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Polysubstance-Involved Opioid Overdose Deaths Among US Youths: 2020 to 2023

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INTRODUCTION

Drug overdoses and poisonings are the third leading cause of death in US children aged 1 to 19 years,[1] and the leading cause of death in young adults aged 19 to 24 years.[2] Most unintentional overdoses in adolescents and young adults (hereafter, "youth") involve opioids, with illicitly-manufactured fentanyl implicated in over three-quarters of fatalities.[3] Among adults aged 25 and older, nearly half of all opioid overdose deaths also involve other substances (most commonly stimulants such as methamphetamine or cocaine).[4] However, among adolescent opioid overdose deaths, such 'polysubstance' involvement is less common.[5] Little is known about the age at which youth overdoses transition from involving only opioids to involving other substances. Understanding the timing of this age-related shift is critical for overdose prevention.

METHODS

We extracted 2020 to 2023 drug overdose fatality data of youth aged 15–24 years from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) database.[6] We identified overdoses involving opioids with and without other substances using a standardized set of *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10)* diagnosis codes[7,8] (Supplemental Table 1), and we extracted death counts and rates stratified by age, sex, race, ethnicity, and census region. We used descriptive statistics with 2-tailed χ^2 to

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compare deaths involving opioids with other substances to opioid-only overdose deaths and significance was set at $P < 0.05$. We conducted analyses using Stata/MP version 18.0 (StataCorp). The Boston University Institutional Review Board did not consider this study to be human subjects research based on use of publicly available, de-identified data.

RESULTS

From 2020 to 2023, there were 22,966 opioid overdose deaths among youth aged 15 to 24 years (Table 1). Fentanyl and other synthetic opioids were most commonly involved (n=21,507; 93.6%). Overall, approximately half of all opioid overdose deaths (n=11,657; 50.8%) involved polysubstance use. Collectively, stimulants (i.e., including methamphetamine, cocaine, and/or other psychostimulants) were involved in 65.3% (n=7,609) of all polysubstance-involved overdose deaths and 33.1% of all opioid overdose deaths.

Polysubstance-involved opioid overdose mortality steadily increased with increasing age, and was (per 100,000): 0.43 among 15-year-olds, 3.49 among 18-year-olds, 8.69 among 21-year-olds, and 15.29 among 24-year-olds. Starting at age 21 and for all older ages, opioid overdose deaths more commonly involved polysubstance use than opioids alone (Figure 1A). Polysubstance-involved overdoses comprised 25.2% of opioid overdose deaths among 15-year-olds, 39.4% among 18-year-olds, 52.8% among 21-year-olds, and 58.1% among 24-year-olds. Collectively, stimulants were the most commonly involved substances other than opioids in these deaths, and were present in 12.4% of opioid overdose deaths among 15-year-olds, 21.1% among 18-year-olds, 33.8% among 21-year-olds, and 40.6% among 24-year-olds (Figure 1B). Benzodiazepines were the next most commonly involved substance in opioid overdose deaths.

DISCUSSION

Fentanyl was involved in more than 9 in 10 opioid overdose deaths among youth; however, the percentage of opioid overdose deaths also involving other substances (most commonly stimulants) steadily rose with increasing age, progressing from adolescence through young adulthood. At age 21 and older, opioid overdoses more commonly involved other substances rather than opioids alone. Previous research found the highest prevalence of stimulant involvement in fentanyl overdose deaths was observed in individuals ages 25 through 54 years, with generally lower rates among adolescents, young adults, and individuals over 64.[4] However, as national data show that the overdose crisis has entered a ‘fourth wave’ in which overdose deaths increasingly involve stimulants in addition to opioids,[4] our results highlight a critical, age-specific transition from deaths involving only opioids to those also involving methamphetamine, prescription stimulants, cocaine, and other substances.

Study limitations include the potential for misclassification of substances involved in deaths in CDC WONDER data, particularly if full toxicology testing or reporting was not conducted at the time a death was documented. Deaths involving newer drugs (e.g., xyzlazine, flualprazolam) are not routinely captured in CDC data. We did not control for cohort or period effects in analyses. Amid high mortality from overdoses involving

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illicitly-manufactured fentanyl and stimulants, these findings suggest that interventions to address overdoses among youth should not have a singular focus on opioids. Indeed, new clinical practice guidelines on the treatment of stimulant use disorder are now available, including recommendations for adolescents.[9] Drug prevention, harm reduction, and addiction treatment need to more broadly incorporate such services to address the rising contribution of stimulants and other substances.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

CDC WONDER	Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research
ICD-10	International Statistical Classification of Diseases and Related Health Problems, Tenth Revision

References

1. Goldstick JE, Cunningham RM, Carter PM. Current Causes of Death in Children and Adolescents in the United States. N Engl J Med. 2022;386(20):1955–1956. [PubMed: 35443104]
2. Centers for Disease Control and Prevention. WISQARS Leading Causes of Death Visualization Tool. Accessed August 30, 2024. https://wisqars.cdc.gov/lcd/?o=LCD&y1=2022&y2=2022&ct=10&cc=UNI&g=00&s=0&r=0&ry=2&e=0&ar=lcd1age&at=groups&ag=lcd1age&a1=0&a2=199
3. Friedman J, Hadland SE. The Overdose Crisis among U.S. Adolescents. N Engl J Med. 2024;390(2):97–100. [PubMed: 38198189]
4. Friedman J, Shover CL. Charting the fourth wave: Geographic, temporal, race/ethnicity and demographic trends in polysubstance fentanyl overdose deaths in the United States, 2010–2021. Addiction. 2023;118(12):2477–2485. [PubMed: 37705148]
5. Lim JK, Earlywine JJ, Bagley SM, Marshall BDL, Hadland SE. Polysubstance Involvement in Opioid Overdose Deaths in Adolescents and Young Adults, 1999–2018. JAMA Pediatr. 2021;175(2):194. [PubMed: 33226412]
6. Centers for Disease Control and Prevention. CDC WONDER Database. Accessed April 11, 2024. https://wonder.cdc.gov/
7. National Vital Statistics System. Provisional Mortality Data from May 2019–April 2020. Accessed February 25, 2025. https://www.cdc.gov/nchs/data/health_policy/Percent-of-Specific-Drugs-Mentioned-in-Combination-May-2019-April-2020.pdf
8. National Center for Health Statistics. Indicator ICD-10-CM Codes.; 2023. https://www.cdc.gov/nchs/dhcs/drug-use/icd10-codes.htm
9. The ASAM/AAAP Clinical Practice Guideline on the Management of Stimulant Use Disorder. J Addict Med. 2024;18(1S):1–56.

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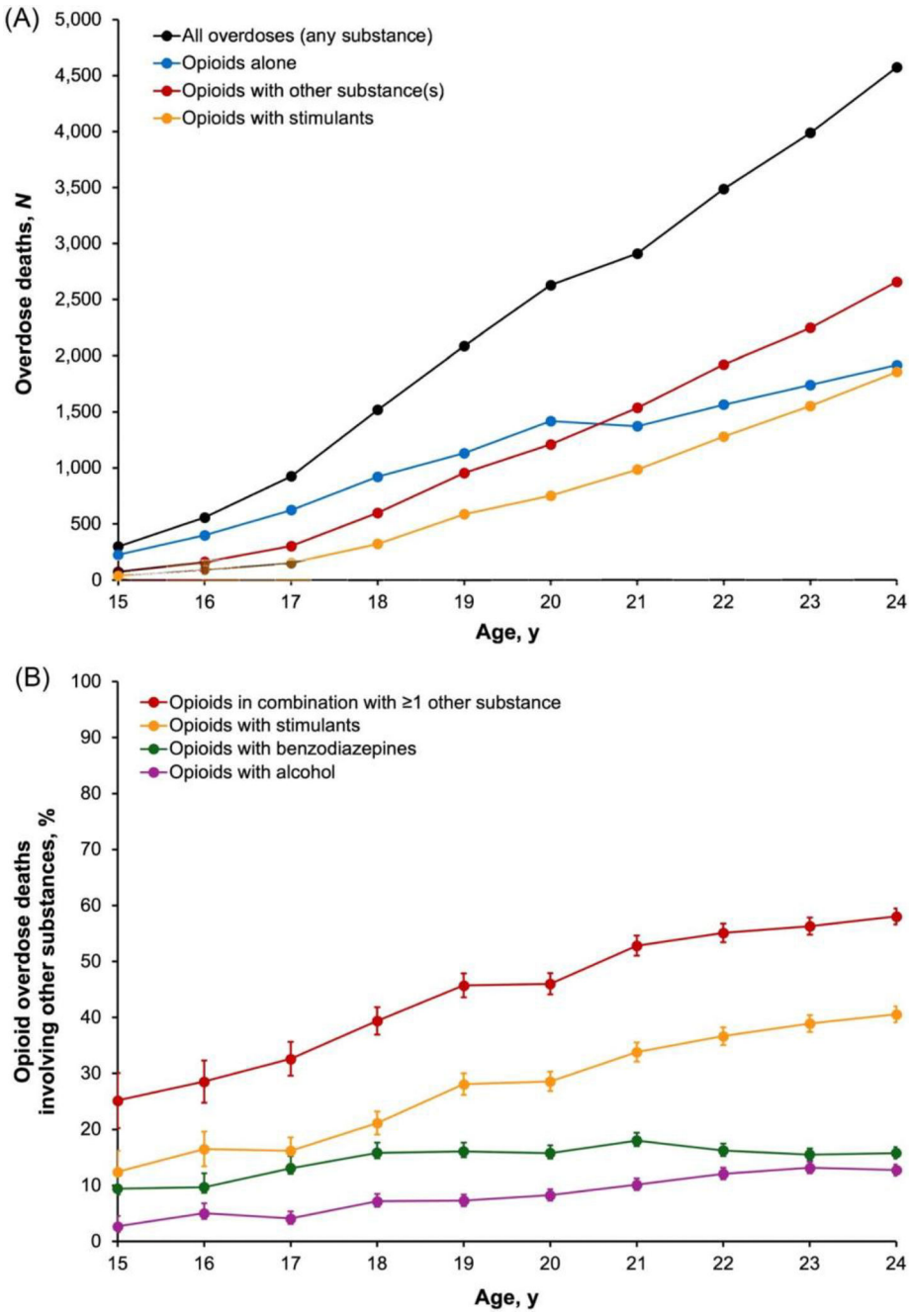


FIGURE 1.

(A) Opioid overdose deaths alone and in combination with other substances including stimulants among US youth aged 15 to 24 years.

(B) Percentage of opioid overdose deaths involving other substances among US youth aged 15 to 24 years.

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TABLE 1.

Characteristics of Opioid Overdose Deaths Among Youth Aged 15 to 24 Years From 2020 to 2023 (N = 22 966)

	Overdose Deaths, n (%)		
Characteristic[a]	**Opioids Plus Other Substances (n = 11 657)**	**Opioids Only (n = 11 309)**	***P* Value**
Age, y			
15–19	2088 (38.8)	3296 (61.2)	<.001
20–24	9569 (54.4)	8013 (45.6)	
Sex			
Male	7921 (49.0)	8233 (51.0)	<.001
Female	3736 (54.8)	3076 (45.2)	
Race and ethnicity			
Non-Hispanic Black	1625 (48.2)	1744 (51.8)	.003
Non-Hispanic white	6523 (50.8)	6319 (49.2)	
Other[b]	423 (54.9)	347 (45.1)	
More than one race	326 (50.2)	323 (49.8)	
Hispanic	2760 (51.7)	2576 (48.3)	
Opioid(s) involved[c]			
Fentanyl and other synthetic opioids[d]	10 781 (50.1)	10 726 (49.9)	<.001
Heroin	797 (57.5)	588 (42.5)	
Methadone	175 (53.7)	151 (46.3)	
Prescription opioids[e]	1315 (59.7)	886 (40.3)	
Other opioids[f]	131 (55.3)	106 (44.7)	
Substance(s) involved[c]			
Psychostimulants other than cocaine	4373 (37.5)	NA	NA
Cocaine	3899 (33.4)	NA	
Benzodiazepines	3624 (31.1)	NA	
Alcohol	2387 (20.5)	NA	
Other substances[g]	1058 (9.1)	NA	
Census region			
Northeast	1719 (54.5)	1435 (45.5)	<.001
Midwest	2230 (46.4)	2573 (53.6)	
South	4427 (50.7)	4301 (49.3)	
West	3281 (52.2)	3000 (47.8)	

Abbreviations: N, total study population; n, subgroup of total population; NA, not applicable.

[a]Includes row percentages comparing youth overdoses involving opioids plus other substances and opioids only within age, sex, race and ethnicity, opioid(s) involved, and census region categories; includes column percentages comparing youth overdoses involving opioids plus other substances between psychostimulants other than cocaine, cocaine, benzodiazepines, alcohol, and other substances.

[b]Includes individuals who are Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander race, and Not Stated; categories were combined to protect decedents' identities.

[c] Deaths involving more than 1 of the substances listed could be counted more than once; thus, percentages add to greater than 100%.

[d] Excludes the synthetic opioid methadone.

[e] Includes oxycodone, hydrocodone, and morphine.

[f] Includes opium and other/unspecified opioids.

[g] Includes cannabis and barbiturates.

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