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One Year Mortality of Patients Treated with Naloxone for Opioid Overdose by Emergency Medical Services

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Abstract

Study objective: Prehospital use of naloxone for presumed opioid overdose has increased markedly in recent years because of the current opioid overdose epidemic. In this study, we determine the one-year mortality of suspected opioid overdose patients who were treated with naloxone by EMS and initially survived.

Methods: This was a retrospective observational study of patients using three linked statewide datasets in Massachusetts: emergency medical services (EMS), a master demographics file, and death records. We included all suspected opioid overdose patients who were treated with naloxone by EMS. The primary outcome measures were death within 3 days of treatment and between 4 days and 1 year of treatment.

Results: Between July 1, 2013 and December 31, 2015, there were 9,734 individuals who met inclusion criteria and were included for analysis. Of these, 807 (8.3% (95% confidence interval (CI) 7.7%-8.8%)) died in the first 3 days, 668 (6.9% (95% CI 6.4%-7.4%)) died between 4 days and 1 year, and 8,259 (84.8% (95% CI 84.1%-85.6%)) were still alive at one year. Excluding those who died within 3 days, 668 of the remaining 8,927 individuals (7.5% (95% CI 6.9%-8.0%)) died within one year.

Conclusion: The one-year mortality of those who are treated with naloxone for opioid overdose by EMS is high. Communities should focus both on primary prevention and interventions for this patient population, including strengthening regional treatment centers and expanding access to medication for opioid use disorder.

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Keywords

naloxone; opioid overdose; emergency medical services

Introduction

The opioid overdose epidemic continues to take thousands of lives in the United States each year and has been called a nationwide public health emergency (1). Emergency medical service (EMS) providers are at the front-line of this epidemic. From July 2016 to September 2017, ED visits for suspected overdose increased 35% (2), and it is likely that most of these patients were transported via ambulance. In fact, EMS providers have had to increase their use of naloxone markedly in response to the epidemic. In a national sample from 2012 to 2016, EMS naloxone administration increased 75.1% (3). Additionally, whereas naloxone was once reserved for advanced life support (ALS) paramedics, now basic life support (BLS) medics administer the antidote in some jurisdictions (4-6). With more potent opioids being used, multiple naloxone administrations by EMS providers are increasing (7).

In Massachusetts, 2,099 people lost their lives to opioid-related overdose in 2016, more than doubling the number in 2013 (8). The state has experienced a disproportionate share of opioid-related deaths in recent years (9). As part of its response to this crisis, the state legislature passed Chapter 55 of the Acts of 2015, which allowed linkage of several previously disparate datasets held by the state for the purpose of learning more about the opioid epidemic (10). The database includes a master demographic file, an EMS incident database (the Massachusetts Ambulance Trip Record Information System, or MATRIS), and death records from the Registry of Vital Records and Statistics. In prior work, we used this resource to determine that the one-year mortality of individuals who were treated for opioid overdose in the emergency department and then were discharged was 5.5% (11).

In this study, we aimed to evaluate individuals treated with naloxone by EMS for suspected opioid overdose. Despite the rising number of EMS naloxone administrations, death due to opioids are also increasing, indicating a need to do something more. Although patients who receive naloxone and are subsequently released from EMS care without transport to an ED are at low risk for immediate mortality, the longer term mortality of these patients is not well-defined (12-14). Reporting a one-year mortality rate to a patient who has received naloxone by EMS, in the setting of a potential near-death experience, may also be the motivation a patient needs to seek help for their opioid use disorder, especially if enhanced community services are available.

In this study, we use Massachusetts' multiple linked datasets to determine the mortality of patients who were treated with naloxone for opioid overdose by EMS. We also evaluate the subsets of those who died within 3 days and those who died between 4 days and one year, to assess both near-term and long-term mortality after the intervention. Finally, for those who died, we aimed to describe demographics and circumstances surrounding the deaths.

Materials and Methods

This was a population-based retrospective cohort study using a linked dataset as part of an epidemiologic study of opioid-related morbidity and mortality that was legislatively mandated in Massachusetts (10). In this analysis, we combined a master demographics list with EMS transports (MATRIS) and death records from the Registry of Vital Records and Statistics that included data from the entire state based on death certificate and medical examiner determinations. The databases were maintained by the Massachusetts Department of Public Health (DPH), who performed a conservative matching procedure to ensure alignment between datasets. To protect patient confidentiality, investigators were provided with a dummy data set that was used to create statistical analysis code that was then provided to DPH, who in turn returned the anonymized results. The linkage process used a nine step deterministic process, which used first name, last name, social security number, date of birth, sex, address, and zip code. A complete description of the overall project, including the patient matching procedure, data dictionaries, and characteristics of the datasets is available online (15). This work was mandated by Massachusetts law using a deidentified dataset and was deemed exempt from review by the Massachusetts DPH Institutional Review Board.

We included patients who received at least one naloxone administration by EMS between July 1, 2013 and December 31, 2015 but did not receive naloxone between January 1, 2013 and June 30, 2013. Since we did not have data prior to January 1, 2013, our data was left-censored so we chose a 6-month exclusion period, in which we ensured that no patient in the cohort had received naloxone by EMS for a minimum of 6 months within Massachusetts. Death records were evaluated until December 31, 2016 to capture the one-year mortality of individuals in the cohort. In our initial work, published previously as an abstract, we evaluated patients who received naloxone by EMS and did not die the same day as EMS administration (16). In that study, we found that 6.5% died the same day as naloxone administration, 9.3% died within one year and 84.3% were alive at one year. Excluding those who died the same day as naloxone administration, 9.9% died within one year. After that publication, we discovered that a) many patients may have received naloxone for other purposes, such as altered mental status due to hypoglycemia or another intoxicant such as alcohol, and b) if someone received naloxone near the end of one calendar day and then died even minutes into the next day, that patient would have been included in the one-year mortality cohort.

For this study, we therefore performed a more in-depth analysis on patients who received naloxone and were also considered to have a suspected opioid overdose based on run sheet descriptive criteria (Appendix 1). We stratified patients with a cut-off of surviving at least the first three days, as opposed to just one day, as patients may have received naloxone, been admitted, and then died within the next 3 days in-hospital. This was consistent with our prior work with the ED cohort that showed the largest incidence of deaths was in the first 3 days after treatment. Also, as we were not able to determine the ED disposition of the included patients (e.g. admitted vs. discharged), surviving the first 3 days was used as a surrogate. We performed a separate sensitivity analysis using 7 days as a cut-off, and the results were not substantially different (8.3% died within 3 days and 9.2% died within 7 days), so we decided

upon 3 days as the cut-off point. The primary outcome measure was death from any cause after the first recorded EMS naloxone administration during the study period.

A master demographics file was merged with EMS transport and death record data. Age was defined as the age of the patient in years as reported as of December 31, 2015, regardless of age at time of overdose or death. Mortality rates were computed for those who died within 3 days and those who died between 4 and 365 days. Descriptive statistics are reported for demographic characteristics and death data, and comparisons between the two cohorts of individuals who died were compared. Analysis was performed using SAS Studio 3.5 (SAS Institute, Cary, NC).

Results

Between July 1, 2013 and December 31, 2015, there were 9,734 unique individuals who met inclusion criteria for analysis (Figure 1), indicating an average of 324.5 first-time naloxone administrations for opioid overdose per month over the 30 months of the study. Of the included patients, 807 (8.3% (95% confidence interval (CI) 7.7%-8.8%)) died in the first 3 days, 668 (6.9% (95% CI 6.4%-7.4%)) died between 4 days and 1 year, and 8,259 (84.8% (95% CI 84.1%-85.6%)) were still alive at one year. Excluding those who died within 3 days, 668 of the remaining 8,927 individuals (7.5% (95% CI 6.9%-8.0%)) died within one year. Figure 2 demonstrates the number of deaths per months in the cohort that died between 4 and 365 days. The highest mortality occurred in the first month, and then was stable over the remaining 11 months.

Table 1 demonstrates the differences between the individuals who died within 3 days and those who died between 4 and 365 days after first recorded naloxone administration. Those who died within 3 days were more likely to be younger (median age 46.0 vs 54.0 years) and male (67.8% vs 61.1%). There was no difference in the race/ethnicity of the decedents or the recorded rate of homelessness. Those who died within 3 days were more likely to have an opioid-related cause of death recorded than those who died between 4 and 365 days (46.6% vs. 36.8%). The manner of death (more likely accidental if within 3 days) and location of death (much more likely in the hospital if within 3 days) were also significantly different.

Limitations

The data in this study were provided by a single state and relied on details from large administrative datasets that were not originally collected for the purpose of research. It is possible that there were errors in the dataset linkages or omissions in data capture. Although the criteria for EMS treatment of overdose were developed in a rigorous fashion, we are not able to validate them. Since fewer than 50% had death records indicating opioid-related overdose as the final cause of death, misclassification is possible. Likewise, as we could not detect the disposition of patients after EMS treatment, we used a cut-off of 3 days after overdose to determine if the individual survived that initial overdose. It is possible that patients were admitted to the hospital and died in the hospital after three days as a result of their initial overdose, which would also be a misclassification error. That 96.8% of individuals who died within 3 days had a location of death in a hospital likely indicates that

our determination is accurate. If patients were treated for overdose or were not a resident of Massachusetts and died in other states, it would not have been captured in our data. Finally, because of our data was left-censored, we excluded 819 individuals (7.7%) who had EMS naloxone administration in the 6 months prior to the start of the study. These individuals are high risk with repeat naloxone administration and may have influenced the results had they been included.

Discussion

Our study demonstrates that the one-year mortality of patients who received naloxone by EMS is quite high. About 1 in 12 people (8.3%) died within 3 days, and an additional 1 in 15 (6.9%) died between 4 days and 1 year. These numbers underscore what a serious medical problem opioid use disorder is, and how fatal it can be. As comparison, a study of patients with ST-segment elevation myocardial infarction (STEMI) who received primary percutaneous coronary intervention found a one-year mortality rate of 7.3% (17). Yet, the way we treat overdose victims is quite different than those who suffer other medical problems. For a STEMI, patients who call 911 are brought by ambulance to a designated center of expertise, rushed to the catheterization lab by a multidisciplinary team that is available at any time of the day or night, and then treated aggressively with medications that lower risk and provided with close follow up. Contrast that to the experience of a typical overdose victim who may be observed in the hallway of an ED for a few hours and is then discharged with a list of detoxification centers which often have limited bed availability.

Another tragic statistic is comparison of death rates for patients who received naloxone for opioid overdose compared with the general population. For 2017, the average life expectancy in the United States was 78.6 years, with a death rate of 863.8 deaths per 100,000 population (18). In our cohort, the median age of those who died within 3 days was 46 years, and just 54 years for those who died between 4 and 365 days. Drug overdose deaths are now a significant reason why the U.S. annual life expectancy has dropped for the past three years (18).

Several findings from our study are of interest beyond the one-year mortality rate. First, the median age of patients who died was higher than expected. Our prior work looking at one-year mortality of patients who were treated in the ED for opioid overdose showed a lower median age of 39 years, and the significance is unclear. It is also of interest that many patients treated with naloxone by EMS (3,818 of 14,407, or 26.5%) did not ultimately have an opioid-related issue and were excluded from analysis. These instances could indicate times when EMS administered naloxone treatment for a patient with altered mental status which could have been from a separate reason, like alcohol intoxication.

Compared with the general population, a disproportionately high number of people who died were homeless, highlighting homelessness as a significant risk factor associated with death within a year. For those who died within 3 days, the vast majority (97%) died in the hospital. However, for those who survived at least 3 days beyond an initial overdose, about one-quarter had a location of death reported as a private residence, likely representing individuals who used drugs alone. For harm reduction purposes, education is needed to

reinforce that people who misuse opioids should never use alone, and family and peers of people who misuse opioids should have ready access to a naloxone rescue kit at their place of residence. It is also important to acknowledge that, when combining all deaths within 1 year, 2.3% (n=34) were deemed due to suicide, highlighting that overdose survivors should be screened for suicide risk.

Fortunately, there are new models being created that are cause for optimism. A study from Yale determined that immediately starting buprenorphine for patients who seek help in the emergency department for opioid use disorder results in a markedly increased 30-day treatment retention rate (19). This practice is also cost effective (20). Another model is to have a follow-up visit by EMS and/or police in the days after a naloxone reversal, which has the benefit of directing people to harm reduction services, providing naloxone rescue kits, and enhancing community engagement (21). Expansion of programs like these that shepherd patients directly into treatment from the emergency department and increase community resource may ameliorate the opioid overdose crisis.

In conclusion, the one-year mortality of those who are treated with naloxone for opioid overdose by EMS is high. Survivors of opioid overdose should know this important mortality statistic. Communities should focus both on primary prevention and interventions for this patient population, including strengthening regional treatment centers, community-based outreach for opioid overdose survivors, and expanding immediate access to medication for opioid use disorder.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1:
Flow diagram of included and excluded subjects.

Figure 2:
Number of deaths per month for patients who died between 4 and 365 days of prehospital naloxone administration (n=668).

Table 1:

Comparison of demographic and death data records for individuals who died within 3 days and those who died between 4 and 365 days. P values <0.05 (in bold) are considered statistically significant.

Cohort (n)	Died within 3 days (n=807)	Died between 4 and 365 days (n=668)	p value
Age, years (median <interquartile range>)	46.0 <33.0-58.0> years	54.0 <36.0-71.0> years	p<0.01
Gender (from death records)	67.8% (n=547) male	61.1% (n=408) male	p<0.01
Race/ethnicity (from death records)	86.1% (n=695) white 4.6% (n=37) black 6.3% (n=51) Hispanic 3.0% (n=24) other	88.9% (n=594) white 3.1% (n=21) black 5.8% (n=39) Hispanic 2.1% (n=14) other	p=0.32
Homeless	6.6% (n=53) homeless	8.5% (n=57) homeless	p=0.15
Opioid-related overdose (from death record)	46.6% (n=376) opioid-related	36.8% (n=246) opioid-related	p<0.01
Manner of death	41.9% (n=338) natural causes 50.7% (n=409) accidental 2.7% (n=22) suicide 4.7% (n=38) other/pending investigation	53.4% (n=357) natural causes 39.5% (n=264) accidental 1.8% (n=12) suicide 5.2% (n=35) other/pending investigation	p<0.01
Location of death	96.8% (n=781) hospital 1.4% (n=11) residence 1.7% (n=14) nursing home/other/unknown	50.2% (n=336) hospital 25.4% (n=170) residence 24.1% (n=161) nursing home/other/unknown	p<0.01