

Supplementary Online Content

Whitley P, LaRue L, Fernandez S, Passik SD, Dawson E, Jackson RD. Analysis of urine drug test results from substance use disorder treatment practices and overdose mortality rates, 2013-2020. *JAMA Netw Open*. 2022;5(6):e2215425. doi:10.1001/jamanetworkopen.2022.15425

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. National, State, and County-Level Overdose Mortality Estimates Used in the Current Study

Overdose Mortality Deaths/Rates	Underlying Cause of Death (UCD) ^a	Multiple Cause of Death (MCD) ^b	Synthetic Opioid Status	Stratification	Study Purpose
National Monthly MCD	ALL	ALL		Group By: Month; Multiple Cause of death	Correlation
National Monthly MCD Plus Synthetic Opioids	ALL	ALL	and T40.4	Group By: Month; Multiple Cause of death	Correlation
National Monthly MCD Minus Synthetic Opioids	ALL	ALL	not T40.4	Group By: Month; Multiple Cause of death	Correlation
State Yearly MCD	ALL	ALL		Group By: State; Year; Multiple Cause of death	Correlation
State Yearly MCD Plus Synthetic Opioids	ALL	ALL	and T40.4	Group By: State; Year; Multiple Cause of death	Correlation
State Yearly MCD Minus Synthetic Opioids	ALL	ALL	not T40.4	Group By: State; Year; Multiple Cause of death	Correlation
State Monthly Total	ALL	ALL		Group By: State; Month	Regression models
Ohio County Yearly MCD	ALL			Group By: County; Year; Multiple Cause of death	Correlation
Ohio County Quarterly Total	ALL			Group By: County; Month (summed to quarter)	Regression models

a. All overdose mortality measures include at least one of the following Underlying Cause of Death (UCD) ICD-10 Codes: Drug poisonings (overdose) Unintentional (X40-X44); Drug poisonings (overdose) Suicide (X60-X64); Drug poisonings (overdose) Homicide (X85); Drug poisonings (overdose) Undetermined (Y10-Y14)

b. Overdose mortality measures include at least one of the following Multiple Cause of Death (MCD) ICD-10 Codes: T40.1 (Heroin); T40.2 (Other Opioids); T40.4 (Synthetic Opioids); T40.5 (Cocaine); T43.6 (Methamphetamine)

eTable 2. Yearly US Urine Drug Test Positivity Rates Stratified by Presence of Synthetic Opioids

Drug Category	Rate Type	2013, No. (%)	2014, No. (%)	2015, No. (%)	2016, No. (%)	2017, No. (%)	2018, No. (%)	2019, No. (%)	2020, No. (%)
Synthetic Opioids	Total	1,241 (2.1)	2,591 (3.7)	5,287 (5.9)	4,789 (7.2)	4,337 (8.5)	4,940 (9.5)	7,633 (13.1)	10,449 (19.1)
Methamphetamine	Total	1,259 (2.2)	2,690 (3.8)	6,263 (7.0)	7,626 (11.5)	7,664 (15.0)	8,463 (16.3)	9,897 (16.9)	11,465 (21.0)
Methamphetamine	Plus Synthetic Opioids	33 (0.1)	97 (0.1)	363 (0.4)	714 (1.1)	927 (1.8)	1,399 (2.7)	2,314 (4.0)	4,307 (7.9)
Methamphetamine	Minus Synthetic Opioids	1,226 (2.1)	2,593 (3.7)	5,900 (6.6)	6,912 (10.4)	6,737 (13.2)	7,064 (13.6)	7,583 (13.0)	7,158 (13.1)
Cocaine	Total	4,602 (7.9)	7,678 (11.0)	9,168 (10.2)	5,975 (9.0)	4,889 (9.6)	4,808 (9.3)	6,344 (10.9)	5,389 (9.9)
Cocaine	Plus Synthetic Opioids	163 (0.3)	604 (0.9)	1,559 (1.7)	1,506 (2.3)	1,544 (3.0)	1,723 (3.3)	2,863 (4.9)	2,796 (5.1)
Cocaine	Minus Synthetic Opioids	4,439 (7.7)	7,074 (10.1)	7,609 (8.5)	4,469 (6.7)	3,345 (6.5)	3,085 (6.0)	3,481 (6.0)	2,593 (4.7)
Heroin	Total	2,337 (4.0)	4,410 (6.3)	6,288 (7.0)	3,677 (5.5)	2,484 (4.9)	2,809 (5.4)	2,680 (4.6)	2,593 (4.7)
Heroin	Plus Synthetic Opioids	65 (0.1)	530 (0.8)	1,559 (1.7)	1,329 (2.0)	1,152 (2.3)	1,263 (2.4)	1,504 (2.6)	1,694 (3.1)
Heroin	Minus Synthetic Opioids	2,272 (3.9)	3,880 (5.5)	4,729 (5.3)	2,348 (3.5)	1,332 (2.6)	1,546 (3.0)	1,176 (2.0)	899 (1.6)
Other Opioids	Total	12,513 (21.6)	17,662 (25.2)	23,685 (26.5)	14,706 (22.2)	9,878 (19.3)	9,150 (17.7)	9,569 (16.4)	8,803 (16.1)
Other Opioids	Plus Synthetic Opioids	614 (1.1)	1,630 (2.3)	3,914 (4.4)	3,445 (5.2)	3,087 (6.0)	3,278 (6.3)	4,569 (7.8)	5,054 (9.2)
Other Opioids	Minus Synthetic Opioids	11,899 (20.5)	16,032 (22.9)	19,771 (22.1)	11,261 (17.0)	6,791 (13.3)	5,872 (11.3)	5,000 (8.6)	3,749 (6.9)

Yearly UDT positives (No.) and positivity rates (%) calculated for the 5 drug classes and stratified by co-detection of synthetic opioids. Total positivity rate is not stratified by detection of synthetic opioids. Positivity rate is calculated as the number of positives (or co-positives) divided by the total number of samples times 100. Synthetic opioids can only be estimated for the total positivity rate.

eTable 3. Spearman Correlation for Yearly State-Level (n = 24) Overdose Mortality Rates With Corresponding Urine Drug Test Positivity Rates

Year	Rate	Synthetic Opioids	Methamphetamine	Cocaine	Heroin	Other Opioids
2013	Total	0.14	0.80	0.57	0.54	0.04
2014	Total	0.65	0.80	0.68	0.63	0.25
2015	Total	0.61	0.85	0.77	0.66	0.31
2016	Total	0.80	0.85	0.83	0.61	0.51
2017	Total	0.77	0.71	0.75	0.42	0.38
2018	Total	0.80	0.73	0.69	0.11	0.31
2019	Total	0.80	0.68	0.73	0.09	0.30
Median	Total	0.77	0.80	0.73	0.54	0.31
2013	Minus Synthetic Opioids	NA	0.79	0.52	0.54	-0.03
2014	Minus Synthetic Opioids	NA	0.82	0.67	0.64	0.23
2015	Minus Synthetic Opioids	NA	0.82	0.74	0.63	0.27
2016	Minus Synthetic Opioids	NA	0.86	0.70	0.62	0.35
2017	Minus Synthetic Opioids	NA	0.78	0.54	0.42	0.12
2018	Minus Synthetic Opioids	NA	0.75	0.51	0.43	0.17
2019	Minus Synthetic Opioids	NA	0.70	0.59	0.78	0.33
Median	Minus Synthetic Opioids	NA	0.79	0.59	0.62	0.23
2013	Plus Synthetic Opioids	NA	-0.11	0.38	0.49	0.20
2014	Plus Synthetic Opioids	NA	-0.05	0.81	0.86	0.64
2015	Plus Synthetic Opioids	NA	0.08	0.78	0.86	0.63
2016	Plus Synthetic Opioids	NA	0.42	0.89	0.86	0.81
2017	Plus Synthetic Opioids	NA	0.46	0.81	0.79	0.76
2018	Plus Synthetic Opioids	NA	0.62	0.86	0.68	0.76
2019	Plus Synthetic Opioids	NA	0.80	0.69	0.50	0.65
Median	Plus Synthetic Opioids	NA	0.42	0.81	0.79	0.65

Spearman correlation for state level mortality and UDT positivity rates stratified by drug category , year of collection and synthetic opioid co-detection. Each correlation represents the state level mortality and UDT positivity rate correlation for a given year. The mortality rates and the UDT positivity rates have been standardized (mean=0, sd=1).

eTable 4. Spearman Correlation for Yearly Urine Drug Test Positivity Rate vs Overdose Mortality Rate for Select States

State	Synthetic Opioids	Methamphetamine	Cocaine	Heroin	Other Opioids
Arizona	0.96 **	0.64	0.43	0.39	0.64
California	0.57	0.89 *	-0.21	-0.54	0.54
Florida	0.96 **	0.96 **	0.43	0.39	0.25
Georgia	-0.04	0.96 **	0.68	-0.64	-0.07
Indiana	0.93 **	0.96 **	0.39	0.21	-0.71
Kentucky	0.86 *	1.00 ***	0.71	0.71	0.50
Louisiana	0.14	0.36	-0.46	-0.11	-0.57
Maryland	0.96 **	0.89 *	0.89 *	0.57	0.39
Michigan	-0.36	0.96 **	0.54	0.04	-0.46
Minnesota	0.82 *	0.89 *	0.89 *	0.25	0.04
Mississippi	0.86 *	0.89 *	0.32	0.89 *	0.14
Nevada	-0.50	-0.57	-0.04	-0.96 **	0.68
New York	0.36	0.93 **	-0.93 **	-0.54	-0.46
North Carolina	0.64	0.86 *	0.96 **	0.64	0.46
Ohio	0.93 **	1.00 ***	0.96 **	0.82 *	0.46
Oklahoma	0.18	0.93 **	-0.23	0.18	0.14
Oregon	0.57	1.00 ***	0.64	0.64	-0.61
Pennsylvania	0.96 **	1.00 ***	0.32	-0.21	-0.21
Tennessee	0.96 **	0.93 **	0.25	0.43	0.21
Texas	0.32	0.86 *	0.82 *	0.79 *	0.39
Utah	0.18	0.82 *	0.36	0.71	-0.14
Virginia	0.93 **	0.57	0.89 *	-0.39	0.57
Washington	0.93 **	0.96 **	-0.18	0.36	-0.43
Wisconsin	0.79 *	0.86 *	0.75	0.29	0.46
Median	0.80	0.91	0.43	0.32	0.18

Spearman correlation for yearly state level mortality and UDT positivity rates stratified by drug category.

P value designation * <0.05, ** <0.01, *** <0.001

eTable 5. Spearman Correlation for Yearly Urine Drug Test Positivity Rate vs Mortality Rate for Select Ohio Counties

County	Synthetic Opioids	Methamphetamine	Cocaine	Heroin	Other Opioids
Franklin	0.95 **	0.95 **	0.40	0.81 *	-0.07
Cuyahoga	0.71	0.69	0.48	0.79 *	0.81 *
Hamilton	0.62	0.67	0.00	0.43	0.17
Summit	0.88 **	0.88 **	0.40	0.98 ***	0.55
Lucas	0.98 ***	0.54	0.71	0.67	0.74 *
Butler	0.43	0.74 *	0.19	0.97 ***	0.40
Lorain	0.93 **	0.55	0.60	0.38	-0.45
Warren	0.48	0.36	0.38	0.84 **	-0.14
Clermont	0.21	0.38	0.12	0.79 *	0.60
Medina	0.81 *	0.32	0.76 *	0.69	0.17
Fairfield	0.89 **	0.83 *	0.20	-0.07	-0.07
Wood	0.71	-0.05	-0.43	0.69	0.57
Richland	0.83 *	0.94 ***	0.24	0.69	0.17
Allen	0.62	0.83 **	-0.04	0.79 *	0.74 *
Erie	0.62	0.83 **	0.67	0.21	0.43
Marion	0.90 **	0.79 *	-0.48	0.55	0.36
Huron	0.74 *	0.34	0.50	-0.08	0.26
Seneca	0.60	0.59	-0.05	0.24	0.34
Fulton	0.55	0.67	0.06	-0.38	-0.12
Median	0.71	0.67	0.24	0.69	0.34

Spearman correlation for yearly county level mortality and UDT positivity rates stratified by drug category.
 P value designation * <0.05, ** <0.01, *** <0.001