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Factors Associated with Naloxone Administration in an Opioid Dependent Sample

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Abstract

Introduction—Naloxone is a safe and effective antidote for reversing opioid overdose. Layperson administration of naloxone is increasingly common, yet little is known about demographic and clinical factors associated with opioid users' likelihood of having administered naloxone to another opioid user who had overdosed. We examined predictors of reported naloxone administration in the past year.

Methods—Four hundred and sixty-eight patients were interviewed upon admission to brief, inpatient opioid detoxification between May and December of 2015. Between group differences were tested using t-tests for differences in means and χ^2-tests for differences in counts.

Results—Participants averaged 32 years of age, 28.9% were female, and 86.8% were White. Most (86.8%) reported detoxifying from heroin, 69.0% had injected drugs in the last 30-days. One sixth (n=68) of those detoxifying from heroin, but none of those detoxifying from other opioids (n=62) had administered naloxone in the past year. Among the small number of Black/African American participants (n=20), none had administered naloxone, although 90% were heroin users. Respondents were more likely to have administered naloxone if they reported recent injection drug use (IDU), had a history of overdose, or witnessed an overdose in the past year (*ps* < .05), even though less than one-third of bystanders of overdose reported administering naloxone.

Conclusions—Higher opioid-related mortality risk (heroin use, IDU, past overdose) was associated with greater likelihood of reported naloxone administration in the past year. The non-use of naloxone among certain groups—prescription pill users and Blacks—was unexpected.

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Keywords

Naloxone; Layperson administration; Overdose; Opioid detoxification

1. Introduction

Over 2.5 million Americans have a prescription opioid use disorder and 591,000 have a heroin use disorder (CBHSQ, 2016). High rates of fatalities and emergency department (ED) visits are linked to prescription opioid analgesics (Compton, Jones, & Baldwin, 2016; Yokell et al., 2014), and heroin overdose fatalities have more than tripled nationwide from 2010 to 2015, surpassing prescription opioid rates (MMWR, 2017).

Naloxone, a safe and effective antidote for reversing the effects of opioid overdose, has become a key component in efforts to address the epidemic of opioid overdose-related morbidity and mortality. Distributing naloxone to likely bystanders of overdose, primarily illicit opioid users (Wheeler et al., 2015), has been shown to be safe (Doyon et al., 2014), cost-effective (Coffin & Sullivan, 2013), carry little clinical (e.g., increased opioid use) or legal liability risk (C. S. Davis, Burris, Beletsky, & Binswanger, 2016; Doe-Simkins et al., 2014), and is associated with significant reductions in community level overdose deaths (Clark, Wilder, & Winstanley, 2014; McDonald & Strang, 2016). The World Health Organization designates naloxone an “essential medicine” that should be accessible to laypersons likely to witness an overdose (WHO, 2014). Nationally, between late 2013 and early 2015, the distribution of community-based naloxone kits increased 187% and outpatient dispensing of naloxone in retail pharmacies surged 1170% (Jones, Lurie, & Compton, 2016). As of August 2016, forty-four U.S. states offered naloxone kits to laypersons without a standing prescriber-patient relationship (C. Davis & Carr, 2017). Despite the continued increased availability of naloxone and national data showing that the vast majority of layperson naloxone use is administered by opioid dependent individuals (Wheeler et al., 2015), research examining demographic and clinical factors associated with naloxone administration in this population is scarce.

The few existing reviews examining the efficacy of naloxone distribution programs have focused on heroin users (McDonald & Strang, 2016), perhaps because naloxone distribution organizations tend to target settings with higher presence of heroin users, IDUs, and those with a history of overdose (e.g., drug treatment programs, needle exchanges; Green & Doe-Simkins, 2016). Yet, national data from organizations distributing naloxone to laypersons report that heroin was involved in 81.6% and prescription opioids in 14.1% of reported cases of naloxone overdose reversal (Wheeler et al., 2015), thus indicating a need to better understand the role of prescription opioids in naloxone use.

1.1. Current Study and Hypotheses

The current study highlights demographic and clinical factors associated with naloxone administration among persons seeking opioid detoxification. We hypothesized that respondents with a higher risk drug use profile, including recent IDU and overdose history, would be more likely to have administered naloxone in the year prior to entering

detoxification. Based on available prevalence data showing greater layperson administration of naloxone among heroin (as opposed to prescription opioid) users, we expected those seeking detoxification from heroin to be more likely to have administered naloxone. We also expected that respondents who had witnessed an overdose in the past year to demonstrate a greater likelihood for having administered naloxone during this time as these respondents may be embedded in high-risk social networks and have greater awareness of overdose risks (and hence motivation to obtain and use naloxone).

2. Method

2.1. Recruitment

Between May and December 2015, persons seeking inpatient opioid detoxification were approached at the time of admission to Stanley Street Treatment and Resources, Inc. (SSTAR) in Fall River, Massachusetts to participate in a survey research study. Fall River has among the highest prevalence of fatal and non-fatal opioid overdose of all towns in Massachusetts (Fraga, 2017). SSTAR's detoxification program provides evaluation and withdrawal management using a methadone taper protocol, individual and group counseling, and aftercare case management.

Of patients admitted to SSTAR during the recruitment period, 487 were opioid users who were 18 years or older, English-speaking, and able to provide informed consent as approved by the Butler Hospital Institutional Review Board. Nine refused study participation or were discharged before staff could interview them. The remaining 478 persons completed an approximately 15-minute non-incentivized, face-to-face interview administered by non-treating research staff. The 468 patients who provided responses to all the measures of interest constitute the study sample.

In November of 2007, the Massachusetts Department of Public Health implemented an Overdose Education and Naloxone Distribution (OEND) program in communities with high incidence of overdose, including Fall River, the residence of the majority (n = 343, 73.3%) of sample participants. These programs train individuals likely to witness an overdose (bystanders; e.g., drug-using and non-using friends, acquaintances, and family members) on how to reduce overdose risk, recognize signs of an overdose, access emergency medical services, and administer intra-nasal naloxone. Since OEND' conception through September 1, 2016, there have been a cumulative total of 48,222 individual participants trained and given a naloxone kit and 8,149 reported opioid overdose reversals across 16 community based agencies in Massachusetts (OEND, 2016).

2.2. Measures

In addition to age, sex, race, ethnicity, past 30-day IDU, and whether the primary drug from which the respondent was detoxifying from was heroin or prescription opioids, several overdose-related variables were assessed. Prior to completing the interview, overdose was defined as a state in which an individual is “unarousable (couldn't be woken) with shaking or calling (your/their) name because of the drugs consumed.”

2.2.1. Overdose history—Respondents reporting that they had overdosed since their first use of drugs were coded as having ever overdosed.

2.2.2. Witnessed overdose—Respondents were asked how many times in the past year they had been "present when someone else has experienced an overdose."

2.2.3. Naloxone administration—Respondents answered "yes" or "no" to giving naloxone (Narcan)—defined as the "overdose antidote"—to someone they had witnessed overdosing in the past year. We also asked respondents who reported administering naloxone where they had obtained their naloxone kit.

2.3. Analysis Plan

We present means and percentages to describe the sample characteristics and describe substantive differences between persons who had and had not administered naloxone in the past year. Between group differences were tested using t-tests for differences in means and χ^2-tests for differences in counts. We did not conduct multivariate logistic regression analysis because we encountered complete separation in which only persons in one category of the predictor administered naloxone. Additionally, there is strong collinearity between potential predictor variables (e.g., specific opioid of misuse and IDU). However, we conducted auxiliary analyses exploring associations between correlates of administering naloxone.

3. Results

Participants averaged 32.1 (± 8.65) years of age, 28.9% were female, 82.3% were non-Hispanic White, 4.3% were non-Hispanic Black/African American, 9.0% were Hispanic, and 4.5% were of other racial or ethnic origins (Table 1). Most (86.8%) respondents reported heroin as the drug from which they were detoxifying, and 69.0% reported past 30-day IDU. One hundred eighty-two (38.9%) said they had ever overdosed, and 41.5% had witnessed an overdose in the past year. Sixty-eight (14.5% had administered naloxone during the past year.

The likelihood of administering naloxone was associated significantly ($\chi^2 = 9.63$, df = 3, $p = .002$) with race; 14.5% of non-Hispanic Whites, 0.0% of non-Hispanic Blacks, 11.9% of Hispanics, and 33.3% of those with other racial/ethnic identifications reported administering naloxone in the past year (Table 1). Administering naloxone was not associated significantly with other demographic characteristics.

Administering naloxone in the past year was associated significantly ($\chi^2 = 12.15$, df = 1, $p < .001$) with primary opioid of misuse; 16.8% of persons detoxifying from heroin, but none detoxifying from prescription opioids had administered naloxone (Table 1). Persons who had recent IDU (19.5%) were significantly ($\chi^2 = 20.78$, df = *1*, $p < .001$) more likely (19.5%) than non-IDUs (3.5%) to have administered naloxone. Nearly one-quarter (22.0%) of persons who had ever overdosed had administered naloxone ($\chi^2 = 13.30$, df = *1*, $p < .001$); this compares to 9.8% of those who had never overdosed. Administering naloxone was also

associated significantly with witnessing an overdose event during the past year (χ^2 = 106.79, p < .001); 34.5% of overdose bystanders reported administering naloxone in the past year.

We conducted auxiliary analyses exploring associations between correlates of administering naloxone. Given the patterns observed in Table 1, we were especially interested in the degree to which the association between race and naloxone administration might be driven by detoxification drug and/or IDU. Race was not associated significantly with detoxification drug (χ^2 = 1.06, df = 3, p = .788); of note, 18 (90.0%) non-Hispanic Blacks were in detoxification from heroin. Race was associated significantly (χ^2 = 9.63, df = 3, p = .022) with IDU. Rates of IDU were 72.0% for non-Hispanic Whites, 60.0% for non-Hispanic Blacks, 53.7% for Hispanics, and 52.4% for persons with other racial origins.

Locations of naloxone procurement included substance use treatment programs (40.3%), through friends or acquaintances (27.4%), drop-in centers (21.0%), needle exchange centers (4.8%), and through doctors or EMTs (3.2%).

4. Discussion

The rapid expansion of public health programs that provide naloxone and naloxone training to laypersons calls for an enhanced understanding of naloxone use among opioid dependent persons. In the current study, we found that higher opioid-related mortality risk (heroin use, IDU, past overdose) predicted a greater likelihood of reported naloxone administration in the past year. Still, overall, this sample reported low rates of naloxone administration. The majority of respondents who had witnessed an overdose did not administer naloxone, and no respondents identifying as Black or as primarily prescription opioid users reported administering naloxone.

The current findings demonstrate that heroin users, IDUs, and opioid dependent individuals with personal overdose experience appear amenable to administering naloxone. Research is needed to investigate the extent to which these persons are targeted for naloxone distribution and training by prevention trainers, or if these high-risk behaviors themselves, and exposure to risky drug use and overdose, incentivize heroin users to carry and administer naloxone. In contrast, no respondents seeking treatment primarily from prescription opioids had administered naloxone. Prescription opioid users, relative to heroin users, receive less substance use treatment (Moore et al., 2007; Rosenblum et al., 2007; Wu, Woody, Yang, & Blazer, 2011) and, in this sample, were less likely to report prior overdose or witnessing an overdose than heroin users. That only one respondent reported receiving naloxone with a doctor's prescription indicates missed opportunities, particularly for prescription opioid users. Although not yet considered standard practice, co-prescribing naloxone to long-term prescription opioid users in primary care settings predicts fewer opioid-related adverse events (e.g., emergency department visits; Coffin et al., 2016). Therefore, screening, identification, and prescribing naloxone to at-risk prescription opioid users at physicians' offices appears promising. Further, outreach efforts aimed at reducing stigma and raising awareness about naloxone among medical providers and prescription opioid users may be needed. For example, prescription opioid users tend to endorse underestimated perceptions

of overdose risk (Rowe, Santos, Behar, & Coffin, 2016); therefore, highlighting national overdose statistics that challenge misperceptions may be beneficial.

Among respondents witnessing an overdose—bystanders of overdose reported witnessing a mean of 3.5 overdoses in the past year—over two-thirds did not administer naloxone. Research should investigate reasons for non-use, such as lack of preparedness due to the lack of public health intervention; lost or confiscated naloxone (e.g., Lankenau et al., 2012); unwillingness to intervene; or administration by others (bystanders, emergency responders). Given both the fact that a minority of bystander respondents reported administering naloxone, and evidence that laypersons likely to witness an overdose experience escalated overdose risk themselves (Ochoa et al., 2005; Silva, Schrager, Kecojevic, & Lankenau, 2013), continued expansion of naloxone distribution and training is critical.

Although most respondents obtained their naloxone kit at a substance use treatment center or drop-in clinic, both of which are OEND target sites, nearly one in three respondents had obtained naloxone from acquaintances or friends. Future research should examine how naloxone-related behaviors are modeled and communicated in opioid-using social networks as these networks may be promising targets for behavioral modeling, social reinforcement, and normative messaging around naloxone, particularly heroin-using populations. As shown in our auxiliary analysis, no respondents identifying as Black had administered naloxone, perhaps indicating that naloxone is viewed differently in some networks or that distribution has not reached certain racial and ethnic subgroups.

4.1. Limitations

There are several limitations to note. First, we do not know the proportion of respondents who carried or ever carried naloxone, how many times naloxone was used, or whether witnessed overdoses were fatal or non-fatal. Because we don't know who had naloxone and chose not to use it, we can only speculate on reasons for non-use by certain groups. Second, some participants who self-classified as seeking detoxification for prescription opioids also reported recent IDU. While it is not known if IDU was in the form of heroin, cocaine, and/or crushed pills, this overlap indicates imperfect separation between groups. Third, our study population was primarily White, male heroin users from one treatment setting; given our findings regarding race and naloxone use, more research is needed among Black populations. Fourth, future research should assess for potential confounders that were not collected in the current study, such as duration of opioid use disorder, psychiatric or substance use comorbidity, and legal or criminal history. Assessing for fentanyl exposure may be particularly important as fentanyl-adulterated heroin has changed the landscape of overdose risk, both by increasing the risk for overdose and the amount of naloxone needed to reverse it. Finally, the current estimates may not be representative of naloxone administration among opioid dependent persons in other states with different naloxone distribution policies. For example, Massachusetts OEND programming actively distributes naloxone and provides approved training; hence, the rates of use found in this sample may be significantly higher than rates in states without such programming.

4.2. Conclusions

Gaining a better understanding of naloxone administration among people who are opioid dependent is a key component in a harm reduction framework to combat the opioid overdose epidemic. By highlighting demographic and clinical factors associated with naloxone use and non-use among opioid users, the current study may help physicians, policy makers and public health officials better target their investment in distributing naloxone. Moreover, broadening naloxone access and usage through education campaigns, insurance coverage, health provider prescription, and pharmacy sales appears warranted.

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Highlights

1. IDU and prior overdose were associated with past year naloxone administration.
2. Past year naloxone use was associated with having witnessed an overdose.
3. Of those respondents detoxifying from heroin, 16.8% had administered naloxone.
4. No respondents detoxifying from prescription opioids had administered naloxone.
5. No Black/African American respondents had administered naloxone in the past year.

Table 1

Background Characteristics by Administering Naloxone in the Past 12-Months.

	Sample (n = 468)	Administered Naloxone		
		No (n = 400)	Yes (n = 68)	χ^2 or t (p =)
Yrs. Age	32.1 (± 8.65)	32.0 (± 8.69)	33.0 (± 8.51)	-0.85 (.398)
Gender				
Female	135 (28.9%)	115 (85.2%[a])	20 (14.8%[a])	0.01 (.911)
Male	333 (71.2%)	285 (85.6%)	48 (14.4%)	
Years Education	11.8 (± 1.88)	11.8 (± 1.95)	11.9 (± 1.36)	-0.24 (.808)
Race/Ethnicity				
Non-Hispanic White	386 (82.3%)	330 (85.5%)	56 (14.5%)	
Non-Hispanic Black	20 (4.3%)	20 (100.0%)	0 (0.0%)	**9.63 (.022)**
Hispanic	42 (9.0%)	37 (88.1%)	5 (11.9%)	
Other	21 (4.5%)	14 (66.7%)	7 (33.3%)	
Detoxification Drug				
Heroin	406 (86.8%)	338 (83.3%)	68 (16.8%)	**12.15 (<.001)**
Other Opiates	62 (13.3%)	62 (100.0%)	0 (0.0%)	
IDU[a] (Past 30 Days)				
No	145 (31.0%)	140 (96.6%)	5 (3.5%)	**20.78 (<.001)**
Yes	323 (69.0%)	260 (80.5%)	63 (19.5%)	
Ever OD[b]				
No	286 (61.1%)	258 (90.2%)	28 (9.8%)	
Yes	182 (38.9%)	142 (78.0%)	40 (22.0%)	
Present at OD				
No	274 (58.6%)	273 (99.6%)	1 (0.4%)	**106.79 (<.001)**
Yes	194 (41.5%)	127 (65.5%)	67 (34.5%)	

Note: Boldface indicates statistical significance ($p<0.05$). Percentages were calculated within rows of the contingency table and should be compared across rows.

[a] Injection drug use

[b] Overdose