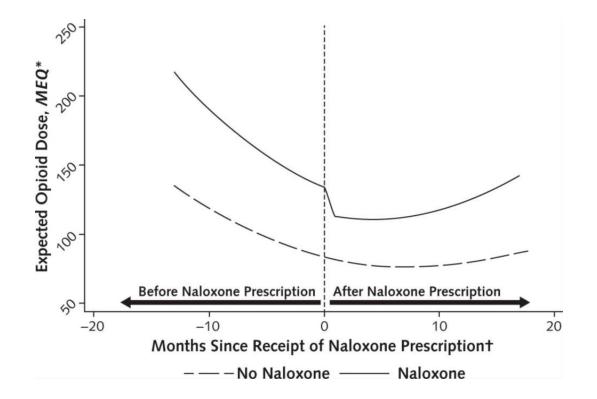


Expected number of opioid-related ED visits per month, by receipt of naloxone prescription. ED = emergency department

Ann Intern Med. 2016;165(4):245-252. doi:10.7326/M15-2771



### From: Nonrandomized Intervention Study of Naloxone Coprescription for Primary Care Patients Receiving Long-Term Opioid Therapy for Pain



Expected opioid dose, by receipt of naloxone prescription. MEQ = morphine equivalent

# Naloxone Basics 101



- MOA: Competitively displaces opioids from receptors
- Half-life: ~ 30 min-1 hour
- Complete, temporary reversal of opioid overdose effects
- May cause acute and severe opioid withdrawal
- Inactivated by first pass metabolism

(95% inactivated, so NO oral route of administration).





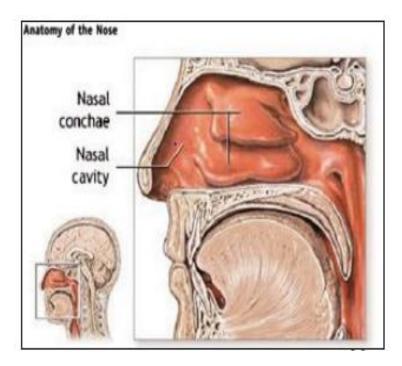
Advantages	Limitations
High absorption for lipophilic drugs with MW<1 kDa Woidance of gastrointestinal and hepatic first-pass effect	Poor permeability for hydrophilic drugs or drugs with MW > 1 kDa (peptides, proteins) Absorption time limited by mucociliary clearance
asma profile similar to the intravenous route: fast onset of action	Low absorption surface in comparison to intestinal mucosa
ase of administration, non-invasive: self-medication	Enzymatic activity of the nasal mucosa, especially with proteins- and peptides-degrading enzymes
ase of use in patients with nausea and vomiting	Variability in the absorption in case of chronic alterations of the nasal mucosa or with simultaneous administration of vasoconstrictive drugs
Cheap drug delivery devices	Local intolerance towards nasal mucosa

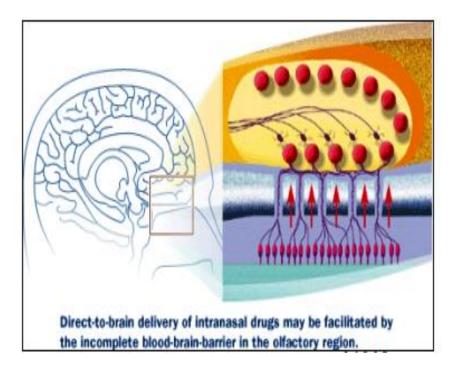
Grassin-Delyle S. Pharmacol Therap. 134; 2012



### **Nasal Physiology**

### **Absorption Pathways**



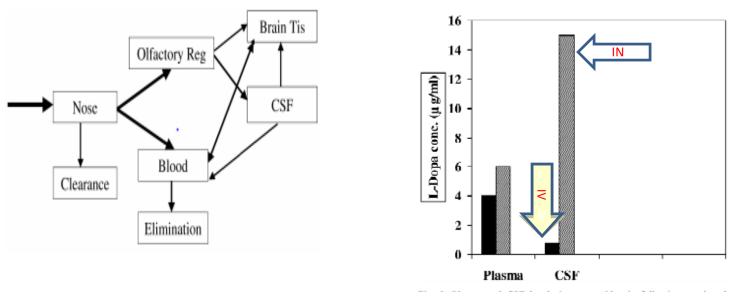


Chhajed S. Int J Pharm Sci Res. 6; 2012



### **Nose to Brain Transport**

### **Plasma vs CSF Concentrations**



Illum L. Eur J Pharm Sci. 11; 2000

# **Ideal Drug Characteristics**



- The more lipophilic the better
- Smaller is better (particle size < 1,000 daltons)
- Volume is important---too much volume increases the amount of drug swallowed & not absorbed!

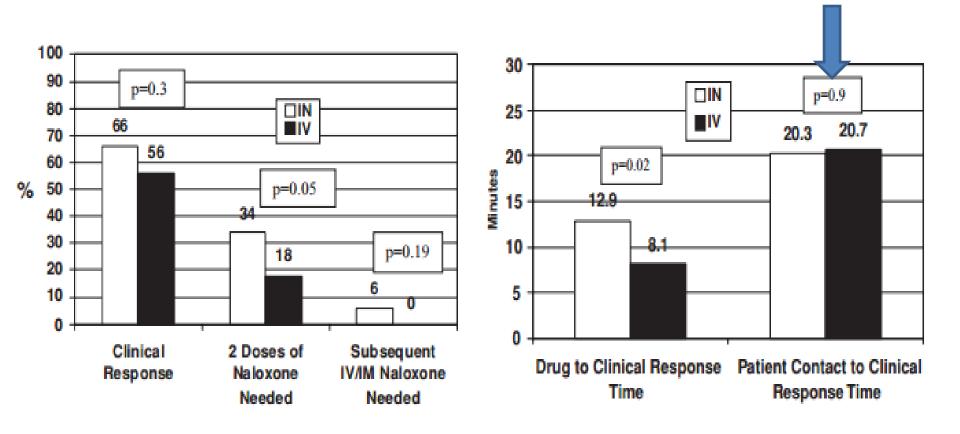




- Increase nasal residual time by applying drug to anterior part of nasal cavity OR add polymer to increase viscosity with mucus.
- Enhance nasal absorption...propylene glycol to increase cell membrane permeability & lipophilicity.
- Modify drug to change the physiochemical properties--change molecular size, solubility, microspheres, or form a salt or ester of the drug.

# Time and Number of Doses

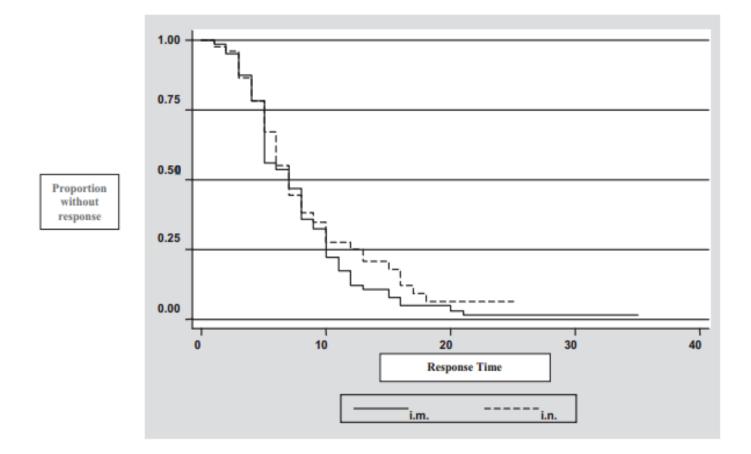




Robertson TM. Prehospital Emergency Care 13; 2009

### IN vs IM Naloxone Response Time





#### Intranasal = dashed line

Kerr D. Addiction. 104;2009

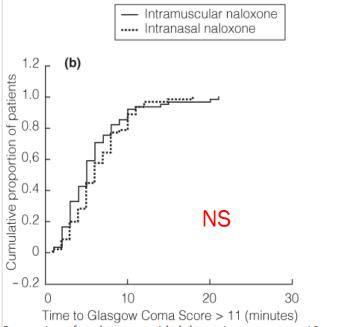
### Route of Administration Comparison



### **Level of Consciousness**

Level of consciousness	Before nalox- one	After nalox- one
Intranasal administration, n (%)		
Coma	12 (24)	0
Stupor	24 (48)	0
Obtundation	14 (28)	0
Lethargic	0	28 (56)
Conscious	0	22 (44)
Intravenous administration, n (%):		
Coma	10 (20)	0
Stupor	28 (56)	0
Obtundation	12 (24)	20 (40)
Lethargic	0	18 (36)
Conscious	0	12 (24)

### **Response Comparison**



Proportion of each group with (a) respiratory rate > 10 per minute, and (b) with Glasgow Coma Scale score > 11 per minute.

Sabzghabee AM Arch Med Sci. 10;2014 Kelly A MJA. 182;2005

## Naloxone Formulations Available



Product	Route of Adminis-tration	Available Strengths	Dosing	Advantage	Price per Dose* (7/2015)	FDA Status
Nasal Spray	IN	4mg	4mg	No training required Easy to use No assembly Tier 2 insurance copay No needles	Varies Least expense for EMS Sold as 2 Pack \$65	Yes
Auto-injector	ΙΜ	0.4mg/ml	0.4mg	No training required Easy to use No assembly Decreased risk of needle stick	\$345	Yes
Multi-use Vial	IM, IV, SC	0.4mg/ml	0.4mg	Multiple doses	\$11.84	Yes
Single Dose Vial	IM, IV, SC	0.4mg/ml	0.4mg	Individual dose	\$18.99	Yes
Prefilled Syringe	Intranasal	1mg/ml	1mg	Easy to use Decreased risk of needle stick	\$19.80	Yes







### The NEW ENGLAND JOURNAL of MEDICINE

# Perspective

### The Rising Price of Naloxone — Risks to Efforts to Stem Overdose Deaths

Ravi Gupta, B.S., Nilay D. Shah, Ph.D., and Joseph S. Ross, M.D., M.H.S.

## The Latest Price



aloxone Product	_		
	Manufacturer	Previous Available Price (yr)	Current Price (2016)
njectable or intranasal, 1 mg-per-milliliter vial (2 ml) (mucosal atomizer device separate)	Amphastar	\$20.34 (2009)	\$39.60
njectable			
0.4 mg-per-milliliter vial (10 ml)	Hospira	\$62.29 (2012)	\$142.49
0.4 mg-per-milliliter vial (1 ml)	Mylan	\$23.72 (2014)	\$23.72
0.4 mg-per-milliliter vial (1 ml)	West-Ward	\$20.40 (2015)	\$20.40
Auto-injector, two-pack of single-use prefilled auto- injectors (Evzio)	Kaleo (approved 2014)	\$690.00 (2014)	\$4,500.00
Nasal spray, two-pack of single-use intranasal devices (Narcan)	Adapt (approved 2015)	\$150.00 (2015)	\$150.00



PHAEMA & NEALTHEARE 4/03/2014 @ 4:05PM 5,094 views

## FDA Rapidly Approves Naloxone Auto-Injector For Heroin And Prescription Opioid Overdose



### Narcan® Nasal Spray by Adapt Pharma





NARCAN<sup>®</sup> (naloxone HCl) Nasal Spray is the first and only FDAapproved nasal form of naloxone for the emergency treatment of a **known or suspected opioid overdose**.

## **Intranasal Naloxone Instruction Sheets**



#### How to identify an opioid overdose:

#### Look for these common signs:

- The person won't wake up even if you shake them or say their name
- Breathing slows or even stops
- Lips and fingernails turn blue or gray
- Skin gets pale, clammy

#### In case of overdose:

 Call 911 and give naloxone If no reaction in 3 minutes, give second naloxone dose
 Do rescue breathing or chest compressions

Follow 911 dispatcher instructions

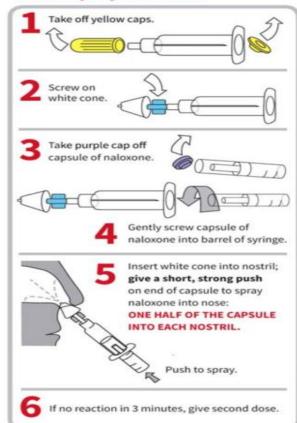
3 After naloxone

Stay with person for at least 3 hours or until help arrives

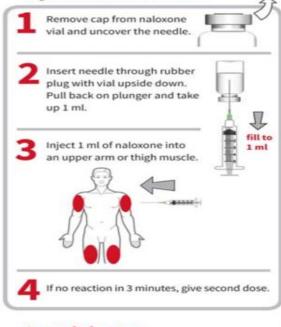
#### How to give naloxone:

There are 3 ways to give naloxone. Follow the instructions for the type you have.

#### Nasal spray naloxone



#### Injectable naloxone



#### Auto-injector

The naloxone auto-injector is FDA approved for use by anyone in the community. It contains a speaker that provides instructions to inject naloxone into the outer thigh, through clothing if needed.

Coffin PO.Ann Intern Med. 2016;165(4):245-252. doi:10.7326/M15-2771



- Price increase over 1000%
- Shortages of nasal sponges
- Evzio Autoinjector

What's

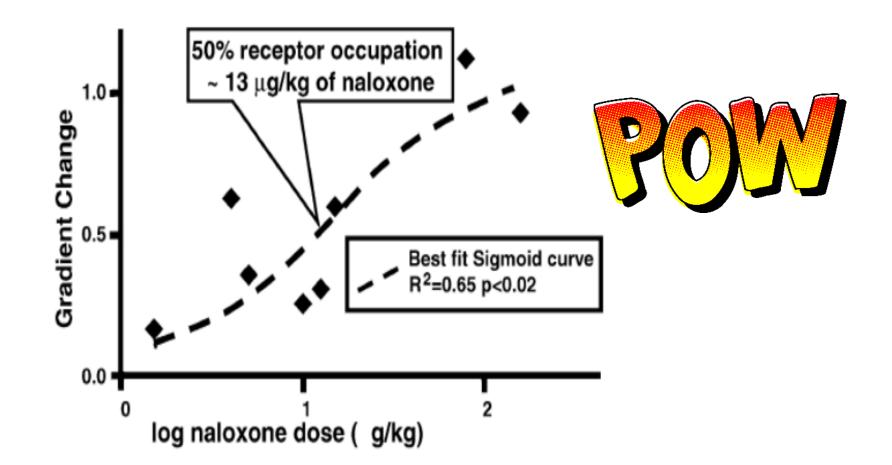
- Nov. 2015 = \$375
- Feb. 2016 = \$1875
- Sept. 2016 = \$2250
- Hospira Naloxone vials
  - \$0.92 to \$21.90
- Adapt Nasal Spray (Nov. 2015)
  - \$63 (discount for EMS and LE agencies)

•new

- Kit comes with 2 doses. Tier 2 copay.



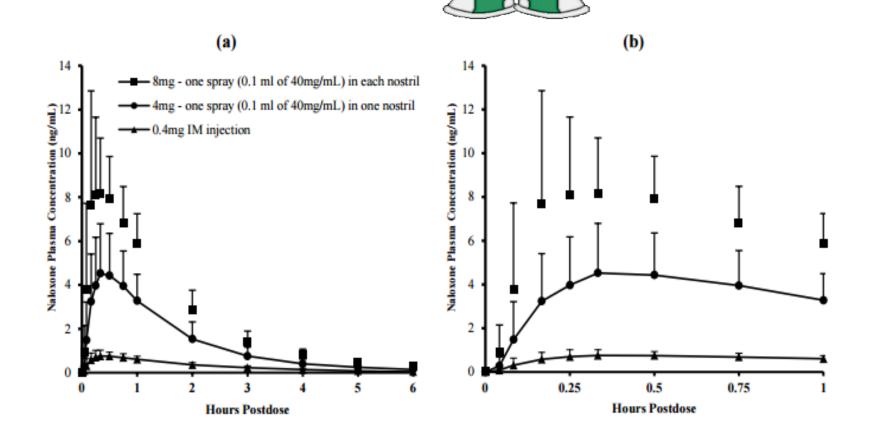




### Why a 4 mg Dose?

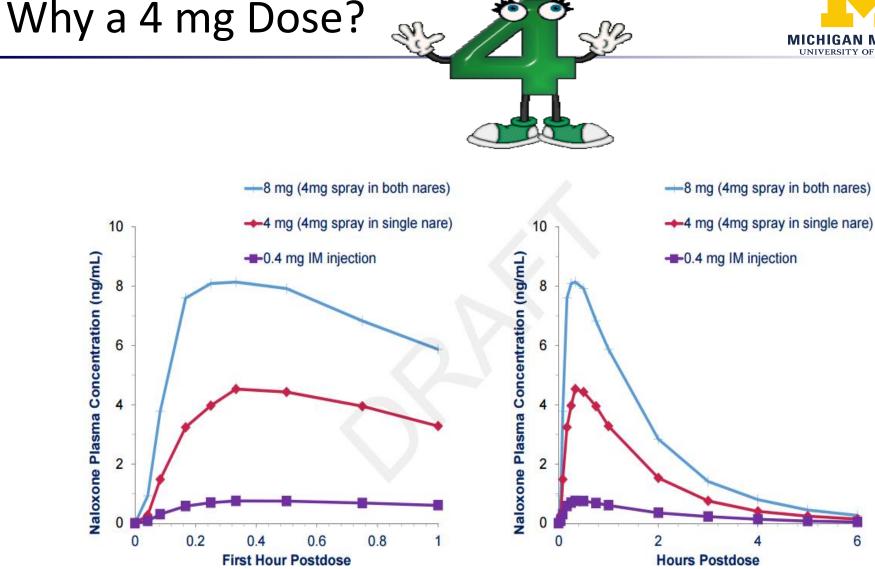






http://www.accessdata.fda.gov/drugsatfda\_docs/label/2015/208411lbl.pdf

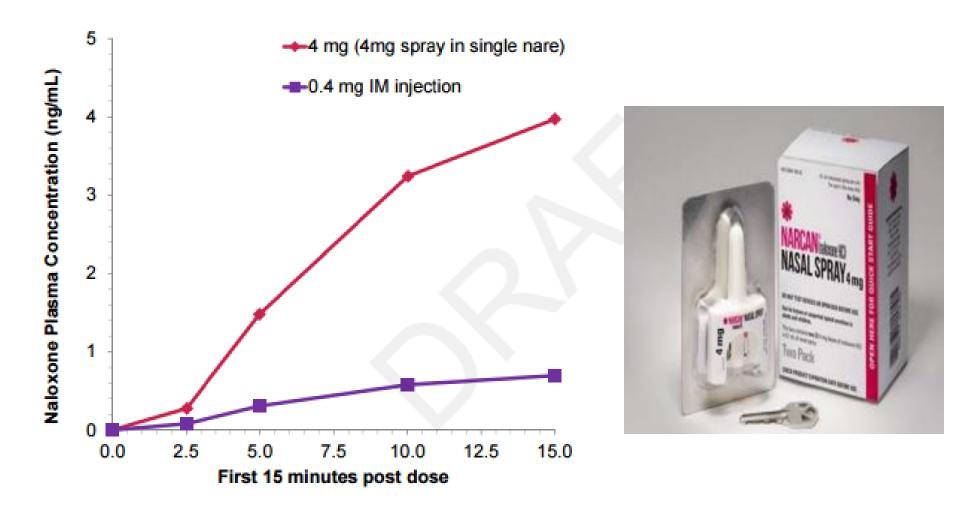




http://www.accessdata.fda.gov/drugsatfda\_docs/label/2015/208411lbl.pdf

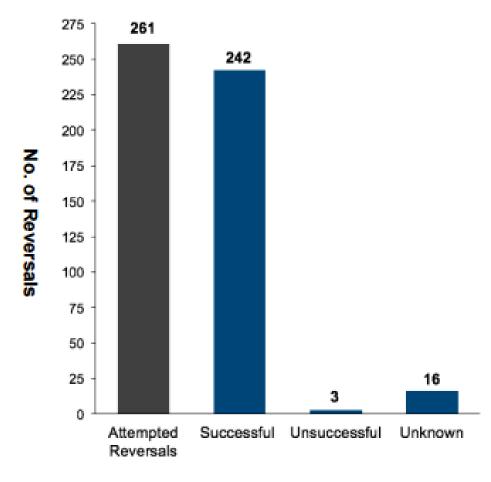
## When Time Matters?





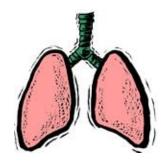
## Success Rate





## **Pulmonary Edema**

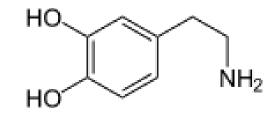
- First case in 1977
- Occurs with doses as low as 80mcg IV
- Onset within 1-60 minutes
- Majority in healthy men < 50 yo
- 2012 Review: 24 published cases, may be hypoxia from opioids that caused the pulmonary edema.







- Increases catecholamine release
  - especially in the presence of hypercapnoea
  - The correction of of hypercapnoea reduces haemodynamic effects.
    - Mills CA (1988)
- There is no clinical evidence to support hypercapnoea correction prior to administration of naloxone





- Can mobilize as usual
- Have oxygen saturation > 92%
- Have a respiratory rate between 10–20
- Have a temperature between 35.0–37.5C
- Have a heart rate of 50–100 bpm
- Have a GCS of 15.

# To Do No Harm

f

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PHOTO ILLUSTRATION BY THE DAILY BEAST

### REALITY CHECK Life Is Hell After Narcan, Heroin's Miracle Cure

The media is hooked on stories of overdoses being magically reversed by wonder drug naloxone, but what follows is arrests, pain, and more addiction.

Neale J, Strang J. Addiction. 2015; 110

## Legislation in Michigan: What's New?





 This standing order is issued pursuant to <u>Michigan's Public</u> <u>Act 383 of 2016</u>, that does not identify particular patients at the time it is issued for the purpose of a pharmacist dispensing the opioid antagonist naloxone.

## Legislation in Michigan: What's New?



 <u>This standing order may be used by Eligible Individuals as</u> <u>a prescription to obtain naloxone from a pharmacy.</u> This order is authorization for pharmacists to dispense naloxone and devices for its administration SOLELY in the FDA-approved naloxone formulations and devices prescribed herein



### **Challenges for Community Programs**



• Prescription and prescriber typically required

• Naloxone cost is increasing, funding is minimal

 Missing people who don't identify as drug users, but have high risk

• Community-based organizations only target IV drug users,

### **Challenges for Community Programs**



- Co-prescribe naloxone with opioids for pain
- Co-prescribe with methadone/ buprenorphine for addiction
- Insurance should fund it
- Increase patient, provider & pharmacist awareness
- Universalize overdose risk...all patients who take >50 oral morphine equivalents per day per the 2016 CDC guidelines.

# And All Ends Well



- Opioid overdose is a public health crisis
- Naloxone is a safe and effective opioid reversal agent
- Multiple routes of administration are available
- Diversion and prescribing of opioids must be addressed





# Naloxone for All?





## **Key Takeaway Points**

- WHO states naloxone can prevent more than 200,000 U.S. deaths.
- "Take home" naloxone was discussed in literature more than 20 years ago!
- Out-patient naloxone use has decreased ED visits for opioid and heroin OD situations.
- Properties of naloxone nasal spray.
- Side effects and opioid withdrawal effects after using naloxone.





- Comparison of intranasal naloxone versus intramuscular naloxone administration.
- Expense and rising "costs" of naloxone.
- Success rate with the use of naloxone.
- Michigan's Public Act 383 of 2016 and its effect on pharmacy technicians and pharmacists.

## Thank you!

