

**EVALUATION OF NALOXONE TAKE-HOME KIT DISTRIBUTION TO  
EMERGENCY DEPARTMENT PATIENTS TREATED AND RELEASED FOR OPIOID  
OVERDOSE**

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**ABSTRACT**

**Purpose:** The United States (U.S.) is encountering an opioid public health crisis. Opioid use disorder (OUD) and overdose has become a top public health issue and a burden on health care costs and mortality rates. In 2016, there were over 33,000 deaths from opioid overdose in the U.S., and 3,383 deaths in Pennsylvania (PA). Due to this public health concern, the Allegheny General Hospital (AGH) Emergency Department (ED) strives to provide all opioid overdose patients with either a prescription for naloxone or naloxone take-home kit prior to patient discharge. Naloxone is an opioid antagonist that binds to opioid receptors. Naloxone therapy is used in opioid overdose because it displaces the opioid drug from the receptors and reverses the effects, particularly death from opioid overdose induced respiratory depression and hypotension.

**Methods:** The primary objective of this retrospective quality improvement study was to determine the number of patients treated and released in the AGH ED for opioid overdose. Secondary objectives included determining the percentage of opioid overdose patients with health insurance, the percentage of opioid overdose patients provided a naloxone prescription or naloxone take-home kit prior to ED discharge, and mean ED length of stay of these patients. Identification of study patients was determined using ED discharge diagnoses; heroin overdose, drug overdose, narcotic overdose, opiate overdose, general overdose, and various trauma diagnoses. Data was obtained using AGH's electronic medical records.

**Results:** From October 1, 2016 through December 31, 2016, a total of 103 unique patients with 106 visits were treated and released for opioid overdose. Patients were mostly male (70.6%), with a mean age 37 years (range 27-64 years). Seventy-nine percent (81/103) of patients were insured. Take-home naloxone was provided in 58 percent (61/106) of ED visits, and mean ED length of stay was 165 minutes (range: 12-733 minutes).

**Conclusion:** This information can be used to anticipate the future volume of patients treated and released in AGH ED for opioid overdose and assist in the design of a sustainable take-home naloxone program.

## TABLE OF CONTENTS

<b>PREFACE.....</b>	<b>IX</b>
<b>1.0 INTRODUCTION.....</b>	<b>1</b>
<b>1.1 OVERVIEW.....</b>	<b>1</b>
<b>1.2 NALOXONE REGULATIONS.....</b>	<b>3</b>
<b>1.3 NALOXONE ACCESS IN THE COMMUNITY .....</b>	<b>4</b>
<b>2.0 EVALUATION OF NALOXONE TAKE-HOME KIT DISTRIBUTION TO EMERGENCY DEPARTMENT PATIENTS TREATED AND RELEASED FOR OPIOID OVERDOSE .....</b>	<b>7</b>
<b>2.1 METHODS.....</b>	<b>7</b>
<b>2.2 RESULTS .....</b>	<b>9</b>
<b>2.3 DISCUSSION.....</b>	<b>11</b>
<b>3.0 CONCLUSION.....</b>	<b>14</b>
<b>APPENDIX: LIST OF DISCHARGE DIAGNOSIS CODES USED IN PATIENT SELECTION .....</b>	<b>15</b>
<b>BIBLIOGRAPHY .....</b>	<b>17</b>

## LIST OF TABLES

Table 1. Baseline characteristics of patient population .....	9
Table 2. Length of stay of patients in the emergency department and times of discharge .....	10

## LIST OF FIGURES

Figure 1. Study population flow diagram .....	9
Figure 2. Number of patients with medical insurance and type of insurance patient had at the time of visit .....	10
Figure 3. Percentage of patients that received naloxone take-home kit at discharge .....	11

## **PREFACE**

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## 1.0 INTRODUCTION

### 1.1 OVERVIEW

#### *Opioid Crisis*

The United States is encountering an opioid public health crisis causing an unprecedented number of opioid overdoses leading to extensive health care costs and increases in preventable mortality.<sup>1</sup> The number of deaths from drug overdoses reached a record high in 2014 of more than 60% of them involving opioids.<sup>2</sup> An opioid overdose may be intentional or accidental. Intentional overdoses occur from the direct misuse of a prescription or illicit opioid, while accidental overdoses may occur secondary to miscalculations of an opioid dose or drug – drug interactions.<sup>3</sup> Reducing opioid overdose is a top public health initiative and the use of rescue naloxone is a key to decrease the number of overdose related deaths.<sup>1</sup>

Opioid drugs include illegal drugs such as heroin, as well as prescription medications used to treat pain such as morphine, codeine, methadone, oxycodone, and fentanyl.<sup>4</sup> All opioids mechanistically work by binding to mu, sigma and kappa ( $\mu$ ,  $\delta$  and  $\kappa$ ) opioid receptors.<sup>4</sup> Stimulating opioid receptors activates “reward centers” in the brain resulting in pain relief and can also affect mood, breathing, and blood pressure.<sup>4,5</sup> Opioid overdose is a medical emergency that requires immediate attention due to its association with hypotension, bradycardia and decreased respiratory rate often times resulting in hospitalization or death.<sup>2</sup> Deaths associated

with opioid overdoses has quadrupled since year 2000. In 2016, there were over 33,000 deaths from opioid overdose in the U.S., and 3,383 deaths in Pennsylvania.<sup>6</sup>

### ***Opioid Overdose Reversal Agents***

Naloxone (Narcan<sup>®</sup>) is a prescription drug with no abuse potential that is considered the standard of care for treatment of opioid overdose.<sup>7</sup> Naloxone is an opioid antagonist that competes and displaces the drug from  $\mu$ ,  $\delta$  and  $\kappa$  opioid receptor sites hence reversing all therapeutic and adverse drug effects.<sup>5</sup> Naloxone is used in inpatient and outpatient settings for rapid detoxification of patients in opioid overdose.<sup>7</sup>

Naloxone can be administered via intramuscular (IM), subcutaneous (SC), intranasal (IN) and intravenous (IV) routes.<sup>7</sup> The initial adult dose of naloxone is 0.4 mg to 2 mg and doses can be repeated to a total dose of 10 mg.<sup>8</sup> The IV formulation is commonly used in emergent situations by health care providers because of its 100% bioavailability and quick onset of action, 1-2 minutes. Naloxone is commercially available in prefilled vials and syringes.<sup>8</sup> IN naloxone is available in two forms; Narcan<sup>®</sup> nasal spray 4 mg per spray and intranasal naloxone generic sold with the mucosal atomization device (MAD) in 2 mg doses (1 per nostril) in the nasal atomizer. The onset of action of IN naloxone is 8-13 minutes.<sup>9</sup>

IN naloxone is effective but in some instances such as nasal mucosa damage may need to be followed by IV doses. One study showed that 83% of patient with an opioid overdose responded to IN naloxone within 3.4 minutes. Sixteen percent of individuals required additional IV naloxone and 5 of the 9 patients in this group has nasal abnormalities which may had decreased IN absorption.<sup>8</sup>

Any naloxone formulations can be included in a naloxone take-home kit however IN naloxone is a safe option because it does not require IV access (decreasing risk of blood borne pathogen exposure) and has been shown to be safe and effective with minimal training.<sup>8</sup> The IM formulation is also a safe alternative however the commercial IM product, Evzio<sup>®</sup> is very costly, greater than \$2300. This product is costly and IM has not showed that it more efficacious than IN. A study conducted comparing IN and IM demonstrated that IN administration has a more rapid onset and intensity as compared to IM.<sup>8</sup> Given this information, IN naloxone is commonly used in naloxone take-home kits and is the formulation included in AGH's naloxone take-home kits.

## **1.2 NALOXONE REGULATIONS**

Due to this overwhelming increase in opioid overdose deaths in recent year's policymakers are focused on fighting this crisis. Federal and State laws are being enacted to increase the public's access to and utilization of naloxone.

### ***United States Regulation***

As of July 2017, all 50 states and the District of Columbia have passed legislation to increase access to naloxone.<sup>10</sup> These regulations include various laws for providing immunity to medical professionals that prescribe and administer naloxone and laypersons that administer.<sup>10</sup> Forty states and the District of Columbia have passed an overdose Good Samaritan law.<sup>10</sup>

Good Samaritan laws also known as 911 immunity laws were developed to increase reporting of overdose by providing some protection from arrest or prosecution for individuals who report an overdose.<sup>11</sup> The scope of which violations and offenses are covered in the good Samaritan laws varies by state.<sup>11</sup> Generally, these laws provide immunity from arrest and prosecution for possession of controlled substances or controlled substance paraphernalia.<sup>11</sup> Some states provide additional immunity from; protective or restraining orders, probation or parole conditions, reporting mitigating factors, civil forfeiture and more.<sup>10</sup>

### ***Pennsylvania Regulation: Act 139***

In 2014, Pennsylvania passed Act 139 which provides a standing order for naloxone. The standing order allows any individual to obtain naloxone without a prescription. The Act also allows first responders to obtain, carry, and administer naloxone in the event of opioid overdose.<sup>12</sup> Bystanders can also administer naloxone to an individual experiencing overdose without any legal ramifications.<sup>12</sup>

## **1.3 NALOXONE ACCESS IN THE COMMUNITY**

### ***Naloxone in Outpatient Settings***

Numerous naloxone community based programs have been successful in providing take-home naloxone to individuals who require chronic opioid medications or are at high risk of overdose. The ease of use and lifesaving potential of naloxone makes it an optimal therapy in the outpatient setting for the reversal of overdose.<sup>3, 13</sup>

The Harm Reduction Coalition (HRC) is a national advocacy group that maintains a database of all organizations that provide naloxone to laypersons.<sup>14</sup> HRC conducted a survey from 1996 – June 2014 at 136 facilities that provided naloxone to laypersons.<sup>14</sup> The survey showed that combined the organizations provided naloxone kits to 152,283 laypersons and received reports of 26,463 overdose reversals.<sup>14</sup>

Take-home naloxone in combination with opioid education has been studied in an ED setting. The ED is a prime location for distribution because patients in active overdose will be taken to the ED directly. A survey was given over a 13 month period to 415 patients treated in an academic, urban, level 1 trauma center ED to evaluate the feasibility of an ED-based overdose prevention and intervention program.<sup>15</sup> Participants received overdose education or overdose education and take-home IN naloxone. A total of 51 (12%) completed the survey, of those 37 (73%) received opioid education and take-home naloxone. Of the 53% of patients that witnessed an overdose, 95% stayed with the patient, 74% called emergency services and 32% used naloxone to reverse the person.<sup>15</sup> Although the study was small with low follow up it showed that ED opioid overdose programs are feasible.

In the ED at AGH, physicians will write a prescription for naloxone to be filled at an outpatient pharmacy or dispense a naloxone take-home kit. Currently, the naloxone take-home kits include educational materials and Narcan® nasal spray. These kits are currently funded by a temporary grant from the Allegheny Health Network (AHN) Center for Inclusion Health.

### ***Cost – effectiveness***

There is limited to no relevant literature on the clinical and cost-effectiveness of naloxone administered in a home or community setting.<sup>16</sup> Proving cost-effectiveness for a naloxone take-home kit program can be challenging for multiple reasons; one reason is that even after naloxone

is administered to a patient experiencing opioid overdose they are still transported to the ED. Therefore, no cost-savings exist from decreased ED visits or hospitalizations. Also, there is the potential to explain cost-savings by the number of lives that are saved using naloxone however this endpoint is not feasible for most facilities to study, due to lack of follow up and inability to prove the naloxone used was from your facilities naloxone take-home kit program.

One epidemiological modeling study was conducted to evaluate cost-effectiveness of distributing naloxone to heroin users for laypersons reversal.<sup>16</sup> The model showed that naloxone distribution to heroin users is likely to decrease overdose deaths and be cost-effective.<sup>16</sup> The model showed that 6% of overdose deaths were prevented with naloxone distribution and that 1 death was prevented for every 227 naloxone kits distributed.<sup>16</sup> Lastly, the naloxone distribution cost was \$53 and the increased quality adjusted life years was 0.119 with an incremental cost-effectiveness ratio of \$438.<sup>16</sup>

## **2.0 EVALUATION OF NALOXONE TAKE-HOME KIT DISTRIBUTION TO EMERGENCY DEPARTMENT PATIENTS TREATED AND RELEASED FOR OPIOID OVERDOSE**

### **2.1 METHODS**

#### ***Objectives***

The primary objective of this study was to evaluate the number of patients treated and released from the AGH ED for opioid overdose. Secondary objectives included: percentage of patients with health insurance, percentage of patients provided a naloxone prescription or naloxone take-home kit prior to ED discharge, and mean ED length of stay.

#### ***Study Design***

A single center retrospective quality improvement study was conducted in order to determine the number of patients treated and released in the AGH ED for opioid overdose. Electronic medical records from October 1, 2016 to December 31, 2016 were used to identify patients. The study design and protocol were received by the Allegheny – Singer Research Institute (ASRI) Institutional Review Board (IRB), which determined that the study does not meet the definition of Human Subject’s research and did not fall under the purview of its IRB.

A naloxone take-home kit program was started in 2016 at AGH. Then Narcan® nasal spray for the naloxone take-home kits is supplied by a grant from AHN Center for Inclusion Health. This study was conducted at AGH in order to collect population data for those treated and released for opioid overdose in order to design a sustainable naloxone take-home kit program.

### ***Selection of Population***

A report was generated from AGH's electronic health record that included patients with the diagnosis codes listed in Appendix A. There was no standard code used for coding opioid overdose at discharge, therefore multiple diagnoses were selected in order to capture the population of patients treated and released for opioid overdose.

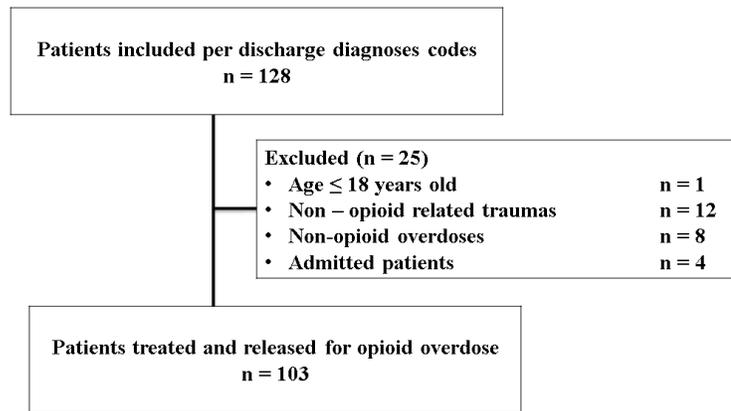
Inclusion criteria stipulated that adults 18 years and older that were treated and released at AGH ED for opioid overdose be included. Exclusion criteria included; admitted patients, non-opioid related traumas, and non-opioid related overdoses. Admitted patients were excluded because these patients would not be offered naloxone take-home kit; kits are only supplied in the ED.

### ***Statistical Analysis***

Descriptive statistics were performed for the primary and secondary objectives; these statistics included; mean, median, and range.

## 2.2 RESULTS

A total of 128 patients were evaluated for study inclusion, of which 25 were excluded, see Figure 1. A total of 103 patients over 106 visits were treated and released for opioid overdose from October 1 to December 31, 2016.



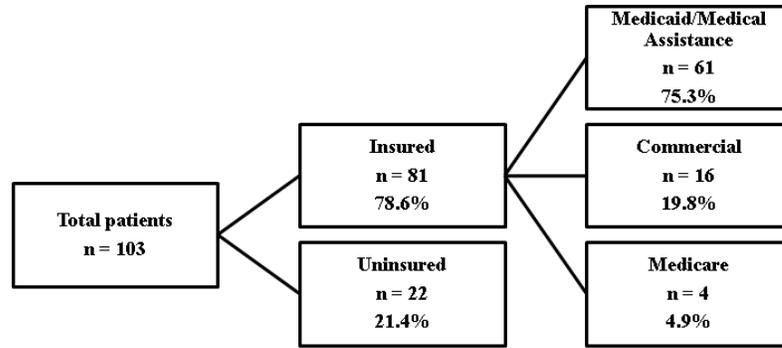
**Figure 1. Study population flow diagram**

### *Characteristics of the population*

The majority of the patient population was male (70.6%), with a mean age of 37 years, see Table 1. Of the 103 patients included, 79% (n = 81) of the patients had medical insurance. A majority of the patients with medical insurance, 75.3% (n = 61) were covered by Medicaid or medical assistance, see Figure 2.

**Table 1. Baseline characteristics of patient population**

Patients	n = 103
Age; mean (range)	37 years (27-64)
Male; n (%)	73 (70.6)
Repeat visits; n (%)	3 (2.9)

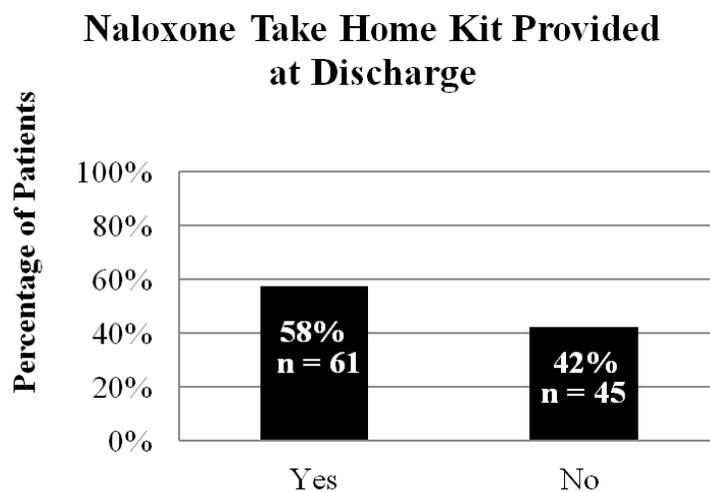


**Figure 2. Number of patients with medical insurance and type of insurance patient had at the time of visit**

The average length of stay (LOS) in the ED was 165 minutes (range 12 – 733 minutes). A majority of the patients were discharged outside of normal business hours of the onsite outpatient pharmacy, 77.4% (n = 82). Sixty five percent (n = 69) of patients were discharged outside of hours in which the pharmacy clinical specialists were present in the ED, see Table 2. At discharge none of the patients received a prescription for naloxone. Fifty eight percent (n = 61) received take-home intranasal naloxone at discharge. Reasons for not receiving a kit were not documented but could have included; refusal, the health care provider did not offer, or the patient left the hospital against medical advice (AMA).

**Table 2. Length of stay of patients in the emergency department and times of discharge**

Visits	n = 106	
ED LOS; mean (range)	165 min (12-733)	
Time of day discharged; n (%)	Outpatient pharmacy hours M-F, 7:00-18:00	24 (22.6)
	Non – outpatient hours	82 (77.4)
Emergency Medicine Clinical Pharmacist Hours; n (%)	Pharmacist hours M-F, 9:00-20:00	37 (34.9)
	Non-Pharmacist hours	69 (65.1)



**Figure 3. Percentage of patients that received naloxone take-home kit at discharge**

In a 3-month period, 103 patients were treated and released for opioid overdose. Based on this it can be predicted that in one year about 412 patients (103 patients x 4) could be treated and released for opioid overdose. Using an estimated cost of about \$140 per Narcan® IN spray it can be predicted that the cost of a naloxone take-home kit program drug cost per year would be approximately \$58,000 at the AGH ED ( $\$140 \text{ per Narcan}^{\circledR} \text{ IN} \times 412 \text{ patients} = \$57,680$ ).

### 2.3 DISCUSSION

The study aim was to collect descriptive data that can potentially be used in the establishment of a sustainable naloxone take-home kit program. The baseline characteristics of patients treated and released for opioid overdoses at AGH ED was found to be similar to that of the Allegheny County area. The total number treated and released in a 3 month period can be

extrapolated to estimate the population that would be served over a longer period of time and to predict the cost of naloxone take home kits.

### ***Limitations***

Limitations to the methods used in this study were that there is no hospital standard for selecting discharge diagnosis code for patients. The codes used are listed in Appendix A, however these may not have captured all the patients treated and released for opioid overdose. The result for the primary objective was most likely an underestimation of the total number of patients treated and released for opioid overdose.

Medical insurance was collected as an endpoint because it had the potential to serve as a possible source of payment for naloxone doses. The limitation to collecting medical insurance data is that not all medical insurance policies cover prescription medications; therefore one cannot assume a patient with medical insurance would have naloxone coverage.

### ***Developing a Naloxone Take-home Kit Program***

One key component to a sustainable naloxone take-home kit program is there being sufficient funds to cover the naloxone. AGH ED receives a grant for the current stock of Narcan® nasal spray. When that supply is completed one way to ensure the program can continue would be to process the naloxone dose through prescription insurance. This study showed that a majority of patients, 78.6% were insured. In order for an insurance claim for a prescription medication to be processed it must be conducted in real time through an outpatient pharmacy.

This possible source of revenue could be justification to continue a naloxone take-home kit program. However, the study also showed that the number of discharges of patients treated

and released for opioid overdose that occurred during the operating hours of the AGH outpatient pharmacy was 22.6%. Since the majority of patients were not seen during operating hours processing an insurance claim through the outpatient pharmacy to provide the naloxone prior to discharge will not be a viable option for the naloxone take-home kit program.

Another option for sustaining the naloxone program is to send patients with a prescription for naloxone if they cannot be given the drug free on site. However this poses two challenges; the first is the pharmacies in the local area do not have extended hours and a majority of patients were seen in off business hours. The second challenge is ensuring compliance with filling the prescription. This patient population is known to leave the ED against medical recommendation and would most likely not go to a pharmacy to fill and pay for a prescription. Some of the patients are in the ED for times as short as 12 minutes.

### ***Education***

The study results showed that 58% of patients treated and released for opioid overdose received naloxone at discharge. The AGH ED's goal is to have 100% of patients that are treated and released for opioid overdose receiving naloxone at discharge. The reason that patients did not receive naloxone take-home kit is unknown. Providing education of ED providers to increase awareness about the naloxone take-home kit program, where the kits are located, and how to dispense the kits may increase the number dispensed in the future.

### **3.0 CONCLUSION**

The data collected in this retrospective study can be used to assist in the design of a sustainable take-home naloxone program. The future steps for the AGH ED are to educate ED providers to provide naloxone take-home kits available at the ED for all patients treated and released for opioid overdose and develop a sustainable naloxone take-home kit program at AGH ED that might include relevant payers providing a supply of naloxone to patients during off hours.

**APPENDIX: LIST OF DISCHARGE DIAGNOSIS CODES USED IN PATIENT  
SELECTION**

Accidental heroin overdose  
Altered mental status; heroin  
Barotrauma, otic, initial encounter  
Blunt trauma to chest, initial  
Chipped tooth; Facial trauma  
Drug overdose  
Encounter for post-traumatic  
Facial trauma  
Fall; Laceration; Traumatic  
Fall; Traumatic hematoma  
Heroin abuse  
Heroin overdose  
heroin overdose; accidental or unintentional  
heroin overdose; aspiration into respiratory tract  
heroin overdose; drug abuse  
Laceration; trauma  
Narcotic overdose; accidental or unintentional  
Overdose  
Overdose of heroin  
Overdose, accidental or unintentional  
Overdose drug; accidental or unintentional  
Overdose; Heroin overdose; accidental or unintentional

Trauma

Trauma; neck pain

Traumatic dislocation

Traumatic ecchymosis of right

Traumatic hematoma of eyelid

Traumatic hematoma of forehead

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