Supplementary Online Content

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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