Opioids and Stimulants: What Are They and How Are People Using Them?



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Introduction

Opioids and stimulants* are separate classes of substances, with different effects. However, these drugs are linked: people who use one may be introduced to the other, one may be substituted for the other, or mask the withdrawal effect of the other. Despite the clear connection between opioids and stimulants, clinical guidelines and interventions often address just one drug, ignoring the important issue of polysubstance use.

Objectives

- 1. Examine the combined opioid/stimulant picture.
- 2. Review opioid and stimulant trends in availability, use, and impacts.
- 3. Compare opioids and stimulants in terms of drug effects and motivations for use.
- 4. Examine the factors that drive "co-use", that is, using opioids and stimulants simultaneously or sequentially.

This info brief will not be covering treatment topics. Treatment information can be found here.

*Unless otherwise specified, the term "opioids" refers to drugs like heroin, morphine, oxycodone and fentanyl. "Stimulants" refers to cocaine and methamphetamine. We are not including prescription-type stimulants such as methylphenidate or amphetamine in this review as they are much less likely to be a sole drug involved in substance use disorder or to result in serious health consequences.

How Cocaine and Methamphetamine Differ

- Cocaine and methamphetamine increase levels of dopamine in the brain dramatically, but methamphetamine is associated with much higher levels of dopamine increases than cocaine (NIDA, 2020).
- Cocaine is metabolized much more quickly than methamphetamine, which means that
 methamphetamine stays in the brain longer exerting its effects for longer. Specifically, the
 effects of cocaine decrease by half in about one hour compared to twelve hours for
 methamphetamine (NIDA, 2020).
- Cocaine is derived from a plant; methamphetamine is human made/"synthetic" (NIDA, 2020).
- Both cocaine and methamphetamine have been associated with the emergence of psychotic symptoms in the people who them; however, research indicates that that people who use methamphetamine may be more likely to experience psychotic symptoms, and at higher levels, than those who use cocaine (Alexander et al., 2017; Mahoney at al., 2008).

Opioids and Stimulants: Connecting the Trends

Methamphetamine Increasing Among People Who Use Opioids

Treatment and health care providers, law enforcement and researchers have watched the opioid epidemic evolve, now well over a decade. The predominant opioid has changed (e.g., heroin → prescription opioids → heroin → fentanyl) as policy and systems of care attempt to catch up with the opioid most accessible in the moment. More recently, methamphetamine re-entered the picture, its wide availability apparent to those working in opioid use disorder (OUD) treatment, where high rates of methamphetamine use are observed among patients (Jones, Underwood, & Compton, 2020). Among those not in treatment, data from a nationally representative sample also indicates a rise in methamphetamine use among people who use heroin (Strickland, Havens, & Stoops, 2019).

When asked about the methamphetamine uptick, people with OUD note that methamphetamine has become increasingly available in the markets where they typically buy opioids and that the relative absence of certain opioids have made getting methamphetamine more attractive (Ellis, Kasper, & Cicero, 2018). These types of reports indicate interrelated drug trends and drug markets that opioids and stimulants share.

Deaths Involving Stimulants and Opioids

With the recent rise of stimulant use comes a rise in stimulant-related deaths. Nationally, deaths involving cocaine increased 27% between mid-2019 and mid-2020; psychostimulant deaths (including methamphetamine) increased 27% during this time period (Centers for Disease Control and Prevention, 2021).

An increase in methamphetamine-related deaths is also apparent in Washington State, whereby these deaths have increased dramatically, from 83 in 2008 to 531 in 2018 (ADAI, 2020a). The percentage of these deaths in which opioids are present varies year to year between 30% and 47% (ADAI, 2020a) while the proportion involving just methamphetamine has consistently been approximately half. Cocaine deaths have remained relatively flat in the most recent decade (ADAI, 2020b); the presence of opioids in cocaine-related deaths is also fairly consistent over time, around 60% for much of the past decade (ADAI, 2020b).

Conclusions/Clinical Takeaways

- Widespread methamphetamine availability has meant: 1) a wave of people with OUD initiated methamphetamine use; and 2) stimulants and opioids are available in the same environments, likely fueling the use of both.
- National and statewide opioid- and stimulant-related death statistics demonstrate the interconnected nature of these substances, as well as the inherent risks in their combined use.

Opioids & Stimulants: Myths and Facts

Myth: One way to reverse an opioid poisoning is to administer a stimulant like cocaine or methamphetamine.

Fact: Stimulants do not address the slowed/stopped breathing that opioids cause and which leads to death. The opioid blocker, naloxone, can temporarily counteract opioids. In fact, opioid poisoning deaths in which stimulants have been present have risen dramatically in recent years, pointing to stimulant use as a potential risk factor in these deaths.

Myth: People can only die from too much opioid use, but too much meth can't kill a person.

Fact: People can and do die from too much cocaine or meth ingestion. In recent years, methamphetamine-related deaths have risen substantially, and a large proportion involve no other drug, indicating risks associated with using it.

Myth: People don't use cocaine anymore.

Fact: Many people use cocaine, have use disorder, and die from overdoses. Just because it's not in the news doesn't mean it's not happening. Drug trends are ever changing and influenced by geography, drug markets, social context, and other factors. It's important to avoid assumptions about what people are using. If appropriate, ask clients directly what they are using. Examining reliable, up-to-date data sources on local drug trends can also help you stay informed.

Myth: Withdrawal from stimulants is easy compared to being in opioid withdrawal.

Fact: It's true that opioid withdrawal can entail some severe physical symptoms (e.g., pain; vomiting; diarrhea) that are not present for people in stimulant withdrawal. But stimulant withdrawal can be debilitating in other ways that might not seem obvious to the onlooker. In particular, stimulant withdrawal is often accompanied by extreme depression and anhedonia (an inability to experience pleasure). Like physical withdrawal, people may desperately want to avoid this state, leading people back to a known and immediate solution: stimulant use.

Comparing Opioids and Stimulants

Effects of Use: What it Looks Like and Feels Like to Use Opioids and Stimulants

Being distinct classes of drugs, opioids and stimulants operate differently within the body and produce largely discrete effects and experiences. People who have taken opioids will likely breathe more slowly, they may feel relief from pain, relaxed or drowsy, confused, happy or even euphoric. While opioids are depressants in that they depress or slow down bodily functions, in some people they have a paradoxical effect and some report feeling "energized" when on opioids. Stimulants can also produce feelings of happiness and euphoria. Because stimulants are "uppers" they also make many people feel energized and agitated, breathing may speed up, and appetite typically decreases.

Opioid and stimulant effects on the body and brain differ greatly and in turn so do the <u>behaviors</u> of people who use them. What it looks like when people use drugs (i.e., behaviors) varies enormously, but a few examples are listed here.

- A person who recently used opioids may look sedated, have difficulty keeping their eyes open, seem indifferent, content or "out of it."
- A person on stimulants may seem happy or appear agitated; the person may engage in productive, even
 frenetic, behavior or express unusual thoughts and behavior (e.g., see or hear things not present to
 others).

Stimulants and opioids can have opposite effects, which may make it seem like it would be straightforward to identify when a person has used one or the other. In practice, the clinical picture can be much more complicated; Figure 1 shows the overlap of opioid and stimulant effects.

Withdrawal symptoms

Another factor that muddies the clinical picture is withdrawal, which occurs when a person's body adapts to regular use of that drug, and the system "rights itself" by counteracting the drug's effects. Withdrawal effects are the opposite effects of the drug itself, and like the drug's effects, can look very different for opioid versus stimulant withdrawal.

- Opioid withdrawal is typically marked by acute physical symptoms (vomiting, diarrhea, flu-like symptoms). People who take opioids can feel sedated and euphoric, and thus withdrawal effects can mean a person is agitated, unable to sleep, and experiences anxiety.
- There are few physical withdrawal symptoms associated with stimulants. Stimulant use can increase energy and be very pleasurable. Consequently, withdrawal can mean the person experiences fatigue and depressed mood, in particular "anhedonia" (inability to experience pleasure). Extreme sleepiness is both a withdrawal effect and it could result from lack of sleep due to the effects of stimulants.

Opioid withdrawal can sometimes appear as though the person is experiencing the effects of stimulants and vice versa. For example, the opioid withdrawal effects of agitation and anxiety can appear as acute stimulant effects. Stimulant withdrawal effects include extreme fatigue and slowing down (also called psychomotor retardation), which in turn can overlap with opioid effects (e.g., "nodding off"). When we view the behavior of others, we may have an assumption about the drug and withdrawal effects we are seeing. Context and knowledge of the person can help make a more accurate guess. Nonetheless, it is important to remember that we might not know what we are seeing. If appropriate, we can ask people directly what they have been using.

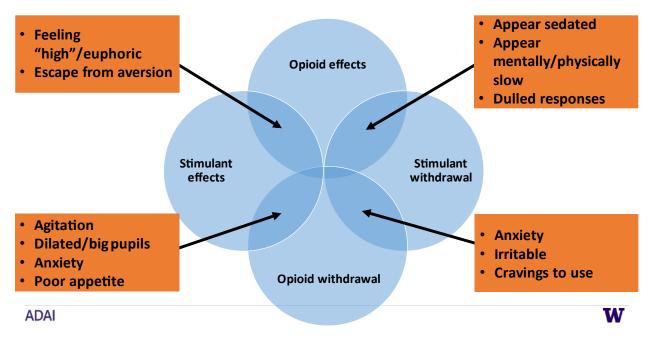


Figure 1. Overlap between opioid and stimulant effects/withdrawal effects.

What Drives Use?

Most substance use is motivated by people's desire to seek pleasure and avoid pain, and this is generally the case across substance categories including opioids and stimulants. Yet, use patterns and people's reports about why they use certain drugs reveal some nuanced differences between opioid and stimulant use.

For individuals using opioids regularly, physical dependence will develop. When people with physical dependence stops using abruptly, they will go into withdrawal. Avoiding withdrawal is an important motivator underlying stimulant use (May, Aupperle, & Stewart, 2020); however, withdrawal avoidance is arguably more instrumental in driving opioid use. "Using just to stay well" is a concept well-known to people with OUD, and avoiding sickness associated withdrawal is often cited as the primary reason for increased or continued use (Cicero & Ellis, 2017; Hartwell et al., 2012).

People who use stimulants tend to exhibit binge use (i.e., repeated consumption in a concentrated time; Cheng et al., 2010; Roy et al., 2017). Binge use can be understood as the person repeatedly seeking the pleasurable effects that stimulants can produce. But people may also use stimulants to improve productivity or functionality (Lende et al., 2007). In other words, it may not be bursts of "pleasure" that drive stimulant use at this stage, it might be that people are seeking bursts of these other functional effects to do things like generate income, care for home/children, or have the energy to face circumstances associated with housing instability. Additionally, people may use stimulants to enhance sexual experiences or increase sociability (Dias, Heckert & Sanchez, 2005). These binges tend to end when a person cannot get more drugs or is physically or mentally exhausted from use.

Methamphetamine and the Brain

Both opioids and stimulants affect the brain in the short- and long-terms, but the most profound changes to the brain and cognitive functioning are associated with methamphetamine use. Through neuroimaging, scientists compared the brains of people who use methamphetamine and people who do not. Such images show differences in brain activity, and the areas of the brain that seem most impacted for people who use methamphetamine. These brain changes can manifest as problems for the individual who uses methamphetamine, including deficits in thinking, motor skills, memory loss, and distractibility. This specific aspect of methamphetamine is important to keep in mind when working with people who use methamphetamine, for example the need for accommodations when receiving services (e.g., shorter treatment encounters, check for understanding, use of tools like reminders).

Conclusions/Clinical Takeaways

- As two separate classes of drugs, opioids and stimulants exert different effects on the person who uses them, have different negative and positive impacts, and have some distinct motivations for use.
- Differences between opioids and stimulants also mean that their use is maintained by different processes.

	Opioids	Stimulants
Drug effects	Relief from pain, feeling relaxed, drowsy, confused, happy/euphoric, respiratory depression	Increased energy, attention, respiration, heart rate, appetite suppression, enhanced mood
Withdrawal effects	Flu-like symptoms (vomiting, diarrhea, discomfort, pain), anxiety, agitation	Sedation, depressed mood, inability to experience pleasure, psychomotor retardation, dulled responses
Motivations for use primarily driven by:	Withdrawal/Negative Affect: Once physiologically dependent, use patterns are marked by avoidance of withdrawal symptoms	Binge/Intoxication: Use patterns marked by repeatedly seeking pleasure/other effects of the substance

Co-use of Opioids and Stimulants

Using one substance represents its own unique difficulties, but adding another substance complicates the clinical picture significantly. Researchers find that people who use both opioids and stimulants are more negatively impacted than those who use only one in the following ways:

- Higher likelihood of injection as the route of administration (Daniulaityte et al., 2020; Glick et al., 2018;
 Shearer et al., 2020);
- Higher rates of viral hepatitis (Chawarski et al., 2020; Shearer et al., 2020);
- Poorer physical (Timko et al., 2017) and mental health status (Shearer et al., 2020; Timko et al., 2017);
- Riskier drug use including preference for fentanyl over heroin (Daniulaityte et al., 2020)
- Less stably housed (Chawarski et al., 2020; Daniulaityte et al., 2020; Glick et al., 2018);
- Higher likelihood of unemployment (Chawarski et al., 2020)
- Poorer SUD treatment outcomes like retention (Wang et al., 2017).

Opioids and Stimulants: Are Two Better Than One?

Co-using opioids and stimulants does not typically correspond to two distinct sets of behaviors. Instead, using one may increase the use of the other; or in some cases the use of one may substitute the use for the other. The reasons people report co-using opioids and stimulants fall into these categories:

- Using both can feel good; people say that using opioids and stimulants at the same time produces a greater effect than either on its own (Ellis, Kasper, & Ciero, 2018; Leri, Bruneau, & Steward, 2003; Palmer et al., 2020).
- One drug may enhance the effects of the other. For example, people report that methamphetamine prolongs the effects of opioids, increasing the amount of time before a person goes into opioid withdrawal (Palmer et al., 2020).

- People may use one drug to temper negative effects of the other, such as countering the sedating effects of opioids by taking stimulants. Or, to counter feeling "edgy" from stimulants, people may take opioids, especially as a person is coming down off stimulants (Ellis et al., 2018; Palmer et al., 2020).
- Drug availability, or lack thereof, may also influence people's tendency to substitute one drug to counteract or help manage the withdrawal symptoms of the other (Ellis et al., 2018; Leri et al., 2003; Palmer et al., 2020).
- Co-use may be a product of environmental factors. That is, both substances being highly available in the current environment may predict use of both (Ellis et al., 2018).

Methadone/Buprenorphine Plus Stimulants

OUD treatment often includes medications (methadone or buprenorphine) as a primary component. These treatments have strong evidence supporting their use to effectively treat OUD (Fullerton et al., 2014; Hser et al., 2016; Mattick et al., 2009; Mattick et al., 2014), and to reduce mortality (Larochelle et al., 2018; Pierce et al., 2016; Wakeman et al., 2020). In a treatment context, OUD medication plus stimulant use represents a unique instance of "co-use." In this case, "co-use" refers to concurrent use of illicit stimulants with the ingestion of medications for OUD, and this combination may be something that people seek for similar and different reasons than they seek out stimulant and illicit opioid use.

Stimulant use is common among patients on medications for OUD and while it can increase the likelihood of treatment discharge, many who stay on buprenorphine eventually reduce their methamphetamine use (Tsui et al., 2020). Low-barrier buprenorphine programs that do not prohibit stimulant use have found that ongoing methamphetamine use is not associated with how long people stay on buprenorphine (Hood et al., 2020). When asked their reasons for using stimulants while taking methadone or buprenorphine for OUD, patients give some of the reasons listed above, like stimulants' capacity to counter the sedating effects of methadone (McNeil et al., 2020). Reversal of sedation may be especially important for individuals taking methadone as it is long-acting, and people report that reversing sedation is critical for survival strategies and daily functioning, like working (McNeil et al., 2020). Another unique aspect of a long-acting opioid like methadone is that the effects are steady but less intense than a short acting opioid like heroin, fentanyl or oxycodone. People maintained on medications for OUD indicate that they miss the intense effects of short-acting opioids and may have a desire to achieve intoxication and therefore do so with stimulants (McNeil et al., 2020; Palmer et al., 2020). In short, people taking medications for OUD cite many reasons for using stimulants, even if their OUD is being treated with effective medications.

Conclusions/Clinical Takeaways

- Opioid-stimulant co-use is associated with higher severity in numerous biopsychosocial domains.
- People report many reasons to co-use opioids and stimulants, including practical reasons like to function better or avoid withdrawal, or for pleasurable effects.
- Use of medications for OUD does not directly address stimulant use, and reasons to use stimulants may still be present or in some cases magnified for these patients. Many people who stay on medications for OUD reduce their methamphetamine use, underscoring the importance of continuing to work with these patients who also use stimulants.

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Citation: Peavy KM, Banta-Green C, Owens M. Opioids and Stimulants: What Are They and How Are People Using Them? Seattle, WA: Addictions, Drug & Alcohol Institute, University of Washington, April 2021. http://adai.uw.edu/pubs/pdf/2021opioidsstimulants.pdf