Methamphetamine-Related Mortality in the United States: Co-Involvement of Heroin and Fentanyl, 1999–2021

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Objectives. To examine trends in methamphetamine-related mortality in the United States from 1999 to 2021 and the extent to which these deaths co-involved heroin or fentanyl.

Methods. We obtained final and provisional data from the CDC WONDER (Centers for Disease Control and Prevention Wide-ranging ONline Data for Epidemiologic Research) multiple causes of death database for deaths that involved methamphetamine and deaths that involved both methamphetamine and heroin or fentanyl mong US residents aged 15 to 74 years. We plotted the age-adjusted methamphetamine-related mortality rate by year and quantified the proportion of deaths with heroin or fentanyl co-involvement. Finally, we used joinpoint regression to quantify trends in the methamphetamine mortality rate and proportion of deaths with heroin or fentanyl co-involvement.

Results. From 1999 to 2021, there was a 50-fold increase in the methamphetamine mortality rate, which was accompanied by an increasing proportion of deaths that co-involved heroin or fentanyl, peaking at 61.2% in 2021.

Conclusions. Unprecedented increases in methamphetamine-related mortality have occurred during the last decade, and an increasing proportion of these deaths co-involved heroin or fentanyl.

Public Health Implications. Stark increases in methamphetamine-related mortality and heroin or fentanyl co-involvement warrant robust harm reduction efforts, especially for people who engage in polysubstance use. (*Am J Public Health*. Published online ahead of print February 2, 2023:e1–e4. https://doi.org/10.2105/AJPH.2022.307212)

AJPH Published online ahead of print February 2, 2023

A staggering increase in drug overdose deaths was observed in the United States in 2020.[1] Moreover, the Centers for Disease Control and Prevention (CDC) reported that 2021 included the deadliest rolling 12-month period for drug overdose deaths on record thus far.[2] Prepandemic data show upward trends in methamphetamine use,[3] methamphetamine and heroin co-use,[4] and methamphetamine-related mortality in the United States.[3] In 2019, more than half of all psychostimulant overdose deaths also involved opioids,[5] suggesting that the second (i.e., heroin) and third (i.e., fentanyl) waves of the opioid overdose crisis may be driving recent methamphetamine-related mortality. Given the steep increases in overall drug overdose mortality observed in 2020 and 2021,[1,2] an updated examination of the trends in methamphetamine-related mortality is warranted. Moreover, it is critical to contextualize these deaths within the ongoing opioid overdose crisis by examining the extent to which methamphetamine-related mortality may be exacerbated by the co-involvement of heroin and fentanyl.

Qualitative data suggest that the co-use of methamphetamine and opioids is motivated by a desire to achieve specific embodied experiences not attained by methamphetamine or opioid use alone.[6] Moreover, a recent qualitative study suggests that there is significant variation in the presentation and severity of stimulant-involved overdoses ("overamping"), which may limit the ability of people who use stimulants to recognize and respond to an overdose.[7] The last 2 decades have also been marked by increased contamination of the unregulated drug

supply with fentanyl and fentanyl-related analogs,[8,9] suggesting that intentional and unintentional co-use may be catalyzing methamphetamine-related mortality in the United States. In this descriptive epidemiological analysis, we quantify the trends in methamphetamine-related mortality and the proportion of these deaths that also involved heroin or fentanyl, including time-sensitive changes not captured in prepandemic data.

METHODS

We obtained 1999–2021 death certificate data from the CDC Wide-ranging ONline Data for Epidemiologic Research (WONDER) final (for 1999 through 2020) and provisional (for 2021) multiple causes of death databases.[10] We examined the annual number of deaths involving methamphetamine and the age-adjusted overdose mortality rates per 100 000 population among US residents aged 15 to 74 years. We included causes of death in the following categories (*International Classification of Diseases, 10th Revision* codes): accidental/unintentional poisoning (X40–X44), intentional self-poisoning/suicide (X60–X64), assault/homicide (X85), and undetermined intent (Y10–Y14). In addition, methamphetamine-related deaths included deaths with a contributing cause of poisoning by psychostimulants with abuse potential (T43.6). We then examined what proportion of methamphetamine-related deaths co-involved heroin (T40.1) or other synthetic narcotics (T40.4; i.e., fentanyl and fentanyl-related analogs) each year. As a post hoc analysis for comparison, we also examined the annual number of cocaine-related deaths (T40.5), age-adjusted cocaine mortality rate, and the proportion of cocaine-related deaths that also included heroin or fentanyl over the same time period.

We quantified trends in the age-adjusted methamphetamine mortality rate and proportion of deaths with heroin or fentanyl co-involvement using joinpoint regression, which uses permutation to fit a series of straight lines on a logarithmic scale to aggregated data to estimate annual percent change (APC) trends of variable length and the slopes of these trends (*b*). We also estimated 95% confidence intervals (CIs) with each APC and reported the corresponding *P* value. The APC was considered statistically significant if the *P* value was less than .05. We conducted analyses with Stata/MP version 17.0 (StataCorp LP, College Station, TX) and Joinpoint Regression Program version 4.9.1.0 (National Cancer Institute, Bethesda, MD https://surveillance.cancer.gov/joinpoint/).

RESULTS

From 1999 to 2021, there were 135 433 methamphetamine-related deaths among US residents aged 15 to 74 years, and 42.8% of these deaths also involved heroin or fentanyl. Across these 23 years of data, there was a 58-fold increase in the annual number of methamphetamine-related deaths (545 methamphetamine-related deaths in 1999 vs 32 353 methamphetamine-related deaths in 2021; Figure 1, panel a) and more than a 50-fold increase in the age-adjusted methamphetamine-related mortality rate (0.27 deaths per 100 000 in 1999 vs 13.93 deaths per 100 000 in 2021; Figure 1, panel b). Annual co-involvement of heroin or fentanyl ranged from 7.3% (2005) to 61.2% (2021), with stark increases observed over the last decade. Post hoc analyses suggest there have also been increases in cocaine-related mortality and co-involvement with heroin or fentanyl, but these trends were more variable over time (Figure A, available as a supplement to the online version of this article at http://www.ajph.org).

The age-adjusted methamphetamine-related mortality rate increased annually by 20.1% from 1999 to 2005 (APC = 20.1%; 95% CI = 14.9, 25.6; $P < .001$; $b = 0.18$), remained stable from 2005 to 2008 (APC = −8.6%; 95% CI = −29.7, 18.8; $P > .05$; $b = -0.09$), continued to increase 21.8% annually from 2008 to 2014 (APC = 21.8%; 95% CI = 14.9, 29.1; $P < .001$; $b = 0.20$), and further increased by 32.5% annually from 2014 to 2021 (APC = 32.5%; 95% CI = 28.0, 37.2; $P < .001$; $b = 0.28$). The proportion of methamphetamine-related deaths with heroin or fentanyl co-involvement decreased by 6.6% annually from 1999 to 2005 (APC = −6.6%; 95% CI = −9.4, −3.6; $P < .001$; $b = -0.07$), increased by 8.9% annually from 2005 to 2010 (APC = 8.9%; 95% CI = 2.7, 15.5; $P < .01$; $b = 0.09$), and increased by 17.3% annually from 2010 to 2021 (APC = 17.3%; 95% CI = 15.8, 18.8; $P < .001$; $b = 0.16$).

DISCUSSION

Consistent with overall drug overdose deaths observed in 2020 and 2021,[1,2] our results suggest that methamphetamine-related mortality has accelerated over the last 2 decades, peaking in 2021. Importantly, this was accompanied by a dramatic growth in the percentage of these deaths that co-involved heroin or fentanyl. The proportional increases in methamphetamine-related mortality and illicit opioid involvement suggest that these stimulant deaths are largely driven by polysubstance use. Intentional

AJPH Published online ahead of print February 2, 2023

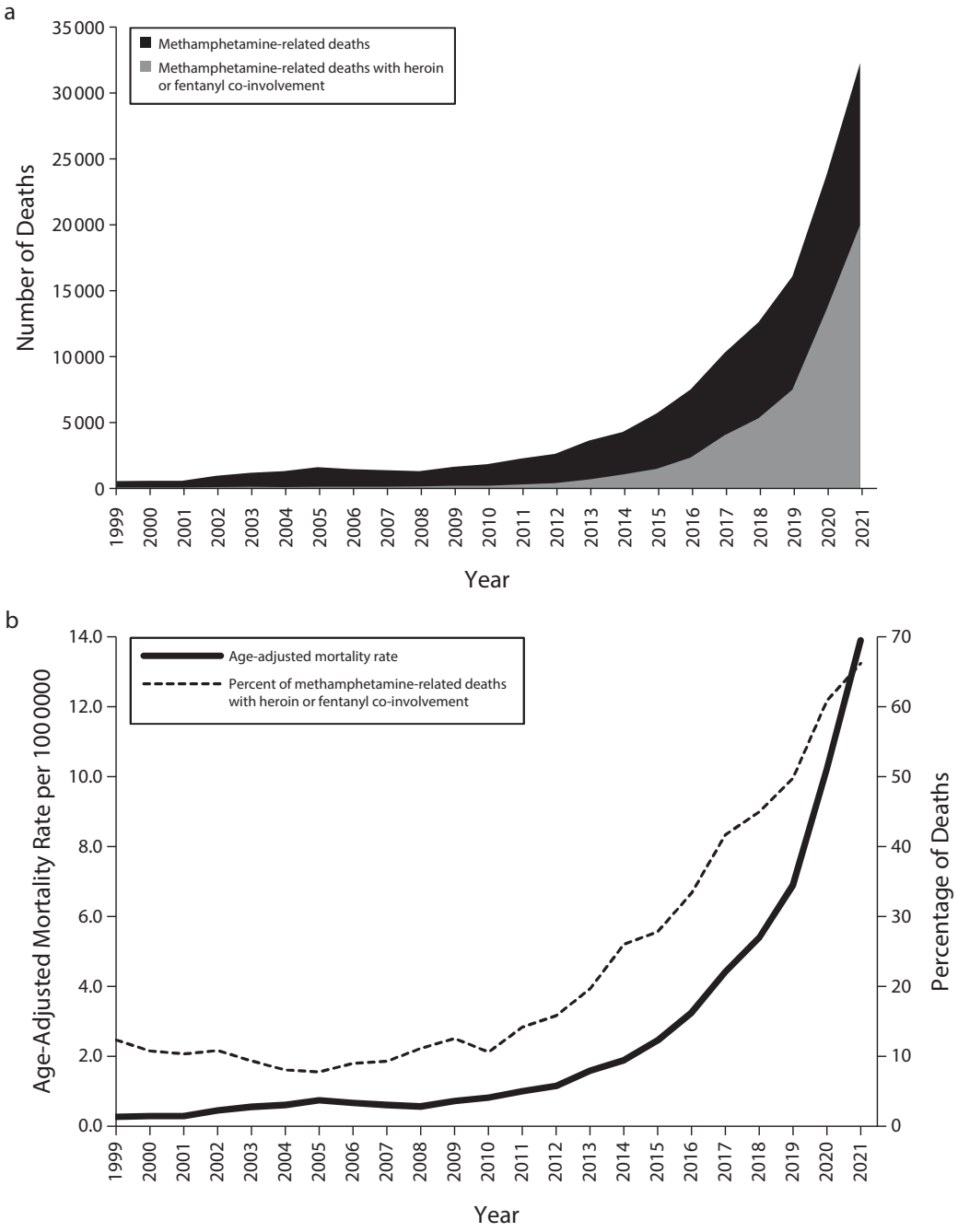

FIGURE 1— Number (a) and Rate (b) of Deaths Involving Methamphetamine and Its Co-Involvement With Heroin or Fentanyl Among People Aged 15–74 Years: CDC WONDER, United States, 1999–2021

Note. CDC WONDER = Centers for Disease Control and Prevention Wide-ranging ONline Data for Epidemiologic Research. Methamphetamine-related deaths included causes of death in the following categories (*International Classification of Diseases, 10th Revision* codes): accidental/unintentional poisoning (X40–X44), intentional self-poisoning/suicide (X60–X64), assault/homicide (X85), and undetermined intent (Y10–Y14) with a contributing cause of poisoning by psychostimulants with abuse potential (T43.6). Methamphetamine-related deaths that involved heroin or fentanyl included deaths with a contributing cause of poisoning by psychostimulants with abuse potential (T43.6) and a contributing cause of poisoning by heroin (T40.1) or other synthetic narcotics (T40.4).

co-use of stimulants and opioids has increased over time,[4] which appears to be motivated in part by desire, pleasure, and control.[6] However, the illicit drug supply in the United States has also become increasingly toxic with the adulteration of street opioids and other drugs with fentanyl and fentanyl-related analogs.[8,9]

AJPH Published online ahead of print February 2, 2023

This study has some limitations. Deaths of nonresidents (e.g., nonresident aliens, nationals living abroad, residents of Puerto Rico, Guam, the Virgin Islands, and other US territories) are not recorded in CDC WONDER[10] and were not included in the current study. Additionally, deaths in which toxicology tests were not performed or were unable to detect the substances examined here were excluded. However, the exclusion of nonresidents and death certificates without drug-specific information is likely to result in an underestimation of methamphetamine-related mortality. Similarly, data for 2021 are provisional and therefore subject to reporting lags, necessitating future updates. Additional research is needed to examine whether there have been any shifts in unique subgroup risks for methamphetamine-related mortality by age, race/ethnicity, and gender over time.

PUBLIC HEALTH IMPLICATIONS

Findings from the current study demonstrate that methamphetamine-related mortality has increased dramatically over the last 2 decades, with the greatest annual increases occurring from 2014 to 2021. Moreover, an increasing proportion of these methamphetamine deaths co-involved heroin or fentanyl over time, with the greatest annual increases occurring from 2010 to 2021. Our results show that both the age-adjusted methamphetamine mortality rate and co-involvement of heroin or fentanyl were the greatest in 2021, with neither trend showing any sign of abatement. These findings underscore the need to develop, implement, and expand the availability and accessibility of robust harm reduction services, with particular attention to polysubstance use. AJPH

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PUBLICATION INFORMATION

Full Citation: Hoopsick RA, Yockey RA. Methamphetamine-related mortality in the United States: co-involvement of heroin and fentanyl, 1999–2021. *Am J Public Health*. Published online ahead of print February 2, 2023:e1–e4.

Acceptance Date: December 15, 2022.

DOI: https://doi.org/10.2105/AJPH.2022.307212

CONTRIBUTORS

R. A. Hoopsick conceptualized the study, conducted the statistical analyses, and wrote the first draft of the manuscript with sections contributed by R. A. Yockey. Both authors reviewed and approved the final version of this manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

HUMAN PARTICIPANT PROTECTION

The University of Illinois Urbana-Champaign institutional review board determined that this study was exempt from review.

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AJPH Published online ahead of print February 2, 2023