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EMS naloxone administration as non-fatal opioid overdose surveillance: 6-year outcomes in Marion County, Indiana

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ABSTRACT

Background and Aims Despite rising rates of opioid overdose in the United States, few studies have examined the frequency of non-fatal overdose events or mortality outcomes following resuscitation. Given the widespread use of naloxone to respond to overdose-related deaths, naloxone administration may provide a useful marker of overdose events to identify high-risk users at heightened risk of mortality. We used naloxone administration by emergency medical services as a proxy measure of non-fatal overdose to examine repeat events and mortality outcomes during a 6-year period. **Methods** We conducted a retrospective investigation of all cases in Marion County, Indiana between January 2011 and December 2016 where emergency medical services used naloxone to resuscitate a patient. Cases were linked to vital records to assess mortality and cause of death during the same time-period. We used Cox regression survival analysis to assess whether repeat non-fatal overdose events during the study period were associated with the hazard of mortality, both overall and by cause of death. **Results** Of 4726 patients administered naloxone, 9.4% (n = 444) died an average of 354 days [standard deviation (SD) = 412.09, range = 1–1980] following resuscitation. Decedents who died of drug-related causes (34.7%, n = 154) were younger and more likely to have had repeat non-fatal overdose events. Patients with repeat non-fatal overdose events (13.4%, n = 632) had a ×2.07 [95% confidence interval (CI) = 1.59, 2.71] higher hazard of all-cause mortality and a ×3.06 (95% CI = 2.13, 4.40) higher hazard of drug-related mortality. **Conclusions** Among US emergency medical service patients administered naloxone for opioid overdose, those with repeat non-fatal opioid overdose events are at a much higher risk of mortality, particularly drug-related mortality, than those without repeat events.

Keywords Drug overdose, emergency medical services, mortality, naloxone, opioid, surveillance.

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INTRODUCTION

Rising rates of opioid use in the United States have contributed to an epidemic in recent decades, termed the 'opioid crisis' [1,2]. To illustrate, up to 4.9% of adults in the United States report opioid use in any given week [3]. Moreover, despite reductions in prescribing rates in recent years, rates of opioid prescribing are nearly three times as high today relative to 1999 [4], fueled in part by revised guidelines for the management of chronic pain [5,6]. Concurrent with the rise in opioid prescribing and use, the mortality rate for drug poisoning quadrupled from 1998 to 2008 [7]. During a similar time period, hospitalizations for prescription opioid, sedative and tranquilizer poisoning increased by 65% [8]. Opioids accounted for the vast majority (73.8%) of all prescription drug deaths [7] and 40% of all drug poisoning deaths [9].

Despite growing opioid use, identification of high-risk opioid users remains challenging in practice. Past efforts to identify users at heightened risk of non-fatal overdose —particularly repeat overdose—and death have relied on users' self-reports of prior overdose events [10,11], longitudinal cohort analysis of users' self-reported use and overdose events [12] and population-level surveillance of changes in overdose events and mortality [13]. Few empirical efforts have adopted surveillance strategies easily replicable in practice to identify and intervene around high-risk users. We are aware of only one investigation using existing

data sources (i.e. emergency department records) to individually track the frequency of repeat overdose events, which found that repeat overdose events during a 1-year surveillance period were associated with greater risk of additional and more severe overdose events [14].

Naloxone has grown in popularity as a tertiary prevention strategy to combat opioid overdose fatalities, including for emergency medical responders who have observed dramatic increases in suspected opioid overdose encounters [15]. Naloxone is an opioid antagonist that can be administered intravenously, intramuscularly, subcutaneously or intranasally, and displaces and blocks opioid agonists from receptor sites, effectively reversing an opioid overdose [16]. Its effectiveness has been well established [17], with few adverse events following administration [18]. Because of its effectiveness, there are growing efforts to distribute naloxone in community settings, including among first responders [19]. State policies for naloxone distribution by emergency medical services (EMS) currently authorize paramedics to administer naloxone, although fewer states have policies permitting emergency medical technician (EMT)-level responders to administer naloxone [20].

Given the increased availability of naloxone as a first response to suspected opioid overdoses, naloxone administration by EMS may provide a useful marker of overdose events to identify high-risk users. Although multiple investigations have examined short-term mortality outcomes following naloxone administration by pre-hospital emergency services [21–24], fewer studies have explored naloxone administration as a means of overdose surveillance [25–27]. To that end, we used naloxone administration as an indicator of opioid overdose events to examine mortality following non-fatal overdose, explore the frequency of non-fatal overdose events and causes of mortality and identify characteristics of non-fatal overdose patients at heightened risk of mortality.

METHODS

Data sources

Study data come from Marion County, the largest county in the state of Indiana. Indiana has been hit hard by the recent opioid epidemic and has the 19th highest mortality rate (13.2 per 100 000 population) for overdose deaths in the United States [7]. Well above the national average, drug poisoning is the leading cause of death (COD) from injury in Indiana [9]. In recent years, Indiana has experienced an increase in overdose-related deaths [28]. As the largest city, Indianapolis has been home to a large majority of these deaths with recent increases in heroin- and fentanyl-related overdose deaths [29].

We requested secondary, administrative records from Indianapolis-EMS and death certificates from the Marion County Public Health Department. EMS staff queried an electronic patient care records database containing medical information captured when responding to a scene or transporting a patient for all cases where naloxone was administered from 1 January 2011 to 31 December 2016. These data were provided to Marion County Public Health Department epidemiologists and linked to death certificate data (i.e. sex, date of birth and COD based on International Classification of Diseases [ICD] codes 10th revision) using patient name and social security number. Data were provided to the study team in anonymous form and approved by the university Institutional Review Board (IRB; protocol no. 1606303640).

Our sampling frame included all patients who had naloxone administered by EMS from 2011 to 2016 (n = 4786). Patients were included if they received naloxone and were resuscitated successfully. We excluded 51 cases where naloxone was administered and the patient could not be resuscitated and died during the EMS contact, and nine cases where information on the date of the naloxone event could not be obtained. The final sample included 4726 patients who were administered naloxone by EMS at least once during the study period and resuscitated. For patients with multiple events where EMS administered naloxone, the most recent EMS response defined the baseline period, resulting in an aggregate exposure time of 9329 person-years.

Measures

Our main outcome was mortality, both overall and by COD, following the most recent non-fatal overdose event. Non-fatal overdose events were operationalized as EMS contacts where naloxone was administered, the patient was resuscitated and the patient survived at least 1 day following resuscitation. To examine whether COD was associated with drug use, we recorded ICD-10 codes provided by vital records. Cases where the underlying COD was associated with drug poisoning or where drug poisoning was determined to be a contributing factor were coded as drug-related. All other cases were coded as non-drug-related mortality. A full list of ICD codes and corresponding dichotomous coding is available via an online supplement (Supporting information, Table S1). Exposure period (days) was measured as time from most recent non-fatal overdose event to either date of death or end of the study period (i.e. 31 December 2016).

Covariates included sex, age (years at most recent non-fatal overdose event), any repeat non-fatal overdose event and number of repeat non-fatal overdose events (count). A repeat non-fatal overdose event was defined as a previous event during the study period for which EMS responded, administered naloxone and the patient was resuscitated; administration of multiple naloxone doses during the same event were not counted as repeat overdose

events. We additionally investigated time between overdose events (i.e. intermittency) in days.

Statistical analysis

First, we conducted descriptive statistics on all study variables. Secondly, we conducted bivariate comparisons (i.e. χ^2, Cramer's *V*, *t*-tests) of COD by age, sex and repeat non-fatal overdose events. Thirdly, we computed crude (CMR) and standardized (SMR) mortality rates. The CMR is a measure of the death rate among the study sample. The SMR compares the number of predicted deaths for the sample—based on population-level mortality data adjusted by age and sex and each person's exposure period—to the observed number of deaths. We computed SMRs based on county-level mortality rates stratified by age and sex from 2011 to 2015. Fourthly, we employed Cox proportional-hazards regression to model the effect of repeat non-fatal overdose events on the hazard of mortality during the exposure period; all models were controlled for age and sex. To display the survival curves, we use a Kaplan–Meier analysis.

RESULTS

Mortality outcomes

During the study period, 4726 patients had a non-fatal overdose event. Mortality outcomes were examined for an average follow-up period of 720.46 days [standard deviation (SD) = 614.82, range = 0–2190]. Approximately one-tenth (9.4%, *n* = 444) died during the follow-up period and the average time from last non-fatal overdose to death was 354 days (SD = 412.09, range = 1–1980). The all-cause mortality incidence rate was 4.76 per 100 person-years for the overall sample. All-cause mortality for patients with any repeat non-fatal overdose during the study period was 7.93 per 100 person-years compared with 4.44 per 100 person-years among those with a single event. For the overall sample, the SMR was 5.41, adjusted for age and sex. The SMR was 4.84 among patients with single non-fatal overdose events and higher for patients with any repeat non-fatal overdose event (SMR = 16.19). For COD, 34.7% (*n* = 154) of deaths were drug-related; the most common ICD-10 codes were accidental poisoning (X44 and X42). The remaining 65.3% (*n* = 260) were non-drug-related with common causes, including chronic obstructive pulmonary disease (*n* = 36), atherosclerotic heart disease of native coronary artery (*n* = 15) and unspecified dementia (*n* = 15). Thus, although 9.4% of the full sample died during the study period, only 3.3% died from drug-related causes. However, during the study period, patients were increasingly more likely to have died from drug-related than non-drug-related causes (Table 1).

Table 2 presents a modified life table showing the frequency and proportion of decedents among all patients who had a non-fatal overdose event, by COD. The time from most recent event to death ranged from 1 to 1980 days. Among all decedents (*n* = 444), nearly one-third died within 1 month of the most recent non-fatal overdose event. However, this trend varied by type of death. Patients who died of non-drug-related causes were more likely to die during the 1-month period following a non-fatal overdose relative to patients who died of drug-related causes. Similar trends were evident during the second month following a non-fatal overdose. Overall, two-thirds of decedents died during the first 12 months following non-fatal overdose, although this was slightly lower for drug-related deaths.

Table 1 Drug-related mortality and non-drug-related mortality by year of most recent non-fatal overdose.

	Drug-related n = 154		*Non-drug-related n = 290*	
Year	*n*	*%*	*n*	*%*
2011	18	24.0	57	76.0
2012	28	36.4	49	63.6
2013	17	25.0	51	75.0
2014	47	42.7	63	57.3
2015	30	36.1	53	63.9
2016	14	45.2	17	54.8

Table 2 Terminal events by month for overall mortality, drug-related mortality and non-drug-related mortality.

	Overall mortality n = 444		*Drug-related mortality n = 154*		*Non-drug-related mortality n = 290*	
Month of terminal event	*n*	*%*	*n*	*%*	*n*	*%*
Month 1	120	27.0	30	19.5	90	31.0
Month 2	34	7.7	10	6.5	24	8.3
Month 3	30	6.8	10	6.5	20	6.9
Month 4	10	2.3	2	1.3	8	2.8
Month 5	10	2.3	2	1.3	8	2.8
Month 6	11	2.5	6	3.9	5	1.7
Month 7	15	3.4	8	5.2	7	2.4
Month 8	9	2.0	4	2.6	5	1.7
Month 9	11	2.5	5	3.2	6	2.1
Month 10	10	2.3	5	3.2	5	1.7
Month 11	14	3.2	8	5.2	6	2.1
Month 12	4	0.9	1	0.6	3	1.0
More than 12 months	166	37.4	63	40.9	103	35.5

Age and sex by COD

Table 3 presents descriptive statistics for the sample overall and by COD. Those who died from drug-related causes

Table 3 Sample characteristics of non-fatal overdose patients overall and by drug-related and non-drug-related mortality.

	Patients who received naloxone n = 4726			*Drug-related deaths n = 154*			*Non-drug-related deaths n = 290*				
	Mean	*SD*	*Range*	*Mean*	*SD*	*Range*	*Mean*	*SD*	*Range*	*d.f.*	*P-value*
Age[a]	39.5	15.9	9–96	37.8	13.1	18–88	62.9	16.2	19–95	442	< 0.001
Repeat non-fatal overdose[a]	1.2	0.7	1–12	1.4	1.2	1–12	1.1	0.6	1–5	442	< 0.001
Sex[b]	*n*	%		*n*	%		*n*	%			
Female	1764	37.3		56	36.4		118	40.7		1	0.374
Male	2962	62.7		98	63.9		172	59.3			
Repeat non-fatal overdose[b]											
1 Repeat non-fatal overdose	4094	86.6		113	73.4		264	91.0		3	< 0.001
2 Repeat non-fatal overdose	432	9.1		30	19.5		15	5.2			
3 Repeat non-fatal overdose	114	2.4		6	3.9		6	2.1			
4 or more non-fatal overdoses	86	1.8		5	3.2		5	1.7			

[a]*t*-test; [b]χ^2. d.f. = degrees of freedom; SD = standard deviation.

were significantly younger than those who died from other causes, 37.8 and 62.9 years, respectively (t = 16.64, $P < 0.001$). Sex was not significantly associated with COD (P = 0.374). Figure 1 illustrates the age density by COD and shows that the age distribution for drug-related deaths was positively skewed, such that younger adults were more represented than older adults. In contrast, the age density of non-drug-related deaths was roughly normally distributed, although centered at an average age of 63.9 years.

Repeat non-fatal overdose events overall and by COD

Most patients, 86.6% (n = 4049), had only one non-fatal overdose event during the study period; of the remaining 13.3% (n = 632), the frequency of repeat non-fatal overdose events ranged from one to 12 (mean = 1.2; SD = 0.7), with 68.4% (n = 432) having two events, 18.0% (n = 114) three and 13.6% (n = 86) four or more (Table 3). There were no differences in the likelihood of any repeat non-fatal overdose event and sex (χ^2 = 3.41; P = 0.065, Cramer's V = 0.27); however, those with a repeat non-fatal overdose event were significantly younger than those without; 35.7 years and 40.1 years, respectively (t = 6.48, $P < 0.001$). Examination of the intermittency of overdose events suggested the time between events decreased with each subsequent overdose. Among patients with repeat non-fatal overdose events, the time between events averaged 350.36 days (SD = 408.64, n = 632) between the first and second, 252.18 days (SD = 295.49, n = 201) between the second and third and 199.52 days (SD = 286.40, n = 86) between the third and fourth. Among patients who died during the follow-up period, the likelihood of any repeat non-fatal overdose event differed significantly by COD; 26.6% of those who died from drug-related causes had a repeat event during the study period compared to 9.0% of those who died from non-drug-related causes (χ^2 = 26.29; $P < 0.001$, Cramer's V = 0.24); however, those who died of non-drug-related causes died sooner (Table 2) and would have less exposure time for additional non-fatal overdose events.

Table 4 presents results of Cox regression survival analyses modeling the hazard of mortality overall and by COD following the most recent non-fatal overdose event.

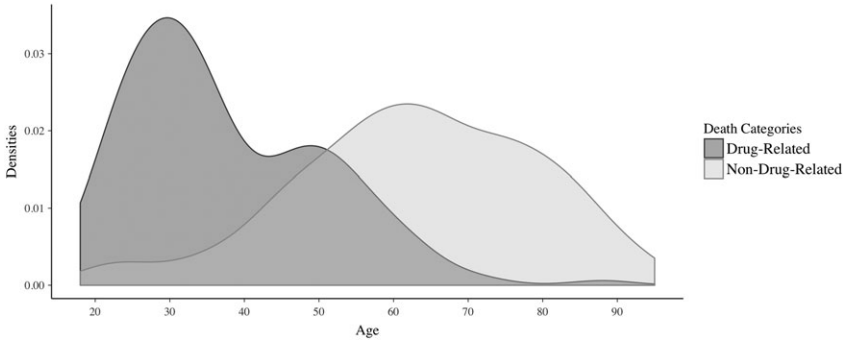

Figure 1 Age at death distribution and density by drug-related mortality and non-drug-related mortality following non-fatal overdose

Table 4 Cox regression predicting the hazard of mortality overall and by drug-related and non-drug-related mortality.

	Overall mortality				*Drug-related mortality*				*Non-drug-related mortality*			
Covariates	*HR*	*95% CI*	*Wald* χ^2	*P-value*	*HR*	*95% CI*	*Wald* χ^2	*P-value*	*HR*	*95% CI*	*Wald* χ^2	*P-value*
Repeat non-fatal overdose event												
No	Reference				Reference				Reference			
Yes	2.07	(1.59–2.71)	28.65	< 0.001	3.06	(2.13–4.40)	36.6	< 0.001	1.50	(0.99–2.27)	3.68	0.056
Age (years)	1.05	(1.05–1.06)	375.15	< 0.001	1.00	(0.99–1.01)	0.486	0.486	1.08	(1.07–1.08)	510.26	< 0.001
Sex												
Female	Reference				Reference				Reference			
Male	1.19	(0.98–1.44)	3.04	0.081	1.19	(0.73–1.42)	0.11	0.917	1.34	(1.05–1.67)	5.67	0.017

HR = hazard ratio; CI = confidence interval.

Controlling for age and sex, any repeat non-fatal overdose increased the hazard of mortality more than twofold [hazard ratio (HR) = 2.07, 95% confidence interval (CI) = 1.59, 2.71, $P = < 0.001$]. Similarly, each additional non-fatal overdose was associated with a 36% (HR = 1.36, 95% CI = 1.22, 1.51, $P < 0.001$) increase in hazard of mortality (see Supporting information, Table S2). In predicting the hazard of a drug-related death, Table 4 shows that patients with repeat non-fatal overdose events had a more than three times higher hazard of mortality compared to patients with one non-fatal overdose event during the study period (HR = 3.06, 95% CI = 2.13, 4.40, $P < 0.001$). Further, each additional non-fatal overdose increased the hazard of drug-related mortality by 48% (HR = 1.48, 95% CI = 1.32, 1.67, $P < 0.001$) (see Supporting information, Table S2). Finally, for non-drug-related mortality, having a repeat non-fatal overdose event resulted in a 50% increase in the hazard of mortality (HR = 1.50, 95% CI = 0.99, 2.27, $P = 0.056$), and each additional event increased the hazard by 23% (HR = 1.23, 95% CI = 1.03, 1.48, $P = 0.024$; see Supporting information, Table S2). Figure 2 displays the Kaplan–Meier curve for all-cause drug-related mortality, and non-drug-related mortality for those with and without a prior non-fatal overdose event.

DISCUSSION

A sharp increase in opioid use in recent decades has contributed to rising numbers of overdose-related deaths, placing a growing burden on emergency services to respond to this epidemic [30]. The pharmaceutical drug naloxone, which reverses opioid overdose, is used by EMS responders throughout all 50 states to respond to opioid overdose events [20]. The growing use of naloxone as a first response to opioid overdose provides a potentially useful mechanism to track individual overdose events and inform identification of users at heightened risk for repeat overdose and mortality. We used EMS data on naloxone administrations to examine 6-year trends in the frequency of non-fatal opioid overdose events and associated mortality outcomes.

Our findings showed that one out of 10 patients who had a non-fatal overdose event to which EMS responded with the use of naloxone died during an average 2-year follow-up period. The all-cause CMR (4.76 per 100 person-years) was much higher than rates reported in the literature on opioid users more broadly (CMR = 2.09 per 100 person-years), but our SMR was much lower (5.41) than similarly published rates (14.66) [31]. Overall, the vast majority of patients (78.7%) had only a single non-fatal overdose event and survived during the course of the study period. The findings also revealed that only 3.3% of patients who had a non-fatal overdose event died of drug-related causes, which is particularly important given public

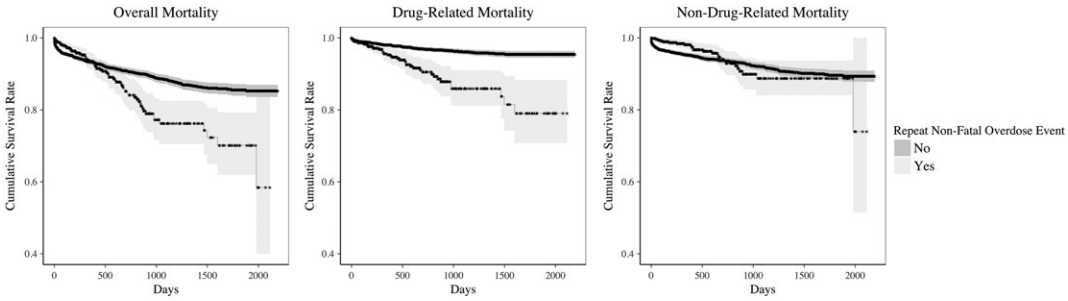

Figure 2 Kaplan–Meier survival plots for overall mortality, drug-related mortality and non-drug-related mortality by those with and without repeat non-fatal overdose events

bias suggesting that naloxone encourages more dangerous drug-use behaviors [32].

Our use of naloxone administration as an indicator of opioid overdose events suggested several subpopulations who may be at heightened risk of mortality: specifically, older adults with chronic health conditions and younger adults with potentially greater substance use. Decedents who died of drug-related causes were an average age of 38 years. In contrast, the two-thirds of decedents who died of non-drug-related causes were an average age of 63 years and more likely to die from chronic health conditions, such as chronic obstructive pulmonary disease, heart disease and dementia. Among older adults, research suggests that substance use disorder is increasing dramatically because of the aging baby-boomer cohort [33] and that this population has different risk factors for prescription misuse [34]. Although we were unable to identify specific substances (i.e. opioid or otherwise; prescription or illicit) implicated in opioid overdose events, it is worth noting that a considerable proportion of overdose events (26.4%) involved adults aged 50 years and older, yet this population was less likely to have had a repeat non-fatal overdose event or die from a drug-related overdose. Given limited research on the physical health correlates of opioid use [35,36], future studies are needed to clarify the interplay between physical and other chronic health problems, prescribed opioid use and misuse and mortality in older adults.

Our investigation is among the first to examine frequency of repeat non-fatal overdose events using EMS naloxone administration as a method of surveillance. Expanded access to naloxone is generally viewed as a promising policy to address opioid overdose due to the drug's effectiveness in decreasing overdose deaths [37], cost-effectiveness [38] and limited potential for adverse events [39]. However, critics have argued recently that naloxone may enable or escalate drug use by proving a safety net and that naloxone is being administered to the same person for multiple overdose events [39]. Contradicting these concerns, we found 13.4% of patients had repeat encounters with EMS where naloxone was administered during a 6-year period. More problematic than the prevalence of repeat overdose events was the heightened risk of mortality associated with repeat EMS encounters where naloxone was administered; patients with repeat encounters had a 65% higher rate of all-cause mortality and were more than twice as likely to die from drug-related causes relative to patients with a single encounter. Thus, our exploratory findings suggest that prior naloxone administration may be a suitable proxy measure of opioid-involved overdose to identify and intervene around patients at increased risk of drug-related mortality.

Our findings support calls for a multi-tiered public health response to the opioid crisis, leveraging primary, secondary and tertiary prevention strategies [40]. These efforts include reducing the availability of illicit and prescription opioids [41]. Current evidence suggests that physicians may not receive adequate training on opioid prescribing. As of 2015, only 23 states had any continuing medical education requirements on opioid prescribing or other pain-management topics for select doctors. Only five states had requirements for most or all physicians. The state of Indiana, for example, has no requirements [42]. Strategies to reduce the availability of prescription opioids may be particularly salient for older adults, who are more likely to be prescribed opioids [43] and are at increasing risk of opioid abuse with suicidal intent [44]. Moreover, older adults, along with racial minorities and men, may be more likely to receive services from EMS in response to an opioid overdose rather than emergency departments [25]. Thus, EMS contacts may serve as an opportunity to identify and intervene for high-risk opioid users by diverting patients to opioid addiction therapies and other harm-reduction strategies, which have been shown to reduce the potential for opioid overdose in high-risk users [45]. Increasingly, for example, communities are developing 'quick response teams' composed of specially trained police officers, EMS personnel and treatment providers who provide first response, service referral and follow-up to patients with suspected overdose [46–48]. More recently, EMS agencies have developed 'leave behind' programs that

allow naloxone to be left with a patient or family member following a non-fatal overdose [49,50]. Although still in their infancy, these efforts highlight the growing recognition of EMS as a promising point of intervention in response to the opioid epidemic.

Limitations

First, our investigation was exploratory and retrospective, and data sources were limited to available administrative records on EMS use of naloxone. Additional information regarding patient characteristics, substances involved in overdose events or medical interventions provided by EMS or in the emergency department were not available. As a result, we could not explore how often naloxone was administered for prescription opioid overdoses—whether medications were acquired legally and used correctly—or illicit opioid overdoses. While Indianapolis EMS protocols prescribe the use of naloxone opioid overdose specifically [51], we do not know how often it was administered incorrectly or whether an overdose patient was resuscitated without naloxone. There is evidence that naloxone is increasingly being administered for symptoms of respiratory depression [52] or altered mental state [26] to rule out overdose as a potential explanation. Although we were unable to verify this trend via chart review, our findings suggested that patients administered naloxone during recent years (i.e. 2014–16) were increasingly more likely to die of drug-related—versus non-drug-related—causes relative to those administered naloxone in earlier years (i.e. 2011–13), providing some evidence contradicting this trend.

Secondly, we relied upon a single source of overdose data. Although naloxone administration has been shown to be a suitable proxy measure in tracking variation in opioid overdose over time [25] and has been used in other investigations to indicate overdose [53] and overdose severity [53], EMS naloxone administration as a method of surveillance has been shown to underestimate opioid-involved overdoses relative to criterion measures such as chart review [26]. These criticisms are common to many methods of overdose surveillance, however, and underscore the inherent trade-off between the accessibility of metrics for establishing evidence of an opioid overdose and the accuracy and comprehensiveness of surveillance efforts. Our exploratory investigation suggests that naloxone administration may have utility as a method of opioid surveillance, particularly for identifying repeat overdose patients.

Thirdly, we examined non-fatal overdose events during only a 6-year period. As such, we could not address prevalent users who may have overdosed prior to 2011. Given the life-time course of opioid addiction [54,55], this is a frequent limitation of time-limited overdose surveillance investigations. However, our 6-year surveillance period represents an improvement over prior investigations of repeat overdose events using existing data sources [14]. Finally, our investigation of overdose events and mortality rates was restricted to a single county in one US state, limiting the generalizability and scope of our results. We could not capture overdose events or deaths occurring outside the county, potentially undercounting overdose events and lowering study mortality rates. Future efforts are needed to broaden the geographic surveillance of non-fatal opioid overdose events.

CONCLUSIONS

Emergency medicine interactions can be a crucial point of contact between opioid users and the health-care system. Interventions delivered in this setting have shown promise in reducing overdose risk and increasing treatment engagement. Our findings suggest that repeat non-fatal overdose events are an opportunity to identify and intervene with high-risk opioid users who are at greater risk of drug-related mortality. Targeted intervention efforts are needed for opioid users with chronic health conditions who are more likely to die from non-drug-related causes. Few intervention efforts have been developed to target opioid abuse or misuse in older adults, yet these efforts will prove necessary as this population continues to use emergency response resources.

Declaration of interests

None.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 A full list of ICD codes and corresponding dichotomous coding.

Table S2 Cox regression predicting the hazard of mortality overall and by drug-related and non-drug-related mortality using continuous measure of repeat non-fatal overdose events.