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Evaluating disparities in prescribing of naloxone after emergency department treatment of opioid overdose

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ABSTRACT

Introduction: Patients who initially survive opioid-related overdose are at high risk for subsequent mortality. Our health system aimed to evaluate the presence of disparities in prescribing naloxone following opioid overdose.
Methods: This was a retrospective cohort study of patients seen in our health system, which comprises two academic centers and eight community hospitals. Eligible patients had at least one visit to any of our hospital's emergency departments (EDs) with a diagnosis code indicating opioid-related overdose between May 1, 2018, and April 30, 2021. The primary outcome measure was prescription of nasal naloxone after at least one visit for opioid-related overdose during the study period.
Results: The health system had 1348 unique patients who presented 1593 times to at least one of the EDs with opioid overdose. Of included patients, 580 (43.2%) received one or more prescriptions for naloxone. The majority (68.9%, n = 925) were male. For race/ethnicity, 74.5% (1000) were Non-Hispanic White, 8.0% (n = 108) were Non-Hispanic Black, and 13.0% (n = 175) were Hispanic/Latinx. Compared with the reference age group of 16–24 years, only those 65+ were less likely to receive naloxone (adjusted odds ratio [aOR] 0.41, 95% confidence interval [CI] 0.20–0.84). The study found no difference for gender (male aOR 1.23, 95% CI 0.97–1.57 compared to female). Hispanic/Latinx patients were more likely to receive a prescription when compared to Non-Hispanic White patients (aOR 1.72, 95% CI 1.22–2.44), while no difference occurred between Non-Hispanic Black compared to Non-Hispanic White patients (aOR 1.31, 95% CI 0.87–1.98).
Conclusions: Naloxone prescribing after overdose in our system was suboptimal, with fewer than half of patients with an overdose diagnosis code receiving this lifesaving and evidence-based intervention. Patients who were Hispanic/Latinx were more likely to receive naloxone than other race and ethnicity groups, and patients who were older were less likely to receive it. Health systems need ongoing equity-informed implementation of programs to expand access to naloxone to all patients at risk.

1. Introduction

Patients who are discharged after an opioid-related overdose are at high risk for mortality. Recent studies show that one-year mortality of patients discharged from the emergency department (ED) after overdose ranged from 5.3% to 5.5%, meaning that roughly 1 of every 20 patients was dead within a year (Leece et al., 2020; Weiner et al., 2020). It is particularly concerning given that most deaths occurred in those under

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age 55 (Wilson et al., 2020). The COVID-19 pandemic has exacerbated the problem (Centers for Disease Control and Prevention, 2020), and the United States recently experienced its highest ever annual all-cause overdose-related deaths, with >100,000 lives lost in the 12-month period ending in April 2021 (National Center for Health Statistics, 2022).

Just as COVID-19 has disproportionately affected minoritized groups (Dixon et al., 2021), so too has the opioid overdose epidemic. In Philadelphia, numbers of overdoses among Black people during the pandemic exceeded those of White individuals for the first time in recent history (Khatri et al., 2021). Disparities have also been reported in Alabama (Patel et al., 2021) and Kentucky (Ochalek et al., 2020), and a nationwide study reported that overdose-associated cardiac arrests rose about 40% nationally in 2020, with larger relative increases seen among Black and Latinx patients (Friedman et al., 2021). In the state where we primarily practice (Massachusetts), opioid-related overdose deaths increased by 5% in 2020 compared with 2019, but the increase specifically among Black men was 69% (Commonwealth of Massachusetts, 2021). Between 2019 and 2020, the number of overdose-related deaths decreased for White individuals but increased for Black individuals in Massachusetts (DiGennaro et al., 2021).

As society works to identify primary prevention and secondary prevention of overdoses, such as implementation of prevention programs and prescribed drug diversion monitoring, an urgent need exists for tertiary prevention (rescuing the patient at the time of an overdose) (Mathis et al., 2018). The primary means of saving lives after an opioid overdose is naloxone (Mathis et al., 2018). Community-wide distribution of naloxone is an evidence-based intervention to reduce overdose deaths (Walley et al., 2013; Clark et al., 2014; Wheeler et al., 2015). Providing a naloxone rescue kit after an opioid overdose is also effective (McDonald & Strang, 2016; Moustaqim-Barrette et al., 2021; Strang et al., 2019). Guidance has been published by the American College of Emergency Physicians to encourage take-home naloxone programs, eliminating any barriers to receiving the kits (Samuels et al., 2015). At several hospitals in our health system, in addition to the ability for providers to write a prescription for naloxone, protocols are in place to dispense naloxone directly to at-risk patients.

Given the recent racial and ethnic disparities in opioid-related overdose and death reported in the literature, our health system aimed to evaluate the presence of disparities in prescribing naloxone following an opioid overdose visit to any of our hospitals' EDs. In this analysis, we evaluated differences in age, gender, race/ethnicity, and primary language of the patient. If disparities exist, they may represent an opportunity for process improvement and clinician education.

2. Methods

This was a retrospective cohort study of patients seen in two large academic centers and seven community hospitals in Massachusetts and one community hospital in New Hampshire. The combined annual number of ED visits is approximately 400,000. In November 2020, our system implemented a deliberate program to address disparities in health care titled "United Against Racism," and this project was part of our substance use steering committee's efforts at identifying differences in substance use disorder–related care. The Mass General Brigham Human Research Committee approved the protocol.

Patients eligible for inclusion in the study were those who had at least one visit to any of our hospitals' EDs with a diagnosis code indicating opioid-related overdose (Appendix 1) between May 1, 2018 and April 30, 2021. The primary outcome measure was prescription (including written prescription or dispensation) of nasal naloxone during at least one visit for opioid-related overdose. The prescription could have occurred at ED discharge or after discharge from hospitalization if the patient was admitted but the study included it only if the treatment episode began with an ED visit for overdose. The study team then analyzed prescription rates for differences by comparing: 1) age at incidence of first overdose during the study period binned into categories (for patient confidentiality); 2) gender (as indicated by the patient); 3) a combined variable of race and ethnicity; and 4) primary language. Demographic data are self-reported and input by registration staff the first time that the patient visits our health care system. For individuals who present unconscious, the study used information from ambulance personnel or patient identification cards and confirmed it with the patient whenever possible. To avoid potential multicollinearity between race and ethnicity, the study combined those variables into the categories "Hispanic," "Non-Hispanic White," "Non-Hispanic Black," "Non-Hispanic Other," and "Unknown" (Agency for Healthcare Research and Quality, 2018). These data are contained in our electronic health record and are input when a patient is first registered in our hospital system.

We first present data using descriptive statistics with unadjusted chi-square analysis comparing categorical variables against the primary outcome. We then conducted a multivariable logistic regression model to determine association of demographics with the naloxone prescription outcome. A Hosmer-Lemeshow test ($p > 0.05$) revealed adequate model fit and generalized variance inflation factors (GVIF) computed with the R package "car" (Fox and Weisberg, 2019) indicated low concern for multicollinearity (GVIF values were <2.0). The study used R version 4.0.3 for all analyses.

3. Results

During the study period, 1348 unique patients presented 1593 times to one of our EDs with opioid overdose. Evaluating unique visits, the individual hospital rate of prescribing ranged from 13.3% to 65.6%. The two academic medical centers were more likely to prescribe compared to the eight community hospitals (42.8% vs 37.9%, $p = 0.037$). The most common dispositions were: discharge from the ED (73.0%, $n = 1161$), admission to hospital (13.9%, $n = 222$), and eloped/left against medical advice (9.7%, $n = 155$). The rate of naloxone prescribing after each of these dispositions was: 45.6% ($n = 529$) for discharged patients, 21.6% ($n = 48$) for admitted patients, and 30.3% ($n = 47$) for patients who eloped/left without being seen.

As the primary outcome of the study was to ascertain prescription of at least one naloxone kit and several patients presented more than once for overdose, we present the remainder of the analyses at the patient level. The study excluded six patients from further analysis because of missing values in the age variable. The study had no missing gender values. Of included patients, 580 (43.2%) received at least one prescription for naloxone after any ED visit. Table 1 displays demographic characteristics and naloxone prescription rates.

Table 2 and Fig. 1 demonstrate the adjusted odds ratio (aOR) estimates. When compared to the 16–24 year age group, those older than age 65 were less likely to receive naloxone (aOR 0.41, 95% confidence interval [CI] 0.20–0.84). When compared to the non-Hispanic White group, patients who were Hispanic/Latinx were more likely to receive naloxone (aOR 1.72, 95% CI 1.22–2.44), as were those with "other" race/ethnicity (aOR 2.68, 95% CI 1.28–5.61). Notably, no differences existed among other age groups, patient gender, or primary language, including no significant difference between non-Hispanic Black patients compared to non-Hispanic White patients (aOR 1.31, 95% CI 0.87–1.98).

4. Discussion

In this analysis of patients who survived opioid overdose and who were treated in one of our health system's EDs, less than half (43.2%) received either a prescription for naloxone or take-home naloxone. This suboptimal implementation of naloxone for a high-risk patient group indicates the need for ongoing quality improvement. Furthermore, the study saw no differences between groups who received naloxone based on age and race/ethnicity. A low rate of prescribing has been described

Table 1
Demographic characteristics of included patients and naloxone prescription rates.

		Total	Naloxone prescribed		p value[a]
			Yes	No	
		n = 1342	n = 580 (43.2%)	n = 762 (56.8%)	
Age group (years)	16–24	64 (4.8%)	31 (5.3%)	33 (4.3%)	**0.01**
	25–34	384 (28.6%)	187 (32.2%)	197 (25.9%)	
	35–44	422 (31.4%)	181 (31.2%)	241 (31.6%)	
	45–54	224 (16.7%)	90 (15.5%)	134 (17.6%)	
	55–64	170 (12.7%)	71 (12.2%)	99 (13.0%)	
	65+	78 (5.8%)	20 (3.4%)	58 (7.6%)	
Gender	Female	417 (31.1%)	164 (28.3%)	253 (33.2%)	0.06
	Male	925 (68.9%)	416 (71.7%)	509 (66.8%)	
Race/ ethnicity	Hispanic/ Latinx	175 (13.0%)	93 (16.0%)	82 (10.8%)	**0.004**
	Non-Hispanic Black	108 (8.0%)	49 (8.4%)	59 (7.7%)	
	Non-Hispanic White	1000 (74.5%)	403 (69.5%)	597 (78.3%)	
	Other[b]	32 (2.4%)	20 (3.4%)	12 (1.6%)	
	Unknown	27 (2.0%)	15 (2.6%)	12 (1.6%)	
Primary language	English	1293 (96.3%)	561 (96.7%)	732 (96.1%)	0.89
	Non-English	32 (2.4%)	12 (2.1%)	20 (2.6%)	
	Unknown	17 (1.3%)	7 (1.2%)	10 (1.3%)	

[a] p-Values calculated with Chi-square analysis. Bolded values indicate results statistically significant at the $p < 0.05$ level.
[b] The "Other" race/ethnicity category included Asian (n = 10), American Indian or Alaska Native (n = 1), two or more (n = 13), and "other", as recorded in our electronic health record (n = 8).

Table 2
Adjusted odds ratios (aOR) for receiving a prescription for naloxone (n = 1342).

Effect		aOR	95% confidence interval[a]
Age group (years)	16–24	Ref	
	25–34	1.07	0.63–1.83
	35–44	0.85	0.50–1.44
	45–54	0.73	0.42–1.29
	55–64	0.81	0.45–1.45
	65+	0.41	**0.20–0.84**
Gender	Female	Ref	
	Male	1.23	0.97–1.57
Race/ethnicity	Non-Hispanic White	Ref	
	Hispanic/Latinx	1.72	**1.22–2.44**
	Non-Hispanic Black	1.31	0.87–1.98
	Other	2.68	**1.28–5.61**
	Unknown	2.34	0.93–5.87
Language	English	Ref	
	Non-English	0.54	0.25–1.19
	Unknown	0.55	0.17–1.76

[a] Bolded values indicate results statistically significant at the $p < 0.05$ level.

in other hospitals as well. In a study from Ohio, another state with high incidence of opioid overdose, 30.9% of patients received naloxone at ED discharge (Lane et al., 2021). In Alberta, Canada, 49% of eligible ED patients were offered take-home naloxone, with higher rates of offering to those who were found unconscious or if they had used an illegal opioid (O'Brien et al., 2019). An exception is in Rhode Island, where a comprehensive postoverdose care pathway led to 66% of eligible ED patients receiving naloxone (Reddy et al., 2021). Other studies, however, have reported lower rates, such as 25.1% in Illinois, where there were informational and financial barriers to program development (Eswaran et al., 2020) and another ED where naloxone prescribing was low enough (16.3%), that it prompted the investigators to create an electronic health record automated prompt to remind providers to prescribe naloxone, an intervention which was effective (Marino et al., 2019).

One possible explanation for the suboptimal rates may be failures at the provider level or system level to offer naloxone to patients. Although one study found that while emergency physicians were willing to perform opioid-related harm reduction interventions, including prescribing naloxone, many lacked confidence to do so, and cited inadequate knowledge, time, training, and institutional support as barriers (Samuels et al., 2016). A 2019 survey in Massachusetts found that only 64% of emergency physicians felt very prepared to prescribe naloxone to prevent overdoses, 45% believed opioid use disorder to be a treatable disease, and just 10% reported caring for patients with OUD to be satisfying (Davidson et al., 2019), potentially indicating stigma and hopelessness among providers that may discourage providing harm-reduction modalities like naloxone. More work is clearly needed to educate clinicians about addiction treatment, the benefits of harm reduction, and the detrimental role of stigma. Another potential reason for suboptimal rates may be patients' willingness to accept naloxone. The research from Alberta described that naloxone was not accepted in 23.8% of cases in which it was offered, including 27.5% of refusing patients who reported that they already had a kit (O'Brien et al., 2019). A similar study from Vancouver also evaluated reasons that patients accepted a kit, and 65.6% reported saving other people as a reason, which may be a way for prescribers to motivate patients to accept the medicine (Kestler et al., 2019). Analyzing prescribing barriers was out of the scope of this research; however, it is a critical question that warrants further investigation.

The primary goal of our study was to evaluate differences in naloxone receipt by age, gender, race/ethnicity, and primary language. We initially hypothesized that Black and Latinx patients would have been offered naloxone less frequently than White patients because of both individual-level prejudice and systemic racism. Instead, we found no differences between White and Black patients during the time period of our analysis. Furthermore, we discovered that Hispanic/Latinx patients were more likely to receive naloxone at discharge than White patients. While greater naloxone provision to Hispanic/Latinx patients is important given increases in overdose among Hispanic/Latinx patients (Cano, 2020; Chen et al., 2021; Cano, 2021), the reasons for these findings are unclear. One optimistic possibility is that these findings reflect upon our system-wide plan to address race, ethnicity, and language disparities (Kilbanksi, 2020). However, this increased likelihood of prescribing naloxone to Hispanic/Latinx individuals could reflect bias among providers that this population of patients is more at risk of repeat overdose. Analyzing the underlying causes is subject to further analysis. Previous research has demonstrated that providers perceive Black patients to be at higher risk of opioid misuse compared to White patients (Hirsh et al., 2020). In addition, provider bias about non-White patient groups and perceived risk for misuse have been identified as a reason for disparities by race and ethnicity in prescribing opioids to treat pain (Santoro & Santoro, 2018). Likewise, as commercially insured non-Hispanic Black and Hispanic individuals are less likely to receive follow-up for OUD care after opioid overdose (Kilaru et al., 2020), increased naloxone prescribing for certain groups may represent biased thinking among providers that these patients may be less likely to follow up on treatment.

The importance of the ED as a location for dispensing naloxone to all at-risk patients cannot be understated. Our study was unable to determine if the naloxone provided was just a prescription or an actual take-home kit because, in several of our hospitals, the take-home naloxone is dispensed directly to the patient in the ED after a provider writes the prescription. However, take-home naloxone is clearly advantageous, particularly as the barrier to a patient going to a pharmacy to pick up the

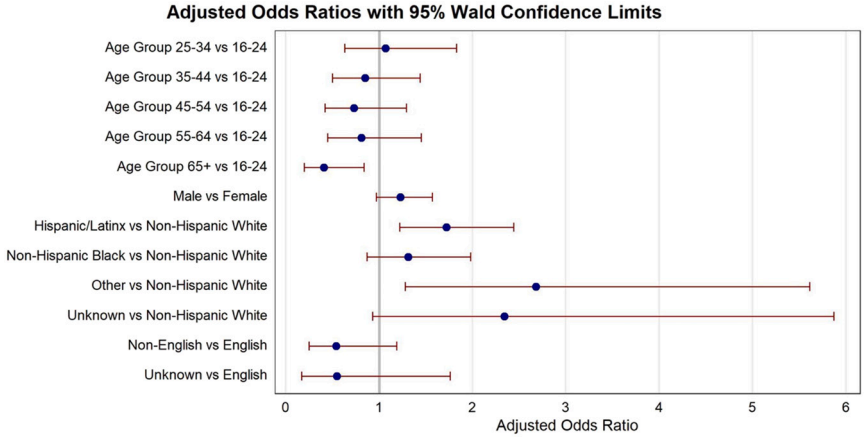

Fig. 1. Adjusted odds ratios of compared values for receiving a prescription for naloxone.

prescription is significant (Weiner & Hoppe, 2021), co-pays at pharmacies may be an additional barrier (Barenie et al., 2020), and pharmacies in more socioeconomically disadvantaged neighborhoods are less likely to carry naloxone (Egan et al., 2020; Abbas et al., 2021). Removing barriers within the ED itself could also be helpful, including allowing nurses and social workers to dispense naloxone to patients without needing to rely on a provider to write an order or prescription.

We evaluated if differences occurred in naloxone provision based on patient age, as we expected differences in the reasons for overdose, such as more prescription opioid (vs. illicit) overdoses and provider expectation of overdose in older adults to be a one-time accident. In the adjusted analysis, we found that patients older than 65 years were less likely to receive naloxone than the reference group (16–24-year-olds). Possible reasons for this finding may include older adults' higher likelihood of having an opioid prescription, as found in a Canadian study (O'Brien et al., 2019), in addition to the possibility of not being well-represented in the public perception of who may be at risk for an opioid-related overdose. Unfortunately, the rate of opioid-related hospitalizations for patients aged 65 years and older increased significantly in past years, including a 34.3% increase in opioid-related hospitalizations and a 74.2% increase in opioid-related ED visits between 2010 and 2015 (Weiss et al., 2018), highlighting the importance of also offering naloxone to patients in this age group.

The final outcomes of interest were the determination of whether primary language or gender of the patient was associated with differential rates of naloxone prescribing. The study included language in the analysis in case barriers to communication existed that led to differences. In the adjusted analysis, a significant difference did not occur between those with English as their primary language and those with other primary languages. Since the percentage of non-English speakers in our cohort was low (2.4%), the lack of difference may be due to inadequate power and should be interpreted with caution. The study included gender given the numerous differences in overdose incidence, outcomes, and comorbidities between the sexes (McHugh, 2020). Our study found no differences in naloxone prescribing to females vs. males. However, we were unable to identify patients who were transgender or gender diverse from our electronic health record data, and some of these individuals have unmet behavioral health needs (Hughto et al., 2021). Larger studies are needed to better assess possible differences in both patient characteristics.

Our study is subject to several limitations. This was a retrospective study that relied on diagnosis codes and may have not included patients for whom our studied diagnoses codes were not documented. Also, we were unable to determine if the naloxone was prescribed or dispensed, and we were unable to capture if naloxone was offered but refused by the patient, a data point that may be important to record in the future should naloxone prescribing after non-fatal overdose become more frequently used as a quality measure. We did not limit the analysis to patients who were discharged from the ED, as we wanted to capture prescription naloxone at any point in their care, including after hospital admission or if they eloped/left without being seen. Although we measured patient-level factors, we did not investigate differences in the characteristics of the providers caring for the patients, which may have influenced outcomes. We also did not examine reasons for different hospitals having different rates of naloxone prescribing and whether underlying socioeconomic factors exist in these communities that contribute to these differences. Finally, Massachusetts has suffered disproportionately from the opioid overdose epidemic (Friedman & Akre, 2021) and has stringent laws mandating provision of medication for OUD to eligible patients from EDs (Commonwealth of Massachusetts, 2018). As a result, the EDs in Massachusetts may be more apt to provide naloxone compared with other states.

In conclusion, naloxone prescribing after an opioid overdose in our system was suboptimal, with fewer than half of patients with an overdose diagnosis code receiving this lifesaving and evidence-based intervention. Furthermore, patients who were Hispanic/Latinx were more likely to receive it than other race and ethnicity groups, and patients who were older were less likely to receive it—findings that warrant attention and that we are sharing with providers in our health system. Research should further evaluate the reasons for differences in naloxone prescribing by ethnicity and age; such research could validate these findings and guide future interventions to improve naloxone access. Hospitals should take part in ongoing implementation of programs to expand access to naloxone, like the “Levels of Care” project in Rhode Island (Samuels et al., 2021), which combined naloxone distribution with behavioral counseling, referral to treatment, and buprenorphine treatment initiation for patients who survived an overdose.

Presentations

An abstract based on this work was presented at the American Society of Addiction Medicine 53rd Annual Conference, Hollywood, FL, April 2022.

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CRediT authorship contribution statement

Conceived the ideas or experimental design of the study: SGW, ADC, NMB, CC, SEW.

Performed data collection: NMB, CC.
Data analysis and interpretation: NMB, CC.
Primary author: SGW.
Provided revisions to the scientific content of the manuscript: ADC, NMB, CPR, CC, EJS, CD, MSJ, SEW.

Declaration of competing interest

The authors declare no potential conflict of interest.

Appendix. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jsat.2022.108785.

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