Naloxone Dispensing via Retail Pharmacies

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FDA Meeting
December 17, 2018

Overview

1. **Promise** of pharmacy-based naloxone rescue kit distribution
2. **Barriers** of pharmacy-based naloxone rescue kit distribution
3. **Opportunities** for pharmacy-based naloxone rescue kit distribution

Pharmacy-based naloxone rescue kit distribution

Promise


The Chicago Recovery Alliance
ANY POSITIVE CHANGE
CHICAGO RECOVERY ALLIANCE
any positive change
One shot naloxone save...
DEATH
NOT BREATHING
NOT RESPONSIVE

AMA
AMERICAN MEDICAL ASSOCIATION

"The **AMA** has been a longtime supporter of increasing the availability of Naloxone for patients, first responders and bystanders who can help save lives and has provided resources to bolster legislative efforts to increase access to this medication in several states."

www.ama-assn.org/ama/pub/news/news/2014-07-naxolene-product-approval.page

NATIONAL DRUG CONTROL STRATEGY

2013

Community management of opioid overdose

World Health Organization

American Pharmacists Association
Improving medication use. Advancing patient care.
APhA

"**APhA** supports the pharmacist's role in selecting appropriate therapy and dosing and initiating and providing education about the proper use of opioid reversal agents to prevent opioid-related deaths due to overdose"

www.pharmacist.com/policy/controlled-substances-and-other-medications-potential-abuse-and-use-opioid-reversal-agents-2

ASAM
American Society of Addiction Medicine

Public Policy Statement on the Use of Naloxone for the Prevention of Drug Overdose Deaths

ASAM Board of Directors
April 2010

"Naloxone has been proven to be an effective, fast-acting, inexpensive and non-addictive opioid antagonist with minimal side effects... Naloxone can be administered quickly and effectively by trained professional and lay individuals who observe the initial signs of an opioid overdose reaction."

www.asam.org/docs/publicy-policy-statements/1naloxone-1-10.pdf

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NATIONAL DRUG CONTROL STRATEGY

2013

Community management of opioid overdose

ASAM

Surgeon General's Advisory on Naloxone and Opioid Overdose

April 5, 2018

I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, ***knowing how to use naloxone and keeping it within reach can save a life.***

BE PREPARED. GET NALOXONE. SAVE A LIFE.

State laws nationwide have drastically increased patients' ease of access to naloxone through pharmacies

The great majority of states permit pharmacies…

- Naloxone distributed without a prescription via standing orders, collaborative practice agreements or pharmacist prescribing authority
- People not at risk themselves for overdose may receive naloxone via 3rd party distribution
- Pharmacist immunity from liability for furnishing naloxone
- Mandated insurance coverage (RI)

Check out PDAPS.org – Prescription Drug Abuse Policy System for the latest state overdose and naloxone laws

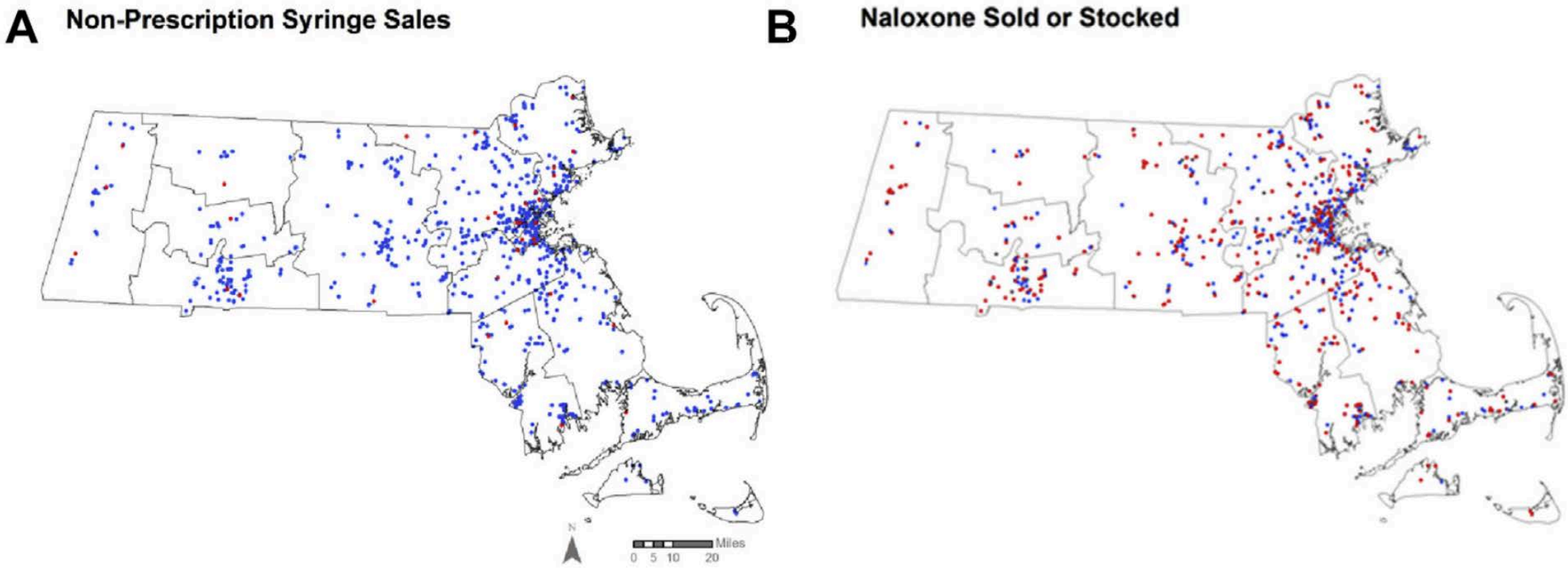
Pharmacy-based naloxone rescue kit distribution

Barriers

Slow Adoption - Despite pharmacy naloxone laws, many pharmacies do not stock or dispense

- IN – 2.5yrs later telephone survey
  - 58% of pharmacies stock and 50% of pharmacists not comfortable dispensing to people who inject
    - Meyerson DAD 2018
- NY – 3yrs later telephone survey
  - 37.5% of NYC pharmacies stocked; willing to dispense
    - NYT 4/12/2018
- CA – 2yrs later 1209 retail pharmacies randomly selected
  - 24% dispensing naloxone without prescription
  - 50% stocking naloxone
  - 60% willing to bill insurance for naloxone
    - Puzantian JAMA 2018

Massachusetts pharmacies, 2015: 97% sell syringes, 45% sell naloxone



Stopka T et al. JAPHA 2017; 57:S34-S44.

Accessing naloxone at pharmacies

Perspectives of people with chronic pain, substance use disorders, caregivers, and pharmacists in 2015 – MA and RI

- **Some fear about consequences from obtaining pharmacy naloxone**
  - "I think that if you go to the pharmacist and…bring it up that you are interested in getting Narcan…automatically red flags go up in that pharmacist's mind. Why do you want Narcan? Do you think you are going to overdose? Then all of a sudden there you are the criminal again."
- **Some pharmacists were concerned about offending patients**
  - "I think it, for me, I think it might ruin a relationship even knowing the background of somebody, but you don't want to step over those boundaries where you would ruin a relationship, then they will go and talk to their friends, "Oh, she thinks I'm an addict."

Green et al. JAPhA 2017

Accessing naloxone at pharmacies

"…[You can take] the stigma away [from naloxone] by making it…as common as…'Do you want fries with that?" – Caregiver, MA

- **Others have had a good experience**
  - "He asked me if I knew how to use it and I said yeah and that was it. So I mean I think it should be that easy, because there are, there are some people who will give you a hard time, you know."
- **Opt-out offer of naloxone considered promising strategy by all groups**
  - "If it was up to me, every single opiate prescription that was being filled would also be dispensed with Narcan. Even if the patients aren't using them or the families aren't using it, it would help, I think, to over time kind of reduce the stigma and that Narcan is only for heroin."

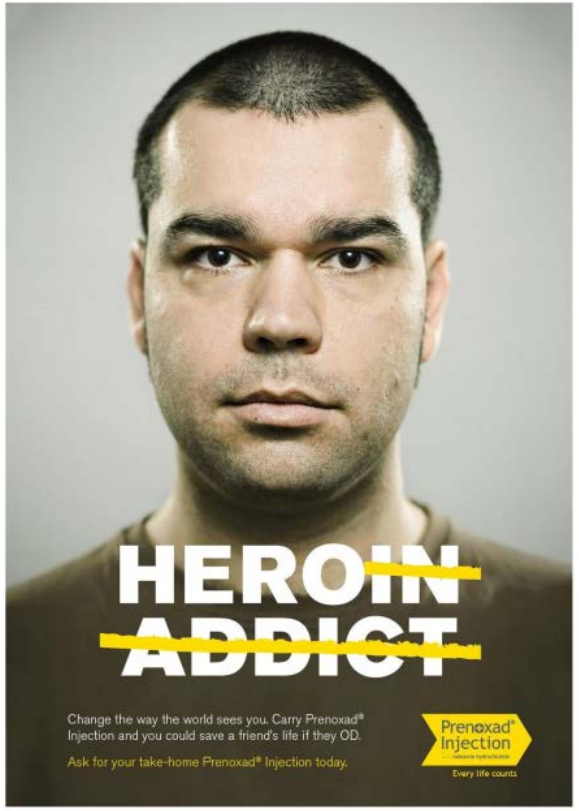
Green et al. JAPhA 2017

Pharmacy-based naloxone rescue kit distribution

Opportunities

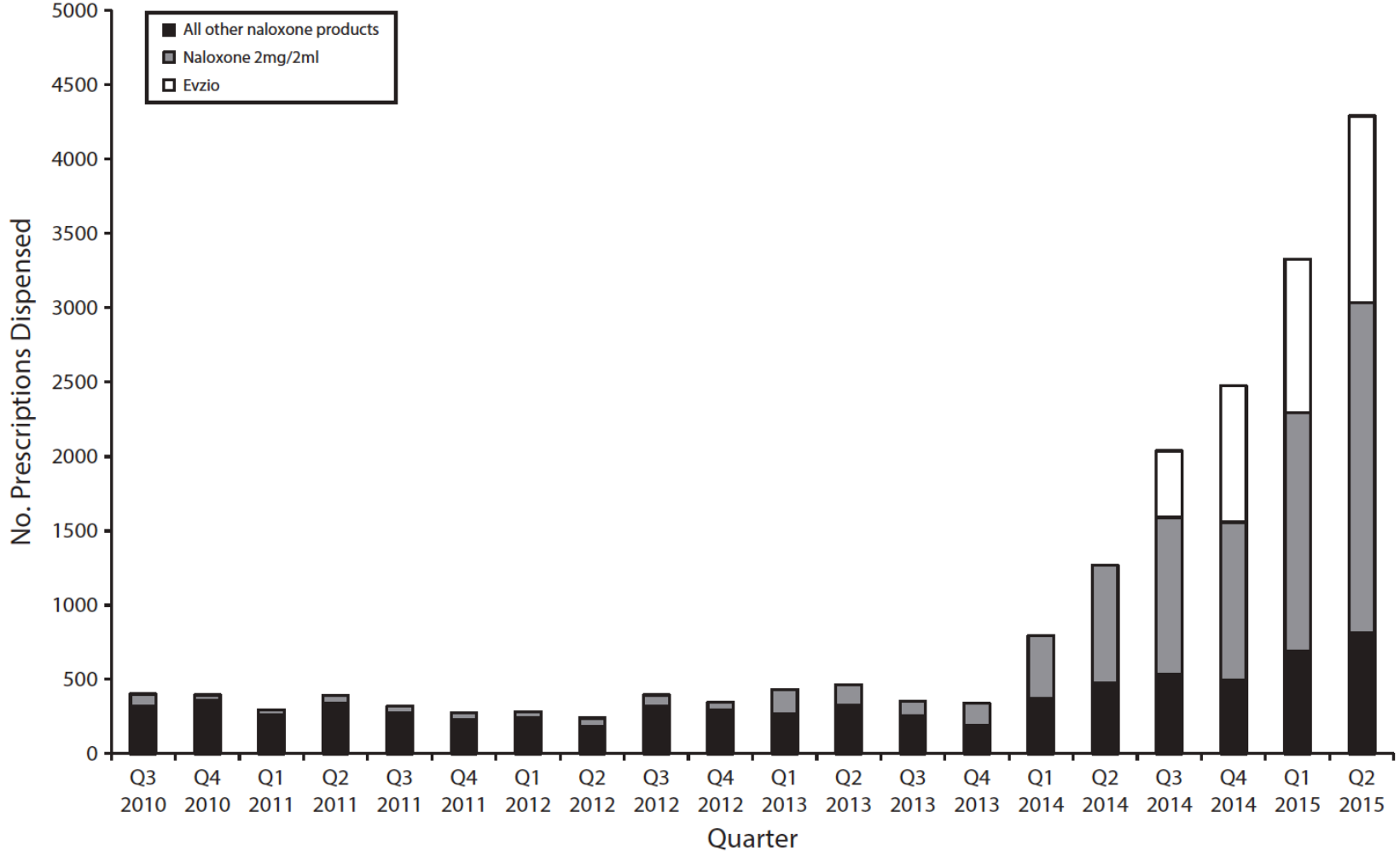
Naloxone through community programs are ahead

- 2013 – Harm reduction programs distributed 130,000+ doses
  - Wheeler et al. MMWR 2015
- 2017 – Mass harm reduction programs distributed 60,000+ doses
  - MA DPH program data



But pharmacy naloxone is picking up

Naloxone dispensed from retail pharmacies, 2010-2015



Jones et al. Increase in Naloxone Prescriptions Dispensed in US Retail Pharmacies Since 2013. AJPH 2016 Vol 106, No. 4

Patience Pays Off

- TX – 3yrs later 2317 chain pharmacies with a standing order
  - 69% stocked + willing to dispense SO naloxone
  - 80% willing to dispense to third-party (rescuer)
  - 50% willing to bill insurance for third-party (rescuer)
    - Evoy JAMA 2018
- MA – 4 yrs later 200 randomly selected pharmacies
  - 79% successful purchase
    - Pollini NIDA R01 prelim data

Green et al. Harm Reduction Journal
DOI 10.1186/s12954-015-0058-x

HARM REDUCTION JOURNAL

CASE STUDY Open Access

Orienting patients to greater opioid safety: models of community pharmacy-based naloxone

Traci C. Green[1,2,3,7*], Emily F Dauria[3], Jeffrey Bratberg[4], Corey S. Davis[5] and Alexander Y Walley[6]

"Opt-out" offer of naloxone to Everyone…..

- Any opioid prescription
- Any opioid/benzo rx combination
- Any disease/opioid combination
- Any methadone
- Any buprenorphine
- Any naltrexone
- Transitions of care
- Friends and family of those at risk
- Syringe buyer request
- Addiction treatment
- Correctional institution
- Behavioral health

North Dakota retail opt-out pilot

- 3 North Dakota retail pharmacies with pharmacist prescribing authority
- 16% (10/59) patients (with MME >50) offered naloxone in one month pilot
- 5-10min of pharmacist time per prescription
- Co-pay typically <$10
- Training for pharmacist and technicians could improve uptake
- Automatic MME calculation could facilitate eligibility determination

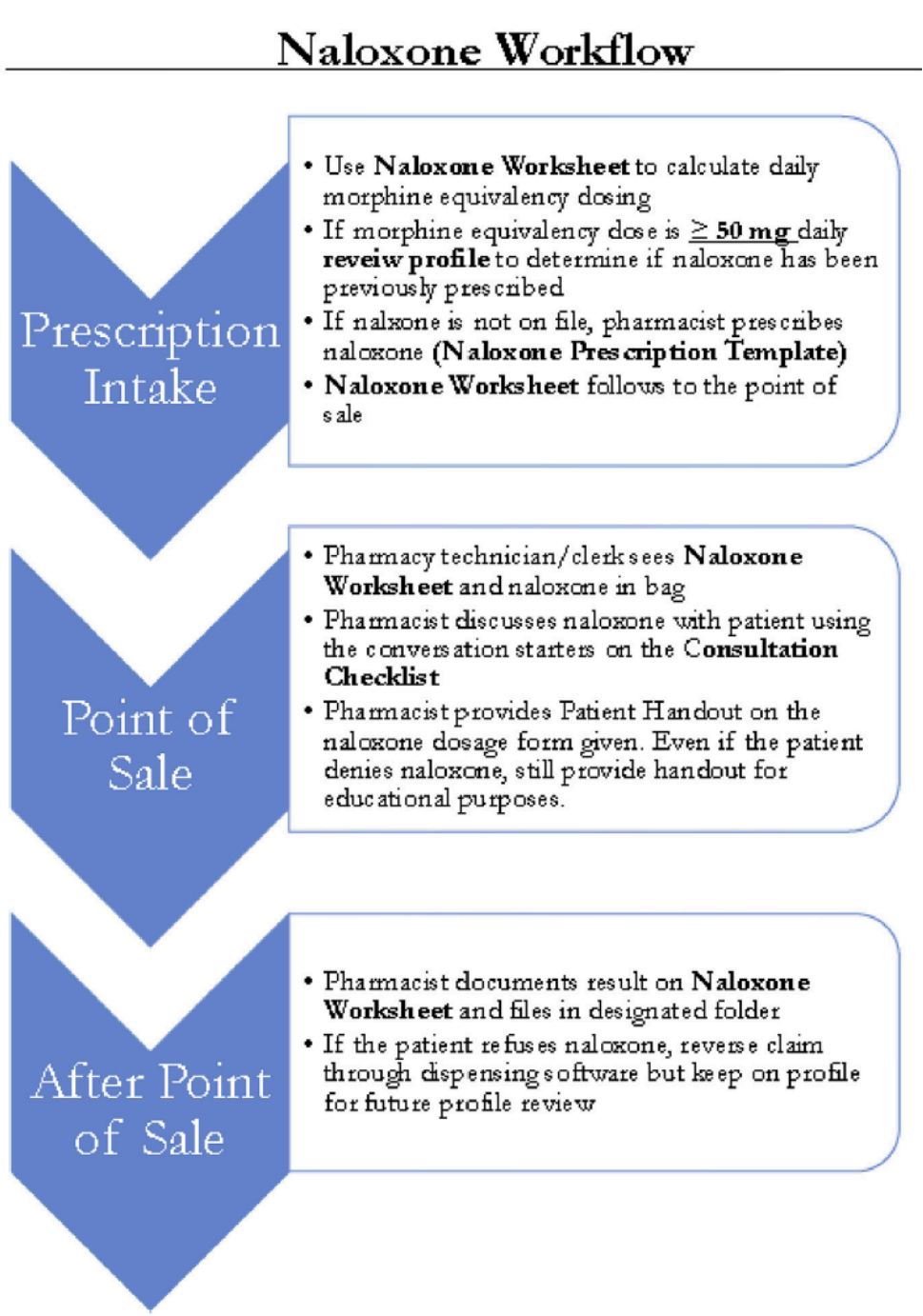
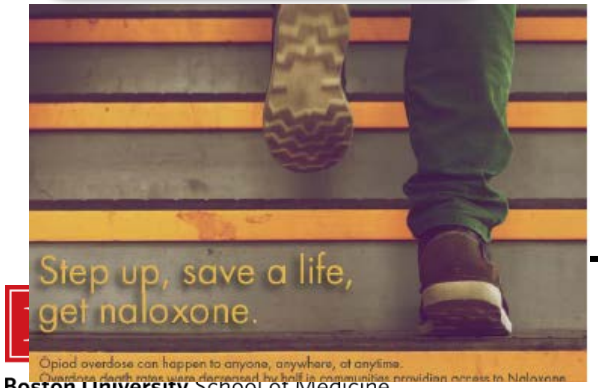


Fig. 1. Incorporation of opt-out naloxone dispensing within the pharmacy workflow.

Prescriber writes prescription
Patient fills at pharmacy

- Setting: clinic with insured patients
- Pharmacies alerted to prescribing plans
- Informational brochure, patient fills
- Prescriber-pharmacy communications key



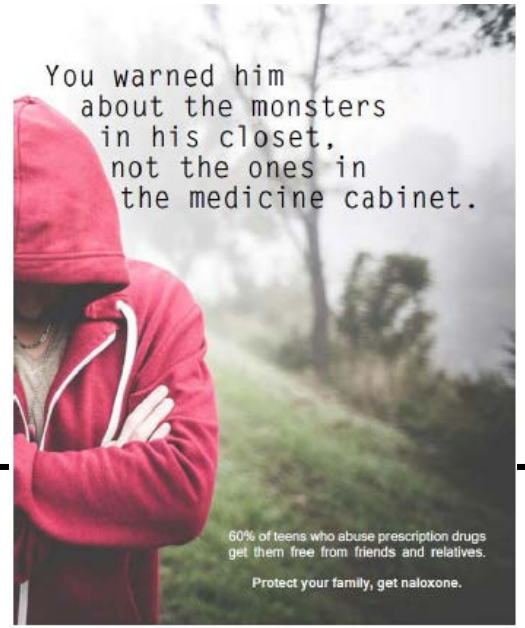
Pharmacy provides naloxone directly to customer

- Without prescriber contact under a standing order
- Training needed

  Passive or active models:
  Naloxone co-prescription
  Universal offer, may require clear policy direction

Pharmacy provides naloxone to patients in treatment center/clinic

- Without prescriber or pharmacy contact under a standing order, distribution model
- Patient training done on-site at clinic, facilitates facility-level compliance and sustainability



Pharmacy provides naloxone to patients in mobile setting

- Without prescriber contact under a standing order

  Event or venue-based, rapid deployment
- Training needed, technology for mobile labeling/billing

  Patient training done in-field by pharmacy

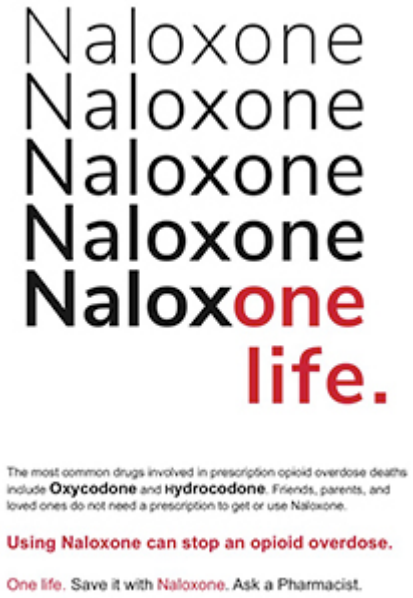
Prevent-protect.org

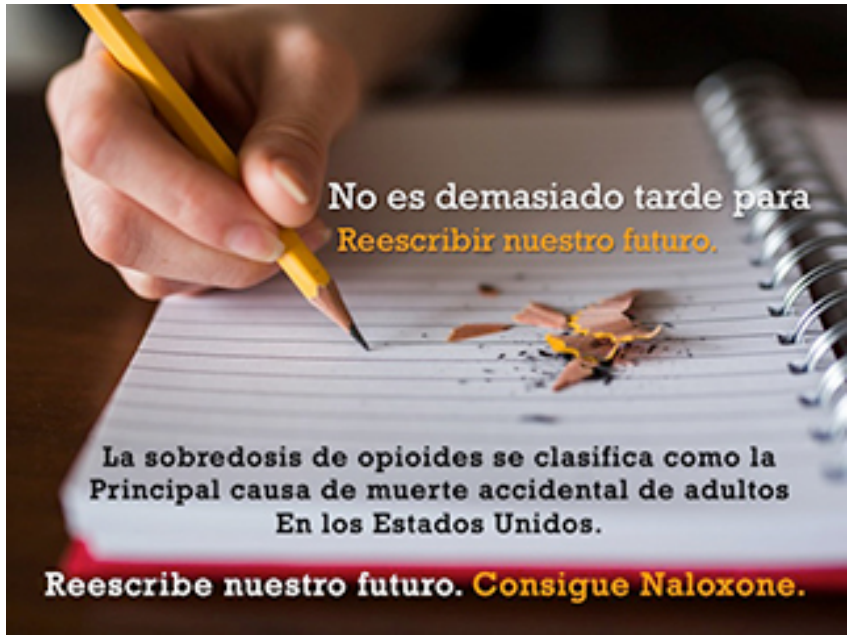
Prescribetoprevent.org

- Resources and guidance for:
  - Pharmacy goers
  - Naloxone advocates (CBOs, health depts)
  - Prescribers
  - Pharmacists
- Spanish/English versions
- Implementation and Dissemination
  - Adopted by: Chicago, Austin, Philadelphia, New York, Virginia, PA Attorney General's Office, Rite Aid
  - AHRQ Director's February 2018 blog post
  - Surgeon General's communications

Overdose and Naloxone Posters at prevent-protect.org

- Posters adapted for www.prevent-protect.org website, Spanish language versions, featured in-pharmacy





On-site safety at pharmacies

Not secure | prevent-protect.org/community-resources-1/safety-policies/

» Safety Policies

As service providers and public health professionals who work with people who use drugs, we know that sometimes people use drugs in our facilities. Particularly in the case of injection drug use, a bathroom or other private area at a trusted services agency may be the safest and most secure location when the alternative is using outdoors, in business bathrooms, or similarly problematic places.

Many programs, and even businesses, have taken steps to improve safety and hygiene in places where people might use drugs. The first goal is to protect clients and staff. When done thoughtfully, such strategies can also foster therapeutic relationships by promoting open and frank dialog with drug using clients.

Examples of steps that can be taken include:

- Training staff on overdose response including the use of naloxone, equipping spaces or individuals with overdose rescue kits, and adopting policies and procedures for overdose management.
  This is a sample policy developed for on-site overdoses– it was created for pharmacies, but can easily be adapted to different venues.

MORE COMMUNITY RESOURCES

- Customizeable Posters
- Downloadable Materials
- Agency Outreach
- Safety Policies

WHAT IS NALOXONE?

NALOXONE: (also called Narcan® or Evzio®) is a prescription medicine that can stop an overdose. Parents, relatives and friends can get it to administer to someone who is overdosing on heroin or medicines like OxyContin® or Percocet®.

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6:39 AM 5/23/2018

Overview

1. **Promise** of pharmacy-based naloxone rescue kit distribution
2. **Barriers** of pharmacy-based naloxone rescue kit distribution
3. **Opportunities** for pharmacy-based naloxone rescue kit distribution

Realistic Expectations!

Addiction is a chronic relapsing condition

Over time treatment works
People get better, if the stay alive

Engage people before, at, and after health system touchpoints

awalley@bu.edu

Naloxone co-prescribing

Phillip Coffin, MD MIA FACP FIDSA
San Francisco Department of Public Health
University of California San Francisco

DISCLOSURES

Have directed NIH and CDC-funded studies addressing opioid overdose and naloxone access

Naloxone for Opioid Safety Evaluation

METHODS

DESIGN:

- Nonrandomized intervention study
- Six safety net clinics of SF Department of Public Health
- 2013 to 2015

INTERVENTION:

- Established clinic recommendation to co-prescribe naloxone with opioids
- Supported staff in prescribing naloxone
- Assisted clinic champion in obtaining brochures (developed by study staff), obtaining atomizers (MAD devices unavailable at pharmacies), location to store supplies, and troubleshooting
- Pharmacy assistance

MEASURES:

- Chart abstraction of all patients on long-term opioid therapy
- Interviews with patients offered naloxone prescriptions
- Surveys of providers in naloxone-providing clinics

FUNDING:

- NIDA - R21DA036776

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
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.prescribetoprevent.org

SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

Opioid safety and how to use naloxone

A GUIDE FOR PATIENTS AND CAREGIVERS

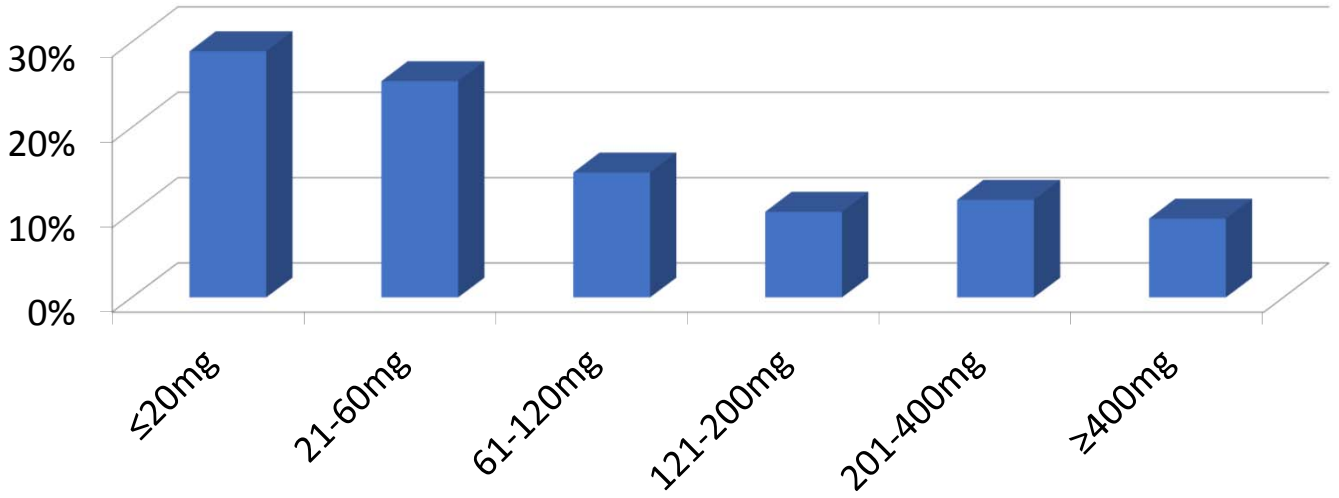
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

Characteristics of Patients on Long-term Opioids for Pain

	Number (%)
Total	1985 (100)
Female	822 (41.4)
Mean Age (SD)	56.7 (10.8)
Race/Ethnicity	
Black	960 (48.4)
White	606 (30.5)
Hispanic/Latino	265 (13.4)
Other	154 (7.8)
Patients with SFGH ED Visits from 2013-early 2015	
Any visit / Annual rate	1061 (53.5) / 2.0
Opioid-related / Annual rate	246 (12.4) / 0.6
Opioid over-sedation / Annual rate	67 (3.4) / 0.1
Deaths during study	
All-cause	59 (3.0)
Opioid poisoning	5 (0.3)

Source: Coffin PO, Behar E, Rowe C, et al. Nonrandomized intervention study of naloxone coprescription for primary care patients receiving long-term opioid therapy for pain. Ann Intern Med. 2016.

MEQ Dose Prescribed at Baseline



*Opioid agonist treatment not included in calculation
**Highest dose was 4,200mg

Source: Coffin PO, Behar E, Rowe C, et al. Ann Intern Med. 2016.

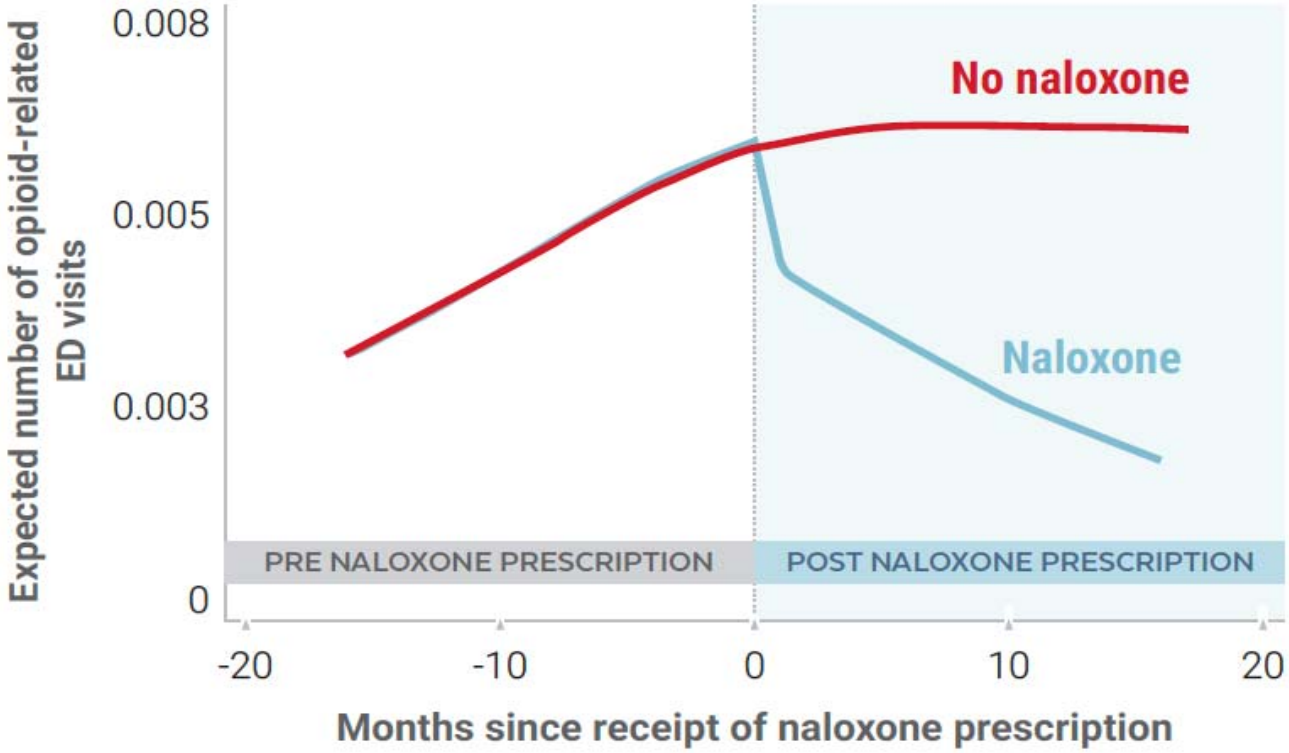
Predictors of Receiving a Naloxone Rx

	aOR
Age (5 year units)	0.94 (0.89-1.00)
Log MEQ dose	1.73 (1.56-1.92)
Opioid-related ED visit in 12 months prior to program	2.54 (1.54-4.18)
Non-significant parameters	
Race/ethnicity	
Gender	
Provider type	
Number of PMR patients seen by provider	

Model also adjusted for patient clinic, number of days elapsed between the earliest data of program initiation (2/1/13) and patient baseline data and number of years elapsed between patient baseline date and subsequent follow-up date

Source: Coffin PO, Behar E, Rowe C, et al. Ann Intern Med. 2016.

OPIOID RELATED EMERGENCY DEPARTMENT VISITS BY RECIPIENT OF NALOXONE PRESCRIPTION AMONG PRIMARY CARE PATIENTS ON OPIOID THERAPY FOR CHRONIC PAIN*



Prescribing naloxone to 29 patients averted 1 opioid-related emergency department visit in the following year.

Source: Coffin PO, Behar E, Rowe C, et al. Ann Intern Med. 2016.

*In a population with a rate of opioid-related emergency department visits of 7/1000 person years.

Related research on ED utilization

Opioid OD ED Visits in MA	
	ARR (95% CI)
No implementation	ref
Low naloxone implementation (1-100/100k pop)	0.93 (0.80 - 1.08)
High naloxone implementation (>100/100k pop)	0.92 (0.75 - 1.13)

Source: Walley, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. BMJ. 2013.

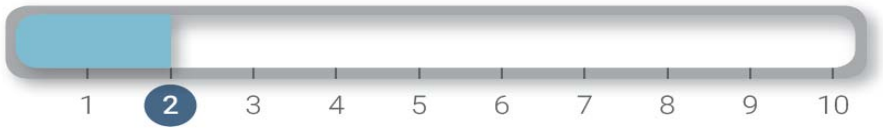
Demographics of Patients Offered Naloxone (N=60)

	Percent
Female	45%
Race/Ethnicity	
Black / African-American	55%
White	27%
Latino/Hispanic	8%
Other	10%

Source: Behar E, Rowe C, Santos GM, Murphy S, Coffin PO. Primary Care Patient Experience with Naloxone Prescription. Ann Fam Med. 2016

Characteristics of Patients Offered Naloxone

	Percent
Ever taken opioids not as prescribed	53%
Ever witnessed an overdose	53%
Previously received take-home naloxone	10%
History of overdose / bad reaction	37%
Overdose	*20%*
"Bad reaction" consistent with overdose	*17%*
Perceived risk of personal overdose	Low (2 out of 10)



Source: Behar E, Rowe C, Santos GM, Murphy S, Coffin PO. Ann Fam Med. 2016

Patient Perceptions and Disposition of Naloxone

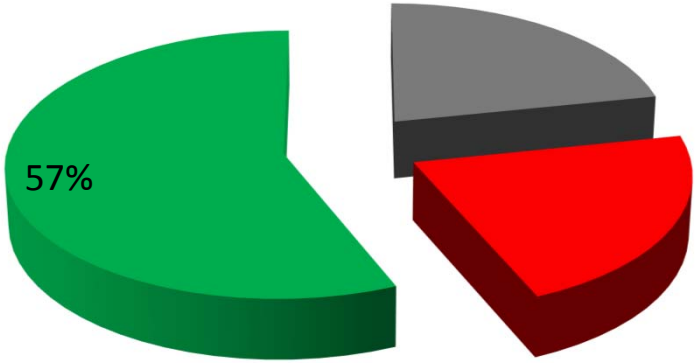
	Percent
Somewhat/very confident in ability …	
… of patient to use naloxone	86%
… of person patient trained to use naloxone	88%
Would want naloxone in the future	98%
Naloxone should be available to all or some patients with chronic pain	97%

Source: Behar E, Rowe C, Santos GM, Murphy S, Coffin PO. Ann Fam Med. 2016

Patient Reactions to Naloxone Offer

Neutral

Positive
- Benefits community
- Appreciated offer
- Increased trust/improved relationship



Negative
- Prescription unnecessary
- Felt judged by provider
- Scared

Source: Behar E, Rowe C, Santos GM, Murphy S, Coffin PO. Ann Fam Med. 2016

Contents lists available at ScienceDirect

Addictive Behaviors

journal homepage: www.elsevier.com/locate/addictbeh

Short Communication

No evidence of compensatory drug use risk behavior among heroin users after receiving take-home naloxone

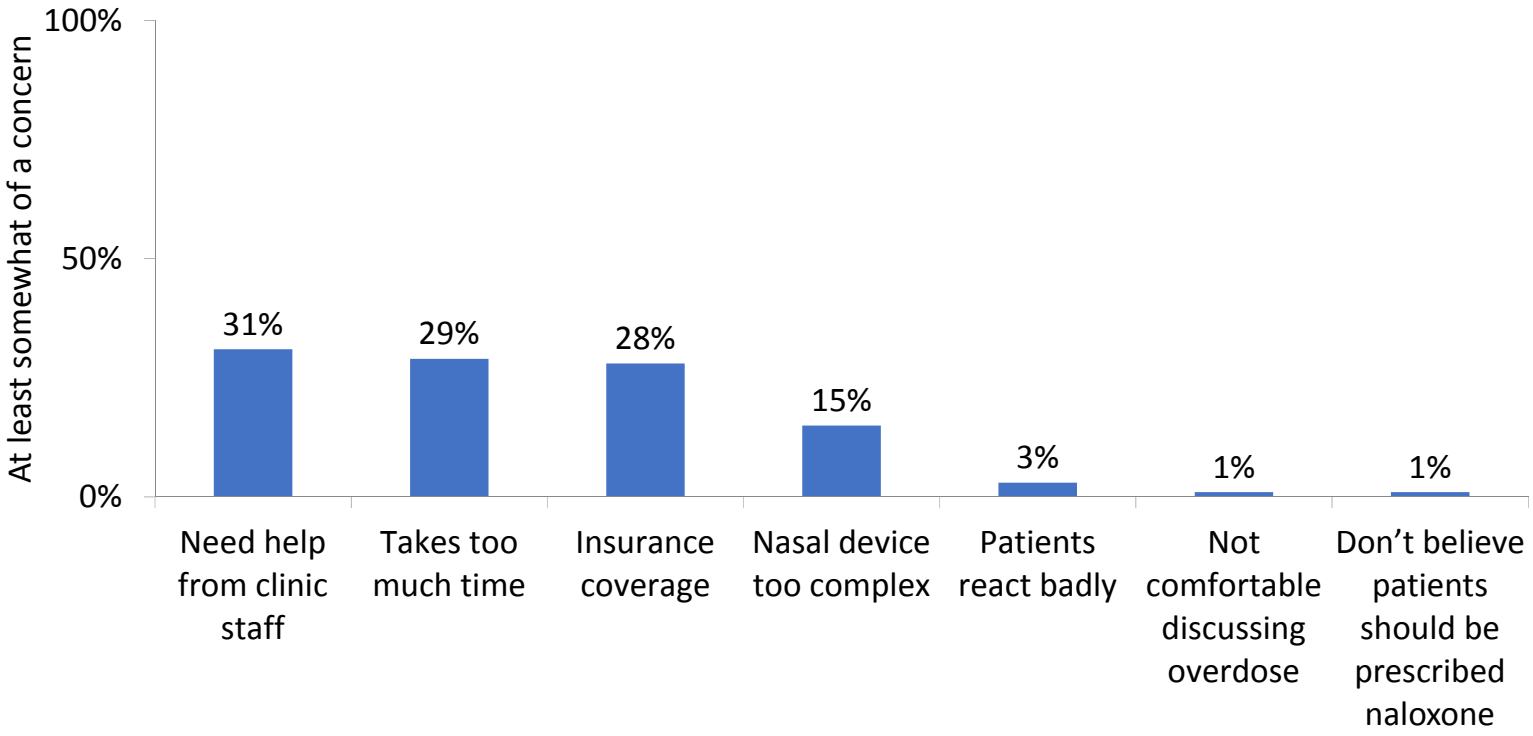
Jermaine D. Jones *, Aimee Campbell, Verena E. Metz, Sandra D. Comer

PCP Uptake and Acceptance of Naloxone Co-Prescribing Program (N=111)

	%
Prescribed naloxone (~6m)	79%
Likely to prescribe naloxone in future	
Very/Moderately	85%
Somewhat	13%
Not	1%
Effect on prescribing opioids	
Might prescribe less	23%
No effect	72%
Might prescribe more	4%

Source: Behar E, et al. Acceptability of naloxone co-prescription among primary care providers treating patients on long-term opioid therapy for pain. J General Internal Medicine. 2016

PCP Concerns with Prescribing Naloxone



Source: Behar E, et al. J General Internal Medicine. 2016

PCP Comments on Prescribing Naloxone

"I expected the decreases in deaths from overdose – but I hadn't thought about how this simple act of prescribing potentially lifesaving treatment has opened up other important conversations that have allowed me to provide better, safer and more compassionate care to my patients"

"The conversation about naloxone has changed the dynamic between discussions of harms and benefits."

Source: Behar E, et al. J General Internal Medicine. 2016

Naloxone Co-Prescribing Systematic Review

- 17 papers
- Willingness to prescribe increased over time
- Most studies implemented universal prescribing
- Most had prescribers providing education and take-home materials
- Challenges included prescriber knowledge about education
- Benefits included “resetting the culture around opioids”

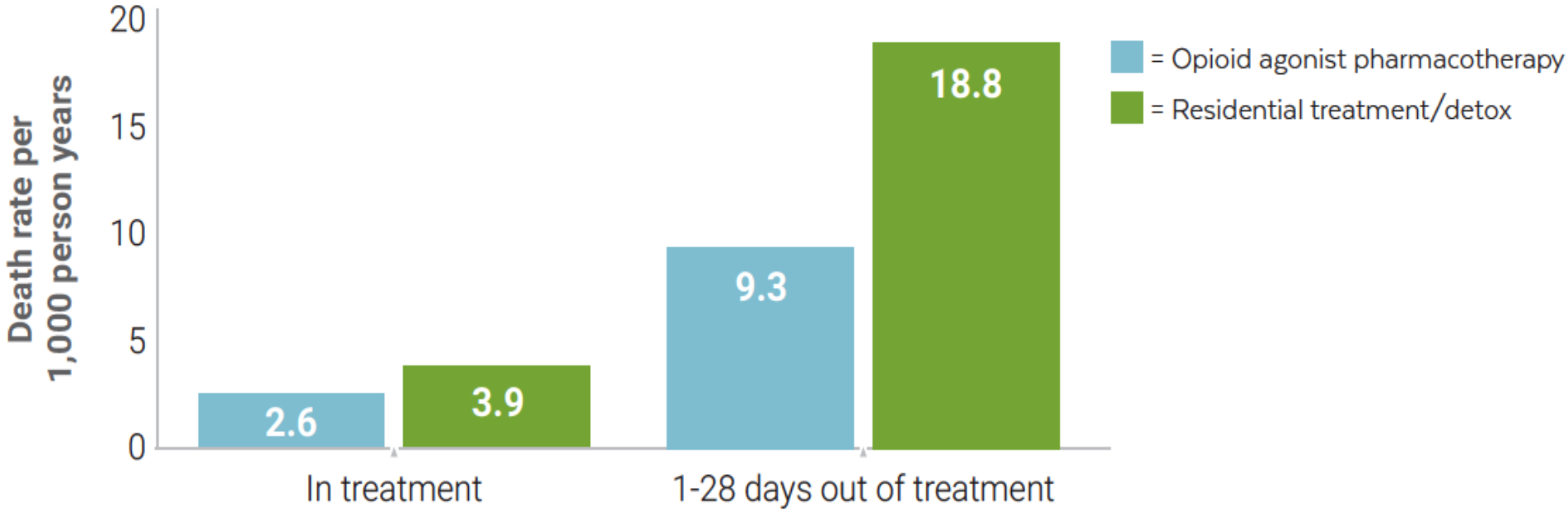
Behar, Bagnulo, Coffin. Preventive Medicine 2018

If naloxone supply is limited … who should get it first?

Predictors of Using Naloxone to Reverse an Overdose in a Community Distribution Program	Adjusted Odds Ratio
Use heroin	1.85
Use methamphetamine	1.71
Previously witnessed OD	2.02

Source: Rowe C, Santos GM, Vittinghoff E, Wheeler E, Davidson P, Coffin PO. Predictors of participant engagement and naloxone utilization in a community-based naloxone distribution program. Addiction. 2015;110(8):1301-1310.

OPIOID OVERDOSE DEATH RATE PER 1,000 PERSON YEARS AMONG 151,983 PEOPLE WITH OPIOID USE DISORDER SEEKING TREATMENT IN THE UNITED KINGDOM



Source: Pierce M, Bird SM, Hickman M, et al. Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England. Addiction. 2016;111(2):298-308.

Conclusions

- Naloxone co-prescribing is feasible and acceptable to patients and providers, even when using complex devices
- The term “overdose” is problematic for patients
- Naloxone co-prescribing may positively influence opioid use behaviors, patient-provider relationships, and the frequency of opioid-related ED visits
- Low-threshold distribution models remain the most powerful means to expand naloxone access, upon which the vast majority of data are based

Thank you!

PHILLIP.COFFIN@UCSF.EDU

Take-Home Naloxone Use in New Mexico

Joanna Girard Katzman, MD, MSPH

Senior Associate Director, ECHO Institute, Project ECHO

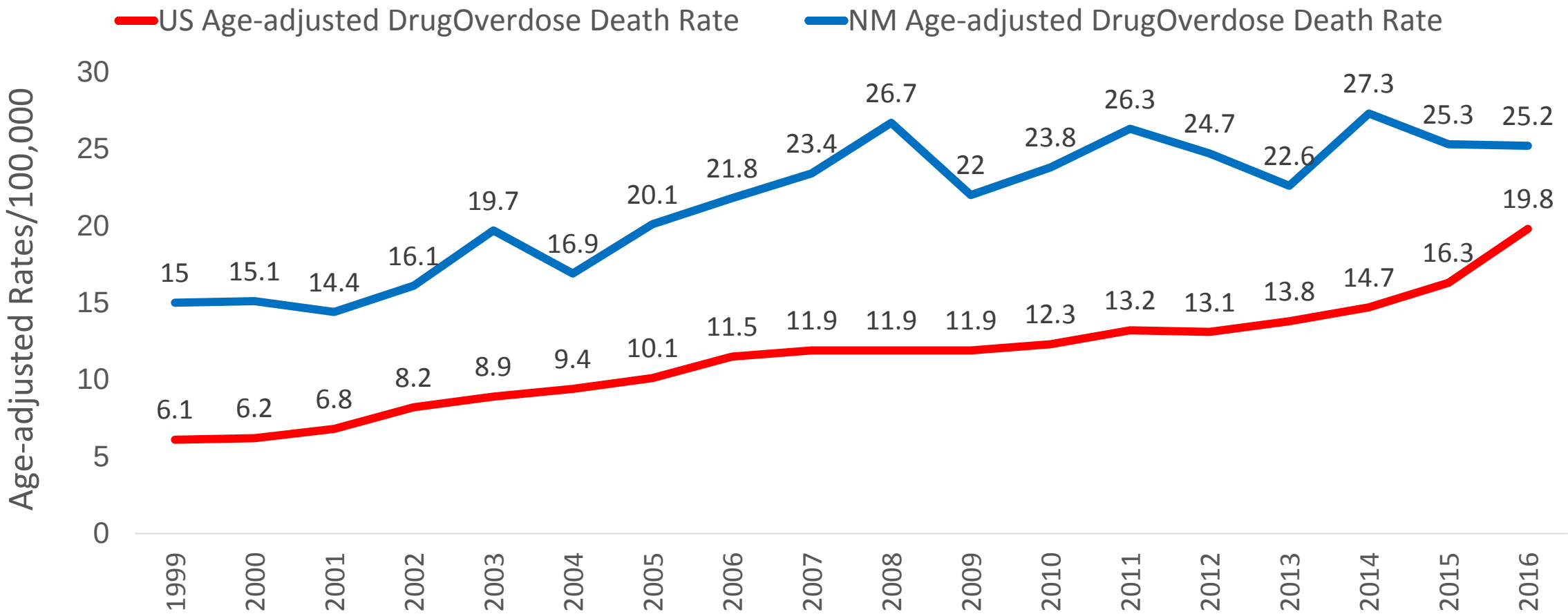
Professor, Neurology University of New Mexico School of Medicine, UNM Health Sciences Center

Albuquerque, New Mexico

Disclosure:

Small grant with Adapt Pharma

Background: US versus New Mexico Drug Overdose Mortality 1999-2016



Data source: CDC WONDER

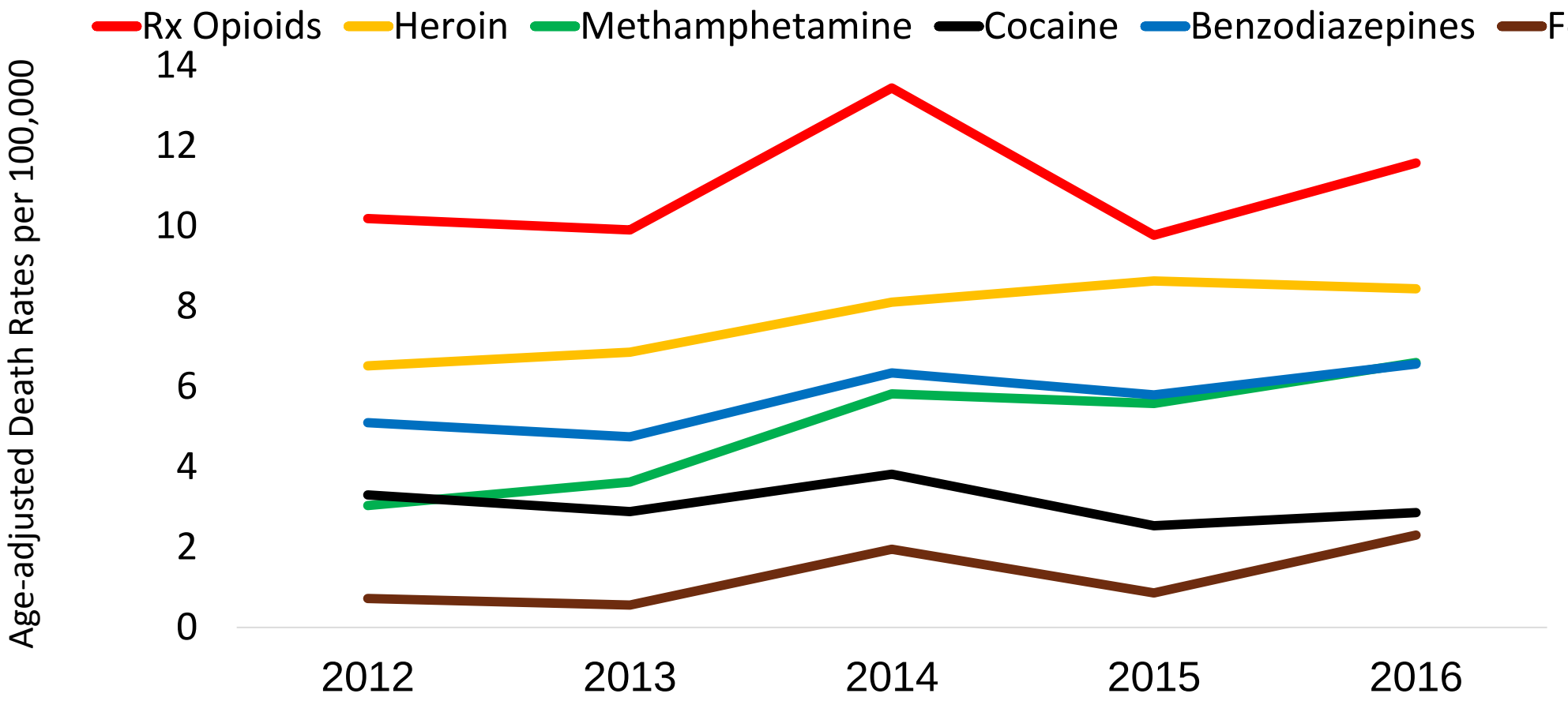
Drug Overdose Mortality by State 2005 vs. 2016

Drug Overdose Mortality by State: 2005		
Location	Drug Overdose Death Rate	Deaths
New Mexico	20.1	373
Utah	19.3	438
Nevada	18.7	457
Kentucky	15.3	638
Louisiana	14.7	661
Tennessee	14.5	872
Rhode Island	14.3	156
Arizona	14.1	794
Oklahoma	13.8	478
Florida	13.5	2,371
Pennsylvania	13.2	1,613
Washington	13.0	850
Colorado	12.7	608

Drug Overdose Mortality by State: 2016		
Location	Drug Overdose Death Rate	Deaths
West Virginia	52.0	884
Ohio	39.1	4,329
New Hampshire	39.0	481
Pennsylvania	37.9	4,627
Kentucky	33.5	1,419
Maryland	33.2	2,044
Massachusetts	33.0	2,227
Rhode Island	30.8	326
Delaware	30.8	282
Maine	28.7	353
Connecticut	27.4	971
New Mexico	25.2	500
Tennessee	24.5	1,630

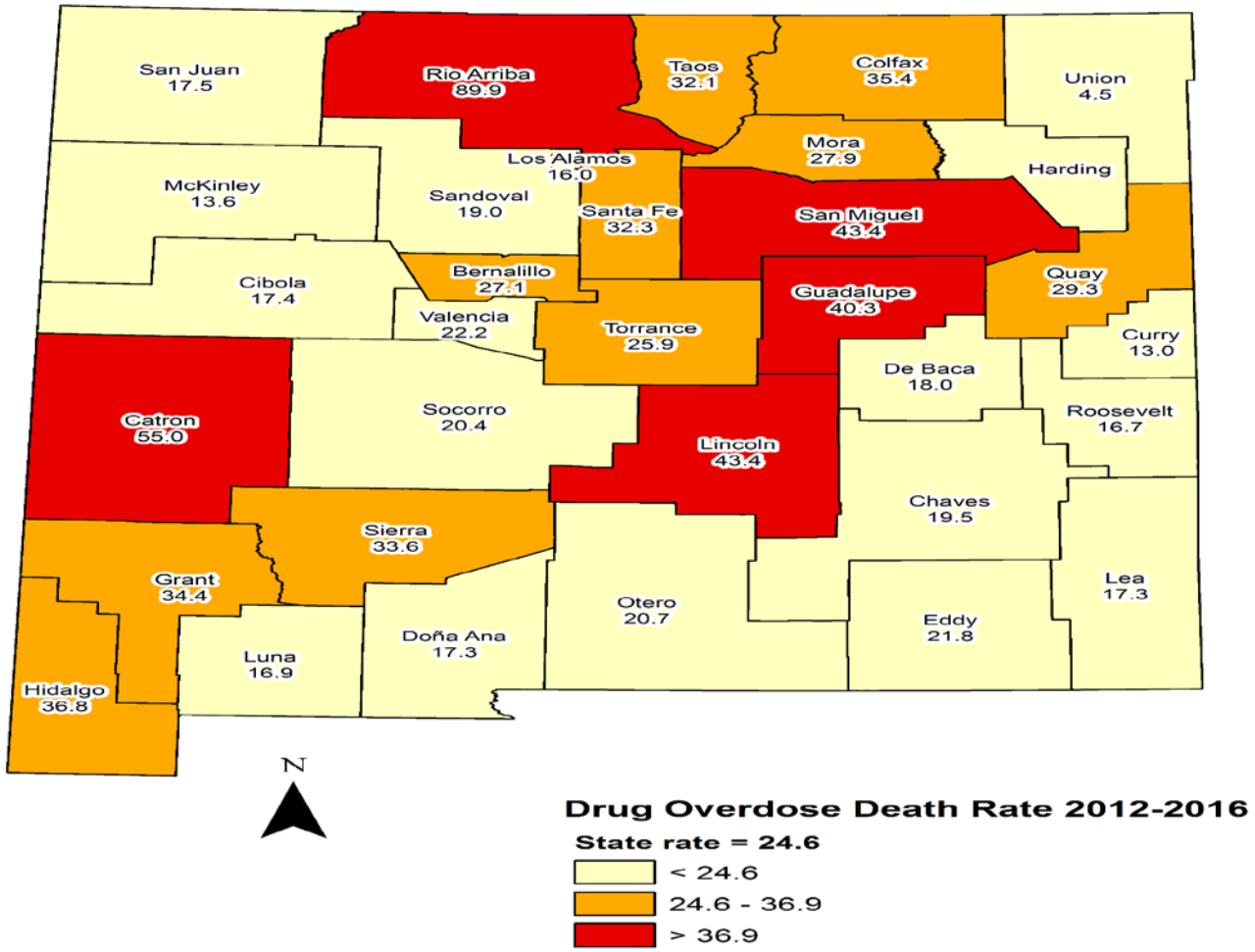
Source: https://www.cdc.gov/nchs/pressroom/sosmap/drug_poisoning_mortality/drug_poisoning.htm

Background: Drug Overdose Death Rates for Selected Drugs, New Mexico 2012-2016



Drug categories are not mutually exclusive
Rates are age adjusted to the US 2000 standard population
Source: Bureau of Vital Records and Health Statistics death data; UNM/GPS population estimates

Age-Adjusted Drug Overdose Death Rate by New Mexico County of Residence, 2012-2016



Rates (per 100,000 population) are age-adjusted to the

US 2000 standard population.

Source: Bureau of Vital Records and Health Statistics,

UNM/GPS population estimates

Bhatt S, Katzman JA, Duensing K, Martinez D, Swift R (2017) New Mexico Naloxone Legislation: Targeting Those Most in Need. J Drug Abuse. Vol.3 No.4:27.

Naloxone-Related Legislation in New Mexico

2001 Authority to Administer, Prescribe, Dispense, and Distribute Naloxone

2007 Good Samaritan Law

2014 Medicaid Coverage

2014 Pharmacist Prescriptive Authority

2016 Naloxone Standing Order

2017 New Mexico House Bill 370 - Mandates take-home naloxone, prescription for naloxone and opioid overdose education for:

- All patients in **Opioid Treatment Programs**
- **Inmates released with diagnosis of OUD**
- **Law Enforcement** agencies

UNM Pain Center
Universal Precautions Model for Naloxone Study

Study site and term: Conducted at University of New Mexico Pain Center from 2013-2015

Intervention: Opioid overdose education and take-home naloxone given to all patients using an opioid analgesic, regardless of amount

Hypotheses:

- Overdose risks are fluid
- Eventual recipient of naloxone is unknown
- Education can be short (10-15 minutes) and medication is safe

Takeda, Katzman, Dole, et al, Co-prescription of naloxone as a Universal Precautions model for patients on chronic opioid therapy: an observational study. *Substance Abuse*. 2016, 37:4, 591-596

Results of UNM Pain Center Universal Precautions Naloxone Study

Patient cohort: UNM Pain Center patients diagnosed with chronic pain *and treated with a chronic opioid (either by PCP or at UNM)*

Study participants: N=206, enrolled July 2014 - June 2016

Morphine equivalent dose:

- Mean: 122.3 (SD 134.6)
- Median: 90 mg/day

Participants who used take-home naloxone: 1 (no death was reported)

Takeda, Katzman, Dole, et al, Co-prescription of naloxone as a Universal Precautions model for patients on chronic opioid therapy: an observational study. *Substance Abuse*. 2016, 37:4, 591-596

The concept of

- very brief opioid overdose education (10 min)
- Take-Home Naloxone (vs. prescription)
- Universal Precautions for high risk groups (risk is fluid)

Study Design then used at the University of New Mexico Addiction Program

Naloxone Use within an OTP Setting: Prospective Cohort Study (at 3 months)

Table 1. Demographics and Medication Treatment		
Demographics	**n**	**%**
Sex		
Female	174	71.3
Male	70	28.7
Race		
Hispanic/White	154	63.1
Non-Hispanic/White	66	27.1
American Indian/Alaska Native	12	4.9
Black or African American	2	0.8
Asian	1	0.4
Not reported	8	3.3
Unknown	1	0.4
Age		
18-29	4	1.6
20-29	92	37.7
30-39	64	26.2
40-49	30	12.3
50-59	36	14.8
≥ 60	18	7.4

Table 1. Demographics and Medication Treatment		
Demographics	**n**	**%**
Medication Treatment		
Methadone	193	79.4
Buprenorphine	42	17.3
Naltrexone (oral or intramuscular)	6	2.5
No opioid replacement therapy	3	1.2
Companion Attendance		
Present	25	10.3
Not present	219	89.8

1- Study Demographics matched OTP population

2- Most study participants received overdose education *without* a companion

Katzman, Takeda, Bhatt. An Innovative Model for Naloxone Use Within an OTP Setting: A Prospective Cohort Study, *J Addict Med*, 2017

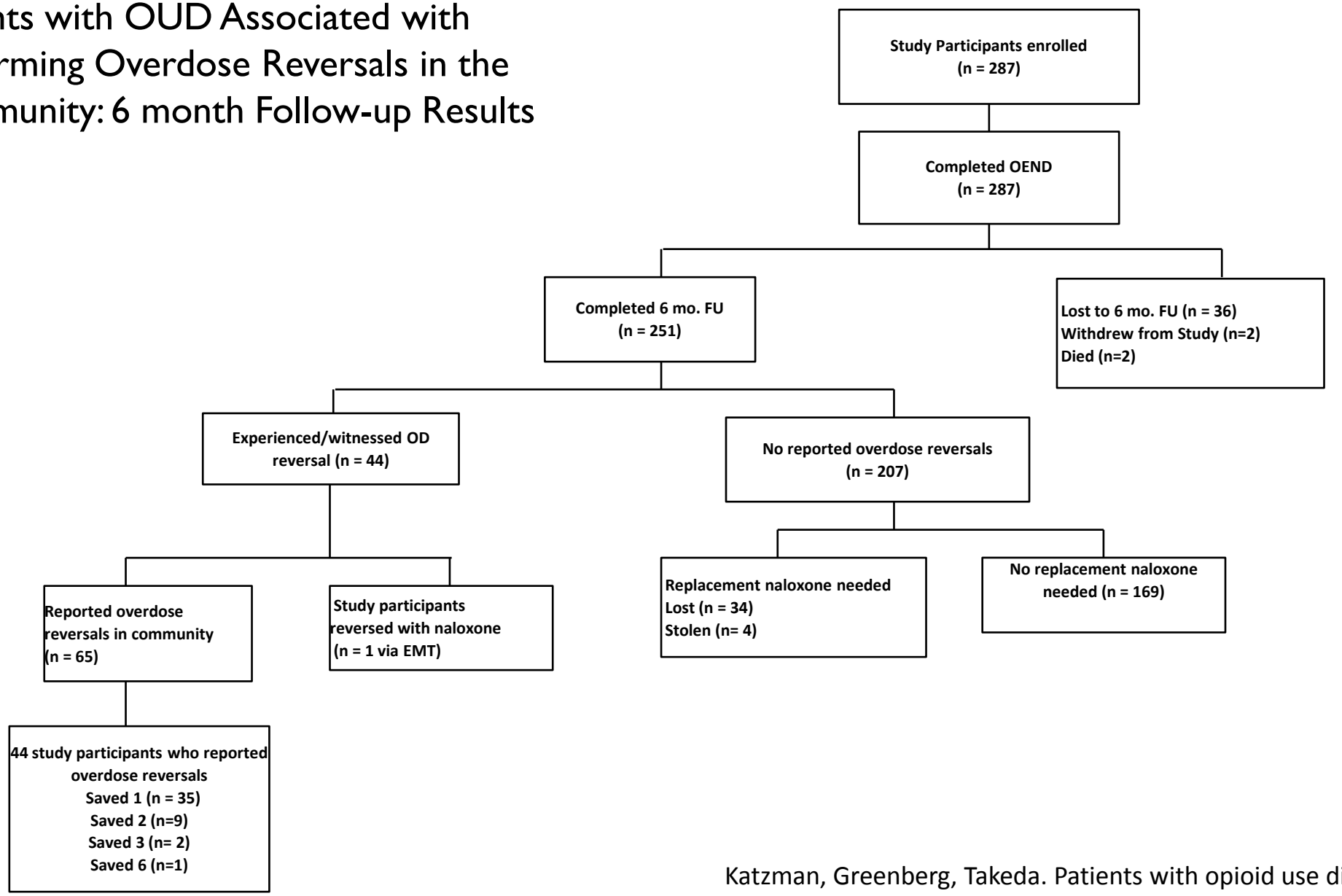
Prior Naloxone Prescriptions for Study Participants

- Fifteen (15) of the 244 study participants* (6.75%) received *prior* naloxone prescription from the UNM Addiction Clinic.

- Each of these 15 study participants denied traveling to the pharmacy to pick up their naloxone prescription.

*Katzman, Takeda, Bhatt. An Innovative Model for Naloxone Use Within an OTP Setting: A Prospective Cohort Study, *J Addict Med*, 2017

Patients with OUD Associated with Performing Overdose Reversals in the Community: 6 month Follow-up Results



Katzman, Greenberg, Takeda. Patients with opioid use disorder associated with performing overdose reversals in the community. *J Addict Med.* 2018

6 Months of Patient Enrollment: Naloxone Doses Used

TABLE 2. Variable Distributions Regarding Community Members Reversed with the Prescribed Naloxone

VARIABLE	n	%
Number of naloxone doses used		
One	28	43%
Two	35	54%
Three	2	3%
911 was called		
Yes	30	46%
No	35	54%
Relationship to study participant		
Acquaintance	5	8%
Family member	11	17%
Friend	36	55%
Significant other	4	6%
Stranger	9	14%

115 Community Overdose Reversals

80% of victims known to the responder

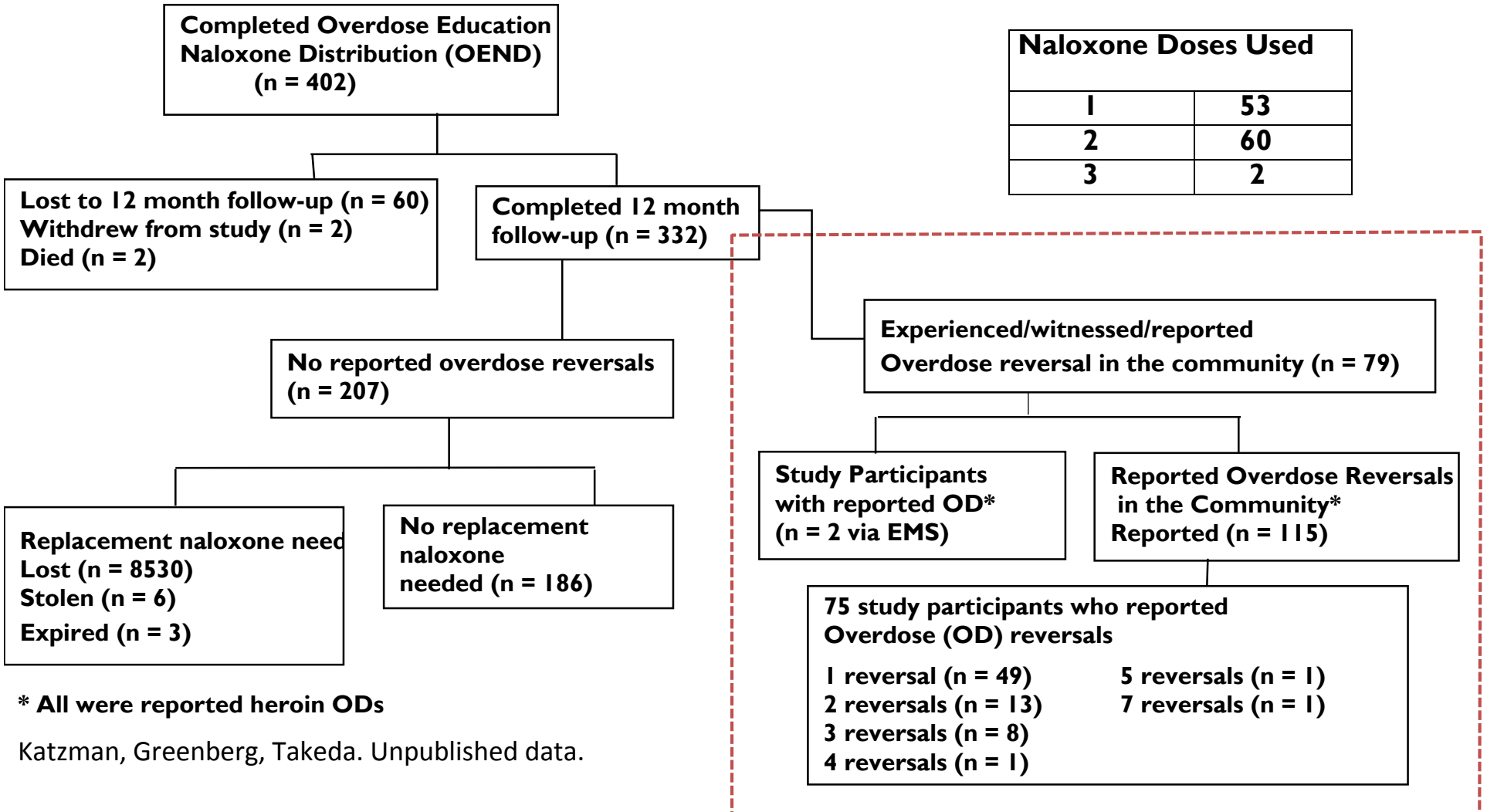
Katzman, Greenberg, Takeda. Patients with opioid use disorder associated with performing overdose reversals in the community. *J Addict Med.* 2018

Logistic Regression Analysis:
Patients with OUD Most Likely to Reverse Another Person (6 month data)

Characteristic	Odds Ratio
Younger Age (18-44)	2.64
Hispanic	2.93
Witnessed Prior Overdose	5.51
Have Been Reversed Before	3.07
Two or More Elicit Medications in UNM Toxicology Screen	4.59
Missing Toxicology Screen	2.98

Katzman, Greenberg, Takeda. Patients with opioid use disorder associated with performing overdose reversals in the community. *J Addict Med.* 2018

Patients with OUD Associated with Performing Overdose Reversals in the Community:
12-month Follow-up Results



Naloxone Doses Used	
1	53
2	60
3	2

*** All were reported heroin ODs**

Katzman, Greenberg, Takeda. Unpublished data.

Patients with OUD Associated with Performing Overdose Reversals in the Community: 12 month Follow Up Results:

- 115 Community overdose reversals
- 80% of victims known to the responder
- Naloxone Doses Used:

1 dose given for 53 reversals

2 doses for 60 reversals

3 doses for- 2 reversals

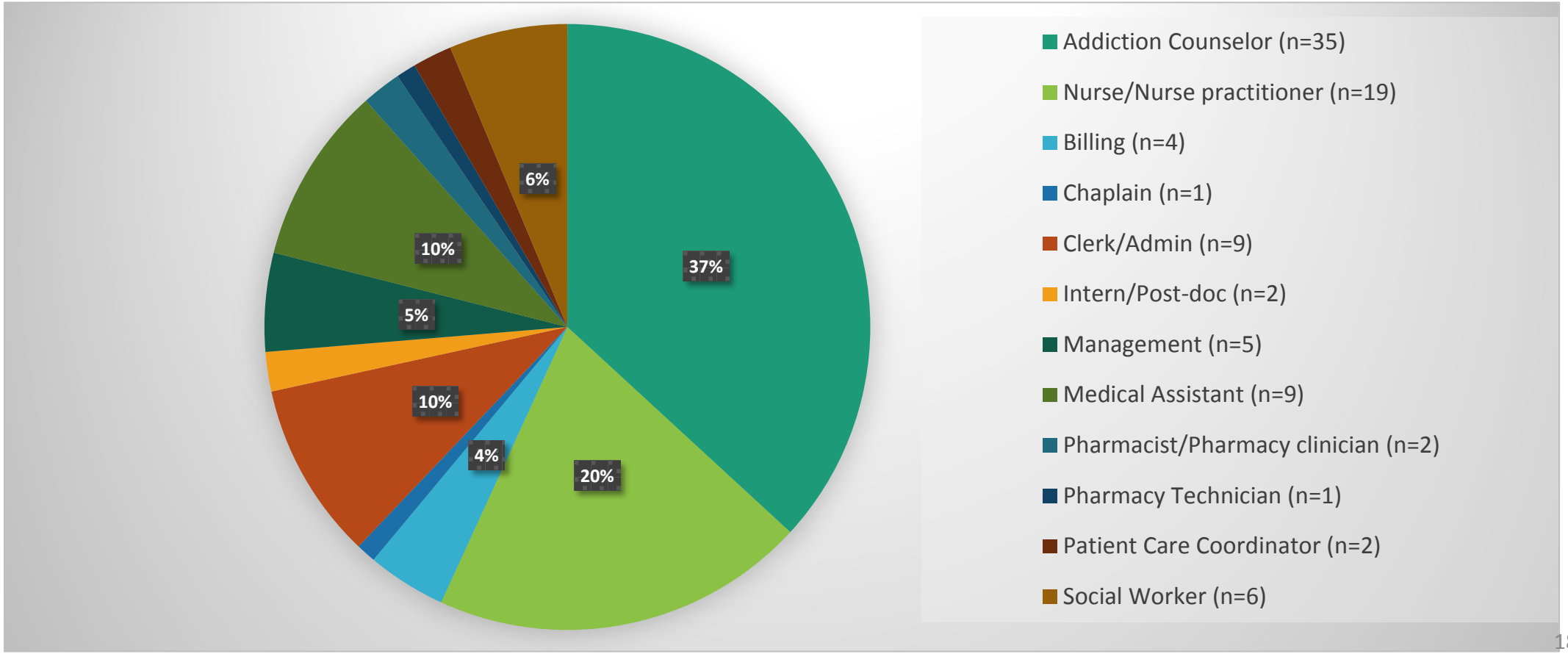
- All reversals reported to be heroin-related

Katzman, Greenberg, Takeda, Moya, Bhatt, unpublished.

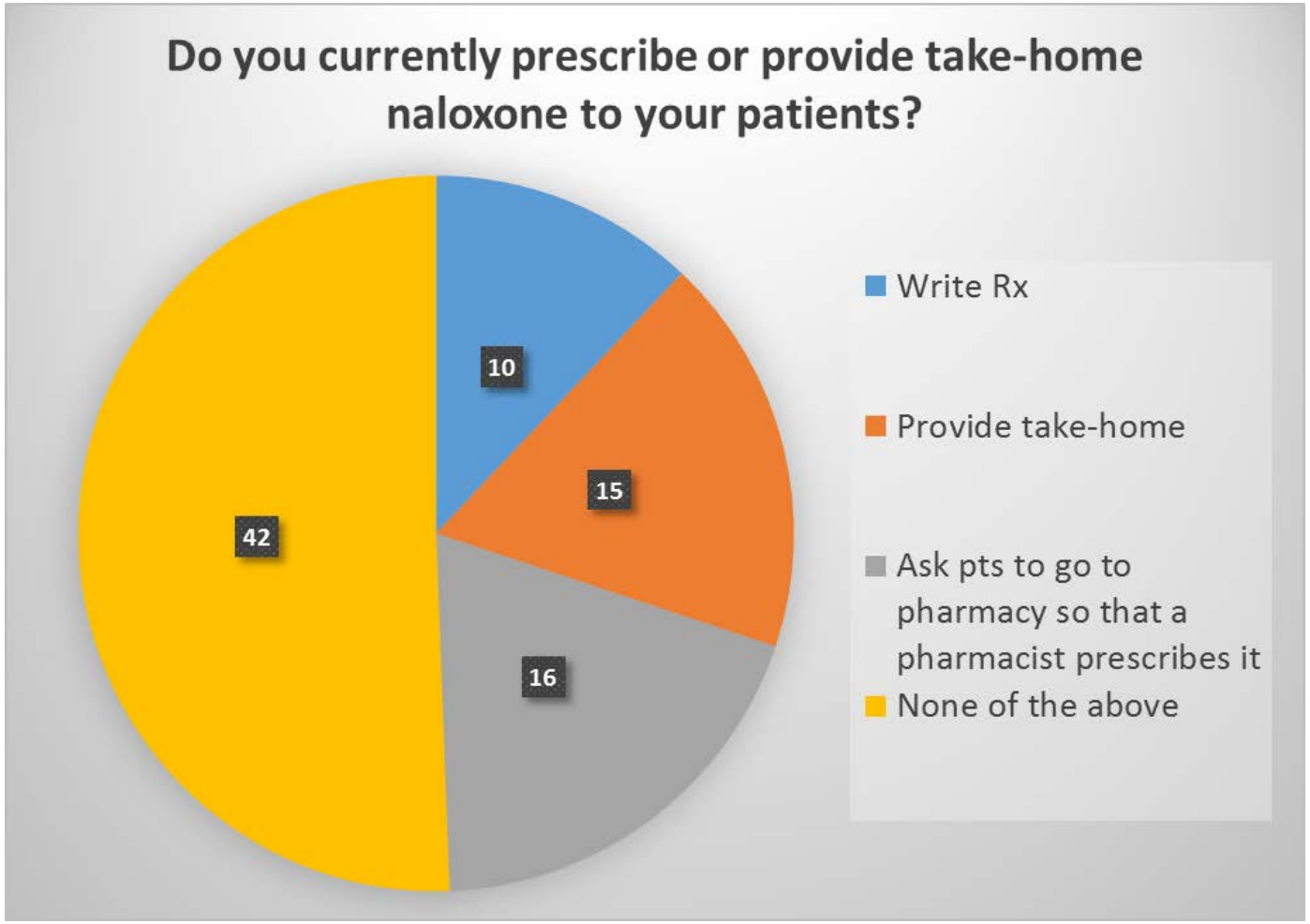
Barriers to Naloxone Prescribing:

Provider Survey Results from 9 NM Outpatient Treatment Programs

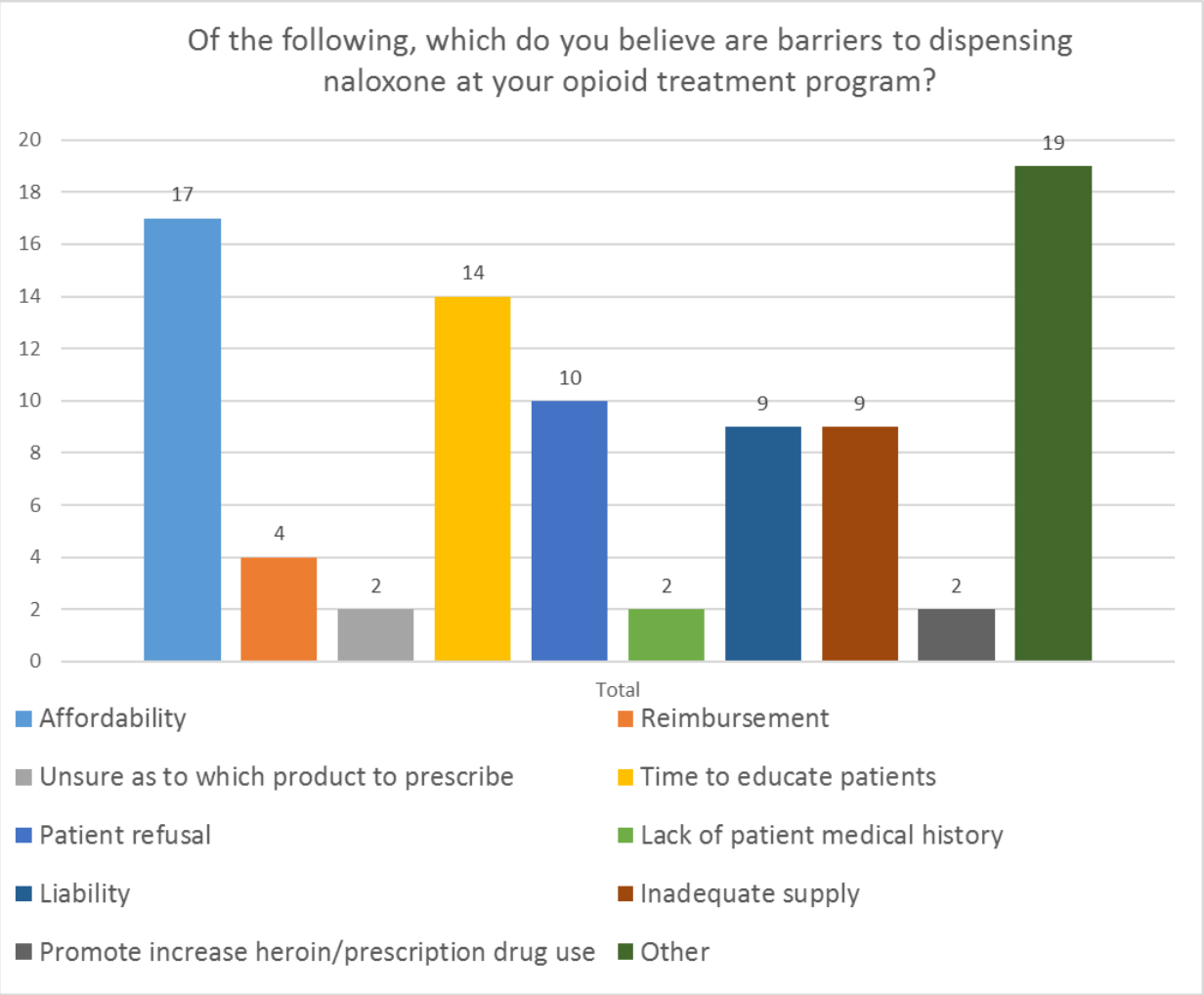
Survey Participants (n = 95)



Barriers to Naloxone Prescribing:
Provider Survey Results from 9 NM Outpatient Treatment Programs

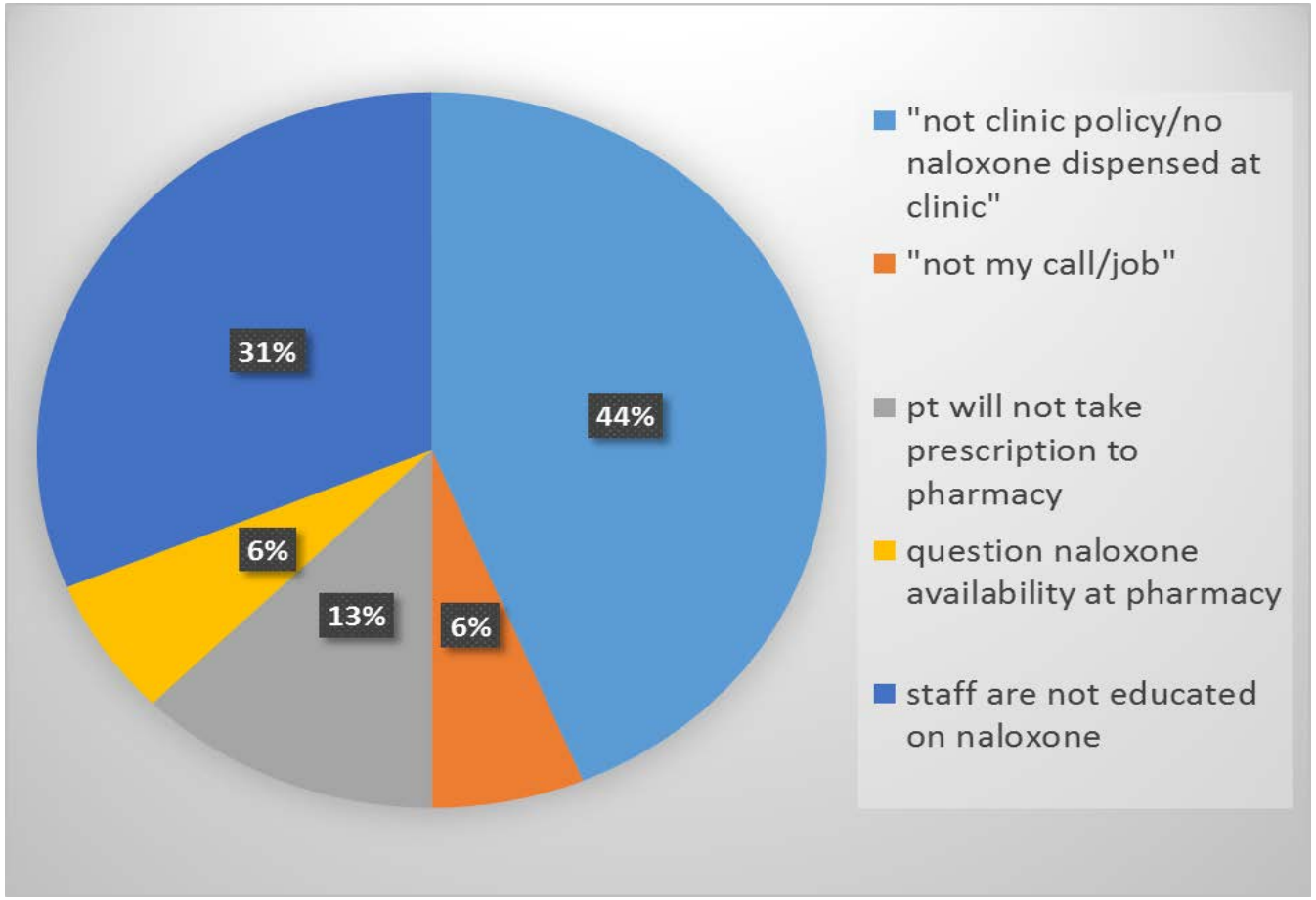


Barriers to Naloxone Prescribing:
Provider Survey Results from 9 NM Outpatient Treatment Programs



Barriers to Naloxone Prescribing:
Provider Survey Results from 9 NM Outpatient Treatment Programs

Other Barriers to Naloxone Prescribing (19% of respondents)



Naloxone Doses: Distribution and Reported Reversals in New Mexico's Harm Reduction Program, 2018 Q 1&2

	2018 Q1 & 2		
County	Naloxone Doses Dispensed	Reversals	People Trained
Bernalillo	576	249	803
Catron	6	0	0
Chaves	78	0	57
Cibola	62	0	2
Colfax	18	9	31
Curry	20	10	19
De Baca	4	2	2
Dona Ana	70	26	167
Eddy	98	28	78
Grant	40	20	49
Guadalupe	0	0	2
Harding	0	0	0
Hidalgo	0	0	1
Lea	10	4	15
Lincoln	4	2	6
Los Alamos	8	4	10
Luna	4	2	3
McKinley	0	0	0
Mora	0	0	0
Otero	4	2	20
Quay	16	4	10
Rio Arriba	396	191	529
Roosevelt	0	0	1
San Juan	50	21	27
San Miguel	60	14	66
Sandoval	38	18	60
Santa Fe	446	215	523
Sierra	6	3	10
Socorro	4	2	37
Taos	38	17	54
Torrance	0	0	2
Union	0	0	0
Valencia	4	2	6
Unknown/Missing	0	0	0
New Mexico	2,060	845	2,590

41 Percent (on average) of Naloxone Doses Dispensed were used in a opioid reversal

Reversal defined as patient outcome ok

County defined as where the recipient resides

These are not individual level data-

as the actual individual may have been reversed more than once

Naloxone Distribution in New Mexico

- New Mexico Department of Health Harm Reduction Services (Since 2001)
- Law Enforcement Agencies (68 agencies to date using naloxone in policing vehicles)
- Retail pharmacies (through 2017 - 79% of New Mexico outpatient pharmacies have dispensed naloxone)
- Behavioral Health Services Division-Office of Substance Abuse Prevention (BHSD-OSAP): 3 funding streams, 2 federal and 1 local.

Lessons Learned in New Mexico So Far

1. Take Home Naloxone successful in reversing community members if given to patients at opioid treatment programs
2. Targeted Naloxone distribution through Harm Reduction programs (syringe exchange programs and other key sites) critical for overdose reversals
3. Correctional Facilities now providing take-home naloxone and opioid overdose education to inmates released with OUD- (robust data not yet available)
4. Over 68 Law enforcement agencies, including the BIA, abiding by the House Bill 370, carrying naloxone in all their police cars.
5. Barriers still exist in mandating Take Home Naloxone to some of the OTPs throughout New Mexico

Development, Manufacturing, and Commercialization Costs for Naloxone and Other Nasal Sprays

Daniel Wermeling, Pharm.D., FCCP, FASHP

Emeritus Professor, University of Kentucky College of Pharmacy

CEO, AntiOp Inc.

Disclosures

- Refer to Meeting Conflict of Interest Statement
- All naloxone related assets of AntiOp and my former naloxone assets are now owned by other companies
- I have no financial stake in any naloxone companies or products
- I do not consult for any companies in the naloxone field
- This presentation is a general outline of single-dose nasal spray product cost of goods ***and costs of a start up company commercializing its first product***
- I do not rely on any proprietary information of other parties. I do rely on 25 years of experience developing single-dose nasal spray products and startup companies

AntiOp Partnered with Indivior to Market Nalscue™

- Aptar mono-dose device
- Lower naloxone concentration
- Two sprayers per dose (one per nostril)
- An anti-microbial preservative included in the formula instead of “sterile” product

FRANCE:

2016: Authorization for Temporary use

2017: Approved

What are the Components of Product Cost?

Three Big Buckets

1. Development costs – an investment typically with contractors
2. Product Manufacturing and Distribution
3. Operational costs at two levels:
   - Corporate direct research expenses
   - Corporate operations

What are the Components of Product Cost?
Of the three…

1. Development costs – an investment
2. Product Manufacturing and Distribution
3. Operational costs at two levels:
   - Research and Development
   - Corporate operations

Who will develop alternate naloxone formulations?

- BIG Companies? – **No**
- Start-up, Small, Medium, and Generic Companies – Yes

- **Marginal corporation cost per product** is greater than in a large company

Cost to Develop, Cost to Produce, Cost to Distribute:

- $ 25 Million over 5 years as initial **at-risk investment cost**
- **Amortize investment and operational/pre-revenue costs into a per unit basis if commercialized**
- Inverted Pyramid of expenses – Expenses increase with progress
- Research and Development – Early development is cheap while later stages are expensive

Cost to Develop, Cost to Produce, Cost to Distribute:

- Evaluations **required** for New Drug Application
    - **Active** ingredient: non-clinical (**animal**) pharmacology/safety **summary**
    - **Inactive** ingredients: Non-clinical (**animal**) pharmacology/safety **summary**
    - **Human pharmacokinetics**
    - **Pediatric** population evaluations
    - **"Human factors"** studies (can potential patients follow the instructions?)

Cost to Develop, Cost to Produce, Cost to Distribute:

- **FDA User fee** for NDA submission (in excess of $2.5 million)
- **Post-approval FDA-required studies** (post approval commitment studies)

Cost to Develop, Cost to Produce, Cost to Distribute:

- **Product development**
  - Select appropriate *inactive* ingredients with naloxone
  - Select appropriate device
  - Testing formulation/container interactions
  - Testing in production and post-production stability
  - Batches: Research, Engineering and 3 Commercial scale batches
  - Compliance and Quality Testing/documentation
  - CMC section for NDA filing
  - Continued stability testing for 2-3 years on R & D batches made and many commercial batches
  - Purchase product supplies/components for commercial manufacturing
  - Take risk by manufacturing launch/commercial supply before FDA approval
- **Sterile products and nasal spray geometry testing are expensive**

Cost to Develop, Cost to Produce, Cost to Distribute:

- First 250,000-unit commercial batch:
- **Cost** of **naloxone hydrochloride**, like most off-patent drugs, is **immaterial**
- $ **3.5 million** for sprayer components acquisition, formulation materials, aseptic sprayer preparation, assembly of sprayers and labelling
- $ **Up to 1 Million** for release testing and 2-year controlled storage and stability testing
    - Physical, chemical, microbiological, and spray pattern physics tests at 8-10 time points thru shelf life

Cost to Develop, Cost to Produce, Cost to Distribute:

- Of the first **250,000 units**:
  - 25,000 Units (10%) retained and dedicated to QC testing and Stability testing (yield = 225,000 units) over 2-3 years
- Secondary and tertiary packaging, package insert and patient instructions
- Shipping, insurance, returns, rebates, damaged or expired product
- At this scale, ex-factory, could easily be **$20-30/commercial package**

Cost to Develop, Cost to Produce, **Cost to Distribute**:

Distribution is not a free service

- **Each vendor in the chain** before and after manufacturing adds cost
- Final vendor: A Pharmacy
- Royalty to Patent Holder (maybe 5- 10% of commercial sales)
- Managing multiple purchase contracts at various price-points below
- FDA Annual Product fee ($250,000/product strength/year)
- Customer Service
- Medical Information Staffing and responses
- Capture of Safety events, creating safety reports, submission to FDA
- FDA annual reports: safety events, chemistry changes, post-marketing status commitments

Startup and Small Company **Operations** Costs

- Rent, building(s), maintenance, utilities, taxes and fees
- Employees for all required functions (internally or outsourced)
- Medical information and marketing
- Pharmacovigilance
- Compliance/Quality Assurance
- Insurance (product liability, workers comp., lawsuits, director and officer, etc.)
- Patent litigation if a generic entrant
- Purchasing, finance and accounting
- Attorneys
- IT/computing
- Financial and SEC management if there are equity investors and or debt instruments
- Bankers
- Interest on debt, etc. – Cost of capital

Circling Back

- **Do we have societal success with naloxone products?**
  - **Adequate distribution for the need?**
  - Why not? High Cost and low volume versus the reverse?
  - **Do costs impact success?**
  - Are other policies impacting success?
- If no, is the cost of the technology and the build up too great?
- Can the cost of current technology have cost curve bent downward with high volumes?
- Thought experiments!!
  - If consumer purchase price product specification of $ 20 was set *a priori*, what technology can satisfy this price specification?
  - How can we make it rain naloxone nationwide?

Potential Solutions (1) – Alternative products

- Use a **cheaper technology** – Example: Blow-fill-seal with a preserved formulation.
- ***Non-sterile is cheaper***
- Are two **doses**/pack *really* necessary?
- Extend shelf-life
- ***What would FDA accept?***

Potential Solutions (2) – FDA

- FDA could add naloxone products to list of products eligible for **priority review voucher,** as for neglected tropical diseases, rare pediatric diseases. (These areas now successfully seeing increased attention and drug development/commercialization.)

https://priorityreviewvoucher.org/

- FDA could eliminate nasal spray pattern geometry requirements
- Approve preserved versus aseptic products
- FDA could trim post-approval commitment studies required
- FDA could encourage preserved, non-sterile options
- Eliminating User Fee for naloxone: saves over $ 2.5 million

Potential Solutions (3) – OTC? Developers?

- Rx to OTC ***increases access***
- Rx to OTC ***does <u>not</u> decrease cost*** to produce <u>nor</u> decrease corporate costs or overhead (only removes pharmacy)
- Rx to OTC **may cut insured persons off their insurance support**, unless other changes made
- Therefore, is cost still a barrier to access?
- Non-Profit status may help if investment comes from gifts/donations, but production, distribution and operations remain. (You have to generate a profit to forego one)

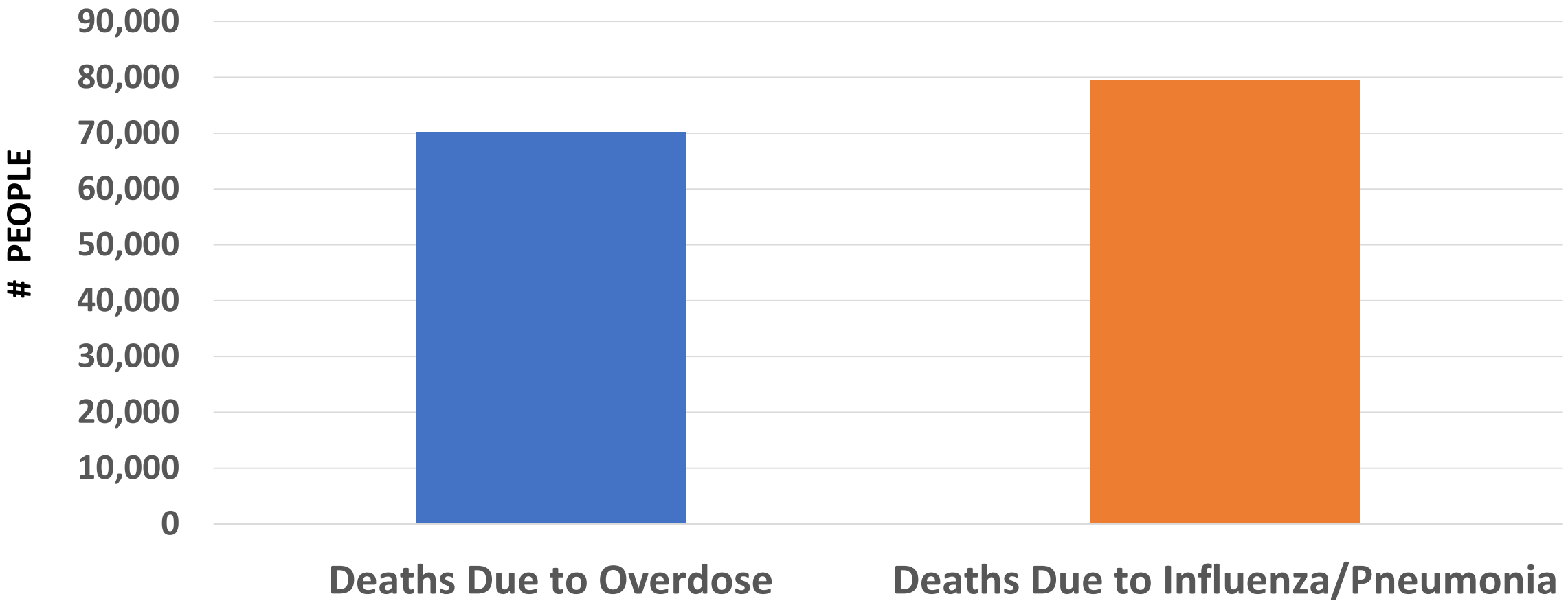
Potential Solutions (4) –Purchase Commitment

- What would the unit cost be if there was a commitment to purchase **10 million units**, or larger volume, annually?
- Governments (federal, state and local) work together to establish production quotas and negotiate price on much higher volumes. Industry can then respond but **they need Purchase Orders**!! Both sides have to make a commitment so production costs covered and product is available for distribution.
- Flip business model to **high volume –> lower cost**, from the reverse of what we have today

Potential Solutions (5): Vaccine Model for Health Care Delivery and Finance?

- We use **public health catastrophe terminology** when describing the issues
- We do not systematically use these methods broadly, in this case, especially in rural circumstances, and diffuse populations
- Example – **Influenza vaccine** and bio-weapons national defense
  - CDC works with the 5 producers of flu vaccine to design the antigens for the injection
  - These companies have a partial built in purchase because all levels of government are purchasers. Influenza vaccine is covered by insurance or patients have a very low co-payment. It is a low-cost product.
  - **Volume keeps costs down. (>160 Million doses influenza vaccine/year)**
  - **ASPR/BARDA funding**

U.S. Deaths in 2017 (or 2017-2018 Flu Season)



Potential Solutions (5): Vaccine Model for Health Care Delivery and Finance?

- Another thought experiment:
  - What would we do, how would it work, if a **nasal Ebola vaccine** was available and needed for an emergency North American prevention/treatment program?
  - What would it cost and how is it covered?

Conclusions

- **Some cost issues may be addressable**
- Stake holders will need to have **frank conversations** about organized Purchase Order agreements to increase volume to have an impact. Refills will be frequent and need to be accounted for in production. Think **25 million** units initial order!
- **New and cheaper technology** for mass distribution should be considered. Non-sterile products are cheaper to make with no sterility testing. Nasal spray physics testing requirements adds no value but adds cost
- Could one argue, through Rx human factors study results, FDA has the data for **OTC?** But, can the business model be sustained, or is cost the same? Beware of a race to the bottom, like what we had for naloxone injection, and only 2 manufacturers remain
- This presentation is an educated **opinion** and other points of view certainly exist

Thank You!

See Appendix for Additional Slides

Daniel Wermeling, Pharm.D.

Telephone – 859-221-4138

Email: dpwermeling@gmail.com

We Have Had Sub-optimal Naloxone Commercialization

- Insufficient Distribution to Have an Impact:
  - ~ 25 Million units/year needed to have impact
  - 1 to 1.5 million units distributed last year
- FDA User Fees are expensive
- Distribution (not cost) impaired by Rx status
- Standard of Care not articulated or adopted yet
- Do purchasers have an ability to pay? Why not?
- Insurance benefits are inconsistent
- Does not fit traditional health care finance and delivery for most of product released

Hypothetical Cost Build For A Commercial Unit Package (Assumes a Certain Volume and Amortization Time)

- **$ 25**: Direct production cost for one saleable unit
- $ 50: $ 25 **+** $ 25 for direct research and development
- $ 90: $ 50 **+** $ 40 for corporate operations
- $ 100: $ 90 **+** $ 10 for Patent holder royalty & price at wholesaler level
- $ 115: $ 100 **+** $ 15 – Shipping, insurance, wholesale mark up, and pharmacy acquisition cost
- **$ 135**: $ 115 **+** $ 20 – **Retail pharmacy transaction with small or no patient co-insurance charge**

Additional factors

- First years are unlikely to recoup investment, product, operational and investment costs
- Remember, you are operating at the starting line with a $ 25 Million development and $ 5 Million first batch embedded cost and 1-2 years of operating loss
- So, the final story is entirely dependent on sales, meaning number of units sold over time. Can enough units be sold at the price indicated to satisfy all the product, corporate, investment and market demands? What is the sales volume break-even point for the company at each of the three levels? When in the commercial cycle does this occur? These determine willingness for new manufacturers to enter the market.

Narcan® Distribution Collaborative

Expanding Access in Hamilton County, Ohio and the Impacts

By

Tim Ingram, Health Commissioner

Hamilton County Public Health

Cincinnati, Ohio

HAMILTON COUNTY PUBLIC HEALTH

PREVENT. PROMOTE. PROTECT.

ACCREDITED HEALTH DEPARTMENT • PUBLIC HEALTH ACCREDITATION BOARD • PHAB Advancing public health performance

NDC NARCAN DISTRIBUTION COLLABORATIVE

Credits

- Shawn A. Ryan, MD, MBA-BrightView Health
- Michael Lyons, MD, MPH – UC-Dept of Emergency Medicine
- Adapt Pharma-Emergent BioSolutions
- Five Health Care Systems and their Foundations
- Interact For Health and Deaconess Foundations
- Hamilton County Heroin Coalition—Bd of County Commissioners

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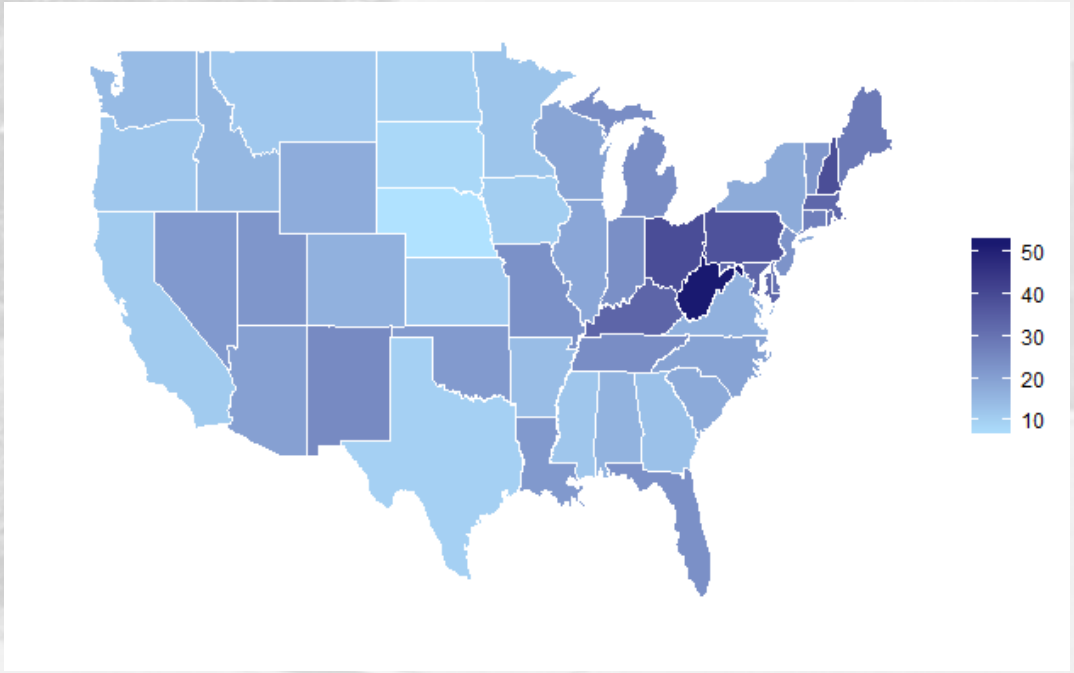
NDC NARCAN DISTRIBUTION COLLABORATIVE

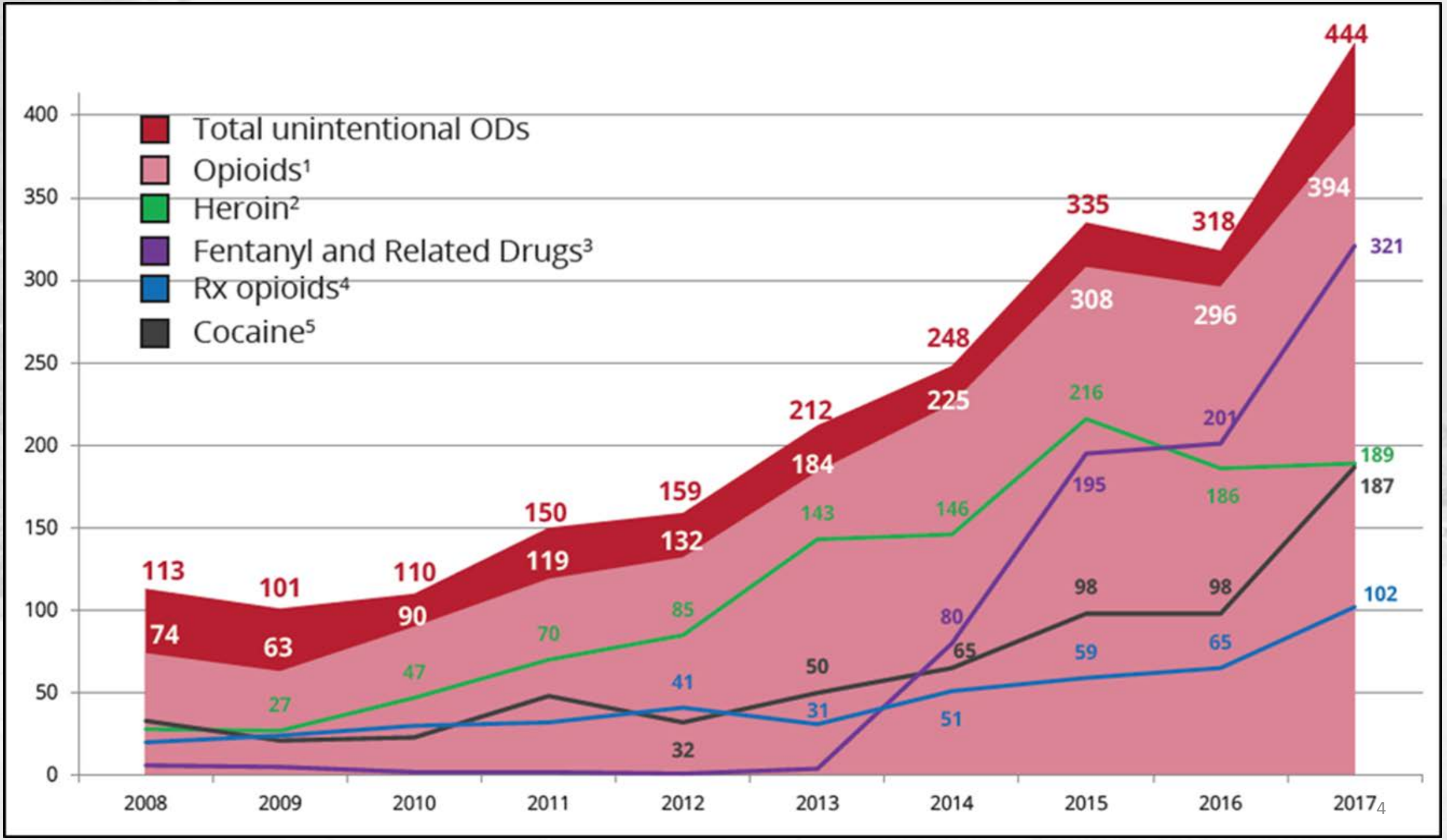
Background



- US age-adjusted overdose rates in 2016, by state (per 100,000 population):
- Ohio is 2nd (39/100,000; 31% increase in 2016)
- Kentucky is 5th (34/100,000; 12% increase in 2016)
- Indiana is 15th (24/100,000; 23% increase in 2016)
- All three states had statistically significant increases in overdose deaths from 2015—2016

**United States Center for Disease Control and Prevention (CDC)*
https://www.cdc.gov/drugoverdose/data/statedeaths.html

HAMILTON COUNTY PUBLIC HEALTH
PREVENT. PROMOTE. PROTECT.


Total unintentional ODs
Opioids[1]
Heroin[2]
Fentanyl and Related Drugs[3]
Rx opioids[4]
Cocaine[5]
400
350
300
250
200
150
100
50
0
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
113
101
110
150
159
212
248
335
318
444
74
63
90
119
132
184
225
308
296
394
27
47
70
85
143
146
216
186
189
41
31
51
59
65
102
32
50
65
98
98
187
80
195
201
321

Primary Goals:

A. Rapidly and substantially increase distribution of 12,500 cartons (25,000 doses) of Narcan® (naloxone) throughout the community.

B. Reduce by >50% both the number of fatal opioid overdoses and those resulting in intensive care unit (ICU) admission.

Primary Outcomes Measures:

1) Number of naloxone doses distributed.
2) Number of naloxone doses administered.
3) Number and proportion of opioid overdoses that result in death or ICU admission.

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Advancing public health performance

NDC
NARCAN DISTRIBUTION COLLABORATIVE

Table 1. Naloxone provided in Hamilton County, October 1, 2017 thru September 30, 2018

	Total	Current (Sep-18)	Average per Month	Peak Month
	N	N	Median (IQR)	N
NDC NARCAN® cartons, take-home use	10,711	676	926 (661-1,148)	1,718
NDC NARCAN® cartons, 1st responder administration	406	0	6 (0-73)	120
Non-NDC Project DAWN NARCAN® cartons*	84	15	12 (0-15)	25
Non-NDC, 1st responder administration NARCAN® cartons	1,002	27	54 (26-126)	267
Prescriptions for naloxone (any formulation)	2,531	215	211 (163-239)	319

** Project DAWN distribution data for Hamilton County is available from January thru September 2018. Project DAWN is a community-based naloxone distribution program providing additional naloxone to individuals throughout the region, on a much smaller scale than NDC.*

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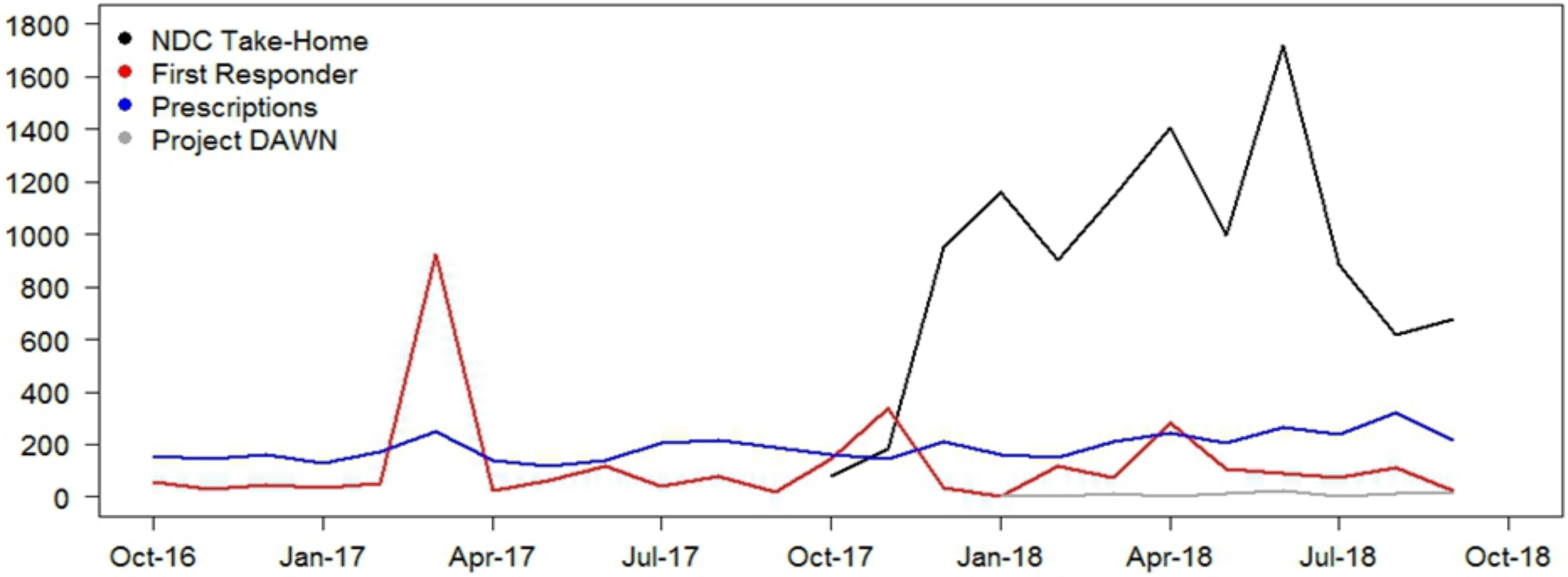
Naloxone Distributed in Hamilton County*



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Residential Zip Codes of Individuals Distributed NARCAN® Cartons in Ohio, Kentucky, and Indiana (N = 6,285)

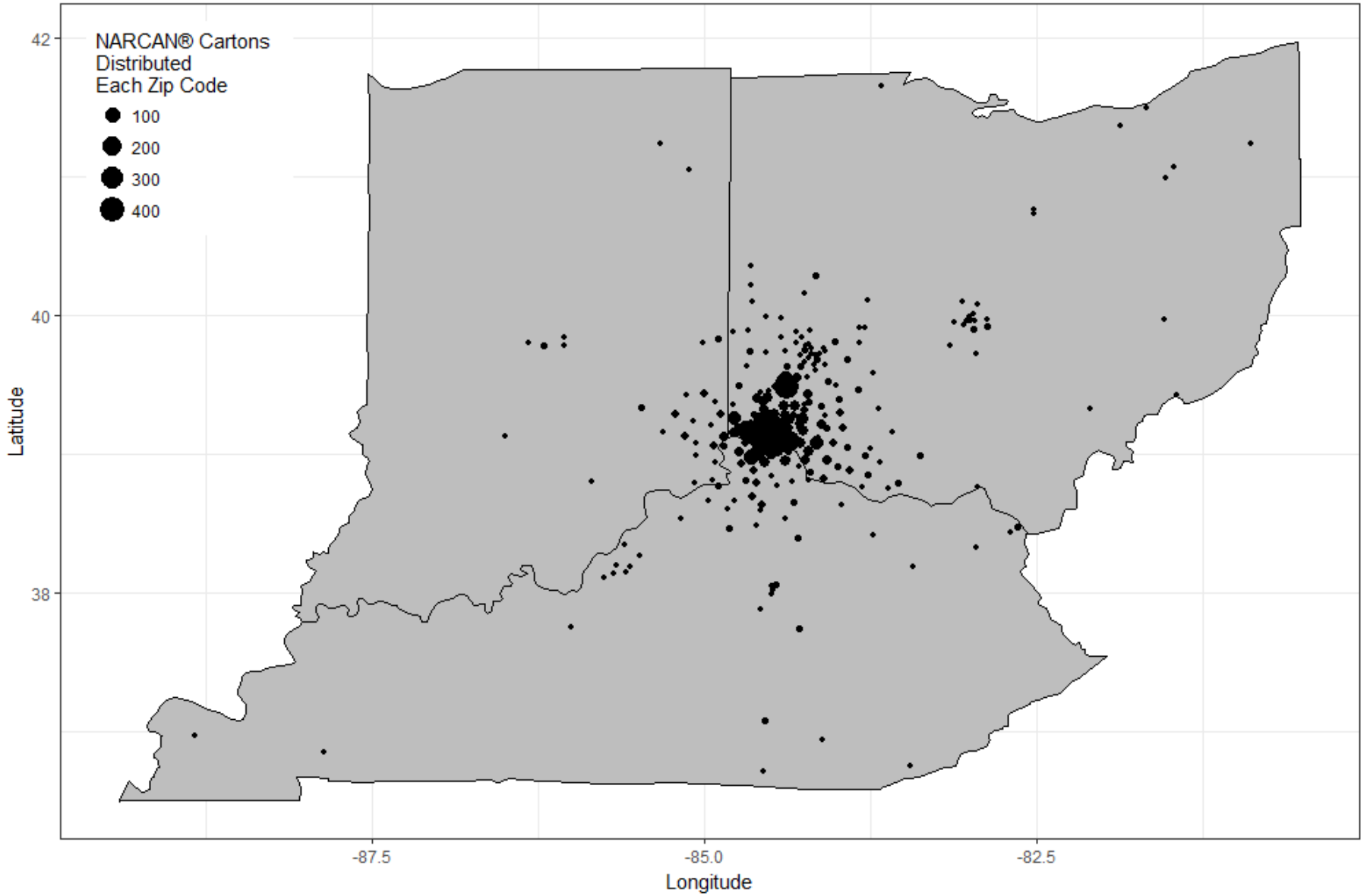

Table 2. Description of data collection for NDC take-home NARCAN® distribution to individuals

Data Collection Type	N
Total cartons distributed to sites	**11,117**
Cartons with individual recipient data expected	10,353
Cartons with individual recipient data received	8,288
Cartons with individual recipient data not expected*	764
Types of individual data received	**8,288**
Survey (shown in Tables 3—6, and Figure 2)	8,100
Medical records only (shown in Table 3)	188

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Table 3. Types of sites where individuals were distributed NDC take-home NARCAN® cartons (N = 8,288)

Site Type	Distributes Cartons to…	N	(%)
Syringe Exchange	Injection drug users exchanging needles	3,703	(44.7)
Correctional Facility	Inmates and visitors to correctional facilities	1,460	(17.6)
Treatment Provider	Clients, employees, and on-hand for community members	1,140	(13.8)
Community Outreach	Community event participants and staff/employees of community organizations	738	(8.9)
Social Service Agency	Clients, employees, and volunteers	620	(7.4)
Nonprofit	Employees, volunteers, and clients	233	(2.8)
ED Pharmacy	ED overdose patients	188	(2.3)
Public Health	Community events participants, employees, and to have on hand at center	93	(1.1)
Nonprofit/Treatment Provider	Clients, employees, and on-hand for community members	28	(0.3)
Faith-Based Organization	Individuals at high-risk for injection drug use and employees	18	(0.2)
Quick Response Teams	Employees to distribute on QRT runs	15	(0.2)
Law Enforcement	Kept on site and employees to have on hand	13	(0.2)
Urgent Care	Employees to have on hand	5	(0.1)
Nonprofit Pharmacy	Community members/patients	1	(0.0)
Missing	Unknown	33	(0.4)

Table 4. Request type for individuals distributed NDC take-home NARCAN® cartons, by site type (N = 8,100)*

	Self-Request (n=3,393)		Staff-Initiated (n=3,832)		Missing Data (n=875)	
Site Type	**n**	**%**	**n**	**%**	**n**	**%**
Syringe Exchange	1,055	(31.1)	2,396	(62.5)	252	(28.8)
Correctional Facility	972	(28.6)	246	(6.4)	242	(27.7)
Treatment Provider	794	(23.4)	143	(3.7)	203	(23.2)
Community Outreach	468	(13.8)	182	(4.7)	88	(10.1)
Social Service Agency	21	(0.6)	535	(14.0)	64	(7.3)
Nonprofit	53	(1.6)	180	(4.7)	0	(0.0)
Public Health	20	(0.6)	73	(1.9)	0	(0.0)
Nonprofit/Treatment Provider	0	(0.0)	28	(0.7)	0	(0.0)
Faith-Based Organization	0	(0.0)	0	(0.0)	18	(2.1)
Quick Response Teams	2	(0.1)	13	(0.3)	0	(0.0)
Law Enforcement	0	(0.0)	13	(0.3)	0	(0.0)
Urgent Care	0	(0.0)	5	(0.1)	0	(0.0)
Nonprofit Pharmacy	1	(0.0)	0	(0.0)	0	(0.0)
Missing	7	(0.2)	18	(0.5)	8	(0.9)

** Does not include the 188 cartons distributed to individuals from ED pharmacies*

Table 5. Reasons for receiving NDC take-home NARCAN® carton (N = 8,100)*

Reason (each person may select more than 1)^	n	%
“If I overdose” (individual use)	2,814	(34.7)
“If family/friend overdoses”	2,285	(28.2)
“If I see someone overdose”	3,768	(46.5)
“Location to have on hand”	658	(8.1)
“Unknown”	1,776	(21.9)
Missing	961	(11.9)

** Does not include the 188 cartons distributed to individuals from hospitals/pharmacies*
^ Of the 7,139 (88.1%) individuals who responded, 2,361 selected > 1 reason (675 selected two, 1,571 selected three, and 115 selected all four possible options)

Table 6. Prior opioid use history, individuals distributed an NDC take-home NARCAN® cartons (N=8,100)*

	Yes		No		Not available		Missing	
Prior opioid history question (% is by row)	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
Administered Narcan®, ever	3,225	(39.8)	3,616	(44.6)	974	(12.0)	285	(3.5)
Overdosed on opioid, ever	2,286	(28.2)	4,519	(55.8)	1,016	(12.5)	279	(3.4)
If ever overdosed, did you overdose multiple times?^	1,635	(71.5)	605	(26.5)	40	(1.7)	6	(0.3)
Injected drugs, ever	3,910	(48.3)	2,776	(34.3)	1,133	(14.0)	281	(3.5)
If ever IVU, have you injected in past 30 days?¥	3,305	(84.5)	459	(11.7)	132	(3.4)	14	(0.4)
Received opioid treatment, ever	3,080	(38.0)	3,550	(43.8)	1,175	(14.5)	295	(3.6)

** Does not include the 188 cartons distributed to individuals from hospitals/pharmacies*
^ Only applicable if answered "yes" to opioid overdose, ever (n = 2,286)
^^ Only applicable if answered "yes" to injected drugs, ever (n = 3,910)

Table A: Drug overdose outcomes in Hamilton County, comparing eight months prior to the start of NDC compared to the eight months NDC was implemented.

	Eight Months Pre NDC Feb 17-Sep 17	Eight Months Post NDC Oct 17-May 18	% Change
Drug Overdose Outcomes			
ED Visits*	2,911	1,690	-41.9
EMS Runs*	3,063	1,910	-37.6
Drug Overdose Deaths – Hamilton County Residents	333	230	-30.9
Opioid Overdose Deaths – Hamilton County Residents	290	201	-30.7

** Data for ED Visits and EMS Runs does not allow for opioid-related specificity*

Table B: Drug overdose outcomes in Hamilton County, 2017 compared to 2018.

	Year to Date Jan-May 2017	Year to Date Jan-May 2018	% Change
Drug Overdose Outcomes			
ED Visits*	1,920	1,021	-46.8
EMS Runs*	1,935	1,087	-43.8
Drug Overdose Deaths – Hamilton County Residents	211	147	-30.3
Opioid Overdose Deaths – Hamilton County Residents	184	124	-32.6

** Data for ED Visits and EMS Runs does not allow for opioid-related specificity*

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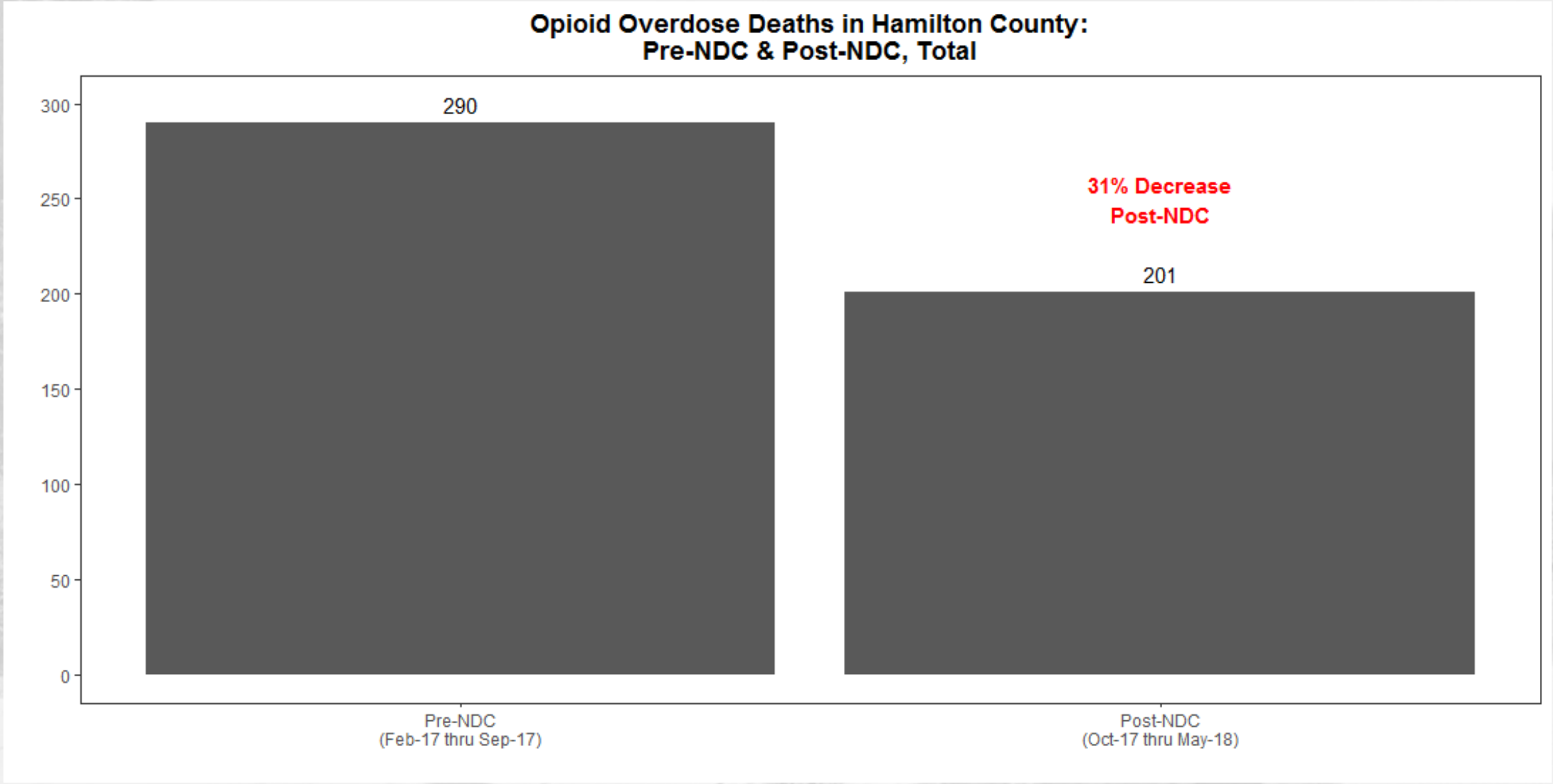

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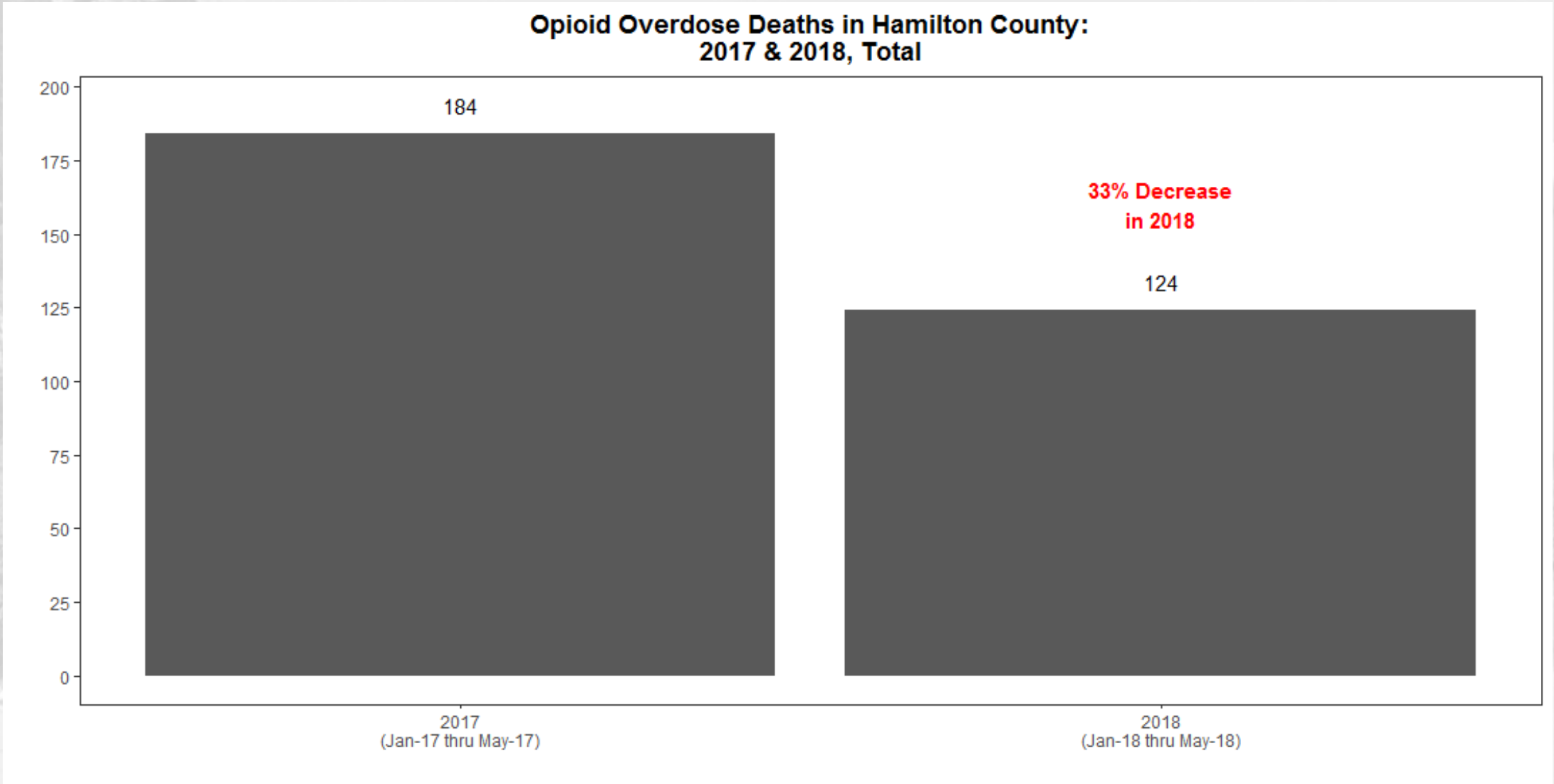

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Summary

- Opioid Drug Deaths decreased by 30.7% over the last eight months compared with Pre-NDC in Hamilton County, Ohio
- Emergency Dept visits and EMS transport runs have decreased overall for all drug overdoses in 2018
- No adverse health events reported to date as a result of administering Narcan®
- The NDC work will continue into 2019.

References

- Narcan® Distribution Collaborative Report: October 2018, revised December 3, 2018, University of Cincinnati Medical Center (subject to change as more data becomes available).
- Hamilton County Public Health Overdose Surveillance, https://www.hamiltoncountyhealth.org/
- Hamilton County Coroner's Office Drug Overdose Death Data
- Centers for Disease Control and Prevention, Opioids Portal https://www.cdc.gov/opioids/
- Ohio Dept of Health, EpiCenter Surveillance and ODH Public Health Data Warehouse, https://odh.ohio.gov/wps/portal/gov/

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Thank-You

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COMMUNITY NALOXONE PROGRAMS

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BACKGROUND

Ideal responses to witnessed opioid-related overdose:

- Call 911
- Perform rescue breathing until EMS arrives

- At least 85% overdoses are witnessed (McGregor 1998)

BACKGROUND

- Substantial barriers to calling 911
- Good Samaritan laws are limited in efficacy
- Treating OD deaths as homicides is a barrier
- Less than 50% of overdose witnesses call 911 (Coffin 2009)

- **We have broken the 911 system for people who use drugs**

ORIGINS OF COMMUNITY NALOXONE

Naloxone distribution to people who use drugs:

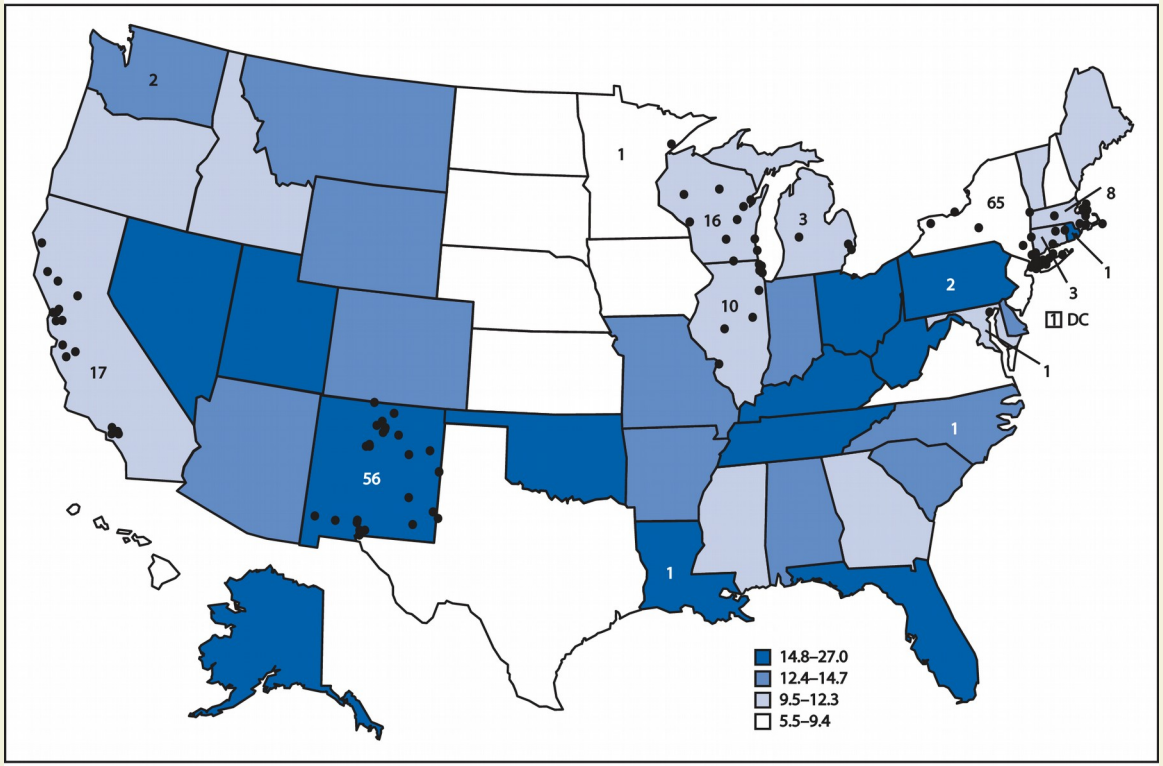
- Like needle exchange, started by drug users and those close to them in the late 1990s
- Research and public health follow

RESEARCH

- Naloxone distribution to people who use drugs is feasible (Simini 1998, Strang 1999, Dettmer 2001, Seal 2003…)
- Naloxone use by people who use drugs is safe (Bigg 2002, Seal 2005, Galea 2006, Piper 2007, Doe-Simkins 2009, Enteen 2010, Wagner 2010, Lankenau 2013, Jones 2017…)
- Distributing naloxone to people who use drugs reduces mortality and is cost effective (Walley 2013, Coffin 2013, Bird 2016, McDonald 2016, Coffin 2018)
- Immediate naloxone use 'at the scene' reduces morbidity (Gonzva 2013)

SPREAD OF COMMUNITY PROGRAMS

FIGURE 2. Number (N = 188) and location* of local drug overdose prevention programs providing naloxone in 2010 and age-adjusted rates† of drug overdose deaths§ in 2008 — United States

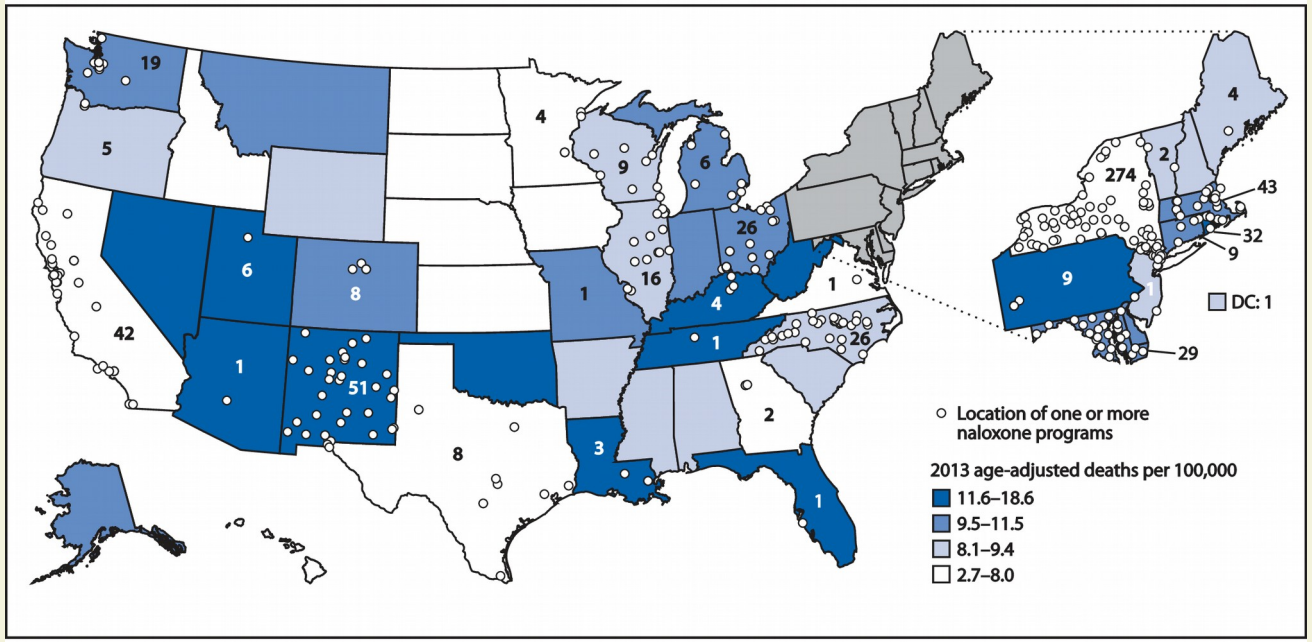


* Not shown in states with fewer than three local programs.
† Per 100,000 population.
§ **Source:** National Vital Statistics System. Available at http://www.cdc.gov/nchs/nvss.htm. Includes intentional, unintentional, and undetermined.

Wheeler et al MMWR 61(6) 2012 - 188 sites in 2010

SPREAD OF COMMUNITY PROGRAMS

FIGURE 2. Number* and location of local drug overdose prevention programs providing naloxone to laypersons, as of June 2014, and age-adjusted rates† of drug overdose deaths§ in 2013 — United States



* Total N = 644; numbers on map indicate the total number of programs within each state.
† Per 100,000 population.
§ CDC, National Center for Health Statistics; Compressed Mortality File 1999–2013 on CDC WONDER Online Database, released January 2015.

Wheeler et al MMWR 64(23) 2015 - 644 sites in 2014

IMPACT

- 152,283 lay persons trained to use naloxone 1996-2014
- 26,463 reported reversals 1996-2014

- OSNN purchasing group: currently 89 programs in 34 states
- 506,000 doses distributed in 2017
- 752,000 doses 2018 YTD
- Projected ~1 million doses 2018

OTHER LAY PERSONS

Reversal rates per kits issued

- Opioid users: 21%
- Friends/family: 7%
- Agency staff: 1%
- Law enforcement: 3%

(Banta-Green, U. Washington, *Naloxone in WA*, SAMHSA PDO, first two years data)

SUMMARY

- **The person most likely to witness an overdose is another person who uses drugs**
- **Naloxone distribution should treat people who use drugs as the priority target population**

FDA POSSIBLE ACTIONS

Clarify that injectable naloxone is approved for community distribution

- Packaging language on Adapt's nasal Narcan and Evzio's autoinjector have led SAMHSA and other funders to believe only these devices are FDA approved for use by non-medical personnel, and that community distribution of injectable forms of naloxone may be off-label use
- IM injectable naloxone is the cheapest and most widely distributed form of naloxone

FDA POSSIBLE ACTIONS

Change shelf life to 5 years

- FDA/DOD Shelf Life Extension Program (SLEP) says true shelf life of naloxone is at least 60 months (Lyon 2006)
- Current shelf life of all products is no more than 24 months
- This is a logistical and economic burden on community programs

FDA POSSIBLE ACTIONS

Make some products OTC

- The need for standing orders and physician involvement in purchasing processes is a significant barrier for some community programs, particularly small programs in rural areas

THANK YOU

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