MILLENNIUM HEALTH℠

Millennium Health Signals Report™

National Drug Use Trends

Volume 2

Published February 2020

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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.

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Foreword

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For the first time in decades, the U.S. Centers for Disease Control and Prevention projected a decline in drug overdose deaths for 2018, which is largely due to a reduction in prescription opioid-involved deaths and a leveling of heroin-involved deaths. We hope the final numbers align with the projected decline in these deaths. Unfortunately, however, deaths related to synthetic opioids, primarily illicitly manufactured fentanyl, and stimulants are on the rise.[1] Millennium Health researchers helped call attention to this trend in our initial installment of the Signals Report last year, reporting an 1800% rise in the co-positivity of fentanyl with heroin in urine drug test (UDT) results and in two publications in *JAMA Network Open*.[2,3,4] In the first study, we identified a 798% increase and an 1850% increase in UDT positivity rates for non-prescribed fentanyl among results positive for methamphetamine and cocaine, respectively.[3] The second study analyzed near real-time UDT positivity rates for cocaine, methamphetamine, and heroin, both with and without illicit fentanyl, uncovering an alarming uptick in methamphetamine and illicit fentanyl positivity at a national level.[4]

This second volume of the Signals Report expands on this research to provide an important, in-depth look at regional and state impacts, which vary greatly. Within the report, we focus on these three topics:

1. National, regional, and state findings for the use of cocaine, heroin, methamphetamine, and fentanyl
2. Co-positivity rates of fentanyl with select drugs of abuse geographically
3. An investigation into kratom, a DEA "drug of concern"

We close this report having Kevin Zacharoff, MD, walk us through a timeline of initiatives aimed at easing the substance abuse crisis in the United States, concluding that no "silver bullet" likely exists for this crisis, but with coordinated efforts informed by timely data and education, we may have a shot in reducing the toll of substance abuse, which is an outcome that we all desire.

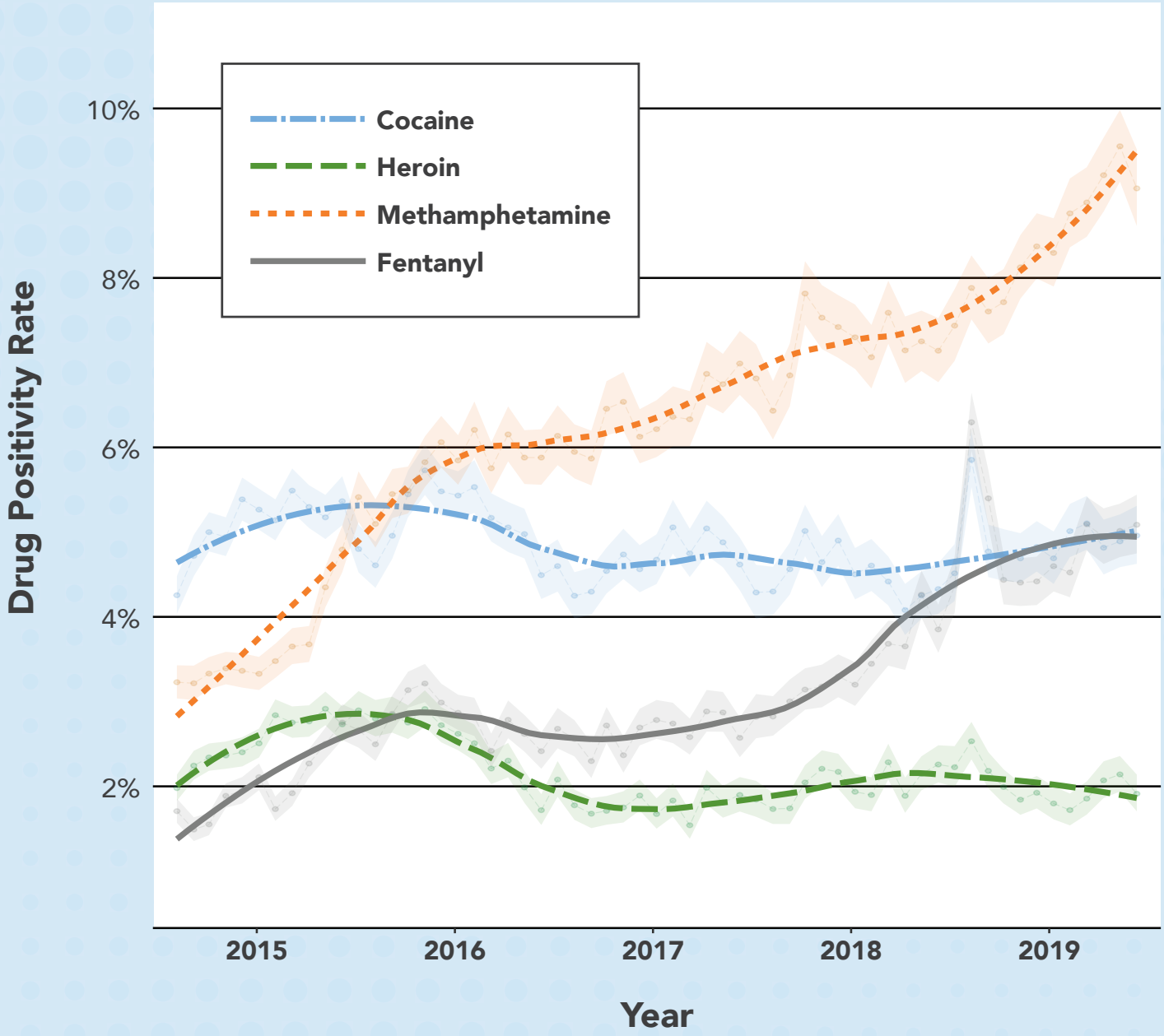
The ultimate goal of our organization in conducting this research and providing the Signals Report is to better arm those fighting the substance abuse crisis with timely information that may improve the efficient use of available resources and ultimately curb the significant impact of drug overdose deaths. Clinicians across the country reading this report will be able to identify which analyzed drugs of abuse are most relevant to their locale and can help educate patients about these trends and their associated risks. As a leading specialty laboratory providing drug testing services across the U.S., Millennium Health researchers are able to access data spanning over a decade in order to identify trends in a more timely manner than traditional data sources, such as drug overdose deaths. This analytic capability coupled with clinical expertise allow our organization to serve as a trusted partner to clinicians, policy makers, public healthcare agencies, and most importantly patients.

We thank you for your continued interest in our Signals Report and relying on us for your clinical testing needs.

Section 1

National and Regional Positivity Rates of Drugs of Abuse: The Shifting Winds of Drug Abuse Trends

Figure 1. Cocaine, Heroin, Methamphetamine, and Fentanyl Positivity Rates Total Sample Population



Background

Drug overdose deaths continue to be the leading cause of injury-related death in the United States.[1] It is important to characterize which substances contribute to these overdose deaths in order to design timely strategies mitigating this risk. As discussed in previous publications and numerous sources, fentanyl is the leading contributor to overdose deaths, involved in over 40% of all overdose deaths.[2,3,4] Overdose deaths associated with stimulants are also on the rise. According to provisional CDC data for 2018, the number of overdose deaths involving cocaine have doubled from the previously observed peak in 2006 and have even surpassed those involving prescription opioids with numbers now similar to deaths involving heroin.[2] Deaths associated with methamphetamine have increased 5-fold since 2010, along with increasing reports of methamphetamine confiscations by law enforcement.[5] Based on these factors, it is important at this time to not only observe the trends happening across the country with fentanyl, but also with heroin, cocaine, and methamphetamine.

In this analysis, we evaluate the positivity rates of each of these individual drugs for the first time regionally, using data from January 2015 through November 2019, to describe near real-time trends in cocaine, fentanyl, heroin, and methamphetamine. Characterizing the landscape of these drugs of abuse can help in discerning differences in national and regional patterns appearing from the drug individually versus those emerging from the deadly mixture of these drugs (intentionally or unintentionally) with fentanyl, which we will describe in Section 2.

Methods

Millennium Health conducted a retrospective analysis of over one million de-identified urine drug test (UDT) results from January 2015 through November 2019 for patient specimens submitted for testing by clinicians as part of patient care. The analysis included specimens with tests ordered for definitive drug testing by liquid chromatography-tandem mass spectrometry (LC-MS/MS) to detect the presence of 6-MAM (a heroin metabolite), methamphetamine, benzoylecognine (a cocaine metabolite) and fentanyl (including testing for the parent drug fentanyl and its metabolite norfentanyl). Specimens from patients with reported fentanyl, cocaine, or methamphetamine prescriptions were excluded from the analysis. Prescribed medications were reported by the ordering clinician and were not verified by Millennium Health.

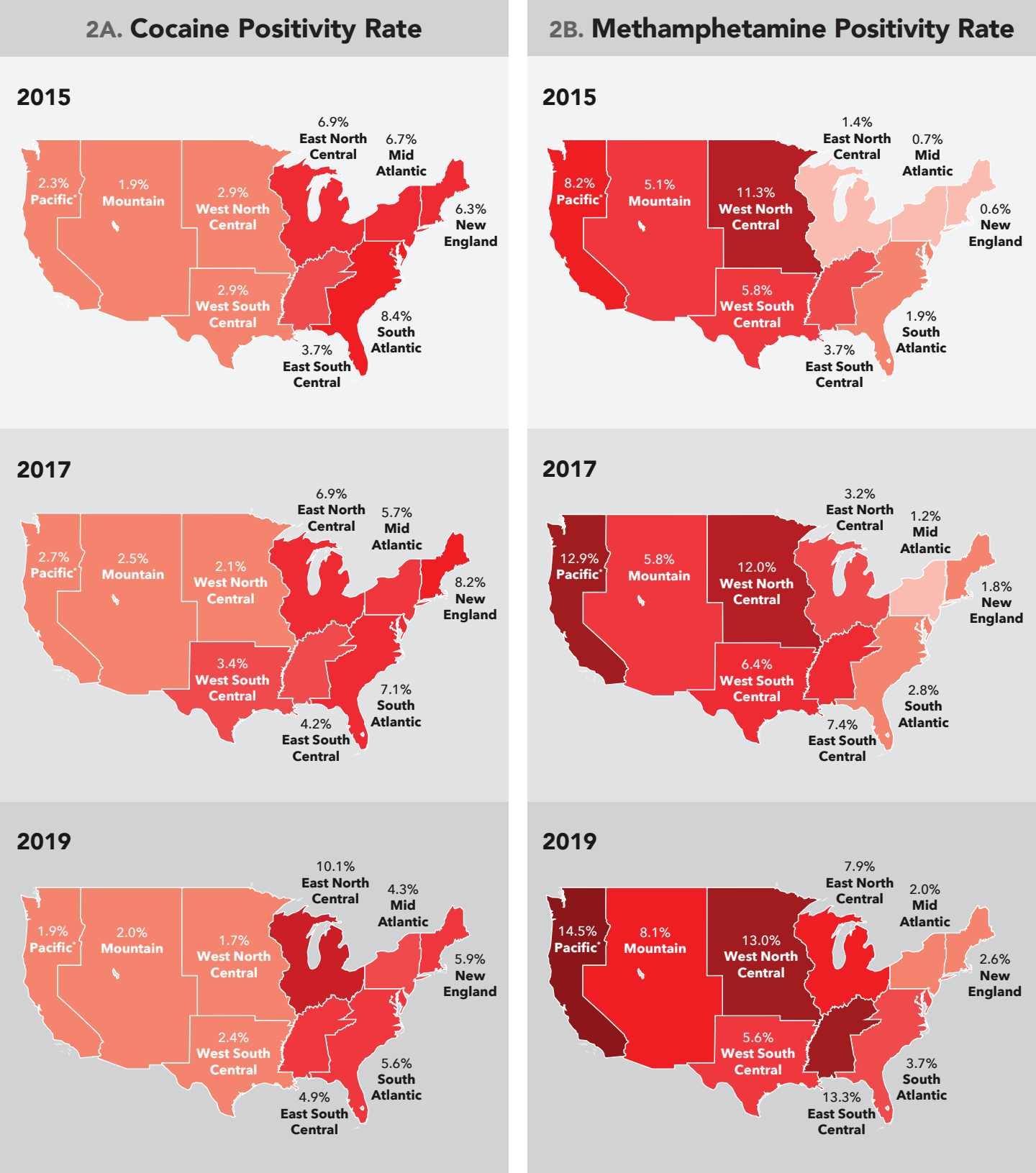
Findings

Nationally, methamphetamine and fentanyl UDT positivity rates have both increased substantially since 2015, rising by 129.6% and 145.8%, respectively. Cocaine and heroin positivity have both declined nationally since 2015, down by 2.5% and 21.4%, respectively (Figure 1, Table 1). Together, these results mark a sizeable shift in illicit drug use in the U.S.

For each of the drugs analyzed, positivity rates varied substantially by U.S. region across the 5 year time span of this study (Figures 2A-D, Table 1). A heat map of the results show that positivity rates for fentanyl and methamphetamine increased by varying degrees across each region, with the exception of a slight decline in methamphetamine positivity for the West South Central region in the last two years of the study. The most substantial

National and Regional Positivity Rates of Drugs of Abuse: The Shifting Winds of Drug Abuse Trends *(continued)*

Figure 2. Drug Positivity in UDT Across U.S. Regions, 2015-2019

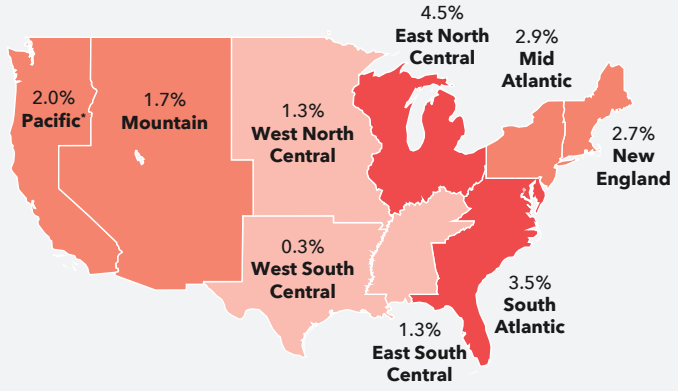


*Pacific Region includes Alaska and Hawaii. (States not shown.)

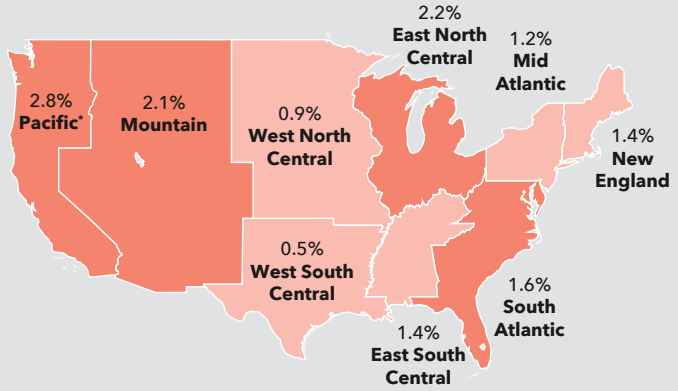
Figure 2. Drug Positivity in UDT Across U.S. Regions, 2015-2019 *(continued)*

2C. Heroin Positivity Rate

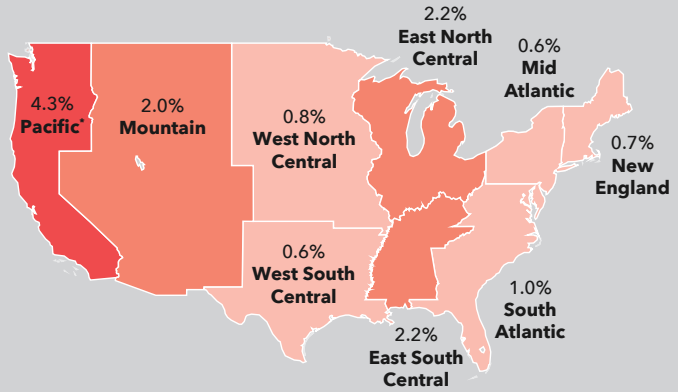
2015



2017

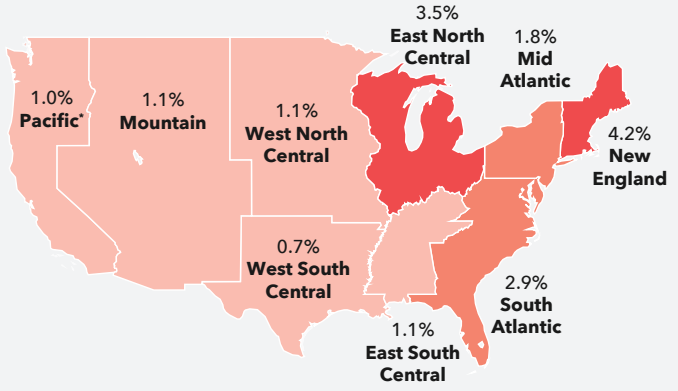


2019

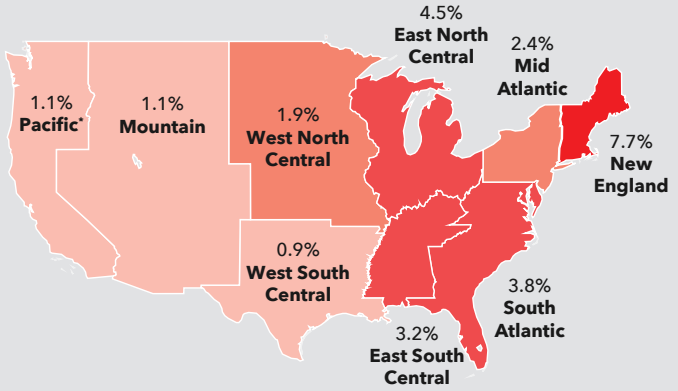


2D. Fentanyl Positivity Rate

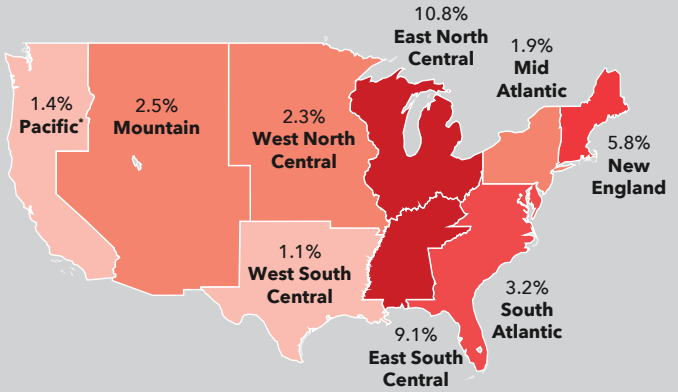
2015



2017



2019



Positivity Rate

0% 20%

*Pacific Region includes Alaska and Hawaii. (States not shown.)

National and Regional Positivity Rates of Drugs of Abuse: The Shifting Winds of Drug Abuse Trends *(continued)*

Table 1. Cocaine, Heroin, Fentanyl, and Methamphetamine Positivity in UDT by U.S. Region

Regions	Cocaine			Fentanyl			Heroin			Methamphetamine		
	2015	2019	% Change	2015	2019	% Change	2015	2019	% Change	2015	2019	% Change
East North Central	6.94%	10.07%	45.15%	3.54%	10.76%	204.02%	4.46%	2.22%	-50.24%	1.44%	7.90%	450.49%
East South Central	3.66%	4.92%	34.38%	1.13%	9.05%	698.31%	1.28%	2.23%	74.60%	3.72%	13.28%	256.77%
Mid Atlantic	6.70%	4.30%	-35.84%	1.80%	1.94%	7.43%	2.86%	0.59%	-79.33%	0.67%	1.98%	197.80%
Mountain	1.91%	2.02%	6.08%	1.05%	2.46%	133.06%	1.68%	1.95%	16.20%	5.10%	8.09%	58.62%
New England	6.27%	5.92%	-5.61%	4.22%	5.81%	37.74%	2.71%	0.65%	-75.87%	0.56%	2.64%	369.55%
Pacific	2.29%	1.91%	-16.50%	1.02%	1.35%	32.42%	2.00%	4.28%	113.75%	8.24%	14.45%	75.34%
South Atlantic	8.35%	5.63%	-32.57%	2.85%	3.23%	13.41%	3.45%	0.97%	-71.82%	1.86%	3.68%	98.00%
West North Central	2.88%	1.68%	-41.65%	1.09%	2.25%	106.98%	1.31%	0.75%	-43.09%	11.28%	12.98%	15.11%
West South Central	2.85%	2.37%	-16.98%	0.65%	1.12%	72.00%	0.34%	0.60%	73.82%	5.84%	5.60%	-4.22%
U.S. Total	5.07%	4.95%	-2.45%	2.01%	4.93%	145.81%	2.54%	2.00%	-21.44%	3.70%	8.49%	129.64%

Change in Positivity Rate: -80% 0% +700%

changes occurred in fentanyl positivity for the East South Central region, which increased by 689.3%, and in methamphetamine positivity for the East North Central region, which increased by 450.5%. While the majority of regions experienced a decline in positivity rates for cocaine and heroin, these substances also exhibited substantial regional differences, including increased positivity among a few regions.

The ten states with the highest UDT positivity rates for each drug are presented in Table 2. It is note-worthy that 24 states among 8 regions are represented across the four drugs analyzed, suggesting that high rates of drug use are not limited to one, or even a few, states or regions of the country.

A limitation of our analysis was the reliance on accurate and complete reports of prescribed medications by the ordering clinician. Our results were compiled from samples collected in a healthcare setting, and thus may not be reflective of the entire population using cocaine, methamphetamine, heroin, or fentanyl.

Table 2: Top 10 States for Drug Positivity in 2019

Rank	Cocaine	Methamphetamine	Heroin	Fentanyl
1	**Maryland** (14.6%)	**Arkansas** (28.7%)	**Washington** (6.3%)	**Kentucky** (16.2%)
2	**Maine** (13.8%)	**Iowa** (20.8%)	**New Mexico** (6.0%)	**Ohio** (13.6%)
3	**Ohio** (12.2%)	**Washington** (20.7%)	**Alaska** (4.9%)	**Maryland** (13.0%)
4	**Virginia** (10.7%)	**Kentucky** (20.3%)	**Kentucky** (4.0%)	**Maine** (10.1%)
5	**North Carolina** (10.0%)	**Minnesota** (16.5%)	**Utah** (3.2%)	**New Hampshire** (9.6%)
6	**Louisiana** (7.3%)	**New Mexico** (15.5%)	**Virginia** (3.1%)	**Illinois** (8.6%)
7	**Kentucky** (7.1%)	**Alaska** (13.5%)	**Nevada** (3.0%)	**Virginia** (8.3%)
8	**Illinois** (6.2%)	**Montana** (12.3%)	**Ohio** (2.7%)	**Arizona** (4.1%)
9	**Wisconsin** (5.3%)	**Missouri** (10.5%)	**Oregon** (2.6%)	**New Mexico** (3.4%)
10	**New Mexico** (5.3%)	**Idaho** (9.8%)	**California** (2.5%)	**Louisiana** (3.3%)

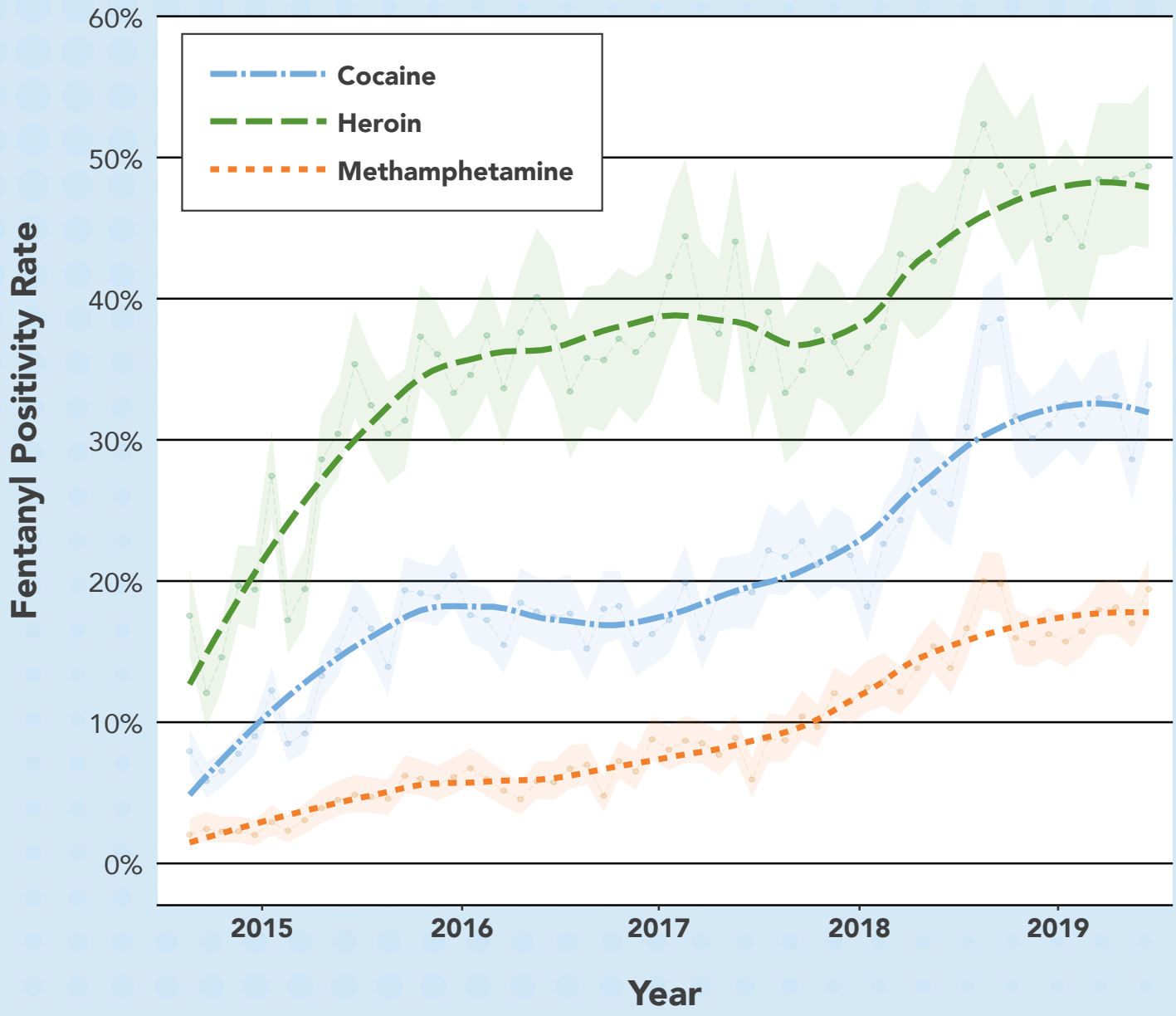
Conclusions

These data indicate that the national positivity rates for fentanyl and methamphetamine have risen substantially since 2015; however, these increases appear largely region dependent. For example, although there was substantially increased positivity for fentanyl in the East North Central and East South Central regions, fentanyl positivity elsewhere increased by varying, lesser degrees. Methamphetamine has exploded across most of the country, explaining at least in part, the 5-fold increase in death rates due to methamphetamine since 2010.[2] Perhaps unexpectedly, cocaine positivity rates decreased in many regions, but again, appeared region-specific, revealing a rise in at least 3 regions, indicating continued popularity there. Finally, the substance that clearly seems to be falling out of favor is heroin, which fell by 21.4% nationally over the 5 year time period of this study. However, in true form, this trend also reflected regional specificity, whereby the positivity rate for the Pacific region more than doubled, while it lost more than half of its positivity in other regions, such as New England and the Mid Atlantic. While shifts in regional patterns may be explained by several factors, the DEA primarily identifies drug trafficking patterns and user preference as driving forces behind regional drug availability.[5] Regardless of what drives these trends, knowledge of them is critically important for targeting efforts aimed at combating drug abuse nationwide.

Section 2

Co-Positivity Rates of Fentanyl with Select Drugs of Abuse: A 2020 Update to a Worsening Public Health Crisis

Figure 1. Fentanyl Positivity Rates in the Cocaine, Heroin, or Methamphetamine Positive Populations



Background

Fentanyl is increasingly being combined with other illicit drugs, which increases the risk of overdose.[1,2] In fact, much of the observed rise in cocaine- and methamphetamine-related drug overdose deaths have been attributed to the involvement of fentanyl.[3] Thus, it is important to continue to monitor the infiltration of fentanyl into the drug supply, whether that be through intentional mixing or unintentional contamination. It's also important to consider users' actions, such as the deliberate combination of fentanyl with a stimulant for a "speedball" effect.

The profitability of fentanyl is likely contributing to its rise in use and adulteration of other drugs.

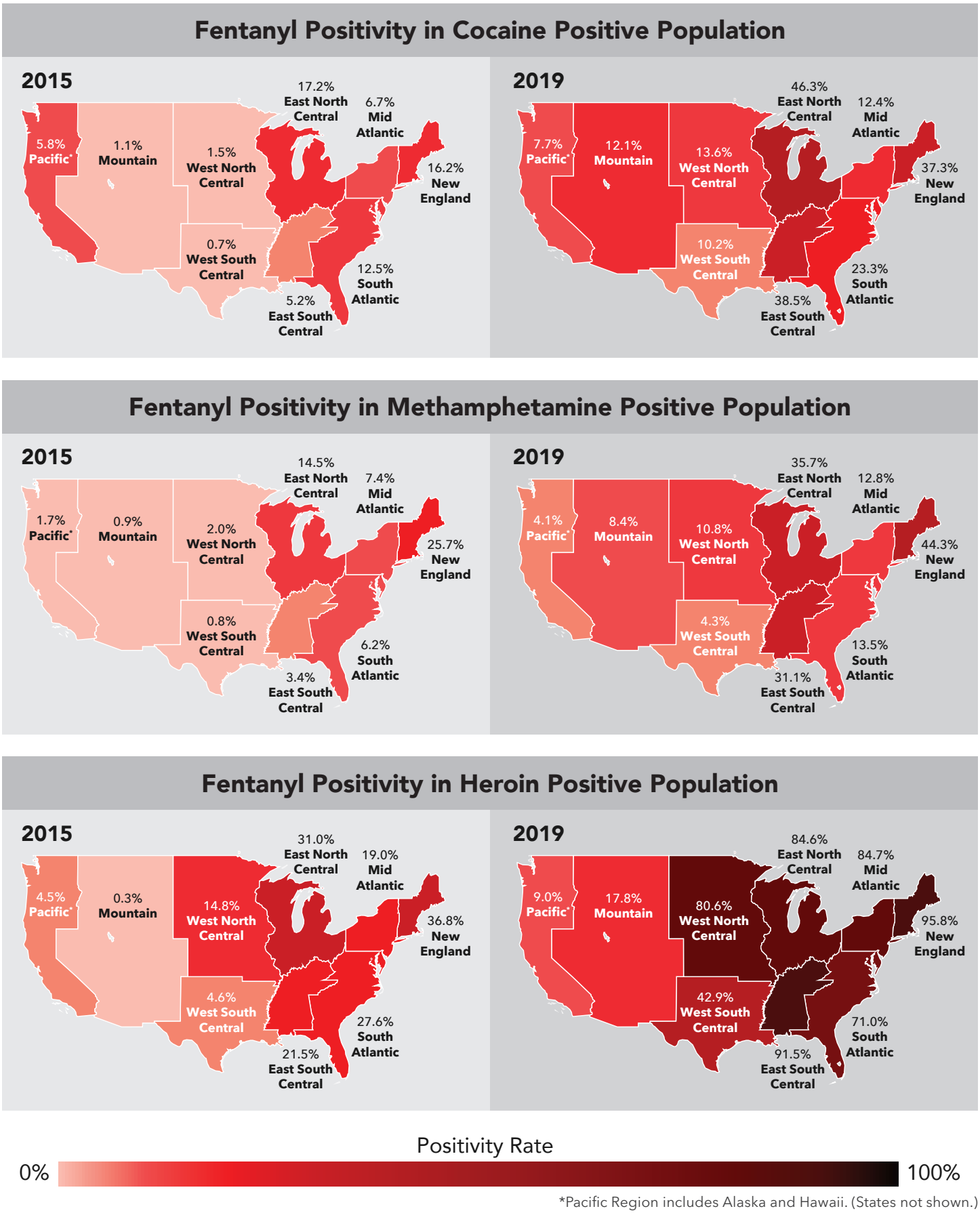
Table 1. Fentanyl Positivity in the Cocaine, Heroin, and Methamphetamine Positive Populations by U.S. Region

Regions	Cocaine			Heroin			Methamphetamine		
	2015	2019	% Change	2015	2019	% Change	2015	2019	% Change
East North Central	17.20%	46.26%	168.97%	30.99%	84.63%	173.11%	14.45%	35.69%	147.04%
East South Central	5.15%	38.48%	646.71%	21.53%	91.49%	324.86%	3.38%	31.05%	819.51%
Mid Atlantic	6.65%	12.40%	86.66%	18.96%	84.72%	346.82%	7.42%	12.81%	72.63%
Mountain	1.07%	12.06%	1022.72%	0.27%	17.83%	6480.50%	0.85%	8.41%	891.15%
New England	16.17%	37.33%	130.78%	36.80%	95.83%	160.45%	25.71%	44.33%	72.39%
Pacific	5.77%	7.74%	34.10%	4.48%	8.99%	100.84%	1.69%	4.14%	144.27%
South Atlantic	12.53%	23.29%	85.83%	27.56%	70.97%	157.48%	6.17%	13.49%	118.44%
West North Central	1.48%	13.58%	819.58%	14.81%	80.56%	443.75%	2.00%	10.80%	441.17%
West South Central	0.67%	10.20%	1431.30%	4.59%	42.86%	834.29%	0.76%	4.31%	468.82%
U.S. Total	10.62%	32.94%	210.19%	22.76%	48.10%	111.31%	3.24%	17.48%	438.89%

Change in Positivity Rate

Co-Positivity Rates of Fentanyl with Select Drugs of Abuse: A 2020 Update to a Worsening Public Health Crisis *(continued)*

Figure 2: Heat Map of UDT Positivity for Cocaine, Heroin, or Methamphetamine with Non-Prescribed Fentanyl by Region (January 2015 through November 2019)



*Pacific Region includes Alaska and Hawaii. (States not shown.)

In 2018, the DEA reported that for every $3,300-$5,000 paid for 1 kg of fentanyl, revenue to the drug trafficking organization could be as high as $2 million. In contrast, $5,000 paid for 1 kg of heroin may result in revenue of $80,000.[4] The difference is staggering. Illicit fentanyl results in significant profit because as a synthetic opioid, it can be cheaply produced. Also, its potency allows drug trafficking organizations to dilute fentanyl for use in several ways, such as cutting heroin with fentanyl to extend the heroin supply or pressing fentanyl in tablet form to sell as counterfeit prescription pills.[4]

Last year, in the Millennium Health Signals Report Volume I (2019), we characterized UDT positivity trends nationally and regionally for the co-occurring positivity rate of non-prescribed fentanyl with heroin. This year, we expand our analysis to build on that, as well as our previously published work that observed these trends on a national level.[5] In this section, we go beyond national trends to focus on regional and state data on the co-positivity rates of fentanyl with heroin, cocaine, or methamphetamine from January 2015 through November 2019.

Methods

Millennium Health conducted a retrospective analysis of over one million de-identified UDT results from January 2015 through November 2019 for patient specimens submitted for testing by clinicians as part of patient care. The analysis included specimens with tests ordered for definitive drug testing by liquid chromatography-tandem mass spectrometry (LC-MS/MS) to detect the presence of 6-MAM (a heroin metabolite), methamphetamine,

Table 2: Top 10 States with Highest Positivity Rates of Co-Occurring Fentanyl with Cocaine, Methamphetamine or Heroin

Rank	Cocaine Positive Population	Methamphetamine Positive Population	Heroin Positive Population
1	**Kentucky** (49.4%)	**Ohio** (38.8%)	**Maryland** (96.7%)
2	**Ohio** (49.2%)	**Kentucky** (37.1%)	**Kentucky** (93.9%)
3	**Maryland** (48.4%)	**Florida** (23.0%)	**Missouri** (92.6%)
4	**Maine** (44.4%)	**Michigan** (18.4%)	**Ohio** (85.7%)
5	**Virginia** (41.5%)	**Arizona** (15.0%)	**Virginia** (83.6%)
6	**Arizona** (21.4%)	**New Mexico** (13.4%)	**New York** (82.4%)
7	**Florida** (20.8%)	**Louisiana** (12.9%)	**Florida** (78.5%)
8	**Louisiana** (16.8%)	**Missouri** (12.3%)	**Louisiana** (60.4%)
9	**Michigan** (14.6%)	**Minnesota** (11.7%)	**New Mexico** (27.8%)
10	**New York** (11.8%)	**California** (5.3%)	**Arizona** (21.7%)

benzoylecognine (a cocaine metabolite) and fentanyl (including testing for the parent drug fentanyl and its metabolite norfentanyl). Specimens from patients with reported fentanyl, cocaine, or methamphetamine prescriptions were excluded from the analysis. Prescribed medications were reported by the ordering clinician and were not verified by Millennium Health.

Findings

Nationally, UDT positivity rates for non-prescribed fentanyl among specimens positive for cocaine, heroin, or methamphetamine have increased since 2015 (Figure 1, Table 1). From 2015 through 2019, positivity rates for non-prescribed fentanyl increased by 210.2% in the cocaine-positive population (from 10.6% to 32.9%), 111.3% in the heroin-positive population (from 22.8% to 48.1%), and 438.9% in the methamphetamine-positive population (from 3.2% to 17.5%). While rates of non-prescribed fentanyl among methamphetamine-positive specimens were relatively lower in 2019 (at 17.5% versus 32.9% and 48.1% for the cocaine-positive and heroin-positive populations, respectively), this group displayed the most dramatic increase since 2015.

Fentanyl positivity rates among those also positive for heroin, cocaine, or methamphetamine varied substantially by U.S. region (Table 1, Figure 2). The greatest change was in the Mountain region, where non-prescribed fentanyl among heroin-positive specimens increased by a massive 6480.5%! A heat map shows that non-prescribed fentanyl is found with heroin, cocaine, or methamphetamine predominantly in the Central and Eastern regions, but the Western region also exhibited a large increase over the time frame analyzed (Figure 2).

The top ten states with the highest UDT positivity rates for each category are spread across 14 different states in 9 regions, suggesting that this trend is not limited to one area of the country (Table 2).

A limitation of our analysis was the reliance on accurate and complete reports of prescribed medications by the ordering clinician. Additionally, the source of non-prescribed fentanyl cannot be definitively ascribed to fentanyl being "spiked" into the heroin, cocaine, or methamphetamine, as these substances may also be combined by the user for desired effect or may be deliberately or unintentionally (as a contaminant) added to the illicit supply by drug trafficking organizations. Our results were compiled from samples collected in a healthcare setting, and thus may not be reflect the entire population using heroin, cocaine, or methamphetamine.

Conclusions

These data indicate that the national positivity rates for heroin, cocaine, and methamphetamine with concomitant non-prescribed fentanyl have risen dramatically in urine drug tests since 2015. Nationally, nearly half of heroin-positive specimens and one-third of cocaine-positive specimens were also positive for non-prescribed fentanyl, while methamphetamine-positives among non-prescribed fentanyl grew most dramatically over the study time frame.

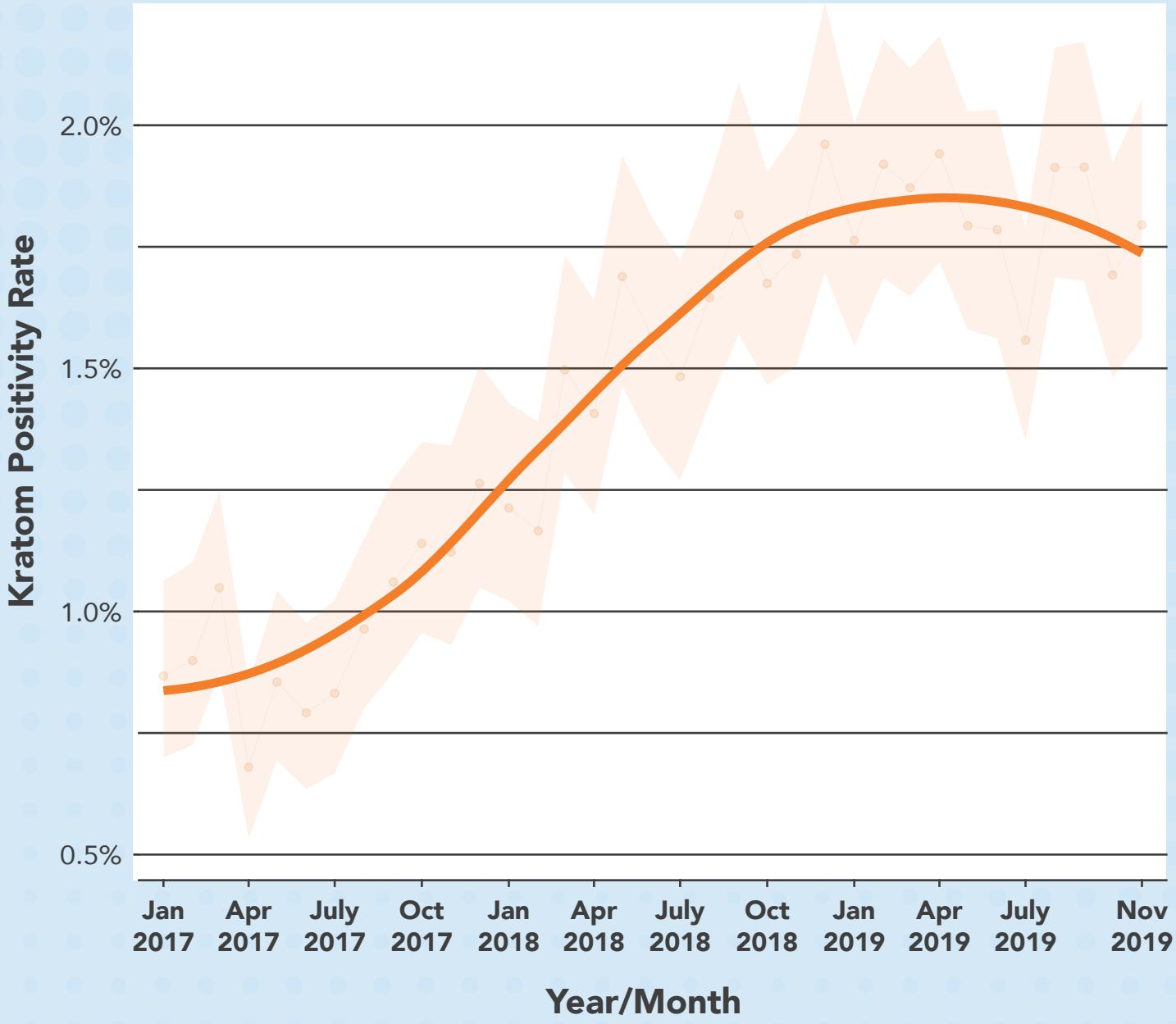
Regionally, rates increased across all areas analyzed, though the extent of these changes varied greatly. While the highest rates of concomitant fentanyl are generally in the Central and Eastern regions of the U.S., several regions in the West experienced major shifts over time.

These rate changes nationally and across each region are concerning because the combination of fentanyl with heroin, cocaine, or methamphetamine greatly increases the risk of overdose and potentially death, particularly if the user is opioid-naïve. The considerable changes noted in this analysis suggest that fentanyl-involved drug overdose deaths may continue to rise. Clinicians should be aware that patients presenting for treatment of suspected drug overdose or substance use disorder may have been exposed, knowingly or unknowingly, to multiple substances, including fentanyl. At risk users may benefit from fentanyl-specific messaging, as well as access to naloxone, in order to mitigate the risk of drug overdose.

Section 3

Kratom: An Investigation into a "Drug of Concern"

Figure 1. Kratom Positivity Rates in the Sample Population



Background

Kratom (*Mitragyna speciosa*) is a tree native to Southeast Asia, particularly in Thailand and Malaysia.[1] It contains the active alkaloids mitragynine and 7-OH mitragynine, which are opioid receptor agonists and contribute to the pharmacologic activity of kratom.[2] The activity is dose-dependent, with stimulant-like effects at lower doses and opioid-like effects at higher doses, lasting 2-5 hours.[1] Kratom is sometimes used for medicinal purposes, such as to relieve pain, or as a drug of abuse alone or in combination with other substances. Kratom may also be used to relieve the symptoms of opioid withdrawal.[2]

Over the last decade, kratom has become readily available through the Internet and numerous vendors as herbal plant material, powder, encapsulated powder, or extract.[3,4] The exact number of users in the U.S. remains unclear; however, data from the American Kratom Association suggests that there are presently an estimated 5 million users.[5]

Kratom is not currently scheduled under the Controlled Substances Act, but the Drug Enforcement Administration (DEA) has labeled it a "drug of concern," and the U.S. Department of Health and Human Services (HHS) has recently recommended classifying the drug a Schedule I substance.[6] Since 2010, several states and cities have passed legislation banning or limiting the sale and use of kratom.[2,7]

In 2018, the Centers for Disease Control and Prevention (CDC), U.S. Food and Drug Administration (FDA), and state and local health officials all identified kratom and kratom-containing products as likely contributors to an outbreak of Salmonella infections in 41 states.[8,9] In a separate FDA analysis, different kratom products were found to contain "significant levels of lead and nickel at concentrations that exceed safe exposure for oral daily drug intake," leading long-term users of kratom to potentially develop heavy metal poisoning, which can include nervous system or kidney damage, anemia, high blood pressure, and/or increased risk of certain cancers.[10] In addition, the FDA has issued letters to companies warning them against making claims that kratom products can be used to treat opioid withdrawal and pain.[6] From 2011-2017, data from the National Poison Data Systems reported that calls to poison control centers associated with kratom exposures increased by nearly 5000%.[11] This coincides with CDC data from July 2016 through December 2017 which found kratom in postmortem toxicology results in 152 unintentional overdose deaths.[12]

Kratom remains a controversial compound with ongoing concerns for safety and efficacy.[13] At the present time however, neither the National Survey on Drug Use and Health or Monitoring the Future Survey include kratom in their reports.[2] As such, our analysis set out to identify positivity rates of kratom, with and without other drugs of abuse, in urine drug tests over time. Timely awareness of these trends supports the targeted development of interventions to curb the impact on public health.

Methods

Millennium Health conducted a retrospective analysis of over 400,000 de-identified urine drug tests (UDT) results from January 2017 through November 2019 for patient specimens submitted for testing by clinicians as part of patient care. The analysis was performed on definitive UDT results from liquid chromatography–tandem mass spectrometry (LC-MS/MS) for specimens tested for mitragynine and 7-OH mitragynine.

Mitragynine and 7-OH mitragynine trends were evaluated by looking at positive findings in UDT results. The analysis was performed for each year in the time period as well as by state and U.S. region. Additionally, UDT co-positivity rates of kratom with other substances of abuse including heroin, cocaine, methamphetamine, benzodiazepines, fentanyl and opioids (morphine, codeine, hydrocodone, hydromorphone, oxycodone, oxymorphone) were analyzed. Specimens from patients with reported prescriptions for benzodiazepines, cocaine, methamphetamine, and prescription opioids (including fentanyl) were excluded from the results. Prescribed medications were reported by the ordering clinician and were not verified by Millennium Health.

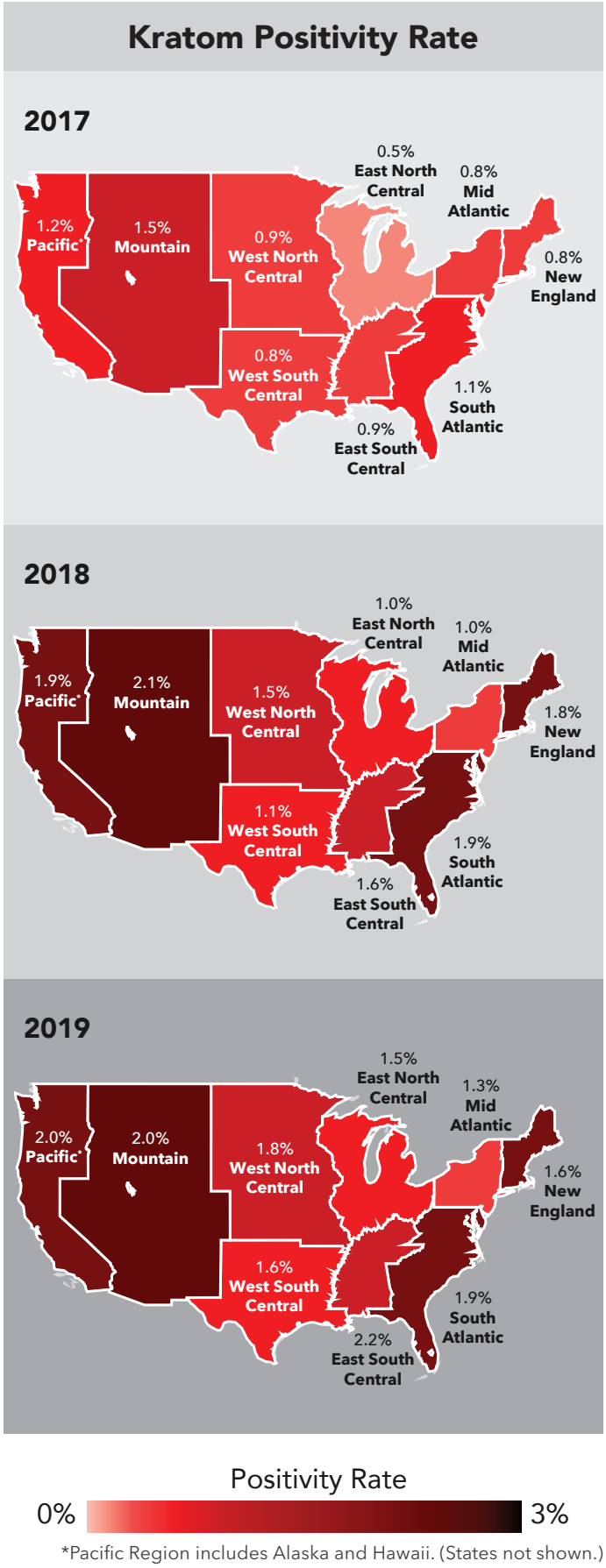
Findings

Overall, we saw the national positivity rate for kratom rise from 0.9% to 1.8% from January 2017 through November 2019. This represents a doubling in urine drug test positivity (Figure 1).

Kratom positivity rates increased in every U.S. region during the study period. For specimens that tested positive for kratom between January 2017 and November 2019, we observed the following regional increases in positivity: East North Central (200.0%), East South Central (144.4%), West South Central (100.0%), West North Central (100.0%), New England (100.0%), South Atlantic (72.7%), Pacific (66.7%), Mid Atlantic (62.5%), and Mountain (33.3%) (Figure 2).

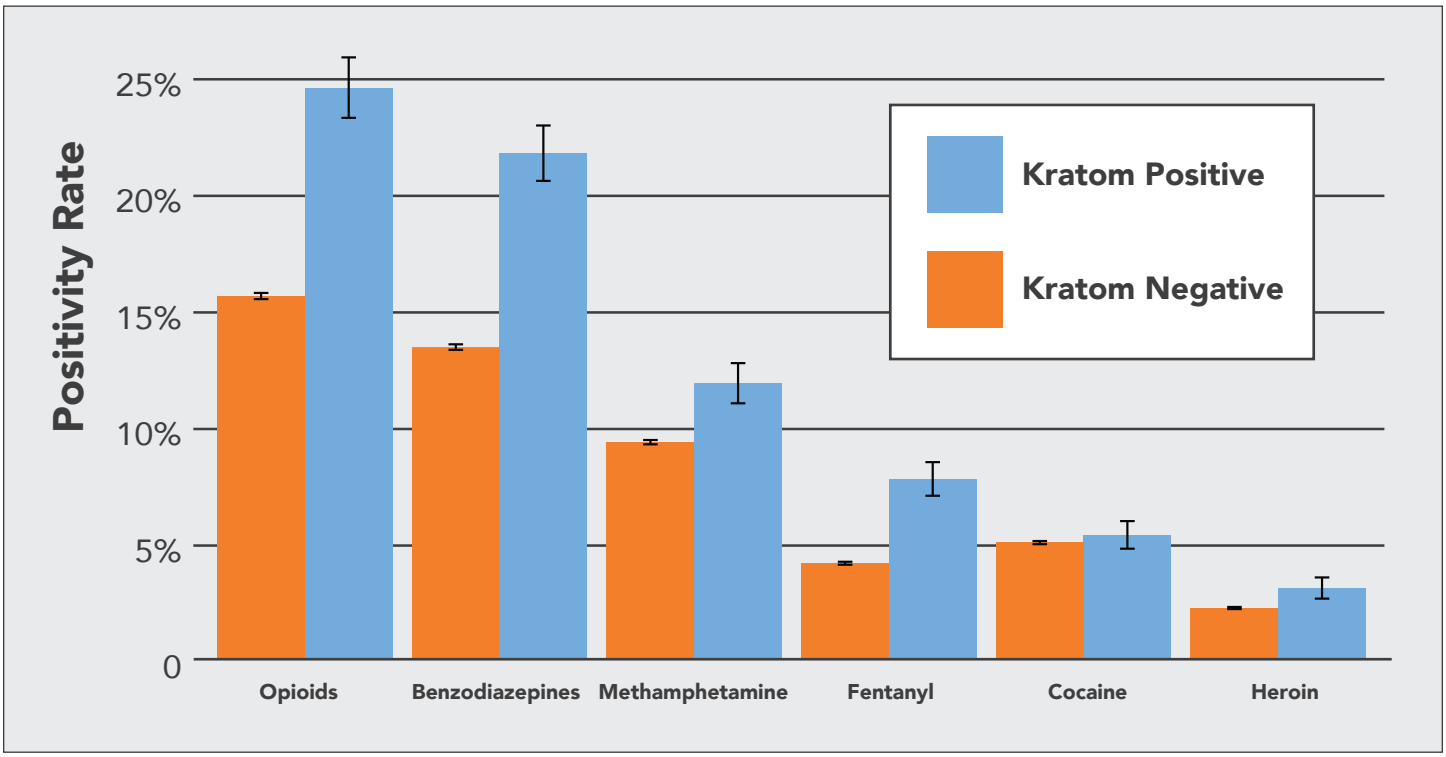
States with the 10 highest positivity rates from January 2017 through November 2019 were Idaho (4.2%), Montana (2.9%), Oregon (2.7%), Colorado (2.3%), Utah (2.3%), Virginia (2.2%), Florida (2.1%), Kentucky (1.9%), Nevada (1.7%), and Missouri (1.7%).

Figure 2: Heat Map of UDT Positivity for Kratom by Region (2017-2019)



*Pacific Region includes Alaska and Hawaii. (States not shown.)

Figure 3. Illicit and Non-Prescribed Drug Positivity Rates Stratified by the Positive or Negative Kratom Population



Urine drug test specimens positive for kratom were also evaluated for co-positivity rates of non-prescribed opioids and benzodiazepines as well as illicit substances. For samples testing positive for kratom over the study period, 24.8% were also found to be positive for opioids, 22.0% for benzodiazepines, 12.0% for methamphetamine, 7.8% for fentanyl, 5.3% for cocaine, and 3.0% for heroin. Positivity rates for these drugs were higher in the kratom positive population versus those negative for kratom (Figure 3).

A limitation of our analysis was the reliance on accurate and complete reports of prescribed medications by the ordering clinician. Our results were compiled from samples collected in a healthcare setting, and thus may not be reflect the entire population using kratom.

Conclusions

Our data suggest that although the national positivity rate for kratom remains low, kratom positive urine drug tests increased nationally and in every U.S. region between January 2017 and November 2019 (Figure 1, Figure 2). Additionally, individuals who were positive for kratom were also more likely to be positive for non-prescribed opioids, benzodiazepines, and illicit substances (Figure 3). Combining kratom with other CNS depressants can result in an increased risk of unintentional overdose. Whether the misuse and abuse of kratom will become a critical health issue remains to be seen. Our findings of frequent co-positivity are consistent with CDC overdose reports, and support the DEA's decision to label kratom a "drug of concern."[12] Therefore, we will continue to closely monitor and report use of kratom.

Conclusion

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The data in this report reinforce the notion that there may in fact be no "silver bullet" for solving the drug overdose epidemic our nation faces today. As we look back over the past 20 years, it may just be overly simplistic for us to conclude that liberal prescribing of opioids alone is the reason for the staggering number of annual drug-related overdoses. Certainly, we must appreciate that the definition of "opioid risk" has evolved to consider not only patient-level risk of adverse effects; it now incorporates household, community, and societal risk of adverse effects along with potential of misuse, abuse, and addiction.

Initially, it was believed that promulgation of guidelines for the use of opioid analgesics to treat chronic pain in non-cancer patients by the American Pain Society and the American Academy of Pain Medicine in 2009 was going to be the way to provide guidance and temper educational deficits. It was thought that with safer and more efficacious prescribing, "opioid risk" could be sufficiently mitigated by consensus.

When the Institute of Medicine (IOM) released the report Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research in 2011, it provided a quantifiable assessment of the social and financial burden of pain in the U.S. The intention was that this report would lead to safer and more effective pain management, prevention of chronic pain, and spark an increase in healthcare provider training. That same year, the Epidemic: Responding to America's Prescription Drug Abuse Crisis plan was released. This drug abuse prevention plan highlighted that non-medical use of prescription opioids was starting to outpace illicit substances like cocaine. The ultimate intention was to promote education of healthcare providers and "tame" the opioid crisis, while maintaining access to medications for those in need.

Prescription Drug Monitoring Programs then became the focus for battling the opioid epidemic as opioid-related overdose deaths continued to rise. The thinking was that enhanced patient and population safety would be achieved by identifying patients receiving multiple prescriptions from different prescribers and prescribed substances that potentially increased the risk of opioid overdoses, such as benzodiazepines.

In 2016, when the Centers for Disease Control and Prevention (CDC) released its Guidelines for Prescribing Opioids for Chronic Pain, it was with the intention of examining the opioid crisis as a true epidemic. While considered by some to be controversial, the intention of these guidelines was to promote safer, more appropriate prescribing of opioid in non-expert settings like primary care. Many components of these guidelines were ultimately adopted by several state agencies, and yielded consequences that included greater fear of

regulatory scrutiny, lower likelihood of prescribing opioids, and in some cases, forced tapering of patients on chronic opioid therapy.

Currently, although naloxone distribution is considered by many to be an effective short-term solution to save lives in the face of opioid-related overdoses, it is not without debate. In 2018, The Department of Health and Human Services issued guidance that recommended prescribing naloxone (or co-prescribing with an opioid) to patients at high risk for an opioid overdose. Controversies surrounding naloxone range from the most effective way to distribute it widely – community-level vs. co-prescribing, to fear about providing a safety net to people who abuse opioids. Opponents feel that this "umbrella" could give a false sense of safety to substance abusers, while proponents feel that there is a relatively low or non-existent risk profile, and that a life saved is better than a life lost.

The Pain Management Best Practices Inter-Agency Task Force published a report in May 2019 to address gaps and inconsistencies in the management of both acute and chronic pain. The task force consisted of experts in diverse disciplines related to pain management, pain advocacy, addiction, recovery, substance use disorders, mental health, and minority health. The impact and effect of this report remains to be seen.

In the final analysis, we need to think about what the data in this report tell us, in addition to what these initiatives over the past 10+ years tell us. The national drug overdose epidemic is multifaceted, has evolved significantly, and will likely continue to do so. Fentanyl has now become the leading contributor to opioid-related overdose deaths, while methamphetamine deaths have increased substantially as well. Clearly, as we see in this report, increases in fentanyl and methamphetamine use will likely expand the role these substances play in overdose deaths. The data in this report show that regionality is a factor; one that many may not often consider. As fentanyl continues to be combined with other substances of abuse, it is hard to predict what may happen, but it is critical that we look at the data to be aware of what has been happening. Could kratom be the next major substance to play a role in this epidemic? While there is likely no "silver bullet" for this crisis, coordinated efforts informed by timely data and education are likely the best shot we have.

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*Conflict of Interest Disclosure: Dr. Zacharoff has received personal fees from Millennium Health.

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