

The Effects of Naloxone Rescue Programs on Opioid-Overdose Outcomes

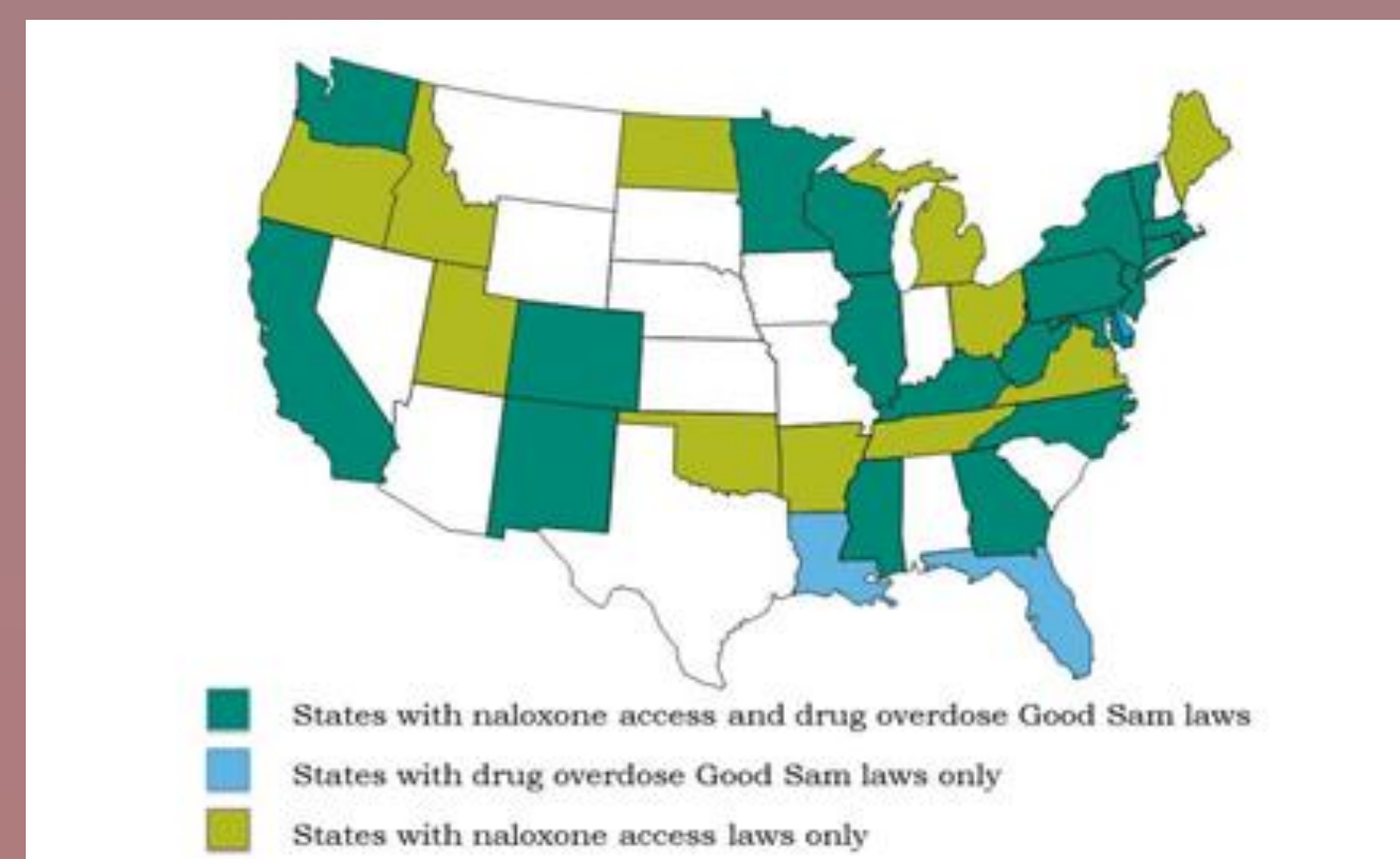
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P → Overdose in Opioid Users **I** → Distribution of naloxone in the context of education and training to nonmedical nonprofessionals **C** → Naloxone administration by emergency first response teams or emergency department staff **O** → Decreased negative overdose outcomes (mortality and cost)

Introduction

The rate of opioid overdose has more than tripled in the United States since 1990. In particular, deaths from prescription opioid overdose now outnumber that due to heroin and cocaine combined, and exceed the number of deaths caused by motor vehicle accidents in 29 states. Nevada is the 4th leading state in opioid overdose-related deaths, with an 80% increase in mortality rates from 1999 to 2010 (11.5/100,000 to 20.7/100,000, respectively). This alarming trend highlights a dire need for interventions that both address opioid misuse, as well as reduce the risk of overdose-related deaths.

Several states have implemented programs and policy changes in attempts to combat the growing opioid misuse problem. Some have expanded the protection of “Good Samaritan” laws to include non-professional third parties in addition to physicians and first responders, which has proven to reduce overall drug-related mortality in general. More specifically, rescue drug laws are showing promise not only in reducing opioid-overdose deaths, but also in decreasing relative accrued costs for inpatient treatment, while increasing public awareness and accurate identification of opioid misuse and overdose.



The current preferred method of treatment for opioid overdose reversal is the administration of an opioid antagonist, Naloxone. When administered appropriately, the drug is highly efficacious; however, its action is time-dependent. Though Naloxone (more commonly called Narcan is not a controlled substance, its use has been largely regulated by laws that pre-date the opioid epidemic. Until recently, its distribution has been limited to emergency departments and medical first response teams, creating unnecessary barriers to the treatment of life-threatening overdoses. There are multiple and multi-faceted reasons one might not receive emergency treatment within the critical window. Most simply, distance from services and lack of access to communication devices are not uncommon. Perhaps more pertinent are bystander or user fears of police involvement, high medical costs, and community stigma.

Drug rescue programs allow Naloxone to be administered by non-professionals outside of hospitals and first-response teams. These programs include educational components such as accurate identification of opioid overdose, CPR training, instructions for appropriate Naloxone administration (including potential for a second dose), and protocol for seeking subsequent medical care. They reach both opioid users, as well as family and friends of users, and individuals living in areas where overdose is common. Thus, drug rescue programs have the potential to overcome the majority of factors contributing to opioid-related overdose deaths.

Resources

Alvar, C., & Brown, J. (2011). *Naloxone: A Review of the Literature*. *Journal of the American Society of Addiction Medicine*, 16(1), 1-10.
Brennan, T. (2011). *Naloxone: A Review of the Literature*. *Journal of the American Society of Addiction Medicine*, 16(1), 1-10.
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Methods

A literature search was performed for Naloxone efficacy in treatment of opioid overdose. NCBI/Pubmed database was searched for studies limited to English. Search terms used were opioid overdose prevention, naloxone, opioid overdose AND naloxone, Opioid overdose mortality. Some specific statistics were gathered from the CDC and Trust for America's Health using a google search. The institution of opioid intervention programs are still in their early stages and there are ethical constraints regarding clinical trials and thus a lack of abundant representative data; specifically, randomly controlled trials. In order to find sufficient evidence of Naloxone outcomes, our search was broadened to include not only systematic reviews but also pilot studies and survey reviews. Because all articles used reviewed the outcomes of opioid overdose prevention programs, they were appropriate for our research question.

Results

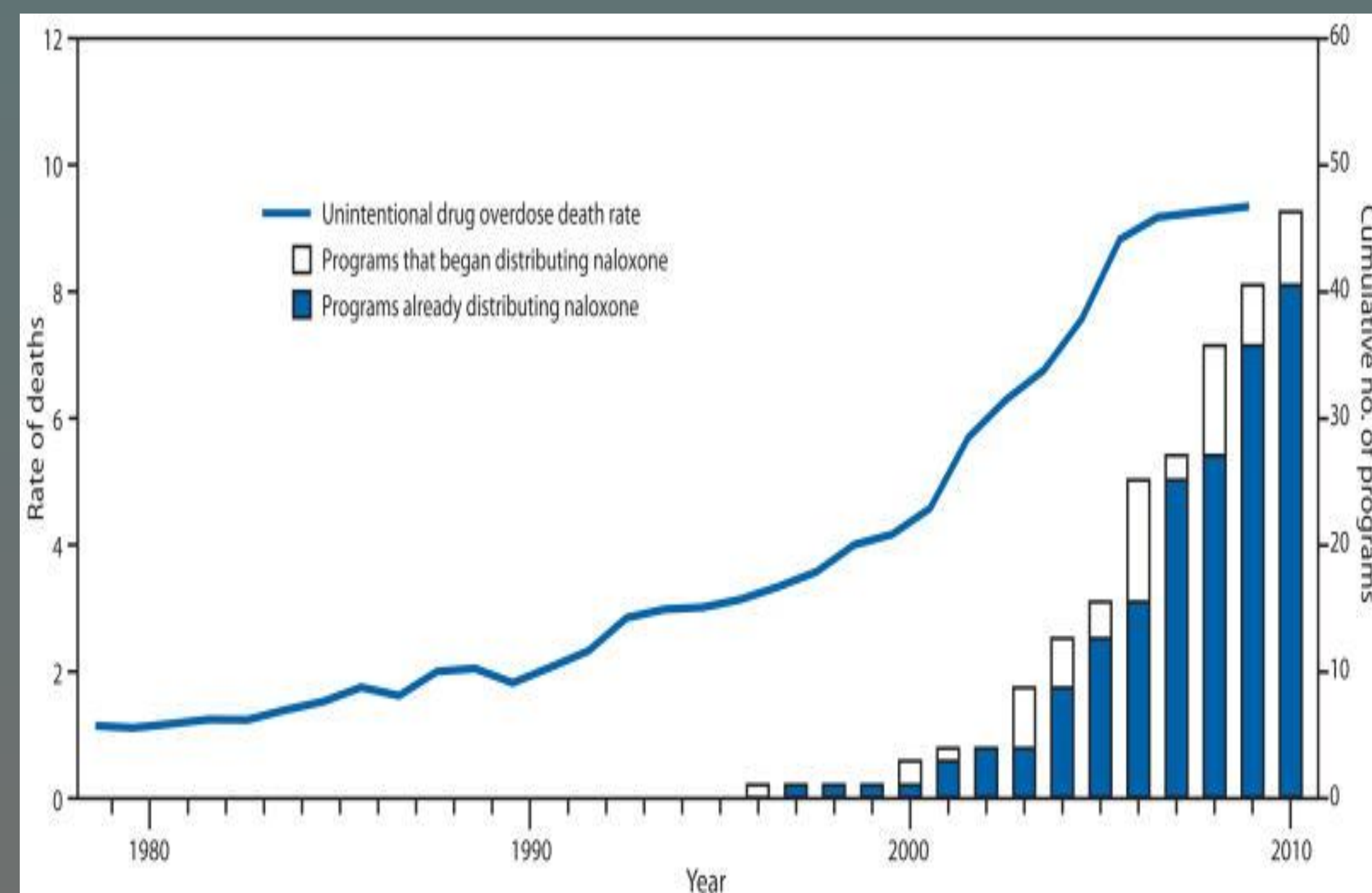
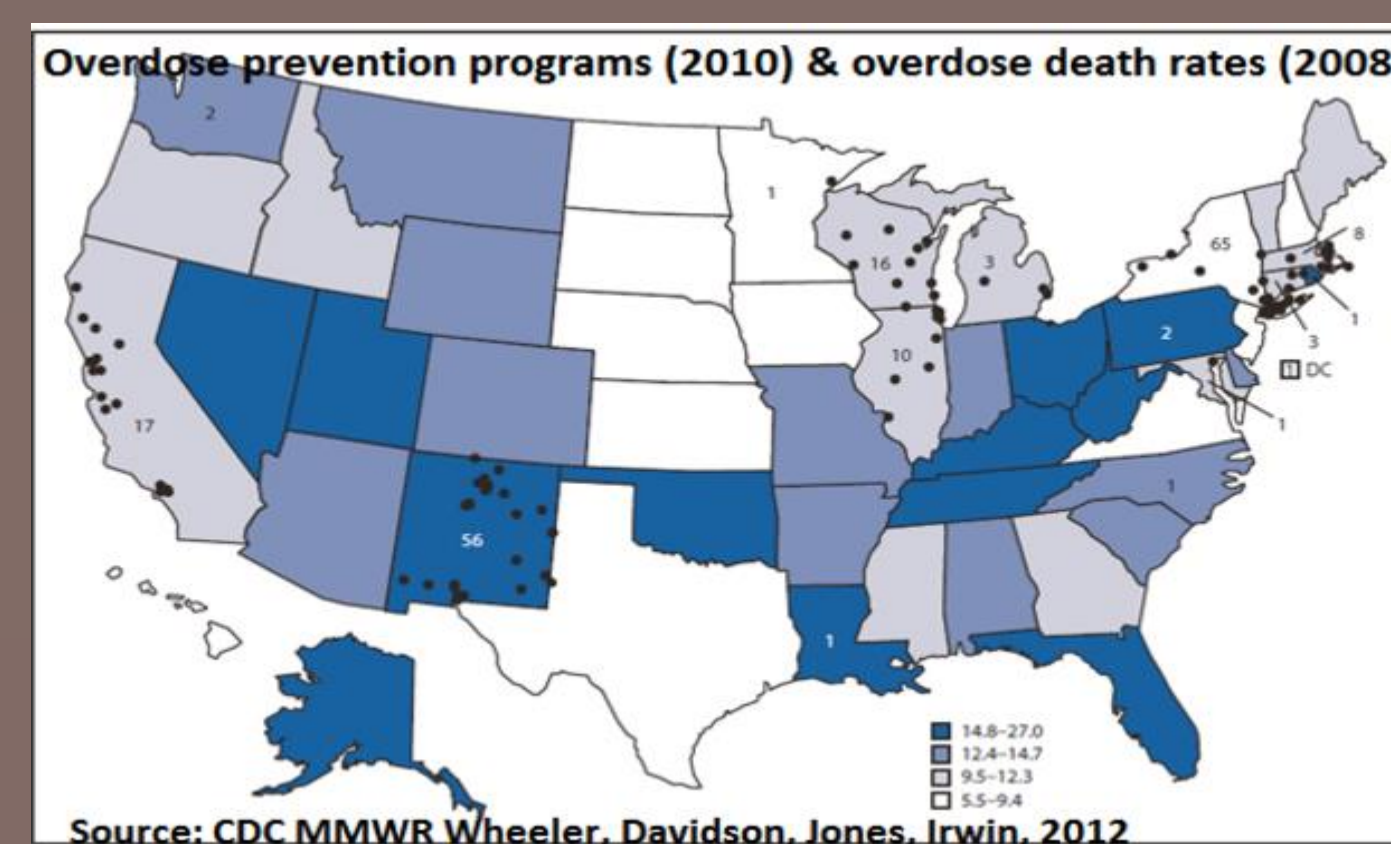


Figure 1. Annual crude rates* of unintentional overdose deaths and number of prevention programs distributing naloxone in the US, 1979-2010. Indicating that with an increase in OOPP's, crude mortality rate has plateaued. * Per 100,000 people
Wheeler, Eliza, Peter J. Davidson, Stephen T. Jones, and Kevin S. Irwin. "Community-Based Opioid Overdose Prevention Programs Providing Naloxone- United States, 2010." *MMWR Morb Mortal Wkly Rep*. 61.6 (2012): 101-05. Web. 26 Apr. 2015.
<<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378715/>>.

Overdose Education and Naloxone Distribution – Overdose Reversals			
OEND Program	# people trained	# overdose reversals	Year data collection began
Chicago Recovery Alliance	36,450	5,430	1996
DOPE project/HRC in San Francisco	5,321	1,500	2003
People's Harm Reduction Alliance in Seattle	8,000	4,967	2005
Harm Reduction Center in Denver	307	101	2012
North Carolina Harm Reduction Coalition	2,232	115	2013
Prevention Point Overdose Prevention Project in Pittsburgh, PA	1,023	1,002	2005
MDPH OEND Massachusetts	>10,000	1,200	2007

Figure 3. Overdose reversal reports collected from community OEND programs . Data indicates number of reported opioid reversals collected by OEND programs through surveys and direct reporting. Time intervals for data collection vary due to implementation time of programs and time of data collection. Data is likely minimized due to underreporting and loss of data, collection errors and reduced follow-up.



Source: CDC MMWR Wheeler, Davidson, Jones, Irwin, 2012

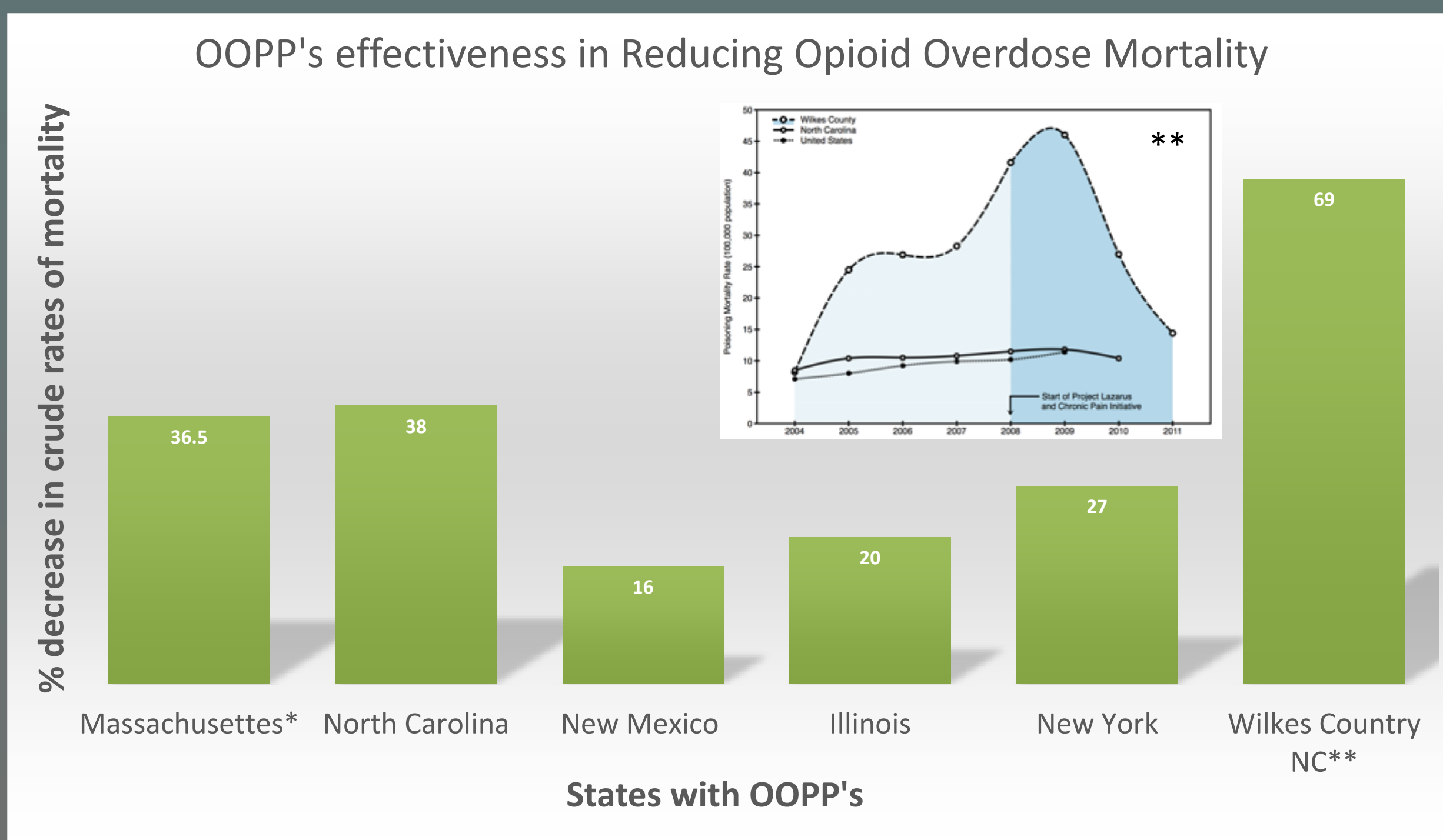


Figure 2. Percent decrease of Crude mortality rate in several states with OOPP's. Data was retrieved from several articles and put into bar graph to show a decrease in crude mortality rate after implementation of overdose prevention programs using “take-home” naloxone. Data reflects collection from different time intervals due to limited available studies and infancy of programs.
*Value is an average decrease in mortality of low implementation programs (1-100 people trained per 100,000; 27%) and high implementation programs (>100 ppl trained per 100,000; 46%) compared to community w/ out OOPP program. ** data directly collected from the Lazarus Project (2009-2011) In Wilkes County NC showing significant decline in overdose mortality after implementation of Lazarus project.

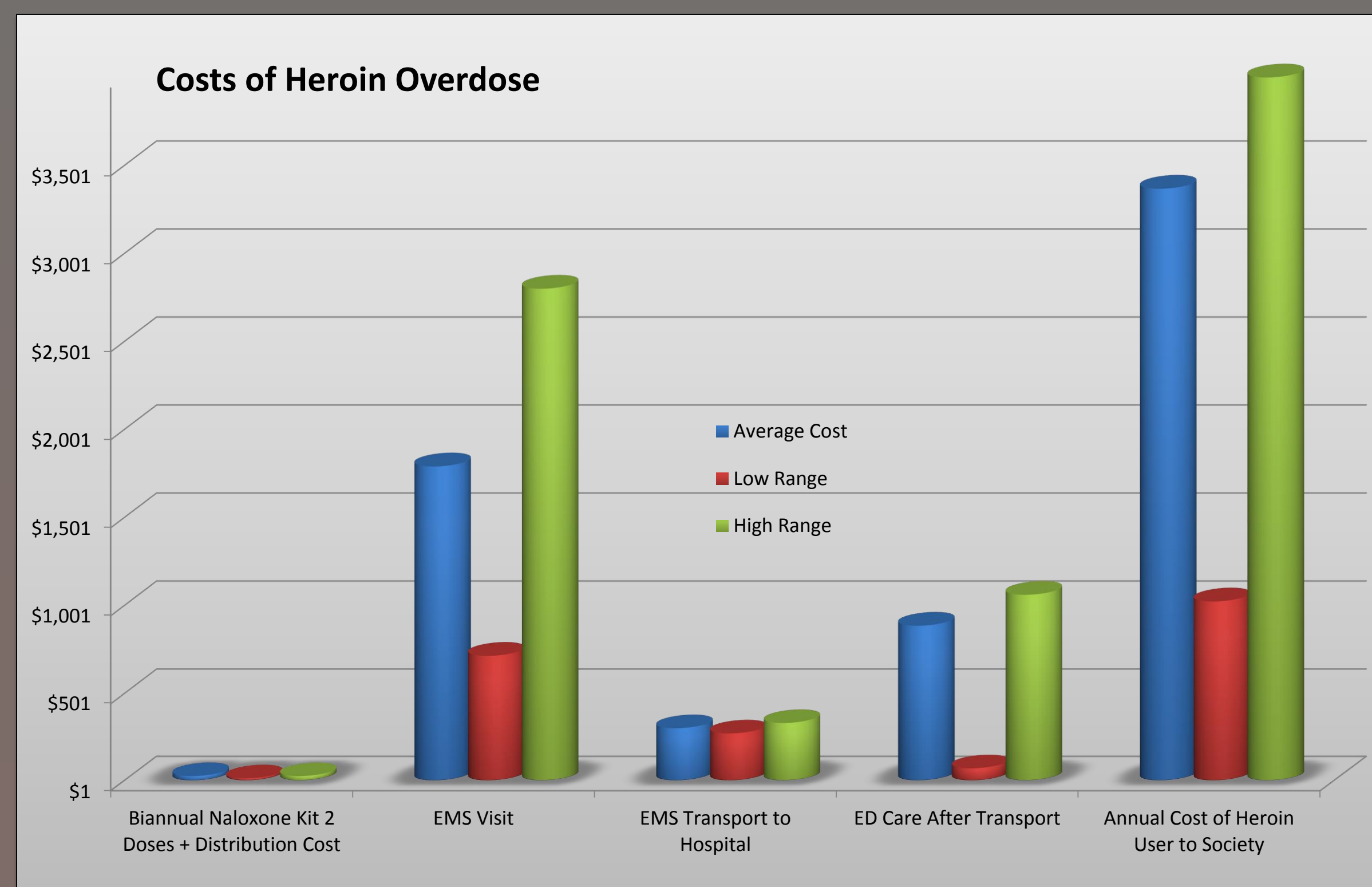


Figure 4. Reflects monetary costs relative to various overdose treatment trajectories. Data was incorporated into a study designed to statistically predict cost-effectiveness of programs distributing naloxone to heroin users, using both deterministic and probabilistic analyses with an integrative Markov and decision analytic model. Conservative values based on assumption of recurrent overdoses and worst-case unwitnessed scenarios were used to avoid overestimating program benefits. Ultimate cost-effectiveness findings represent monetary cost, quality-adjusted life-years (QALYs) and incremental cost per QALY gained.
Preventing fatal overdoses: A systematic review of the effectiveness of take-home naloxones. (2015). In *European Monitoring Centre for Drugs and Drug Addiction*. Retrieved April 26, 2015, from http://www.emcdda.europa.eu/attachments/cjv/ai_234376_en_TDAU1400ENweb.pdf

Clarifications

Opioid- includes both opiates, a natural derivative of opium such as morphine and codeine, and related synthetic and semi-synthetic compounds that act at the opioid receptor (mu receptor). Including but not limited to; hydrocodone (Vicodin), oxycodone (OxyContin, Percocet), heroin and methadone.

Opioid Overdose- occurs when opioid binds the mu receptors in the brain causing them to become desensitized to Carbon dioxide levels in the blood which leads to depressed respiration and can ultimately lead to death.

Naloxone- opioid antagonist that outcompetes opioids for the mu receptor thus inhibiting the effects opioids have on the brainstem and respiration. The primary route of naloxone is by injection (IM) but is now able to be administered via a nasal spray (Narcan) which is the preferred method of administration in non-medically trained individuals.

Conclusions

- The implementation of increased numbers of naloxone distribution programs correlates with a plateau in rates of opioid overdose deaths
- Overall, studies show that naloxone distribution programs reduce opioid overdose mortality, ranging from 6.1 to 69%.
- Naloxone distribution results in large numbers of overdose reversals
- Data indicates that laypersons do utilize naloxone distribution kits in recognized overdose situations
- Naloxone administered by lay persons is equally as effective in reversing overdose and preventing mortality as that administered by emergency medical services
- The cost of naloxone distribution kits is exponentially less than that of alternative emergency service care, even in cases where repeat doses or subsequent medical evaluation are necessary
- Statistical analysis of overdose outcomes including recurrent OD, population-based distribution rates, variability in witnessed events, and monetary expenditures projects that naloxone distribution programs will be “highly cost-effective” even under markedly conservative assumptions

Based on the findings presented, we conclude that the implementation of naloxone distribution programs results in overall improvement of opioid-related overdose outcomes, interpreted as reduced mortality and decreased monetary costs.

Limitations

- Several studies focused on naloxone effectiveness in heroin overdose only, excluding opioid medications
- Several study results were gathered from surveying opioid users and program employees which can lead to underestimated data due to loss of follow-up and/or collection errors.
- Lack of high level evidence research
- Lack of updated data such as vital statistics
- Comparison of programs is difficult due to differences in state laws, difference in program implementation and sheer number of programs as well as differences in opioid overdose demographics
- Not all opioid overdoses result in death, suggesting that opioid reversals were not all “life-saving” treatments and could be attributing more efficacy to naloxone than what truly exists.

Future Direction

Traditionally, opioid overdose treatment has been provided by medical first responders and given in the emergency department. The challenges to this model of treatment include the high rates of non-reporting and access and timing of emergency medical services. This together with the increasing rate of overdose clearly points to the need for a more novel model of prevention and treatment. Many states and communities have recognized this need and have established programs to distribute naloxone, the most common treatment for opioid overdose, to lay people and opioid users. States without these programs continue to have some of the highest opioid overdose mortality rates. Our recommendation moving forward would be to establish naloxone distribution programs in states and communities where they don't exist. This model of treatment works very well when you consider that overdose in drug users is very common, is often witnessed by peers and family members and timely administration of naloxone can prevent mortality and morbidity. Studies have shown that administration of naloxone by peers and family members is successful and they are willing to provide intervention. To support the establishment and expansion of Naloxone distribution programs we recommend the passage of Good Samaritan laws in states where they don't currently exist as lack of this protection has been shown to be a barrier to overdose reporting. Research also suggests that lack of Good Samaritan protection is a barrier to Naloxone administration even in states where distribution programs exist.

We additionally make the following recommendations based on deductive reasoning and good practice principles, however their analysis was either outside the scope of this project or there was insufficient research to report. OOPP programs should include an education component consisting of training for recognizing the signs and symptoms of opioid overdose, how to administer naloxone, and basic life support techniques including CPR and instructions for obtaining appropriate follow-up care. We would recommend that the intranasal form of naloxone be used as this method has shown to be safe, effective and easily administered by a lay-person. Other benefits of this form are the dilute formula, positive side effect profile and reduced risk for needle-stick injury. An auto-injectable form of naloxone was recently approved by the FDA, but long-term adverse effect profiles are not yet available. Finally, we would also recommend overdose education at the time prescriptions for opioids are given. In recent years drug misuse more commonly involves prescription opioids. We believe this would be another level at which outreach can occur.