Millennium Health is an accredited specialty laboratory with over a decade of experience in drug testing services allowing clinicians to monitor the use of prescription medications and illicit drugs and effectiveness of treatment plans. Processing over a million specimens each year allows us to provide real-time analytics regarding emerging drug use trends.

**Customer Service & RADAR® Hotline**
(866) 866-0605
As the nation continues to navigate the impacts of the COVID-19 pandemic, new and alarming drug use trends have emerged. In 2020, more people died of drug overdoses than in any previously recorded year. Combined with suicide and alcohol-related illness, these “deaths of despair” have contributed to a drop in overall life expectancy in the U.S.

These developments have instilled a sense of urgency to address this crisis, with some public health officials calling for radical change. At Millennium Health, we believe it’s more important than ever to do our part by informing public health surveillance efforts and bringing awareness to communities that are most in need of intervention. In 2021, we continued our work through our Emerging Threat Intelligence (ETI) Program, providing reports to the U.S. Department of Health and Human Services and the Ohio Department of Public Safety. We also established a new agreement with Columbia University to provide data assisting their efforts with the HEALing Communities Study (HCS) in New York. According to University Professor, Nabila El-Bassel, PhD, Director, Social Intervention Group, Columbia University and Principal Investigator for the New York research site of HCS, “Millennium Health’s ETI Report will help the community coalitions in HCS to use data to inform their implementation strategies to reduce overdose deaths.”

Sharing vital information to help reduce overdose deaths is a key tenet of Millennium Health, with our researchers contributing multiple, peer-reviewed studies to the literature throughout the year. Using our proprietary, national database of definitive urine drug testing (UDT) results, in 2021, we published current trends in methamphetamine and alcohol use, highlighting factors that influence use. Additionally, collaborative research with Dr. Brendan Saloner of Johns Hopkins University identified patterns of substance use in patients prescribed buprenorphine for opioid use disorder. Many research projects are ongoing, and our team is excited to share these findings in 2022, beginning with the release of our annual Millennium Health Signals Report™.

With volume 4 of this Signals Report, we address some of the most pressing questions regarding substance use trends. First, we evaluate trends in four common illicit substances known to be driving overdose deaths (i.e., fentanyl, methamphetamine, cocaine, and heroin), as well as the populations most likely to test positive for these drugs. In section 2, due to increasing polysubstance use and coinvolved drug overdoses, we assess current trends in the combination of fentanyl with other illicit substances. Lastly, we cover a new and relevant topic for the Signals Report: marijuana use.

We hope this report is useful to your practice and will ultimately help make a difference in the lives of patients, their families, and communities across the nation.
Adjusted positivity rates and 95% confidence interval (CI) values for methamphetamine, fentanyl, cocaine, and heroin were estimated for each month between 2015 and 2021. Rates were adjusted for age, sex, U.S. census division and specialty of the referring clinic using logistic regression. A 3-month moving average of the adjusted positivity rates is shown as a thick line. The vertical line reflects the U.S. national emergency declaration on March 13, 2020.
**Background**

Drug overdose deaths topped 100,000 in the 12-month period ending in April 2021.¹ Largely driven by synthetic opioids, namely illicitly manufactured fentanyl, deaths involving this drug category increased a staggering 60% between 2019 and 2020, contributing to approximately 60% of all drug overdose deaths.¹ Second to synthetic opioids are stimulants, including methamphetamine and cocaine, contributing to approximately 25% and 20% of overdose deaths, respectively.¹ Cocaïne and methamphetamine are each now involved in more deaths than either prescription opioids or heroin. Lastly, while declining slightly overall, heroin was involved in approximately 15% of overdose deaths in 2020.¹

In addition to marijuana, these four drugs persist among the top five substances identified by law enforcement in confiscations across the nation, with methamphetamine remaining at the top of the list in 2020.⁶ Due to its high purity and potency, coupled with low cost, methamphetamine is readily available with the majority of product being smuggled into the U.S. from Mexico.⁷ Cocaïne availability is also steady, likely due to record production in Columbia, which produces about 90% of the cocaine powder reaching the U.S.⁷,⁸

According to the Drug Enforcement Administration (DEA), illicit fentanyl continues to drive the opioid crisis.⁷ Reports on fentanyl identified by law enforcement in confiscations across the U.S. increased from nearly 5,400 in 2014 to over 117,000 in 2020.⁶,⁸ The DEA also seized a staggering 20.4 million counterfeit, fentanyl-laced tablets in 2021; the counterfeit tablets often look remarkably similar to authentic tablets and are increasingly contributing to overdose deaths across the country (Figure 2).⁹,¹⁰

Fentanyl is up to 100 times more potent than morphine and as little as 2 mg can be lethal (Figure 3).¹¹ Of counterfeit pills tested in DEA laboratories, four out of ten pills made with fentanyl contained a potentially lethal dose.¹⁰ Its synthetic nature allows it to be cheaply produced, and it is often mixed with other drugs, such as heroin, to extend or supplant supplies. While the heroin supply remains high, its market is often intertwined with illicit fentanyl; this will be further explored in Section 2 of this report.⁷

![Figure 2. Authentic Oxycodone Tablets (Top) Vs. Counterfeit Oxycodone Tablets Containing Fentanyl (Bottom)](image)

![Figure 3. Potentially Lethal Dose of Fentanyl](image)

Because of widespread availability and lethality of these four illicit drugs, we continue to evaluate their UDT positivity trends over time.
Key Findings

In this section, we evaluated adjusted UDT positivity rates for illicit methamphetamine, fentanyl, cocaine, and heroin. Findings include:

Nationally, between 2015 and 2021, overall UDT positivity increased for fentanyl and methamphetamine, though a downward trend was noted toward the end of 2021; cocaine has remained relatively flat, and heroin has declined (Figure 1).

Among specialties, specimens from pain management practices had the lowest positivity rates for all four drugs and positivity declined or remained flat between 2015 and 2021 (Figure 4).

The highest positivity rates were from substance use disorder (SUD) treatment practices with rates increasing steeply for methamphetamine and fentanyl over time (Figure 4).

Positivity rates are similar based on patient sex; positivity tended to be higher in younger patients, except for cocaine, where use was similar across age groups (Figure 5).

Between 2019 and 2021, fentanyl and cocaine positivity increased in all census divisions, led by the Pacific and Mid Atlantic divisions, respectively; all but one census division increased in methamphetamine positivity, led by New England (Table 1, Figure 6).

Heroin declined in most census divisions (Table 1, Figure 6).
Yearly adjusted positivity rates and 95% CI values for methamphetamine, fentanyl, cocaine, and heroin were estimated for each year and specialty of the referring clinic between 2015 and 2021. Rates were adjusted for age, sex, and U.S. census division using logistic regression.

2021 adjusted positivity rates and 95% CI values for methamphetamine, fentanyl, cocaine, and heroin are shown for age, sex, and specialty of the referring clinic. Rates were adjusted for age, sex, U.S. census division and specialty of the referring clinic using logistic regression.
2019 and 2021 adjusted positivity rates for methamphetamine, fentanyl, cocaine, and heroin were estimated for U.S. census divisions. Rates were adjusted for age, sex, and specialty of the referring clinic using logistic regression.
Conclusions

Overall increases in fentanyl and methamphetamine are concerning, especially when considering these are the top two drugs contributing to drug overdose deaths. However, a shift towards a downward trend in these substances in late 2021 suggest that use may no longer be growing at the exponential rates observed in 2020, surrounding the emergence of the COVID-19 pandemic. We will continue tracking these changes through 2022 to see if the trend continues.

Regionally, as indicated in the heat map, fentanyl’s growth continues in the Western U.S., while methamphetamine gained ground in the New England area. Heroin positivity declined nearly everywhere, while cocaine positivity remained steady or slightly increased across the U.S.

Looking at demographics, it’s notable that trends observed in the rest of our health care population are not reflected in pain management practices, where positivity was consistently low for all drugs over the past six years. Trends in other specialties mirrored those of the national findings, including increases in fentanyl and methamphetamine. SUD treatment had the highest positivity rates, which is consistent with other research suggesting that those with SUD are most likely to test positive for illicit substances.\(^3,12\)

While no significant difference was observed between patient sex, this itself is a notable finding, as other literature has typically indicated higher rates of substance use in men, though sex does not appear to influence development of SUD.\(^13\) This finding suggests the gap in use is perhaps narrowing or may not be significantly different in a population seeking health care. As anticipated, use was generally highest in younger populations, though cocaine use was similar across age groups.

<table>
<thead>
<tr>
<th>U.S. Census Division</th>
<th>Methamphetamine</th>
<th>Fentanyl</th>
<th>Cocaine</th>
<th>Heroin</th>
</tr>
</thead>
<tbody>
<tr>
<td>East North Central</td>
<td>50%</td>
<td>43%</td>
<td>6%</td>
<td>-40%</td>
</tr>
<tr>
<td>East South Central</td>
<td>30%</td>
<td>44%</td>
<td>16%</td>
<td>-40%</td>
</tr>
<tr>
<td>Mid Atlantic</td>
<td>23%</td>
<td>76%</td>
<td>48%</td>
<td>-27%</td>
</tr>
<tr>
<td>Mountain</td>
<td>68%</td>
<td>198%</td>
<td>11%</td>
<td>-2%</td>
</tr>
<tr>
<td>New England</td>
<td>134%</td>
<td>97%</td>
<td>39%</td>
<td>-35%</td>
</tr>
<tr>
<td>Pacific</td>
<td>-4%</td>
<td>427%</td>
<td>25%</td>
<td>-20%</td>
</tr>
<tr>
<td>South Atlantic</td>
<td>45%</td>
<td>80%</td>
<td>12%</td>
<td>-17%</td>
</tr>
<tr>
<td>West North Central</td>
<td>25%</td>
<td>160%</td>
<td>3%</td>
<td>26%</td>
</tr>
<tr>
<td>West South Central</td>
<td>27%</td>
<td>305%</td>
<td>26%</td>
<td>52%</td>
</tr>
<tr>
<td>U.S. Total</td>
<td>40%</td>
<td>134%</td>
<td>20%</td>
<td>-16%</td>
</tr>
</tbody>
</table>

2019 and 2021 adjusted positivity rates for methamphetamine, fentanyl, cocaine, and heroin were estimated for U.S. census divisions. Rates were adjusted for age, sex, and specialty of the referring clinic using logistic regression. The percent change between 2019 and 2021 was estimated as: % change = (2021 rate - 2019 rate)/2019 rate*100.
Adjusted fentanyl positivity rates and 95% confidence interval (CI) values for the heroin, methamphetamine, and cocaine positive populations were estimated for each month between 2015 and 2021. Rates were adjusted for the U.S. census division using logistic regression. A 3-month moving average of the adjusted positivity rate is shown as a thick line. The vertical line reflects the U.S. national emergency declaration on March 13, 2020.
Background

As discussed in Section 1, the number one drug category involved in overdose deaths is synthetic opioids, primarily illicitly manufactured fentanyl, which contributed to approximately 60% of overdose deaths in 2020. Its co-involvement with other substances has also increased across all drug categories. Apart from methamphetamine, which is associated with increasing deaths both alone and in combination with synthetic opioids, deaths involving cocaine and heroin are only increasing when coinvolved with synthetic opioids.

While fentanyl is identified as a single drug in about half of law enforcement reports, it has infiltrated the supply of other drugs. In some cases, the person using the drug is unaware of fentanyl’s presence, which can amplify the risk of overdose. In other cases, drugs are deliberately combined, such as the co-use of opioids and stimulants to counterbalance sedation and stimulation.

There are increasing reports of methamphetamine use among those who also use opioids. A recent study conducted in persons entering treatment for opioid use disorder identified past month use of at least one non-opioid drug in more than 90% of participants; methamphetamine use grew the most, increasing 85% from 2011 to 2018.

Concerns around the contribution of polysubstance use to drug overdose deaths led us to analyze fentanyl combinations with common illicit substances, including methamphetamine, cocaine, and heroin.

Key Findings

In this section, we evaluated adjusted UDT positivity rates for illicit fentanyl in patients testing positive for heroin, methamphetamine, or cocaine. Findings include:

Nationally, in 2021, nearly all (92%) of heroin-positive UDT specimens also contained illicit fentanyl, while 41% of methamphetamine-positive UDT specimens and 36% of cocaine-positive UDT specimens also contained illicit fentanyl (Figure 1).

Between 2019 and 2021, national UDT positivity rates for illicit fentanyl increased by 155% in the methamphetamine-positive population, 81% in the cocaine-positive population, and 42% in the heroin-positive population (Table 1).

Fentanyl co-positivity with heroin, methamphetamine, and cocaine increased in every U.S. census division (Figure 2, Table 1).

The greatest changes in co-positivity were in the West, including the Pacific and Mountain divisions. The West South Central also had over 100% increases in each category (Table 1).

Western states (e.g., Nevada, Utah, Colorado, and Alaska) had the highest increases in co-positivity (Table 2).
Fentanyl positivity rates in the heroin, methamphetamine, and cocaine positive populations were estimated for 2019 and 2021. Rates were estimated for the U.S. census division and year using logistic regression without adjustment for other demographic covariates.
Conclusions

These findings indicate that fentanyl has become extensively intertwined with other substances. Ignoring polysubstance use trends to focus on the opioid epidemic in a silo is shortsighted because of the complications presented by polysubstance use. Unfortunately, clinical guidelines tend to address solitary SUDs, which makes it challenging to develop treatment strategies for those with multiple SUDs. Additionally, there remains no FDA-approved treatment for stimulant use disorder, and chronic use, especially of methamphetamine, can lead to debilitating changes in brain chemistry and diminished quality of life.

Rather than addressing fentanyl alone, treatment and prevention efforts need to take a more global position, accounting for the multiple drugs used along with opioids. Developing strategies to overcome barriers and get patients engaged in treatment is crucial to improving effective outcomes and saving lives.

Table 1. Percent Change from 2019 to 2021 in Fentanyl Positivity in the Heroin, Methamphetamine, and Cocaine Positive Populations by U.S. Census Division

<table>
<thead>
<tr>
<th>U.S. Census Division</th>
<th>Heroin</th>
<th>Methamphetamine</th>
<th>Cocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>East North Central</td>
<td>10%</td>
<td>35%</td>
<td>20%</td>
</tr>
<tr>
<td>East South Central</td>
<td>5%</td>
<td>29%</td>
<td>21%</td>
</tr>
<tr>
<td>Mid Atlantic</td>
<td>22%</td>
<td>94%</td>
<td>55%</td>
</tr>
<tr>
<td>Mountain</td>
<td>102%</td>
<td>306%</td>
<td>163%</td>
</tr>
<tr>
<td>New England</td>
<td>5%</td>
<td>58%</td>
<td>57%</td>
</tr>
<tr>
<td>Pacific</td>
<td>485%</td>
<td>571%</td>
<td>254%</td>
</tr>
<tr>
<td>South Atlantic</td>
<td>13%</td>
<td>148%</td>
<td>42%</td>
</tr>
<tr>
<td>West North Central</td>
<td>16%</td>
<td>179%</td>
<td>31%</td>
</tr>
<tr>
<td>West South Central</td>
<td>112%</td>
<td>471%</td>
<td>324%</td>
</tr>
<tr>
<td>U.S. Total</td>
<td>42%</td>
<td>155%</td>
<td>81%</td>
</tr>
</tbody>
</table>

Fentanyl positivity rates in the heroin, methamphetamine, and cocaine positive populations were estimated for 2019 and 2021. Rates were estimated for the U.S. census division and year using logistic regression without adjustment for other demographic covariates. The percent change between 2019 and 2021 was estimated as: % change = (2021 rate – 2019 rate)/2019 rate*100.

Table 2. Top 10 States with the Highest Percent Increase in Fentanyl Positivity in the Heroin, Methamphetamine, and Cocaine Positive Populations

<table>
<thead>
<tr>
<th>Rank</th>
<th>State</th>
<th>2019 Rate</th>
<th>2021 Rate</th>
<th>% Increase</th>
<th>State</th>
<th>2019 Rate</th>
<th>2021 Rate</th>
<th>% Increase</th>
<th>State</th>
<th>2019 Rate</th>
<th>2021 Rate</th>
<th>% Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Utah</td>
<td>0.0%</td>
<td>31.6%</td>
<td>&gt;5000%</td>
<td>Nevada</td>
<td>0.0%</td>
<td>9.6%</td>
<td>&gt;5000%</td>
<td>Colorado</td>
<td>2.0%</td>
<td>23.7%</td>
<td>1096%</td>
</tr>
<tr>
<td>2</td>
<td>Colorado</td>
<td>2.5%</td>
<td>40.0%</td>
<td>1500%</td>
<td>Utah</td>
<td>0.0%</td>
<td>16.1%</td>
<td>&gt;5000%</td>
<td>Alaska</td>
<td>3.1%</td>
<td>33.3%</td>
<td>983%</td>
</tr>
<tr>
<td>3</td>
<td>Alaska</td>
<td>7.0%</td>
<td>69.0%</td>
<td>886%</td>
<td>Colorado</td>
<td>0.9%</td>
<td>31.7%</td>
<td>3435%</td>
<td>Mississippi</td>
<td>1.3%</td>
<td>12.6%</td>
<td>848%</td>
</tr>
<tr>
<td>4</td>
<td>Washington</td>
<td>9.4%</td>
<td>70.1%</td>
<td>644%</td>
<td>Montana</td>
<td>1.0%</td>
<td>9.6%</td>
<td>869%</td>
<td>Texas</td>
<td>3.8%</td>
<td>18.5%</td>
<td>388%</td>
</tr>
<tr>
<td>5</td>
<td>Montana</td>
<td>10.3%</td>
<td>45.6%</td>
<td>341%</td>
<td>Alaska</td>
<td>4.1%</td>
<td>37.3%</td>
<td>817%</td>
<td>New Mexico</td>
<td>13.5%</td>
<td>51.5%</td>
<td>281%</td>
</tr>
<tr>
<td>6</td>
<td>Oregon</td>
<td>11.4%</td>
<td>48.7%</td>
<td>327%</td>
<td>Arkansas</td>
<td>0.9%</td>
<td>8.0%</td>
<td>807%</td>
<td>Washington</td>
<td>9.4%</td>
<td>32.5%</td>
<td>246%</td>
</tr>
<tr>
<td>7</td>
<td>California</td>
<td>15.9%</td>
<td>55.3%</td>
<td>249%</td>
<td>Washington</td>
<td>4.7%</td>
<td>42.3%</td>
<td>801%</td>
<td>Louisiana</td>
<td>15.3%</td>
<td>51.3%</td>
<td>235%</td>
</tr>
<tr>
<td>8</td>
<td>Arizona</td>
<td>23.9%</td>
<td>66.6%</td>
<td>179%</td>
<td>Texas</td>
<td>2.5%</td>
<td>15.9%</td>
<td>536%</td>
<td>California</td>
<td>9.8%</td>
<td>31.8%</td>
<td>223%</td>
</tr>
<tr>
<td>9</td>
<td>New Mexico</td>
<td>29.3%</td>
<td>60.6%</td>
<td>107%</td>
<td>Oregon</td>
<td>5.6%</td>
<td>24.4%</td>
<td>337%</td>
<td>North Carolina</td>
<td>10.5%</td>
<td>30.3%</td>
<td>190%</td>
</tr>
<tr>
<td>10</td>
<td>Indiana</td>
<td>56.5%</td>
<td>97.4%</td>
<td>72%</td>
<td>California</td>
<td>6.8%</td>
<td>28.6%</td>
<td>320%</td>
<td>Arizona</td>
<td>25.1%</td>
<td>54.4%</td>
<td>117%</td>
</tr>
</tbody>
</table>
Adjusted positivity rate and 95% confidence interval (CI) values for marijuana were estimated for each month between 2015 and 2021. Rates were adjusted for age, sex, U.S. census division and specialty of the referring clinic using logistic regression. A 3-month moving average of the adjusted positivity rates is shown as a thick line. The vertical line reflects the U.S. national emergency declaration on March 13, 2020.
Background

The marijuana, or cannabis, landscape has become increasingly complex as interest in medical and recreational use has grown, and some states have created legislation conflicting with marijuana’s federal status as a Schedule I illicit substance. In 1996, California was the first state to legalize medical marijuana; that number has since grown to include 36 states and the District of Columbia. The regulation of recreational marijuana has also gained momentum, following legalization of retail sales a decade ago in Colorado and Washington. Currently, 19 states have approved recreational use for adults. Other states have allowed access to cannabidiol products, while only 3 states do not allow legal access to any forms of marijuana.18,19

According to the most recent National Survey on Drug Use and Health, marijuana is the most used drug with approximately 49.6 million Americans aged 12 and older reporting use in the past year. According to the same survey, approximately 14.2 million Americans had a marijuana use disorder in the past year, predominantly among those 18 to 25 years old.20

While research efforts have identified some potential medical benefits, marijuana use has intrinsic risks, particularly for younger people and those predisposed to mental health disorders.21 Research indicates that 30% of people using marijuana may have some degree of marijuana use disorder, and the risk of developing a marijuana use disorder is four to seven times more likely in people who use marijuana before the age of 18.22 Negative effects are also more likely with chronic use of high potency products.21

The cannabis plant contains hundreds of chemical compounds. Two of the better characterized cannabinoids include delta-9-tetrahydrocannabinol (THC), which is one of the main psychoactive ingredients, and cannabidiol (CBD), a nonpsychoactive component.23 Though “THC” is the abbreviation commonly referring to delta-9-THC, other isomers of tetrahydrocannabinol exist, such as delta-8-THC. Delta-8-THC is present in small amounts in the marijuana plant and may be isolated into products considered legal in some states.24

Over time, the average THC concentration in marijuana products has risen considerably in both traditional, leafy marijuana and more concentrated products, such as wax or hash oil. For example, the average THC content in confiscated marijuana products seized by the DEA in 1995 was less than 4%, while in 2019, the average was over 14%.25 Some dispensaries advertise smokable marijuana with 30% or more THC content, while some concentrate products exceed 90% THC.7 Increasing potency has led to a rise in emergency department visits and poison control calls relating to marijuana toxicity.26 These trends, along with growing interest in this substance, led us to evaluate marijuana positivity in UDT over time.
Characterizing the Cannabis Landscape (continued)

Key Findings

In this section, we evaluated adjusted UDT positivity rates for marijuana. Findings include:

- Nationally, between 2015 and 2021, the UDT positivity rate for marijuana increased 32% (from 22.9% to 30.3%) (Figure 1)

- The highest positivity rates were noted for male patients and those aged 18-24 years old; the likelihood of testing positive decreased with age (Figure 2)

- Pain management had significantly lower positivity rates than other health care specialties (Figure 2)

- Marijuana positivity increased in every U.S. census division, led by the West South Central (Figure 3, Table 1)
Table 1. Percent Change from 2019 to 2021 in Marijuana Positivity Rate by U.S. Census Division

<table>
<thead>
<tr>
<th>U.S. Census Division</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>West South Central</td>
<td>43%</td>
</tr>
<tr>
<td>West North Central</td>
<td>38%</td>
</tr>
<tr>
<td>East South Central</td>
<td>34%</td>
</tr>
<tr>
<td>South Atlantic</td>
<td>29%</td>
</tr>
<tr>
<td>East North Central</td>
<td>22%</td>
</tr>
<tr>
<td>Mountain</td>
<td>20%</td>
</tr>
<tr>
<td>Mid Atlantic</td>
<td>15%</td>
</tr>
<tr>
<td>New England</td>
<td>15%</td>
</tr>
<tr>
<td>Pacific</td>
<td>2%</td>
</tr>
<tr>
<td>U.S. Total</td>
<td>23%</td>
</tr>
</tbody>
</table>

2019 and 2021 adjusted positivity rates for marijuana were estimated for each Census Division. Rates were adjusted for age, sex, and specialty of the referring clinic using logistic regression. The percent change between 2019 and 2021 was estimated as: % change = (2021 rate - 2019 rate) / 2019 rate * 100.
Characterizing the Cannabis Landscape (continued)

Conclusions

Marijuana positivity has increased remarkably in this health care population. This may be due to increasing legalization and access, changes in public perception of marijuana-related harm, and factors associated with the COVID-19 pandemic. For example, a recent study identified isolation and depression coping as major reasons for increases in marijuana use during the pandemic. While prevailing public opinion is that marijuana is a relatively benign, mood-altering substance, research indicates that use can be harmful, particularly for at-risk populations and when using high potency products. Because of these reasons, monitoring for marijuana via definitive UDT may be warranted in some cases.

Table 2. Top 10 States with the Highest Percent Increase in Positivity Rate From 2019 to 2021 for Marijuana

<table>
<thead>
<tr>
<th>State</th>
<th>2019 Rate</th>
<th>2021 Rate</th>
<th>Percent Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tennessee</td>
<td>14.2%</td>
<td>27.6%</td>
<td>94%</td>
</tr>
<tr>
<td>Illinois</td>
<td>27.5%</td>
<td>48.5%</td>
<td>76%</td>
</tr>
<tr>
<td>Virginia</td>
<td>18.2%</td>
<td>30.7%</td>
<td>69%</td>
</tr>
<tr>
<td>Iowa</td>
<td>29.8%</td>
<td>49.8%</td>
<td>67%</td>
</tr>
<tr>
<td>Idaho</td>
<td>12.1%</td>
<td>19.0%</td>
<td>57%</td>
</tr>
<tr>
<td>Indiana</td>
<td>17.8%</td>
<td>28.0%</td>
<td>57%</td>
</tr>
<tr>
<td>Minnesota</td>
<td>21.6%</td>
<td>33.0%</td>
<td>53%</td>
</tr>
<tr>
<td>Arizona</td>
<td>21.7%</td>
<td>29.8%</td>
<td>37%</td>
</tr>
<tr>
<td>Louisiana</td>
<td>24.8%</td>
<td>33.5%</td>
<td>35%</td>
</tr>
<tr>
<td>Nevada</td>
<td>26.5%</td>
<td>35.0%</td>
<td>32%</td>
</tr>
</tbody>
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2019 and 2021 adjusted positivity rates for marijuana were estimated for states. Rates were adjusted for age, sex, and specialty of the referring clinic using logistic regression. The percent change between 2019 and 2021 was estimated as: % change = (2021 rate – 2019 rate)/2019 rate*100. The 10 states with the highest percent increase in positivity rates were chosen if the 2019 and 2021 positivity rates were significantly different.
This cross-sectional analysis includes evaluation of definitive urine drug testing (UDT) results tested by liquid chromatography-tandem mass spectrometry (LC-MS/MS) from 2 million unique patient specimens across the U.S. and multiple health care specialties. The LC-MS/MS testing method is a laboratory-developed test with performance characteristics determined by Millennium Health, San Diego, California, which is certified by the Clinical Laboratory Improvement Amendments and accredited by the College of American Pathologists for high-complexity testing. Specimens were collected between January 1, 2015, and December 20, 2021. Included specimens were from patients aged 18 years or older. Specimens were collected from health care practices from all 50 states. Each UDT was individually ordered by the clinician based on medical necessity. A single specimen for each patient was selected based on the earliest specimen collection date, and repeated measurements were removed from the sample population. Patient specimens were tested for the following drug categories (all analytes tested are in parentheses): cocaine (benzoylecgonine), methamphetamine (methamphetamine), fentanyl (fentanyl, norfentanyl), heroin (6-monoacetylmorphine) and marijuana (delta-9-tetrahydrocannabinol carboxylic acid [cTHC]). Of note, the LC-MS/MS UDT test used for marijuana is specific for delta-9-THC carboxylic acid, the major metabolite of THC; thus, delta-8-THC is not anticipated to cause a positive result with this method. If any parent drug or metabolite within a drug category was ordered and detected, the drug category was considered positive for that specimen. Specimens with reported prescriptions for any of the UDT drug categories above were excluded from analysis. UDT cannot distinguish between use of pharmaceutical-grade fentanyl and illicitly manufactured fentanyl.

Logistic regression was used to adjust UDT positivity rates by correcting for differences in population characteristics, including U.S. census division, age, sex, and health care specialty. Different model specifications were used depending on the analysis requirements (see figure and table legends for included covariates). Adjusted positivity rates (Least Square Mean marginal probability) and adjusted odds ratios (aOR) were estimated. 95% CI values for aOR and positivity rates were estimated, and P values were Tukey corrected for multiple comparisons where appropriate. Statistical significance for state-level analysis in sections 2 and 3 was performed by comparing 95% CI for 2019 and 2021 positivity rates. Non-overlap of 95% CI indicated significant change. This method is conservative relative to a 5% significance level.
I am delighted to have returned to Millennium Health to join with the talented people throughout the company and specifically, to collaborate on harnessing the power of Millennium Health’s national database of definitive drug test results. The hard work and vision of the company’s cross-functional data program has led to an appreciation of its public health value, as witnessed in the impressive list of collaborators and users of the data who have been driving research and informing policy. The drug test results in the Millennium Health database can be aggregated and employed to aid those involved in the fight against illicit drug use and its multiple harms, including the crisis of drug overdose deaths that has been affecting our country. I am happy to add my experience, knowledge, and relationships garnered over 35 years in the field of clinical psychology, pain management, and substance use disorders to add collaborations to expand the use of these data for the good of public health, and I am honored to have been asked to share my perspective and commentary on this volume.

This edition of the Signals Report has three important and timely sections. The first section updates previous findings related to positivity of the four major illicit drugs (methamphetamine, fentanyl, cocaine, and heroin) that have been driving the substance use and overdose crises over the past several years, and since these drugs continue to remain relevant, have become a cornerstone of the Signals Report. While they indicate that use of heroin continues its decline and cocaine is stable, methamphetamine and fentanyl are on a dramatic, and all too often deadly, rise, including during the pandemic. However, there was a downward trend in these substances in late 2021. Is this a hopeful sign? Does it suggest that use may no longer be growing at the exponential rates observed in 2020? It may be too early to say with certainty, but we will continue tracking these changes through 2022 to see if the trend continues.

Section 1 also presents positivity along with demographic and regional data, and this remains a major issue in SUD treatment, especially for younger populations. However, there is some potentially good news here for clinicians treating patients with pain. We see something for the pain management specialty we did not observe for any other group in our healthcare population; from 2015 to 2021, for all four illicit drugs, the percent positivity remained steady, and at lower rates than any other specialty. We are currently working on a study to further explore trends in positivity for these substances in a cohort of patients with pain prescribed opioids, a timely endeavor as the CDC reconsiders its 2016 opioid prescribing guidelines.

The second section of this edition focuses on copositivity of illicit fentanyl with the three other illicit drugs in section one (heroin, methamphetamine, and cocaine) and examines which groups are more likely to test positive for
these combinations. The continued infiltration of illicit fentanyl into the drug supply is alarming, as the risk of overdose increases for people who use drugs, such as methamphetamine, that on their own were not historically so intimately tied to fatal overdose risk. As discussed in this section, many people may not even know they are ingesting tainted drugs; therefore, the need for definitive urine drug testing, particularly since there is no readily available point-of-care test for fentanyl, may be more warranted than ever. Using definitive testing can also help clinicians obtain a clear picture of what a patient is ingesting to inform the patient’s treatment plan.

The final section of this volume deals with the growing use of cannabis as it has become increasingly available for medical and/or recreational use. When I hear the rhetoric around increased access to cannabis, I am reminded of the early days of the expanded use of opioids; overstatement of benefits and trivialization of risks. No substance under the sun benefits everyone and harms no one; medicines have therapeutic windows. In my own experience and as shown in published literature, the harms may particularly affect the medically ill populations who are treated under supervision with medical cannabis or self-treating and have risk factors for mental health problems or substance use disorders. My hope is that the use of cannabis medically and otherwise will be guided by lessons learned from opioids – to understand that risk does not solely live in substances but in complex interactions between substances and people. When clinicians treat medically ill patients and cannabis use is part of the picture, such patients should be monitored appropriately with UDT and other tools to attempt to strike the best risk-benefit balance possible for that individual.

It is of the utmost importance now to use all available data sources, including definitive UDT, to track substance use trends, considering drug overdose deaths are at the highest level ever recorded. Access to real-time data can inform the aforementioned intervention efforts and even potentially serve as an early warning for changes in the drug use landscape. This information, including trends over time, plus geographic and demographic factors impacting use, can better influence interventions across the continuum of care.
References


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