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Naloxone administration among opioid-involved overdose deaths in 38 United States jurisdictions in the State Unintentional Drug Overdose Reporting System, 2019

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Abstract

Background: The majority of drug overdose deaths in the United States involve opioids, and synthetic opioid-involved overdose death rates are increasing. Naloxone is a key prevention strategy yet estimates of its administration are limited.

Methods: We analyzed 2019 data from 37 states and the District of Columbia in CDC's State Unintentional Drug Overdose Reporting System to estimate the percentage of decedents, by sociodemographic subgroup, who experienced a fatal opioid-involved overdose and had no evidence of naloxone administration.

Results: A total of 77.3% of 33,084 opioid-involved overdose deaths had no evidence of naloxone administration. Statistically significant subgroup differences were observed for all sociodemographic groups examined except housing status. The highest percentages of decedents lacking evidence of naloxone administration were those with highest educational attainment (doctorate or professional degree, 87.0%), oldest (55–64 years, 83.4%; 65 years, 87.3%) and youngest ages (<15 years, 87.5%), and single marital status (84.5%). The lowest percentages of no evidence of naloxone administration were observed for non-Hispanic American Indian/Alaskan Native persons (66.2%) and those ages 15–24 years (70.8%).

Conclusions: More than three-quarters of opioid-involved overdose deaths had no evidence of naloxone administration, underscoring the need to ensure sufficient naloxone access and capacity for utilization. While fatal overdose data cannot fully characterize sociodemographic disparities in naloxone administration, naloxone education and access efforts can be informed by apparent inequities. Public health partners can assist persons who use drugs (PWUD) by maintaining

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Contributors

KQ conceived the study, conducted data analyses, interpreted the data, and wrote the manuscript. SK conceived the study, conducted data analyses, interpreted the data, and revised the manuscript. CH conceived the study, interpreted the data, and revised the manuscript. JO conceived the study, conducted data analyses, interpreted the data, and revised the manuscript. ND interpreted the data and reviewed and revised the manuscript. All authors approved the final article.

Conflict of interest

No conflict declared.

CDC disclaimer

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naloxone supply and amplifying messages about the high risk of using drugs alone among PWUD and their social networks.

Keywords

Naloxone; Harm reduction; Opioid-involved overdose; Overdose mortality; Health disparities

1. Introduction

In 2020, 74.8% of 91,799 drug overdose deaths in the United States involved opioids, and 61.6% involved synthetic opioids, which likely consisted largely of illicitly manufactured fentanyl (IMFs) (CDC WONDER). Preliminary 2021 data suggest that overall drug and synthetic opioid-involved overdose death rates continue to increase (Ahmad et al., 2021). Naloxone is an opioid antagonist medication that can reverse the effects of an opioid overdose when administered in time and is a key overdose prevention strategy.

Evidence suggests that efforts to increase naloxone awareness and access, including through community distribution, can be effective in preventing deaths from opioid overdose (Irvine et al., 2018; McClellan et al., 2018; Mueller et al., 2015; Giglio et al., 2015; Walley et al., 2013; Wheeler et al., 2015). Access to naloxone among laypersons and co-drug use partners and education about overdose recognition and naloxone administration in the general population are critical given the increasing availability of highly potent IMFs in the illicit drug supply. However, stigmatization of persons who use drugs (PWUD), misconceptions that naloxone access increases high-risk drug use, and fear of legal repercussions may hinder naloxone distribution and use, and therefore, its life-saving potential (Lai et al., 2021; Dayton et al., 2020; Crabtree and Masuda, 2019; Carson, 2019; Sisson et al., 2019).

U.S. population estimates of naloxone administration are elusive because naloxone can be administered by various trained and untrained people, including EMS personnel and other first responders, co-drug use partners, and other bystanders, making utilization difficult to monitor. Studies of naloxone administration, access (including ongoing access), and training in subpopulations (e.g., PWUD, individuals with health care coverage, persons receiving EMS response/treatment for an overdose) suggest sociodemographic inequities (Kinnard et al., 2021; Geiger et al., 2020; Dayton et al., 2020; Kim et al., 2020; Ong et al., 2020; Barboza and Angulski, 2020; Reed et al., 2019; Jones et al., 2016; Rowe et al., 2015).

We used data from the Centers for Disease Control and Prevention's (CDC) State Unintentional Drug Overdose Reporting System (SUDORS) to estimate the percentage of decedents who experienced an opioid-involved overdose that potentially could have been reversed with naloxone yet had no evidence of naloxone administration. We also investigated whether sociodemographic subgroup differences in naloxone administration exist in this sample of U.S. overdose decedents.

2. Methods

Data on unintentional and undetermined intent drug overdose deaths that occurred in 37 states and the District of Columbia in 2019 were included. Four jurisdictions reported data

for January-June; six reported data for July-December, and 28 reported data for the full year. Twenty-eight jurisdictions reported data on all overdose deaths, and ten reported data for a subset of counties accounting for an estimated 75% of drug overdose deaths in the jurisdiction. Jurisdictions abstracted data from death certificates and medical examiner/coroner reports, including death scene investigation findings and all drugs detected by postmortem toxicology testing; only cases with medical examiner/coroner reports were included.¹ Data for 2020 were not included to avoid potential emerging trends associated with the COVID-19 pandemic, such as possible changes in naloxone access and drug-use behaviors (e.g., possible changes in PWUD using drugs alone) (Ali et al., 2021).

We classified deaths as having no evidence of naloxone administration (hereafter “no naloxone”) if there was no scene and no witness evidence to suggest naloxone was administered by a layperson, EMS responder, law enforcement officer, firefighter, or health care worker in an emergency room, hospital, or critical care center; or if toxicology testing did not detect naloxone. If buprenorphine and naloxone were detected by toxicology testing, deaths were classified as no naloxone (absent scene evidence) to avoid misclassifying decedents with the combination buprenorphine-naloxone in their system, which is used to treat opioid use disorder.

We examined percentages of no naloxone among deaths with at least one opioid (with or without co-involvement of other drugs) as a cause of death (COD), for seven sociodemographic characteristics: age, sex, race/ethnicity, educational attainment, marital status, housing status, and military service. Cases with missing or unknown values were excluded from subgroup analyses. Frequencies and percentages of no naloxone were estimated in SAS 9.4, SAS Institute. Chi square tests were used to assess subgroup differences; $p < 0.05$ was considered statistically significant.

3. Results

Thirty-eight jurisdictions reported 40,288 overdose deaths during 2019. Of these deaths, 82.1% (33,804) involved at least one opioid as a COD. Among opioid-involved overdose deaths, 77.3% were classified as no naloxone. Among the 6484 decedents without an opioid as a COD, 85.8% were classified as no naloxone (not shown and excluded from further analyses). We observed statistically significant subgroup differences in no naloxone opioid-involved overdose deaths for all sociodemographic characteristics other than housing status (Table 1).

We highlight subgroups with percentages of no naloxone that were 5% higher or lower than the overall percentage among opioid-involved deaths (77.3%). The oldest age groups were among the highest percentages of no naloxone (83.4% for 55–64 years and 87.2% for 65 years); the percentage for those < 15 years was 87.5% but represented only 35 decedents. Those with the highest educational attainment (doctorate or professional degree),

¹For additional SUDORS description see O'Donnell, J., Gladden, R.M., Kariisa, M., Mattson, C.L., 2021. Using death scene and toxicology evidence to define involvement of heroin, pharmaceutical morphine, illicitly manufactured fentanyl and pharmaceutical fentanyl in opioid overdose deaths, 38 states and the District of Columbia, January 2018–December 2019. *Addiction*. 1–8. DOI: [10.1111/add.15768](https://doi.org/10.1111/add.15768).

single, not otherwise specified decedents, and current or former military personnel were also among subgroups with the highest percentages of no naloxone (87.0%, 84.5%, and 82.3%, respectively). In contrast, the subgroups with the lowest percentages of no naloxone were non-Hispanic American Indian/Alaskan Native persons (66.2%) and those ages 15–24 years (70.8%).

4. Discussion

SUDORS data allow us to investigate patterns in reported naloxone administration among overdose decedents that may inform public health strategies and overdose prevention policies. The vast majority had no evidence of naloxone administration. These findings are concerning because of the large proportion of overdose deaths that involve opioids, and, in particular, highly-potent IMFs, for which early and sufficient naloxone administration is critical for survival (O'Donnell et al., 2021). The low percentages of naloxone administration, however, may also reflect naloxone's success, when administered, because the current analysis included only overdose deaths.

Approximately one in five decedents had evidence of naloxone administration that did not prevent the fatal overdose. Information on timing of naloxone administration and whether naloxone was administered appropriately was not available. Fentanyl's short duration of effect may increase frequency of its use, potentially leading to the need for more frequent naloxone administration in addition to the potential need for multiple doses (Kim et al., 2019; Moss and Carlo, 2019). In April 2021, the U.S. Food and Drug Administration approved a higher dose naloxone hydrochloride nasal spray (8 milligrams (mg) versus 2 mg and 4 mg products previously) (USFDA, 2021). SUDORS 2019 data reflect the period before this dosage increase but during which time fatal overdoses involving IMFs and co-use of stimulants and opioids increased (Mattson et al., 2021; O'Donnell et al., 2020a, 2020b). Further, naloxone's duration of effect depends on dose, route of administration, and overdose symptoms (Boyer, 2012). Resuscitation efforts to support breathing and prolonged monitoring for possible return of overdose symptoms are important aspects of post-naloxone care (Boyer, 2012; WHO, 2014). Both the failure to administer naloxone and the administration of naloxone without achieving overdose reversal are adverse outcomes. In addition to increasing naloxone use, mortality prevention strategies can focus on ensuring sufficient doses are administered appropriately in a timely fashion and follow-up care is provided. Both strategies require another person to be present, highlighting the importance of not using drugs alone.

We observed statistically significant differences in the percentages of decedents with no naloxone evidence in all but one of the sociodemographic groups examined, though not all were of substantial magnitude (e.g., only a 2.1% difference between males and females). It is important to interpret findings in the context of the population represented by SUDORS data, i.e., people who died from a drug overdose. Without the complement of those who overdosed and survived, we cannot fully characterize disparities. Stigma towards PWUD varies by the sociodemographic characteristics of both the persons with potentially stigmatizing attitudes and the PWUD (Goodyear and Chavanne, 2020). It is possible that an especially high percentage of no naloxone among some subgroups is influenced by stigma

that impacts naloxone use and/or bias in acknowledging risk of drug overdose among certain populations. For example, 87% no naloxone was observed among those with a PhD or professional degree; however, higher SES individuals may not be well-represented in this sample if they were more likely to survive a drug overdose. Similarly, the high no naloxone among the 65 + age group (87%) might be influenced by misconceptions about low illicit and prescription drug misuse among elderly populations.

Individual, societal, and policy-level factors may play a role in naloxone's administration, which may in turn contribute to sociodemographic differences. Overdose circumstances, such as place (e.g., at home vs. in public, rural vs. urban setting) and presence and type of bystanders to administer naloxone appropriately, are important. Community access to and use of naloxone may be related to funding, training for EMS personnel and other first responders and laypersons, and Good Samaritan laws. Such multi-level influences are suggested by studies of unhoused PWUD for whom inadequate naloxone availability may be associated with this population's greater exposure to public drug use and overdose, more frequent need for naloxone administration, and thus greater need for refills; (Kinnard et al., 2021; Trayner et al., 2020; Deonarine et al., 2016).

Challenges to obtaining high quality overdose data include stigma, legal ramifications, and resources. Data abstraction relies on source data (e.g., death certificates, medical examiner/coroner reports, and toxicology results) that vary in availability and quality across jurisdictions. Misclassification bias may stem from the inclusion of 13,267 decedents (40% of opioid-involved overdose deaths) with unknown naloxone status in the no evidence of naloxone group, and naloxone administration may be higher than 22.7%. Despite limitations to estimating naloxone administration and sociodemographic disparities, this analysis suggests that a high proportion of people who died from opioid-involved overdose in the U.S. in 2019 did not receive naloxone, which might have reversed overdoses and saved lives.

A range of approaches is needed to make naloxone ubiquitous and easily accessible to laypersons as well as EMS personnel and other first responders. The Office of National Drug Control Policy announced the release of a model law that provides states with a potential roadmap for expanding naloxone access and availability (LAPPA, 2021). Expanding access is important as studies have found low rates of the following: co-prescribing naloxone to people with both opioid and benzodiazepine prescriptions; dispensing naloxone prescriptions to those presenting in emergency departments for drug overdose, opioid use disorder, or withdrawal; using insurance to obtain naloxone; and accessing naloxone from retail pharmacies (Guy et al., 2021; Kilaru et al., 2021; Lin et al., 2020; Follman et al., 2019). Further, focusing on such avenues may exacerbate disparities in naloxone access given unequal access to care. Evidence suggests that community-based efforts (e.g., distribution in public place and through syringe service programs, training laypersons) have the potential to be an effective route for reducing fatal overdoses (Irvine et al., 2018; McClellan et al., 2018; Mueller et al., 2015; Giglio et al., 2015; Walley et al., 2013; Wheeler et al., 2015). Innovative approaches used during the COVID-19 pandemic, such as mail-based naloxone, may reduce gaps in naloxone access and use (Wenger et al., 2021). Cultural competence in overdose prevention strategies, such as engaging social networks and

peer educators, will likely be crucial to engaging subpopulations in the use of naloxone. (Dayton et al., 2020).

5. Conclusions

Ongoing efforts by CDC and participating SUDORS jurisdictions to improve the quality of drug overdose data through partnerships and resources for medicolegal death investigators, medical examiners and coroners, and forensic toxicologists are critical to identify gaps in overdose mortality prevention, such as naloxone administration. Future research could aim to link fatal and nonfatal overdose data to better characterize disparities in naloxone administration and successful or unsuccessful use. Analyses of geographic and temporal trends, which may be influenced by variation in programs and policies, the COVID-19 pandemic, and other factors, may inform our understanding of naloxone outcomes. Because inter-related individual and societal factors likely influence naloxone outcomes through various pathways, multivariable models could attempt to examine the influences of overdose circumstances (e.g., rapid onset overdose, EMS response time, presence of bystanders) and whether they differ by sociodemographic characteristics. While surveillance and research are being advanced, public health partners can assist PWUD to maintain adequate naloxone supply and amplify messages about the high risk of using drugs alone among PWUD and their social networks.

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Table 1

Evidence of naloxone administration among opioid-involved overdose deaths by sociodemographic characteristics, State Unintentional Drug Overdose Reporting System (SUDORS), 38 jurisdictions in the United States^a, 2019^b, N = 33,084.

Total	No evidence of naloxone		Evidence of naloxone	
	Number 25,564	Percent 77.3	Number 7520	Percent 22.7
Sex (n = 0 missing/unknown)				
Male	18,062	77.9	5130	22.1
Female	7502	75.8	2390	24.2
Race/ethnicity (n = 310 missing/unknown)				
White, non-Hispanic	18,683	77.6	5381	22.4
Black, non-Hispanic	4029	76.5	1237	23.5
American Indian/Alaskan native, non-Hispanic	196	66.2	100	33.8
Asian/Pacific Islander, non-Hispanic	139	80.8	33	19.2
Multi-race, non-Hispanic	149	72.0	58	28.0
Hispanic	2118	76.5	651	23.5
Age (years) (n = 4 missing/unknown)				
Under 15	35	87.5	5	12.5
15–24	1612	70.8	666	29.2
25–35	6557	73.3	2391	26.7
35–44	6633	76.2	2072	23.8
45–54	5467	79.7	1389	20.3
55–64	4278	83.4	853	16.6
65 +	978	87.2	144	12.8
Educational attainment (n = 1085 missing/unknown)				
8th grade or less	736	78.6	200	21.4
9–12th grade, no diploma	4077	74.9	1365	25.1
High school graduate or GED	13,096	77.4	3825	22.6
College credit, no degree	3648	76.1	1149	23.9
Associate's degree	1430	78.5	391	29.5
Bachelor's degree	1365	81.1	318	18.9
Master's degree	248	80.8	59	19.2
Doctorate or professional degree	80	87.0	12	13.0
Military service (n = 1864 missing/unknown)				
No military service	22,757	77.3	6670	22.7
Current or former military personnel	1475	82.3	318	17.7
Housing status (n = 2171 missing/unknown)				
Not experiencing homelessness	22,828	77.1	6766	22.9
Experiencing homelessness	1021	77.4	298	22.6

Total	No evidence of naloxone		Evidence of naloxone	
	Number 25,564	Percent 77.3	Number 7520	Percent 22.7
Marital status (n = 617 missing/unknown)				
Married, civil union, domestic partnership	3886	74.8	1313	25.2
Never married	14,102	76.2	4415	23.8
Widowed	902	81.8	201	18.2
Divorced	5485	80.7	1312	19.3
Married, civil union, domestic partnership, separated	496	77.7	142	22.3
Single, not otherwise specified	180	84.5	33	15.5

Chi-squared tests compared categories within each sociodemographic characteristic and were statistically significant for all at $p < 0.0001$, except for housing status ($p = 0.8$).

^a38 jurisdictions include the following states and District of Columbia: Alaska, Arizona, Colorado, Connecticut, Delaware, Florida, Georgia, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Dakota, Tennessee, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin.

^bFlorida, Louisiana, Maryland, and Michigan reported data for only January- June 2019. Arizona, Colorado, Kansas, Montana, Oregon, and South Dakota reported data for only July-December 2019.