Saved by the Nose: Bystander-Administered Intranasal Naloxone Hydrochloride for Opioid Overdose

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Administering naloxone hydrochloride (naloxone) during an opioid overdose reverses the overdose and can prevent death. Although typically delivered via intramuscular or intravenous injection, naloxone may be delivered via intranasal spray device. In August 2006, the Boston Public Health Commission passed a public health regulation that authorized an opioid overdose prevention program that included intranasal naloxone education and distribution of the spray to potential bystanders. Participants were taught by trained nonmedical needle exchange staff. After 15 months, the program provided training and intranasal naloxone to 385 participants who reported 74 successful overdose reversals. Problems with intranasal naloxone were uncommon. Overdose prevention education with distribution of intranasal naloxone is a feasible public health intervention to address opioid overdose. *Am J Public Health.* 2009;99:788–791. doi:10.2105/AJPH.2008.146647.

KEY FINDINGS

- Needle-exchange participants have experienced and witnessed high rates of overdoses.
- Needle-exchange participants can successfully recognize an overdose and use intranasal naloxone to reverse potentially fatal opioid overdoses.
- With the support and regulation of the local public health authority, overdose prevention programs can provide training and distribute intranasal naloxone without a direct clinical health care provider–patient encounter.
- Overdose prevention programs that include the distribution of intranasal naloxone by nonmedical personnel are feasible for city public health departments.

RATES OF OPIOID OVERDOSE have increased since the early 1990s because of lower-cost, higher-purity heroin and prescription opioid abuse.[1–5] In Massachusetts, from 1990 to 2006, annual opioid overdose–related fatalities increased over 6-fold, from 94 to 637.[6,7] In response, the Boston Public Health Commission (BPHC) passed a regulation that authorized the development of an overdose prevention program with naloxone distribution through its mobile needle-exchange program. This program is innovative, because it includes the distribution of intranasal naloxone by trained, nonmedical public health workers to potential overdose bystanders for administration to overdose victims. Legal and regulatory barriers to implementation are detailed in the box on page 791.

Naloxone, an opioid antagonist, reverses opioid overdose by displacing opioid agonists, such as heroin or oxycodone, from opioid receptors. It is the standard treatment used by medical personnel. It has no abuse potential, and its only contraindication is a prior allergic reaction, which is rare.[8] Although typically administered intravenously or intramuscularly, it can be administered intranasally.[9–13] Strong interest in overdose prevention training and access to naloxone exists among potential overdose bystanders, including family members[14] and drug-using partners.[15] Overdose prevention programs with naloxone distribution that train and distribute naloxone to people who are likely to witness an overdose have been successfully implemented in several communities, including Chicago,[16,17] New York,[18,19] San Francisco,[20] Baltimore,[15,21] and New Mexico.[8] A 6-program study demonstrated that trained bystanders were similarly skilled as medical experts in recognizing opioid overdose situations, and when naloxone was indicated.[22]

The BPHC started an overdose prevention program with intranasal naloxone distribution as a result of the successful experience of the city's emergency medical services use of the nasal spray as a prehospital treatment for opioid overdose; the concept was also seen as an attractive option because intranasal delivery of the drug eliminates the risks of needlestick injuries and needle disposal. BPHC implemented the program through the needle-exchange program because program participants were considered particularly likely to witness overdoses.

PROGRAM CURRICULUM

All participating needle-exchange program staff—2 nurses and 4 nonmedical public health workers—completed 8 hours of didactic training, a knowledge test, and at least 4 supervised bystander-training sessions. Both the staff training and bystander training were adapted from existing program curricula from other cities that primarily used needle-based naloxone.[8,14,17–21]

The 15-minute bystander training included techniques in overdose prevention. Staff completed a checklist (available as a supplement to the online article at http://www.ajph.org) to ensure participant comprehension. Overdose prevention kits included instructions; 2 luer-lock, prefilled

syringes with 2 mg/2 mL naloxone hydrochloride; and the mucosal atomization device. Participants were instructed to deliver 1 mL (1 mg) to each nostril of the overdose victim. Because most opioid agonists have a longer half-life than naloxone, if overdose symptoms returned, victims could be treated with the second dose.

DATA COLLECTION AND ANALYSIS

From September 2006 to December 2007, during each bystander training, staff completed an enrollment form, recording respondents' demographics and overdose risk factors. When participants returned to the needle-exchange program, staff completed a form detailing overdoses witnessed, use of naloxone, and whether additional doses were needed. Data were maintained in a Microsoft Access 2003 database (Microsoft Corp, Redmond, WA). We compared enrollment data from participants who reported overdose reversals with those who did not with the *t* test of means and the χ^2 or Fisher exact test. We used SAS version 9.1 (SAS Institute, Cary, NC) for all tests of comparison.

DISCUSSION AND EVALUATION

Over 15 months, the program provided education and intranasal naloxone to 385 potential bystanders. At enrollment (Table 1), heroin was the most frequently used drug, followed by cocaine, methadone, benzodiazepines, and alcohol. Opioids were used on a mean of 24.1 of the last 30 days. Cocaine was the drug used most commonly in combination with heroin. Among 224 (64%) who reported a previous overdose, the median number of lifetime overdoses was 2, and among the 303 (92%) who had witnessed an overdose, the median number of lifetime witnessed overdoses was 5.

Follow-up contact was made at least once with 278 (72%) participants, 222 of whom reported no overdoses witnessed and no need for additional doses of naloxone. Among the 57 participants who requested additional doses, 7 had the naloxone lost, stolen, or confiscated, and 50 administered naloxone while observing an overdose (Figure 1). Among the 50 participants (13%) who reported reversing an overdose, 74 successful reversals were reported. Except for mean age (43 vs 39 years; $P < .05$), there were no significant differences between those participants who reported reversing an overdose and those who did not (data not shown). Emergency medical personnel were involved in 21 of the 74 (28%) reported overdoses and were not involved in 39 (53%) reported overdoses. Involvement by emergency medical personnel was not reported in the remainder (data available as a supplement to the online article at http://www.ajph.org). Two previous studies of naloxone distribution programs have reported similar rates of emergency medical personnel involvement (10% to 31%).[20,23]

Among follow-up contacts, problems were uncommon. During 4 overdoses, bystanders could not connect the mucosal atomization device to the syringe, although each resulted in successful reversal. Two administered naloxone nasally directly from the syringe, 1 injected the naloxone intramuscularly, and 1 did not administer naloxone, but delivered rescue breathing and physical stimulation until Boston Emergency Medical Services arrived. Two bystanders reported that naloxone induced withdrawal symptoms, but, in both cases, the victim did not use additional opioids to alleviate symptoms. Two bystanders observed the naloxone wearing off: 1 readministered it after 90 minutes, and 1 reported that the victim became resedated after 20 minutes, when Boston Emergency Medical Services assumed care. Two people had naloxone confiscated at a homeless shelter, 1 reported being expelled from a residential drug treatment program for having the substance, and 3 reported negative interactions with emergency medical personnel,

TABLE 1—Selected Characteristics of Participants (N = 385) in an Overdose Prevention Program With Intranasal Naloxone Distribution: Boston, MA, September 2006–December 2007

	Sample Total	No. (%) or Mean ±SD
Age, y	377	39.6 ± 11
Women	381	129 (34)
Race/Ethnicity	374	
White		245 (66)
Hispanic		81 (22)
Black		45 (12)
Other		3 (1)
HIV status	219	
Positive		26 (12)
Negative		193 (88)
HCV status	246	
Positive		159 (65)
Negative		87 (35)
Days opioids used	351	24.1 ± 10.7
Substance used in the last 30 d	385	
Heroin		273 (71)
Methadone		149 (39)
Buprenorphine		11 (3)
Other opioids		60 (16)
Cocaine		155 (40)
Benzodiazepines		118 (31)
Alcohol		88 (23)
Heroin and cocaine		125 (33)
Heroin and benzos		98 (26)
Heroin and alcohol		69 (18)
Heroin, benzos, alcohol		35 (9)
Clonodine		26 (7)
History of nonfatal overdose	349	
Had a nonfatal overdose		225 (65)
Nonfatal overdoses experienced, median (interquartile range)		2 (1–5)
Nonfatal overdose treated with naloxone		146 (69)[a]
Lifetime witnessed overdose	329	
Had witnessed an overdose		303 (92)
Overdoses witnessed, median (interquartile range)		5 (3–15)

[a]The percentage represents the percentage of respondents who had a nonfatal overdose and answered the question about whether naloxone had been used (n = 212).

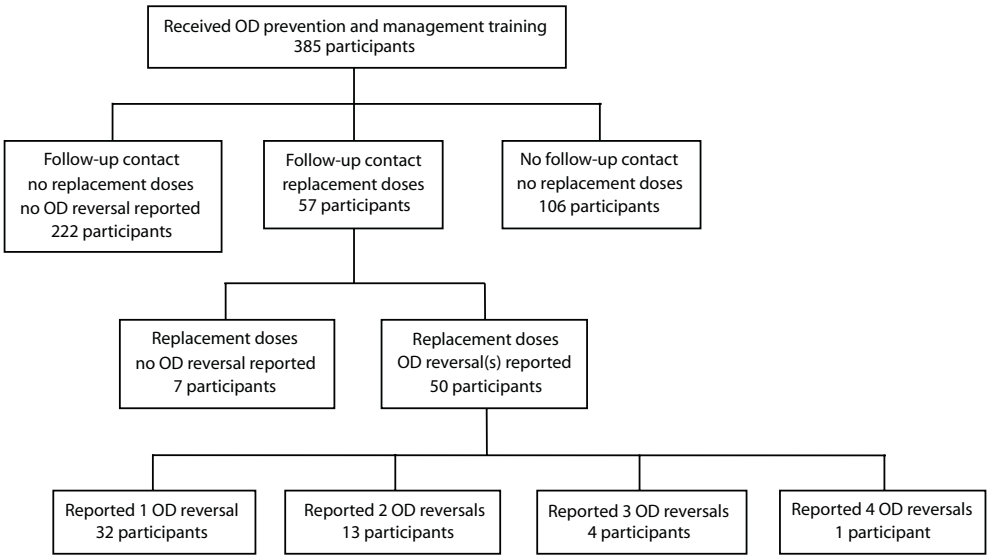

FIGURE 1—Flow chart of follow-up of 385 potential bystanders who received overdose (OD) prevention and management training: Boston, MA, September 2006–December 2007.

none of which resulted in arrest (8 reported positive interactions).

Of the 74 reported reversals, 4 reports were of bystanders not initially enrolled in the program who used intranasal naloxone obtained from peers who were enrolled. Thus, there was some peer-to-peer overdose knowledge and skill transfer beyond the program.

The BPHC overdose-prevention naloxone distribution program was implemented without substantial additional funding. Space, printing costs, and staff time were provided by the existing needle-exchange program. Naloxone kits cost approximately $25.

NEXT STEPS

The BPHC naloxone distribution program is a feasible, successful program that includes distribution of intranasal naloxone by nonmedical staff. The Massachusetts Department of Public Health has identified overdose prevention as a major focus area for new public health initiatives and has expanded the program to 5 additional sites that target needle-exchange participants, staff at substance abuse treatment programs, homeless shelters, and families and friends of opioid users. ■

About the Authors

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Contributors

M. Doe-Simkins and A. Y. Walley, as co-first authors, jointly wrote the first draft and led subsequent revisions of the article. M. Doe-Simkins managed the data collection and assembly of the dataset and was a lead trainer of participants and other staff. A. Y. Walley performed the data analysis and led the institutional review board application. A. Epstein led the development and implementation of the project. P. Moyer provided medical supervision and direction. All authors helped to conceptualize ideas, develop the project, interpret findings, and review drafts of the article.

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Human Participant Protection

This study was approved as an exempt study by the Boston University Medical Center institutional review board.

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Legal and Regulatory Barriers to Implementing an Overdose Prevention Program With Intranasal Naloxone Distribution by Nonmedical Personnel

Barrier	Response
Nonmedical personnel are not authorized to distribute prescription medication and are not authorized to administer a prescription medication to a person who has not been prescribed the medication.	▪ The standard of care for the use of naloxone has for decades included use by prehospital personnel in nonclinical settings operating under standing orders from physicians who are neither on-site nor directly supervising. ▪ Other life saving prescription medications, such as epinephrine injectors for anaphylactic shock,[24] and other devices, such as automated external defibrillators, are used by bystanders and nonmedical personnel. ▪ Other states, such as New Mexico, New York and Connecticut, have addressed this by passing laws that limit the liability of medical and nonmedical personnel who administer and distribute potentially lifesaving medication.[25] ▪ A study of 6 programs that train bystanders to recognize and respond to opioid overdose by using naloxone has demonstrated that trained potential bystanders are similarly skilled as medical experts in recognizing opioid overdose situations and when naloxone is indicated.[22] ▪ A local public health regulation was passed by BPHC, the City of Boston's board of health, identifying the overdose-prevention naloxone distribution program as an official public health program and assuming liability for the work of medical and non-medical personnel involved in the program. ▪ Under the medical license of the Medical Director of Boston Emergency Medical Services, potential bystanders received a standard curriculum about overdose prevention with instructions and demonstration of how to properly use the medication. Receipt of this curriculum was documented by BPHC staff.
Intranasal delivery of naloxone is an off-label method.	▪ Prescriptions drugs may be and are routinely given for any indication not explicitly prohibited by law.[25,26] ▪ While no large scale randomized clinical trials have been conducted, intranasal naloxone has been evaluated in several research studies, with little evidence of adverse events.[9–13] A small randomized trial comparing intranasal with intramuscular delivery of naloxone used by emergency personnel demonstrated that intranasal delivery had a longer time to clinical response (8 minutes vs 6 minutes), but less agitation or irritation (2% vs 13%).[11] ▪ Intranasal naloxone is a first-line treatment for opioid overdose among emergency medical personnel in the local Boston community.