Physicians' Knowledge of and Willingness to Prescribe Naloxone to Reverse Accidental Opiate Overdose: Challenges and Opportunities

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ABSTRACT *Naloxone, the standard treatment for heroin overdose, is a safe and effective prescription drug commonly administered by emergency room physicians or first responders acting under standing orders of physicians. High rates of overdose deaths and widely accepted evidence that witnesses of heroin overdose are often unwilling or unable to call 9-1-1 has led to interventions in several US cities and abroad in which drug users are instructed in overdose rescue techniques and provided a "take-home" dose of naloxone. Under current Food and Drug Administration (FDA) regulations, such interventions require physician involvement. As part of a larger study to evaluate the knowledge and attitudes of doctors towards providing drug treatment and harm reduction services to injection drug users (IDUs), we investigated physician knowledge and willingness to prescribe naloxone. Less than one in four of the respondents in our sample reported having heard of naloxone prescription as an intervention to prevent opiate overdose, and the majority reported that they would never consider prescribing the agent and explaining its application to a patient. Factors predicting a favorable attitude towards prescribing naloxone included fewer negative perceptions of IDUs, assigning less importance to peer and community pressure not to treat IDUs, and increased confidence in ability to provide meaningful treatment to IDUs. Our data suggest that steps to promote naloxone distribution programs should include physician education about evidence-based harm minimization schemes, broader support for such initiatives by professional organizations, and policy reform to alleviate medicolegal concerns associated with naloxone prescription. FDA re-classification of naloxone for over-the-counter sales and promotion of nasal-delivery mechanism for this agent should be explored.*

KEYWORDS *Evidence-based practice, Heroin, Injection drug use, Naloxone, Overdose prevention, Physician behavior, Physician education.*

INTRODUCTION

Fatal heroin overdose among injection drug users (IDUs) is a rapidly growing public health problem, representing one of the highest causes of preventable death in U.S.

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areas where heroin injection is widespread.^{1–3} The epidemiology of morbidity and mortality associated with overdose has been gaining overdue attention.^{1,4–7} Analysis suggests that overdose incidents typically take place with other users present and that death occurs 1–3 hours after the initial injection.^{8–10} This allows ample opportunity for medical intervention to prevent fatalities through the administration of naloxone, a safe and effective opiate antagonist.^{2,4,11,12} A generically-manufactured agent, naloxone is a Class 3 substance that is typically injected but can also be nasally-administered to a victim of an opiate overdose.^{12,13} This substance lacks any psychoactive or addictive qualities; it merely blocks the effects of opiates without any potential for abuse.^{8,14} On standing orders of a physician, first responders routinely administer naloxone through injection when summoned to the scene of drug overdose.^{2,12,15–17} Side effects associated with naloxone treatment for opiate overdose are generally rare.^{12,18,19}

Too often, timely medical attention is not provided to victims of opiate overdose.^{5,11} Witnesses may fail to summon help for fear of legal repercussions to self or to the victim, or mistrust of the medical system.^{3–8,11,15} Equipping drug users with naloxone for administration in the event of an overdose has been introduced in several areas in the United States as well as internationally, with positive results.^{9,20–24}

Naloxone distribution programs have been associated with a drastic reduction in the number of overdose deaths in a community.^{10,20–22} Aside from provision of naloxone, these programs typically include instruction on first-aid techniques, ways to spot and appropriately report signs of the most common adverse reactions, and access to drug treatment and other services. Data suggest that trained clients may use drugs less frequently and be more likely to seek addiction treatment than non-trained counterparts^{20–23} and that they do not increase drug dosage in reliance on the overdose reversal agent.^{20,21} Medical side-effects or other problematic unintended consequences associated with such distribution programs have not, to date, been reported.^{8,9,21,24,25}

Naloxone is a prescription drug, so physician participation is a necessary element in any naloxone distribution program in the U.S. More generally, physicians can help reduce the harmful health consequences of injection drug use by counseling patients about ways to reduce drug use or its risks.^{26,27} Approximately two-thirds of individuals with addiction will see a primary care or urgent care physician every six months, and many others are regularly examined by other medical specialists.^{26,28–32}

Although systematic research on physicians and IDU care has been limited,^{28,30,31,33–35} studies suggest that training, attitudes, and self-efficacy factors influence health care provider participation in harm reduction interventions.^{8,27,28,30–36} Medical professionals may be uncomfortable treating drug users at all,³⁷ or view drug abusing patients as a particularly difficult population not amenable to intervention,³¹ while fearing that their other patients, colleagues, or society at large will perceive caring for IDUs as “softness” on drug abusers.³⁸ These concerns may reflect the widespread social perception that drug abuse is a self-inflicted behavior, less worthy of clinical care and treatment.³¹

Such attitudes act as barriers to effective and sustained treatment and recovery for patients.³⁹ A more detailed understanding of these factors is a precondition to success in efforts to bring about greater physician involvement⁴⁰ (and with that, broader public support) in the care of IDUs, including changes in legal and institutional policies, as well as training and continuing education of physicians.^{28,41}

Here, we report on the naloxone-related results of a national survey of physicians on IDU care.

METHODS

The study sample consisted of 1.5% of physician members of the American Medical Association (AMA) registered in the AMA master file, which includes physicians from all fifty states and Puerto Rico. We limited the study to physicians practicing in specialties and sub-specialties likely to entail treatment of IDUs. The sample was geographically representative of physicians in Internal Medicine, Family Practice, General Practice, Gynecology, Pediatrics/Adolescent Medicine, Emergency Care, Addiction Medicine, Addiction Psychiatry, Endocrinology, Diabetes and Metabolism, Infectious Disease, Obstetrics (Surgery and Gynecology), Physical Medicine, Rehabilitation, and Pain Medicine.

The 46-item survey included a set of items assessing respondent attitudes towards IDUs, as well as items covering their professional experience caring for IDUs and their attitudes on specific interventions, including prescription of syringes, providing office-based opiate replacement therapy, and prescribing naloxone as a means of reducing opiate overdose mortality. Up to four mailings were sent out to each participant, or until a response was obtained. The first, second, and third mailings were sent by first class mail. The fourth mailing was sent by FedEx 2 day delivery. All mailings contained a self-addressed, stamped return envelope.

To increase the response rate, we called physicians with available phone numbers after the first mailing. Physicians were asked if they had received a copy of the survey and if we could fax to them a copy of the survey. Up to 3 faxes were sent to each physician contacted by phone: first immediately after contacting them, and then if there was no response, 1 and 3 weeks later. The data were double entered for accuracy and analyzed using SAS software. All protocols were reviewed and approved by The Miriam Hospital Institutional Review Board (IRB) and the Temple University IRB. Physicians were informed that their responses would be kept confidential and consent was determined by return of the survey.

The main outcome variable in this study was physicians' willingness to consider prescribing naloxone and explaining its use to an IDU patient. The independent variables consisted of composite Likert scales representing the three major components of behavioral intention identified in the Theory of Planned Behavior (TPB): attitudes, subjective norms, and perceived control.⁴² Because the original study was not focused on naloxone prescribing, we used the TPB in this analysis to identify important general factors associated with a willingness to consider providing overdose care to IDU patients as opposed to predicting the intention to prescribe naloxone. The items used to construct these scales were chosen by consensus of the authors from items in a larger study of health care and harm reduction. To facilitate analysis, we rescaled all items to values of 0 to 100 so that higher numbers denote more positive or better attitudes, subjective norms, or perceived control.

Alpha-reliability coefficients were used for scale development and summary. The attitude scale was designed to evaluate physicians' perceptions of IDUs in order to test the null hypothesis that physicians who have negative attitudes towards IDUs would be just as likely to say they would consider prescribing naloxone as those with positive attitudes. Nine items were initially included in this category, but removal of two of them increased the alpha-reliability. The resulting scale pooled responses to 7 items, including "Drug addiction is a behavioral problem, not a

disease” and “If I saw marks on a patient indicating injection drug use (such as track marks), I would regard the patient less favorably.”

Investigators initially classified eleven items as related to subjective norms; two were removed in order to improve the alpha-reliability. The resulting 9-item subjective norms scale was constructed from questions that addressed normative issues, such as “Patients would leave my practice if they realized I was treating IDUs” and “Having IDUs as patients is stressful.” This scale was designed to test the null hypothesis that physicians who perceive that their staffs, patients or colleagues would disapprove of any active efforts to provide harm reduction care to IDUs in the practice would be just as likely to respond that they would consider prescribing naloxone as those who did not report feeling these normative pressures.

The 11-item perceived control scale included “I do not feel I am adequately trained in the treatment of drug addiction” and “Treating drug addiction use isn’t effective.” It also included items aimed at assessing the respondent’s feelings about dealing with possible legal consequences (e.g., “Physicians are not always treated fairly by the medical board.”) This scale was designed to test the null hypothesis that physicians who believe there is little they can do to help IDUs would be just as likely to respond that they would consider prescribing naloxone as those who felt able and authorized to help IDUs (see Table 3).

To create each of the final composite scales, individual items were rescaled to 0–100 and then averaged. Chi-square tests were used to test the significance of the association of physician intention to discuss or prescribe naloxone in relation to their answers to other items on the survey. We used logistic regression models to evaluate the magnitude of associations, as estimated by odds ratios and 95% confidence intervals, between physician responses to survey questions and the outcome response variable of whether or not the physician reported that they would consider prescribing naloxone and explaining its use to an IDU patient. Logistic regression was used for both univariate and multivariable analyses to see if the likelihood of answering “yes” to whether the physician would consider participating in a naloxone distribution program was related to awareness of naloxone distribution and any of the composite measures. *P*-values of ≤ 0.05 were considered as statistically significant.

We assessed the reliability of the composite scales using the alpha reliability coefficient. The attitude scale had an alpha reliability of 0.51, the subjective norms scale had an alpha reliability of 0.65, and the perceived control scale had an alpha reliability of 0.54, suggesting that the scales reasonably captured the information contained in their individual sub-components. Additionally, we compared the *r*-square values between each scale pair, finding that the scales explain about 37% to 42% of each other. These results suggest that each scale measures different, but not totally independent domains.

RESULTS

The initial study sample included 3,435 physicians. In the process of data collection, we found that 146 (4.3%) were deceased or retired, and 442 (12.8%) were unreachable because of incorrect contact information. This left 2,847 eligible physicians for our study. Two hundred eighty eight physicians (10.1%) refused to participate, while 69.2% ($n=1,971$) were non-responders. Thus, a total of 588 (20.6%) physicians responded to the survey, and over 95% of these responders

answered the two items related to prescription of naloxone. Similar to the overall population of US physicians, males (70%) were overrepresented in our sample; of those who responded to the race question (slightly less than half of the overall sample), 83% identified as white, with Asians (9%), Hispanics (5%), and Blacks (3%) comprising the remainder.

Only 23% of 571 physicians responding to this question indicated that they “had heard” of prescribing naloxone to IDUs as a strategy to prevent overdose. A slight majority (54%) of 563 responders indicated that they would never “consider prescribing naloxone and explaining its use to an IDU patient.” Demographics of the sample are presented in Table 1. Among demographic characteristics (age, gender, race, specialty, and geographic region), only age was a significant predictor of having heard of the strategy, with the mean age of those who reported having heard about this intervention being slightly older than those who responded negatively (mean = 51 vs. 48, $p = 0.006$). Physicians willing to consider prescribing naloxone were slightly older than those who would not. Physicians who answered “yes” to this item were also significantly more likely to be aware of IDUs in their patient population, to provide information about drug treatment, and to report knowledge of syringe exchange and the legality of prescribing syringes to IDUs in their locality (see Table 2).

TABLE 1. Descriptive statistics of respondents to item willingness to prescribe naloxone ($n = 563$)

	ALL ($n = 563$)	Yes, would consider prescribing naloxone ($n = 261$)	No, would NOT consider prescribing naloxone ($n = 302$)	p -value
Age in years, mean $\pm$ SD (n)				
At survey	48.9 $\pm$ 11.0 (563)	48.6 $\pm$ 10.2 (261)	49.1 $\pm$ 11.6 (302)	0.53
At graduation	26.6 $\pm$ 3.3 (563)	27.0 $\pm$ 3.6 (261)	26.3 $\pm$ 3.1 (302)	0.0222
Gender, % female	29.8% (168/563)	29.9% (78/261)	29.8% (90/302)	0.98
Race, % (n)	$N = 429$	$N = 199$	$N = 230$	0.22
White, nonhispanic	45.0% (193)	45.7% (91)	44.3% (102)	
Black, nonhispanic	1.6% (7)	1.5% (3)	1.7% (4)	
Hispanic	2.6% (11)	2.5% (5)	2.6% (6)	
Asian	4.7% (20)	2.0% (4)	7.0% (16)	
Other	0.2% (1)	(0)	0.4% (1)	
Unknown	45.9% (197)	48.2% (96)	43.9% (101)	
Specialty, % (n)	$N = 563$	$N = 261$	$N = 302$	0.12
Primary	80.6% (454)	82.8% (216)	78.8% (238)	
Adolescent	0.9% (5)	1.5% (4)	0.3% (1)	
Emergency med.	12.8% (72)	11.9% (31)	13.6% (41)	
Specialist	5.7% (32)	3.8% (10)	7.3% (22)	
Region, % (n)	$N = 556$	$N = 256$	$N = 300$	0.10
Northeast	26.6% (148)	27.7% (71)	25.7% (77)	
South	26.1% (145)	24.2% (62)	27.7% (83)	
Midwest	23.6% (131)	20.3% (52)	26.3% (79)	
West	23.7% (132)	27.7% (71)	20.3% (61)	

TABLE 2. Respondent characteristics stratified by willingness to prescribe naloxone (n = 563)^a

	ALL (n = 563) ^a	Yes, would consider prescribing naloxone (n = 261)	No, would NOT consider prescribing naloxone (n = 302)	p-value
Aware of naloxone strategy	22.9% (129/563)	25.7% (67/261)	20.5% (62/302)	0.15
% with IDUs in practice	41.2% (229/556)	47.5% (122/257)	35.8% (107/299)	0.0053
Provides information on drug treatment to patients	97.1% (542/558)	98.8% (255/258)	95.7% (287/300)	0.0253
Knows if syringe prescription is legal	21.4% (120/560)	27.4% (71/259)	16.3% (49/301)	0.0014
Knows whether syringe exchange program operates in local area	44.2% (246/557)	51.8% (133/257)	37.7% (113/300)	0.0008

^aTable includes data for (n = 563) physicians who responded to question about willingness to prescribe naloxone.

After adjusting for age at medical school graduation and geographical location, we found that all three composite scales had robust positive associations with a willingness to consider prescribing naloxone to IDU patients (see Table 3). This finding suggests that better attitudes towards IDUs, assigning less importance to peer and community pressure not to treat IDUs, and increased confidence in ability to provide meaningful help to IDUs would all increase the willingness of a physician to deal with overdose prevention among her own IDU patients, or to prescribe naloxone to drug using patients.

DISCUSSION

Researchers conducting national postal surveys of US physicians have generally reported response rates between 44–65%.^{43–45} In designing this study, we adopted techniques that had helped past survey initiatives overcome the significant barriers to participation that exist in this population.^{43–45} Despite these efforts, the 20% response rate in this survey was substantially lower than that achieved by the studies we emulated.^{43–45} Considering the similarity between the study samples and research processes, one explanation for this discrepancy is the subject matter of our survey. There is evidence that many US physicians are not comfortable, knowledgeable, nor interested in providing care to IDUs.^{27,28,31,37,46,47} The fact that roughly twice to three times as many doctors chose to participate in past postal surveys on other subjects suggests that US physicians are reluctant to discuss injection drug use and IDU care in their practice. Other surveys of medical personnel on topics related to injection drug use, including naloxone distribution have reported comparably low response rates.^{27,35,48}

Consideration of why so many physicians turned away from answering this survey is also informed by the responses of those who did participate. In our sample, over 65% reported that they “usually” or “always” ask patients about the

TABLE 3. Relationship of physicians’ consideration of naloxone prescription with composite scales

	Yes, would consider prescribing naloxone (n = 261)	No, would NOT consider prescribing naloxone (n = 302)	Unadjusted Odds Ratio (OR)	Adjusted Odds Ratio
Scale	Median Scale value <q1–q3> (n)		Odds Ratio per 10 point increase (and 95% CI), p-value	
Attitude	57 <50–68> (260)	54 <43–61> (299)	1.45 (CI: 1.26–1.67) p ≤ 0.0001	1.41 (CI: 1.22–1.67) p ≤ 0.0001
Subjective norm	53 <47–64> (259)	47 <39–56> (299)	1.69 (CI: 1.45–1.97) p ≤ 0.0001	1.66 (CI: 1.42–1.94) p ≤ 0.0001
Perceived control	54 <48–61> (259)	52 <45–59> (299)	1.32 (CI: 1.11–1.56) p = 0. 0013	1.28 (CI: 1.07–1.52) p = 0.0058

use of individual illicit drugs, while over 40% reported having IDUs among their patients. The former datapoint is roughly twice the proportion reported in a recent comprehensive national physician survey,²⁷ suggesting that our sample was skewed towards individuals who were more aware of drug use issues.

It is telling that even within this group, less than one in four (23%) responders had ever heard of prescribing naloxone as a tool for preventing opiate overdose, and that a majority (54%) said they would never consider prescribing naloxone. These results are consistent with similarly low proportions of health providers reporting willingness to participate in naloxone distribution in smaller, regional surveys.^{35,41} The dramatic successes of the IDU care programs established to date show that even a few committed physicians can make a big difference,⁴⁹ but IDU care will remain sub-optimal without change that reaches deeper into the physician population.

Changing healthcare provider attitudes and behavior is slow and difficult.^{30,42} As our study suggests, in order to impact physicians’ intention to prescribe naloxone, several different behavioral motivators must be addressed, including negative attitudes towards IDUs, pessimism in treating drug use, and fear of social or professional disapproval. Robust evidence has now established that harm reducing interventions like overdose prevention, better syringe access, and drug treatment do provide real health benefits to the IDU population and the broader community, including considerable savings in the use of public resources.^{10,12,50,51} Side effects of naloxone administration and danger of overdose reversal have been found to be minimal,¹⁹ and providers’ concerns about proper care can be addressed by bundling distribution programs with resuscitation and monitoring techniques.^{8,13,19,41} A nasal delivery system can assuage provider anxiety about improper injection of the agent.^{13,35} Communicating this evidence to physicians is the most immediate step to address the lack of knowledge and sense of treatment futility our survey highlights. Informing health providers about the mechanisms of such treatment can also serve as a vehicle for addressing the stigma of treating IDUs.

Such information transfer may occur during medical school and residency, where instruction in the realm of substance abuse, including injection drug use is

generally understood to be inadequate.^{28,47} Continuing medical education courses are also a promising forum for reaching a broad population of practising healthcare providers.³⁵ Greater focus on IDU care as a matter of quality improvement in health care institutions and managed care organizations may be promoted by organizations themselves and by accreditation bodies. Professional organizations can also do more to promote evidence-based, public health-driven approaches to drug use and better care for IDUs.

Addressing medicolegal anxiety among providers presents another avenue for action. The *de facto* “deputation” of the patient to act as health care provider in injection of naloxone may raise provider or the prescription recipient’s concerns about civil or criminal liability for unauthorized practice of medicine. Similar concerns have arisen with patient-administered therapy for sexually transmitted infections.⁵² New York State and New Mexico legislatures dealt with this concern by passing laws broadly immunizing participating health care professionals from civil and criminal liability that may result from naloxone prescription programs.^{53,54} There is some anecdotal evidence that malpractice liability concerns may also be a barrier.⁸ Legislative reform shielding prescribing physicians from liability and fast-track approval of nasal, rather than injection-based, delivery mechanisms can effectively address this as well.⁸

Sustained, creative and multi-faceted efforts are needed to improve health care for IDUs in the U.S. Such efforts should include promoting physician participation in interventions to reduce overdose morbidity and mortality. It should be noted, however, that overdose interventions deploying naloxone could be as well or even better assisted by a change in the status of naloxone under U.S. FDA regulations. Naloxone is now classified as a prescription drug. A change in its status to over-the-counter would require collection of data showing that consumers can safely use the drug without physician supervision or special prior training. Physicians and public health professionals in this country may fear that making naloxone available without requiring recipients to undergo resuscitation and other training may lead to widespread misuse, but Italy’s experience shows that naloxone reclassification for over-the-counter sales produces positive results with no reported complications.²⁵ In order to evaluate whether prescription reform is warranted in the US context, more research is needed to ascertain the public health benefit and cost-effectiveness of naloxone provision schemes that forgo or minimize recipient training; wider reach and lower costs of such initiatives have to be weighed against the purported benefits that flow from providing a training intervention and other services—including gateways to treatment—at the point of distribution.

The switch of a drug to over-the-counter status in the U.S. is typically made at the request of a manufacturer, which bears the costs of conducting the necessary studies and going through the administrative procedure. In the case of naloxone (a generic drug), the public health community would need to play an active role in promoting reclassification reform. A manufacturer of an intra-nasal delivery mechanism that would make naloxone easier and safer to administer may be persuaded to invest in an FDA reclassification process. If the market does not provide sufficient incentives to manufacturers to mount such an effort, the FDA should exercise its legal authority to pursue reclassification in the public interest on its own initiative. The National Institutes for Drug Abuse, Centers for Disease Control and Prevention, and other relevant federal agencies can assist by supporting the necessary research and surveillance to document safety and effectiveness.

CONCLUSION

Growing evidence suggests that physicians can provide care that contributes to recovery and reduces the risks of morbidity and mortality associated with drug abuse. Physician reluctance to provide such care has many roots, including lack of training, negative attitudes towards drug users, doubts about the efficacy of interventions, real and perceived legal barriers, and fear of social, professional, and material detriment. Efforts to improve IDU access to naloxone through the primary care context include policy reform to address physicians' legal concerns, better education about what constitutes evidence-based practice, greater attention to public health and quality improvement activities, and a stronger voice from professional organizations. Recognition of formidable barriers in the existing prescription-based scheme should also inspire urgency in considering nasal delivery systems and FDA reclassification as promising avenues for reform to promote the distribution of naloxone with the related reduction in overdose deaths.

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