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| **Supplemental Digital Content 2. Mann-Kendall Correlation Analysis of Co-Positivity OR Values** |
| *Analyte* | *Regions* | *Tau* | *P Value* |
| **Benzodiazepines** | **US Total** | **-0.3333333** | **0.452370346** |
| **Buprenorphine** | **US Total** | **0.59999996** | **0.132854939** |
| **Cocaine** | **US Total** | **0.33333331** | **0.452370405** |
| **Alcohol** | **US Total** | **-0.3333333** | **0.452370346** |
| **Fentanyl** | **US Total** | **0.99999994** | **0.008534908** |
| **Heroin** | **US Total** | **0.86666662** | **0.024170518** |
| **Methadone** | **US Total** | **-0.2** | **0.70711422** |
| **Other Opioids** | **US Total** | **0.73333329** | **0.060289145** |
| **THC** | **US Total** | **0.19999999** | **0.70711422** |
| Benzodiazepines | East North Central | -0.6 | 0.132854968 |
| Buprenorphine | East North Central | -0.4666666 | 0.25965631 |
| Cocaine | East North Central | -0.0666667 | 1 |
| Alcohol | East North Central | -0.3333333 | 0.452370346 |
| Fentanyl | East North Central | 0.73333329 | 0.060289145 |
| Heroin | East North Central | 0.59999996 | 0.132854939 |
| Methadone | East North Central | -0.2 | 0.70711422 |
| Other Opioids | East North Central | -0.3333333 | 0.452370346 |
| THC | East North Central | -0.6 | 0.132854968 |
| Benzodiazepines | East South Central | -0.9999999 | 0.008534921 |
| Buprenorphine | East South Central | -0.4666666 | 0.25965631 |
| Cocaine | East South Central | -0.4666666 | 0.25965631 |
| Alcohol | East South Central | -0.8666666 | 0.024170551 |
| Fentanyl | East South Central | 0.59999996 | 0.132854939 |
| Heroin | East South Central | 0.46666664 | 0.25965631 |
| Methadone | East South Central | -0.9999999 | 0.008534921 |
| Other Opioids | East South Central | 0.73333329 | 0.060289145 |
| THC | East South Central | 0.19999999 | 0.70711422 |
| Benzodiazepines | Mid Atlantic | -0.2 | 0.70711422 |
| Buprenorphine | Mid Atlantic | 0.73333329 | 0.060289145 |
| Cocaine | Mid Atlantic | 0.33333331 | 0.452370405 |
| Alcohol | Mid Atlantic | -0.0666667 | 1 |
| Fentanyl | Mid Atlantic | 0.73333329 | 0.060289145 |
| Heroin | Mid Atlantic | 0.59999996 | 0.132854939 |
| Methadone | Mid Atlantic | 0.33333331 | 0.452370405 |
| Other Opioids | Mid Atlantic | -0.2 | 0.70711422 |
| THC | Mid Atlantic | -0.3333333 | 0.452370346 |
| Benzodiazepines | Mountain | 0.19999999 | 0.70711422 |
| Buprenorphine | Mountain | 0.86666662 | 0.024170518 |
| Cocaine | Mountain | 0.59999996 | 0.132854939 |
| Alcohol | Mountain | -0.0666667 | 1 |
| Fentanyl | Mountain | 0.86666662 | 0.024170518 |
| Heroin | Mountain | 0.73333329 | 0.060289145 |
| Methadone | Mountain | 0.46666664 | 0.25965631 |
| Other Opioids | Mountain | 0.99999994 | 0.008534908 |
| THC | Mountain | -0.6 | 0.132854968 |
| Benzodiazepines | New England | 0.33333331 | 0.452370405 |
| Buprenorphine | New England | 0.33333331 | 0.452370405 |
| Cocaine | New England | -0.0666667 | 1 |
| Alcohol | New England | -0.2 | 0.70711422 |
| Fentanyl | New England | 0.46666664 | 0.25965631 |
| Heroin | New England | 0.19999999 | 0.70711422 |
| Methadone | New England | -0.3333333 | 0.452370346 |
| Other Opioids | New England | 0.46666664 | 0.25965631 |
| THC | New England | 0.33333331 | 0.452370405 |
| Benzodiazepines | Pacific | -0.8666666 | 0.024170551 |
| Buprenorphine | Pacific | 0.46666664 | 0.25965631 |
| Cocaine | Pacific | -0.3333333 | 0.452370346 |
| Alcohol | Pacific | -0.9999999 | 0.008534921 |
| Fentanyl | Pacific | 0.86666662 | 0.024170518 |
| Heroin | Pacific | 0.99999994 | 0.008534908 |
| Methadone | Pacific | 0.46666664 | 0.25965631 |
| Other Opioids | Pacific | 0.99999994 | 0.008534908 |
| THC | Pacific | -0.9999999 | 0.008534921 |
| Benzodiazepines | South Atlantic | -0.7333333 | 0.060289178 |
| Buprenorphine | South Atlantic | -0.2 | 0.70711422 |
| Cocaine | South Atlantic | 0.46666664 | 0.25965631 |
| Alcohol | South Atlantic | -0.3333333 | 0.452370346 |
| Fentanyl | South Atlantic | 0.99999994 | 0.008534908 |
| Heroin | South Atlantic | 0.46666664 | 0.25965631 |
| Methadone | South Atlantic | -0.2 | 0.70711422 |
| Other Opioids | South Atlantic | -0.3333333 | 0.452370346 |
| THC | South Atlantic | 0.33333331 | 0.452370405 |
| Benzodiazepines | West North Central | 0.06666666 | 1 |
| Buprenorphine | West North Central | 0.33333331 | 0.452370405 |
| Cocaine | West North Central | 0.59999996 | 0.132854939 |
| Alcohol | West North Central | 0.33333331 | 0.452370405 |
| Fentanyl | West North Central | 0.59999996 | 0.132854939 |
| Heroin | West North Central | 0.73333329 | 0.060289145 |
| Methadone | West North Central | 0.46666664 | 0.25965631 |
| Other Opioids | West North Central | 0.59999996 | 0.132854939 |
| THC | West North Central | 0.59999996 | 0.132854939 |
| Benzodiazepines | West South Central | 0.06666666 | 1 |
| Buprenorphine | West South Central | -0.2 | 0.70711422 |
| Cocaine | West South Central | -0.2 | 0.70711422 |
| Alcohol | West South Central | -0.2 | 0.70711422 |
| Fentanyl | West South Central | 0.73333329 | 0.060289145 |
| Heroin | West South Central | -0.2 | 0.70711422 |
| Methadone | West South Central | -0.9999999 | 0.008534921 |
| Other Opioids | West South Central | -0.4666666 | 0.25965631 |
| THC | West South Central | 0.73333329 | 0.060289145 |

**Supplemental Digital Content 2. Mann-Kendall Correlation Analysis of Co-Positivity OR Values**

*Notes:*

A Mann Kendall correlation test was performed for each of the nine co-positivity regression models. The Mann Kendall test is a simple non-parametric test often used to evaluate if there is a monotonic increase or decrease in a variable over time. This test was used to determine if the OR from Table 3 was increasing or decreasing for a given census division and drug or drug class. The total US OR was also evaluated for each drug model. Other opioids include codeine, hydrocodone, hydromorphone, morphine, oxycodone, and oxymorphone.