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Original Article

Trend analysis of drug overdose deaths before and during the COVID-19 pandemic

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Abstract: Data from a single state indicated there was an increase in opioid overdose related emergency services during the COVID-19 pandemic. The current study examined the provisional rolling 12-month drug overdose deaths between January 2019 and October 2021 at the national, state, and specific-drug levels, to identify trends in drug-overdose deaths before and during the COVID-19 pandemic. The trend in provisional U.S. drug overdose deaths accelerated at the beginning of the pandemic (December 2019). This acceleration slowed in the middle of pandemic (October 2020). Additionally, there was significant state and drug heterogeneity of drug overdose deaths.

Keywords: COVID-19, pandemic, overdose, opioids

Introduction

Opioid overdose related emergency services increased during the COVID-19 pandemic (January 14, 2020 to October 26, 2020) in Kentucky [1]. Similarly, there was a greater number of emergency department visits for non-fatal opioid overdoses during the first 4 months of the COVID-19 pandemic in Virginia [2]. These studies highlight a significant impact of the pandemic on the ongoing drug overdose epidemic, but only in individual states. The current study examined the provisional rolling 12-month drug-overdose deaths between January 2019 and October 2021 at the national, state, and specific-drug level.

Methods

Provisional death counts of drug overdose from January 1, 2019 to October 31, 2021 were obtained from the Centers for Disease Control and Prevention website [3]. Drug overdose deaths were identified using specific multiple cause-of-death International Classification of Diseases (ICD)-10 codes, including: T40.0 (opium), T40.1 (heroin); T40.2 (natural and semi-synthetic opioids, such as morphine, codeine, oxycodone, hydrocodone, hydromorphone, and oxymorphone), T40.3 (methadone), T40.4 (synthetic opioid analgesics other than methadone, such as fentanyl and tramadol), T40.5 (cocaine), T40.6 (other unspecified opioids), T43.6 (psychostimulants with abuse potential, such as methamphetamine). Opioid overdose deaths were identified by the presence of any of the following ICD-10 codes: T40.0, T40.1, T40.2, T40.3, T40.4, or T40.6.

Counts of the rolling 12-month deaths ending each month during the study period were plotted. Percentage changes at the monthly level were calculated by comparing the rolling 12 month deaths ending in any given month to the deaths ending in the previous month, using the latter as 100%. The percentage changes for each month were computed as input for trend analysis of the entire study period, for the best fit of the drug overdose deaths. A log-linear regression was carried out in the Stata software (version 16) with two turning points assumed for trend analysis [4, 5]. Subsequently, the trend analysis results were confirmed using Joinpoint software (NCI, NIH, version March 2021). With turning points identified in the trend analysis, state-specific rolling 12 months drug overdose deaths ending October 2021 were compared with that ending in December

2019 (the identified first turning point), using the latter as 100% for each state. Only the states with no less than 90% of reporting completeness on drug types were included. Differences in the proportion of drug types were analyzed using Chi-square test. A *p*-value < 0.05 was considered significant.

Results

The provisional 12-month deaths from drug overdose ending on January 1, 2019, were 67,697 and those ending on October 31, 2021, were 101,035. There were significant increases over time (33,338 or 49.01%). More importantly, when monthly percentage changes (MPC) were used to examine the pattern of increase, statistical analysis fitted the entire study period into three phases: January 2019 to December 2019, MPC=0.41; December 2019 to October 2020, MPC=2.70; October 2020 to October 2021, MPC=0.92 (**Figure 1A**). MPCs during the pandemic were higher than before the pandemic (P < 0.001 for both), suggesting that drug overdose deaths became worse during the pandemic.

There was state heterogeneity in the uptrend of drug overdose deaths. As December 2019 was identified by statistical analysis as a turning point, the drug overdose deaths for each state in the rolling 12 months ending December 2019 was used as a baseline to calculate the percentage of increase of the rolling 12 months ending October 2021. While several states exhibited only modest percentages of increase (**Figure 1B**, dark blue color), several other states exhibited strikingly higher percentages of increase (dark red color).

There was also heterogeneity in the proportions of types of drugs causing deaths. The proportion of opioid deaths slightly decreased from December 2019 (60.79%) to October 2021 (59.05%, P < 0.001). Cocaine, heroin, and prescription opioids all exhibited a decrease in their respective proportions in drug overdose deaths. Notably, the proportions of synthetic opioid overdose deaths and psychostimulants with abuse potential both increased during the same time period (**Figure 1C**, 44.34% to 51.41%, P < 0.001 and 19.80% to 23.66%, P < 0.001, respectively), attenuating the decreasing trends in opioids and other drugs existing prior to the COVID-19 pandemic [6]. The trend analyses by drug type showed that the proportion of opioid deaths among all drug overdose deaths had an increasing trend during March 2020 to January 2021 (MPC=0.177, 95% confidence intervals [CI], 0.141 to 0.213, P < 0.001), which however, was attenuated after January 2021 (MPC=-0.424, 95% CI, -0.46 to -0.388, P < 0.001, **Table 1**). Strikingly, the proportions of synthetic opioid overdose deaths and psychostimulant deaths increased throughout the study period of January 2019 to October 2021, respectively (**Table 1**). The proportions of synthetic opioid overdose deaths increased most during November 2019 to December/2020 (MPC=1.177, 95% CI, 1.107 to 1.247) and those of psychostimulants increased most during July 2020 to October 2021 (MPC=1.088, 95% CI, 1.029 to 1.146) and appeared to continue an increasing trend.

Discussion

The trend of provisional U.S. drug overdose deaths accelerated at the beginning of the COVID-19 pandemic (December 2019). This acceleration has slowed since the middle of pandemic (October 2020) which appeared to coincide with the rollout of mass vaccination in the U.S. [7] although the MPC was still higher than pre-pandemic (January 2019 to December 2019). It is interesting to speculate that psychosocial stressors during the early phase of the pandemic might have contributed to the steep acceleration in monthly percentage increase, which partially subsided with the resolution of first COVID-19 wave around August 2020. Additionally, there was significant state and drug heterogeneity of drug overdose deaths. The increasing trends in the proportion of synthetic opioid overdose deaths and psychostimulant deaths are particularly concerning. As such, while the COVID-19 pandemic overall accelerated drug-overdose epidemic, the heterogeneity in drug-overdose deaths argues for state- or region-specific and drug-specific strategies to combat the epidemic.

This study has several limitations. Death numbers were provisional and included both U.S. residents and foreigners, while the foreigners' deaths were usually in the 200s and were excluded in the final counts [3]. Compared to multiple variable regression analysis, trend analysis focuses on the trajectory of changes

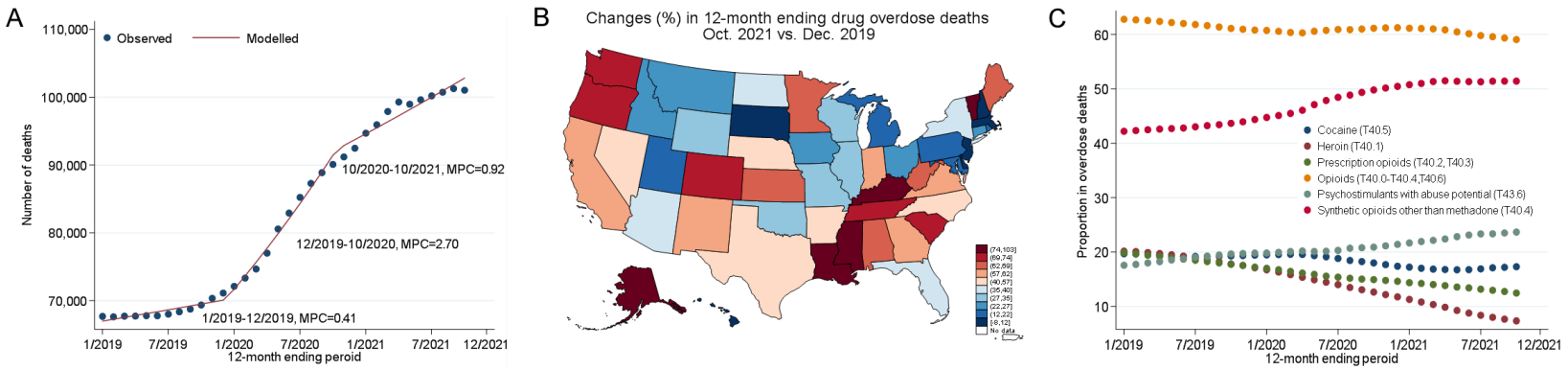

Figure 1. Trend analysis of drug-overdose deaths before and during the COVID-19 pandemic. A. Trend analysis of 12-month ending drug overdose deaths in the U.S. from January 2019 to October 2021; B. Heatmap of state-specific drug-overdose deaths increase (%) from December 2019 to October 2021; C. Proportion of drug types in drug overdose deaths over time. MPC: monthly percentage change.

Table 1. Trends in proportions of specific drugs in the months ending in Oct. 2021: drug-overdose deaths over time by drug type

Drug type (ICD-10 code)	Jan. 2019	Oct. 2021	Trend segment 1			Trend segment 2			Trend segment 3		
	N (%)	N (%)	Dates	MPC (95% CI)	P	Dates	MPC (95% CI)	P	Dates	MPC (95% CI)	P
Cocaine (T40.5)	14,731 (19.68)	22,216 (17.29)	1/2019-5/2020	-0.011 (-0.086 to 0.065)	0.776	5/2020-3/2021	-1.486 (-1.663 to -1.309)	< 0.001	3/2021-10/2021	0.449 (0.185 to 0.714)	0.002
Heroin (T40.1)	15,089 (20.15)	9,424 (7.34)	1/2019-12/2019	-1.486 (-1.625 to -1.347)	< 0.001	12/2019-12/2020	-3.135 (-3.271 to -2.997)	< 0.001	12/2020-10/2021	-4.77 (-4.925 to -4.614)	< 0.001
Natural & semi-synthetic opioids, including methadone (T40.2, T40.3)	14,880 (19.87)	15,993 (12.45)	1/2019-8/2020	-1.434 (-1.478 to -1.39)	< 0.001	8/2020-3/2021	-1.167 (-1.418 to -0.915)	< 0.001	3/2021-10/2021	-1.655 (-1.853 to -1.457)	< 0.001
Opioids (T40.0-T40.4, T40.6)	46,996 (62.77)	75,853 (59.05)	1/2019-3/2020	-0.294 (-0.312 to -0.275)	< 0.001	3/2020-1/2021	0.177 (0.141 to 0.213)	< 0.001	1/2021-10/2021	-0.424 (-0.46 to -0.388)	< 0.001
Psychostimulants with abuse potential (T43.6)	13,142 (17.55)	30,388 (23.66)	1/2019-10/2019	1.273 (1.147 to 1.399)	< 0.001	10/2019-7/2020	0.356 (0.206 to 0.505)	< 0.001	7/2020-10/2021	1.088 (1.029 to 1.146)	< 0.001
Synthetic opioids, excluding methadone (T40.4)	31,585 (42.19)	66,035 (51.41)	1/2019-11/2019	0.381 (0.290 to 0.472)	< 0.001	11/2019-12/2020	1.177 (1.107 to 1.247)	< 0.001	12/2020-10/2021	0.117 (0.026 to 0.207)	0.014

MPC, monthly percentage change; CI, confidence intervals; ICD-10, International classification of diseases, 10th edition.

without considering some confounding variables. Opioid overdose deaths could include multiple substances; hence, the proportion of deaths when combined was higher than 100 percent. The accelerated trend in drug-overdose deaths starting in December 2019 coincided with the timing of COVID-19 pandemic emergence. However, this coincidence does not necessarily suggest a causal relationship between the two.

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Disclosure of conflict of interest

None.

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