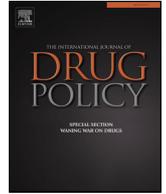




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Research Paper

Attitudes and availability: A comparison of naloxone dispensing across chain and independent pharmacies in rural and urban areas in Alabama

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ABSTRACT

Background: Fatal opioid overdoses remain the leading cause of accidental deaths in the United States, which have contributed to implementation of standing order laws that allow pharmacists to dispense naloxone to patients. Although pharmacy distribution of naloxone is a promising approach to increase access to this intervention, understanding barriers preventing greater uptake of this service is needed.

Methods: Data for the current study were collected via telephone survey assessing the availability of various formulations of naloxone at chain and independent pharmacies in rural and urban areas in Birmingham, Alabama ($N = 222$). Pharmacists' attitudes toward naloxone and potential barriers of pharmacy naloxone distribution were also assessed. One-way analysis of variance (ANOVA) and logistic regression analyses were utilized to examine differences in stocking of naloxone in chain and independent pharmacies and to determine predictors of the number of kits dispensed by pharmacies.

Results: Independent pharmacies were less likely to have naloxone in stock, especially those in rural areas. Furthermore, rural pharmacies required more time to obtain all four formulations of naloxone, and offered less extensive training on naloxone use. Pharmacists endorsing the belief that naloxone allows avoidance of emergent treatment in an overdose situation was associated with fewer dispensed kits by the pharmacies. Over 80% of pharmacists endorsed at least one negative belief about naloxone (e.g., allowing riskier opioid use). Pharmacists noted cost to patients and the pharmacy as contributing to not dispensing more naloxone kits.

Conclusion: The current study demonstrates the lower availability of naloxone stocked at pharmacies in independent versus chain pharmacies, particularly in rural communities. This study also highlights several barriers preventing greater naloxone dispensing including pharmacists' attitudes and costs of naloxone. The potential benefit of standing order laws is not being fully actualized due to the structural and attitudinal barriers identified in this study. Strategies to increase naloxone access through pharmacy dispensing are discussed.

Introduction

Drug overdoses are the leading cause of accidental deaths in the United States, with a majority of those involving opioids, and have played a significant role in the decline of life expectancy for the third consecutive year (Centers for Disease Control & Prevention, 2017; Hedegaard, Miniño & Warner, 2018). While the overprescribing of analgesic medications and subsequent tightening of prescribed opioids caused many to transition to heroin, more recently, synthetic opioids mixed with heroin have become the primary cause of concern in the emerging opioid epidemic (Drug Enforcement Administration, 2015,

2016). These drug cocktails are highly potent and often sold to persons who use drugs who are unaware of their contents (Compton, Jones & T Baldwin, 2016; Drug Enforcement Administration, 2015, 2016). The dramatic increase in overdose deaths has been one important factor in the implementation of naloxone training programs and public policy changes to make naloxone available in most states at local pharmacies (Davis & Carr, 2015).

Naloxone is an opioid antagonist that rapidly counters opioid overdose by temporarily reversing the effects of respiratory depression and loss of consciousness (Pharmacists, 2015). An increasingly popular method for preventing fatal opioid overdose is naloxone training and

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distribution programs targeted at persons who use opioids (Walley et al., 2013). Persons trained by community-based organizations exhibit improved accuracy in recognizing overdose symptoms and responding in overdose scenarios (Green, Heimer & Grau, 2008; Kwon, Moody, Thigpen & Gauld, 2019). Despite the success of community-based programs, their ability to combat the growing opioid crisis is limited. Rural populations in particular have difficulty accessing community-based services such as naloxone, methadone, and buprenorphine, even when they are Medicaid-eligible (Deck & Carlson, 2004; Quest, Merrill, Roll, Saxon & Rosenblatt, 2012). The paucity of resources in rural communities is especially problematic because opioid use and overdose rates are often higher in rural communities (Dunn et al., 2016; Havens et al., 2007; Paulozzi & Xi, 2008; Rigg, Monnat & Chavez, 2018; Wunsch, Nakamoto, Behonick & Massello, 2009).

Pharmacies have been shown to be accessible intervention sites for persons who use opioids (Crawford et al., 2014; Fuller et al., 2007; Jones, Lurie & Compton, 2016). Studies examining syringe access and disposal programs in urban settings have found that persons who inject drugs utilize pharmacy-based services and that pharmacists' attitudes towards persons who inject drugs improved through providing services and training (Crawford et al., 2014; Fuller et al., 2007). Widespread access to naloxone in pharmacies has been facilitated by state level policy changes intended to expand naloxone distribution (Davis & Carr, 2015; Green, Dauria, Bratberg, Davis & Walley, 2015). This has predominately taken the form of standing order laws, which enable pharmacists to provide naloxone to persons who use opioids without a prescription from a healthcare provider. Prescription audit data indicate that such policies have increased naloxone access, with naloxone sales increasing tenfold from 2013 to 2015 (Davis & Carr, 2015).

Although there has been increased utilization of pharmacy-based naloxone distribution, there are several structural barriers preventing greater uptake. While chain pharmacies implement standing order laws across the nation (Davis & Carr, 2017), independent pharmacies are not under any corporate mandate to stock naloxone. Furthermore, the clientele of pharmacies in rural areas face barriers including distance and transportation (Martin, Baker & Piper, 2015; Rose, Lutnick & Kral, 2014). Finally, the cost to obtain naloxone may be prohibitive for uninsured patients. In addition to structural barriers, attitudinal barriers by pharmacists may also prevent patients with opioid use disorder from seeking naloxone (Freeman et al., 2017; Rudolph et al., 2018; Zaller, Yokell, Green, Gaggin & Case, 2013). These may include ethical beliefs that pharmacists have towards naloxone itself or racial biases that influence their willingness to sell and advertise naloxone to certain demographics, a trend that has been noted in prior studies (Compton, Cottler, Decker, Mager & Stringfellow, 1992; Costenbader, Zule & Coomes, 2010).

While these beliefs have been studied qualitatively in urban areas, few studies have employed a quantitative approach to assessing pharmacists' attitudes towards naloxone (Rose et al., 2014; Zaller et al., 2013). Additionally, the number of pharmacies that actually stock naloxone is relatively unknown, as is the quantity and number of formulations in stock. As such, the purpose of the current study is to determine (i) the number of pharmacies around the Birmingham, Alabama area that stock naloxone, (ii) the naloxone formulations that pharmacies have in stock, (iii) pharmacists' attitudes towards naloxone, dispensing of naloxone, and how these attitudes impact dispensing of naloxone, and (iv) whether there are notable differences between chain and independent pharmacies in rural versus urban locations. We hypothesized that (i) chain pharmacies and those localized in urban areas would report having naloxone in stock more frequently than independent and rural pharmacies; (ii) chain and urban pharmacies would provide more comprehensive naloxone use instructions to patients than independent or rural pharmacies; (iii) chain and urban pharmacies would have greater variation of naloxone formulations than independent and rural pharmacies; and (iv) pharmacists at chain stores

or in urban areas would have more positive attitudes about naloxone than those working in independent or rural pharmacies.

Material and methods

Data collection

Data for the present study were collected between May and September 2018 via a telephone survey questionnaire investigating the availability of naloxone in pharmacies, as well as pharmacists' attitudes towards naloxone. Through a comprehensive search of phone numbers and addresses, researchers identified 320 potential pharmacies in two counties located in a state with standing order laws in place (Jefferson County and Walker County, Alabama) that contained both rural and urban areas. Approximately 30% ($n = 98$) of those identified pharmacies were unreachable (e.g., disconnected phone lines [$n = 13$], no answer despite multiple calls during business hours [$n = 17$], personal phone line [$n = 28$], inaccurately listed as a current pharmacy [$n = 40$]). Of the 222 pharmacies successfully contacted, all but one responded to initial questions related to stocking and formulations of naloxone. Pharmacists at 125 (56.3%) locations completed the full survey instrument, rather than solely responding to stocking questions. Pharmacists who declined to complete the entirety of the survey (43.7%; $n = 97$) cited various reasons including time constraints (48.5%; $n = 47$), not being interested in participation (35.1%; $n = 34$), not stocking naloxone (7.2%; $n = 7$), or not being familiar with naloxone (9.2%; $n = 9$).

Measures

The survey questionnaire included 12 items assessing the pharmacy's ability to stock naloxone (e.g., is naloxone currently in stock and if not, how long in hours or days would it take for it to be in stock), available formulations of naloxone, levels of training offered to patients requesting naloxone, and pharmacists' attitudes regarding various aspects of dispensing naloxone kits. All questions regarding pharmacists' attitudes towards naloxone were answered with a "Yes," "No," or "Unsure" response. Inquiries ranged from perceptions regarding the efficacy of naloxone, to whether or not naloxone encourages riskier usage of opioids. Pharmacists were also queried about barriers that potentially contribute to the pharmacy not dispensing more naloxone kits (e.g., lack of staff training, expense issues, patients not needing it, etc.). Finally, pharmacists reported demographic information including age, sex, race, and the number of pharmacists employed at their location. The survey instrument (see Appendix A) was developed based on previous pharmacy surveys (Nielsen & Van Hout, 2016; Stewart, Thomas, & Tutag-Lehr, 2018; Thompson, Rao, Hayes & Purtill, 2018). The entire phone survey took about 10 minutes to complete and pharmacists did not receive an incentive for engaging in the study. Participants in this study all identified as pharmacists. If a pharmacy technician answered the phone, the research assistant requested to speak to the pharmacist or called back at a time when a pharmacist could be available. Research assistants attempted to contact pharmacists up to three times during business hours before agreement or refusal to participate was confirmed.

Procedures

Initially, pharmacists were asked about their pharmacy's current stock of naloxone kits, including generic brands of the injection and nasal spray, as well as the EVZIO® auto injector and Narcan™ nasal spray. The type of training offered to patients who express interest in purchasing naloxone and who request instruction was also queried (e.g., verbal instructions, written instructions, video instructions, no training). For these initial questions, research assistants requested information as if they were a patient. Once initial stocking and training

availability questions were answered, research assistants disclosed the purpose of the call and asked pharmacists whether they would consent to participate in answering additional questions. This approach, including the initial deception and then disclosure of the purpose of the study, was approved by the University of Alabama at Birmingham Institutional Review Board and served the purpose of procuring stocking and training information without potential bias associated with knowledge of participating in a research study.

Data analytic approach

Descriptive statistics were computed using chi-square procedures. Chi-square analyses were utilized to determine whether there were differences in stocking of naloxone, type of training provided to patients, and attitudes among independent and chain pharmacies in urban and rural areas. Prior to conducting analyses related to the hypotheses of the study, data were tested to ensure that all assumptions for the intended analyses were met. Standard recommendations for assumption testing procedures were followed (Tabachnick & Fidell, 2013). Two data points for the number of kits dispensed were classified as outliers and truncated. However, results were not impacted by the transformation and the original data points were therefore retained. Rurality was computed into a dichotomous variable (rural or urban) based on population density. Per Census Bureau guidelines, cities were considered rural if the reported population density was less than 1000 people per square mile (Ratcliffe, Burd, Holder & Fields, 2016). Pharmacies were partitioned into categories based on their being a national chain (e.g., CVS, Walgreens) or an independently owned pharmacy. A dichotomous variable reflecting pharmacists' attitudes was computed such that pharmacists holding at least one negative attitude was coded as "1" and holding no negative attitudes was coded as "0."

A linear regression analysis was conducted to examine the relationship between pharmacists' attitudes about naloxone and the number of kits dispensed. Pharmacists' attitudes were regressed on number of kits dispensed. Demographic variables (age, sex, and median household income) were controlled for in the regression analysis.

Results

Pharmacist and pharmacy characteristics

Pharmacies at which the pharmacist completed the entirety of the survey and those at which the pharmacist only responded to initial stocking questions did not differ statistically in terms of rurality ($X^2 = 1.72, p = 0.190$) or whether they had dispensed kits in the past month ($X^2 = 0.89, p = 0.347$). However, pharmacists at chain pharmacies were more likely to complete the entirety of the survey as compared to those at independent locations ($X^2 = 12.18, p < 0.001$). Pharmacies with naloxone in stock were also more likely to complete the whole survey instrument ($X^2 = 21.13, p < 0.001$). The majority of pharmacists who consented to demographic questions were female (64.7%), Caucasian (87.9%), and were an average age of 40.7 years old. Approximately 41.0% ($n = 91$) of pharmacies were located in rural areas and 59.0% ($n = 131$) were in urban areas. The final sample consisted of pharmacies classified as chains (47.3%; $n = 105$) and independently owned pharmacies (52.7%; $n = 117$). Rural areas were more likely to have independent pharmacies (58.2%) than chain pharmacies (41.8%; [$t(90) = 30.44, p < 0.001$]). Conversely, urban areas were more likely to have chain pharmacies (51.1%) as compared to independent pharmacies (48.9%; [$t(130) = 33.95, p < 0.001$]). For a full summary of pharmacist and pharmacy characteristics, see Table 1.

Naloxone availability by pharmacy type in rural and urban areas

In the month prior to being contacted, 69.7% of pharmacies had not

Table 1
Pharmacist ($n = 116$) and pharmacy ($N = 222$) characteristics*.

Variable (range)	% (N) or Mean (SD)	
Pharmacist age (22–89)**	40.6	(11.7)
Pharmacist gender		
Female	64.7	(75)
Male	35.3	(41)
Pharmacist race		
Caucasian	87.9	(102)
African American	6.0	(7)
Other	6.0	(7)
Number of pharmacists employed (1–9)**	2.6	(1.3)
Pharmacy Location		
Rural	41.0	(91)
Urban	59.0	(131)
Pharmacy Type		
Independent	52.7	(117)
Chain	47.3	(105)
Pharmacy has naloxone in stock		
Yes	104	(52)
No	96	(48)
Number of kits dispensed in the last month (0–10)**	0.66	(1.5)

* Not all pharmacists opted to answer demographic questions.

** Mean and standard deviation are presented.

dispensed any naloxone kits. There were no statistically significant differences in dispensing across rurality or pharmacy type. At the point of contact, there was a significant difference in stocking in terms of rurality and pharmacy type, with 28.6% of chain pharmacies and 11.0% of independent pharmacies in rural areas having naloxone kits in stock ($X^2 = 22.73, p < 0.001$). Similarly, 39.2% of chain pharmacies in urban areas had naloxone in stock, as compared to only 10.8% of independent pharmacies ($X^2 = 39.88, p < 0.001$). There were also significant differences in the amount of time it would take for rural versus urban pharmacies to obtain naloxone with rural pharmacies taking longer to obtain the generic intramuscular injection ($X^2 = 11.42, p = 0.044$), generic nasal spray ($X^2 = 14.03, p = 0.015$), and EVZIO® auto injection ($X^2 = 13.22, p = 0.021$) forms of naloxone. There was no significant difference in the amount of time it would take to stock Narcan™ nasal spray for pharmacies in rural or urban areas ($X^2 = 8.10, p = 0.151$). Rural pharmacies most frequently reported that they were not able to obtain any formulation of naloxone; whereas, urban pharmacies typically reported being able to get any formulation in stock within 24 hours. While rural pharmacies most commonly indicated never being able to stock naloxone, others did endorse the ability to obtain it within 72, or even 24 hours (See Table 2).

There was a significant difference between rural and urban pharmacies in terms of the type of training they offered to patients when dispensing naloxone kits ($X^2 = 17.09, p = 0.002$). Rural pharmacies typically communicated solely verbal instructions (20.4%), while urban pharmacies most often provided both verbal and written instructions (19.9%).

3. Naloxone formulation availability

During the month prior to being contacted, pharmacies in rural areas had dispensed a total of 52 naloxone kits ($M = 0.87$) while pharmacies in urban areas had dispensed 70 ($M = 0.51$). There was no statistically significant difference in the number of kits dispensed between rural and urban areas. In rural areas, an equal percentage of independent and chain pharmacies had dispensed at least one kit in the past month (Independent: 19.2%, $n = 10$; Chain: 19.2%, $n = 10$). However, in urban areas, 20.0% ($n = 14$) of chain pharmacies had dispensed at least one kit in the last month as compared to only 4.3% ($n = 3$) of independent pharmacies. Both rural and urban pharmacies were most likely to have Narcan™ nasal spray in stock. However, the number of formulations of naloxone offered significantly differed

Table 2
Naloxone formulations stocked in independent and chain pharmacies in rural and urban areas.

Variable	Rural Independent% (n = 53)	Rural Chain% (n = 38)	Urban Independent% (n = 64)	Urban Chain% (n = 67)
Generic Intramuscular Injection				
In stock	7.7	15.8	9.4	7.6
Can be in stock in <24 h	15.4	15.8	17.2	40.9
Can be in stock in 24–72 h	28.8	7.9	14.1	28.8
Can be in stock in >72 h	5.8	5.2	0.0	3.0
Never available to be stocked	42.3	55.3	59.4	19.7
Generic Naloxone Nasal Spray				
In stock	2.0	10.5	3.1	24.2
Can be in stock in <24 h	17.6	21.1	20.3	31.8
Can be in stock in 24–72 h	25.5	5.3	17.2	22.7
Can be in stock in >72 h	5.9	5.2	0.0	0.0
Never available to be stocked	49.0	57.9	59.4	21.2
Narcan™ Nasal Spray				
In stock	3.8	60.5	12.5	72.7
Can be in stock in <24 h	15.4	13.2	18.8	10.6
Can be in stock in 24–72 h	30.8	5.3	14.1	10.6
Can be in stock in >72 h	5.8	7.8	0.0	4.5
Never available to be stocked	44.2	13.2	54.7	1.5
EVZIO® Auto Injector				
In stock	0.0	7.9	3.1	6.1
Can be in stock in <24 h	15.4	18.4	17.2	40.9
Can be in stock in 24–72 h	23.1	13.2	17.2	31.8
Can be in stock in >72 h	7.7	5.2	0.0	1.5
Never available to be stocked	53.8	55.3	62.5	19.7

between chain and independent pharmacies in rural ($X^2 = 12.23$, $p < 0.001$) and urban areas ($X^2 = 8.21$, $p = 0.004$). In rural areas, 8.8% of chain pharmacies offered more than one formulation of naloxone. Unfortunately, none of the independent pharmacies in rural areas carried more than one formulation. In urban areas, 13.7% of chain pharmacies and 3.8% of independent pharmacies had more than one formulation in stock. See Table 4.

Pharmacist attitudes and barriers to distribution

Pharmacists' attitudes regarding naloxone and barriers to dispensing naloxone kits are presented in Table 3. A large percentage (49.1%) of pharmacists endorsed the belief that naloxone allows persons who use opioids to continue using at riskier levels than they would without the availability of naloxone. There was a statistically significant difference in endorsement of this attitude across chain and independent pharmacies in rural areas ($X^2 = 6.56$, $p = 0.010$). Only 14.0% of pharmacists at chain locations endorsed this attitude, while 34.0% of pharmacists at rural independent pharmacies felt that obtaining naloxone is related to increased risky opioid use. Additionally, 42.1% of pharmacists felt that naloxone allows persons who use opioids to avoid seeking substance use treatment, while 45.7% endorsed the belief that naloxone allows avoidance of emergency treatment following an overdose. These attitudes did not differ based on pharmacy type or rurality.

Chi-square analyses were conducted to examine the relationship between pharmacists' attitudes, type and location of pharmacy, and dispensing of naloxone kits. Endorsement of the attitude that naloxone allows persons who use opioids to avoid seeking emergency treatment in an overdose situation was related to not dispensing kits in the past month for chain pharmacies in both rural ($X^2 = 6.30$, $p = 0.012$) and urban areas ($X^2 = 4.99$, $p = 0.026$). For chain pharmacies in urban areas, holding the belief that the availability of naloxone allows for riskier opioid use was associated with not dispensing kits ($X^2 = 4.08$, $p = 0.043$). In terms of barriers to dispensing a greater quantity of kits, the perception of low demand for naloxone was associated with no kits being dispensed in independent pharmacies in rural ($X^2 = 11.23$, $p = 0.004$) and urban areas ($X^2 = 6.86$, $p = 0.032$) and chain pharmacies in rural areas ($X^2 = 7.23$, $p = 0.027$). See Table 4 for results of chi-square analyses that highlight differences among chain and

independent pharmacies in rural and urban areas.

A linear regression was conducted to examine the relationship between pharmacists' attitudes about naloxone and the number of naloxone kits dispensed by pharmacies. Pharmacists' attitudes were regressed on number of kits dispensed. Median household income, and pharmacist age and sex were controlled for in the analysis. Endorsement of the attitude that naloxone allows persons who use opioids to avoid seeking emergent treatment following an overdose was a statistically significant predictor of number of kits dispensed ($t = -2.12$, $p = .037$), indicating that pharmacists maintaining this attitude contributes to fewer kits being disseminated.

On a whole, 81.4% of pharmacists endorsed at least one negative belief about naloxone. There was no statistically significant difference in negative attitudes based on demographic variables or rurality. However, in rural areas pharmacists at independent pharmacies (53.2%) were more likely to hold at least one negative attitude ($X^2 = 5.65$, $p = 0.017$) compared to chain pharmacists (27.7%). Despite varying opinions, the majority of pharmacists agreed that naloxone is effective (95.2%) and provides a useful service to the community (97.5%).

In terms of barriers to dispensing naloxone, most pharmacists (56.5%) agreed that patients not being able to afford it contributed to their not dispensing more naloxone kits. Almost half of pharmacists (42.4%) stated that low demand by patients contributed to their not dispensing more naloxone kits. There were no statistically significant differences in these attitudes based on rurality or pharmacy type. Approximately half of pharmacists (46.4%) acknowledged that expense, reimbursement issues, or costs of stocking contributed to them not dispensing more naloxone kits. There was a statistically significant difference in endorsement of this belief based on rurality and pharmacy type ($X^2 = 15.48$, $p = 0.017$), with independent pharmacies in rural areas more frequently indicating this as a barrier.

Discussion

Though pharmacy-based naloxone distribution appears to be a promising approach to increasing access to this life-saving intervention, results of the current study attest to the outstanding barriers preventing greater utilization of this service, especially in rural areas (Crawford et al., 2014; Fuller et al., 2007). Despite standing order

Table 3
Pharmacist attitudes and barriers to dispensing naloxone among chain and independent pharmacies in rural and urban areas.

Question	Rural Indep. (n = 53)%	Rural Chain (n = 38)%	Urban Indep. (n = 64)%	Urban Chain (n = 66)%	X ²	p
Do you think dispensing naloxone provides a useful service to the community?	22.8	20.3	17.3	37.4	5.68	.128
Do you think the use of naloxone allows opioid users to avoid seeking emergent treatment following an overdose?	12.4	5.7	10.5	17.1	3.76	.289
Do you think the use of naloxone allows opioid users to avoid seeking substance abuse treatment following an overdose?	14.0	6.5	9.3	12.1	5.36	.147
Do you think the use of naloxone allows opioid users to continue using at riskier levels than they would without the availability of naloxone?	15.7	6.5	10.2	16.7	7.30	.063
Did expense, reimbursement issues, or costs of stocking contribute to this pharmacy not dispensing more naloxone kits?	16.0	8.0	11.2	11.2	15.48	.017*
Did patients not wanting it contribute to this pharmacy not dispensing more naloxone kits?	8.8	7.2	8.8	17.6	8.62	.196
Did patients not being able to afford it contribute to this pharmacy not dispensing more naloxone kits?	14.5	11.3	10.5	20.2	3.05	.802

Note. Percentages displayed indicate endorsement of listed attitude; *p-value < 0.05.

policies, approximately 70% of pharmacies in the current sample had not dispensed any kits in the past month. Furthermore, approximately only 11% of independent pharmacies in rural and urban areas reported having naloxone in stock. While standing order laws have boosted naloxone purchases, this effect appears to be concentrated to chain pharmacies (Gertner, Domino & Davis, 2018; Xu, Davis, Cruz & Lurie, 2018). The full potential benefits of this legislation are not being actualized, namely due to insufficient availability at independently owned pharmacies (Davis & Carr, 2015).

Pharmacists in rural areas most frequently indicated an inability to stock naloxone. Though the remaining rural pharmacies were able to obtain naloxone within 72 hours, the lack of immediate availability serves as a barrier for individuals in rural areas due to potential distance and transportation issues. In addition to being less likely to have naloxone in stock, rural pharmacies, specifically those that are independently owned, also tended to carry fewer formulations of naloxone. Previous research has found that having various naloxone formulations in stock may contribute to an increased dissemination of kits, potentially because it allows patients the opportunity to select a type of naloxone they feel most comfortable administering (Carpenter et al., 2018).

In addition to availability differences, the training offered to patients also differed based on rurality. Training in rural areas often consisted of exclusively verbal instructions, while pharmacies in urban areas had a slightly more comprehensive instructional approach utilizing both verbal and written instructions. Moreover, training in chain pharmacies often consisted of verbal or verbal and written instructions, while independent pharmacies provided no training or verbal instructions only. Providing satisfactory training to patients is imperative, as it may enhance confidence in their ability to administer naloxone in an overdose situation and thus render them more likely to utilize a kit.

Pharmacists also considered reimbursement and time constraints, as well as the financial limitations of patients, as preventing wider distribution of naloxone. Inadequate reimbursement and time constraints have been previously noted by pharmacists as barriers to providing thorough training to patients (Bakhireva et al., 2017; Zaller et al., 2013). These findings suggest that the financial expense incurred by pharmacists for stocking and training costs, as well as by patients when purchasing kits, are important targets for reducing access barriers to naloxone.

Similar to previous research, pharmacist attitudes pertaining to concerns about naloxone remain prevalent (Rose et al., 2014; Zaller et al., 2013), with over 80% of the pharmacists in this study endorsing at least one negative belief. A considerable percentage of the pharmacists in this study believed that naloxone encourages opioid use at riskier levels and allows persons who use opioids to avoid seeking emergent and substance use treatment. Pharmacists endorsing the belief that naloxone allows persons who use opioids to avoid seeking emergent treatment in an overdose situation was a contributing factor to pharmacies dispensing fewer naloxone kits. This indicates that pharmacists holding negative attitudes toward naloxone may be one of the many factors influencing underwhelming naloxone dissemination. Of note, pharmacists at rural independent pharmacies were more likely to hold this belief than their urban counterparts. Overall, these attitudes stand in contrast with the existing literature, which suggests that possession of naloxone does not encourage risky opioid use and that naloxone distribution may actually serve as a motivating factor to seeking treatment (Jones, Campbell, Metz & Comer, 2017; McClellan et al., 2018; Wagner et al., 2010). The differing attitudes toward naloxone underscores the need for increased naloxone-focused education to pharmacists.

The current study benefited from comprehensively sampling every identifiable and accessible pharmacy in two counties and asking questions about availability and formulations of naloxone prior to notifying the pharmacist that this was a research study. Pharmacies were evenly distributed across rural and urban regions as well as across chain and

Table 4
Differences among chain and independent pharmacies in rural and urban areas.

Variable	Rural Independent% (n = 53)	Rural Chain% (n = 38)	Urban Independent% (n = 64)	Urban Chain% (n = 66)	X ²	p
Pharmacy has naloxone in stock					64.43**	<0.001
Yes	18.9	68.4	21.9	77.3		
No	81.1	31.6	78.1	22.7		
Naloxone formulations stocked					69.40**	<0.001
0	86.8	31.6	79.7	26.9		
1	13.2	47.2	12.5	46.3		
>1	0.0	21.1	7.8	26.9		
Do you think the use of naloxone allows opioid users to continue using at riskier levels than they would without the availability of naloxone?					8.06*	.045
Yes	65.4	28.0	57.9	44.7		
No	34.6	72.0	42.1	55.3		

* p-value < 0.05.

** p-value < 0.001.

independent types. Additionally, pharmacist demographics did not differ based on rurality. To our knowledge, this is one of the first attempts to quantitatively gauge pharmacist attitudes regarding naloxone distribution and the duration it would take to have various formulations in stock. Additionally, the inclusion of survey questions assessing barriers to naloxone distribution from the pharmacist perspective provides a unique insight into the factors restricting greater access and dissemination. Moreover, the comparison of these variables and attitudes between independent and chain pharmacies sheds light on the differences between pharmacy types. Although the nature of this study provided a snapshot view of naloxone access, it does not objectively account for the amount of naloxone that pharmacies in the county are distributing over extended periods. Also, it is important to recognize that, in some instances, pharmacists have only limited interactions with patients. It is often pharmacy technicians who interact with patients for everyday purchases and the dispensing of medication. As such, it may be equally important to gauge the attitudes and beliefs of technicians since they are the primary point of contact for many customers. Furthermore, while this study made use of the Census Bureau's definition of rurality to dichotomize included cities and townships as rural or urban, it should be noted that this is one of numerous categorization methods. The methods used herein are primarily to delineate the Birmingham metropolitan area and surrounding high-density suburban areas from low-density suburban areas and rural outskirts. This is not, however, a complete capture of the gradations in rurality present in the area nor are the rural environments near a large city such as Birmingham akin to the remote rural areas in other parts of the state. It should also be noted that a sample of convenience was utilized and an a priori power analysis was not conducted, thereby limiting assurance that the sample size yielded adequate power to detect the statistical differences explored.

Future studies should attempt to acquire an objective inventory report detailing the number of naloxone kits dispensed by pharmacies over an extended period of time in addition to querying pharmacists over the phone. For the current study, participation was restricted solely to pharmacists in order to maintain a similar level of expertise and remain consistent with previous research. However, including pharmacy technicians in future studies may provide valuable information, as they likely have more interactions with patients as compared to pharmacists. Future studies should also focus on developing education courses for pharmacists in order to determine whether changing misperceptions would lead to an increase in naloxone distribution and therefore proper treatment for patients. Finally, future studies should focus on creating awareness programs to aide in education of the need to stock naloxone, specifically in low dispensing rural-independent pharmacies as well as creating an awareness to the public that naloxone is readily available in these locations.

Conclusion

Substantial barriers to dispensing naloxone persist, despite recent legislation aimed at increasing this life-saving intervention. Though standing order laws are intended to facilitate the access of naloxone, the potential benefit of this legislation is partially negated by the underwhelming level of stocking in pharmacies, especially in independent pharmacies. Furthermore, the current study found no differences in dispensing of naloxone based on rurality. Yet, rural pharmacies were less likely to have naloxone in stock, had fewer formulations in stock, required more time to obtain naloxone, and offered less comprehensive training than urban pharmacies. Inaccurate attitudes criticizing naloxone still exist among pharmacists even though research consistently finds these criticisms to be unfounded. Overall, the current study emphasizes the progress that still needs to occur in terms of successfully implementing interventions to lessen the current opioid crisis.

CRediT authorship contribution statement

Michelle L. Sisson: Formal analysis, Writing - original draft, Writing - review & editing. **Kristina B. McMahan:** Data curation, Writing - original draft, Writing - review & editing. **Keith R. Chichester:** Formal analysis, Writing - original draft, Writing - review & editing. **James W. Galbraith:** Conceptualization, Writing - review & editing. **Karen L. Cropsey:** Conceptualization, Data curation, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

All authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.drugpo.2019.09.021](https://doi.org/10.1016/j.drugpo.2019.09.021).

References

- Bakhireva, L. N., Bautista, A., Cano, S., Shrestha, S., Bachyrycz, A. M., & Cruz, T. H. (2017). Barriers and facilitators to dispensing of intranasal naloxone by pharmacists. *Substance Abuse*, 1–11. <https://doi.org/10.1080/08897077.2017.1391924>.
- Carpenter, D. M., Dhamanaskar, A. K., Gallegos, K. L., Shepherd, G., Mosley, S. L., &

- Roberts, C. A. (2018). Factors associated with how often community pharmacists offer and dispense naloxone. *Research in Social and Administrative Pharmacy*. <https://doi.org/10.1016/j.sapharm.2018.07.008>.
- Centers for Disease Control and Prevention. (2017). *Understanding the epidemic*. Centers for Disease Control and Prevention.
- Compton, W. M., Cottler, L. B., Decker, S. H., Mager, D., & Stringfellow, R. (1992). Legal needle buying in St. Louis. *American Journal of Public Health*, 82(4), 595–596. <https://doi.org/10.2105/AJPH.82.4.595>.
- Compton, W., Jones, C., & T Baldwin, G. (2016). *Relationship between nonmedical prescription-opioid use and heroin use*, 374, *New England Journal of Medicine* 154–163.
- Costenbader, E. C., Zule, W. A., & Coomes, C. C. (2010). Racial differences in acquisition of syringes from pharmacies under conditions of legal but restricted sales. *International Journal of Drug Policy*, 21(5), 425–428. <https://doi.org/10.1016/j.drugpo.2009.12.006>.
- Crawford, N. D., Amesty, S., Rivera, A. V., Harripersaud, K., Turner, A., & Fuller, C. M. (2014). Community impact of pharmacy-randomized intervention to improve access to syringes and services for injection drug users. *Health Education & Behavior*, 41(4), 397–405. <https://doi.org/10.1177/1090198114529131>.
- Davis, C. S., & Carr, D. (2015). Legal changes to increase access to naloxone for opioid overdose reversal in the United States. *Drug and Alcohol Dependence*, 157, 112–120. <https://doi.org/10.1016/j.drugalcdep.2015.10.013>.
- Davis, C., & Carr, D. (2017). State legal innovations to encourage naloxone dispensing. *Journal of the American Pharmacists Association*, 57(2), S180–S184. <https://doi.org/10.1016/j.japh.2016.11.007>.
- Deck, D., & Carlson, M. J. (2004). Access to publicly funded methadone maintenance treatment in two western states. *The Journal of Behavioral Health Services & Research*, 31(2), 164–177. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/15255224>.
- Drug Enforcement Administration. (2015). DEA issues nationwide alert on fentanyl as threat to health and public safety. Retrieved from <https://www.dea.gov/press-releases/2015/03/18/dea-issues-nationwide-alert-fentanyl-threat-health-and-public-safety>.
- Drug Enforcement Administration. (2016). *Counterfeit prescription pills containing fentanyls: A global threat*. (DEA-DCT-DIB-021-16). Retrieved from https://content.govdelivery.com/attachments/USDOJDEA/2016/07/22/file_attachments/590360/fentanyl%2Bpills%2Breport.pdf.
- Dunn, K. E., Barrett, F. S., Yepez-Laubach, C., Meyer, A. C., Hruska, B. J., Petrush, K., & Bigelow, G. E. (2016). Opioid overdose experience, risk behaviors, and knowledge in drug users from a rural versus an urban setting. *Journal of Substance Abuse Treatment*, 71, 1–7. <https://doi.org/10.1016/j.jsat.2016.08.006>.
- Freeman, P. R., Goodin, A., Troske, S., Strahl, A., Fallin, A., & Green, T. C. (2017). Pharmacists' role in opioid overdose: Kentucky pharmacists' willingness to participate in naloxone dispensing. *Journal of the American Pharmacists Association*, 57(2, Supplement), S28–S33. <https://doi.org/10.1016/j.japh.2016.12.064>.
- Fuller, C. M., Galea, S., Caceres, W., Blaney, S., Sisco, S., & Vlahov, D. (2007). Multilevel community-based intervention to increase access to sterile syringes among injection drug users through pharmacy sales in new york city. *American Journal of Public Health*, 97(1), 117–124. <https://doi.org/10.2105/AJPH.2005.069591>.
- Gertner, A. K., Domino, M. E., & Davis, C. S. (2018). Do naloxone access laws increase outpatient naloxone prescriptions? Evidence from medicaid. *Drug and Alcohol Dependence*, 190, 37–41. <https://doi.org/10.1016/j.drugalcdep.2018.05.014>.
- Green, T. C., Dauria, E. F., Bratberg, J., Davis, C. S., & Walley, A. Y. (2015). Orienting patients to greater opioid safety: Models of community pharmacy-based naloxone. *Harm Reduction Journal*, 12, 25. <https://doi.org/10.1186/s12954-015-0058-x>.
- Green, T. C., Heimer, R., & Grau, L. E. (2008). Distinguishing signs of opioid overdose and indication for naloxone: An evaluation of six overdose training and naloxone distribution programs in the united states. *Addiction (Abingdon, England)*, 103(6), 979–989. <https://doi.org/10.1111/j.1360-0443.2008.02182.x>.
- Havens, J. R., Oser, C. B., Leukefeld, C. G., Webster, J. M., Martin, S. S., O'Connell, D. J., et al. (2007). Differences in prevalence of prescription opiate misuse among rural and urban probationers. *The American Journal of Drug and Alcohol Abuse*, 33(2), 309–317. <https://doi.org/10.1080/00952990601175078>.
- Hedegaard, H., Miniño, A. M., & Warner, M. (2018). *Drug overdose deaths in the United States, 1999–2017*. NCHS Data Brief: Centers for Disease Control and Prevention.
- Jones, C. M., Lurie, P. G., & Compton, W. M. (2016). Increase in naloxone prescriptions dispensed in us retail pharmacies since 2013. *American Journal of Public Health*, 106(4), 689–690. <https://doi.org/10.2105/AJPH.2016.303062>.
- Jones, J. D., Campbell, A., Metz, V. E., & Comer, S. D. (2017). No evidence of compensatory drug use risk behavior among heroin users after receiving take-home naloxone. *Addictive Behaviors*, 71, 104–106. <https://doi.org/10.1016/j.addbeh.2017.03.008>.
- Kwon, M., Moody, A. E., Thigpen, J., & Gauld, A. (2019). Implementation and evaluation of an opioid overdose and naloxone distribution training in a pharmacist laboratory. *American Journal of Pharmaceutical Education*, ajpe7179. <https://doi.org/10.5688/ajpe7179>.
- Martin, S. L., Baker, R. P., & Piper, B. J. (2015). Evaluation of urban-rural differences in pharmacy practice needs in Maine with the Mappna. *Pharmacy Practice*, 13(4), 669. <https://doi.org/10.18549/PharmPract.2015.04.669-669>.
- McClellan, C., Lambdin, B. H., Ali, M. M., Mutter, R., Davis, C. S., Wheeler, E., et al. (2018). Opioid-overdose laws association with opioid use and overdose mortality. *Addictive Behaviors*, 86, 90–95. <https://doi.org/10.1016/j.addbeh.2018.03.014>.
- Nielsen, S., & Van Hout, M. C. (2016). What is known about community pharmacy supply of naloxone? a scoping review. *International Journal of Drug Policy*, 32, 24–33. <https://doi.org/10.1016/j.drugpo.2016.02.006>.
- Paulozzi, L. J., & Xi, Y. (2008). Recent changes in drug poisoning mortality in the united states by urban-rural status and by drug type. *Pharmacoepidemiology and Drug Safety*, 17(10), 997–1005. <https://doi.org/10.1002/pds.1626>.
- Pharmacists, The American Society of Health-System. (2015). Naloxone hydrochloride. Package leaflet: Information for the patient.
- Quest, T. L., Merrill, J. O., Roll, J., Saxon, A. J., & Rosenblatt, R. A. (2012). Buprenorphine therapy for opioid addiction in rural Washington: The experience of the early adopters. *Journal of Opioid Management*, 8(1), 29–38. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/22479882>.
- Ratcliffe, M., Burd, C., Holder, K., & Fields, A. (2016). *Defining rural at the U.S. census bureau*. United States Census Bureau Census.gov.
- Rigg, K. K., Monnat, S. M., & Chavez, M. N. (2018). Opioid-related mortality in rural America: Geographic heterogeneity and intervention strategies. *International Journal of Drug Policy*, 57, 119–129. <https://doi.org/10.1016/j.drugpo.2018.04.011>.
- Rose, V. J., Lutnick, A., & Kral, A. H. (2014). Feasibility of providing interventions for injection drug users in pharmacy settings: A case study among San Francisco pharmacists. *Journal of Psychoactive Drugs*, 46(3), 226–232. <https://doi.org/10.1080/02791072.2014.921745>.
- Rudolph, S. E., Branham, A. R., Rhodes, L. A., Hayes, H. H., Moose, J. S., & Marciniak, M. W. (2018). Identifying barriers to dispensing naloxone: A survey of community pharmacists in north carolina. *Journal of the American Pharmacists Association*, 58(4, Supplement), S55–S58. <https://doi.org/10.1016/j.japh.2018.04.025> e53.
- Stewart, B., L. Thomas, R., & Tutag Lehr, V. (2018). *Pharmacists' knowledge, support, and perceived roles associated with providing naloxone in the community*, 10, *Currents in Pharmacy Teaching and Learning* 1013–1021.
- Tabachnick, B., & Fidell, L. (2013). *Using multivariate statistics* ((6th ed.)). Pearson.
- Thompson, E. L., Rao, P. S. S., Hayes, C., & Purtil, C. (2018). Dispensing naloxone without a prescription: Survey evaluation of Ohio pharmacists. *Journal of Pharmacy Practice* 897190018759225. <https://doi.org/10.1177/0897190018759225>.
- Wagner, K. D., Valente, T. W., Casanova, M., Partovi, S. M., Mendenhall, B. M., & Hundley, J. H. (2010). Evaluation of an overdose prevention and response training programme for injection drug users in the skid row area of Los Angeles, CA. *International Journal of Drug Policy*, 21(3), 186–193. <https://doi.org/10.1016/j.drugpo.2009.01.003>.
- Walley, A. Y., Xuan, Z., Hackman, H. H., Quinn, E., Doe-Simkins, M., Sorensen-Alawad, A., et al. (2013). Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: Interrupted time series analysis. *BMJ (Clinical Research ed.)*, 346, f174. <https://doi.org/10.1136/bmj.f174>.
- Wunsch, M. J., Nakamoto, K., Behonick, G., & Massello, W. (2009). Opioid deaths in rural Virginia: A description of the high prevalence of accidental fatalities involving prescribed medications. *The American Journal on Addictions / American Academy of Psychiatrists in Alcoholism and Addictions*, 18(1), 5–14. <https://doi.org/10.1080/10550490802544938>.
- Xu, J., Davis, C. S., Cruz, M., & Lurie, P. (2018). State naloxone access laws are associated with an increase in the number of naloxone prescriptions dispensed in retail pharmacies. *Drug and Alcohol Dependence*, 189, 37–41. <https://doi.org/10.1016/j.drugalcdep.2018.04.020>.
- Zaller, N. D., Yokell, M. A., Green, T. C., Gaggin, J., & Case, P. (2013). The feasibility of pharmacy-based naloxone distribution interventions: A qualitative study with injection drug users and pharmacy staff in Rhode Island. *Substance Use & Misuse*, 48(8), 590–599. <https://doi.org/10.3109/10826084.2013.793355>.