

SYSTEMATIC REVIEW

Toxicology

Naloxone distribution programs in the emergency department: A scoping review of the literature

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Abstract

This scoping review summarized the literature regarding naloxone distribution from emergency departments (EDs) without a prescription. Our intention was to examine various naloxone distribution programs, their methodologies, and the level of effectiveness of each. Understanding these key aspects of naloxone distribution could lead to improved standardized protocols, saving countless additional lives from opioid overdose. This review evaluated studies reporting naloxone distribution from EDs in the United States. The included studies were written in English and published between January 1, 2017, and December 31, 2022. Searches were performed using PubMed and Embase. A total of 129 studies were reviewed, with only 12 meeting the necessary criteria for analysis. Heterogeneity was found across naloxone distribution programs, including how patients were identified, how naloxone was dispensed to patients, and the specific naloxone products made available. The protocols included various methods, such as patient screening, where information used for this screening was sometimes obtained from health records or patient interviews. Some programs detailed only the distribution of naloxone, while others included additional interventions such as behavior counseling, peer support, and education. In four studies, patients received buprenorphine with naloxone kits. The various programs differed in their implementation but were generally successful in improving naloxone distribution. However, among the studies reviewed, the percentage of ED patients receiving naloxone varied from ~30% to 70%, suggesting that certain program elements may be more impactful. Further research is needed to identify key elements of the most impactful programs in order to improve naloxone distribution and improve patient odds of surviving an opioid overdose.

KEYWORDS

emergency department, opioid overdose, substance use disorder, take-home naloxone

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1 | INTRODUCTION

1.1 | Background

The rate of opioid-related overdose deaths has been increasing over the past two decades. In 2021, there were 70,601 deaths from overdoses involving synthetic opioids (other than methadone) in the United States, compared with over 40,000 deaths in 2019.¹ The opioid overdose epidemic is often described as happening in three waves. In the first two waves, prescription opioids followed by heroin accounted for the greatest share of opioid-related deaths.² Recently, during the third wave, illicitly manufactured fentanyl has become increasingly prevalent.² Opioid-related overdoses contribute significantly to mortality in the United States. Furthermore, opioid-related hospitalizations³ and increased use of emergency medical services for opioid events⁴ place a significant burden on the healthcare system.

Opioid overdoses can be mitigated by medical interventions. Naloxone is an opioid antagonist that reverses opioid binding at the mu receptor, thereby preventing respiratory depression.⁵ Naloxone can be administered intranasally (IN) or by injection, which can be intramuscular, subcutaneous, or intravenous.⁵ Real-world studies highlight that in the majority of situations, naloxone administration is successful in reversing opioid overdose and saving patients' lives.^{6,7} At the population level, increased availability of and training on naloxone is associated with a decrease in overdose death rates.^{8,9} Legislation increasing access to naloxone has also been associated with lower overdose death rates.¹⁰

1.2 | Importance

Several strategies can be used for distributing naloxone, including community-based and pharmacy distribution, over-the-counter availability, and distribution from healthcare facilities.¹¹ Emergency departments (EDs) may be a particularly effective venue for naloxone distribution, as many individuals experiencing overdoses or other health outcomes related to both licit and illicit opioid use are seen in EDs. Distributing naloxone to these patients may help to prevent future adverse outcomes. The American College of Emergency Physicians supports naloxone distribution in EDs as an important intervention to prevent overdose deaths.¹²

Although the ED is an effective venue for naloxone distribution,¹³ there is still a need to increase the frequency of naloxone distribution to patients from EDs. One large US study found that only 7.4% of ED visits for opioid-related overdoses resulted in a naloxone prescription.¹⁴ In comparison, a Canadian study reported that nearly 50% of discharged overdose patients were offered take-home naloxone (THN), where naloxone is immediately provided to the patient rather than a prescription.¹⁵ Multifaceted THN programs, including not only immediate naloxone access, but also peer recovery coaching, provision of medication for opioid use disorder (OUD), and harm reduction supplies may be needed to further reduce incidence of opioid over-

TABLE 1 Search terms used for literature reviews.

<p>"naloxone" AND "emergency department" AND ("dispense" OR "distribute" OR "distribution" OR "dispensing" OR "take-home") AND ("challenges" OR "barriers")</p>
<p>"naloxone" AND "emergency department" AND ("dispense" OR "distribute" OR "distribution" OR "dispensing" OR "take-home") AND ("successful" OR "effective" OR "best practice")</p>
<p>"naloxone" AND "emergency department" AND ("dispensing" OR "dispense" OR "distribution" OR "take-home" OR "take home") AND ("success" OR "impact" OR "effective" OR "strategies" OR "outcome")</p>

doses. The scientific literature suggests significant deficits in providing naloxone to patients who have suffered an opioid overdose.¹⁶

1.3 | Goals of this investigation

Given the importance of improving access to naloxone in preventing fatal opioid overdoses and that the ED may be an underused venue for increasing naloxone distribution to at-risk patients, understanding existing naloxone programs is important. Therefore, this review seeks to analyze naloxone distribution from EDs with a focus on understanding the different methods used by each program, their impact, and implementation recommendations.

2 | METHODS

2.1 | Design

The development of this scoping review was informed by the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines.¹⁷ The inclusion criteria for this literature review comprised of studies reporting naloxone distribution from EDs in the United States and examining only peer-reviewed literature published in English. Additionally, studies were required to have some aspect of quantitative analysis to be included in this review. Articles describing protocols that provided a naloxone prescription were excluded.

2.2 | Search strategy

A comprehensive search for relevant articles was conducted within two databases, PubMed and Embase. Due to the extensive history of naloxone use, search criteria were limited to the date of publication ranging from January 1, 2017, to December 31, 2022. Searches were conducted to include "naloxone," "emergency department," and at least one variant of "distribution" with additional terms focusing on success, impact, strategies, or outcomes. A complete list of search terms is provided in Table 1.

2.3 | Selection of studies

The results from searches using both databases were collected and exported to a reference handling software EndNote. Initial screening was performed to exclude duplicates and others that did not meet the necessary inclusion criteria, such as non-English publications. Studies were then screened more closely through title and abstract information to exclude any that did not match the inclusion criteria for relevance, including restrictions of EDs in the United States and associated quantitative analysis. Remaining articles that met all inclusion criteria had full texts reviewed and author agreement for data synthesis and inclusion within this review.

3 | RESULTS

Figure 1 shows the results from the literature search on PubMed and Embase. Initial searches of the two databases resulted in a total of 257 studies identified. One hundred twenty-eight duplicates were removed, leaving 129 studies that were retrieved and evaluated. After reviewing of the titles, abstracts, and full texts, 117 studies were excluded because they did not meet the inclusion criteria. This resulted in a total of 12 studies that met the inclusion criteria for review.

Table 2 presents the characteristics of the included studies. One study used an approach combining education plus behavioral intervention and examined differences in overdose between a treatment group that received naloxone and a control group that did not.¹⁸ Additional studies evaluated the impact of screening for naloxone distribution,¹⁹ the impact of THN,^{20–22} acceptance of naloxone by drug users,²³ and clinicians' compliance with naloxone recommendations.²⁴ Four studies assessed the impact of a naloxone program, one of which paired naloxone distribution with peer recovery coaching.^{25–28} Finally, one study focused specifically on racial and ethnic differences among patients provided naloxone at discharge.²⁹ The methodologies of these studies varied, where one used an interventional approach,¹⁸ seven used a cross-sectional approach,^{19,20,22,24–26,29} three used a longitudinal cohort approach,^{21,23,28} and one study was a retrospective time period analysis.²⁷

Although published between 2017 and 2022, studies were conducted between 2013 and 2020. The oldest study was conducted between 2013 and 2015,¹⁸ while five studies had some data collection that took place in 2020.^{20,21,26,27,29} Many of the studies collected data in multiple years. Most studies considered patients as their unit of analysis; however, two studies used encounters, meaning that some individuals could have been seen multiple times,^{24,26} and two other studies used naloxone kits distributed as their unit of analysis.^{25,27} Sample sizes varied from a low of 30 ED opioid-related patients²³ to a high of 1036 opioid-related ED encounters.²⁴ All studies were conducted across different geographic regions of the United States.

The endpoints of the different studies varied. One intervention study compared the proportion of overdose-related events between the interventional group that received naloxone and the control group that did not.¹⁸ Devries et al.¹⁹ examined the percentage of

patients who accepted naloxone, while others examined the percentage of patients who received THN,^{21,22,24,26} or the number of naloxone kits that were distributed.^{10,25,27–29} One study tracked the movement of the naloxone kits after distribution using global positioning system (GPS) tracking with patient consent.²³ Several studies also had secondary outcomes including time to first overdose after receiving THN,¹⁸ characteristics of patients accepting naloxone,¹⁹ barriers to and facilitators of naloxone dispensing,²⁰ other interventions received,²¹ and factors associated with naloxone provision or distribution.^{22,24,28,29}

Table 3 shows the characteristics of the naloxone programs. Seven studies included a screening protocol for identifying patients for whom naloxone would be dispensed. These protocols typically focused on the reasons why patients were seen in the ED, which were usually related to opioids or a history of opioid use.^{18,21–23,25,26,29} In one study, this screening involved an interview.¹⁹ In other studies, inclusion was determined by having a referral for treatment related to opioids.^{24,28} One study left the distribution of naloxone to the discretion of the clinician.²⁰ Another study compared the number of distributed kits over time, but did not specify the patients who received them.²⁷

Although all interventions involved naloxone distribution, there were variations in additional components and distribution methods. Some studies utilized interventions involving multiple components, such as counseling and education.^{18,19,21,23–27,29} Four programs included buprenorphine distribution in addition to naloxone.^{21,24,26,27} Additional variations concerned the formulation of naloxone provided, including four studies that involved IN naloxone,^{21,25,28,29} others that used intramuscular naloxone,^{20,22} and one study that included both IN and intramuscular formulations.¹⁹ Among the studies that reported number of doses provided, the most common were two doses,^{21,22,29} with others providing either one²⁵ or three²⁰ doses.

Different methods were used to distribute naloxone to patients. Some studies reported that naloxone was distributed by either the hospital or research staff,^{18,23} by the hospital's pharmacy,¹⁹ or by nurses.^{21,22,28,29} In one study, various healthcare professionals, including pharmacists, nurses, and physicians, initiated the process of dispensing naloxone.²⁰ Naloxone dispensing machines were also used in multiple studies.^{24,25,28} The source and/or funding for naloxone varied across studies, such as donations,²⁰ grant funding,^{20,26} hospital pharmacy,²⁰ and hospital purchase.^{28,29} Two studies included some form of compensation for study participants.^{18,23}

Table 4 includes results from both the primary and secondary outcomes of the reviewed studies. Banta-Green et al.¹⁸ found no significant differences in ED visits, hospitalizations, or overdoses between the intervention group that received naloxone and the control group. In this study, the time to first overdose did not significantly differ between the two groups. The authors mentioned that the study's sample size of 241 opioid-related patients may limit its generalizability due to the high degree of housing instability (70% impermanently housed) and social factors among this vulnerable population.

Among the studies that focused on the proportion of patients who received naloxone, Devries et al.¹⁹ found that more than 60% of the patients in the study "accepted naloxone recommendations," and about

TABLE 2 Study characteristics and outcomes.

Study	Objective	Year	Study design	Sample size	Primary outcome	Other outcomes
Banta-Green et al., 2019	To assess the impact of an intervention for patients following ED visits, which included THN among other components	2013–2015	Intervention	241 ED opioid-related patients	Proportion of overdose related events between the intervention group that received naloxone and the control group that did not	Time to first overdose
Devries et al., 2019	To evaluate the outcomes of routine screening for the provision of THN in an ED	2016	Cross-sectional	182 ED opioid-related patients	Recommended and accepting THN or being prescribed naloxone	Characteristics of those accepting or declining naloxone
Eswaran et al., 2020	To evaluate a THN program in an ED	2018–2020	Cross-sectional	669 ED opioid-related patients	THN kits dispensed	Barriers to and facilitators of naloxone kit dispensing
Jacka et al., 2022	To examine different factors that impact patients THN	2017–2020	Cohort	742 ED opioid-related patients	Percent of patients who received THN	Other types of interventions received
Kestler et al., 2017	To examine the acceptance of THN among ED patients	2015	Cross-sectional	241 ED opioid-related patients	Percent of patients who THN	Factors associated with THN
Lai et al., 2020	To examine whether patients who use drugs accept naloxone	2017–2018	Cohort	30 ED opioid-related patients	Movement of naloxone kit off hospital grounds	Factors associated with naloxone provision
Lane et al., 2021	To assess how clinicians in an ED follow naloxone practice recommendations	2018–2019	Cross-sectional	1036 ED opioid-related encounters	Patient provided naloxone	Factors associated with naloxone provision
Mullenix et al., 2020	To improve the availability of naloxone through naloxone kit distribution	2017–2019	Cross-sectional	220 naloxone kits distributed to patients for opioid-related reasons	Number of naloxone kits distributed	
Moore et al., 2021	To assess a point-of-care distribution of naloxone in the ED	2020	Cross-sectional	208 opioid-related patient ED encounters	Obtainment of naloxone	
Ramdin et al., 2022	To assess the effect of a peer recovery program on naloxone kit distribution	2017–2020	Retrospective, time period analysis	238 naloxone kits distributed to patients to the ED for opioid-related reasons	Distribution of naloxone kits	
Reddy et al., 2021	To assess racial/ethnic differences in naloxone provided at discharge among ED patients	2017–2020	Cross-sectional	735 ED opioid-related patients	Naloxone distribution	Factors related to naloxone distribution
Samuels et al., 2018	To assess the impact of an ED naloxone program	2014–2015	Cohort	151 ED opioid-related patients	Receiving naloxone	Receiving naloxone and recovery coaching

Abbreviations: ED, emergency department; THN, take-home naloxone.

TABLE 3 Characteristics of take-home naloxone (THN) programs.

Study	Year	Participants	Intervention	Distribution method	Source of naloxone
Banta-Green et al., 2019	2013–2015	<p>Inclusion: reason for visit related to opioids, use of non-prescribed opioids, use of other opioids and drugs, a higher daily use of prescribed opioids, or enrollment in opioid agonist therapy.</p> <p>Exclusion: refusing medical record access, cannot communicate in English, suicide ideation, cognitive or psychiatric impairment, no-contact information provided, younger than 18 or older than 70 years, not living in WA, treatment for sexual assault, currently having naloxone.</p>	<p>The intervention included overdose education, behavior change counseling, and a naloxone kit. A \$20 gift card was provided for participating.</p>	<p>Given THN kit by staff.</p>	
Devries et al., 2019	2016	<p>Screening: a screening tool that was based on prescribing guidelines for naloxone was used. An interview was conducted to identify potential good candidates for naloxone. Questions focused on factors such as receiving emergency care for events due to opioids, history of non-medical opioid use or overdose, and other health issues.</p>	<p>The intervention included training in how to recognize and prevent opioid overdose, and how to use naloxone in the event of respiratory depression among. Patients were asked whether they accepted or declined naloxone. The naloxone available at the medical center's pharmacy include intramuscular with syringes, intranasal with atomizer and autoinjector. Funding was available for those with limited resources.</p>	<p>Following the patient's decision about whether they wanted to receive naloxone, the ED clinicians decided whether to prescribe naloxone, which was distributed through institution's pharmacy.</p>	
Eswaran et al., 2020	2018–2020	<p>Naloxone provision left to clinicians' discretion. Kits were mostly dispensed during ED visits for medical events involving opioids. Kits were not dispensed to patients prescribed opioids.</p>	<p>THN kit included "3 vials of naloxone 0.4-mg solution in a light-protective bag, three individually wrapped hypodermic 3 cm³ syringes with 23 G x1" needles, and a 1-page insert containing basic instructions for recognizing opioid overdose and administering naloxone." There was no cost to the patient for the kit. A custom electronic medical record was created for dispensing the kits. Clinical pharmacists in the ED were required to complete an online training titled "Prescribe-to-Prevent."</p>	<p>Naloxone dispensed directly to patients in multiple clinical settings. THN dispensed directly to patients by treating provider or through standing order. Naloxone prescribed and filled in the same setting.</p>	<p>Initially a donated supply, then the supply was funded by a grant. Finally, hospital pharmacy agreed to fund naloxone.</p>
Jacka et al., 2022	2017–2020	<p>Participants were eligible for inclusion in the study if they were identified at risk for or received care for an opioid overdose based on ICD-10 codes. Participants had to be 18 years of age or older. Patients were excluded if they were in: police custody.</p>	<p>Patients were provided with THN, behavioral counseling, treatment referral, and buprenorphine initiation. Two doses of intranasal naloxone were given to patients at no cost by a nurse in the ED. Video provided education about the use of naloxone. Behavioral counseling would be provided by "peer recovery specialists, ED social work, or an ED psychiatrist." Patients referred to "formal addiction treatment at an outpatient addiction medicine specialty clinic" during discharge.</p>	<p>THN included two doses of "4 mg nasal Narcan." Given to patient at no cost. Ordered by treating physician and a nurse dispensing to the patient.</p>	

(Continues)

TABLE 3 (Continued)

Study	Year	Participants	Intervention	Distribution method	Source of naloxone
Kestler et al., 2017	2015	16 years old or older who met defined criteria for being at high opioid risk, provided informed consent, and were able to administer naloxone.	Research assistants approached candidates for THN. A nurse would dispense the actual kit. The kit "contained 2 vials of 0.4 mg naloxone, syringes with self-retracting needles, gloves, a rescue breathing barrier mask, and an instructional diagram." Later modifications included the inclusion of three vials because of the frequent need for additional doses to reverse fentanyl overdoses. Even patients who did not participate in the study were offered THN.	Dispensed by nurse.	
Lai et al., 2020	2017–2018	Patients 18 years or older who came to the ED for an opioid-related reason.	Participants received a naloxone training session that had information about how to recognize an overdose and administer intranasal naloxone. Following the training they were given the kit. A \$40 gift card was provided for participating.	Staff running the study were involved in the distribution of the naloxone.	
Lane et al., 2021	2018–2019	Patients who were 18 years or older, seen between January 1, 2018, and November 30, 2019, discharged from the hospital, and treated with buprenorphine in the ED or referred to substance use treatment.	Standardized ED buprenorphine treatment or outpatient OUD referral protocol, including training and naloxone provision. THN was stocked in the automated medication dispensing system to any ED patient, without need for a physician order or prescription.	THN kept in an "automated medication dispensing system" and was distributed to patients for free.	
Moore et al., 2021	2017–2019	Patients were included in the study if they had evidence of illicit opioid use, used methadone or buprenorphine at home, had opioid and benzodiazepine prescriptions. Additionally, if patients were at the ED for opioid overdose or had a history of overdose. Patients could also be included if they were recently released "from incarceration, mandatory detoxification, or substance treatment program." Patients could be excluded if they were younger than 18 years, had trauma or psychiatric-related complaints, were being seen by hospice, had suicide ideation, or had an impaired mental capacity.	Patients were screened for naloxone eligibility by physicians, medical students, pharmacists, and/or nurses. For patients who were eligible, an order was placed in the patient's electronic health record. The order documented that the patient qualified for the kit and "triggered the nurse to screen the training video" and prompted the nurse to dispense kits. Due to state law, patients were required to be trained about how to use naloxone before it was dispensed. A publicly available video was used for this training. After watching the video, patients were provided with a naloxone kit by the nurse.	An order was placed into the electronic health record for the naloxone kit to be distributed along with other parts of the intervention.	The supplies in the naloxone kit were bought using funds obtained both from the institution and a grant.

(Continues)

TABLE 3 (Continued)

Study	Year	Participants	Intervention	Distribution method	Source of naloxone
Mullenmix et al., 2020	2020	Patients were adults or adolescents who received treatment after an opioid overdose.	Developed a program charter with the seeking "to provide an organized foundation for the program to clarify team members' responsibilities and support meeting outcome goals. The charter identified key team members and organizational stakeholders and described the overall program vision, deliverables, and metrics." The intervention involved providing naloxone and education to patients. Those present at discharge, such as friends and family, were encouraged to participate. The naloxone that was distributed was 4 mg nasal spray.	Naloxone was directly provided to patients. Naloxone was kept in an automated medication dispensing machine.	
Ramdin et al., 2022	2017–2020	Different time periods were compared for when ED guidelines for buprenorphine induction were introduced, when naloxone kits began being dispensed, when a peer navigator program began, the beginning of the SARS-CoV-2 pandemic, and the end of the first wave of the pandemic.	At different points in time, buprenorphine induction, naloxone kit distribution, and peer-navigation were all introduced.		
Reddy et al., 2021	2017–2020	Patients who were identified as being at-risk for opioid overdose at discharge at their ED visit were referred to treatment. A clinic would then contact the patient after their ED visit for them to come to the clinic. Patients can then decide whether to receive treatment. Treatment included THN, behavioral counseling, and referrals.	Providing THN, behavior counseling, and treatment referral. The kits included two doses of 2 mg intranasal naloxone.	Given to patients by an ED nurse. No charge.	Purchased by hospital administration.
Samuels et al., 2018	2014–2015	Patients were referred for treatment based on an electronic medical order. This order generated a message with patient information. Clinic schedules follow-up visit with patient to enter THN treatment program.	THN orders were built into electronic medical record order. Patients in the study were provided with either "usual care," THN or THN along with a peer recovery. The THN had "two doses of 2 mg intranasal naloxone, a mucosal atomizer device, and pictorial and verbal assembly and administration instructions in English and Spanish."	Naloxone was kept in a medication dispensing machine and then given to the patients by the nurse.	The naloxone was purchased by the hospital.

Abbreviations: ED, emergency department; OUD, opioid use disorder.

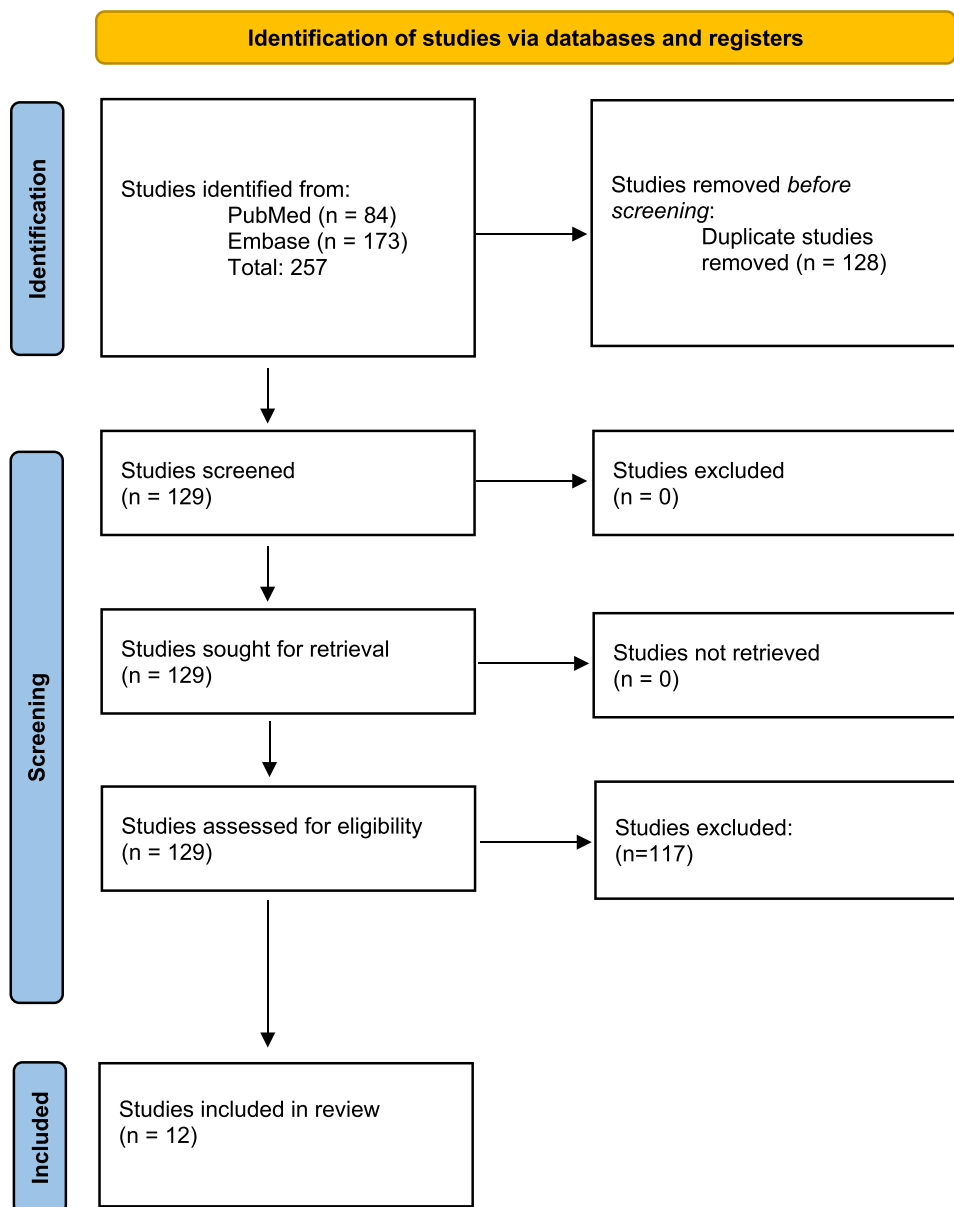


FIGURE 1 Prisma flow diagram describing articles screened for inclusion.

one-third were prescribed naloxone. The study also examined factors associated with accepting naloxone and found that three factors had a significant association: (1) taking an opioid for pain or other conditions, (2) taking antidepressants, and (3) knowing someone who takes opioids that the patient was concerned about.¹⁹ Three studies found that naloxone was accepted by approximately 70% of patients.^{21,22,29} Several factors were associated with accepting naloxone, including witnessing overdose in others, concern about their own overdose, being female, and injection drug use.¹⁸ Reddy et al.²⁹ reported that the racial/ethnic origins of the patients did not influence the distribution of THN. Samuels et al.²⁸ found that 17.2% of patients received THN alone, 47.7% received both THN and peer recovery coaching, and the remaining patients received standard care. Lane et al.²⁴ reported the lowest rate of THN with only about 30% of patients.

Of the studies that focused on the amount of THN distributed, Eswaran et al.²⁰ found that of 168 kits distributed in the ED, there were at least three cases where kits were used to reverse an overdose. In this study, factors that were identified as barriers to naloxone distribution included a lack of knowledge of ED medication dispensing rules and financial factors.²⁰ Lai et al.²³ found that out of 30 naloxone kits distributed, 24 were taken off the hospital grounds, while six kits remained on site. Lane et al.²⁴ conducted a multivariate analysis and found that initiation of buprenorphine treatment for OUD was associated with a 94% decrease in the odds of receiving naloxone. Mullennix et al.²⁵ reported that there were 250 naloxone kits distributed in the first year of the program. In Moore et al.,²⁶ there were 134 electronic THN orders, 117 (87.3%) of which were distributed to patients. Ramdin et al.²⁷ found a significant increase in

TABLE 4 Study outcomes.

Study	Primary outcome	Other outcome(s)
Banta-Green et al., 2019	"24% of the 241 participants had at least one overdose event, 85% had one or more ED visits, and 55% had at least one hospitalization." No significant differences were identified between intervention and comparison groups.	Among those in the intervention group there was a lower time to first event than those in the comparison group.
Devries et al., 2019	Of the 58 patients who were candidates to receive THN "36 (62.1%) accepted a naloxone recommendation and 19 (32.8%) were prescribed naloxone."	Several individual screening questions correlated significantly with naloxone prescription include: "Do you take an opioid for pain or other conditions?," "Do you take antidepressants?," and "Do you know someone who takes opioids that you are concerned about?"
Eswaran et al., 2020	Over a 16-month period, there 669 visits to the ED due to opioid overdose. Among these visits, there 168 kits distributed "accounting for 10.5 per month." These kits were used to reverse at least three overdoses.	Barriers to naloxone distribution included "lack of knowledge regarding the allowability of ED medication dispensing, as well as financial barriers, such as the need to obtain a supply of naloxone."
Jacka et al., 2022	There were 742 patients "discharged after an opioid overdose" and 966 visits. Of these 966 visits THN was provided at 637 (69%). Over 51% of the patients were provided with "behavioral counseling and treatment referral." Among the physicians in the study, in at least one instance almost all of them provided THN, behavioral counseling, or treatment referral.	
Kestler et al., 2017	68.2% of patients accepted the THN.	Factors significantly associated with THN acceptance were "witnessing overdose in others," "concern about own overdose death," "female sex," and "injection drug use."
Lai et al., 2020	24 naloxone kits were taken off the grounds of the hospital.	
Lane et al., 2021	30.9% of the eligible patients had naloxone provision.	In a multivariate analysis buprenorphine administration was associated with a lower odd of receiving naloxone.
Mullennix et al., 2020	There were over 250 THN kits distributed in the first year of the program.	
Moore et al., 2021	During the 18 months examined there were 134 THN orders and from these orders 117 kits were dispensed, so the obtainment rate for kits was 87.3%. In over 90% of cases, the indication for THN was heroin use.	
Ramdin et al., 2022	There was an increase in naloxone kits distributed during the program.	
Reddy et al., 2021	66% of the study patients in the study received THN when they were discharged from the ED.	The most common intervention was THN followed by behavioral counseling. This pattern was true among all racial/ethnic groups. No significant differences in providing THN were found according to the race/ethnicity of the patient.
Samuels et al., 2018	Among the 151 adults who were included in the study "60 (39.7%) received usual care, 26 (17.2%) received THN alone, and 72 (47.7%) received THN and a peer recovery coach."	

Abbreviations: ED, emergency department; THN, take-home naloxone.

the number of naloxone kits distributed after the introduction of a program.

Commonly, authors have concluded that it is possible to successfully implement a THN program in an ED, although specific methodologies have varied, as shown in Table 5.^{20,22,23} Jacka et al.²¹ reported

success with their multifaceted intervention, which included naloxone distribution. Program elements such as peer recovery programs had positive impacts, such as increasing administration of naloxone kits and buprenorphine.²⁷ Reddy et al.²⁹ reported no significant differences in providing THN based on race or ethnicity. Less successful outcomes

TABLE 5 Study conclusions and recommendations.

Study	Conclusion	Recommendations
Banta-Green et al., 2019	The "brief, one-time intervention" used in this study may not be enough to reduce the probability of "serious overdose events."	Different interventions including "direct referral and provision of housing and opioid agonist treatment medications" may be more likely to have a larger impact on the risk of opioid overdose among "this high acuity population in acute care settings."
Devries et al., 2019	Screening programs for THN may be an effective method for identifying patients who are at a high risk for opioid overdose. Screening was associated with THN recommendations, but not actual receipt of the THN.	It may be effective to use shorter questionnaires for screening with two or three questions. Other data sources can also be used for screening in electronic health records, including opioid use history or opioid prescriptions can reliably help flag patients for a naloxone prescription."
Eswaran et al., 2020	The success of the THN program may have been positively impacted by the fact it included "interdisciplinary and interdepartmental collaboration, understanding of state regulations and hospital processes, and organizational buy-in."	When trying to start a THN program, it may be helpful to consider dispensing procedures under the state pharmacy practice act and "other state-specific considerations such as PMP reporting requirements and civil liability protections for pharmacists dispensing naloxone."
Jacka et al., 2022	A program that includes the distribution of naloxone, behavioral counseling, and treatment referral "can be successfully integrated into usual emergency care and maintained over time with high reach and adoption."	Additional research is needed to find strategies that can be implemented at a low cost and still increase THN dissemination.
Kestler et al., 2017	THN ED program can help "to improve access to THN and awareness in individuals most vulnerable to overdoses."	It may be effective to focus on individuals who are most likely to accept THN as part of a THN program.
Lai et al., 2020	About 10%–20% of the participants did not take the naloxone kits from the campus of the hospital.	There is a need for more research to study how to address participants' concerns about interactions with prehospital personnel and fears of law enforcement action when emergency medical services are activated in response to an opioid overdose.
Lane et al., 2021	A majority of the patients that were given an opioid-use disorder intervention did not receive THN or a naloxone prescription, despite it being freely available. Additionally, patients who received "buprenorphine were less likely to receive naloxone than patients only referred to outpatient treatment."	A "treatment bundle" including both naloxone and buprenorphine "may be a helpful conceptual model to promote high quality, comprehensive ED care for patients with potential OUD."
Mullennix et al., 2020	An interdisciplinary team and clinical nurse specialists are needed for creating a successful ED naloxone program.	Different "site-specific factors" should be considered when creating a naloxone program. These factors include: "anticipated insurance coverage of naloxone products within the community, financial resources available to the hospital through philanthropy or grants, bias within the healthcare culture, the availability of other resources (e.g., education), and the engagement of frontline clinical champions to help lead the practice change."
Moore et al., 2021	The distribution of naloxone in an ED can be successful. Other hospitals can replicate what was done in the program described in this paper.	Programs should focus on the need to overcome barriers such as obtaining naloxone, education, and working with the pharmacy.
Ramdin et al., 2022	The type of peer recovery support programs such as the one described in this paper "can have an impact on administration of naloxone kits and buprenorphine."	Further research should examine "whether or not these peer recovery support programs have the potential to cause a long-term culture change in the ED."
Reddy et al., 2021	The study did not observe racial and ethnic differences in the provision of naloxone.	Future study should seek to examine "barriers to behavioral counseling within ED settings and factors contributing to racial inequities in post-overdose emergency care." Additionally, there is a need for "provider training in addiction, substance use disorders, implicit bias and anti-racism, and patient engagement skills."
Samuels et al., 2018	Following the introduction of the program there was a decrease in "repeat ED visitation for opioid overdose among individuals getting take home naloxone."	"ED peer recovery consultation and naloxone administration may be effective interventions to decrease time to initiation of medication for OUD and reduce mortality among ED patients treated after opioid overdose."

Abbreviations: ED, emergency department; THN, take-home naloxone; OUD, opioid use disorder; PMP, prescription monitoring program.

were also reported, such as Banta-Green et al.,¹⁸ who concluded that “one-time intervention in acute care settings” was not adequate for reducing overdoses. Lane et al.²⁴ concluded that a majority of the patients who were targets for receiving naloxone did not take it and that patients who received buprenorphine were less likely to accept naloxone compared to patients who received a referral for outpatient treatment.

Other studies found mixed results with program outcomes. Devries et al.¹⁹ concluded that while screening was helpful for identifying patients in need of naloxone, screening did not “correlate with naloxone receipt.” Lai et al.²³ found that while patients were willing to accept naloxone with geolocation technology, 20% did not take “their smart naloxone kit off the hospital campus.” This 20% could be partially explained by the fact that patients were offered a \$40 gift card for accepting the naloxone kit, incentivizing patients who had little interest. Mullennix et al.’s²⁵ conclusion was that THN programs are feasible, but they require engagement with an interdisciplinary team. Samuels et al.²⁸ found that there was “decreased repeat ED visitation for opioid overdose among individuals getting THN.”

The recommendations made in the included studies also varied. Banta-Green et al.¹⁸ concluded that “more intensive interventions” aimed at improving housing and addiction treatment are needed to reduce overdoses. Other recommendations focused on the need for naloxone programs to confirm dispensing procedures with state policy and to identify low-cost implementation strategies.^{20,21} Kestler et al.²² suggested that programs should focus on individuals most likely to accept THN and, resources permitting, develop strategies to engage subgroups that are less likely to accept naloxone. Lai et al.²³ recommended considering patients’ potential concerns about “interactions with prehospital personnel and fears of law enforcement action” during opioid overdose response. Additional recommendations included using a “treatment bundle” for suspected OUD to improve ED care, citing lower odds of naloxone provision with buprenorphine treatment, and the need to engage multiple stakeholders in interventions to increase naloxone deployment.^{24,25} Other areas of focus included the need to overcome barriers such as obtaining naloxone, providing education, working with pharmacies, and the role of peer recovery support navigators on both naloxone and buprenorphine.^{26,27} Reddy et al.²⁹ encouraged developing an understanding of barriers to counseling and increased training of clinicians in “addiction, substance use disorders, implicit bias and anti-racism, and patient engagement skills.” Samuels et al.²⁸ suggested that peer recovery consultation in the ED with naloxone administration may be an effective method to decrease the time to OUD medication initiation and to “reduce mortality among ED patients treated after opioid overdose.”

3.1 | Limitations

There are limitations to the inferences that can be made from the articles reviewed. Except for one study, the reviewed articles did not use an experimental approach. As a result, it is impossible to quantitatively determine the programs’ effectiveness or which aspects had the greatest impact. Additionally, because the studies generally did not

focus on clinical outcomes (such as overdoses, deaths, etc.), it cannot be determined which elements led to improved patient outcomes.

4 | DISCUSSION

This scoping review was performed to summarize the literature regarding naloxone distribution from EDs in the United States and to highlight key elements and themes across programs. Our findings revealed diverse approaches to distributing naloxone from the ED in the United States. Most of the studies that were conducted did not focus on patient outcomes in preventing overdose but rather on program outcomes such as the number and proportion of patients given naloxone.

A common program element was a screening protocol for identifying patients to whom naloxone should be distributed. Screening included factors such as an ED visit related to opioid use or having a history of OUD, and the information used for this screening could come from healthcare records or patient interviews. Overall, targeted screening could be a useful tool to identify patients likely to benefit from naloxone, as well as to gauge the likelihood of acceptance, highlighting any possible barriers that could be addressed by additional support such as peer recovery or specific education. There were also differences in the extensivity of naloxone distribution programs, where certain programs only distributed naloxone, whereas others provided additional services such as counseling, peer support, and education. Naloxone formulations varied between IN and intramuscular routes, and some programs also provided buprenorphine with the naloxone. Additionally, the methods used for getting naloxone to patients differed and included direct distribution by the staff, distribution through the pharmacy, or the use of a naloxone dispensing machine.

The heterogeneity of these programs highlights the need for further research on how the most successful program outcomes correlate with improved patient outcomes, which would translate the success of naloxone distribution to improved opioid overdose outcomes. Connecting the diverse methodologies explored in this review to improved patient outcomes could emphasize the need for and lead to the development of consistent guidelines and protocols for naloxone distribution in EDs. These protocols could implement the effective elements for naloxone distribution reported across the studies examined, including screening for identifying candidates for distribution, the best methods for distribution, and other interventions such as counseling that should accompany naloxone. Such protocols may make it easier for more EDs to implement naloxone distribution programs with consistent and effective methodologies that can be assessed for improved patient outcomes.

Overall, the programs described in the identified articles were successful for naloxone distribution. In most cases, success was determined by assessing the proportion of identified patients who obtained THN. However, only one of the studies examined patient outcomes pertaining to preventing opioid overdose. Additional research is needed to evaluate the impacts of ED naloxone programs on patient outcomes.

The findings from this study show that naloxone distribution programs have been implemented with various methodologies. Many of

these programs appeared to be successful in terms of increasing the distribution of naloxone, but there remains a need for standardizing successful methodologies. This standardization would help EDs across the United States to improve program outcomes, meaning increased naloxone distribution. Additionally, more research is needed to correlate improved program outcomes with improved patient outcomes in preventing opioid overdose fatalities.

AUTHOR CONTRIBUTIONS

Mohan K. Sindhwani and Adam Friedman conceived and designed the study. Mohan K. Sindhwani supervised data collection. Mohan K. Sindhwani, Scott G. Weiner, and Donald Stader provided critical review and analysis of data. Mohan K. Sindhwani, Donald Stader, and Scott G. Weiner drafted the initial manuscript. All authors provided critical review, revisions, and final approval for the submitted manuscript.

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