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QUALITY IMPROVEMENT

Implementation of an Electronic Health Record Alert to Improve Naloxone Coprescribing for Adult Patients With Cancer at Risk for Opioid Overdose

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Authors' disclosures of conflicts of interest are found at the end of this article.

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Abstract

The Centers for Disease Control and Prevention and U.S. Public Health Service recommend that clinicians prioritize coprescribing take-home naloxone (THN) for patients with cancer receiving opioids in high doses or in the presence of a concomitant high-risk medication. Despite this, THN coprescribing rates remain low. The aim of this quality improvement project (QIP) was to determine if the implementation of an electronic health record (EHR) alert could result in increased THN coprescribing rates in patients with cancer at risk for opioid overdose. This pre- and post-intervention QIP was conducted in an outpatient medical oncology clinic in the Mountain West region of the US. Opioid prescriptions for the management of cancer-related pain totaling ≥ 100 morphine milligram equivalents (MME) per day or with a concomitant high-risk medication were eligible for inclusion (N = 224). An EHR alert was developed to notify the provider when eligibility criteria were met, prompting them to coprescribe THN. The primary outcome measure to increase THN coprescribing rates for opioid prescriptions totaling ≥ 100 MME per day was 38% at the end of the post-intervention period, a 29 percentage point increase from baseline (odds ratio [OR] = 6.57, 95% confidence interval [CI] = 1.85–23.39, p = .003). The coprescribing rate for opioid prescriptions with a high-risk medication was 57% at completion of the project, a 53 percentage point increase from baseline (OR = 30.67, 95% CI = 8.91–105.59, p < .001). This project established the practicality and success of THN coprescribing alert implementation and can be utilized as a roadmap for other practices to achieve safe opioid prescribing for patients with cancer.

Pain is one of the most prevalent and frightening cancer-related symptoms, with approximately 30% to 50% of patients with cancer experiencing pain at the time of diagnosis (Ruano et al., 2022). Significant resources have been dedicated to studying the pathophysiology and management of cancer-related pain over the years. Despite these efforts, opioids remain a cornerstone of treatment due to their rapid efficacy, tolerability, and lack of a ceiling effect, allowing higher doses to provide continued pain relief (Dalal & Bruera, 2019). Opioids, while effective for pain relief, also carry significant risks, including misuse, overdose, and even death. These dangers are especially apparent in the United States, which is currently facing an unprecedented opioid epidemic. From 1999 to 2020, approximately 564,000 deaths occurred due to opioid overdoses, with nearly half of these fatalities linked to prescription opioids (CDC, 2022).

The opioid epidemic has significantly impacted the management of cancer-related pain. It has heightened provider awareness of the potential for opioid misuse, even in a population once thought to be largely exempt, while also increasing patient awareness about the risks of opioid misuse and overdose. Reflecting national trends, there was a notable rise in opioid-associated deaths among patients with cancer and a two-fold increase in opioid-related emergency department (ED) visits for overdoses between 2006 and 2016 (Afezolli et al., 2023). Additionally, media coverage of the epidemic has altered patient perceptions of opioids and their associated risks, which may lead to behavior changes. For instance, some patients may modify or tamper with long-acting opioid formulations to reduce perceived risks, inadvertently increasing the risk of overdose (Afezolli et al., 2023).

In response to the opioid epidemic, many government agencies, including the Centers for Disease Control and Prevention and U.S. Public Health Service, have issued guidelines for safe opioid prescribing (Dalal & Bruera, 2019). These guidelines include the recommendation that providers consider prescribing take-home naloxone (THN), an opioid antagonist, when also prescribing opioids for patients at an increased risk of overdose (CDC, 2022). This practice is referred to as naloxone coprescribing. As national opioid prescribing guidelines have historically excluded patients receiving treatment for cancer-related pain, oncology providers have begun to look to professional organizations for population-specific guidelines. For example, the National Comprehensive Cancer Network (NCCN) has published guidelines recommending that THN be made available to patients deemed at high risk for overdose but has stopped short of providing specific clinical criteria for when to coprescribe (Swarm et al., 2019).

Despite these recommendations, THN coprescribing rates remain low across all clinical settings. In fact, a study to evaluate coprescribing rates in ambulatory clinics and EDs across the US found that in the almost 50,000 patient visits that met inclusion criteria, THN was coprescribed with opioids < 0.1% of the time (Gruver et al., 2020). Similar trends were observed locally in the outpatient medical oncology clinic at Cheyenne Regional Medical Center (CRMC), as baseline data obtained from the clinic revealed that only 1 in approximately 22 patients at increased risk for opioid overdose received a coprescription for THN.

Current literature supports the coprescription of THN for all patient populations at increased risk of overdose, including those receiving treatment for cancer-related pain. Expanding on the NCCN guidelines, Dalal and Bruera (2019) recommend that clinicians prioritize coprescribing THN for patients with cancer taking more than 100 morphine milligram equivalents (MME) per day or for those using opioids in combination with other high-risk factors, such as concurrent benzodiazepine use, a known history of substance misuse, pulmonary conditions (e.g., chronic obstructive pulmonary disease), or liver dysfunction. Calculations of MME help standardize opioid dosages by converting different opioids into morphine equivalents, allowing for better assessment of potency and overdose risk.

Additionally, substantial evidence supports interventions designed to increase coprescribing rates, such as electronic health record (EHR) alerts and order pathways. A study by Heiman and colleagues (2022) demonstrated the effectiveness of such measures, showing a significant rise in THN coprescribing rates following the implementation of an EHR alert (odds ratio [OR] = 5.66, 95% confidence interval [CI] = 4.11–7.78, $p < .001$).

METHODS

Context

The medical oncology clinic at CRMC is a hospital-based outpatient clinic providing care to adult (age 18 and older) patients with cancer in Southeast Wyoming. The organization uses Epic (Epic Systems Corporation) for its EHR. According to baseline data, the clinic generates 540 opioid prescriptions per year, 224 of which were eligible for inclusion for this QIP. Prescriptions for opioids totaling greater than or equal to 100 MME per day or opioids prescribed with a concomitant high-risk medication (defined as a benzodiazepine, benzodiazepine-related hypnotic, gabapentinoid, skeletal muscle relaxant, or barbiturate) were eligible for inclusion. Prescriptions from the pain management clinic or the organization's supportive care (formerly palliative care) and hospice teams were excluded, as naloxone is prescribed independently by these services according to their own criteria.

Intervention and Study of the Intervention

It was determined that the principal driving factors for low coprescribing rates included (1) limited provider knowledge regarding evidence-based recommendations for coprescribing in patients with cancer, (2) lack of patient education regarding risk factors for overdose and importance of THN coprescribing, and (3) the absence of clear clinical criteria and prompting by the EHR for when to coprescribe. Prior to this project, the decision of when to coprescribe THN was at the discretion of the provider or by request from the patient and/or caregiver.

To address these factors, three primary interventions were developed with the intention of increasing THN coprescribing rates. These included (1) implementation of an EHR coprescribing alert, (2) development and dissemination of evidence-based provider education, and (3) the creation and distribution of evidence-based patient education.

A new EHR alert was developed by the project lead with assistance from a senior Epic analyst and input from the director of quality and safety. The EHR alert was designed to notify the ordering provider when the patient was at increased risk of opioid overdose. For the purposes of this project, increased risk was defined as patients receiving greater than or equal to 100 MME per day or those receiving opioids with a concomitant high-risk medication (as defined previously). Utilizing data from the patient's active medication list, including drug classification and total daily MME, the EHR was able to determine eligibility. Based on the eligibility criteria, the alert was then activated at the time an opioid or high-risk medication order was placed. As shown in Appendix A, once displayed, the alert would notify the ordering provider that the patient was at increased risk of overdose, prompting them to prescribe THN. If prescribed, the provider would then be prompted by the EHR via a second alert to document if THN education was provided to either the patient and/or caregiver. If naloxone was not prescribed or the alert was overridden by the provider, it would continue to activate with each opioid or high-risk medication prescription until THN was prescribed or added to the patient's active medication list.

In addition to the EHR alert, a patient handout summarizing the use of THN for the prevention of opioid overdose was developed by the project lead (Appendix B). Prior to implementation, it was reviewed by the director of the oncology service line, director of the medical oncology clinic, and all medical oncology providers. Following approval, copies of the handout were then printed and placed in each exam room to distribute to patients and/or caregivers. A copy was also saved to the clinic shared drive, which the clinic staff could then upload and send via the patient portal or print and deliver via mail. Patient and/or caregiver education was performed by trained clinic staff either in person, by phone, or via the patient portal. For consistency, and to streamline clinic workflow, a call script and preformatted text block were created for staff to use when contacting patients.

Ahead of the EHR alert implementation, all clinic staff attended a 1-hour education session. This training was developed by the project lead using evidence-based practice and included a summary of the literature and guideline recommendations for THN coprescribing in patients with cancer. The training also included education on how to use the newly developed EHR alert, as well as proper documentation of patient and/or caregiver education.

Measures

The two outcome measures for the project were developed based on expert opinion from Dalal and Bruera (2019) with the intent of evaluating the overall impact of the project, which was to increase THN coprescribing rates for outpatient medical oncology patients at CRMC. These two measures included the percentage of opioid prescriptions totaling greater than or equal to 100 MME per day and the percentage of opioid prescriptions with a concomitant high-risk medication that received a coprescription for THN.

Four process measures were developed to evaluate compliance with the interventions. The first two process measures included the percentage of eligible patients properly identified by the EHR alert and the percentage of times the alert was utilized by staff. These two measures were created to evaluate the accuracy and usability of the alert. The second two process measures were developed for quality and safety purposes. This included the proportion of medical oncology staff that were educated about THN coprescribing and the percentage of patients that received education on the indications for and proper use of THN.

Finally, two balancing measures were developed to assess for unintended consequences that may have resulted due to the implementation of the interventions. Most importantly, this included the percentage of unintentional naloxone administrations resulting in emergency department (ED) visits or hospitalizations for pain crisis. The mean National Research Corporation (NRC) survey score for the question "Did the provider explain things?" was also monitored to ensure consistency in patient satisfaction following the implementation of the interventions.

Baseline and post-intervention patient demographics (e.g., age, sex, MME/day) were obtained from the EHR outpatient opioid prescribing report. The pre- and post-intervention data for the outcome and balancing measures were obtained from existing organizational reports with assistance from a senior Epic analyst as well as a data analyst employed by CRMC. For both outcome measures, data were collected monthly. For the balancing measures, data were collected twice, during both the pre- and post-intervention phases. Data for proper patient identification, alert utilization, and patient education were also collected monthly and obtained from EHR reports, which were newly developed and verified. Staff education was assessed via survey in the post-intervention period.

Analysis

The EHR alert implementation took place on October 1, 2023, and was followed by 6 months of post-intervention data collection, which was aggregated by month. Categorical variables for the pre-intervention (April 2023 through September 2023) and post-intervention periods (October 2023 through March 2024) were evaluated using descriptive statistics. The primary project aim was evaluated using Fisher's exact test, and statistical significance was set at $p < .05$. The accuracy of the EHR alert, provider utilization, provider education, patient education, and ED visits or hospitalizations for pain crisis due to unintentional naloxone administration were tracked at the appropriate interval and analyzed using a comparison of means with confidence intervals. A run chart adhering to Institute for Healthcare Improvement (IHI) run chart rules was utilized to monitor the NRC survey scores.

Ethical Considerations

All data utilized for the project were collected and treated in accordance with the policy and procedures of the project site. The project was deemed a quality improvement project by the University of Colorado Bridge Committee, and thus exempt from full institutional review board approval.

RESULTS

Outcome Measures

Baseline and post-intervention patient demographics are summarized in Table 1. At baseline, 42% ($n = 47$) of prescriptions totaled greater than or equal to 100 MME per day. This was compared to 28.2% ($n = 29$) in the post-intervention period. Pre-intervention data showed that 65.2% ($n = 73$) of eligible prescriptions were for opioids prescribed with a concomitant high-risk medication. This was compared to 78.6% ($n = 81$) post intervention. Most eligible prescriptions were prescribed to women. This was true for both the pre- and post-intervention time frames. Remarkably, 100% ($n = 5$) of THN coprescriptions in the

Table 1. Patient Demographics

	Pre-Intervention		Post-Intervention	
	Eligible prescriptions, *N* (%)	**THN coprescriptions, *n* (%)**	**Eligible prescriptions, *N* (%)**	**THN coprescriptions, *n* (%)**
No.	112	5	103	53
Age, yr				
18–34	0 (0)	0 (0)	2 (1.9)	0 (0)
35–64	64 (57.1)	5 (100)	72 (69.9)	36 (67.9)
> 65	48 (42.9)	0 (0)	29 (28.2)	17 (32.1)
Sex				
Female	62 (55.4)	0 (0)	63 (61.2)	29 (54.7)
Male	50 (44.6)	5 (100)	40 (38.8)	24 (45.3)
MME/day				
< 25	26 (23.2)	0 (0)	30 (29.1)	10 (18.8)
25–49	16 (14.3)	0 (0)	14 (13.6)	11 (20.8)
50–74	22 (19.6)	1 (20)	22 (21.4)	15 (28.3)
75–99	1 (0.9)	0 (0)	8 (7.8)	6 (11.3)
≥ 100	47 (42.0)	4 (80)	29 (28.2)	11 (20.8)
With HRM	73 (65.2)	3 (60)	81 (78.6)	46 (86.8)

Note. THN = take-home naloxone; MME = morphine milligram equivalents; HRM= high-risk medication.

pre-intervention period were for men, compared to only 45.3% (n = 24) post intervention.

As displayed in Table 2, the primary outcome measure to increase THN coprescribing rates for opioid prescriptions totaling greater than or equal to 100 MME per day was 38% at the end of the post-intervention period (OR = 6.57, 95% CI = 1.85–23.39, p = .003). This was a 29 percentage point increase from baseline and well above the established goal of 30%. Similarly, the THN coprescribing rate for opioid prescriptions with a concomitant high-risk medication was 57% at completion of the project (OR = 30.67, 95% CI = 8.91–105.59, p < .001). This too was well above the established goal of 15% and was an impressive 53 percentage point increase from baseline. Of note, the reasons for not coprescribing THN were captured in the comments section of the EHR alert. Of these documented reasons, the most common were inadequate time and/or EHR access, and patient and/or caregiver refusal.

Process Measures

Table 3 displays the outcomes for the process measures, which also yielded remarkable results. Consistent with the pre-intervention goals, all staff members received education prior to the project start date, and all eligible patients were properly identified by the newly developed EHR alert. In addition, 100% of patients who received a coprescription received proper education on the indications for and administration of THN. Utilization

Table 2. Comparison of Baseline and Post-Intervention Take-Home Naloxone Rates

	Pre-intervention (*N* = 112)	**Post-intervention (*N* = 103)**	**Odds ratio (95% CI)**	***p* value***
≥ 100 MME per day, *n* (%)	4 (9%)	11 (38%)	6.57 (1.85–23.39)	.003[a]
Opioid with HRM, *n* (%)	3 (4%)	46 (57%)	30.67 (8.91–105.59)	< .001[a]

Note. MME = morphine milligram equivalents; HRM = high-risk medication. [a]p < .05

Table 3. Comparison of Process and Balancing Measure Outcomes to Goal

	Goal percentage	Observed percentage (95% CI)
Clinic staff education	100%	100% (N/A)
Eligible patients identified by EHR alert	100%	100% (N/A)
EHR alert utilization by staff	50%	84.62% (75.54%–91.33%)
Patient education	100%	100% (N/A)
Unintentional naloxone administrations	0%	0% (N/A)

Note. EHR = electronic health record. Confidence intervals for proportions were calculated using the Clopper-Pearson method.

of the EHR alert by staff was 84.62% (95% CI = 75.54%–91.33%). This was excellent when compared to the established goal of 50%.

Balancing Measures

As shown in Table 3, there were no ED visits or hospitalizations for pain crisis due to unintentional naloxone administration during the intervention time frame. The run chart utilized to monitor the NRC survey score for the question "Did the provider explain things?" is shown in Figure 1 and demonstrates no significant variance in the average NRC survey score. Overall, these findings suggest there was no negative impact on the measures related to the implementation of the interventions, which was the intended goal.

DISCUSSION

Summary

The development and implementation of an EHR alert resulted in a significant increase in THN coprescriptions for patients with cancer at an increased risk of opioid overdose. This included a 29 percentage point increase in coprescribing rates for prescriptions totaling greater than or equal to 100 MME per day, and a 53 percentage point increase for opioid prescriptions with a concomitant high-risk medication. Alert utilization by staff was excellent, as was proper patient education on the indications for and administration of THN. There were no unintentional naloxone administrations resulting in ED visits or hospitalizations for pain crisis, and patient satisfaction scores did not decrease from baseline.

Interpretation

Consistent with the established project outcome and existing literature, successful application of evidence-based education and the development and implementation of an EHR coprescribing alert resulted in a substantial increase in THN prescriptions for patients with cancer at increased risk of opioid overdose.

The majority of THN prescriptions in the post-intervention phase were provided to women between the ages of 35 and 64 receiving an opioid with a concomitant high-risk medication. This was compared to the pre-intervention period when the majority of THN prescriptions were prescribed to men between the ages of 35 and 64 receiving greater than or equal to 100 MME per day. Breast cancer is a disease occurring predominantly in middle-aged women, and these patients were overrepresented in the clinic population, which may account for these findings. In addition, patients with breast cancer experience several treatment-related side effects, including postsurgical pain, nausea, and chemotherapy-induced peripheral neuropathy, which are often managed with high-risk medications such as opioids, benzodiazepines, gabapentinoids, and skeletal muscle relaxants.

The data also revealed that most eligible opioid prescriptions in the pre-intervention period were totaled greater than or equal to 100 MME per day (42%, $n = 47$), whereas the majority of prescriptions in the post-intervention period totaled less than 25 MME per day (28.2%, $n = 29$). These findings may suggest that the implementation of the EHR alert not only influenced THN coprescribing rates but may have also impacted opioid prescribing practices in the clinic.

As previously mentioned, the most common reasons for not coprescribing were inadequate time and/or EHR access. This was most likely related to

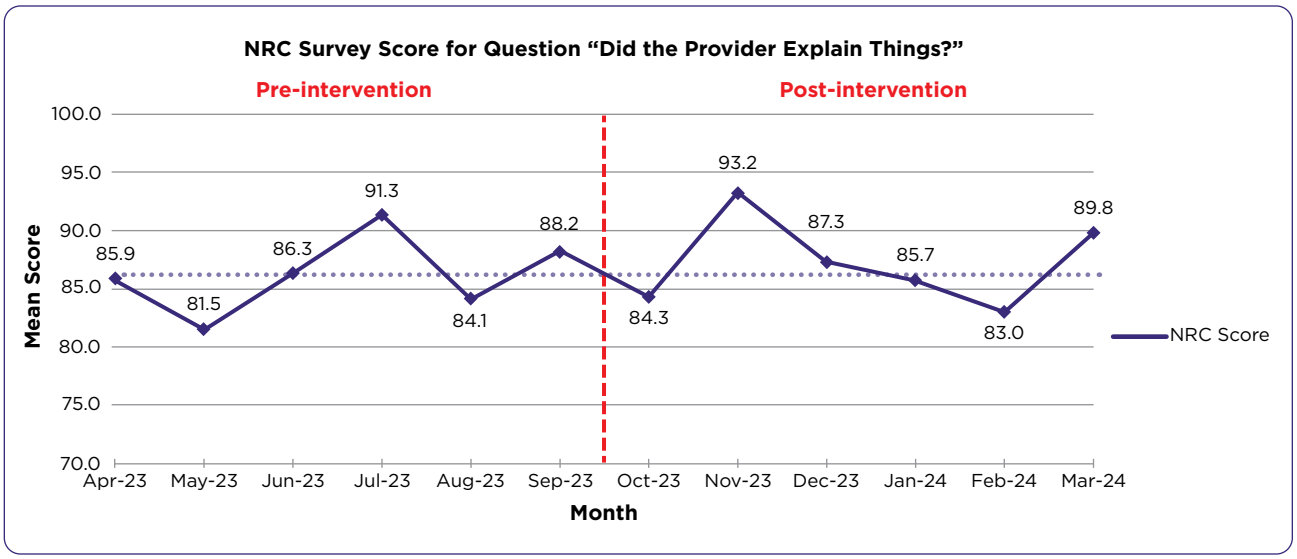

Figure 1. National Research Corporation (NRC) survey scores for the question "Did the provider explain things?"

two phenomena: (1) biometric multifactor authentication devices in the clinic exam rooms, which are required for the prescribing of controlled substances, did not work reliably, and (2) there was limited provider time due to a staffing shortage.

Limitations

This study had several limitations. First, the project was conducted in a rural hospital-based outpatient medical oncology clinic and may not be applicable to all settings. It is also possible that unmeasured confounding contributed to the observed effects, specifically increased societal awareness and acceptability of naloxone unrelated to the interventions of this project. In addition, patients with other high-risk features for opioid overdose, such as a history of substance misuse or concomitant pulmonary or liver disease, were not captured by the EHR alert. Lastly, it is not known whether naloxone was dispensed to the patient at the pharmacy, only that it was prescribed.

CONCLUSIONS

This successful quality improvement project demonstrates the effectiveness of evidence-based education and EHR coprescribing alerts in improving THN coprescribing rates within the oncology population, with minimal organizational cost beyond Epic support and staff training. While the findings are not generalizable, they offer a scalable model for other organizations aiming to enhance safe opioid prescribing. The study's implications extend beyond oncology, providing a practical framework that can be adopted in various healthcare settings to address the national opioid epidemic, improve patient safety, and promote safer opioid prescribing practices. ●

Disclosure

The authors have no conflicts of interest to disclose.

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Appendix A. EHR Alert for Naloxone Coprescription

Patient Safety Concern (1)

This patient is at risk for unintentional opioid overdose and a naloxone prescription is recommended.
!! Morphine milligram equivalent per day (MME/day)

Signing this order will affect the patient's morphine milligram equivalent per day (MME/day) for outpatient orders. Review the information below to ensure opioid dosing will remain within appropriate limits.

Cumulative MME/day (100 mg max recommended)
AFTER signing: **118.8 mg !** Before signing: **28.8 mg**

UNSIGNED OUTPATIENT OPIOIDS	MME/day
oxyCODONE-acetaminophen (PERCOCET) 5-325 mg per tablet Take 2 tablets by mouth every 4 (four) hours as needed for pain. Normal, Disp-20 tablet, R-0 Maximum MME/day: 90 MME/day for this order	90 mg

OTHER ACTIVE OUTPATIENT OPIOIDS	MME/day
fentaNYL (DURAGESIC) 12 mcg/hr Place 1 patch onto the skin every third day, historical med	28.8 mg

Order | Do Not Order | NALOXONE 4 MG/ACTUATION NASAL SPRAY

Acknowledge Reason

Doesn't Meet Criteria | See Comments

Appendix B. Naloxone: Use for the Prevention of Opioid Overdose

What is naloxone and how does it work?

Naloxone (Narcan®) is a life-saving medication that can temporarily reverse an overdose by blocking the effects of opioids. Naloxone can restore normal breathing in a person whose breath has slowed, or even stopped, as a result of opioid overdose.[1]

Potential risk factors for opioid overdose include:[2]

- Age > 65 years
- Concurrent medical conditions (e.g., lung disease, liver disease)
- Use of other high-risk medications or substances (e.g., alcohol, benzodiazepines)
- Use of high-dose opioids or extended release formulations

Signs and symptoms of an opioid overdose may include:[1,3]

- Unresponsiveness or loss of consciousness
- Shallow or slow breathing
- Small, constricted "pinpoint" pupils
- Gasping or no breathing at all
- Blue lips and blue fingertips

What to do if you suspect an opioid overdose[1,3]

- Call 911 immediately.
- If available, give naloxone as directed. Giving naloxone to a person who has not taken an opioid medication will not hurt them.
- Lay the person on their side to prevent choking.
- Stay with the person until emergency services arrive.

How to Administer Naloxone

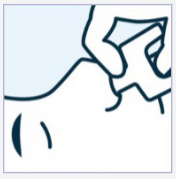
1

Remove the nasal spray from the box. Do not prime or test the nasal spray, as you may waste all or part of the medication.

2

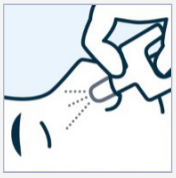
Hold the nasal spray with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle.

3



Gently insert the tip of the nozzle into one nostril, until your fingers on either side of the nozzle are against the bottom of the nose.

4



Press the plunger firmly to give the dose. You may give additional doses every 2 to 3 minutes until the person responds or help arrives.

Scan the QR code or visit https://www.cdc.gov/stopoverdose for resources on how to respond to an opioid overdose.

[1]https://www.cdc.gov/overdose-resources/pdf/Naloxone_FactSheet_Family_and_Caregivers_How_and_When_to_use_Naloxone_508.pdf
[2]https://www.who.int/news-room/fact-sheets/detail/opioid-overdose
[3]https://www.samhsa.gov/substance-use/treatment/overdose-prevention/opioid-overdose-reversal