Facilitators and Barriers to Naloxone Kit Use Among Opioid-Dependent Patients Seeking Treatment at Medication Assisted Therapy Clinics in North Carolina, USA

by

Prasana Khatiwoda

Duke Global Health Institute
Duke University

Date:_____

Approved:

_____
Rae Jean Proeschold-Bell, Supervisor

_____
Christina S. Meade

_____
Lawrence P. Park

Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Duke Global Health Institute
in the Graduate School of Duke University

2016

ABSTRACT

Facilitators and Barriers to Naloxone Kit Use Among Opioid-Dependent Patients Seeking Treatment at Medication Assisted Therapy Clinics in North Carolina, USA

by

Prasana Khatiwoda

Duke Global Health Institute
Duke University

Date:_____
Approved:

_____
Rae Jean Proeschold-Bell, Supervisor

_____
Christina S. Meade

_____
Lawrence P. Park

An abstract of a thesis submitted in partial
fulfillment of the requirements for the degree
of Master of Science in the Duke Global Health Institute
in the Graduate School of Duke University

2016

Abstract

Naloxone – an opioid antagonist that reverses the effects of opioids, including potential death from overdose – is increasingly being distributed in non-medical settings. We conducted a mixed methods study administering a survey to 100 treatment seekers and pursuing observant participation at four methadone/buprenorphine Medication Assisted Therapy (MAT) clinics in North Carolina, USA. Female participants were more likely to have gotten a kit and to carry it with them, whereas male participants were more likely to have witnessed an overdose and to have made use of naloxone. Men discussed the difficulties of carrying the naloxone kits, which are currently too large to fit in a pocket. Public health officials may be relieved to know that naloxone users intend to call emergency services.

Dedication

This paper is dedicated to all who have lost a loved one to drug addiction and to those who are currently struggling.

Contents

List of Tables

Acknowledgements

This research was supported by the Duke Global Health Institute. We would like to thank Tessie Castillo, Loftin Gregory Wilson, and Hyunnie Namkoong, together with all the NCHRC staff members, for assisting with recruitment and providing valuable insights. We would also like to show our gratitude to Caesar Lubanga-kene for double-coding all the open-ended responses in this study.

1. Introduction

According to the 2015 World Drug Report, an estimated 246 million people between the ages of 15 and 64 years worldwide in 2013 used an illicit drug, primarily belonging to the opioid, cocaine, cannabis and amphetamine-type stimulant group, and just over 10% of those users met diagnostic criteria for drug dependence. An estimated 12.19 million people were intravenous drug users (IDU). The report also indicated that in 2013, an estimated 187,000 drug-related deaths were reported globally, often as a result of drug overdose (UNODC, 2015).

Naloxone is an opioid-antagonist drug that can be administered to persons experiencing opioid overdose in order to reverse the overdose and save their lives. Because naloxone is administered by friends or bystanders and not by the opioid users themselves, it is a means for opioid users and their loved ones to keep each other safe. Naloxone was first invented in 1961, but it was not approved by the US Food and Drug Administration to treat overdose until 1971, after its benefits became clear. Since then it has been used widely around the world in medical settings. The idea of distributing naloxone to opioid users rather than medical providers as a harm reduction strategy was first suggested in 1992 (Strang et al., 1996), and in 1995, Germany and England became the first countries to distribute naloxone to opioid users (Dettmer et al., 2001). Nevertheless, there remain numerous barriers to expanding the distribution of naloxone, including a country's national policies, state laws, awareness campaigns, and

procedures used by local groups to distribute naloxone to opioid users. Naloxone distribution is an interesting harm reduction strategy as it acknowledges the important role that peers play in drug use, as well as in prevention of drug overdose.

The current study focuses on naloxone use in the state of North Carolina, United States (US), but its distribution has also been studied in other countries. Naloxone is widely accessible in England, where it has enjoyed legal status permitting its use by non-medical providers since 2005 (Strang et al., 2006). Studies on the effectiveness of naloxone programs suggest the importance of training opioid users and their friends and family members to recognize overdose symptoms and to use naloxone kits (Strang et al., 2008; Strang et al., 2000; Williams et al., 2013). While this literature has focused on factors that would improve the use or willingness to use naloxone by bystanders who already possess naloxone kits, we know little about the factors that influence people's decisions to get or carry such a kit. This study seeks to identify the main facilitators of, and barriers to, these aspects of naloxone distribution from the perspective of opioid-dependent persons and their friends and family members. It also aims to highlight how naloxone law in the US affects the distribution of naloxone in non-medical settings, thereby providing information on how the tensions between conflicting US policy paradigms play out in the implementation of this harm reduction policy.

Even though opioid overdose is widely accepted as a preventable phenomenon with a cost-effective solution, the implementation of policies and programs to support

harm reduction interventions such as naloxone distribution is greatly affected by the country's politics, policies and law. The US has historically resisted harm reduction policies globally and nationally (Wood et al., 2009). Politics and media have for decades created an environment that has shaped prohibitionist, zero-tolerance drug policies focusing on drug control through the criminal justice system (Wood et al., 2009; Brocato & Wagner, 2003), giving rise to immense spending on law enforcement and incarceration, stigmatization of drug users and on/off again bans on federal spending for harm reduction approaches like needle exchange programs. This resistance to harm reduction policies in the US stems from the general belief that if harm from or the risk of drug use were to be reduced, it would increase drug use. Along those same lines, some believe that implementation of harm reduction programs condones drug use (MacCoun, 1997). This way of thinking greatly affects successful implementation of any harm reduction approach, including naloxone distribution, in the US. The success of this approach in countries like the Netherlands and England as due to a change in their traditional national drug policy, adopting a more pragmatic approach to drug addiction control through public health intervention and justice (Marlatt, 1996).

To better understand naloxone regulations in the US, it is helpful to understand both the legal and illegal use of opioid drugs in the country. It is also important to understand the mindset of substance use treatment in the US as it influences policies on naloxone, which is seen as a temporary measure to reverse overdose and not as a way to

prevent future substance use and overdose. We provide below the history and current US context of opioid use, opioid overdose and substance use treatment, followed by a description of how naloxone is currently distributed in the US.

1.1 Opioid drugs

The class of opioid drugs includes substances derived from the poppy plant (e.g., morphine, heroin, opium) and synthetic or semi-synthetic drugs that have similar modes of activity (e.g., methadone, percocet, oxycontin, vicodin, pethedine, fentanyl). Opioid drugs may be administered orally or by snorting, injecting, or smoking. They work through opioid receptors found principally in the central and peripheral nervous system, together with the gastro-intestinal system.

Due to their analgesic effect, opioids are used in medical settings to increase one's pain threshold. In addition to this medical benefit, opioids are commonly abused to produce euphoria. Most Americans have access to opioids such as Hydrocodone and OxyCodone through medication prescribed for pain relief (Manubay et al., 2011).The non-medical use of opioids entails taking prescription drugs that are not prescribed by a physician, or taking prescribed drugs in quantities greater than prescribed (Jones et al., 2014). Heroin is another form of opioid which is illegal in the US and not obtained through prescription. But whether legal or illegal, the repeated use of opioids can lead to tolerance, dependence and addiction. The adverse effects of opioids include nausea, vomiting, drowsiness, and, in large quantities, respiratory suppression and death.

Overdose occurs when excess of opiates bind to the μ2 receptors in the brain stem, desensitizing it to carbon dioxide levels in the blood so that breathing mechanisms are not triggered, leading to respiratory failure (Darke et al., 1996; Sporer, 2003).

In 2014, opioid use prevalence in the US was 3.8% compared to the global average of 0.7% (UNODC, 2015). According to the National Prescription Audit, the number of opioid prescriptions ballooned from an estimated 76 million in 1991 to 207 million in 2013; by 2013, an estimated 1.9 million Americans were abusing or were dependent on opioid drugs (NSDUH, 2014). This rise can be traced to liberal laws on prescribing opioids for chronic pain, pain management standards that facilitate over-treatment, and aggressive marketing by pharmaceutical companies (Laxmaiah Manchikanti et al., 2012). As a response to the growing abuse of prescription opioids, some measures were taken to control this, including state-run Prescription Drug Monitoring Programs (Manchikanti et al., 2005; Manubay et al., 2011) and implementation of Risk Evaluation and Mitigation Strategies (Slevin & Ashburn, 2010) to limit opioid prescription by physicians and decrease inappropriate access to these medications. Also, a new formulation of the widely abused prescription opioid OxyContin was introduced in 2010. This abuse-deterrent OxyContin cannot be crushed or dissolved, making it difficult to inject or inhale (methods that increase the euphoric property of the drug).

The number of heroin users in the US nearly doubled between 2005 and 2012 (Substance Abuse and Mental Health Services Administration, 2013). In 2013, an estimated 517,000 Americans were living with heroin addiction (NSDUH, 2014). The use of prescription opioids was a primary risk factor for heroin abuse, with four out of five heroin users reporting addiction to prescription opioids before switching to heroin (Muhuri et al., 2013). The US Centers for Disease Control and Prevention also reported that people addicted to painkillers were 40 times more likely to abuse and be dependent on heroin (CDC, 2015). Additionally, past studies report that heroin use is common among patients with a history of abusing prescription opioids that can be obtained over-the-counter (Volkow, 2014; Cicero et al., 2014). The rise in heroin use in the US can thus be attributed to the growing availability, use and abuse of prescription opioids, while changes in prescription law and the introduction of abuse-deterrent OxyContin have been suggested as explanations for the shift from prescription opioids to heroin (Muhuri et al., 2013). Heroin is as addictive as prescription opioids (Maher et al., 2005), with the additional danger of drug impurity; it is often mixed with other drugs, of which users may be unaware.

1.2 Overdose

The most common cause of death among drug users is overdose, and opioid products are highly associated with overdose deaths (UNODC, 2015). The CDC has reported drug overdose as the leading cause of injury-related deaths in the US, with

43,982 drug overdose deaths in 2013 alone (CDC, 2015). Of these drug overdose deaths, 51.8% involved prescription drugs. The United Nations Office on Drugs and Crime also reports a global shift in opioid use from prescription OxyContin to heroin, fueling the growing global trend in heroin-related deaths (UNODC, 2015).

In the US, the rate of drug overdose from opioids varies widely across states. In 2014, West Virginia had the highest drug overdose rate (31.3 per 100,000 population), which was more than eight times that of the state with the lowest rate, North Dakota. In North Carolina in 2014, the opioid overdose death rate was 12.6 per 100,000 people (CDC, 2015). Risk factors for opioid overdose include intravenous administration, poly-drug use, and drug impurity (Miller, 2009; Darke & Hall, 2003). In addition, abstinence for even brief periods of time (e.g., due to incarceration or hospitalization) and then returning to use the same amount of opioid as before the abstinence exposes users to greater risks of overdose because their tolerance to opioid drugs will be reduced (Darke & Hall, 2003).

1.3 Treatment approaches to substance abuse

In most parts of the world, drug treatment counsels abstinence. In the US, patients usually visit outpatient centers for group therapy, peer interaction, and counseling. In both outpatient centers and residential treatment programs, the main aim is to achieve complete abstinence. In contrast, approaches based on harm reduction aim to minimize the dangers to individuals and society associated with substance abuse.

Harm reduction recognizes that the singular goal of abstinence may not be realistic; it involves setting up a hierarchy of goals, aiming for more pragmatic results first, and, if possible, followed by abstinence later (Brettle, 1991). In the harm reduction approach, patients in therapy consider a variety of potential harms that come from substance use and make plans to decrease them, even if they do not plan to achieve abstinence from all substances. Methadone/buprenorphine maintenance or Medication Assisted Therapy (MAT) is an example of such a harm reduction strategy. Prescribed as an alternative to heroin and other opioids, methadone and buprenorphine are long-acting synthetic opioids; studies have shown that they can reduce opioid withdrawal and cravings associated with opioid dependence (Amato et al., 2005).

Opioid overdose prevention programs are another example of such harm reduction in practice. Programs provide overdose education, distribute naloxone to opioid users and their families and friends, and seek to change laws and policies to increase bystander response in cases of overdose. Many harm reduction organizations in the US have incorporated overdose prevention programs in their services, helping drug users and their families and friends gain access to naloxone.

1.4 Naloxone

Naloxone received US Food and Drug Administration approval in 1971. Over the next 40 years, injectable naloxone became the drug of choice to reverse overdoses in hospitals settings (Wermeling, 2010). With the rise in opioid-related overdose deaths,

naloxone has increasingly been tested for use outside of medical settings. Studies suggest that opioid users frequently witness drug overdose by others; some studies report that more than 70% of heroin-using participants have witnessed an overdose (Bennett & Higgins, 1999; McGregor et al., 1998). At the same time, instant death due to opioid overdose is not particularly common. In most cases, death occurs 1 to 3 hours post-injection (Zador et al., 1996; Monforte, 1977). The effects of naloxone last for 20 to 90 minutes (Tenenbein, 1984), providing sufficient time for persons to seek medical care. Naloxone is highly effective (Walley et al., 2014), safe to use, has no potential for abuse or effect on individuals who have not taken opioids (CDC, 2012) and requires minimal training to use (Doe-Simkins et al., 2014). Because most overdoses take place in the company of others with sufficient time to act, the morbidity and mortality associated with opioid overdose is a largely preventable phenomenon with the timely administration of naloxone prior to seeking emergency medical care.

The first naloxone distribution program in the US began in 1996 in Chicago. Nearly 20 years later, over 600 opioid overdose prevention programs in the US provide naloxone to drug users, their friends and family members (CDC, 2015). But despite various naloxone distribution efforts and opioid overdose prevention approaches, universal access to naloxone remains a challenge in the US, partly due to legal barriers.

Although naloxone is a prescription drug, it is not a controlled substance as it has no abuse potential (Doe-Simkins et al., 2014). However, naloxone is subjected to laws

that regulate prescription drugs in medical settings (21 U.S.Code § 353) and which prohibit drugs from being prescribed to persons other than the individual to whom the drug will be administered, or to any person the physician has not personally examined. This prohibits physicians from prescribing naloxone to distribution programs. Unless federal law is changed, to increase naloxone access in the US, each state must pass a law allowing the drug to be prescribed by physicians to individuals who may use it on someone else and to be prescribed to a person with whom the prescriber does not have a prescriber-patient relationship. To increase access to naloxone, the majority of states have now changed their laws to remove these restrictions. These changes are typically known as Naloxone Access Laws. There are various components to these laws and each state has different variations of them (Davis & Carr, 2015).

In addition, bystanders are deterred from acting when witnessing an overdose for fear of being arrested if drugs or paraphernalia are present. To increase bystander response, a state must also pass a law to protect overdosing persons and bystanders from arrest, charge, and/or prosecution, encouraging them to call emergency services without fear of legal consequences. These laws are known as a 911 Good Samaritan Law or Medical Amnesty Laws. Most states in the US have now passed these laws, which typically provide that people who experience a drug overdose or persons who witness an overdose and seek help for the overdosing person cannot be arrested, charged and/or prosecuted for possession of small amounts of drugs or drug paraphernalia.

Increasingly, these laws provide protection from offenses such as underage drinking as well, and some also provide protection from violations of probation and parole. Despite these variations between states, the goal of these laws is to remove the fear of criminal repercussion for calling 911 to report an overdose, and to instead focus efforts on getting help to the overdosing person (Davis & Carr, 2015).

In North Carolina, the North Carolina Harm Reduction Coalition successfully encouraged legislators to pass Senate Bill 20, which entered into effect in April 2013, and Senate Bill 154, which entered into effect in 2015. These bills encompass both a 911 Good Samaritan Law and a Naloxone Access Law. Senate Bill 20 authorized medical providers in North Carolina to prescribe naloxone to a person to use on others, and provided immunity from prosecution for possession of small amounts of drugs and drug paraphernalia for people who seek medical care for a person who is overdosing as well as for the victim. Senate Bill 154, passed in 2015, further expanded protections for 911 callers to include protection from having their probation or parole violated, and included pharmacists on the lists of groups immune from civil or criminal liability for dispensing naloxone (General Assembly of North Carolina, 2013, 2015).

1.5 North Carolina Harm Reduction Coalition: Overdose Prevention Project

The North Carolina Harm Reduction Coalition (NCHRC) Overdose Prevention Project began operating in August 2013. The NCHRC has over 200 volunteer contractors

who help dispense free naloxone kits at various locations in North Carolina. Following the passage of the 911 Good Samaritan/Naloxone Access bill (2013's Senate Bill 20), the NCHRC has been able to distribute kits in diverse settings such as MAT clinics, community outreach centers, drug user hangouts, drug courts, jails, homeless camps, law enforcement centers, community parks and bus stops. There is no legal requirement for the receiver of the kit to be trained, and the law provides immunity to anyone who uses the naloxone kit in a medical emergency situation. When distributing the kits, NCHRC volunteers provide a short verbal training on how to recognize overdose symptoms and how to use the kit, as well as a pamphlet on naloxone utilization and law. The NCHRC reported that as of January 2016, it had distributed 22,277 naloxone rescue kits, leading to the reversal of 1,989 overdoses (personal communication with North Carolina Harm Reduction Coalition, 2016). The overdose prevention data are based on the reports of people who inform NCHRC staff about their experiences using the kit, usually when asking for a replacement or via outreach.

A NCHRC naloxone kit contains two 1 mL single-doses of naloxone in two separate vials placed inside a small UV-protected pouch, two 3 mL 23 gauge IM syringes, a brochure explaining how to recognize overdose and how to load and give naloxone, and contact information and information about the 911 Good Samaritan and Naloxone Access Law (2013's SB20 and 2015's SB154). It also contains a label with the prescribing physician's name, date of prescription and serial number. All of these are

placed inside a clear plastic pouch. Naloxone is administered by injecting 1 mL of naloxone intramuscularly into the upper arm, buttocks or thigh. If there is no response within two minutes, another 1 mL dose is given the same way. The syringes are intentionally large for two reasons. First, the large size allows injecting through heavy clothing and jackets, facilitating faster response. In addition, some people in the US are opposed to giving out needles that might be used for injecting illegal drugs into the veins. The large syringes in the naloxone kits are meant for intramuscular injection rather than injection into the bloodstream via the veins; if used to inject a drug intended for a euphoric high or pain relief, much of it would be wasted through injection outside the veins. After receiving an injection of naloxone, it is recommended that the individual receive emergency medical attention, usually by calling the emergency response number 911 to ensure the individual is out of medical harm.

These kits are distributed by NCHRC in almost all of the more than 40 MAT clinics in the state of North Carolina. The clinics where this study was conducted introduced naloxone distribution in 2014-2015. The Hickory Metro Treatment Center introduced it in 2014, and the naloxone distribution program has been conducted there every 3 months since. At Crossroads Treatment Center of Ashville, naloxone distribution was also introduced in 2014 and the program is conducted every month due to the large population of opioid-drug dependent patients in the area. At the BAART

Community Healthcare Treatment Center in Durham, naloxone distribution was started in 2015 and is conducted every three months.

Despite considerable evidence of positive outcomes from using naloxone as an antidote for opioid overdose, its use remains limited due to the lack of wide access to naloxone and the fear of criminal prosecution by prescribers, bystanders and first responders who would administer naloxone to overdosed drug users. However, US federal government agencies are now coming together to make naloxone more accessible in both medical and community settings. Even so, little research has been done on the actual use of naloxone kits in the field, and the present literature is limited in reporting what encourages people to get and carry a naloxone kit.

The current study sought to identify the facilitators of, and barriers to, using naloxone kits among opioid users seeking treatment at MAT clinics in North Carolina. It aimed to identify:

1) How opioid users seeking treatment at methadone clinics hear about naloxone kits and what factors relate to them getting the kit for themselves; and
2) Perceived facilitators of, and barriers to, carrying the kit, using it, and calling 911 when they witness an overdose or a near overdose.

This study makes a unique contribution to the literature by focusing on the variables related to the willingness of MAT patients to get and carry a naloxone kit.

2. Methods

We used a mixed methods approach consisting of: 1) observant participation and 2) surveys which included both close-ended questions analyzed quantitatively, and open-ended questions analyzed qualitatively.

Observant participation: Between June and August 2015, we accompanied the NCHRC staff to four MAT clinics in three North Carolina cities: Hickory, Asheville and Durham. The study's first author was a volunteer for the NCHRC and worked as an intern with the NCHRC at that time. She sat at a table set up by the NCHRC staff and listened when methadone/buprenorphine treatment-seekers asked the staff questions about how to use naloxone, or reported when they had used naloxone to reverse an overdose. Treatment-seekers and staff also engaged in conversation about their experiences, as well as their friends' experiences, with drug use, laws and law enforcement. On each observation day, the first author wrote field notes on these conversations. We used the field notes to identify additional themes during the coding of the open-ended survey items and to help us interpret the quantitative survey findings.

Survey recruitment and data collection*:* We recruited participants with help from NCHRC staff. People come to MAT clinics seeking methadone/buprenorphine to prevent cravings for opioids; they must often wait in line. All participants have a history

of using opioid drugs, either prescription opioid or heroin, for which they are currently seeking treatment at the MAT clinic. However, their current drug use or the choice of drug was not asked because one of the requirements of the treatment center is that they stop taking any drugs except the prescribed methadone or buprenorphine and participants would have been reluctant to share that information. When clients arrived at MAT clinics in Hickory, Asheville or Durham, North Carolina, this study's first author or a NCHRC staff member approached them and asked study eligibility questions, specifically being 18 years and above, being fluent in English and having heard of naloxone as a drug to reverse opioid overdose, regardless of whether they had ever possessed a naloxone kit. Eligible individuals were asked if they were interested in taking a 5-7 minute anonymous survey about naloxone. If they were interested, we followed a verbal consent process and then handed them a paper survey to self-administer. If they had reading barriers, we read the questions aloud in private. As compensation for their time, we provided light refreshments (e.g., donuts) while they completed the survey. All procedures were approved by the Duke University Arts & Sciences Institutional Review Board.

2.1 Measures

For the current study, all eligible participants were asked to answer a survey questionnaire on their naloxone use and their opinions about the current law. The questionnaire had a total of 15 questions divided into sections covering general

questions about naloxone kits, participants' experiences with using a naloxone kit, their practices in carrying the kit, their willingness to call 911 after using the kit and their opinions about the current law.

Information on participants hearing about the naloxone kit and factors relating to getting the kit for themselves, carrying it, using it and their willingness to call 911 was assessed with both open and closed ended questions that directly answered the study's aim and objectives. Additional information on their opinions about the law was assessed with an open ended question.

All questions were created by the author of this paper, following which the questions were reviewed by 3 content r experts who gave feedback. The questions were then modified accordingly to make it clear and understandable.

2.2 Analysis

Survey Data Analysis*:* We used univariate frequency tables to characterize the sample on gender, race, receipt of a kit, carrying the kit, and using the kit, witnessing overdose, receiving training on using the kit, confidence level with kit use, desire for changes in the law, and willingness to call the public emergency phone number 911. These data are presented as counts and percentages.

To examine the relation between the outcome variables (which included getting the kit, carrying the kit, and using the kit) and selected predictor variables, we conducted cross tabulation analysis and reported the frequency and percentages.

Finally, due to the small sample size, we used Fisher's Exact Test to assess the strength of the statistical associations between variables. All statistical analyses were conducted with SPSS version 22.

We analyzed open-ended survey questions through qualitative content analysis of the responses. We first created a list of all responses and then developed data-driven codes with definitions and examples of each. The first author assigned each participant response a code. A collaborator then independently coded the responses; few discrepancies occurred and all were reconciled by consensus.

3. Results

A total of 100 participants from MAT clinics in Hickory (N=36), Durham (N=38) and Asheville (N=26) took the survey. The sample was 58.6% female and predominantly White (90.8%), with 7.1% identifying as Black or African-American, and 2% identifying as neither White nor Black/African-American.

3.1 Facilitators and barriers to getting the naloxone kit

As seen in Table 1, 81% of female and 63% of male participants reported having ever gotten a naloxone kit. A majority (68%) reported receiving a kit from the NCHRC, 14% from a harm reduction coalition other than the NCHRC, 13% from a friend or family member, and 5% from a doctor or paramedic. Sixty-two percent of female and 46% of male participants reported that they had received training on how to use a naloxone kit. Of the 71 participants who had gotten a kit, 24% of females and 12% of males reported always carrying it. Twenty-one participants reported carrying a kit when they witnessed an overdose, and of those, 80% of females and 91% of males indicated that they had used naloxone from the kit to try to reverse the overdose. Sixty-nine percent of female and 66% of male participants thought current laws need to be changed to facilitate people calling 911 in cases of overdose.

Table 1: Experience with overdose and naloxone kits by gender

	Male % (n)	Female % (n)
Have you ever gotten a kit? (N=99)		
Yes	63.4% (26)	81.0% (47)
No	36.6% (15)	19.0% (11)
How often do you carry the kit? (N=71)		
Always	12.0% (3)	23.9% (11)
Sometimes/mostly	56.0% (14)	56.5% (26)
Never	32.0% (8)	19.6% (9)
Have you ever used the kit? (N=21)		
Yes	90.9% (10)	80.0% (8)
No	9.1% (1)	20.0% (2)
Have you ever been trained in using a naloxone kit? (N=99)		
Yes	46.3% (19)	62.1% (36)
No	53.7% (22)	37.9% (22)
How confident are you that you can use a naloxone kit right now? (N=99)		
Not at all confident	7.3% (3)	1.7% (1)
Slightly confident	4.9% (2)	8.6% (5)
Moderately confident	19.5% (8)	13.8% (8)
Very confident	36.6% (15)	32.8% (19)
Extremely confident	31.7% (13)	43.1% (25)
Have you ever witnessed an overdose? (N=99)		
Yes	78.0% (32)	67.2% (39)
No	22.0% (9)	32.8% (19)
Do you think there needs to be a change in the law? (N=99)		
Yes	65.9% (27)	69.0% (40)
No	34.1% (14)	31.0% (18)

Would you call 911 after witnessing an overdose? (N=99)		
Yes	90.2% (37)	96.6% (56)
No	9.8% (4)	3.4% (2)

Table 2 compares participants who had and who had not received a naloxone kit. Participants were more likely to have received a kit if they had been informed about naloxone through the NCHRC or a methadone clinic, or if they had friends or family who had ever gotten a kit.

Table 2: Experiences among people who have versus have not gotten a kit for themselves: Possible facilitators and barriers to getting a kit (N=100)

	"Have you ever gotten a kit for yourself?"		Fishers Exact Test, 2-tailed
Variables	Yes	No	
How did you first hear about naloxone kits? (*multiple responses possible* N=107)			
Family and friends % (n)	57.9% (11)	42.1% (8)	
NCHRC and/or MAT clinic % (n)	81.3% (61)	18.7% (14)	0.07
Media % (n)	66.7% (4)	33.3% (2)	
Other % (n)	57.1% (4)	42.9% (3)	
One or more friends have ever gotten a kit			
Yes % (n)	82.4% (42)	17.6% (9)	0.07
No % (n)	65.3% (32)	34.7% (17)	

A family member has ever gotten a kit			
Yes %(n)	88.5% (23)	11.5% (3)	0.07
No % (n)	68.9% (51)	31.1% (23)	

- "How did you first hear about naloxone/narcan kit" was a multiple response option item with "check all that apply" as an instruction. Total response size was thus more than 100 (n=107).

Among those who had never gotten a kit (n = 26), the primary barrier reported was accessibility, i.e., they did not know where to get one (Table 3).

Table 3: Primary barrier indicated to getting a kit for people who have never gotten a kit (N=26)

Categories	Frequency	Percent
- Did not know where to get it	13	50.0%
- Not at high risk of overdose	4	15.4%
- Don't know, just didn't get it	3	11.5%
- Didn't know it was available	3	11.5%
- Concerned kids will get hold of it	2	7.7%
- Fear of discrimination/prosecution by the police	1	3.8%
Total	26	100.0%

Responses to the open-ended survey items included:

"I had heard of these before, they showed it on the news, I think. I just didn't know where to get them from. Do you guys come here often? Will I get this at the pharmacy?" (White female)

"Didn't know where to get it from. I heard they sell it at the drug store. I didn't think about going. I didn't know it was free here." (White female)

3.2 Facilitators and barriers to carrying the naloxone kit

Table 4 shows that women and persons with friends or family members who possessed naloxone kits more often carried the kit with them.

Table 4: Factors and experiences related to the frequency of carrying a kit by people who have ever gotten a kit for themselves (N=72)

	"How often do you carry a kit with you?"			Fishers Exact Test, 2-tailed
Variables	Never %	Sometimes/ mostly %	Always %	
Gender				
Male	32.0%	56.0%	12.0%	0.35
Female	19.6%	56.5%	23.9%	
Ever witnessed an overdose?				
Yes	20.0%	62.0%	18.0%	0.42
No	31.8%	45.5%	22.7%	

Friend has ever gotten a kit Yes No	20.0% 28.1%	55.0% 59.4%	25.0% 12.5%	0.40
Family member has ever gotten a kit Yes No	26.1% 22.4%	47.8% 61.2%	26.1% 16.3%	0.45

Among the 57 participants who reported having received a kit but not always carrying it, the most commonly reported reason was that they felt they did not need it since they were no longer around drugs (Table 5). As one participant wrote:

"I usually give away the kits that I get. I do not feel comfortable carrying it with me because I have a small child that's why I am no longer using illegal drugs." (White female)

Another commonly reported barrier related to the logistics of carrying the kit. Complaints about the logistics of carrying kits were brought up numerous times. As one male participant described in the survey:

"It's too big to carry in my pocket, so I leave it in my backpack and often times I just forget it in my car." (White male)

Table 5: Primary barrier indicated to carrying a kit among people who have ever gotten a kit but who do not always (i.e., never/sometimes/mostly) carry a kit (N=57)

Categories	Frequency	Percent
Don't see self as at risk of overdose anymore	12	21.1%
Logistics of carrying a kit: difficult to carry, awkward to carry	11	19.3%
I forget to carry it	11	19.3%
Fear of prosecution/fear of police	9	15.8%
Fear of discrimination/embarrassment	7	12.3%
Concern for children around getting the kit	4	7.0%
Nothing, I just don't think it's necessary	3	5.3%
Total	57	100.0%

Among the participants who responded that they sometimes or mostly carry the kit, 61% said they sometimes or mostly carry it whenever they go out to a place such as a club, party, or festival where they think people might need it. As one female participant stated in the survey:

"When I go places, big parties, when I know a person might need a kit." (White female)

3.3 Facilitators and barriers to using the naloxone kit

Of the 72 participants who had witnessed an overdose, 29% were in possession of a naloxone kit at the time. Among those who had a kit with them, 86% (18 participants) reported using it. The survey included an open-ended question asking participants who did not use the kit why they did not use it. Only three participants answered this question, and each indicated:

"I didn't know how to use it."

3.4 Willingness to call 911 and opinions on current law

In response to the question, "Would you ever call 911 after witnessing an overdose or a near overdose?", 94% of participants stated that they would. Among the 74 participants who had gotten a kit for themselves, the figure was 96%, and among the 14 participants who reported always carrying the kit, 93%. Only 6% of participants indicated that they would not call 911. The most common reasons for not calling were not trusting the police and preferring to take action by oneself. One participant stated:

"If I have the kit then I would rather not call, I would rather take action myself because I don't trust cops. I don't want to go to jail for trying to save someone. They say it's not going to happen, but I don't trust them." (White male)

Sixty-eight percent of participants thought there need to be changes in current laws to make it easier for people to call 911 when they witness an overdose or near overdose. The most frequently cited concern was the need for greater protection for callers to ensure that police do not charge them for being present at the scene. For example, some participants stated:

"The laws have to understand that it's not a matter of trying to make an arrest but a matter of saving lives, because there would be deaths that could've been prevented. If someone wasn't scared that they will be going to prison, they would call more." (White male)

"The cops always come in and search when you call 911 to save a life. I don't want my house searched. Seeking medical care is great but not jail time." (White female)

"Even when people want to call they don't call 911 till they get rid of what they have on them. There should be no arrest if the cops come at that time, no matter what you have. It would save some time." (Unknown race and gender)

3.5 Data collection through observant participation

During the course of data collection, many participants mentioned confusion around how to use the naloxone kit. The most frequently raised question was whether naloxone should be administered in the same way as shown in one of the scenes from the movie "Pulp Fiction," in which a bystander injects an overdose reversal drug directly into the heart. Male participants also mentioned difficulties carrying the kit. In particular, they thought the kit was too large to be easily carried.

4. Discussion

Death due to overdose has become a major public health problem in the US. With the drug naloxone, morbidity and mortality due to opioid overdose is preventable. Naloxone has been used for many years by medical first responders. However, with the prevalence rate of overdose increasing, strategies beyond medical providers are needed. Because overdose often occurs in the company of friends and family, it is important to find ways for non-medical bystanders to respond quickly. But even with numerous efforts to expand naloxone kit distribution programs (Wheeler et al., 2015), naloxone often remains unavailable at the time and place where it is needed.

Prior research has asked naloxone kit distribution staff about the facilitators of, and barriers to expanding naloxone access to laypersons (Doyon et al., 2014). The current mixed-methods study adds to this literature by focusing on finding the barriers that prevent people who are themselves dependent on opioid drugs from getting a naloxone kit, carrying it once they have gotten it, and making use of it to counter overdose. This study also highlighted the potential facilitators that encourage people to obtain and use the kit. In addition, because laws may influence actions taken by bystanders, willingness to seek medical help and access to naloxone, this study also focused on participants' perceptions of, and opinions on, changing laws to facilitate 911 calls following an overdose reversal.

We found that women were more likely than men to get or carry a kit, even though they were slightly less likely to have witnessed an overdose or used naloxone from the kit. Past studies have shown that men are more likely to experience opioid overdose (WHO, 2014). Our study sample included more female than male participants. Women were more likely to report having received naloxone training, having greater confidence in using the kit, and having friends and family members with a kit. For men, the primary reported barrier to carrying the kit was logistical: it was too large to carry in their pockets, while women could carry it in their purses. Nevertheless, men were more likely to have witnessed an overdose and to have used naloxone at the time to counter it. This finding highlights the need to design a kit that is small enough to carry in a pocket.

The major barrier reported by participants to getting the kit was lack of knowledge about its availability. The majority of participants who had gotten a kit reported learning about it through the NCHRC and/or a MAT clinic where NCHRC can hang up posters about the law; most (68%) received the kit from the NCHRC. This finding is not surprising given that we recruited respondents in MAT clinics where the NCHRC does outreach work. A third reported source of learning about naloxone kits was through media sources, including the internet, television, and radio. Media sources are not to be underestimated; one of the most common questions asked by participants was about administering naloxone in the way it was done in the movie "Pulp Fiction." This suggests that television programs and movies can be valuable tools in informing

people about the risks of drug overdose and the use of overdose reversal drugs such as naloxone.

Of the participants who had gotten kits for themselves, only 19% reported that they always carried it. The leading reasons for not carrying the kit were practical: forgetting it at home or thinking that there was no reason to carry it when not around drugs. This was often related to the logistics of carrying a kit. After getting a kit, the inconvenience of carrying it around can encourage people to leave it at home, and lead to forgetting that they have it. On the other hand, participants who said they sometimes or mostly carried the kit did so when attending parties, clubs or festivals, suggesting that they take the kit with them when they think they are more likely to encounter overdose.

Among participants who had witnessed an overdose and had a kit with them at the time, 86% used it; the main reason for not using it was "I didn't know how to." Thus the main factors related to bystanders not administering naloxone were not having the kit with them in the first place, followed by not knowing how to use it. Our findings also suggest that having been trained to administer naloxone does not relate to actually using the kit. This may be due to the small sample size in our study, although direct conversation with participants suggested that most of them were highly confident about using naloxone to prevent overdose and thought that official training would not contribute to their knowledge, particularly knowledge on how to use a needle. Taken

together, our findings suggest that to increase bystander response to overdose, one should focus on informing people who spend time with opioid users about the existence of naloxone kits and the importance of carrying kits with them.

Opponents to the expansion of naloxone distribution programs in the US have expressed concern that having a naloxone kit may decrease people's willingness to call 911 for overdose emergencies, thereby putting them at medical risk because they may not seek appropriate medical care. We found that out of 100 participants, 94 indicated that they would call 911. However, this finding may also be due to the fact that our sample was predominantly White, and a study with more Black or other race participants could produce a different result. We found that among participants who had possessed a naloxone kit, 96% indicated that they would call 911. Thus, an overwhelming majority of participants planned to call 911 in case of an overdose, and action to the contrary should not be of great concern to policy makers. Although knowledge of the need to seek medical care following an overdose reversal appears widespread, naloxone kit distributers should continue to give this message.

We found that, despite legislation giving immunity to drug users when they call for assistance with overdose, and despite participants claiming that they would call 911, they were concerned about being arrested when they call police for help. The new laws still does not provide protection from being arrested (only from being prosecuted) but does add protection from probation and parole violations, which might encourage some

people who are on probation or parole to call 911. Hence, it is very important to focus on informing the population about the existing law. Additionally, it is important to ensure that the police adhere to the existing law. Engaging and training law enforcement on the law is essential.

4.1 Implications for policy and practice

After sharing these findings with the NCHRC volunteers, they informed us that one of the main challenges they face in expanding the naloxone distribution through MAT clinics was convincing the patient population about the overdose risk that they or their associates face with opioid use. The general belief among the participants at the methadone clinic was that, since they are seeking treatment currently, they no longer face overdose risk anymore. However, this is not true since methadone itself is an opioid drug and there is a high chance of patients relapsing, or possibly still continuing with their drug use outside without the knowledge of the treatment provider.

This information and the findings from the current paper highlight the need to address various issues preventing naloxone use to save lives. Future policies and practices should be focused on solving some of the main reasons discouraging people to get and carry a naloxone kit, such as designing a kit small enough to carry in a pocket and working on expanding information about the kits' availability and accessibility, together with current state laws.

Additionally, the clinics face their own problem with funding for the services they provide, which do not include naloxone distribution. All naloxone for these clinics is provided free of charge from NCHRC, funded by various grants and not federal or state funds. So if NCHRC's funding sources were ever decreased or cut, they may lose access to naloxone. Future policies should focus on expanding naloxone distribution through pre-existing infrastructures working for harm reduction intervention. Main structures that should be targeted for funding should be MAT clinics and syringe exchange programs.

4.2 Study strengths and limitations

This study had several limitations. Specifically, we used a very brief survey in order to increase participation, but its brevity limited the information collected about the participants. The study could benefit from a fuller understanding of participants' duration of opioid use and type of opioid used (i.e., prescription versus heroin), as well as their age. Secondly, the survey did not assess whether participants who had witnessed an overdose did so before or after getting a naloxone kit; we therefore cannot infer whether witnessing an overdose influences a person to get a kit. Thirdly, this survey only informs about MAT clinic patients' willingness to call 911 in case of an overdose emergency. A study involving active drug users not in treatment could produce a different finding. Future studies may consider collecting this information in order to identify more fully the facilitators of, and barriers to, naloxone kit usage.

5. Conclusion

In conclusion, opioid users are at risk of overdose and overdose-related death. Although one way to prevent these risks is to stop using opioids, this can be difficult due to drug dependence. This study sought to understand the facilitators and barriers to naloxone use among opioid users in North Carolina seeking MAT treatment. Naloxone kits offer a means of "harm reduction from below" – a way for opioid users to protect their lives. We found that opioid users who know about naloxone kits are willing to carry and use them, giving them a vital tool for overdose reversal.

Appendix A: Survey Questions

Section 1: General Questions about Naloxone/Narcan Kits

S1.1) How did you first hear about Naloxone/Narcan Kits? (Check all that apply.)

- ☐ From a friend/peer
- ☐ From my family
- ☐ Through Methadone Clinics
- ☐ Through the North Carolina Harm Reduction Coalition
- ☐ From the Internet
- ☐ Other, specify:_____

S1.2) Have you ever gotten a Kit for yourself?

☐ Yes

Where have you gotten a Naloxone/Narcan Kit from? (Check all that apply.)

- ☐ I got one from my friends and peers
- ☐ I got one from my family
- ☐ I got one from the North Carolina Harm Reduction Coalition (NCHRC)
- ☐ I got one from a Naloxone distribution program other than NCHRC
- ☐ Other, specify:_____

☐ No

If you have never gotten a Kit for yourself, what has prevented you from getting one?

_____

_____

S1.3) Have you ever had a complete training (other than a brief verbal instruction) on how to use Naloxone/Narcan Kits?

☐ No

I haven't been trained because:

_____

_____

_____

_____

☐ Yes, my training was from:

- o A friend/a family member
- o The internet
- o The North Carolina Harm Reduction Coalition (NCHRC)
- o A Naloxone distribution program other than NCHRC
- o Other, specify: _____

Section 2: Experiences with Using Naloxone/Narcan Kits

S2.1) How confident are you that you could use Naloxone/Narcan right now to reverse an overdose?

- ☐ Not at all confident
- ☐ Slightly confident
- ☐ Moderately confident
- ☐ Very confident
- ☐ Extremely confident

If you are not at all, slightly or only moderately confident that you could use Naloxone, what would you need to become more confident?

- ☐ More information
- ☐ More practice
- ☐ Other, specify: _____

S2.2) Have you ever witnessed an overdose or near overdose?

- ☐ No, I have never witnessed an overdose or near overdose
- ☐ Yes, but I did not have Naloxone/a Narcan Kit with me
- ☐ Yes, I have and I **did** have Naloxone/ a Narcan Kit with me

2b) Did you use the Naloxone/Narcan Kit at that time?

- ☐ Yes, I did
- ☐ No, I did not

2c) If No, what prevented you from using the Kit?

_____
_____
_____
_____
_____

S2.3) We are trying to improve Naloxone trainings. What questions do you have about using Naloxone/Narcan Kits for overdose reversals?

I would like to know:

_____
_____
_____

Section 3: Practices in carrying Naloxone/Narcan Kit

S3.1) How often do you carry a Kit with you?

- ☐ I have never gotten a Kit for myself
- ☐ Never, even though I have had a Kit
- ☐ Sometimes. Please tell us when:_____
  _____
- ☐ Most of the time
- ☐ Always

S3.2) What usually prevents you from carrying Naloxone/a Narcan Kit with you?

_____

S3.3) Do you have one or more friends who carry Naloxone/a Narcan Kit?

☐ Yes
☐ No

S3.4) Do you have any family members who carry Naloxone/a Narcan Kit?

☐ Yes
☐ No

Thanks for answering these questions so far. Now we have a few questions about what happens after Naloxone is used. It is recommended that the person who nearly overdosed get medical attention. We would like your help to understand whether medical attention is commonly sought or not and if not, what gets in the way.

Section 4: After using Naloxone/Narcan

S4.1) Would you ever call 911 after witnessing an overdose or a near overdose?

☐ Yes
☐ No

If no, why not?:
_____
_____
_____

S4.2) Would you ever seek medical care (not through 911) after personally experiencing an overdose or urge someone to seek medical care after experiencing an overdose or a near overdose?

☐ Yes
☐ No

If no, why not?
_____
_____
_____
_____

S4.3) Do you think there need to be changes in the current laws to make it easier for people to call 911 when they witness an overdose?

- ☐ Yes
- ☐ No

If yes, in your opinion, what should these changes be?

_____
_____
_____
_____
_____
_____
_____

Section 5: Tell us a little about you

S5.1) What is your race or ethnicity? (Mark all that apply.)

- ☐ Black or African American
- ☐ White
- ☐ Latino/Hispanic
- ☐ American Indian (or Alaska native or Native American)
- ☐ Asian or Asian American
- ☐ Other:_____

S5.2) What is your gender?

- ☐ Male
- ☐ Female
- ☐ Transgender
- ☐ Other

Is this the first time you have taken this exact survey?

- ☐ Yes, this is the first time
- ☐ No, I have already taken this survey this summer

Thank you for taking this survey! Your answers will be combined with the answers from other people and used to improve Naloxone training.

References

21 U.S. Code § 353. (n.d.). *Exemptions and consideration for certain drugs, devices, and biological products.* Available from: https://www.law.cornell.edu/uscode/text/21/353#fn002029-ref.

Amato, L., Davoli, M., Perucci, C. A., Ferri, M., Faggiano, F., & Mattick, R. P. (2005). An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. *Journal of Substance Abuse Treatment, 28*(4), 321-329.

Bennett, G. A., & Higgins, D. S. (1999). Accidental overdose among injecting drug users in Dorset, UK. *Addiction, 94*(8), 1179-1189.

Brettle, R. P. (1991). HIV and harm reduction for injection drug users. *AIDS, 5*(2), 125-136.

Brocato, J., & Wagner, E. (2003). Harm reduction: A social work practice model and social justice agenda. *Health & Social Work, 28*(2), *117.*

Centers for Disease Control and Prevention. (2012). Community-based opioid overdose prevention programs providing naloxone—United States, 2010. *Morbidity and Mortality Weekly Report*, *61*(6):101–105.

Centers for Disease Control and Prevention. (2015). *National Vital Statistics System mortality data.*

Centers for Disease Control and Prevention. (2015, June 19). Opioid Overdose Prevention Programs Providing Naloxone to Laypersons — United States, 2014. *Morbidity and Mortality Weekly Report*, *64*(23);631-635.

Cicero, T., Ellis, M., Surratt, & Kurtz, S. (2014). The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years. *JAMA Psychiatry*, *71*(7):821-826. doi:10.1001/jamapsychiatry.2014.366.

Cicero, T., Ellis, M., Surratt, H., & Kurtz, S. (2014). The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years. *JAMA Psychiatry 71*(7), 821-826. doi:10.1001/jamapsychiatry.2014.366.

Darke, S., & Hall, W. (2003). Heroin overdose: research and evidence-based intervention. *Journal of Urban Health*, *80*(2), 189-200.

Darke, S., Ross, J., & Hall, W. (1996). Overdose among heroin users in Sydney, Australia: Prevalence and correlates of non-fatal overdose. *Addiction*, *91*(3), 405-411.

Davis, C., & Carr, D. (2015). Legal changes to increase access to naloxone for opioid overdose reversal in the United States. *Drug and Alcohol Dependence, 157*, 112-120.

Dettmer, K., Saunders, B., & Strang, J. (2001). Take home naloxone and the prevention of deaths from opiate overdose: two pilot schemes. *British Medical Journal, 322(7291)*, 895–896.

Doe-Simkins, M., Quinn, E., Xuan, Z., Sorensen-Alawad, A., Hackman, H., Ozonoff, A., & Walley, A. Y. (2014). Overdose rescues by trained and untrained participants and change in opioid use among substance-using participants in overdose education and naloxone distribution programs: a retrospective cohort study. *British Medical Journal*, *14*(1), 297.

Doyon, S., Aks, S. E., & Schaeffer, S. (2014). Expanding access to naloxone in the United States. *Clinical Toxicology, 52*(10), 989-992.

General Assembly of North Carolina. (2013). *Senate Bill 20.* Retrieved from: http://www.ncga.state.nc.us/Sessions/2013/Bills/Senate/HTML/S20v7.html.

Jones, C., Paulozzi, L., & Mack, K. (2014). Sources of Prescription Opioid Pain Relievers by Frequency of Past-Year Nonmedical Use: United States, 2008-2011. *JAMA Intern Medicine*, *174*(5):802-803. doi:10.1001/jamainternmed.2013.12809.

Laxmaiah Manchikanti, M. D., Standiford Helm, I. I., MA, J. W., PhD, V. P., MSc, J. S., & DO, P. (2012). Opioid epidemic in the United States. *Pain Physician, 15*, 2150-1149.

MacCoun, R. (1997). *The psychology of harm reduction: comparing alternative strategies for modifying high-risk behaviors.* Paper presented at the 1996 Wellness Lectures, University of California, Santa Monica. (Reprinted by Rand/RP-6 11) .

Maher, C., Martin, T., & Childers, S. (2005). Mechanisms of mu opioid receptor/G-protein desensitization in brain by chronic heroin administration. *Life sciences, 77*(10), 1140-1154.

Manchikanti, L., Whitfield, E., & Pallone, F. (2005). Evolution of the National All Schedules Prescription Electronic Reporting Act (NASPER): A public law for balancing treatment of pain and drug abuse and diversion. *Pain Physician, 8*(4), *335*.

Manubay, J., Muchow, C., & Sullivan, M. (2011). Prescription drug abuse: epidemiology, regulatory issues, chronic pain management with narcotic analgesics. *Primary Care: Clinics in Office Practice, 38*(1), 71-90.

Marlatt, G. (1996). Harm reduction: Come as you are. *Addictive behaviors, 21*(6), 779-788.

Mcgregor, C., Darke, S., Ali, R., & Christie, P. (1998). Experience of non-fatal overdose among heroin users in Adelaide, Australia: circumstances and risk perceptions. *Addiction*, *93*(5), 701-711.

Miller, P. G. (2009). Safe using messages may not be enough to promote behaviour change amongst injecting drug users who are ambivalent or indifferent towards death. *Harm Reduction Journal*, *6*(18), 10-1186.

Monforte, J. R. (1977). Some observations concerning blood morphine concentrations in narcotic addicts. *Journal of Forensic Sciences*, *22*(4), 718-724.

Muhuri, P. K., Gfroerer, J. C., & Davies, M. (2013). Associations of nonmedical pain reliever use and initiation of heroin use in the United States. The CBHSQ Data Review.

National Survey on Drug Use and Health (NSDUH). (2014). *Available from: http://www.samhsa.gov/data/sites/default/files/NSDUH-SR200-RecoveryMonth2014/NSDUH-SR200-RecoveryMonth-2014.htm%20v*.

North Carolina Harm Reduction Coalition. (2015). *Available from: http://www.nchrc.org/*.

PK, M., JC, G., & MC, D. (2013). Associations of nonmedical pain reliever use and initiation of heroin use in the United States.

Slevin, K., & Ashburn, M. (2010). Primary care physician opinion survey on FDA opioid risk evaluation and mitigation strategies. *Journal of opioid management*, *7*(2), 109-115.

Sporer, K. A. (2003). Strategies for preventing heroin overdose. *British Medical Journal*, *326*(7386), 442-444.

Strang, J., Best, D., Man, L.-H., Noble, A., & Gossop, M. (2000). Peer-initiated overdose resuscitation: fellow drug users could be mobilised to implement resuscitation. *International Journal of Drug Policy*, *11*, 437–445.

Strang, J., Darke, S., Hall, W., Farrell, M., & Ali, R. (1996). Heroin overdose: the case for take-home naloxone. *British Medical Journal*, *312*(7044), 1435.

Strang, J., Kelleher, M., Best, D., Mayet, S., & Manning, V. (2006). Emergency naloxone for heroin overdose: Should it be available over the counter? *British Medical Journal, 333*(7569), 614–615.

Strang, J., Manning, V., Mayet, S., Best, D., Titherington, E., Santana, L., & Semmler, C. (2008). Overdose training and take-home naloxone for opiate users:prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. *Addiction, 103*(10), 1648-1657.

Substance Abuse and Mental Health Services Administration Rockville, MD. (2013). Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings. *NSDUH Series H-46, HHS Publication No. (SMA),* pp. 13-4795.

Tenenbein, M. (1984). Continuous naloxone infusion for opiate poisoning in infancy. *The Journal of Pediatrics*, 105(4), 645-648.

UNODC. (2015). World Drug Report. p. Retrieved from: http://www.unodc.org/wdr2015/.

Volkow, N. (2014). Prescription Opioid and Heroin Abuse. *Available from: http://www.drugabuse.gov*.

Walley, A. Y., Xuan, Z., Hackman, H. H., Quinn, E., Doe-Simkins, M., Sorensen-Alawad, A., & Ozonoff, A. (2013). Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. *British Medical Journal, 346*, f174.

Wermeling, D. P. (2010). Opioid harm reduction strategies: focus on expanded access to intranasal naloxone. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 30*(7), 627-631.

Wheeler, E., Jones, T. S., Gilbert, M. K., & Davidson, P. J. (2015). Opioid overdose prevention programs providing naloxone to laypersons—United States, 2014. *Morbidity and Mortality Weekly Report, 64*(23), pp. 631-635.

WHO. Data available from: http://www.who.int/substance_abuse/information-sheet/en/. (n.d.).

Williams, A. V., Strang, J., & Marsden, J. (2013). Development of Opioid Overdose Knowledge (OOKS) and Attitudes (OOAS) Scales for take-home naloxone training evaluation. *Drug and Alcohol Dependence, 132*(1), 383-386.

Wood, E., Werb, D., Marshall, B., Montaner, J., & Kerr, T. (2009). The war on drugs: a devastating public-policy disaster. *The Lancet, 373*(9668), 989-990.

Zador, D., Sunjic, S., & Darke, S. (1996). Heroin-related deaths in New South Wales, 1992: toxicological findings and circumstances. *Medical Journal of Australia*, *164*(4), 204-206.