



# Comparative Human Factors Evaluation of Two Nasal Naloxone Administration Devices: NARCAN<sup>®</sup> Nasal Spray and Naloxone Prefilled Syringe with Nasal Atomizer

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## ABSTRACT

**Introduction:** Opioid overdose rescue situations are time-critical, high-stress scenarios that frequently require nonmedical first responders or bystanders to intervene and administer naloxone to avoid opioid-induced fatalities. Training nonmedical personnel to respond during such mentally constraining situations presents the human factors challenge of how best to design a safe and effective lay delivery system. This paper comparatively evaluates the ease of use of two nasal naloxone administration products: NARCAN<sup>®</sup> Nasal Spray and a naloxone prefilled syringe with nasal atomizer (PFS-NA).

**Methods:** We evaluated the use requirements and usability of NARCAN<sup>®</sup> Nasal Spray versus a naloxone PFS-NA using a systems-oriented method. First, we determined the use requirements of different user groups. Next, we focused on constructing a human factors task analysis of both products. Finally, we conducted a comparative risk assessment of the tasks that were different between the two products.

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**Results:** Inexperienced users, such as nonmedical first responders and bystanders, are at the highest risk of incorrectly administering naloxone, particularly in high-stress emergency opioid overdose situations. The device *Preparation* and *Medication Delivery* tasks most differentiate the use of NARCAN<sup>®</sup> Nasal Spray and a PFS-NA. The level of task complexity and number of steps within those tasks is substantially greater for a PFS-NA than for the NARCAN<sup>®</sup> Nasal Spray.

**Conclusions:** NARCAN<sup>®</sup> Nasal Spray requires fewer steps and is easier to administer than a naloxone PFS-NA. Thus, using NARCAN<sup>®</sup> Nasal Spray should increase the likelihood that non-medical personnel correctly deliver naloxone in time-critical, high-stress opioid overdose rescue situations.

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**Keywords:** Naloxone; NARCAN<sup>®</sup>; Opioids; Overdose

## INTRODUCTION

Opioid overdose fatalities in the United States have drastically risen over the past two decades, leading to the development of training initiatives for nonmedical first responders and bystanders on when and how to administer the opioid reversal agent naloxone [1]. This authorization and promotion of lay users to respond

to opioid overdoses prior to the arrival of emergency medical services (EMS) has already resulted in a reduction in opioid fatalities in areas with increased public access to naloxone [2, 3]. The goal of human factors research is to design devices that address the challenges faced by different user groups in various use environments and thus reduce the risks associated with using such products. Naloxone use by nonmedical personnel poses human factors design challenges as the medication administration device needs to effectively guide the user to correctly administer naloxone during time-critical emergency overdose scenarios.

Naloxone was developed in the 1960s and was the first opioid overdose reversal agent largely free of adverse effects, resulting in it quickly becoming the standard rescue medication for overdose management [2, 3]. Naloxone is currently available as a prefilled syringe (PFS) that the user can build into an intramuscular (IM) or intranasal (IN) kit by separately purchasing and adding a standard needle or nasal atomizer, respectively. Compared with IM naloxone, use of IN naloxone reduces the risk of a needlestick, which is important given the high prevalence of blood-borne illnesses among those with opioid use disorders [3]. However, the IN PFS kit is an off-label use [4]. The Food and Drug Administration (FDA) recently approved administration of naloxone by bystanders via NARCAN<sup>®</sup> Nasal Spray (approved

in 2015; ADAPT Pharma, Inc., Radnor, PA) [3]. NARCAN<sup>®</sup> Nasal Spray (Fig. 1) costs \$125 for two doses [5], whereas a PFS and independently added nasal atomizer (PFS-NA) (Fig. 2) costs approximately \$44 for a single dose [5, 6]. The average insurance co-pay for both products, either the two doses of NARCAN<sup>®</sup> Nasal Spray or the one dose of a PFS-NA, is approximately \$17 [6–8].

The need for nonmedical personnel to appropriately deliver naloxone during opioid overdoses is well known and increasing. However, the safety of lay prehospital naloxone administration has not been established [9], and standardized medication administration training programs are limited. Additionally, the naloxone PFS-NA was recalled by the FDA in 2016 because the nasal atomizer was not reliably converting the fluid medication into a spray [10]. Despite these uncertainties, studies suggest that the risks involved in lay naloxone administration outweigh the dangers posed by an opioid overdose, particularly when users are not trained in other respiratory support methods [3].

Prior usability research found that no untrained, and about 60% of trained, users were able to successfully administer a full dose of naloxone using a PFS-NA [11], whereas >90% of untrained users were able to successfully administer a full dose using NARCAN<sup>®</sup> Nasal Spray [12]. These studies provide



**Fig. 1** NARCAN<sup>®</sup> Nasal Spray Kit (*left*); named components NARCAN<sup>®</sup> Nasal Spray Kit (*right*). Reused with permission from ADAPT Pharma, Inc



**Fig. 2** Naloxone prefilled syringe with nasal atomizer (*left*); named components of Prefilled Syringe with Nasal Atomizer Kit (*right*)

information about lay users' ability to administer naloxone but do not provide insights on why users commit more errors when using a PFS-NA.

Human factors is a discipline that focuses on how people interact with products in specific use environments (cf. [13]). The goal of human factors research is to optimize the design of a product to match the capabilities and limitations of the users, thus making product use safer and more effective [14]. In this paper, we conducted a human factors evaluation of NARCAN<sup>®</sup> Nasal Spray versus a PFS-NA by assessing the ease of use of administering each IN naloxone product in time-critical emergency situations. We hypothesized that increased task complexity and coupling lead to greater risk of incorrectly administering naloxone when using a PFS-NA compared with the NARCAN<sup>®</sup> Nasal Spray.

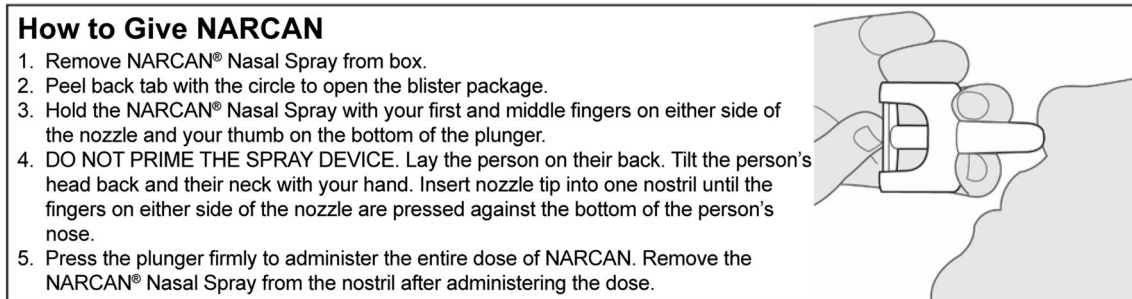
## METHODS

For this study, we employed a systems-oriented human factors evaluation approach to determine the differences in task complexity and risk between NARCAN<sup>®</sup> Nasal Spray and a PFS-NA.

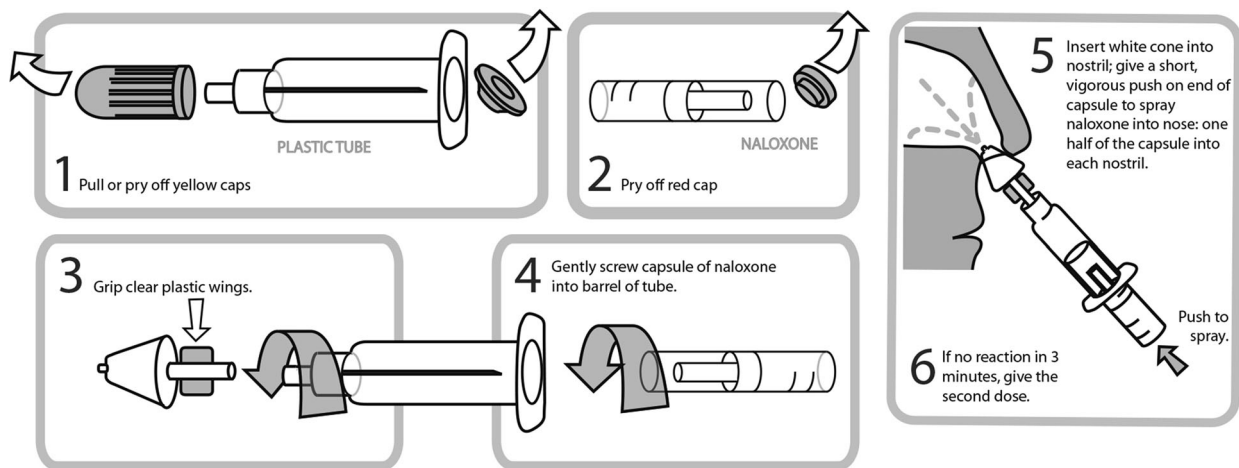
This article does not contain any studies with human participants or animals performed by any of the authors.

We first conducted a literature review to create an independent list of use requirements for different user groups. We used Google Scholar with the search terms {"naloxone"}, {"Narcan"}, {"opioid crisis"}, and {"opioid overdose"} as well as similar variations to build a database of articles. We also searched resources from government and public awareness organizations, such as the Centers for Disease Control and Prevention (CDC) and the Association for Addiction Professionals, for information about opioid abuse and opioid overdose rescue procedures. This search was conducted in October 2018. No papers were excluded based on publication date, but additional weight was given to newer articles citing current opioid use and treatment regimens.

We then constructed a task analysis of NARCAN<sup>®</sup> Nasal Spray and a PFS-NA by performing a mock administration using each product's respective Instructions for Use (IFU) (Figs. 3, 4). The intent of the task analysis was to determine the tasks, subtasks, and workflow involved in administering naloxone with each kit. We performed this analysis in accordance



**Fig. 3** NARCAN® Nasal Spray administration instructions [30]. Adapted with permission from ADAPT Pharma, Inc



**Fig. 4** Naloxone prefilled syringe with nasal atomizer instructions [31]. Reused with permission from Project Lazarus

with the 2016 FDA guidance “Applying Human Factors and Usability Engineering to Medical Devices” [15].

Finally, we constructed a risk assessment of all administration tasks that were substantially different between NARCAN® Nasal Spray and a PFS-NA. The goal of the risk assessment was to determine which tasks posed the greatest risk of preventing successful naloxone administration. We performed the assessment in accordance with the 2007 International Organization for Standardization standard “ISO 14971: Medical devices—Application of risk management to medical devices” [16].

## RESULTS

The following sections describe the results for each stage of the human factors evaluation,

which included exploring the use requirements for naloxone and conducting a task analysis and risk assessment of NARCAN® Nasal Spray and a PFS-NA.

### Use Requirements

Naloxone is used by emergency medical personnel and nonmedical personnel in a wide range of circumstances. Nonmedical personnel may include nonmedical first responders, bystanders that are also using opioids, and non-using bystanders. Understanding the perspectives, needs, and training (or lack thereof) on naloxone administration for each user group provides a framework for the development of effective drug delivery products.

## User Groups

Levels of user training with drug delivery devices impacts how quickly and accurately users can administer medication in rescue situations. EMS personnel often administer naloxone and assist with mechanical ventilation via a bag valve mask after arriving on the scene of an opioid overdose. EMS personnel are trained to handle chaotic, high-stress situations in uncontrolled environments and have the expertise to quickly and accurately react to overdose emergencies.

Increasing numbers of nonmedical first responders (e.g., police and firefighters) and bystanders (e.g., opioid users and non-users) are being trained on how to administer naloxone for opioid overdoses prior to the arrival of EMS [3]. Law enforcement response training typically includes information about three basic elements: (1) how to recognize the symptoms of an opioid overdose, (2) how to react to an opioid overdose, and (3) how to recognize and react to opioid-induced events [17]. Both opioid-using and non-using bystanders are often trained similarly to first responders through community courses [18], with recent co-prescribing and peer administration efforts already resulting in a decrease in opioid-related deaths [1, 3]. However, this limited training for non-medical personnel may make recalling rescue procedures difficult given the added mental constraints posed by emergency opioid overdose situations.

## User Needs

Determining the user's needs involves ascertaining how they go about reaching their goals. The following sections discuss the goals, context, and obstacles lay users encounter during naloxone administration within the framework of the user-centered design process.

### **Goal: Prevent Overdose Fatality**

The primary goal of pre-EMS naloxone administration is to prevent an opioid overdose fatality. Figure 5 shows an overview of the process of treating an overdose with naloxone. The

challenges users face include determining when or if they should administer the medication, how they should administer it, and if they have administered the appropriate dose. The product-based difficulties users encounter center on how the medication is administered; this is further explored in the task analysis and risk assessment sections.

### **Context: Emergency Situation**

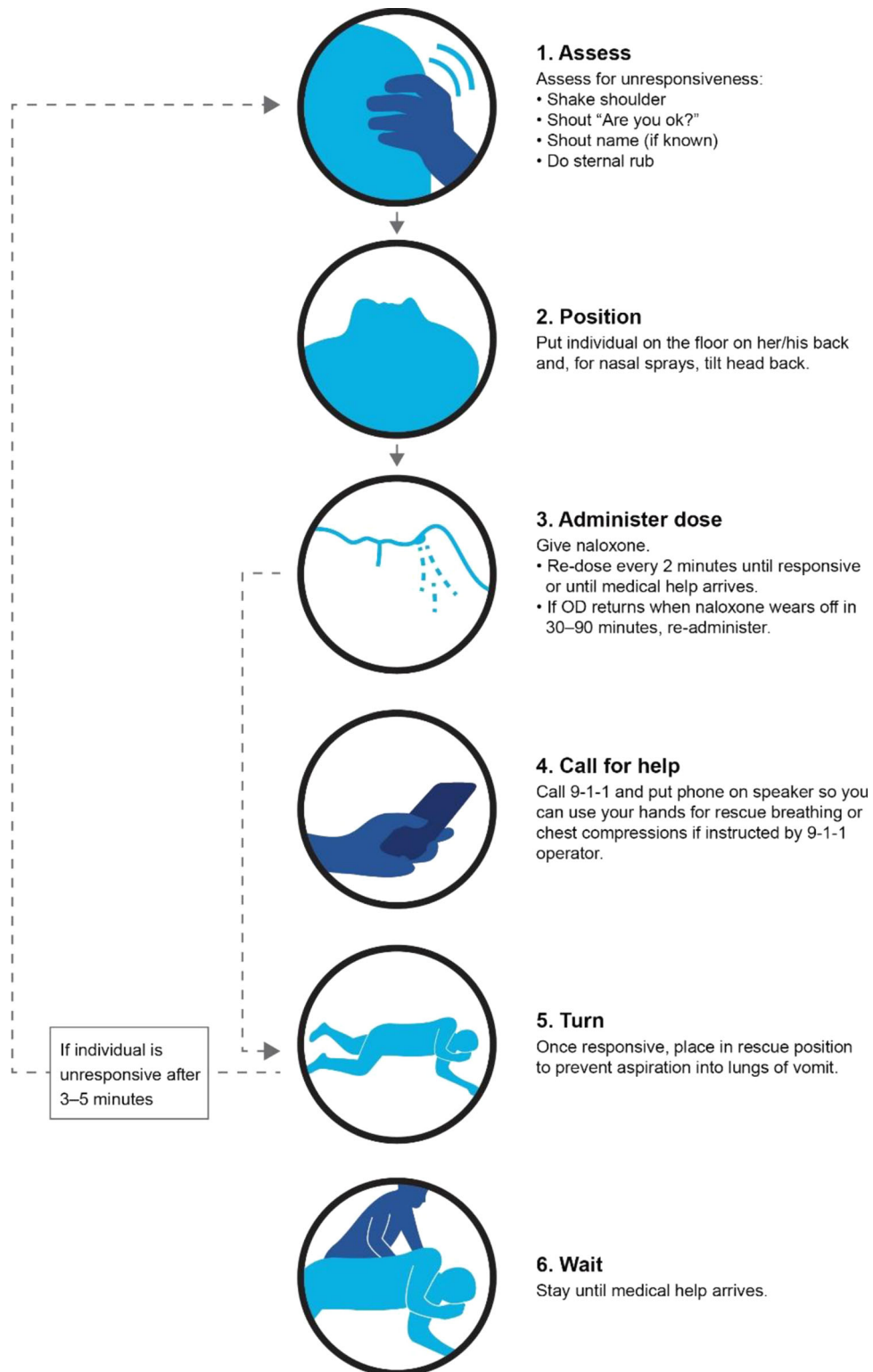
Naloxone administration during opioid overdoses has become even more time-critical with the use and increased abuse of synthetic opioids, such as illicitly manufactured fentanyl. Fentanyl is estimated to be 50–100 times more potent than morphine [19, 20] and may result in an overdose fatality seconds or minutes after use. This leaves no time for the arrival of EMS [21], thus placing the burden of emergency naloxone administration on bystanders.

Emergency situations are time-critical, high-pressure scenarios that can induce a stress response impacting the user's cognitive ability to adapt to task demands. Nonmedical first responders and bystanders with either limited or no training on naloxone administration are particularly susceptible to these cognitive impairments. Stress may cause users to (cf. [22]):

- Narrow their attention toward one central task.
- Lose the ability to coordinate or integrate information, particularly across different mediums.
- Have a lower level of accuracy when performing tasks.
- Have difficulty making decisions.

Product design features that mitigate the impact of emergency stress minimize the working memory load required to use the device. This is accomplished by visually displaying information, reducing the number of tasks required to administer the medication, and closely grouping items or instructions intended to be used together [22]. As observed in Figs. 4 and 6, using a PFS-NA involves assembling more components that have a higher level of complexity than using NARCAN® Nasal Spray. This may cause lay users to have more difficulty administering a PFS-NA.





**Fig. 5** Naloxone administration process [29]

**Obstacles: Access to Naloxone**

Several obstacles exist to appropriately using nasal naloxone, including knowledge of and about the medication and its administration, awareness of bystander overdose intervention laws, and the reliability of medication administration kits. Each of these factors directly impacts a product’s ease of use.

Studies suggest that increased naloxone co-prescribing and peer utilization efforts have reduced opioid overdose fatalities [1, 3]. However, opioid users often lack sufficient knowledge of naloxone: what it is, how to obtain it, and how to use it. For example, in a study by Kirane et al. [23], researchers interviewed 100 opioid users and found that while 65% of patients correctly identified that naloxone could be used for opioid overdose reversal, only 33% knew where to obtain a rescue kit. In addition, 19% thought prosecuting bystanders who responded at the scene of an overdose was legal [23].

**Task Analysis**

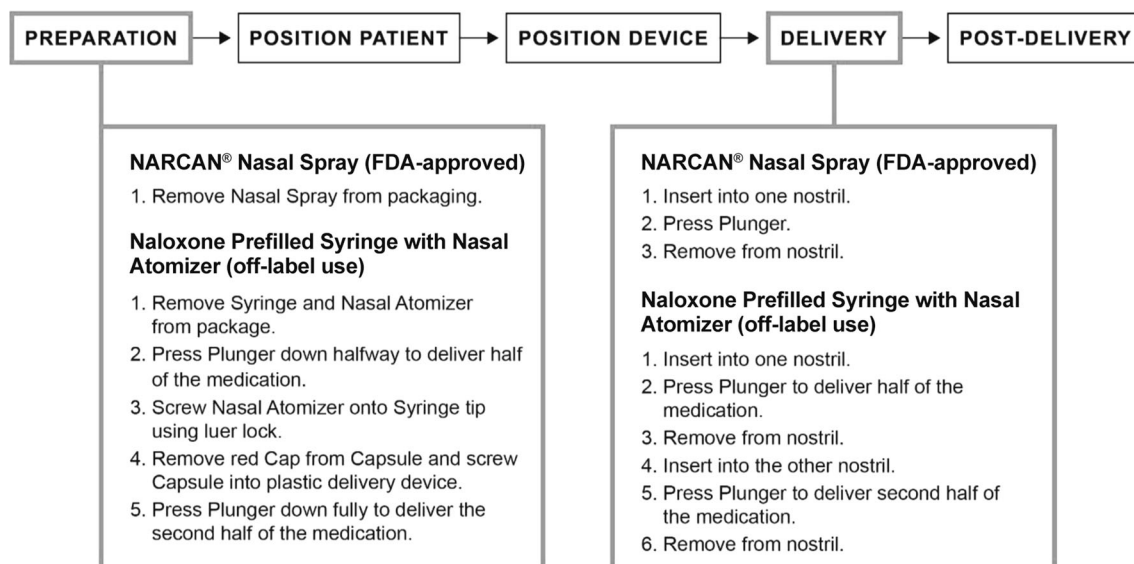
The task analysis that we performed assigned each element of naloxone administration into one of five major tasks: (1) *Preparation*, (2) *Positioning of the Patient*, (3) *Positioning of the Device*, (4) *Delivery*, and (5) *Post-Delivery* (see Fig. 6). The highlighted boxes in Fig. 6 represent those tasks

with steps that were substantially different between a PFS-NA and NARCAN® Nasal Spray. The dropdown boxes on the illustration detail the specific steps required to use each product. For the tasks of *Preparation* and *Delivery* of medication, a PFS-NA requires substantially more steps than the NARCAN® Nasal Spray, potentially requiring more time and a more highly skilled user. The risks involved in each step of the *Preparation* and *Delivery* process are compared in the risk assessment.

**Risk Assessment**

A product risk is the chance that someone may be harmed by use of the product. A comparison of the risks involved in using NARCAN® Nasal Spray versus a PFS-NA provides insight into adverse outcomes that might occur due to the inappropriate use of either kit. The two tasks that most differentiated the products were *Preparation* and *Delivery* of medication.

The preparation of a PFS-NA and NARCAN® Nasal Spray both start with removing the products from their respective packaging. The device workflows then diverge, with a PFS-NA requiring more steps than NARCAN® Nasal Spray. Each additional PFS-NA step (see Fig. 6) opens multiple avenues for failure modes that may result in incorrect assembly of the kit. During the



**Fig. 6** High-level summary of tasks involved in IN naloxone administration

*Preparation* task, most failure modes result in delayed therapy or no therapy, which may cause harm to the overdose victim, such as brain damage or death [3, 24]. This suggests that use of a PFS-NA is likely to result in more adverse events than use of NARCAN<sup>®</sup> Nasal Spray.

The *Delivery* of naloxone also differs between the two products. With a PFS-NA, the user administers half the dose of medication in each nostril. This means users must maintain an awareness of the amount of medication they are administering and must remember to administer half the syringe into each nostril. Contrastingly, NARCAN<sup>®</sup> Nasal Spray only requires the user to deliver a single dose into one nostril. A lay user's emergency stress response may thus make it more difficult to correctly administer naloxone when using a PFS-NA.

## DISCUSSION

The opioid crisis is widespread, and naloxone temporarily mitigates the life-threatening respiratory depression that causes opioid overdose fatalities. Given the speed of illicit fentanyl, its rising use, and the risk of consuming opioids laced with fentanyl [25], saving opioid overdose victims' lives increasingly depends on the ability of nonmedical first responders and lay bystanders to appropriately administer naloxone rescue treatments. This study evaluated the ease of use of administering IN naloxone in time-critical emergency situations with two different products: NARCAN<sup>®</sup> Nasal Spray and a PFS-NA.

Opioid overdoses caused over 140,000 non-fatal emergency department visits and over 42,000 fatalities in 2017 [26, 27]. The symptoms of opioid overdose are pinpoint pupils, unconsciousness, and respiratory depression [28]; respiratory depression may cause death [3]. The treatment for opioid overdoses is to combat this suppressed breathing physically through cardiopulmonary resuscitation (CPR) and pharmacologically through naloxone administration.

Naloxone use in emergency opioid overdose situations is common and promoted for non-medical users, making it important to evaluate this user group's needs. Lay administration keeps overdose victims alive until EMS arrive. Lay users,

however, often have minimal training on naloxone administration and are more likely to experience mental limitations due to stress in emergency situations. The human factors task and risk assessments revealed that compared with NARCAN<sup>®</sup> Nasal Spray, a PFS-NA involved substantially more steps to complete the *Preparation* and *Delivery* tasks. The task simplicity of NARCAN<sup>®</sup> Nasal Spray should thus aid lay users in correct medication administration.

Real-world findings from the Association for Addiction Professionals support the results from this study. Data indicate that a PFS-NA is difficult to assemble and that users commonly break or misuse kit components [29]. Our risk analysis strengthens usability study results from Edwards et al. [11] and Krieter et al. [12], which suggest that untrained users are unlikely to successfully administer naloxone using a PFS-NA and are more likely to successfully administer the medication using NARCAN<sup>®</sup> Nasal Spray.

The primary limitation of this comparative human factors analysis was that the task analysis did not involve actual opioid users. Future research might include evaluating these products with opioid users or using an expanded set of human factors techniques, such as time-and-motion analysis. This would provide further insights into the safety of each IN naloxone administration method.

## CONCLUSIONS

Training nonmedical personnel to use naloxone presents the human factors challenge of how best to design a safe and effective delivery system for lay users given the added mental constraints posed by emergency situations. From a human factors perspective, nonmedical emergency responders and bystanders are more likely to correctly and successfully administer NARCAN<sup>®</sup> Nasal Spray than a naloxone PFS-NA.

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**Compliance with Ethics Guidelines.** This article does not contain any studies with human participants or animals performed by any of the authors.

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## REFERENCES

1. Fairbairn N, Coffin PO, Walley AY. Naloxone for heroin, prescription opioid, and illicitly made fentanyl overdoses: challenges and innovations responding to a dynamic epidemic. *Int J Drug Policy*. 2017;46:172–9.
2. McDonald R, Campbell ND, Strang J. Twenty years of take-home naloxone for the prevention of overdose deaths from heroin and other opioids-conception and maturation. *Drug Alcohol Depend*. 2017;178:176–87.
3. Rzasa Lynn R, Galinkin JL. Naloxone dosage for opioid reversal: current evidence and clinical implications. *Ther Adv Drug Saf*. 2018;9(1):63–88.
4. US Food and Drug Administration. FDA news release: FDA moves quickly to approve easy-to-use nasal spray to treat opioid overdose. 2015. <https://wayback.archive-it.org/7993/2017011122937/https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm473505.htm>. Accessed Oct 2018.
5. Medi-Span. *Clinical drug information report naloxone*. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc.; 2018.
6. Bound Tree. MAD mucosal atomization devices. 2019. <https://www.boundtree.com/Airway-&Oxygen-Delivery/Intubation-Aids/MAD-Mucosal-Atomization-Devices/p/group000154>. Accessed 28 Jan 2019.
7. IQVIA (IMS Health & Quintiles). Narcan out of pocket cost by payer: FIA claims data. Time period: Jan 2017 to Dec 2017. Plymouth Meeting, PA (1 IMS Drive): IQVIA; 2018.
8. Association for Accessible Medicines. 2018 generic drug access & savings in the U.S. (AAM-2018SR-070918-P). 2018. <https://accessiblemeds.org/sites/>

- [default/files/2018\\_aam\\_generic\\_drug\\_access\\_and\\_savings\\_report.pdf](#). Accessed 28 Jan 2019.
9. Wermeling DP. Review of naloxone safety for opioid overdose: practical considerations for new technology and expanded public access. *Ther Adv Drug Saf*. 2015;6(1):20–31.
  10. Teleflex Medical. Urgent medical device recall notification: LMA<sup>®</sup> MDA Nasal<sup>™</sup> intranasal mucosal atomization device. 2016. [https://www.ct.gov/dmhas/lib/dmhas/newsworthy/mad\\_recall.pdf](https://www.ct.gov/dmhas/lib/dmhas/newsworthy/mad_recall.pdf). Accessed Oct 2018.
  11. Edwards ET, Edwards ES, Davis E, Mulcare M, Wiklund M, Kelley G. Comparative usability study of a novel auto-injector and an intranasal system for naloxone delivery. *Pain Ther*. 2015;4(1):89–105.
  12. Krieter P, Chiang N, Gyaw S, et al. Pharmacokinetic properties and human use characteristics of an FDA-approved intranasal naloxone product for the treatment of opioid overdose. *J Clin Pharmacol*. 2016;56(10):1243–53.
  13. Sanders MS, McCormick EJ. Human factors in engineering and design. 7th ed. New York, NY: McGraw-Hill Book Company; 1993.
  14. Schaeffer NE. The role of human factors in the design and development of an insulin pump. *J Diabetes Sci Technol*. 2012;6(2):260–4.
  15. US Food and Drug Administration. Applying human factors and usability engineering to medical devices: guidance for industry and Food and Drug Administration staff. 2016. <https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/UCM259760.pdf>. Accessed 19 Nov 2018.
  16. International Organization for Standardization. ISO 14971: medical devices—application of risk management to medical devices. 2nd ed. Geneva, Switzerland: International Organization for Standardization. 2007. <https://www.iso.org/standard/38193.html>. Accessed 12 Mar 2019.
  17. National Training and Technical Assistance Center (NTTAC). Law enforcement training. 2018. <https://bjatta.bja.ojp.gov/tools/naloxone/Law-Enforcement-Training>. Accessed Oct 2018.
  18. Ready.gov. Community emergency response team. 2018. <https://www.ready.gov/community-emergency-response-team>. Accessed Oct 2019.
  19. Morgan J, Jones AL. The role of naloxone in the opioid crisis. *Toxicol Commun*. 2018;2(1):15–8.
  20. O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM. Deaths involving fentanyl, fentanyl analogs, and U-47700—10 states, July–December 2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(43):1197–202.
  21. Somerville NJ, O'Donnell J, Gladden RM, et al. Characteristics of fentanyl overdose—Massachusetts, 2014–2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(14):382–6.
  22. Wickens CD. Designing for stress. In: Driskell JE, Salas E, editors. *Series in applied psychology. Stress and human performance*. Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.; 1996. pp. 279–295.
  23. Kirane H, Ketteringham M, Bereket S, et al. Awareness and attitudes toward intranasal naloxone rescue for opioid overdose prevention. *J Subst Abuse Treat*. 2016;69:44–9.
  24. National Association of State Head Injury Administrators. Brain injury and opioid overdose: fast facts. 2018. [https://www.nashia.org/pdf/brain\\_injury\\_opio\\_id\\_final\\_june\\_7\\_2018.pdf](https://www.nashia.org/pdf/brain_injury_opio_id_final_june_7_2018.pdf). Accessed 28 Jan 2019.
  25. US Food and Drug Administration. Exploring naloxone uptake and use public meeting. 2015. <https://www.fda.gov/downloads/Drugs/NewsEvents/UCM469456.pdf>. Accessed 19 Nov 2018.
  26. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) national practice guideline for the use of medications in the treatment of addiction involving opioid use. *J Addict Med*. 2015;9(5):358–67.
  27. Centers for Disease Control and Prevention (National Center for Injury Prevention and Control). Drug overdose deaths. 2017. <https://www.cdc.gov/drugoverdose/data/statedeaths.html>. Accessed 19 Nov 2018.
  28. World Health Organization. Management of substance abuse: information sheet on opioid overdose. 2018. [https://www.who.int/substance\\_abuse/information-sheet/en/](https://www.who.int/substance_abuse/information-sheet/en/). Accessed 19 Nov 2018.
  29. Elliott R, Braucht G. Don't run—call 9-1-1: overdose prevention. 2018. <https://www.naadac.org/dont-run-call-9-1-1-overdose-prevention>. Accessed 19 Nov 2018.
  30. ADAPT Pharma, Inc. Quick start guide: opioid overdose response instructions. 2015. <https://www.narcan.com/static/NARCAN-Quick-Start-Guide.pdf>. Accessed 31 Jan 2019.
  31. Project Lazarus. Prescriber naloxone packet. 2019. [https://docs.wixstatic.com/ugd/540bd6\\_94c5e66994254431bd6b5f3ce3eda5ff.pdf](https://docs.wixstatic.com/ugd/540bd6_94c5e66994254431bd6b5f3ce3eda5ff.pdf). Accessed 28 Jan 2019.