In both the mass media and scientific reports, people who use drugs tend to be classified by the substances they use: as heroin, crack cocaine, or methamphetamine users. This classification obscures a central fact about illicit substance use, which is that most people who use drugs, and certainly most people who use illicit opioids, use multiple substances. For example, in a national sample of people who used opioids and were seeking treatment, 96 percent reported having used at least one non-opioid substance in the past month. Among these individuals, roughly one third reported methamphetamine use, a third reported cocaine/crack use, and a third reported heavy alcohol use. In a national sample of heroin users in 2015–16, 93 percent reportedly used at least one drug in addition to heroin, and more than 40 percent had used three or more drugs in the past year. These data confirm that polysubstance use is the norm.

When it comes to the opioid overdose epidemic, understanding polysubstance use plays an increasingly pivotal role. The number of overdose deaths involving heroin plus a synthetic narcotic (predominantly fentanyl) has risen 200-fold since 2010. In 2017, these polysubstance deaths exceeded heroin-only overdose deaths for the first time. The trend continued into 2018, when more than 9,000 overdoses involved heroin and fentanyl, whereas roughly 6,000 involved heroin alone (Figure 1).

In 2017–2018, according to data reported from 25 states by the Centers for Disease Control and Prevention, multiple opioids (e.g., heroin and fentanyl) were involved in 68 percent of heroin deaths and 52 percent of illicitly manufactured fentanyl (IMF) deaths. Similar upward trends occurred in fatal polysubstance-
related overdoses involving stimulants. Overdose deaths involving stimulants (mostly methamphetamine) and opioids increased 10-fold, and those involving methamphetamine and fentanyl increased almost 50-fold from 2010 through 2018. Similar increases were seen in overdose deaths involving cocaine and opioids (Figure 2).

Finally, fatal overdoses involving benzodiazepines and opioids or fentanyl have risen sharply since 2010, accounting for more than 14,000 deaths in 2018. The presence of alcohol is not routinely included in national overdose data, although we know that alcohol and opioids are a dangerous mix. For example, between 2015 and 2018 in San Francisco, California, 23 percent of opioid overdose deaths were co-attributed to acute toxicity from alcohol.4

![National Drug Overdose Deaths Involving Heroin](image)

**Figure 1.** National Overdose Deaths Involving Heroin, by Other Synthetic Narcotic (Opioid) Involvement, Number Among All Ages, 1999–2018

**Impact of Illicitly Manufactured Fentanyl on Polysubstance Use and Overdose**

The increasing presence of IMF in U.S. drug markets has played an important role in polysubstance use. IMF is a synthetic opioid (or narcotic) manufactured in laboratories (rather than cultivated, like heroin) and is several times more powerful than heroin. The contamination of the heroin supply with IMF led to a dramatic upsurge in fatal overdoses in the United States beginning in 2014.5 IMF has also been used unintentionally when methamphetamine and cocaine were laced with it. Although it is likely that some contamination of the heroin supply continues, IMF is now a known entity among people who use illicit opioids. It is gradually replacing heroin in East Coast drug markets and is increasingly becoming a drug of choice. Because IMF is much more powerful
than heroin, there is evidence that people are using methamphetamine or cocaine with IMF to balance its overwhelming narcotic effects. Both unintentional and intentional polysubstance use have increased since IMF emerged on the scene.

**Reasons for Polysubstance Use**

Epidemiological data show us that polysubstance use is common and sometimes dangerous. However, these data provide limited insight into why people use multiple substances. The relatively small amount of in-depth research into this issue identifies some reasons. One reason, mentioned above, is that people seek to balance the effects of different substances. For example, they may seek to counteract the stimulant effects of methamphetamine with alcohol or an opioid. Similarly, sometimes people use benzodiazepines or marijuana to “come down” from stimulant drugs.

Intensification of a drug effect is another reason for polysubstance use, such as using multiple opioids to sustain a deeper or longer feeling of pleasure. Given that substance use treatment is often not immediately available, people sometimes engage in polysubstance use to manage their own gradual withdrawal from opioids by using substances that ease the symptoms, such as alcohol or benzodiazepines.

Finally, polysubstance use can result from market forces such as scarcity and price, which lead people to supplement a relatively expensive or hard-to-find substance with another that is cheaper or more widely available. For example, in some locales, heroin has become less widely available while IMF has flooded the illicit drug market. This contributes to two types of polysubstance use: first, people supplement the scarcer heroin with IMF; second, as we mentioned above, people use methamphetamine to mitigate the effects of IMF, which has a more immediate and intense narcotic effect than heroin.

![National Drug Overdose Deaths Involving Cocaine, by Opioid Involvement, Number Among All Ages, 1999-2018](image)

*Figure 2. National Drug Overdose Deaths Involving Cocaine, by Opioid Involvement, Number Among All Ages, 1999–2018*
Unanswered Questions About Polysubstance Use

Despite its broad presence, polysubstance use continues to be inadequately understood and poorly defined. Most studies define it as use of multiple substances over a period of 30 days or longer. Yet when it comes to the overdose risk related to polysubstance use, timing is everything. We need a much more finely tuned understanding of the timing and sequencing of polysubstance use at a daily level to understand overdose risk. For example, using two substances concurrently is more dangerous than using them a few hours apart, yet we do not know how frequently or why people choose concurrent use over sequential use. We also need to learn about the situational factors that encourage polysubstance use and determine which can potentially be addressed or ameliorated. Furthermore, most studies of polysubstance use exclude alcohol, even though alcohol in combination with opioids substantially increases the risk of overdose.

In addition, polysubstance use poses unique challenges to the success of substance use treatment. There is broad recognition that polysubstance use is common in treatment populations. In fact, addressing polysubstance use is considered a best practice in substance use screening and treatment, even if the type of treatment is effective for a specific substance use disorder, such as medication-assisted treatment for opioid use disorder. Unfortunately, knowledge is limited about substance use treatment modalities (e.g., cognitive behavioral therapy, dialectical behavioral therapy) that are best suited for treating polysubstance use. Moreover, people with a history of polysubstance use vary in their patterns of polysubstance use, patterns of substance use disorder, presence or absence of co-occurring mental disorders, and other factors. More research and evaluation are needed to identify evidence-based strategies that improve treatment outcomes among subgroups of people who use multiple substances.

COVID-19, Overdose, and Polysubstance Use

The COVID-19 pandemic affects nearly every aspect of life, and substance use is no exception. According to The Washington Post, suspected overdoses in the United States increased 28 percent in April 2020 and 54 percent in May 2020. These increases appear to have multiple causes: (1) social isolation, lack of employment, and uncertainty about the future can lead to increased substance use; (2) using drugs alone increases the risk of fatal overdose because there is no one else present to intervene when overdose occurs; and (3) the supply and availability of illicit substances is less predictable. Though only anecdotal data are currently available, it appears that the contamination of substances like heroin and cocaine with IMF is once again on the rise. In addition, people may choose to mix drugs because of limited availability during the pandemic. Finally, many may face a lack of access to substance use treatment, which has been curtailed in some areas by shelter-in-place orders and the pressing demands of COVID-19 treatment. Because of these compounding factors, the challenges posed by polysubstance use will likely increase during this public health crisis.

Ways Forward

It is clear that polysubstance use can be dangerous, and many harm-reduction groups already provide good guidance on reducing the risks involved in mixing drugs. COSSAP grantees should ensure that their local organizations intentionally address polysubstance use whenever appropriate. Consider reviewing the National Harm Reduction Coalition’s Opioid Overdose Risks and Prevention page on Mixing Drugs for more information.
However, there are still significant gaps in our knowledge, emphasizing the need for additional research. We need a stronger understanding of how and why polysubstance use occurs to develop specific risk-prevention strategies. We also need additional research to inform effective intervention and treatment strategies for people using multiple substances. As we gain new knowledge, we can continue to refine and improve our approach to the opioid overdose epidemic as it continues to evolve.

References


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