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Signal of increased opioid overdose during COVID-19 from emergency medical services data

Svetla Slavova[a,b,*], Peter Rock[b], Heather M. Bush[a], Dana Quesinberry[b,c], Sharon L. Walsh[d,e]

[a] Department of Biostatistics, University of Kentucky, Lexington, KY, United States
[b] Kentucky Injury Prevention and Research Center, University of Kentucky, Lexington, KY, United States
[c] Department of Health Management and Policy, University of Kentucky, Lexington, KY, United States
[d] Department of Behavioral Science, University of Kentucky, Lexington, KY, United States
[e] Center on Drug and Alcohol Research, University of Kentucky, Lexington, KY, United States

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ABSTRACT

Background: Individuals with opioid use disorder may be at heightened risk of opioid overdose during the COVID-19 period of social isolation, economic distress, and disrupted treatment services delivery. This study evaluated changes in daily number of Kentucky emergency medical services (EMS) runs for opioid overdose between January 14, 2020 and April 26, 2020.

Methods: We evaluated the statistical significance of the changes in the average daily EMS opioid overdose runs in the 52 days before and after the COVID-19 state of emergency declaration, March 6, 2020.

Results: Kentucky EMS opioid overdose daily runs increased after the COVID-19 state emergency declaration. In contrast, EMS daily runs for other conditions leveled or declined. There was a 17% increase in the number of EMS opioid overdose runs with transportation to an emergency department (ED), a 71% increase in runs with refused transportation, and a 50% increase in runs for suspected opioid overdoses with deaths at the scene. The average daily EMS opioid overdose runs with refused transportation increased significantly, doubled to an average of 8 opioid overdose patients refusing transportation every day during the COVID-19-related study period.

Conclusions: This Kentucky-specific study provides empirical evidence for concerns that opioid overdoses are rising during the COVID-19 pandemic and calls for sharing of observations and analyses from different regions and surveillance systems with timely data collection (e.g., EMS data, syndromic surveillance data for ED visits) to improve our understanding of the situation, inform proactive response, and prevent another big wave of opioid overdoses in our communities.

1. Introduction

In the midst of the ongoing opioid epidemic in the U.S., the new crisis of the COVID-19 pandemic may put individuals with opioid use disorder at higher risk of overdose as others have recently noted (Becker and Fiellin, 2017; Wakeman et al., 2020). Historically, the primary evidence-based treatments for opioid use disorder (OUD) (i.e., methadone and buprenorphine) require in-person and often frequent (sometimes daily) visits that are in whole or part precluded under widespread stay-at-home orders. Public health departments, which are often a safety net for provision of harm reduction interventions (i.e., syringe service programs, naloxone distribution, etc.) are under tremendous strain and may offer reduced support while they focus resources on responding to the COVID-19 pandemic. Additionally, anxiety and depression compounded by social isolation and economic uncertainty during the pandemic may increase the risk of relapse in those who are abstinent and increase the likelihood of individuals to be alone when using opioids - both of which are factors related to increased risk of fatal overdose.

While the federal government has rapidly moved to revise policies to offer telemedicine and eliminate barriers to care (ONDCP, 2020), the structural barriers related to rapid implementation of these practice changes has been challenging. To address concerns regarding increased risk for those suffering with OUD in this rapidly changing environment, monitoring of early warning systems may provide critical data to identify changes in overdose patterns and inform public health

* Corresponding author at: Department of Biostatistics, University of Kentucky, Healthy Kentucky Research Building RB2, Office 261, 760 Press Ave, Lexington, KY 40536, United States.
E-mail address: ssslav2@email.uky.edu (S. Slavova).

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response.

We hypothesized that the COVID-19 pandemic would result in significant increases in opioid overdoses. This study examined emergency medical services (EMS) runs for opioid overdose for temporal changes from the period prior to and after stay-at-home orders were placed in Kentucky for COVID-19.

2. Methods

The primary analysis for this study used data from the Kentucky State Ambulance Reporting System, supported by the Kentucky Board of EMS and examined emergency response records (excluding inter-facility transports) for opioid overdose in the Commonwealth of Kentucky from January 14, 2020 to April 26, 2020. EMS Opioid Overdose Runs (OOR) were identified by a previously described algorithm (Lasher et al., 2019), which incorporates information from the EMS narrative and specific field entries on primary/secondary impression, naloxone administration, and positive response to naloxone. EMS OOR were further split into runs that resulted in transportation to an emergency department (ED) (OOR-Transport) or a refusal for transportation to ED (OOR-Refusal). A third category, EMS runs for suspected opioid overdose with death at the scene, was included in the descriptive analysis but due to small daily counts was not analyzed with a regression analysis.

The outcomes for primary analyses were the daily number of EMS OOR. Daily EMS OOR and their 7-day moving averages were visualized in comparison to all other EMS runs (i.e., excluding runs for opioid overdoses). Descriptive statistics (means and standard deviations) were used to describe the daily number of EMS runs for the period before and after the COVID-19 state emergency declaration.

Segmented regression analysis for interrupted time series (Bernal et al., 2017; Wagner et al., 2002) with autoregressive error model (SAS, 2020; Slavova et al., 2018) was used to model the daily EMS OOR linear trends in the two segments of the study period, before and after March 6, 2020, the day of the state emergency declaration. The analysis estimated the changes in both the intercept and the slope for before and during COVID-19 study periods. The date of the state emergency declaration marked the beginning of the COVID-19-related study period but the wide adoption of social distancing occurred more than one week later. In order to identify the actual change point in the EMS OOR trends, a sequence of segmented regression analyses was performed and every day between March 6 and March 30, 2020 was tested as a change point/interruption for the established pre−COVID-19 trend of daily number of EMS OOR. Models with different change points were compared based on the maximum likelihood estimates for the Akaike's Information Criteria (AIC) and the model with the lowest AIC was considered the best fit. The modeling identified that the best segmented regression analysis fit for EMS OOR-Transport was achieved for the change point of March 18, 2020; for the EMS OOR-Refusal, the best change point was March 20, 2020. Model assumptions and fit were evaluated with diagnostic tools. Analysis was performed with SAS statistical software (PROC AUTOREG); two-sided significance level of 0.05 was used. Parameter estimates and 95% confidence intervals were reported. For a sensitivity analysis, the segmented regression analysis was also performed for EMS OOR data for the period January 14, 2019 to April 26, 2019. This study was approved by the University of Kentucky Institutional Review Board.

3. Results

Overall, there was an increase in the total number of EMS OOR during the COVID-19 study period compared to the pre−COVID-19 period (Table 1). Specifically, there were 2456 EMS OOR-Transport (1133 during the pre−COVID-19 period vs. 1323 during the COVID-19 period; 17% increase), 605 EMS OOR-Refusal (223 vs. 382; 71% increase), and 30 EMS runs for suspected opioid overdose with death at the scene (12 vs. 18; 50% increase). At the same time, there was a noticeable decline in the total number of all EMS Transport Runs Excluding OOR-Transport (55,855 vs. 43,478; 22% decline) and almost no change in all EMS Refusal Runs Excluding OOR-Refusal (11,044 vs. 10,957; 0.8% decline).

Fig. 1 illustrates EMS OOR trends in comparison with all EMS Runs Excluding OOR, from January 14, 2020 to April 26, 2020. The solid vertical line marks the date of the state of emergency declaration, March 6, 2020, identifying the first day of a 52-day COVID-19-related study period (ending on April 26, 2020; most recent data available for the study analysis). An equally long pre−COVID-19 period is defined from January 14 to March 5, 2020. As illustrated (Fig. 1A), EMS Transport Runs Excluding OOR-Transport were relatively stable during the pre−COVID-19 period but a drop in the daily mean was observed after the COVID-19 declaration, from 1074 (SD = 74) to 836 (139) (Table 1). In contrast, EMS OOR-Transport (Fig. 1B) began to climb after the COVID-19 declaration; the estimated average number of daily runs during COVID-19, 25.44 (5.38) was higher than the pre−COVID-19 period (21.79 (5.78)). Fig. 1C, EMS Refusal Runs Excluding OOR-Refusal, illustrates approximately leveled numbers over the entire time period (pre−COVID-19 average: 212 (21), during COVID-19: 211 (21)). Average daily EMS OOR-Refusal (Fig. 1D) almost doubled after the COVID-19 declaration (in period before COVID-19: 4.29 (2.04) versus during COVID-19: 7.35 (2.81)). The segmented regression analysis identified that March 18, 2020 was the change point for the EMS OOR-Transport data (minimum AIC; best fit) (Fig. 2A), while March 20, 2020 was the change point that best separated the pre-and during COVID-19 trends for EMS OOR-Refusal data (Fig. 2B).

Segmented regression analysis found that during the pre−COVID-19 period, on average 21.58 (95% CI, 19.40–23.76) opioid overdose patients were transported daily to ED with no significant daily changes (P = .73; Table 2; Case Period; EMS OOR-Transport). However, there was a significant difference in the slope of the daily EMS OOR-Transport regression lines (Fig. 2A) before and after March 18, 2020 (estimated slope change of 0.14; $P = .04$; Table 2; Case Period; EMS OOR-Transport). As such, the impact of COVID-19 on EMS OOR-Transport resulted in a sustained average rate of increase of one opioid overdose per week after March 18, 2020.

The pre−COVID-19 trend for EMS OOR-Refusal was flat (Fig. 2B) with an estimated daily average of 4.28 opioid overdose runs (Table 2, Case Period; EMS OOR-Refusal). This trajectory did not change during COVID-19 period ($P = .93$). However, there was a significant shift in the average number of daily EMS OOR-Refusal after March 20, 2020 (estimated increase of 3.58 runs; $P < .001$) such that the average number of refusals increased to 8 per day after March 20, 2020 (Table 2, Case Period; EMS OOR-Refusal).

To evaluate these results in the context of a comparable time period without COVID-19, the two segmented regression models were fitted for EMS OOR data from Jan 14, 2019 to April 26, 2019. For comparison, March 18 and March 20, 2019 were again selected as the change points for OOR-Transport and OOR-Refusal trends respectively, and separated the time period into two parts. For both OOR-Transport and OOR-Refusals, when compared to the period before the change points, there were no significant changes in the number of runs or rate of runs after the change point (Table 2, Sensitivity Analysis).

4. Discussion

The presented data revealed that EMS runs in response to opioid overdoses have significantly increased since the COVID-19 crisis began. By comparing the period before the emergency declaration was made in Kentucky to the period after the declaration, EMS runs for opioid overdose have increased both in the rate of transportation to ED and, critically, in the number of those who were treated on the scene and refused transportation to ED. It is also clear that these increases are not related to seasonality as a similar change was not noted when

Table 1
Summary Statistics for Kentucky Emergency Medical Services (EMS) Daily Runs during pre – COVID-19 Study Period (January 14, 2020 to March 5, 2020) vs. COVID-19 Study Period (March 6, 2020 to April 26, 2020), by Type of EMS Runs.

	January 14, 2020 to March 5, 2020		March 6, 2020 to April 26, 2020	
Type of EMS runs	No. (%)	Daily Mean (SD)	No. (%)	Daily Mean (SD)
EMS opioid overdose runs with transportation to emergency department (ED) (n = 2456)	1133 (46.13)	21.79 (5.78)	1323 (53.87)	25.44 (5.38)
EMS opioid overdose runs with refused transportation to ED (n = 605)	223 (36.86)	4.29 (2.04)	382 (63.14)	7.35 (2.81)
EMS runs for suspected opioid overdose with death at the scene (n = 30)	12 (40.00)	0.23 (0.43)	18 (60.00)	0.35 (0.65)
All other EMS runs (excluding opioid overdose) with transportation to ED (n = 99,333)	55,855 (56.23)	1074.13 (73.70)	43,478 (43.77)	836.12 (138.83)
All other EMS runs (excluding opioid overdose) with refused transportation to ED (n = 22,001)	11,044 (50.20)	212.38 (21.04)	10,957 (49.80)	210.71 (21.42)

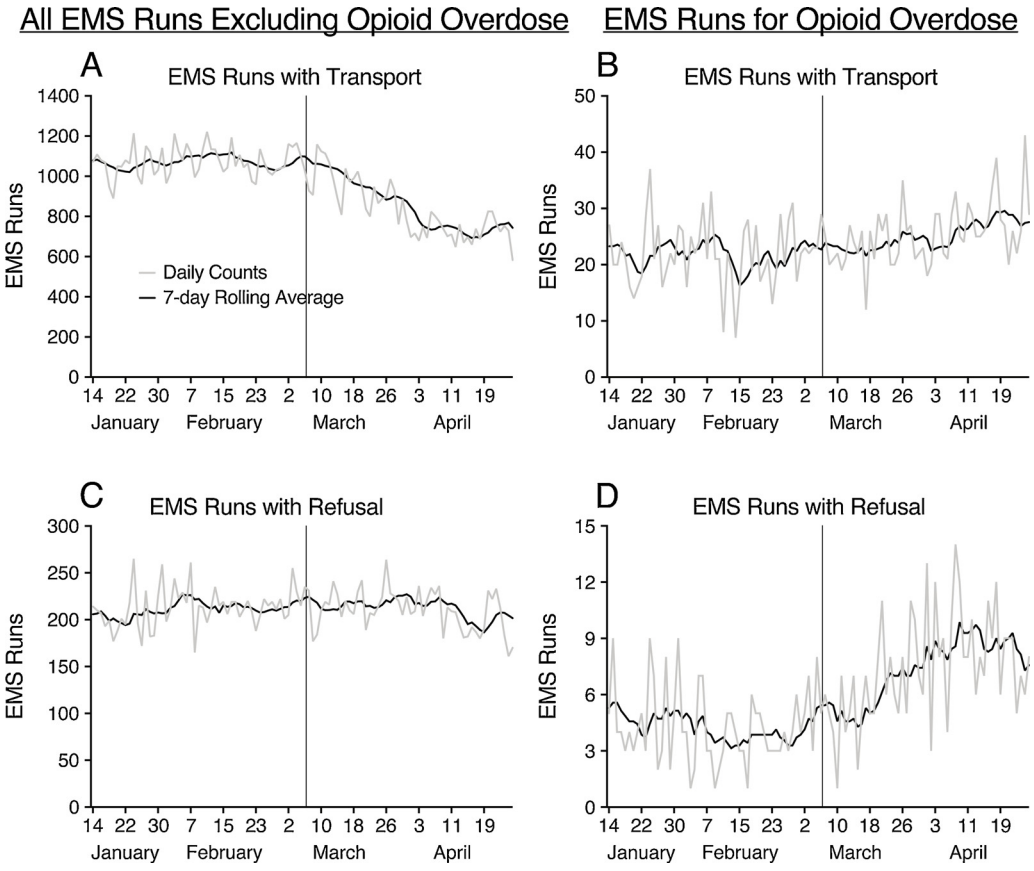

Fig. 1. Daily Series of Number of Kentucky Emergency Medical Services Runs, by Type of Run, January 14, 2020 to April 26, 2020.
Number of Emergency Medical Services (EMS) Daily Runs for All EMS Runs Excluding Opioid Overdose (left panel) and EMS Runs for Opioid Overdose (right panel), further stratified as EMS runs with transportation of the patient to an emergency department (ED) (top row) or with a refusal for transportation to an ED (bottom row), from January 14, 2020 to April 26, 2020. The daily counts are visualized by the gray line; the 7-day rolling averages are visualized by the black line.

comparing the identical timeframe from the preceding year. Importantly, these increases are occurring in the context of decreasing EMS runs for all causes other than opioid overdose, which have declined by over 20% for the same period. These data serve as an early warning and may portend a potential increase in opioid overdose deaths during the COVID-19 crisis.

There are numerous reasons for concern about opioid overdose deaths rising during the COVID-19 pandemic that have been recently enumerated (Alexander et al., 2020; Becker and Fiellin, 2020; Wakeman et al., 2020). For those individuals who are out of treatment and actively using illicit opioids, social distancing increases the likelihood that individuals will use alone more often, with no one to intervene in the event of an overdose. Across the country, individuals are being released early from jails and prisons in order to contain the spread of the virus (Simpson and Butler, 2020); however, these individuals are abruptly reentering society likely without a care plan for their opioid use disorder, if present. Release from incarceration after an extended period of abstinence is recognized as a particularly high risk period for opioid overdose death (Farrell and Marsden, 2008) (Farrell and Marsden, 2008; Merrall et al., 2010). Moreover, the social distancing measures are highly likely to alter the illicit drug market in ways not yet understood. Individuals who were in treatment and successfully abstaining are facing disruptions to their ongoing care due to COVID-19. While the government has taken rapid action to reduce restrictions (e.g., allowing telemedicine, increasing allowed take-home doses of medications for treatment of opioid use disorder)(SAMHSA, 2020), modifying practices and addressing technology gaps require time to be implemented and adopted by both treatment providers and those seeking treatment. Additionally, mutual support groups that meet in person are a common platform for recovery support services, and these are being disrupted by stay-at-home and social distancing orders.

The data here revealed that, in addition to increases in individuals

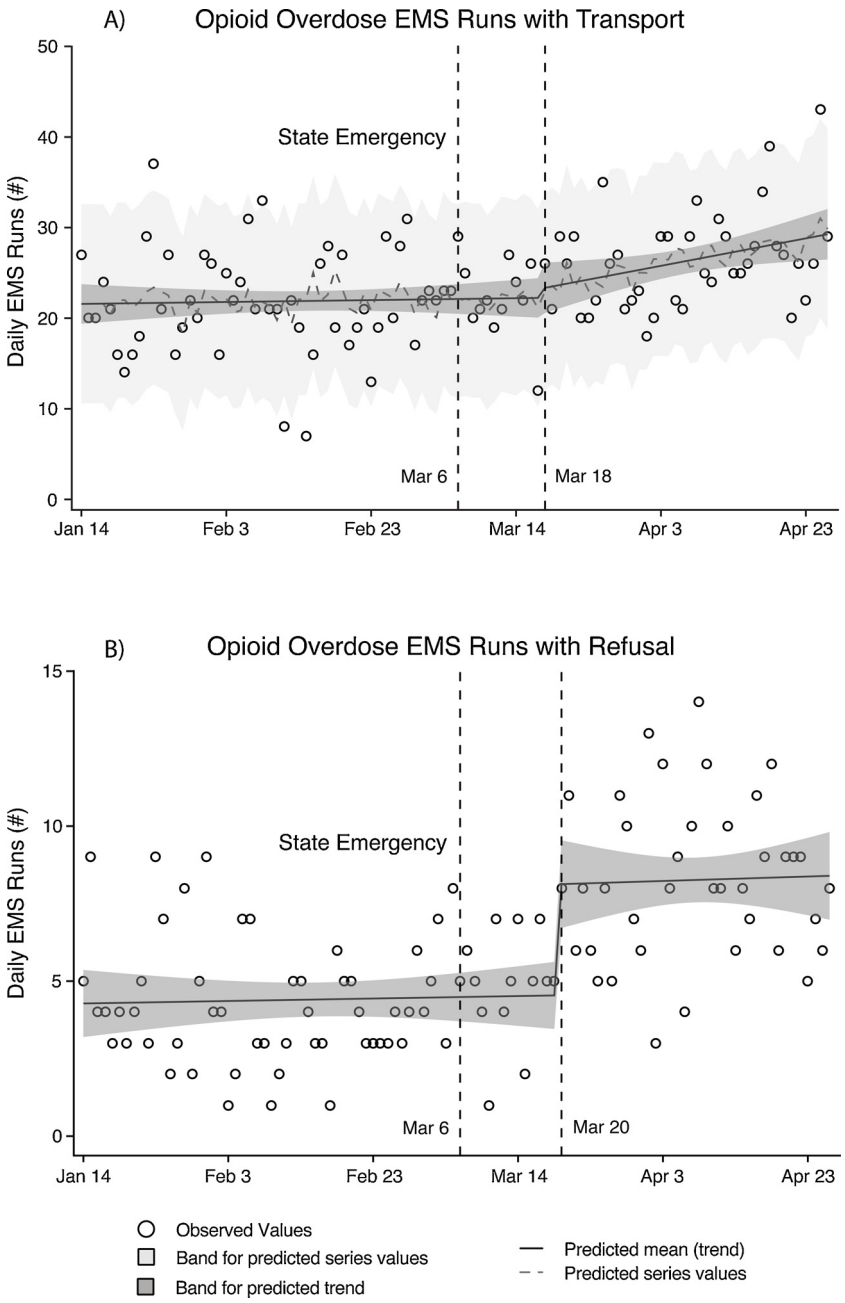

Fig. 2. Trends in Kentucky Emergency Medical Services Daily Runs for Opioid Overdose, January 14, 2020 to April 26, 2020.
(2A) March 18, 2020 was identified as the point of the slope change (estimated change of 0.14 runs/day, 95% CI, 0.01 to 0.28; $P = .04$) from the pre−COVID-19 trend line of EMS daily opioid overdose runs with transportation to ED. (2B) March 20, 2020 was the change point associated with an immediate jump (3.58 runs; 95% CI, 1.76–5.41; $P < .001$) in the level of the average daily EMS opioid overdose runs with refused transportation to ED.

being transported for opioid overdose by EMS, the number of individuals refusing transport has doubled. Individuals with opioid overdose may refuse transportation to the hospital for many reasons, including fear of law enforcement (particularly if they are carrying drugs or paraphernalia), concern over potential cost, embarrassment, or because they are experiencing precipitated withdrawal. In the midst of the pandemic, people are more inclined to stay away from the hospital for fear of exposure to COVID-19 as reflected by news and professional society reports of declines in emergency room admissions.

Effective public health response to the opioid epidemic, especially during a COVID-19 pandemic, depends on timely and accurate data to inform data-driven decisions. The determination of cause of death for suspected drug overdose typically requires medico-legal death investigation and subsequent toxicological tests. States vary widely in the length of time required for final death determinations and reporting, but it is not uncommon for reporting to lag by 6 months or more (Spencer and Ahmad, 2016). Therefore, examination of timely data, such as EMS runs, may provide more rapid information about a change in risk for overdose and inform earlier intervention. The EMS data are a new and underutilized public health surveillance data source with great potential. In Kentucky in particular, the data collection is mandated by state laws (KAR, 2013; KRS, 2019) and allows timely monitoring of existing and newly emerging trends at state and local levels. It also allows capturing of the volume of opioid overdose encounters that are not captured by the emergency department discharge claims data, a traditional source for opioid overdose epidemiology and public health surveillance. A limitation of EMS OOR measure is that the EMS records do not include clinical (i.e. documented by a clinician) diagnosis for

Table 2
Parameter Estimates for Segmented Regression Analysis of Daily Emergency Medical Services (EMS) Runs for Opioid Overdose, January 14, 2020 to April 26, 2020.

	Parameter Estimates[a]			
	Pre-COVID-19 Intercept	Pre-COVID-19 Slope	COVID-19 Intercept Change[b]	COVID-19 Slope Change
Case Period: January 14, 2020 – April 26, 2020				
EMS OOR-Transport (Change Point Mar 18, 2020)	21.58 [19.40, 23.76] ($P < .001$)	0.01 [−0.05, 0.07] ($P = .73$)	0.97 [−2.72, 4.65] ($P = .60$)	0.14 [0.01, 0.28] ($P = .04$)
EMS OOR-Refusal (Change Point Mar 20, 2020)	4.28 [3.20, 5.36] ($P < .001$)	0.004 [−0.02, 0.03] ($P = .78$)	3.58 [1.76, 5.41] ($P < .001$)	0.003 [−0.07, 0.07] ($P = .93$)
Sensitivity Period: January 14, 2019 - April 26, 2019				
EMS OOR-Transport (Change Point Mar 18, 2020)	20.25 [17.63, 22.87] ($P < 0.001$)	0.04 [−0.03, 0.11] ($P = .26$)	−1.12[−5.40, 3.16] ($P = .60$)	−0.12[−0.28, 0.04] ($P = .14$)
EMS OOR-Refusal (Change Point Mar 20, 2020)	3.22 [2.23, 4.20] ($P < 0.001$)	0.002 [−0.03, 0.03] ($P = .89$)	0.93 [−1.65, 2.58] ($P = .27$)	−0.01[−0.06, 0.05] ($P = .76$)

Note: [a]Estimates [95% CI] and (P-values) are presented from the segmented regression models;
[b] Change from the end of the preceding segment.

opioid overdose. A limitation of the study is the reporting from only a single state, but the national EMS data collection has considerable lag. It is likely that other states, particularly those highly affected by the opioid crisis pre−COVID-19, will see similar concerning changes. Further analysis at the local level, supported by additional data sources and input from local stakeholders, can identify the specific factors driving the changes in the trends and inform appropriate local public health response and mitigation strategies.

The emerging trends of increased opioid overdose EMS runs in Kentucky provide empirical evidence for concerns that opioid overdoses are rising during the current COVID-19 pandemic. We want to encourage our colleagues at state and local public health departments, EMS agencies, and health care systems, to share observations and analyses from different regions and surveillance systems with timely data collection (e.g., EMS data, syndromic surveillance data for ED visits) to improve our understanding of the situation, inform proactive response, and prevent another big wave of opioid overdoses in our communities.

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Contributors

All authors contributed to the concept of the study and provided edits to the manuscript. P.R. obtained and pre-processed the data. S.S. conducted the statistical analysis. S.S. and S.W. had equal contribution to drafting the manuscript.

Declaration of Competing Interest

The authors have no competing interests to declare.

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BRIEF REPORT

Opioid Overdose–Related Emergency Department Visits and Accidental Deaths during the COVID-19 Pandemic

Luke N. Rodda · Kelsa L. West · Kathy T. LeSaint

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Introduction

The world became aware of a novel coronavirus disease (COVID-19) in late December 2019, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 presents a heightened threat to human life with its ability to spread efficiently and at a high mortality rate to those with medical comorbidities [1, 2]. Within months, the virus had spread rapidly from its origin in China to parts of Europe, namely Italy and the UK, and to the United States (US). Towards the end of March, the USA had the most cases worldwide [3].

Many US states, counties, and cities enacted travel restrictions and promoted social distancing in order to combat human-to-human spread of COVID-19. In mid-March, San Francisco led the country in enacting these safety measures, and a month later, nearly all of mainland US was under similar restrictions. Early prevention measures included limitations on the use of city-owned facilities, followed by a restriction on public gatherings, and on March 16th, a complete shelter-in-place mandate was ordered [4]. Surrounding San Francisco Bay Area, counties enacted similar measures contemporaneously, and California mandated a statewide shelter-in-home (akin to shelter-in-place) restriction on March 19th [5].

Concomitant to the COVID-19 pandemic, San Francisco has been experiencing an opioid epidemic throughout recent years, starting predominantly in 2016, and largely due to the significant increase of fentanyl availability and, often contemporaneous, use with heroin [6, 7]. News outlets, harm reduction agencies, and professional health societies have since shared

L. N. Rodda · K. L. West
Forensic Laboratory Division, Office of the Chief Medical Examiner, San Francisco, CA, USA

L. N. Rodda (✉)
Department of Laboratory Medicine, University of California, San Francisco, San Francisco, CA, USA
e-mail: luke.rodda@ucsf.edu

K. T. LeSaint
Department of Emergency Medicine, University of California, San Francisco, San Francisco, CA, USA

K. T. LeSaint
California Poison Control System, San Francisco Division, San Francisco, CA, USA

concerns of increased overdose incidents during periods of social distancing [8, 9].

In this study, we describe the prevalence and characteristics of individuals in San Francisco who experienced significant consequences following opioid use, specifically those resulting in emergency department visits and accidental death, in the time of social distancing during the COVID-19 pandemic.

Methods

Patient cases from January 1 through April 18, 2020, were included to capture the immediate time period of mid-March representing before and after social distancing mandates were enacted. Descriptive statistics were used to characterize the cohort of patients. Categorical variables are described via absolute values and percentages.

Opioid Overdose–Related Emergency Room Presentations

Together, the emergency departments at the University of California, San Francisco (UCSF) and its affiliated Zuckerberg San Francisco General Hospital & Trauma Center (ZSFG) serve the largest proportion of patients in the City, each providing care to over 40,000 patients per year. The electronic medical records at both sites were queried for patient chief complaints and final diagnoses of "overdose." Of these, cases were excluded if neither the chief complaint nor the final diagnosis was opiate, opioid, heroin, and/or fentanyl related. Patient-related demographic information such as date of emergency room presentation, age, and sex were collected in addition to the underlying chief complaint.

Opioid Overdose–Related Fatalities

All accidental, homicide, suicide, suspicious, undetermined, and certain natural deaths in San Francisco are investigated by the Office of the Chief Medical Examiner (OCME). During the study period, all available forensic investigation, medical and scientific findings from accidental overdose cases were captured. For the purposes of this study, demographic and toxicological information were collected on each case. Using a previously published method, accidental overdose deaths with fentanyl, norfentanyl, 6-monoacetylmorphine (6-MAM, heroin's primary metabolite), morphine, and/or codeine detected in blood were captured to best determine their relevance in causation of drug toxicity [10]. Contribution of heroin to death was assessed following the model described by Stam et al. [11]. Deaths caused by other drugs were not considered in this study.

Results

Demographics

Males made up four out of five cases in both emergency department presentations and fatal overdoses (Fig. 1). Younger age groups made the majority of emergency presentations while, comparatively, there were more deaths in elderly populations.

Survived Overdoses

During the study period, 365 emergency department patients at UCSF and ZSFG were seen with the chief complaint or final diagnosis of "overdose." Of these, 176 visits were either not opioid-related (e.g., overdose related to acetaminophen) or not clearly opioid-related (e.g., final diagnosis was pneumonia) and, therefore, were excluded. A total of 189 patients were seen for opioid-related overdose and were included in the primary analysis. Seventy-eight percent were male with a median age of 37 years (IQR 30–49). There were no in-hospital deaths in this cohort. Substances consumed by patients included fentanyl ($N = 31$, 16%), heroin ($N = 2$, 1%), and non-specified opioid ($N = 153$, 81%). Following the shelter-in-place enactment period to April 18, UCSF and ZSFG emergency departments saw approximately 2.5 patients per day with opioid overdose, compared with 1.4 patients per day prior to this period (Fig. 2).

Fatal Overdoses

Of the 459 deaths received and accepted by the OCME in the first 109 days of the year in 2020, 121 were opioid-related accidental overdoses. Eighty-two percent were male. Age was unknown in three individuals. The median age for 118 patients with accidental death was 45 years (IQR 35–56). Of accidental overdose death, 95 (78%) were related to fentanyl, 13 (11%) related to heroin, and 13 (11%) related to fentanyl and heroin in

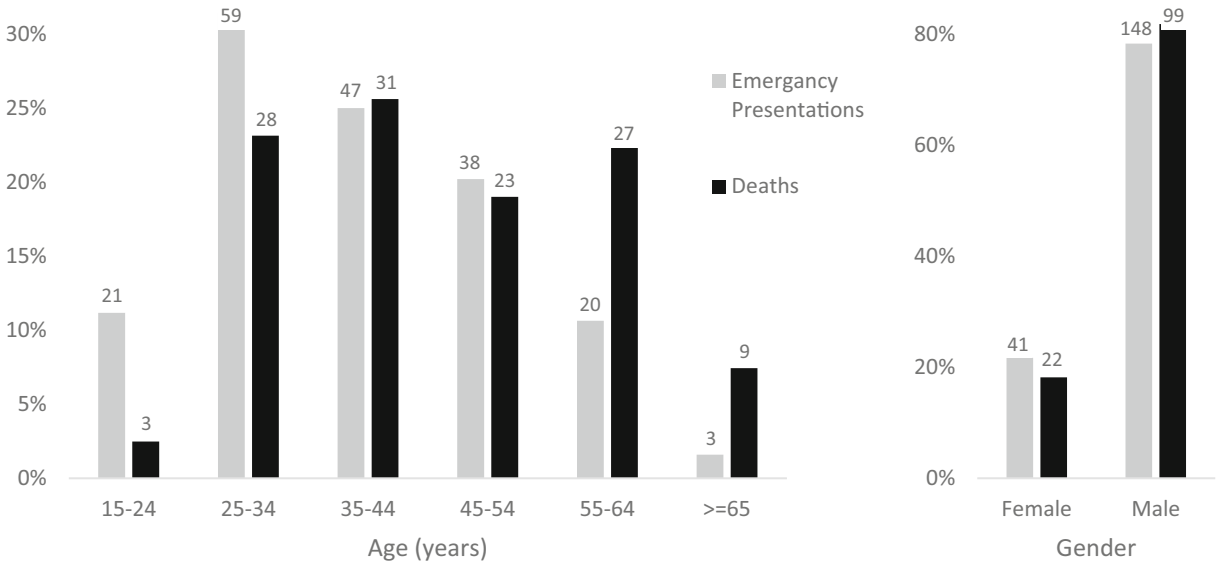


Fig. 1 Gender and ages of individuals who presented to the emergency department or accidentally died due to an opioid overdose from January 1 to April 18, 2020

combination. From March 16 to April 18, there were 1.47 deaths per day, compared with 0.95 deaths per day prior to this period (Fig. 2). In 2020, deaths per day were higher in April than preceding months (Fig. 3). Comparatively, deaths in the months of March and April in 2018 and 2019 were lower than in the month of February in each respective year.

Discussion

Individuals with substance use disorders, particularly those using opioids, are among vulnerable populations with an increased risk of drug-related harms and death during social distancing regulations [1, 12]. The delivery of harm reduction measures is difficult during this unprecedented time—persons who use drugs are more likely to use alone, seek out new sources for drugs as supply chains are disrupted, or use unclean supplies given reduced access to needle and syringe exchange programs [8, 9]. In addition, the risk of death may be increased for users of opioids due to the need for timely reversal treatment such as naloxone. The isolation that comes as a consequence of social distancing may also be a trigger for relapse [12]. Furthermore, reduced access to drug treatment programs and clinics presents as a further risk for relapsing to street-based drugs [13].

The increased number of overdoses seen during our study period may have been related to reduced observations of overdose events as a result of less foot traffic past overdosed individuals who use in public view, or decreased visitation to homes for those using drugs behind closed doors [14]. In addition, reversed overdoses that may not have typically presented to emergency departments and/or medical examiner offices may have become more severe in consequence and required medical and/or death investigation. Based on our results, it appears drug supplies have not been significantly impacted, at least in these initial months of the COVID-19 pandemic. It should also be noted that in recent years, San Francisco has continued to observe increases in fatal overdoses each year, demonstrated when comparing year-to-year total deaths in Fig. 3.

Several limitations exist from this study. First, data collected were only two large emergency departments in the city, but do not reflect all survived overdoses in the city. In addition, emergency department charts were queried for chief complaints and final diagnosis codes, which tend to vary in accuracy and completeness, and therefore, we may have omitted relevant cases or may have been observing an inaccurate, although likely consistent, trend. Furthermore, in most of our emergency department cases, the exact substance(s) contributing to overdose was unknown, resulting in a non-specified opioid chief complaint or final diagnosis. Other limitations include those inherent to cross-sectional studies of this type, such as the inability to establish causation or determine the directionality of relationships. Finally,

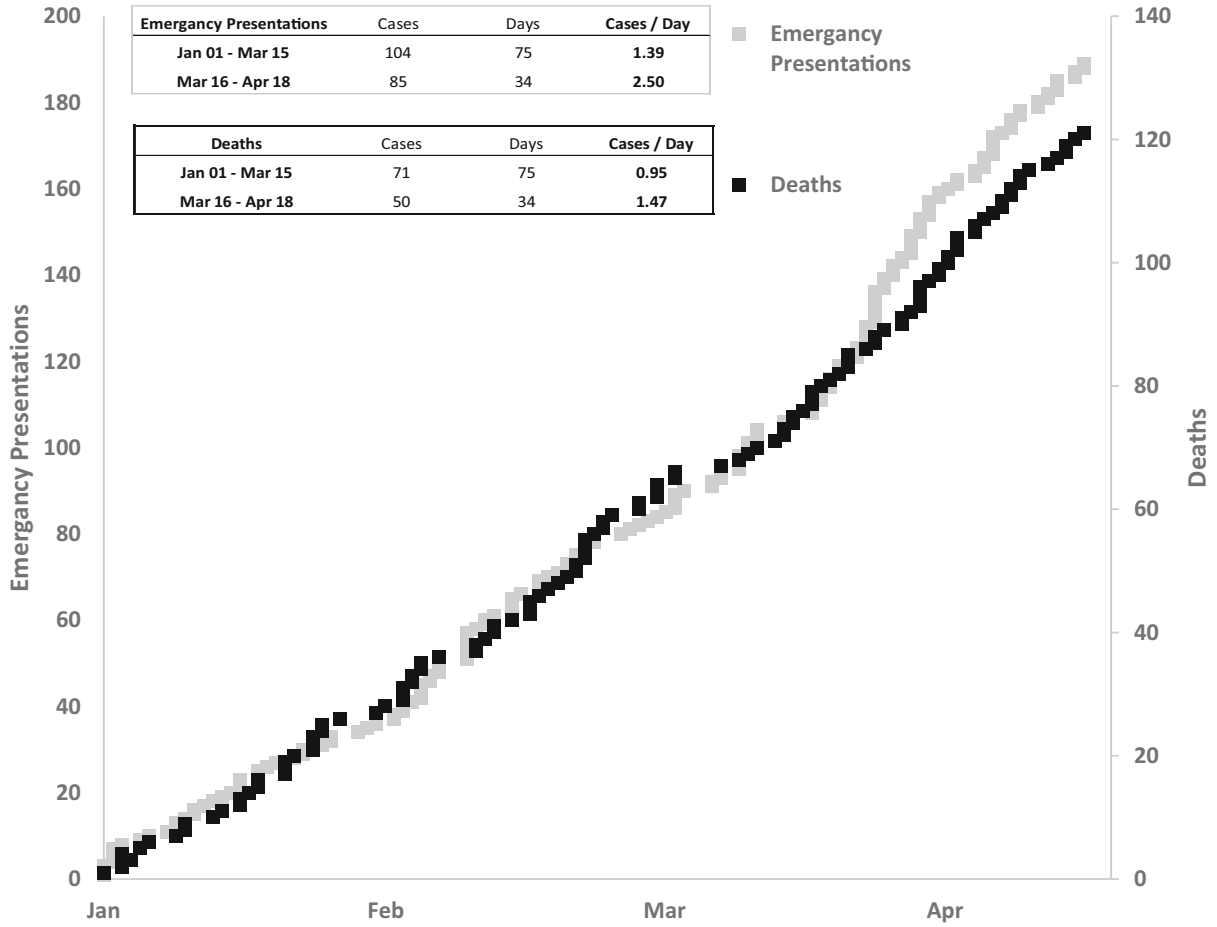
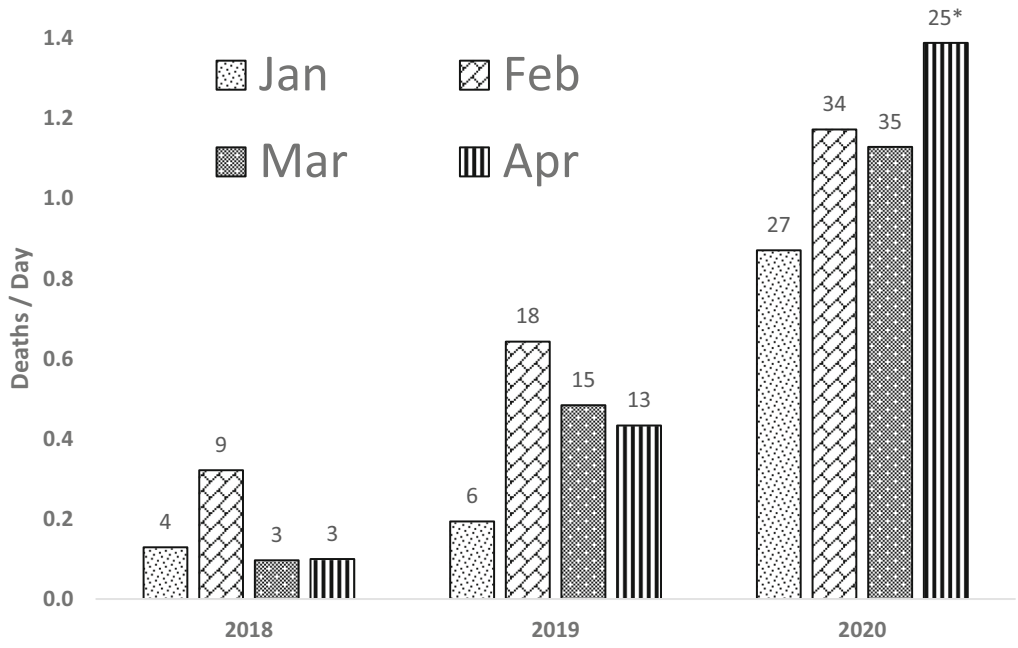


Fig. 2 Emergency department presentations and accidental deaths due to opioid overdose from January 1 to April 18, 2020, following shelter-in-place orders on March 16, 2020

individuals with opioid use disorder may also be particularly susceptible to COVID-19 complications due to substance use–related respiratory problems or hepatic insufficiency and may have affected our number of observed fatalities [14]. Such complications were not considered in this study.

As of April 18, 2020, 665,330 COVID-19-positive-confirmed cases were reported, resulting in 30,384 deaths nationwide [15]. At the same time in San Francisco, there were 1215 cases and 20 COVID-19 deaths [16]. The early enactment of protective measures to reduce the rate and amount of COVID-19 spread within a condensed major US city has likely led to the mitigation of thousands of cases and saving of many lives. Considering other major cities, even with the observed increases in drug overdose deaths, there is undoubtedly a total harm minimization. Furthermore, without San Francisco's developed public health measures to reduce drug harm in the community through resources such as widespread naloxone access and user support services, a larger increase in overdoses may have been observed [17]. Finally, San Francisco's comprehensive drug surveillance systems in UCSF and ZSFG emergency rooms, and OCME decedent investigations, may subsequently demonstrate emphasized overdose data relative to other populations with limited analysis, testing, and/or reporting.

The San Francisco Bay Area likely had the first death from COVID-19 back on February 6, 2020, in Santa Clara County [18]. Although the Bay Area was possibly among one of the first locations exposed in the country, early implementation of the aforementioned measures have proven effective to flatten-the-curve,



* *April 2020 contained cases only up until the study period of April 18.*

Fig. 3 Deaths per day and total deaths per month due to opioid overdose from January 1 to April 18, 2020. The asterisk indicates that April 2020 contained cases only up until the study period of April 18

contain the spread of COVID-19, and reduce overwhelming hospitals and, subsequently, deaths from COVID-19.

Conclusion

Anecdotal commentaries of either drug supply disruption, increased syringe requests, and/or overdoses have been reported in the media. Here, we describe that during the first weeks of a COVID-19 pandemic, emergency room presentations and deaths related to opioid overdose may increase during an isolation period. This report provides useful and immediate information for already strained hospitals, forensic facilities, and public health agencies that come under threat with a simultaneous viral pandemic and drug epidemic.

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