

# Overview of Methamphetamine Usage & Trends in SF

Issue Brief: April 2019

## Background

Methamphetamine, a derivative of amphetamine, is a growing and evolving public health and safety concern, and its illicit use and manufacture have broadened in nature and distribution well beyond California. While methamphetamine use remained stable from 2002 to 2014, more recent evidence indicates an uptick in methamphetamine activity across the country. For example, seizures of methamphetamine by U.S. Customs and Border Protection has tripled since 2012, treatment admissions for methamphetamine has been increasing since 2011, and the US Drug Enforcement Agency has noted that methamphetamine's purity averages above 90 percent while remaining low-cost.<sup>1,2,3</sup> In addition, amphetamine use is now the fourth most common reason to seek drug treatment in the US, after alcohol, opioid, and marijuana use.<sup>4</sup>

In 2017, drug overdose deaths across the US grew by 9.6 percent from the previous year to 70,237, and the rate has more than tripled since 2000 (6.2 to 21.7 per 100,000 population).<sup>5,6</sup> California also saw a 4.5 percent increase in drug overdose deaths from 2016. Largely overshadowed by the opioid epidemic, deaths from illicit psychostimulants such as methamphetamine increased more than 250 percent between 2008 and 2015 after a period of declining amphetamine use.<sup>7</sup> In 2017, illicit psychostimulants were involved in 10,000 overdose deaths – a 33 percent climb from 2016.<sup>8</sup> Overall, deaths

from psychostimulants have jumped from 5 percent of all overdose deaths in 2010 to 14 percent in 2017.<sup>9</sup> It is estimated that methamphetamine use disorder costs the US approximately \$23.4 billion in 2005, and rising rates of amphetamine use resulted in \$2.17 billion in annual hospital costs in 2015.<sup>10,11</sup>

Methamphetamine can be snorted, smoked, ingested orally or rectally, and injected.<sup>12</sup> Due to its synthetic nature, many variations of methamphetamine are produced, and it is referred to by numerous street names such as speed, crank, ice, meth and crystal.<sup>13</sup> It is currently classified by the US Drug Enforcement Administration as a Schedule II stimulant, and it has the ability to rapidly release high levels of dopamine in reward areas of the brain. In contrast to cocaine, which is quickly removed from and almost completely metabolized in the body, methamphetamine has a much longer duration of action, ultimately leading to prolonged stimulant effects.<sup>14</sup>

## Methamphetamine Usage and Trends

According to the 2017 National Survey on Drug Use and Health (NSDUH), approximately 530 people started using methamphetamine each day, and 774,000 people aged 12 or older were current users of methamphetamine.<sup>15,16,17</sup> In fact, the number of current people who use methamphetamine has increased for all

<sup>1</sup> US Customs and Border Protection (2018). CBP Enforcement Statistics FY2018. Retrieved from <https://www.cbp.gov/newsroom/stats/cbp-enforcement-statistics>

<sup>2</sup> Substance Abuse and Mental Health Services Administration (2018). Treatment Episode Data Set (TEDS) 2016: Admissions to and Discharges from Publicly Funded Substance Use Treatment. Retrieved from [https://www.samhsa.gov/data/sites/default/files/2016\\_Treatment\\_Episode\\_Data\\_Set\\_Annual.pdf](https://www.samhsa.gov/data/sites/default/files/2016_Treatment_Episode_Data_Set_Annual.pdf)

<sup>3</sup> US Drug Enforcement Administration (2018). 2016 National Drug Price and Purity Data. Retrieved from <https://ndews.umd.edu/sites/ndews.umd.edu/files/dea-2016-national-drug-price-purity-data.pdf>

<sup>4</sup> Winkelman, T.N.A., Admon, L.K., et al (2018). Evaluation of Amphetamine-Related Hospitalizations and Associated Clinical Outcomes and Costs in the United States. *JAMA Network Open*, 1(6)

<sup>5</sup> Centers for Disease Control and Prevention (2018). Drug Overdose Deaths. Retrieved from <https://www.cdc.gov/drugoverdose/data/statedeaths.html>

<sup>6</sup> Centers for Disease Control and Prevention (2016). Increases in Drug and Opioid Overdose Deaths – United States, 2000–2014. Retrieved from <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm>

<sup>7</sup> Centers for Disease Control and Prevention (2018). Drug Overdose Deaths. Retrieved from <https://www.cdc.gov/drugoverdose/data/statedeaths.html>

<sup>8</sup> Centers for Disease Control and Prevention (2018). Other Drugs. Retrieved from <https://www.cdc.gov/drugoverdose/data/otherdrugs.html>

<sup>9</sup> Centers for Disease Control and Prevention (2017). Drug Overdose Deaths in the United States, 1999–2015. Retrieved from <https://www.cdc.gov/nchs/products/databriefs/db273.htm>

<sup>10</sup> Nicosia, N., Pacula, R., Kilmer, B., Lundberg, R., & Chiesa, J. (2009). The Economic Cost of Methamphetamine Use in the United States, 2005. *Rand Corporation*.

<sup>11</sup> Winkelman, T.N.A., Admon, L.K., et al (2018). Evaluation of Amphetamine-Related Hospitalizations and Associated Clinical Outcomes and Costs in the United States. *JAMA Network Open*, 1(6)

<sup>12</sup> Shrem, M.T. & Halktisi, P.N. (2008). Methamphetamine Abuse in the United States: Contextual, Psychological, and Sociological Considerations. *Journal of Health Psychology*, 13(5) 669-679

<sup>13</sup> Shukla, R.K., Crump, J.L., & Chrisco, E.S. (2012). An evolving problem: Methamphetamine production and trafficking in the United States. *International Journal of Drug Policy*, 23, 426-435

<sup>14</sup> National Institute on Drug Abuse (2013). Methamphetamine. Retrieved from <https://www.drugabuse.gov/publications/research-reports/methamphetamine/what-methamphetamine>

<sup>15</sup> Substance Abuse and Mental Health Services Administration (2018). Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health. Retrieved from <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf>

<sup>16</sup> Prior to 2015, questions about methamphetamine use were asked in the context of questions about the misuse of prescription stimulants because methamphetamine is legally available by prescription (Desoxyn®).

<sup>17</sup> There are limitations to the NSDUH as it does not include homeless, marginally housed, or incarcerated individuals. It also did not detect any increase in opioid use over the past two decades.

**Table 1: Drug Use and Mental Health Status by Percent of Age Group, California (2016-2017)**

Item	12-17	18-25	26+
methamphetamine	0.20	0.96	0.85
heroin	0.05	0.30	0.18
cocaine	0.69	7.99	2.05
substance use disorder	4.63	14.20	6.69
illicit drug use disorder	3.73	7.27	2.15
needing but not receiving treatment for substance use	4.47	13.28	6.42
needing but not receiving treatment for illicit drug use	3.79	6.73	2.02
any mental illness		24.75	17.06
serious mental illness		6.61	3.48
received mental health services		11.34	11.78

age groups from 2016, most significantly 132.3 percent among transitional-aged youth (TAY) ages 18 to 25 years. This population also had increasing rates of serious mental illness and major depressive episodes.<sup>18</sup> In contrast with some other illicit drugs, lifetime methamphetamine use rates are similar between women (7.3%) and men (10.0%), and women represent 38.5 percent of people who use methamphetamine and are more likely than men to report methamphetamine as their primary drug.<sup>19</sup>

### California

California saw similar patterns in 2017, and TAY had the highest rate of methamphetamine use compared to adolescents and older adults.<sup>20</sup> TAY also had the highest use rates for heroin, cocaine, and pain reliever misuse, including substance use disorders and mental illness. However, they were among the least likely to report seeking methamphetamine use disorder treatment.

Among Californians, between 23 and 27 percent of substance-using men who have sex with men (MSM) have reported methamphetamine use in the past 30 days, and approximately 20 percent of trans women in the state have used in the past year.

**Table 2: SUD Treatment Admissions, Methamphetamine Primary Substance, San Francisco (2017)**

Category	Characteristic	%
Sex	Male	73.9%
	Female	26.1%
Race	White	35.6%
	Black/African-American	20.5%
	Hispanic/Latinx	29.5%
Age	18-25	12.0%
	26-44	60.9%
	45+	26.9%
Administration	Smoked	65.7%
	Injected	23.5%
	Inhaled	7.1%
	Oral/other/unknown	3.6%

After alcohol and marijuana, methamphetamine is the third most frequently used substance among MSM and trans women.<sup>21</sup>

### San Francisco

Numerous indicators suggest increasing methamphetamine-related morbidity and mortality in the city (Figure 1). Substance use disorder (SUD) treatment admissions for methamphetamine have continued rising, in addition to hospitalizations, emergency department visits, and law enforcement seizures involving methamphetamine.

Mortality and treatment admission data suggest that people who use methamphetamine in San Francisco are most likely to be male, white, aged 26 and older, and consume the drug through smoking.<sup>22</sup> There is also substantial research supporting a close association between methamphetamine use and sexual risk-taking, especially among MSM. Nearly half (47%) of all patients visiting Psychiatric Emergency Services (PES) are due to methamphetamine use. Among clients with at least eight 5150s (psychiatric holds) nearly 9 in 10 (89.1%) used only methamphetamine, and 1 in 4 (25%) used methamphetamine in addition to opioids, cocaine, and alcohol.<sup>23</sup> Individuals with at least eight 5150s would be considered for conservatorship under Senate Bill (SB)

<sup>18</sup> Substance Abuse and Mental Health Services Administration (2018). Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health. Retrieved from <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf>

<sup>19</sup> Rade, C.B., Desmarais, S.L., et al (2015). Mental Health Correlates of Drug Treatment Among Women Who Use Methamphetamine. *The American Journal on Addictions*, 24: 646–653.

<sup>20</sup> Substance Abuse and Mental Health Services Administration (2018). 2016-2017 National Survey on Drug Use and Health: Model-Based Prevalence Estimates (50 States and the District of Columbia). Retrieved from

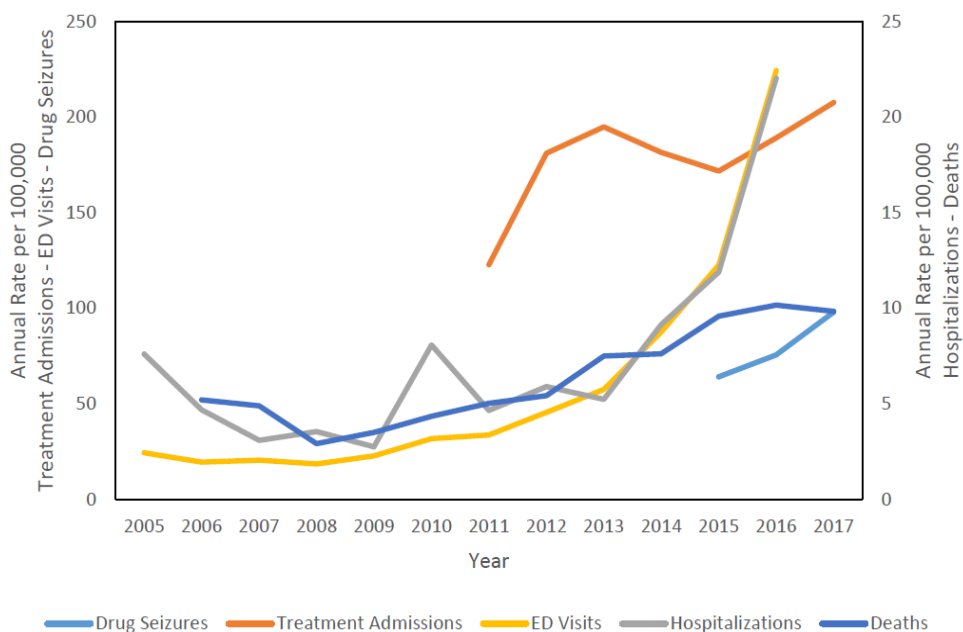
<https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHsaePercentsExcelCSVs2017/NSDUHsaePercents2017.pdf>

<sup>21</sup> Anderson-Carpenter, K.D., Fletcher, J.B., & Reback, C.J. (2017). Associations Between Methamphetamine Use, Housing Status, and Incarceration Rates Among Men Who Have Sex With Men and Transgender Women. *Journal of Drug Issues*, 47(3) 383-395

<sup>22</sup> Coffin, P.O. & Rowe, C. (2018). NDEWS San Francisco Sentinel Community Site (SCS) Drug Use Patterns and Trends, 2018. National Drug Early Warning System.

<sup>23</sup> San Francisco Department of Public Health (2018). CCMS Cohort Report, FY1718 Utilization. Whole Person Care.

**Figure 1: San Francisco Methamphetamine Indicators, 2005-2017**

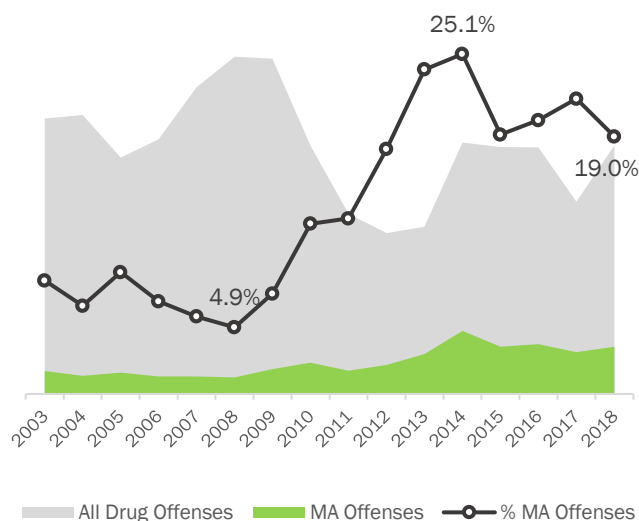


1045. Methamphetamine has been the third most common primary substance for people being admitted to a substance use disorder (SUD) treatment program since 2015, and at least 1,400 have been admitted each year for primary methamphetamine use since 2013.<sup>24</sup> Out of 9,660 program admissions in 2017, nearly 1 in 5 (19%) were for methamphetamine as the primary substance.

methamphetamine-involved drug arrests occurred in District 6, which include the Tenderloin (36.6%) and SoMa (17.2%) neighborhoods; about 14 percent were in the Mission.<sup>29</sup>

Multiple drug use is common among people who use methamphetamine. Among people who inject drugs in San Francisco, a 2017 survey indicated over half (57.5%) injected methamphetamine, and nearly two-thirds (65%) reported injecting more than one drug, with the most common combination being heroin and methamphetamine (55%).<sup>25</sup> Out of 419 SUD treatment admissions for prescription opioids in SF, methamphetamine was a secondary substance in 10 percent of cases.<sup>26</sup> Among the 54 overdose deaths involving prescription opioids, 22 percent involved methamphetamine.<sup>27</sup>

**Figure 2: Drug & Methamphetamine Offenses, San Francisco (2003-2018)**



The number of methamphetamine arrests has steadily risen since 2003, and the percent of drug arrests involving methamphetamine have trended upward since 2008, from 1 in 20 drug arrests to a peak of 1 in 4 in 2014.<sup>28</sup> In 2018, about 1 in 5 involved methamphetamine. The majority (55.2%) of

<sup>24</sup> Coffin, P.O. & Rowe, C. (2018). NDEWS San Francisco Sentinel Community Site (SCS) Drug Use Patterns and Trends, 2018. National Drug Early Warning System.  
<sup>25</sup> San Francisco Department of Public Health (2018). CHEP Safe Injection Services Survey Results.  
<sup>26</sup> Coffin, P.O. & Rowe, C. (2018). NDEWS San Francisco Sentinel Community Site (SCS) Drug Use Patterns and Trends, 2018. National Drug Early Warning System.  
<sup>27</sup> *ibid*  
<sup>28</sup> San Francisco Police Department (2019). Police Incident Reports: 2003 to Present. Retrieved from <https://data.sfgov.org/browse?category=Public+Safety>  
<sup>29</sup> *ibid*

## Impacts of Methamphetamine Use

Methamphetamine can result in many of the same health impacts as those of other stimulants such as cocaine, including: increased wakefulness and physical activity, decreased appetite, faster breathing, rapid and/or irregular heartbeat, and increased blood pressure and body temperature. Long-term methamphetamine use may also lead to or exacerbate the following symptoms and conditions:

- hallucinations
- psychosis
- violent and aggressive behavior
- anxiety and confusion
- insomnia
- depression
- suicidal ideation
- impulsivity
- reduced motor coordination and memory
- extreme and unreasonable paranoia
- sexual risk-taking
- increased risk of contracting HIV and sexually transmitted infections
- chest pain
- pulmonary diseases
- cardiac and cerebrovascular disease
- respiratory failure
- extreme weight loss
- severe dental problems
- intense itching and skin sores
- Parkinson's-like symptoms
- toxicity of the kidneys and liver
- prenatal complications and birth defects
- increased likelihood of incarceration<sup>30,31, 32</sup>

A study of HIV-positive people who use stimulants in San Francisco found recent use to be associated with inflammation, innate immune activation, neuroendocrine hormone regulation, and neurotransmitter synthesis.<sup>33</sup> Withdrawal symptoms can include anxiety, fatigue, severe depression, psychosis, and intense drug cravings.<sup>34</sup>

<sup>30</sup> Shrem, M.T. & Halktisi, P.N. (2008). Methamphetamine Abuse in the United States: Contextual, Psychological, and Sociological Considerations. *Journal of Health Psychology*, 13(5) 669-679.

<sup>31</sup> National Institute on Drug Abuse (2013). Methamphetamine. Retrieved from <https://www.drugabuse.gov/publications/research-reports/methamphetamine/what-methamphetamine>

<sup>32</sup> Tsai, H., Lee, J.H., et al (2017). Methamphetamine And Common Pulmonary Diseases: A Retrospective Investigation Of Hospital Discharges In California From 2005 Through 2011. *American Journal of Respiratory and Critical Care Medicine*, 195.

<sup>33</sup> Carrico AW, Flentje A, Kober K, Lee S, Hunt P, Riley ED, Shoptaw S, Flowers E, Dilworth SE, Pahwa S, Auizerat BE. (2018). Recent stimulant use and leukocyte gene expression in methamphetamine users with treated HIV infection. *Brain, Behavior, and Immunity*, 71:108-115.

## Overdose Mortality in San Francisco

Deaths determined to have been caused by methamphetamine in San Francisco have steadily increased from 1.8 per 100,000 in 2008 to 11.5 in 2017.<sup>35</sup> Decedents are typically male, white, and average 48.6 years.<sup>36</sup> Methamphetamine is known to increase heart rate and blood pressure, likely exerting strain on the individual's cardiovascular and cerebrovascular systems. A study of overdose deaths in San Francisco found that individuals who died of acute methamphetamine or cocaine poisoning were significantly more likely to have also suffered a cardiac event or cerebral hemorrhage contributing to their demise, when compared to those who died from acute opioid poisoning.<sup>37</sup>

Consistent with patterns of multiple drug use, in 2017, 22 percent of the city's overdose deaths involving cocaine also involved methamphetamine; 35 percent of overdose deaths from fentanyl also involved methamphetamine present in their system.<sup>38</sup> Notably, an episode in February 2018 involved three overdose decedents that tested positive for multiple illicit substances, including methamphetamine and fentanyl. Paraphernalia suggested that either the methamphetamine or the cocaine was laced with fentanyl. Among decedents experiencing homelessness, methamphetamine was the most commonly present (47%) substance in toxicology reports.<sup>39</sup>

Overdose deaths in San Francisco involving methamphetamine and amphetamines have shifted geographically over time. In 2006-2007, deaths were more localized in eastern neighborhoods like South of Market, Western Addition, Union Square, and Mission (Figure 3). Over the following decade, deaths involving those substances spread to eastern and southeastern neighborhoods, including the Bayview, Excelsior, Potrero Hill, Mission Bay, and the Embarcadero (Figure 4).

<sup>34</sup> National Institute on Drug Abuse (2013). Methamphetamine. Retrieved from <https://www.drugabuse.gov/publications/research-reports/methamphetamine/what-methamphetamine>

<sup>35</sup> Coffin, P.O. & Rowe, C. (2018). NDEWS San Francisco Sentinel Community Site (SCS) Drug Use Patterns and Trends, 2018. *National Drug Early Warning System*.

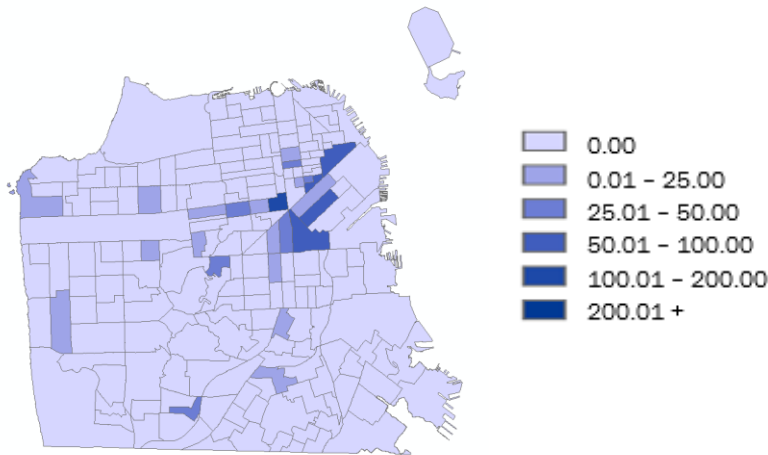
<sup>36</sup> Coffin, P. (2018). Distribution of mortality by substance category and select characteristics, San Francisco, 2006 - 2015. San Francisco Department of Public Health.

<sup>37</sup> Turner, C., Chandrakumar, D., Rowe, C., Santos, G., Riley, E.D., & Coffin, P. (2017). Cross-sectional cause of death comparisons for stimulant and opioid mortality in San Francisco, 2005-2015. *Drug and Alcohol Dependence*, 185: 305-312.

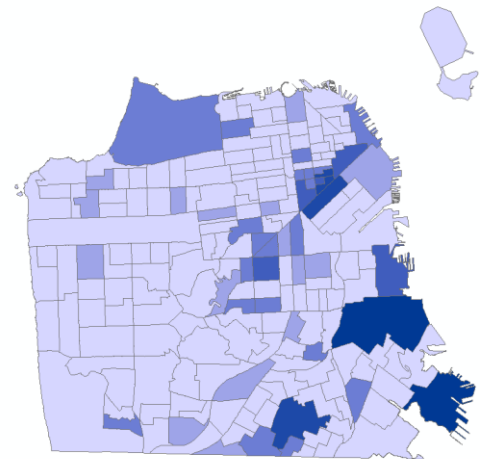
<sup>38</sup> *ibid*

<sup>39</sup> Zevin, B. & Cawley, C. (2019). Homeless Mortality in San Francisco: Opportunities for Prevention. San Francisco Department of Public Health

**Figure 3: Methamphetamine & Amphetamine Overdose Deaths Per 100k, 2006-2007**



**Figure 4: Methamphetamine & Amphetamine Overdose Deaths Per 100k, 2014-2015**



### Characteristics of People Who Use Methamphetamine

According to SAMHSA, methamphetamine use disorder occurs when “someone experiences clinically significant impairment caused by the recurrent use of methamphetamine, including health problems, physical withdrawal, persistent or increasing use, and failure to meet major responsibilities at work, school, or home.”<sup>42</sup> In 2017, an estimated 964,000 Americans aged 12 or older had a methamphetamine use disorder, a 41 percent surge from 2016. While the number of adults 18 and older with methamphetamine use disorder increased, the two-thirds increase among 12-17 year olds was the sharpest among the age groups. Furthermore, an additional 212,000 adults 26 and older developed methamphetamine use disorder.

Models of addiction vary in their emphasis on personality characteristics (e.g. high reactivity, pessimism) and socialization sources (e.g. family, schools, the media, and peer groups) as contributing factors toward substance use disorder.<sup>43</sup> Other studies have shown that women often begin using at an earlier age and develop dependence at a quicker rate than men.<sup>44</sup>

### Opportunities and Challenges for Intervention

Nearly half of people who use visit PES are under the influence of methamphetamine, and clinical and behavioral manifestations often include cognitive impairment, poor memory, elevated rates of psychiatric co-morbidity, short attention span, decreased motivation, and sleep disorders. The presence of powerful trigger and craving responses, ambivalence about the need to stop, and a limited understanding of addiction commonly result in poor retention in outpatient treatment.

There is considerable comorbidity between psychopathology and use of methamphetamine, underscoring the significance of understanding the developmental, contextual, and personality factors which contribute to methamphetamine use. For example, psychiatric comorbidity including depression, personality disorders, and psychoses were found in nearly half of participants diagnosed with methamphetamine dependency.<sup>45</sup> Other studies have shown that 1 in 3 people who use methamphetamine report lifetime mood disorders, and over 1 in 4 report lifetime anxiety disorders. Female users of methamphetamine are more likely to experience depression and anxiety symptoms compared to men.<sup>46</sup>

Psychiatric comorbidity is a major health concern when treating addiction to stimulant drugs such as

<sup>42</sup> Substance Abuse and Mental Health Services Administration (2018). Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health. Retrieved from <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHF2017/NSDUHF2017.pdf>

<sup>43</sup> Shrem, M.T. & Halktisi, P.N. (2008). Methamphetamine Abuse in the United States: Contextual, Psychological, and Sociological Considerations. *Journal of Health Psychology*, 13(5) 669-679.

<sup>44</sup> Brecht ML, O'Brien A, Von Mayrhauser C, Anglin, MD. (2004). Methamphetamine use behaviors and gender differences. *Addictive Behaviors*. 2004; 29:89–106.

<sup>45</sup> Shrem, M.T. & Halktisi, P.N. (2008). Methamphetamine Abuse in the United States: Contextual, Psychological, and Sociological Considerations. *Journal of Health Psychology*, 13(5) 669-679.

<sup>46</sup> Hartwell, E.E., Moallem, N.R., et al (2016). Gender differences in the association between internalizing symptoms and craving in methamphetamine users. *Journal of Addiction Medicine*, 10(6) 395-401.



methamphetamine, and many comorbid symptoms are exacerbated by ongoing methamphetamine use. For example, up to 25 percent of individuals diagnosed with drug-induced psychosis after some years developed a primary psychotic disorder<sup>47</sup> In addition, 38 percent of individuals with methamphetamine-associated psychosis may be diagnosed with schizophrenia due to persistent psychosis.<sup>48</sup> Conversely, remaining abstinent reduces the severity of psychiatric symptoms. Development of treatment interventions may need to consider integrated treatment of both methamphetamine-induced and other Axis I disorders with symptoms such as psychosis, depression and anxiety.<sup>49</sup>

### Current Treatment Options

Although there are no FDA-approved medications for the treatment of methamphetamine use disorder, there have been several studies suggesting potential benefits from mirtazapine, bupropion, methylphenidate, and oxytocin.<sup>50</sup> Furthermore, there preliminary data suggest potential neuroprotection from agents such as n-acetylcysteine.<sup>51</sup> Results overall suggest that fully effective pharmacotherapy may require more than one agent.

Behavioral therapies are currently used to help patients recognize, avoid, and cope with the situations in which they are most likely to use drugs. These approaches include utilizing motivational incentives such as vouchers or small cash rewards to encourage patients to remain abstinent.<sup>52</sup>

Examples of specific behavioral therapies include:

- Contingency management interventions provide tangible incentives in exchange for engaging in treatment and maintaining abstinence.
- The Matrix Model is a 16-week comprehensive behavioral treatment approach that combines behavioral therapy, family education, individual counseling, 12-Step support, drug testing, and encouragement for non-drug-related activities.

- Motivational Incentives for Enhancing Drug Abuse Recovery (MIEDAR) is an incentive-based method for promoting cocaine and methamphetamine abstinence.

### Additional Considerations

- Stigma plays an influential role in the mental and social health of individuals who use drugs and in the success of treatment.
- Populations that may need specific treatment considerations include: female stimulant users; people who inject drugs; individuals under 21 years of age; individuals experiencing homelessness; individuals who take stimulants daily or in very high doses; and individuals with chronic mental illness and/or high levels of psychiatric symptoms at admission.
- Many experts consider use of methamphetamine as a cardiac risk factor and recommend accounting for that in consideration of interventions addressing primary and secondary cardiac risk.<sup>54</sup>
- Studies indicate that people who use methamphetamine consulted with healthcare professionals at roughly similar rates as seen in the general population. Health care providers could potentially serve as a point of engagement, screening, and intervention.<sup>55</sup>
- The lack of consistent usage of ICD-9-CM diagnostic codes has persisted in updated ICD-10 codes and raises concerns that the current coding structures are insufficiently utilized to detect and respond to emerging public health issues related to a variety of psychostimulants.<sup>56</sup>

<sup>47</sup> Bramness JG, Gundersen ØH, Guterstam J, et al. Amphetamine-induced psychosis—a separate diagnostic entity or primary psychosis triggered in the vulnerable?. *BMC Psychiatry*. 2012;12:221. Published 2012 Dec 5. doi:10.1186/1471-244X-12-221.

<sup>48</sup> Kittirattanapaiboon P, Mahatnirunkul S, Booncharoen H, Thummawong P, Dumrongchai U, Chutha W. Long-term outcomes in methamphetamine psychosis patients after first hospitalisation. *Drug Alcohol Rev*. 2010;29(4):456–461.

<sup>49</sup> Salo, R., Flower, K., et al (2011). Psychiatric comorbidity in methamphetamine dependence. *Psychiatry Review*, 186(2-3) 356-361.

<sup>50</sup> Colfax, GN, Santos GM, Das M, Santos DM, Matheson T, Gasper J, Shoptaw S, Vittinghoff E.(2011). Mirtazapine to reduce methamphetamine use: a randomized controlled trial. *Archives of General Psychiatry*, 68(11) 1168-75.

<sup>51</sup> Bavarsad Shahripour, R., Harrigan, M. R., & Alexandrov, A. V. (2014). N-acetylcysteine (NAC) in neurological disorders: mechanisms of action and therapeutic opportunities. *Brain and Behavior*, 4(2), 108-22.

<sup>52</sup> National Institute on Drug Abuse (2013). Methamphetamine. Retrieved from <https://www.drugabuse.gov/publications/research-reports/methamphetamine/what-methamphetamine>

<sup>54</sup> <sup>54</sup> Turner, C., Chandrakumar, D., Rowe, C., Santos, G., Riley, E.D., & Coffin, P. (2017). Cross-sectional cause of death comparisons for stimulant and opioid mortality in San Francisco, 2005–2015. *Drug and Alcohol Dependence*, 185: 305-312.

<sup>55</sup> Herbeck, D.M., Brecht, M.L., & Lovinger, K. (2015). Mortality, causes of death and health status among methamphetamine users. *Journal of Addictive Diseases*, 34(1) 88-100.

<sup>56</sup> Winkelman, T.N.A., Admon, L.K., et al (2018). Evaluation of Amphetamine-Related Hospitalizations and Associated Clinical Outcomes and Costs in the United States. *JAMA Network Open*, 1(6)