



*The National
Academies of*

SCIENCES
ENGINEERING
MEDICINE



opiANT

FOCUSED ON ADDICTION

Presentation at National Academies of Sciences Engineering Medicine

11th October 2017

COI statement

- Full time employee of Opiant Pharmaceuticals Inc.
- Shareholder of Opiant Pharmaceuticals Inc.

Opiant is a specialty pharma focused on addiction

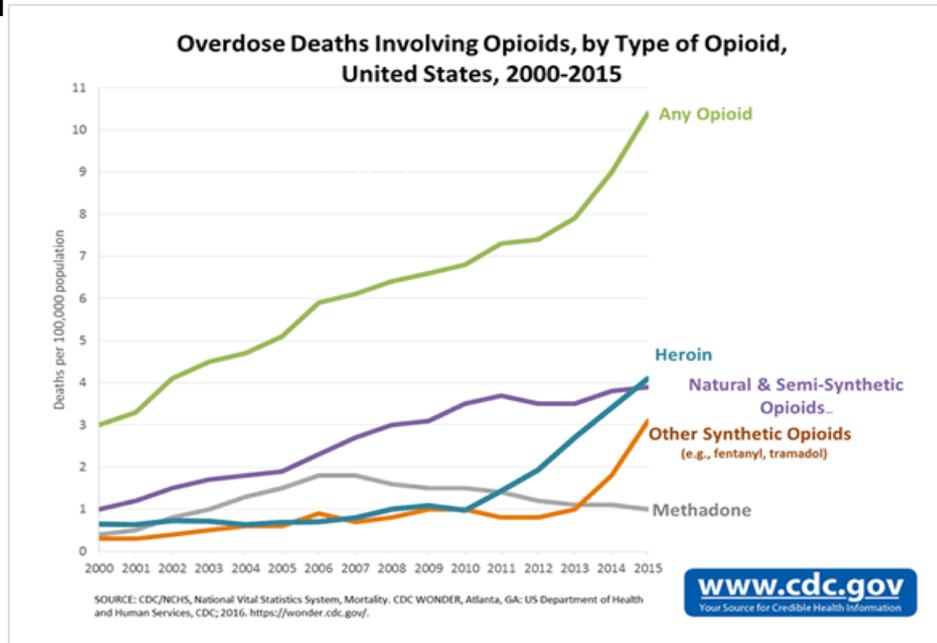
- Based in Santa Monica, CA & clinical operations in London, UK
- Company has single focus on developing pharmacotherapies for addiction
- Particular expertise with opioid_antagonists
- Company origins in Finland

Lead Programs

Indication	Product Candidate / Regulatory Pathway	Pre-clinical	Phase 1	Phase 2	Phase 3	NDA	FDA Approval	Partner	
Opioid Overdose	NARCAN® Nasal Spray 505(b)(2)							 	
Eating Disorders	OPNT001 Opioid Antagonist Nasal Spray 505(b)(2)								
Alcohol Dependence	OPNT002 Opioid Antagonist Nasal Spray / 505(b)(2)								
Opioid Use Disorder	OPNT006 Opioid Antagonist Implant								
Opioid Use Disorder	OPNT 005 Heroin hapten + liposome adjuvant								

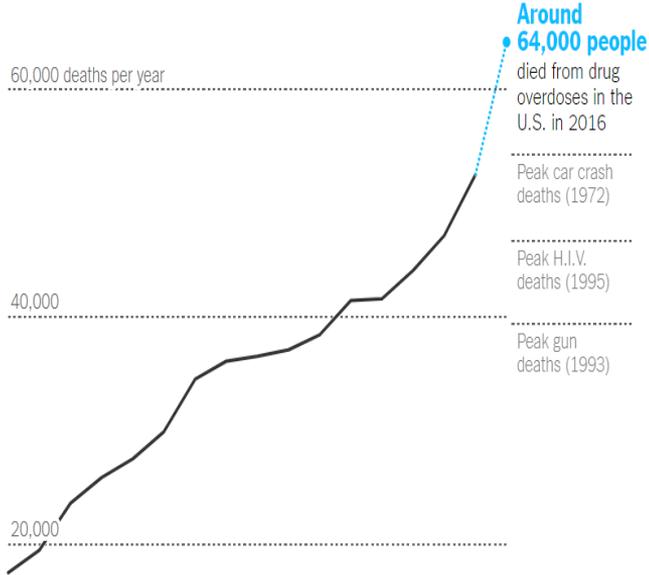
Opioid addiction and overdose: A significant public health crisis

- Opioid overdose deaths have increased dramatically since 2000
- Opioid often used first for pain relief - reverse ladder of elsewhere
- USA – direct to consumer marketing and (mis)marketing to Drs
- Drs reimbursed for pain free patients (Medicaid, pain as vital sign..)
- Dramatic increase in synthetic opioids including fentanyl
- Approximately opioid 33,000 overdose deaths in 2015

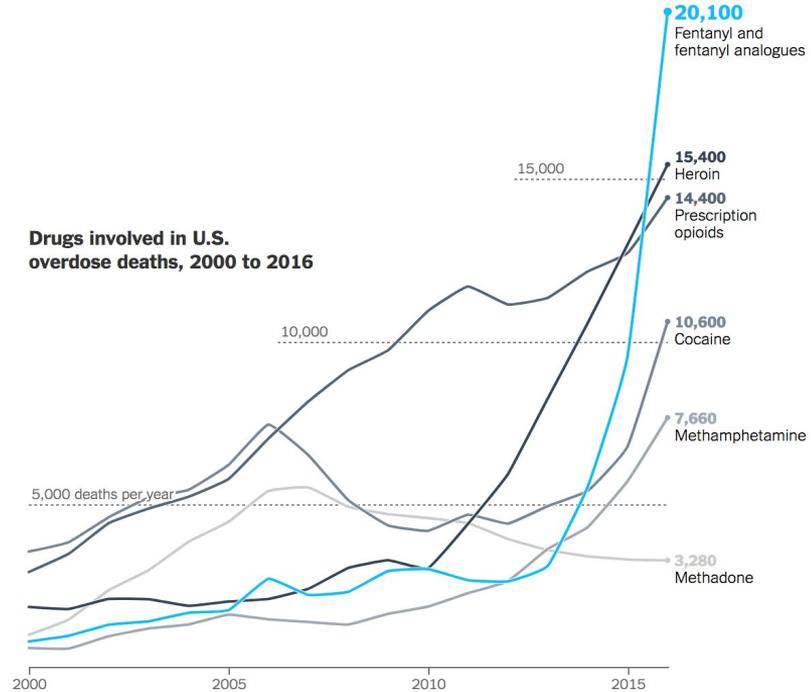


And it's getting worse....53,000 deaths in 2016

Total U.S. drug deaths



Drugs involved in U.S. overdose deaths, 2000 to 2016



Graph from [NY Times Article](#) based on [CDC MMWR Report 2017](#)

U.S.

Heroin Epidemic Is Yielding to a Deadlier Cousin: Fentanyl

By KATHARINE Q. SEELYE MARCH 25, 2016



With permission from Bruce Taylor/NHSP Forensic Lab

Image showing lethal doses of heroin (left) and fentanyl (right)



NEW YORK TIMES, 25 MARCH 2016

Syringes scattered along the ground at a homeless encampment in Lawrence, Mass.
Katherine Taylor for The New York Times

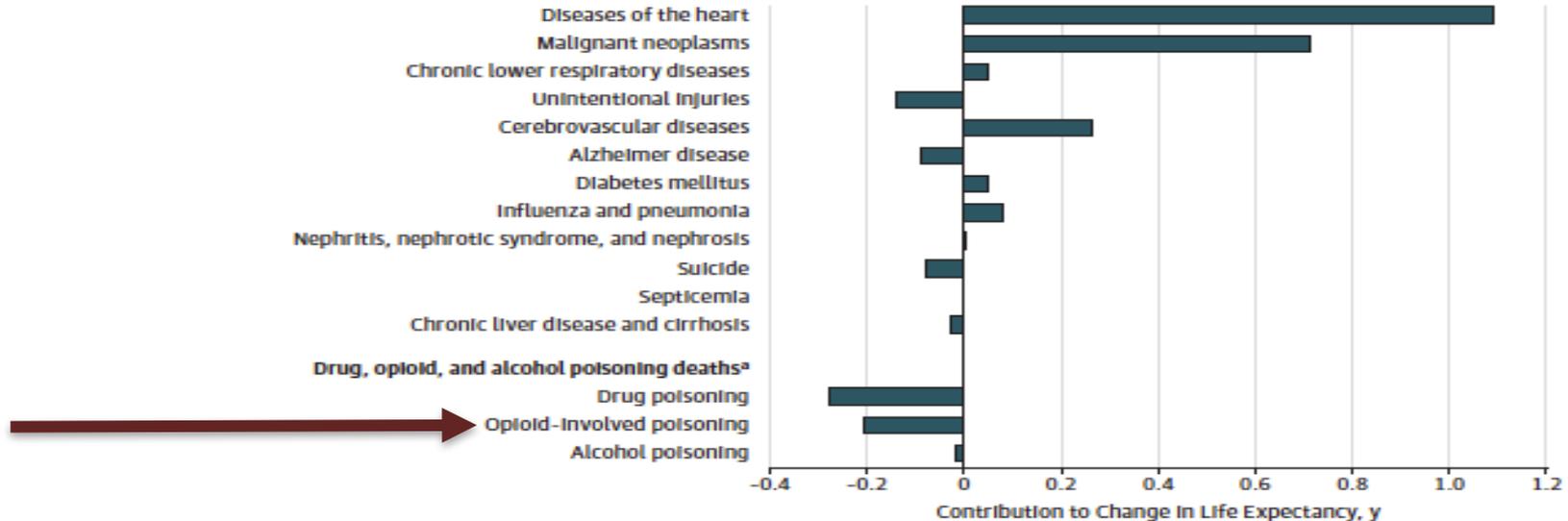
Fentanyl is more potent than heroin, cheap and very accessible

- Gets into brain **quickly**; longer duration of action than heroin
- 50-100x **more potent** than morphine
- **Easier to produce** than heroin
- **Cheaper**
 - estimated wholesale price of heroin is \$65,000/kg.
 - Illicit fentanyl is available for \$13,000/kg (Frank & Pollack, NEJM)
- **Easier to manufacture** and further **modify** into more potent analogs:
 - Synthesis not beyond the skills of a competent chemist
 - Fentanyl is a piperidine - readily derivatized...for example into carfentanil

Opioid Overdoses Have Reduced Life Expectancy In The USA

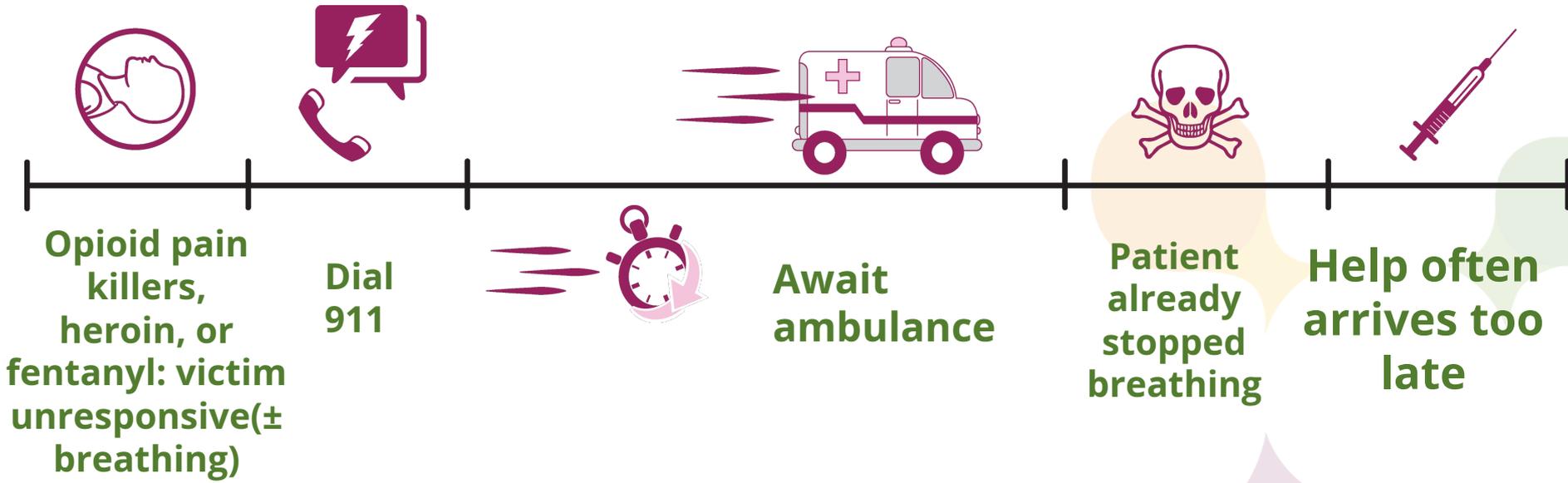
Figure. Contributions of Selected Causes of Death to the Change in Life Expectancy in the United States, 2000-2015

12 Leading causes of death (ranked highest to lowest according to No. of deaths in year 2015)



From Dowell, et al., JAMA, 2017

Naloxone saves lives if given quickly – injections can only be given by qualified personnel



Prior to NARCAN® Nasal Spray, naloxone options often involved needles, were hard to use and expensive

Injectable Naloxone



- Only suitable for trained personnel
- Requires prep time
- Requires a needle

Autoinjectors



- Expensive
- Not needle free

Improved Nasal Kits



- Only suitable for trained personnel
- Requires assembly
- Not FDA-approved
- Low absorption

Concept of Nasal Naloxone first arose from improvised kits



- (1) Remove medication and atomizer
- (2) Pull off both yellow caps from syringe
- (3) Pull off purple naloxone cap from naloxone cartridge
- (4) Attach atomizer onto syringe by the hold wings on the atomizer
- (5) Screw naloxone cartridge into syringe
- (6) Place atomizer tip into patient's nostril
- (7) Push cartridge to administer some naloxone into one nostril
- (8) Push cartridge to administer approximately 1 mL naloxone into the other nostril

Patient Instructions for Intranasal Naloxone Administration

How to Avoid Overdose

- Only take medicine prescribed to you
- Don't take more than instructed

- Call a doctor if your pain gets worse
- Never mix pain meds with alcohol
- Avoid sleeping pills when taking pain meds

- Dispose of unused medications
- Store your medicine in a secure place
- Learn how to use naloxone

- Teach your family + friends how to respond to an overdose

Are they breathing?



Signs of an overdose:

- Slow or shallow breathing
- Coughing for air when sleeping or weird snoring
- Pale or bluish skin
- Slow heartbeat, low blood pressure
- Worst wakes up or respond (rub knuckles on sternum)

Call 911 for help

All you have to say:
"Someone is unresponsive and not breathing"
Give clear address and location.



Airway



Make sure nothing is inside the person's mouth.

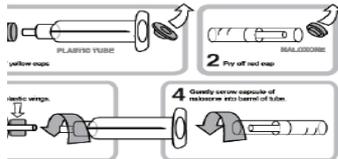
Rescue breathing



Oxygen saves lives. Breathe for them.
One hand on chin, tilt head back, pinch nose closed.
Make a seal over mouth & breathe in 1 breath every 5 seconds
Chest should rise, not stomach

Prepare Naloxone

Are they any better? Can you get naloxone and prepare it quickly enough that they won't go for too long without your breathing assistance?



PrescribeToPrevent.org



Source: Harm Reduction.org

Evaluate + support

- Continue rescue breathing
- Give another 2 sprays of naloxone in 3 minutes if no or minimal breathing or responsiveness
- Naloxone wears off in 30-90 minutes
- Comfort them: withdrawal can be unpleasant
- Get them medical care and help: there's not sea more opiate right away
- Encourage survivors to seek treatment if they feel they have a problem



PK profile of improvised device would not meet FDA standard for approval

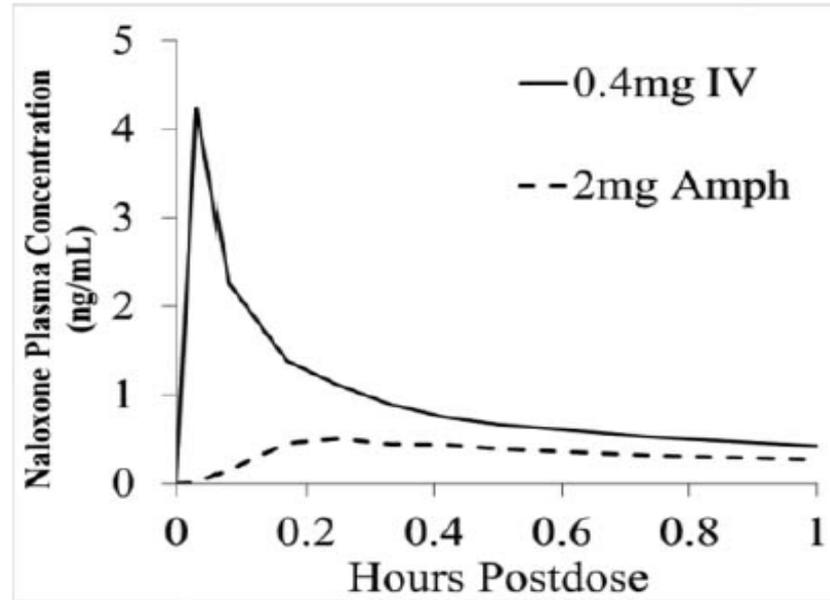


Figure 1. Mean naloxone plasma concentration of improvised nasal naloxone 2 mg/2 mL (2 mg Amph) and naloxone 0.4 mg delivered by intravenous injection (0.4 mg IV) in the first hour post-dose. **Source:** U.S. Patent 9,192,570; WO 2015/095644 AntiOp, Inc.

FDA guidance on novel naloxone products

volunteers. According to the FDA guidance (Hertz, 2012), pharmacokinetic studies will need to “[e]valuate the relative bioavailability of at least two different doses compared to parenteral injection of naloxone (IM, IV or SC). [Studies should] [c]ompare a parenteral dose of naloxone of at least 0.4 mg to dose(s) of the new product that would be expected to result in similar or greater drug exposure. Target plasma naloxone levels [should be] detectable in all subjects for a meaningful duration comparable to approved product.”

FDA advisory committee Oct 2016
recommend a higher dose of a naloxone as a new minimum

Opiant partnered with NIDA in 2012, recognizing the potential magnitude of the opioid crisis

- Alarming data in exposed late 2011:
 - More deaths from OOD than Road Traffic Accidents
 - Widespread prescribing of opioids unique to USA:
- Meanwhile, Opiant had generated encouraging Phase 2 data using nasal naloxone for Binge Eating Disorder.....
- Opiant (then Lightlake Therapeutics), established a Clinical Trial Agreement with NIDA in 2012.....
 - Pilot pK data very encouraging
 - Larger confirmatory pK study established with NIDA in 2013

NARCAN® Nasal Spray was born out of the need to provide a simple-to-use needle-free solution

Key product requirements

Avoidance of needles: people more willing and able to use

Capable of reversing overdose from more potent opioids

Reliable drug delivery: multidirectional, avoids priming and suited for mass production

Easy to use – no assembly required – suitable for anyone to use with no/minimal training

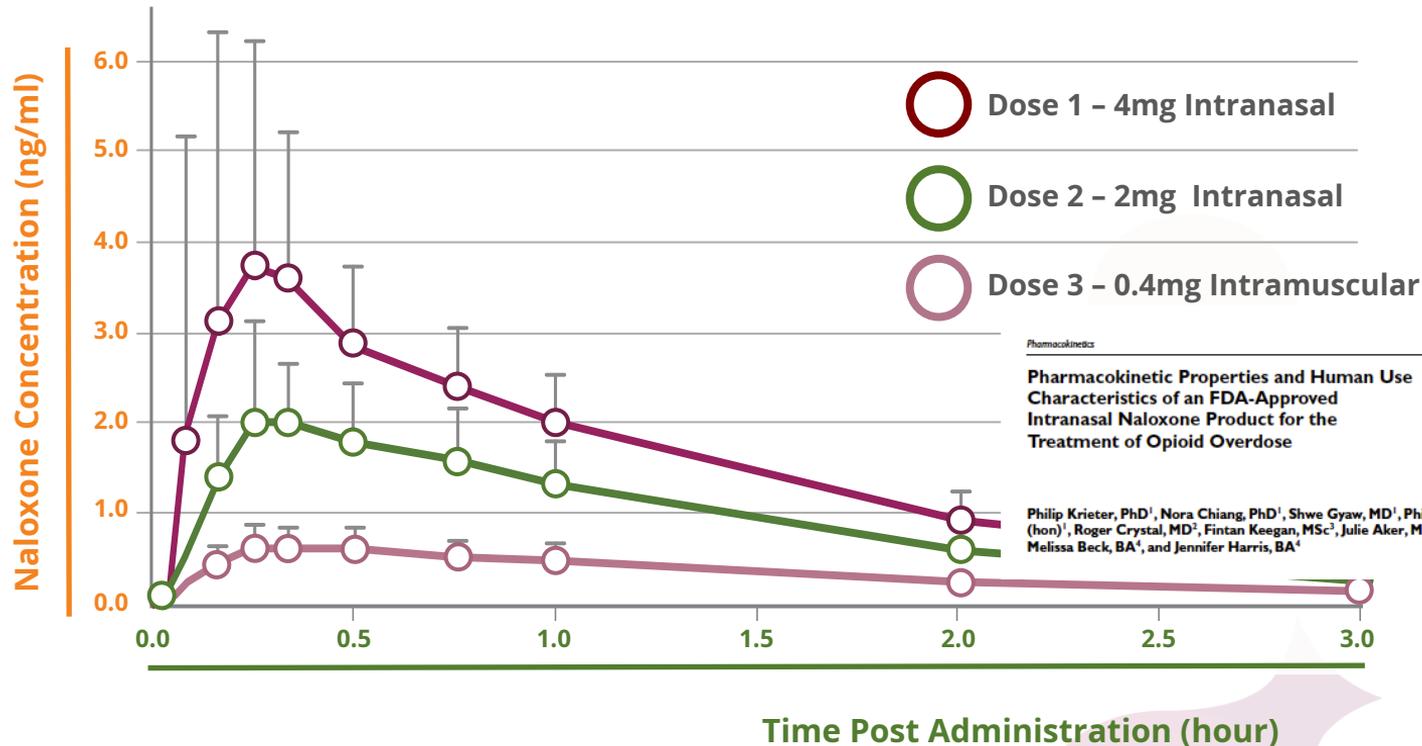
Opiant's solution

Nasal delivery

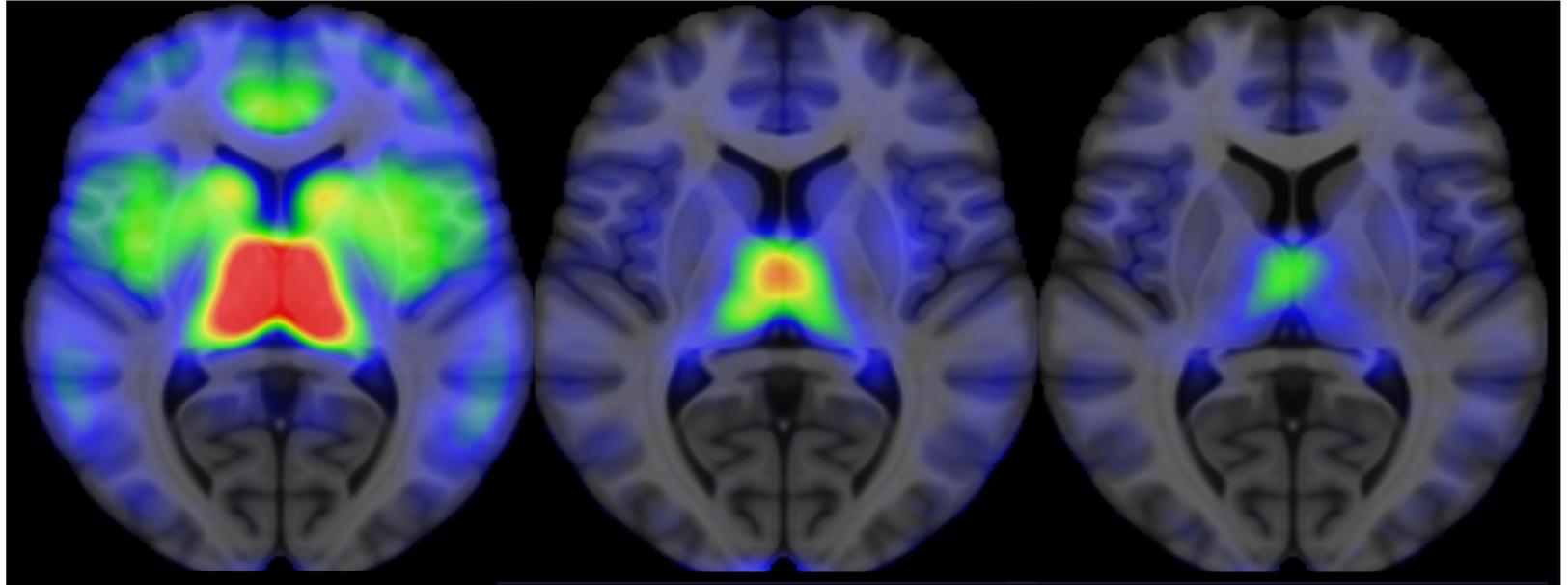
Higher 4mg dose in novel formulation

Aptar Unit dose device

NARCAN® Nasal Spray: both doses: rapid absorption with higher blood levels compared to 0.4mg IM naloxone

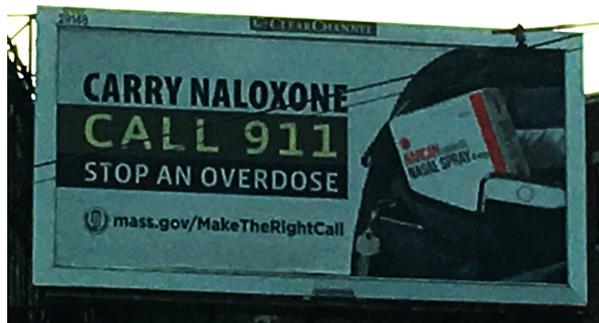


4mg Nasal Naloxone Can Displace [^{11}C] Carfentanil From Brain Opioid Receptors



Scheinin, et al., in preparation

NARCAN® Nasal Spray is becoming the mainstream rescue product across the USA



L.A. sheriff's deputies to carry treat opioid overdose victims



SAVE A LIFE

COLLEGE OF MARIN POLICE OFFICERS
CARRY NALOXONE.

Naloxone given as a nasal spray can reverse the effects of an opioid overdose and save a life. Call 911 if you think someone is having an

Opiant remains committed to developing treatments for OUD and other addictions

- Additional programs in OUD including 6mth opioid antagonist implant and a heroin vaccine
- Phase 2 study in Bulimia
- Alcohol Use Disorder
....significant rise in drinking over last decade....

Alcohol Use Disorder... The next epidemic...

Original Investigation

September 2017

Prevalence of 12-Month Alcohol Use, High-Risk Drinking, and *DSM-IV* Alcohol Use Disorder in the United States, 2001-2002 to 2012-2013

Results From the National Epidemiologic Survey on Alcohol and Related Conditions

Bridget F. Grant, PhD¹; S. Patricia Chou, PhD¹; Tulshi D. Saha, PhD¹; et al

[> Author Affiliations](#)

JAMA Psychiatry. 2017;74(9):911-923. doi:10.1001/jamapsychiatry.2017.2161



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