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Short communication

Accidental drug overdose deaths in Connecticut, 2012–2018: The rise of polysubstance detection?

Taeho Greg Rhee[a,b,c,d,*], Joseph S. Ross[d,e,f], Robert A. Rosenheck[b,c,f], Lauretta E. Grau[g], David A. Fiellin[e,f], William C. Becker[e,h]

[a] Department of Public Health Sciences, School of Medicine, University of Connecticut, Farmington, CT, United States
[b] Department of Psychiatry, School of Medicine, Yale University, New Haven, CT, United States
[c] Mental Illness Research, Education and Clinical Center of New England, US Department of Veterans Affairs Connecticut Healthcare System, West Haven, CT, United States
[d] Yale Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, CT, United States
[e] Section of General Internal Medicine, Department of Internal Medicine, School of Medicine, Yale University, New Haven, CT, United States
[f] Department of Health Policy and Management, School of Public Health, Yale University, New Haven, CT, United States
[g] Department of Epidemiology of Microbial Diseases, School of Public Health, Yale University, New Haven, CT, United States
[h] Pain Research, Informatics, Multi-morbidities and Education Center of Excellence, VA Connecticut Healthcare System, West Haven, CT, United States

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ABSTRACT

Objectives: To examine trends in polysubstance detection associated with drug-related overdose deaths in Connecticut.

Methods: We used 2012–2018 data provided by Connecticut's Office of the Chief Medical Examiner (OCME) on accidental overdose deaths. We estimated annual trends, standardizing the number of deaths per 100,000 Connecticut residents each year. We then conducted stratified analyses by polysubstance use status. We also examined the numbers of deaths involving fentanyl in a separate analysis. We obtained data in April 2019, and statistical analyses were performed from April to September 2019.

Results: The rate of overdose deaths in Connecticut increased from 9.9 per 100,000 residents in 2012 to 28.5 per 100,000 residents in 2018—a 221 % increase—with the majority occurring among persons aged 35–64 (65.3 %), men (73.9 %), and non-Hispanic whites (78.5 %). Among deaths involving fentanyl, the overall deaths escalated from 5.2 deaths per 100,000 residents in 2015 to 21.3 deaths per 100,000 residents in 2018, and more than 50% of these fentanyl-related deaths involved polysubstance use.

Conclusions: Connecticut experienced a more-than doubling of opioid-involved overdose deaths, largely driven by fentanyl and polysubstance use. The role of polysubstance use should be considered in efforts toward reducing opioid-related overdose incidents.

1. Introduction

The current US opioid epidemic has led to catastrophic increases in drug-related deaths, and in 2017, the state of Connecticut had the eighth highest rate of opioid overdose deaths in the United States. While many initiatives have been implemented to reduce opioid prescribing and misuse (Centers for Disease Control and Prevention, 2017; Substance Abuse and Mental Health Services Administration, 2019), simply reducing prescription opioid use may not address the specific toxicological causes of fatal overdoses (Gladden et al., 2019). For instance, overdose may not be simply related to misuse of opioids, but rather to their use in combination with other substances. Although polysubstance use is known to be common among substance users (Cicero and Ellis, 2015; Compton et al., 2016; Connor et al., 2014; Evans et al., 2017; Kandel et al., 2017), little is known about the impact of changing patterns of polysubstance use and the specific agents involved in opioid overdose deaths. In addition, understanding the potential role of polysubstance use in accidental drug overdose deaths may facilitate developing and disseminating drug overdose-related prevention and intervention strategies. Accordingly, we examined trends in polysubstance patterns associated with drug-related overdose deaths in Connecticut.

2. Methods

We used 2012–2018 data provided by Connecticut's Office of the

* Corresponding author at: Department of Public Health Sciences, School of Medicine, University of Connecticut, Farmington, CT, United States.
E-mail addresses: tgrhee.research@gmail.com, rhee@uchc.edu (T.G. Rhee).

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Table 1
Characteristics of accidental drug overdose deaths per 100,000 Connecticut residents by year in Connecticut, 2012–2018.

	2012 (n = 355)	2013 (n = 490)	2014 (n = 557)	2015 (n = 726)	2016 (n = 917)	2017 (n = 1038)	2018 (n = 1018)	*P*-value for overall trends
Drug overdose deaths	9.9	13.6	15.5	20.2	25.6	29.0	28.5	< 0.001
Age, yrs.								
≤ 21	0.6	0.4	0.4	0.8	0.5	0.6	0.6	< 0.001
22-34	2.9	4.2	4.3	5.7	7.8	9.2	7.8	0.951
35-44	2.0	2.9	4.2	4.3	6.7	7.1	7.4	0.048
45-64	4.1	5.9	6.1	8.9	10.8	11.6	11.7	0.508
≥ 65	0.3	0.2	0.4	0.6	0.5	0.5	1.0	0.297
Sex								
Male	7.2	9.7	10.8	14.9	19.1	21.7	21.7	0.005
Female	2.7	3.9	4.6	5.3	6.5	7.3	6.7	0.007
Race/ethnicity								
White	7.6	10.8	13.0	16.5	19.9	22.7	21.2	0.002
Hispanic	1.1	1.4	1.6	2.2	2.8	3.4	3.8	0.048
Black	1.1	1.2	0.8	1.3	2.4	2.5	2.9	0.153
Other[a)]	0.1	0.2	0.1	0.2	0.4	0.4	0.6	0.124
Location of deaths								
Home/residence	4.8	6.7	8.1	11.3	12.9	15.5	15.4	0.072
Hospital	3.7	5.0	5.1	5.7	8.9	8.2	8.8	0.002
Other[b)]	1.3	1.9	2.3	3.0	3.7	5.3	4.3	0.069
Drug-involved								
Opioid	8.2	11.5	14.0	18.3	23.7	26.8	26.4	< 0.001
Non-heroin	3.4	4.3	4.9	6.7	9.9	13.5	15.5	< 0.001
Fentanyl	0.4	1.0	2.1	5.2	13.5	18.9	21.3	< 0.001
Other	4.8	6.9	8.0	8.6	6.2	3.9	2.4	< 0.001
Cocaine	2.9	4.1	3.5	4.8	7.7	9.7	9.7	< 0.001
Benzodiazepine	1.4	2.2	4.3	6.2	6.8	9.2	7.4	< 0.001
Ethanol	1.7	2.3	3.5	4.9	7.1	8.1	7.2	< 0.001
Methamphetamine	0.0	0.1	0.1	0.2	0.2	0.3	0.6	0.001
Other[c)]	0.3	0.3	0.2	0.3	0.2	0.2	0.3	0.002
Polysubstance use								
Opioid only	4.3	6.0	6.1	7.2	8.3	8.3	9.3	< 0.001
Opioid and benzodiazepine	0.9	1.2	2.7	3.7	4.1	5.0	3.7	0.035
Opioid, benzodiazepine and ethanol	0.2	0.4	0.6	0.9	0.9	1.5	1.0	0.067
Opioid, benzodiazepine, ethanol, and other	0.2	0.4	0.7	1.1	1.1	2.0	1.5	0.001
Other non-opioid combinations	1.6	2.1	1.5	2.0	1.9	2.2	2.1	< 0.001

Note: Data were collected from Office of the Chief Medical Examiner, State of Connecticut. a) includes Asian, American Indian, or other racial/ethnic groups; b) includes shelters, motels, roadways or streets, vehicles, or other; and c) includes other street-name drugs.

Chief Medical Examiner (OCME) on accidental overdose deaths. We obtained data in April 2018, and statistical analyses were performed from April to September 2018. Between 2012 and 2018, the OCME documented accidental overdose deaths that occurred in Connecticut. Accidental deaths are caused by external, violent or accidental means, and are not related to any intentional or criminal acts. For each death, drugs listed on the death certificate were identified on the basis of toxicology testing. As there is no precise mechanism to ascertain which drugs were contributing causes of death, multiple drugs were often listed. While comprehensive drug information was provided in the data, information about suicidal intent deaths was not captured in the data. Using this information, we determined the causes of accidental overdose deaths characterized by the following drug classes: benzodiazepine, cocaine, ethanol, methamphetamine, opioid, or other (e.g., cathinone, ketamine, 3,4-methylenedioxymethamphetamine (MDMA) or ecstasy, and phencyclidine (PCP) or Angel dust). Because more than 90% of all accidental overdose deaths in Connecticut involved opioids, we classified polysubstance use in three groups as follows: opioids only, opioids with one additional substance, or opioids with two or more substances.

Analyses conducted in this study are descriptive in nature. We estimated annual trends, standardizing the number of deaths per 100,000 Connecticut residents each year. We also conducted stratified analyses by polysubstance use status to better understand the role of polysubstance use among overdose deaths. We performed a trends analysis between 2012 and 2018, and reported *p*-values to indicate significant trends overtime. Since fentanyl and related analogues are the most potent and lethal opioids, we further examined the numbers of deaths involving fentanyl in a separate analysis. All analyses were performed using Stata 15.1 M P/6-Core (College Station, TX) (StataCorp., 2017). This study examined de-identified data and was exempted from review by the Institutional Review Board at University of Connecticut Health Center.

3. Results

Between 2012 and 2018, 5101 deaths in Connecticut were identified by the OCME as accidental drug overdose deaths. The rate of overdose deaths in Connecticut increased from 9.9 per 100,000 residents in 2012 to 28.5 per 100,000 residents in 2018—a 221 % increase ($p < 0.001$) (Table 1)—with the majority occurring among persons aged 35–64 (65.3 %; $p = 0.048$), men (73.9 %; $p = 0.005$), and non-Hispanic whites (78.5 %; $p = 0.002$). Fentanyl-related overdose deaths, in particular, increased 5361% ($p < 0.001$), while opioid overdose deaths not involving fentanyl decreased by 34% ($p < 0.001$). Among non-opioid substances, methamphetamine-involved overdose deaths increased by 1912 % ($p = 0.001$) and benzodiazepine-involved overdose deaths increased by 446 % ($p < 0.001$).

An increasing number of accidental drug overdose deaths involved polysubstance use (Fig. 1, Panel A). The number of deaths involving an opioid and one additional substance increased from 3.4 deaths per 100,000 residents to 12.4 deaths per 100,000 residents (Fig. 1, Panel B). Similarly, overdose deaths involving an opioid and two or more substances increased from 0.5 deaths per 100,000 residents in 2012 to 4.7 deaths per 100,000 residents in 2018 (Fig. 1, Panel B). When stratified by fentanyl-related overdose deaths, deaths not involving

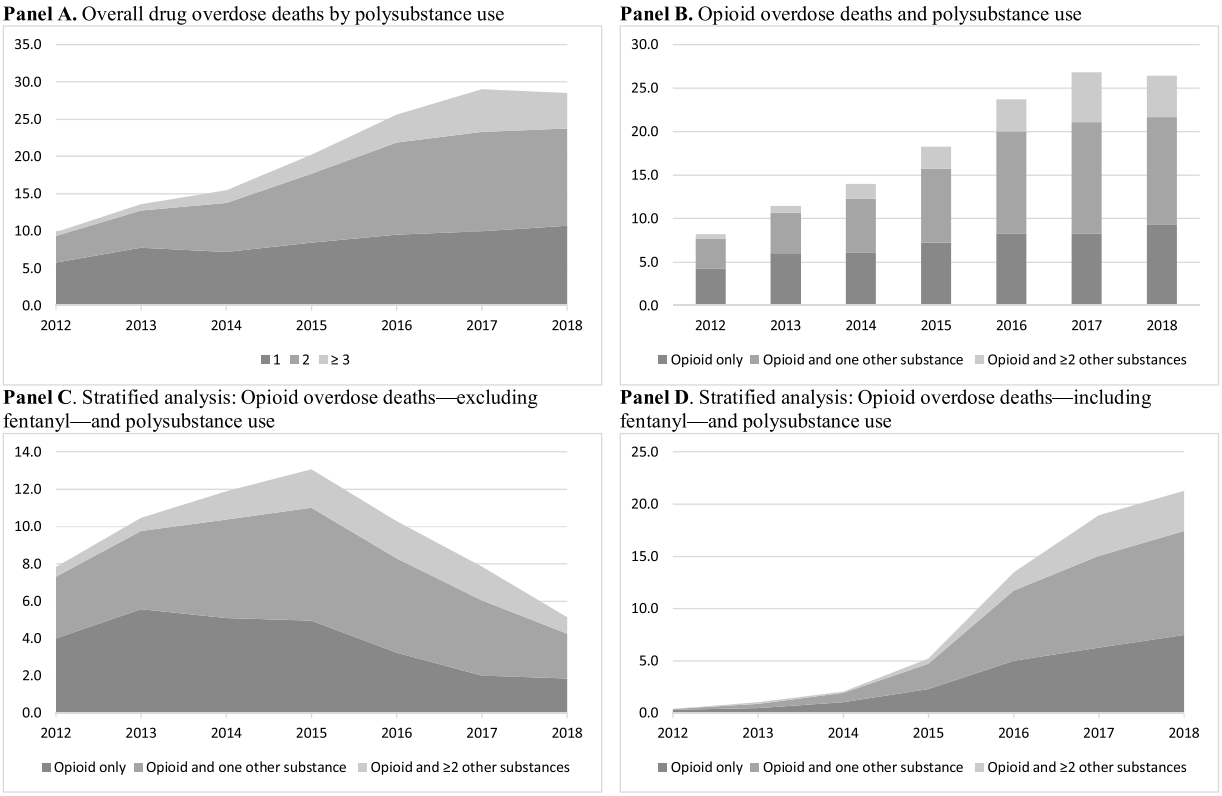

Fig. 1. Trends of accidental drug overdose deaths per 100,000 Connecticut residents by polysubstance use in Connecticut, 2012–2018.
Panel A. Overall drug overdose deaths by polysubstance use.
Panel B. Opioid overdose deaths and polysubstance use.
Panel C. Stratified analysis: Opioid overdose deaths—excluding fentanyl—and polysubstance use.
Panel D. Stratified analysis: Opioid overdose deaths—including fentanyl—and polysubstance use.
Note: Data were collected from Office of the Chief Medical Examiner, State of Connecticut. Y-axis indicates "per 100,000 residents in Connecticut." The following drug classes were considered: opioid, benzodiazepine, cocaine, ethanol, or other.

fentanyl decreased after 2015, but more than 50 % of these deaths involved multiple substances (Fig. 1, Panel C). Among deaths involving fentanyl, the overall deaths escalated from 5.2 deaths per 100,000 residents in 2015 to 21.3 deaths per 100,000 residents in 2018, and more than 50 % of these deaths involved polysubstance use (Fig. 1, Panel D).

4. Discussion

From 2012–2018, Connecticut experienced a more-than doubling of opioid-involved overdose deaths, largely associated with fentanyl and polysubstance use. The rate of opioid overdose deaths in Connecticut is higher than the national average (i.e., 21.7 deaths per 100,000 populations in 2017) (Centers for Disease Control and Prevention, 2018). While our findings may not generalize to other states, the rise in fentanyl-related overdose deaths appears to be widespread in Connecticut (Centers for Disease Control and Prevention, 2018; Peterson et al., 2016). Our findings also raise concerns about the increasing associations of polysubstance use, especially involving fentanyl, with accidental drug overdose deaths.

Our study highlights unique patterns of polysubstance use in the era of the opioid epidemic in Connecticut: a decreasing trend of polysubstance use in opioid overdose deaths not involving fentanyl, and an increasing trend of polysubstance use involving fentanyl-associated overdose deaths since 2015. Future research is needed to determine whether or not those with fentanyl-associated overdose deaths were heavy users of other substances prior to their initiation of fentanyl use. Further, because polysubstance use is associated with overall drug overdose deaths and specifically with fentanyl-related overdose deaths, more research is needed in the patterns of behavioral health (e.g., substance use, mental and physical health status) among individuals with polysubstance use to identify preventable pathways to adverse health outcomes.

Some limitations deserve comment. First, as stated earlier, our data were from a single state (Connecticut) and may not be generalizable to other states. Second, some of trends may be due in part to methodological improvements in toxicological testing of postmortem samples. Despite these limitations, strengths of the study included the use of 2018 data, compared to the National Center for Health Statistics of the Centers for Disease Control and Prevention's most recent data (2017), and the use of detailed descriptive statistics to understand potential roles of polysubstance use in the era of the opioid epidemic.

Opioid-related overdose prevention programs (e.g., prescription drug monitoring programs and academic detailing (Mattson et al., 2018)) and other public health strategies (e.g., provision of access to medication-assisted treatment (Centers for Disease Control and Prevention, 2017)) are increasingly implemented and available throughout the US. However, the role of polysubstance use and specifically use of fentanyl should be targeted in efforts toward reducing opioid-related overdose incidents. Overall, these findings highlight the need for strategies to monitor and rapidly respond to emerging trends in the overdose crisis.

Previous presentation

None.

Disclaimers

Analyses, interpretation, and conclusions are solely those of the author and do not necessarily reflect the views of the Connecticut's Office of the Chief Medical Examiner (OCME).

Author contributions

Study concept and design: Rhee, Ross, and Becker; Data acquisition and statistical analyses: Rhee; Interpretation of data: All authors; Drafting of manuscript: Rhee; Critical revision of manuscript for important intellectual content: All authors.

Funding/support and role of the funder/sponsor

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Compliance with ethical standards

This article does not contain any studies with human participants or animals performed by the authors. All research procedures performed in this study are in accordance with the ethical standards of the Institutional Review Board at University of Connecticut School of Medicine and Yale University School of Medicine.

Rhee reported no financial or other relationship relevant to this article. In the past 36 months, Ross has received research support through Yale University from Johnson and Johnson to develop methods of clinical trial data sharing, from Medtronic, Inc. and the Food and Drug Administration (FDA) to develop methods for post-market surveillance of medical devices (U01FD004585), from the Food and Drug Administration to establish Yale-Mayo Clinic Center for Excellence in Regulatory Science and Innovation (CERSI) program (U01FD005938), from the Blue Cross Blue Shield Association to better understand medical technology evaluation, from the Centers of Medicare and Medicaid Services (CMS) to develop and maintain performance measures that are used for public reporting (HHSM-500-2013-13018I), from the Agency for Healthcare Research and Quality (R01HS022882), from the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH) (R01HS025164), and from the Laura and John Arnold Foundation to establish the Good Pharma Scorecard at Bioethics International and the Collaboration for Research Integrity and Transparency (CRIT) at Yale.

Declaration of Competing Interest

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References

Centers for Disease Control and Prevention, 2017. CDC Guideline for Prescribing Opioids for Chronic Pain. (Accessed July 3 2018). https://www.cdc.gov/drugoverdose/prescribing/guideline.html.

Centers for Disease Control and Prevention, 2018. Drug Overdose Death Data. (Accessed May 17 2019). https://www.cdc.gov/drugoverdose/data/statedeaths.html.

Cicero, T.J., Ellis, M.S., 2015. Abuse-deterrent formulations and the prescription opioid abuse epidemic in the United States: lessons learned from OxyContin. JAMA Psychiatry 72 (5), 424–430.

Compton, W.M., Jones, C.M., Baldwin, G.T., 2016. Relationship between nonmedical prescription-opioid use and heroin use. N. Engl. J. Med. 374 (2), 154–163.

Connor, J.P., Gullo, M.J., White, A., Kelly, A.B., 2014. Polysubstance use: diagnostic challenges, patterns of use and health. Curr. Opin. Psychiatry 27 (4), 269–275.

Evans, E.A., Grella, C.E., Washington, D.L., Upchurch, D.M., 2017. Gender and race/ethnic differences in the persistence of alcohol, drug, and poly-substance use disorders. Drug Alcohol Depend. 174, 128–136.

Gladden, R.M., O'Donnell, J., Mattson, C.L., Seth, P., 2019. Changes in opioid-involved overdose deaths by opioid type and presence of benzodiazepines, cocaine, and methamphetamine - 25 states, July-December 2017 to January-June 2018. MMWR Morb. Mortal. Wkly. Rep. 68 (34), 737–744.

Kandel, D.B., Hu, M.C., Griesler, P., Wall, M., 2017. Increases from 2002 to 2015 in prescription opioid overdose deaths in combination with other substances. Drug Alcohol Depend. 178, 501–511.

Mattson, C.L., O'Donnell, J., Kariisa, M., Seth, P., Scholl, L., Gladden, R.M., 2018. Opportunities to prevent overdose deaths involving prescription and illicit opioids, 11 states, July 2016-June 2017. MMWR Morb. Mortal. Wkly. Rep. 67 (34), 945–951.

Peterson, A.B., Gladden, R.M., Delcher, C., Spies, E., Garcia-Williams, A., Wang, Y., Halpin, J., Zibbell, J., McCarty, C.L., DeFiore-Hyrmer, J., DiOrio, M., Goldberger, B.A., 2016. Increases in fentanyl-related overdose deaths - Florida and Ohio, 2013-2015. MMWR Morb. Mortal. Wkly. Rep. 65 (33), 844–849.

StataCorp, 2017. Stata Statistical Software: Release 15. StataCorp LP., College Station, TX.

Substance Abuse and Mental Health Services Administration, 2019. Number of DATA-waived Practitioners and Newly Certified Per Year. (Accessed May 17 2019). https://www.samhsa.gov/medication-assisted-treatment/training-materials-resources/practitioner-program-data.