RESEARCH LETTER

## Trends in Drug Overdose Deaths Among US Adolescents, January 2010 to June 2021

The illicit drug supply has increasingly become contaminated with illicitly manufactured fentanyls and other synthetic opioid and benzodiazepine analogues.[1] Adolescent drug use rates remained generally stable between 2010 and 2020, with 30.2% and 30.4%, respectively, of 10th-graders reporting any illicit drug use in the past 12 months, which declined to 18.7% of 10th-graders in 2021.[2] However, given the increase in illicit fentanyls and potential associated risks, we assessed shifts in overdose deaths among adolescents.

Supplemental content

**Methods** | We calculated drug overdose deaths per 100 000 population for adolescents (aged 14-18 years), compared with the overall population, from January 2010 to June 2021, using data from the Centers for Disease Control and Prevention WONDER (Wide-Ranging Online Data for Epidemiologic Research) database,[3] containing records on all US deaths for which drug overdose was listed as the underlying cause of death. Values for January to June 2021 were provisional and annualized by proportional scaling. Descriptive trends by specific substance involvement were assessed using *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* multiple cause of death codes (eAppendix in the Supplement) and by ethnicity (Latinx) and race (American Indian or Alaska Native, Black or African American, White) as categorized in the underlying records. Rationale for assessment of race and ethnicity is described in footnote *c* of the **Table**. Analyses were conducted using R version 4.0.3. This study was deemed exempt from review and informed consent by the University of California, Los Angeles institutional review board.

**Results** | There were 518 deaths among adolescents (2.40 per 100 000 population) in 2010, with rates remaining stable through 2019 with 492 deaths (2.36 per 100 000). Deaths increased to 954 (4.57 per 100 000) in 2020 and to 1146 (5.49 per 100 000) in 2021. Between 2019 and 2020, overdose mortality increased by 94.03% and from 2020 to 2021 by 20.05%.

In the overall population, numbers of overdose deaths were higher and rates increased steadily from 2010 (n = 38 329; 12.4 per 100 000) to 2020 (n = 91 799; 27.86 per 100 000) and 2021 (n = 101 954; 31.06 per 100 000). The percent change was 29.48% from 2019 to 2020 and 11.48% from 2020 to 2021 (Table).

**Table. Characteristics of Adolescent Overdose Deaths, 2010, 2019, 2020, and 2021[a]**

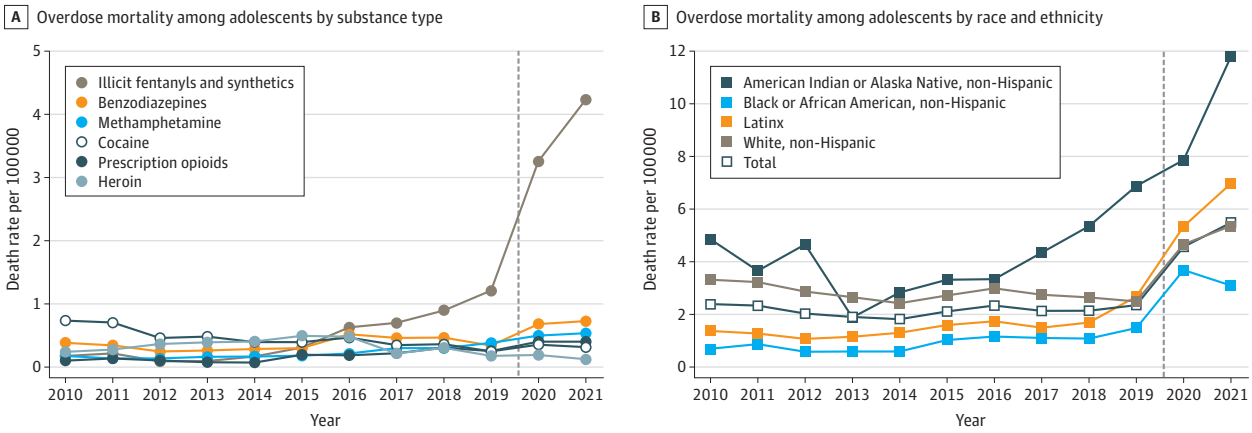
| Characteristics | 2010 | | 2019 | | 2020 | | | 2021[b] | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Deaths, No. | Rate | Deaths, No. | Rate | Deaths, No. | Rate | Change, % | Deaths, No. | Rate | Change, % |
| Total among overall population | 38 329 | 12.41 | 70 630 | 21.52 | 91 799 | 27.86 | 29.48 | 101 954 | 31.06 | 11.48 |
| Total among adolescents | 518 | 2.40 | 492 | 2.36 | 954 | 4.57 | 94.03 | 1146 | 5.49 | 20.05 |
| Substance | | | | | | | | | | |
| Benzodiazepines | 83 | 0.38 | 71 | 0.34 | 142 | 0.68 | 100.13 | 152 | 0.73 | 6.97 |
| Cocaine | 22 | 0.10 | 53 | 0.25 | 84 | 0.40 | 58.59 | 84 | 0.40 | −0.07 |
| Heroin | 52 | 0.24 | 37 | 0.18 | 40 | 0.19 | 8.18 | 26 | 0.12 | −35.04 |
| Illicit fentanyls and synthetics | 38 | 0.18 | 253 | 1.21 | 680 | 3.26 | 168.95 | 884 | 4.23 | 29.91 |
| Methamphetamine | 38 | 0.18 | 80 | 0.38 | 104 | 0.50 | 30.09 | 112 | 0.54 | 7.62 |
| Prescription opioids | 159 | 0.74 | 52 | 0.25 | 74 | 0.35 | 42.40 | 66 | 0.32 | −10.87 |
| Race and ethnicity[c] | | | | | | | | | | |
| American Indian or Alaska Native, non-Hispanic | 11 | 4.86 | 14 | 6.88 | 16 | 7.87 | 14.37 | 24 | 11.79 | 49.89 |
| Black or African American, non-Hispanic | 24 | 0.70 | 46 | 1.49 | 114 | 3.69 | 148.22 | 96 | 3.10 | −15.92 |
| Latinx | 62 | 1.38 | 136 | 2.68 | 276 | 5.35 | 99.44 | 354 | 6.98 | 30.51 |
| White, non-Hispanic | 412 | 3.32 | 281 | 2.50 | 521 | 4.67 | 87.02 | 604 | 5.36 | 14.93 |

[a] Drug overdose deaths among high school–aged adolescents (14-18 years), shown as counts, and rates per 100 000 population for 2010, 2019, 2020, and 2021, compared with values for the all-age US population. Data for adolescents are also stratified by substance involved and race and ethnicity. Year-to-year percentage increases are shown for 2020 (relative to 2019) and 2021 (relative to 2020).

[b] 2021 refers to January to June 2021, and rates and counts have been annualized.

[c] Race and ethnicity were assessed in this study, as categorized in the underlying records, because recent data have suggested that racial and ethnic inequalities in overdose are increasing among the general population and may also be a concern among the adolescent population assessed herein.[5] Trends among Asian individuals were not included because of differences between the representation of this group in the preliminary and final databases used.

Figure. Adolescent Overdose Deaths, 2010-2021




Drug overdose rates per 100 000 adolescents are shown by (A) substance involved and (B) race and ethnicity. The year 2021 refers to January to June 2021, and rates have been annualized. The vertical dashed lines delineate the prepandemic and pandemic periods of observed data.

Among adolescents, fentanyl-involved fatalities increased from 253 (1.21 per 100 000) in 2019 to 680 (3.26 per 100 000) in 2020 and to 884 (4.23 per 100 000) in 2021 (**Figure**, A). In 2021, fentanyls were identified in 77.14% of adolescent overdose deaths, compared with 13.26% for benzodiazepines, 9.77% for methamphetamine, 7.33% for cocaine, 5.76% for prescription opioids, and 2.27% for heroin.

American Indian and Alaska Native adolescents experienced the highest overdose rate in 2021 (n = 24; 11.79 per 100 000), followed by Latinx adolescents (n = 354; 6.98 per 100 000) (Figure, B).

**Discussion** | Beginning in 2020, adolescents experienced a greater relative increase in overdose mortality than the overall population, attributable in large part to fatalities involving fentanyls. In the context of decreasing adolescent drug use rates nationally,[2] these shifts suggest heightened risk from illicit fentanyls, which have variable and high potency.[1] Since 2015, fentanyls have been increasingly added to counterfeit pills resembling prescription opioids, benzodiazepines, and other drugs, which adolescents may not identify as dangerous and which may be playing a key role in these shifts.[1,4]

The highest rates of overdose deaths were among American Indian and Alaska Native adolescents, which have also been reported among adults in this population in 2020.[5] High rates among Latinx adolescents contrast with relatively lower rates among Latinx adults.[5] These adolescent trends fit a wider pattern of increasing racial and ethnic inequalities in overdose that deserve further investigation and intervention efforts.[5]

Study limitations include the observational design that cannot establish causality, that race and ethnicity may be incorrectly assigned in some death investigations, that results from 2021 were provisional and include proportionally scaled values from January to June, and small numbers in some subgroups. In addition, the contribution of factors unique to the COVID-19 pandemic, such as suicidal ideation, mental illness, social isolation, and disruptions to illicit drug markets, cannot be discerned.[6]

Increasing adolescent overdose deaths, in the context of increasing availability of illicit fentanyls, highlight the need for accurate harm-reduction education for adolescents and greater access to naloxone and services for mental health and substance use behaviors.

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*Concept and design:* Friedman, Godvin, Shover, Hansen, Schriger.
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1. Ciccarone D. The rise of illicit fentanyls, stimulants and the fourth wave of the opioid overdose crisis. *Curr Opin Psychiatry*. 2021;34(4):344-350. doi:10.1097/YCO.0000000000000717

2. Monitoring the Future. Data for in-school surveys of 8th, 10th, and 12th grade students, 1975-2021: prevalence trends by drug. Accessed February 7, 2022. http://monitoringthefuture.org/data/21data.htm

3. Centers for Disease Control and Prevention. CDC WONDER database. Accessed December 30, 2020. https://wonder.cdc.gov/

4. Green TC, Gilbert M. Counterfeit medications and fentanyl. *JAMA Intern Med*. 2016;176(10):1555-1557. doi:10.1001/jamainternmed.2016.4310

5. Friedman J, Hansen H. Evaluation of increases in drug overdose mortality rates in the US by race and ethnicity before and during the COVID-19 pandemic. *JAMA Psychiatry*. Published online March 2, 2022. doi:10.1001/jamapsychiatry.2022.0004

6. *Protecting Youth Mental Health: The US Surgeon General's Advisory*. Published 2021. Accessed December 19, 2021. https://www.hhs.gov/sites/default/files/surgeon-general-youth-mental-health-advisory.pdf

## COMMENT & RESPONSE

## Supporting Diagnosis With Next-Generation Artificial Intelligence

**To the Editor** A recent Viewpoint[1] proposed to support diagnosis with next-generation artificial intelligence that not only predicts diagnosis but also accompanies physicians on their journey. The wayfinding metaphor poses interesting research questions about the best way to represent the map from an ergonomic point of view, but it also calls into question the volume of interventions of the system and its level of autonomy. A high volume of alerts accompanied clinical decision support systems for prescription and laboratory ordering. The strategy of alerting physicians initially seemed relevant and necessary to help reduce prescription errors. However, the frequent alerts led to a fatigue phenomenon, and physicians eventually ended up not taking them into account.[2] Likewise, one can imagine observing a fatigue alert linked to the wayfinding provided by next-generation artificial intelligence. Therefore, it is vital to set the recommendation and intervention level of the system.

First, the system should allow time for clinicians to ask questions and take actions on their own, when appropriate. A system that anticipates every clinician move could be irritating and fatiguing, even if always correct. Clinicians are highly qualified professionals who are trained to request help when necessary. Use of a computer system can be stressful and overloading, and may be harmful in several ways. The challenge is therefore to set appropriately for the individual clinician (adjusted for specialty and training level[3]) the type (asynchronous vs dynamic), level (critical vs minor), and time (at consult vs at result return) for interactions.

Second, the system should be more active in the case of life-threatening situations if recommended tests are not ordered, whereas it may be less active in the diagnosis of chronic conditions. For example, the system should be able to prioritize clinical situations such as sepsis,[4] malnutrition, and low back pain,[5] helping the clinician focus on emergencies first and intervene later on lower-priority conditions. At the same time, the system could screen continuously for rare diseases, which may be difficult to diagnose, to help avoid potentially delayed appropriate care. This ability of diagnosis systems using next-generation artificial intelligence to be highly adapted to the clinical context is crucial for the wayfinding to be useful to clinicians.

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1. Adler-Milstein J, Chen JH, Dhaliwal G. Next-generation artificial intelligence for diagnosis: from predicting diagnostic labels to "wayfinding". *JAMA*. 2021;326(24):2467-2468. doi:10.1001/jama.2021.22396

2. Bittmann JA, Rein EK, Metzner M, Haefeli WE, Seidling HM. The acceptance of interruptive medication alerts in an electronic decision support system differs between different alert types. *Methods Inf Med*. 2021;60(5-06):180-184. doi:10.1055/s-0041-1735169

3. Sellier E, Colombet I, Sabatier B, et al. Effect of alerts for drug dosage adjustment in inpatients with renal insufficiency. *J Am Med Inform Assoc*. 2009;16(2):203-210. doi:10.1197/jamia.M2805

4. Wu M, Du X, Gu R, Wei J. Artificial intelligence for clinical decision support in sepsis. *Front Med (Lausanne)*. 2021;8:665464. doi:10.3389/fmed.2021.665464

5. Miotto R, Percha BL, Glicksberg BS, et al. Identifying acute low back pain episodes in primary care practice from clinical notes: observational study. *JMIR Med Inform*. 2020;8(2):e16878. doi:10.2196/16878

**In Reply** We agree with Drs Bousquet and Coulet that worthwhile artificial intelligence wayfinding systems should avoid alert fatigue, support and not preempt clinician judgment, and operate variably in the foreground or background, depending on the clinical context.

The wayfinding analogy in our Viewpoint[1] drew attention to the information clinicians need to determine the next steps in the dynamic diagnostic processes. The diagnostic decision space comprises a myriad of plausible maneuvers (eg, questions, physical findings, laboratory testing, imaging). Wayfinding systems could narrow this space in an adaptive manner that reduces clinician cognitive burden.

Bousquet and Coulet point out that effective systems are not just about the right information but also the right interface (person, channel, format, and time).[2,3] Current clinical decision support systems use interruptive electronic warnings that exacerbate alert fatigue.[4] We envision wayfinding systems that infer clinical context and passively offer guideposts when decision makers are searching for clinical orders or consultations. User testing of prototype clinical order recommender systems for acute hospital medical conditions indicates that physicians readily accept suggestions in more than 95% of cases.[5] Wayfinding is a departure from existing constructs such as manual order sets and interruptive alerts, and it is more like features in YouTube, Netflix, and Amazon that