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**Increasing Overdose Deaths Related to Cocaine and Other Stimulants: Guidance from the New York State Office of Addiction Services and Supports, Medical Advisory Panel**

Purpose: To raise awareness of increasing overdose events and deaths related to cocaine and other stimulant use, and to provide guidance to health care providers on clinically managing and preventing harm from cocaine and stimulant use disorders.

Context: Recently, there have been reports of increasing overdose deaths related to cocaine and other stimulants, both nationally and in New York State (NYS) and New York City (NYC). There are data to suggest that rates of cocaine and other stimulant use\* are increasing, particularly in certain demographic groups and geographic areas.<sup>1</sup> While overdose deaths related to cocaine and/or other stimulants alone are increasing, there are also data to suggest that most of the increase in overdose deaths related to cocaine and other stimulants is related to opioids – particularly high potency synthetic opioids such as fentanyl and analogues – being mixed with cocaine and other stimulants.<sup>2</sup> This “mixing” can occur in two ways – individuals can intentionally use cocaine/stimulants along with or near the same time as opioids (and highly potent opioids may be included in the intentionally used opioids, and the person using may or may not be aware of their presence), or the opioids can be combined with the cocaine/stimulants without the individual using knowing of their presence.

The NYS Office of Addiction Services and Supports (OASAS) Medical Advisory Panel convened a meeting to discuss this burgeoning overdose crisis on October 16, 2019, and offers the following guidance to clinical providers and local public health and mental hygiene authorities in NY.

Overdose Prevention:

- All individuals who use cocaine/stimulants should be provided with overdose prevention education, including but not limited to the following facts: opioids including fentanyl and analogues may be mixed into other drugs; individuals who do not normally use opioids (i.e., who only use cocaine and/or stimulants) would not have a tolerance to opioids and would therefore be at higher overdose risk; using multiple drugs simultaneously is more dangerous than using a single drug at a time; using with a buddy is safer than using alone; using slowly until potency is established is safer than using a usual dose all at once; naloxone should be readily available during any drug use; and tolerance to opioids may be lost (and overdose therefore more likely) after a period of abstinence from opioids (eg., hospital, detox, or criminal justice admission). Information and resources/materials from the NYS Department of Health can be found [here](#) (scroll down to “ESAP/Injection Drug Use/Opioid Overdose”), and information from the NYC Department of Health and Mental Hygiene can be found [here](#).
- All individuals who use cocaine/stimulants should be given or prescribed naloxone for overdose reversal in the community. Since opioids including fentanyl and analogues have also been identified in other drugs such as illicit benzodiazepine pills, MDMA, and synthetic cannabinoids, anyone who uses drugs

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should be provided with naloxone, possibly unless their drug use is exclusively regulated products (eg., alcohol, tobacco). Repeated studies have shown that naloxone distribution decreases overdose deaths and is not associated with increased drug use.<sup>3</sup> Individuals should be educated on how to use naloxone, including the importance of administering naloxone right away (i.e., even before calling 911) in an overdose situation and the fact that multiple doses might be necessary, which are particularly important points in case fentanyl or analogs are involved. Information from the NYS Department of Health about Opioid Overdose Prevention Programs and obtaining naloxone in pharmacies including the Naloxone Copayment Assistance Program can be found [here](#). Information about accessing naloxone from the NYC Department of Health and Mental Hygiene can be found [here](#).

### Treatment:

- There are no medications approved by the United States Food and Drug Administration (FDA) for the treatment of cocaine or stimulant\* use disorders, so the mainstays of treatment are psychosocial approaches and treatment of co-occurring conditions.
- Co-occurring mental health conditions and psychiatric symptoms should be identified and treated vigorously. For instance, co-occurring attention deficit-hyperactivity disorder (ADHD) is common among people with substance use disorders (SUDs). Treatment of ADHD – including with careful use of stimulants – may benefit the SUD. Comorbid depressive symptoms and insomnia are also common – due to protracted stimulant withdrawal symptoms and/or co-occurring psychiatric disorders – and should be proactively treated.
- Co-occurring SUDs should also be identified and treated. In particular, co-occurring opioid use and alcohol use disorders should be treated with FDA-approved medications. Medications for addiction should not be denied or tapered/discontinued solely due to continued drug use. For further guidance on appropriate, person-centered use of medications in OASAS-certified programs, see [here](#). For best practices to increase access to buprenorphine from the NYS Department of Health and OASAS, see [here](#).
- Providers should pay close attention to the physical health of individuals who use drugs, including identifying medical complications of drug use (eg., viral hepatitis, human immunodeficiency virus, skin/soft tissue infections), testing for sexually transmitted infections, providing recommended cancer screenings, etc., and should either provide treatment or refer individuals to other medical providers and help coordinate their care.
- While many approaches including Cognitive Behavioral Therapy have some level of evidence, the single psychosocial approach to cocaine and stimulant use disorders that appears to have the most consistent evidence is contingency management and community reinforcement.<sup>4</sup> However, there are special considerations around providing and billing for this intervention. OASAS plans to issue further guidance on implementing this approach.
- Medications:
  - While there are no medications approved by the FDA for the treatment of cocaine and stimulant use disorders, several medication classes have preliminary evidence for potential benefits. Please see the table below for a summary of possible medication options.<sup>†</sup>
  - Naltrexone may be helpful for relapse prevention in individuals with stimulant use disorder and with early abstinence<sup>5</sup>, and can also treat co-occurring opioid and/or alcohol use disorders. However,

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significant findings have only been shown for oral naltrexone thus far, not for long-acting injectable naltrexone.

- Anticonvulsant agents including topiramate have some evidence for promotion of abstinence in cocaine use disorder<sup>6,7,8</sup> and reduction in use for amphetamine use disorder.<sup>9</sup> Topiramate may also be effective for individuals with comorbid alcohol use disorder.<sup>10</sup>
- Antidepressant medications – particularly bupropion – may be helpful<sup>6,11</sup>, especially for individuals with depressive symptoms or a co-occurring depressive disorder and/or individuals with less severe baseline cocaine/stimulant use.<sup>12</sup> Bupropion is also approved by the FDA to treat tobacco use disorder. There is more preliminary evidence that sertraline may be helpful for relapse prevention in individuals with comorbid cocaine use disorder and depressive symptoms after a period of initial abstinence.<sup>6,13,14</sup> There is also a recent study showing efficacy for mirtazapine for reducing crystal methamphetamine use as well as depressive symptoms, insomnia, and HIV risk behaviors.<sup>15</sup>
- Stimulant medications\*<sup>6,9,11</sup> including formulations of methylphenidate<sup>6,9,16,17</sup> and amphetamines<sup>6,18,19</sup> as well as modafinil<sup>6,20,21,22,23</sup> have evidence for facilitating reduction of use/abstinence and improving treatment retention, and some are also indicated to treat co-occurring ADHD.<sup>24,25</sup> Long-acting and abuse-deterrent formulations (eg., extended-release methylphenidate, extended-release mixed amphetamine salts, lisdexamfetamine) are preferred over short-acting, immediate-release medications. Lisdexamfetamine specifically may be helpful for individuals with comorbid opioid use disorder who are on opioid agonist therapy.<sup>18</sup> Providers should prescribe controlled substances with misuse or diversion potential judiciously to individuals with SUDs, and should ensure frequent and careful monitoring. However, medication doses should be high enough to allow for valid assessment of whether the medication benefits the individual. For instance, individuals with co-morbid ADHD and cocaine or stimulant use disorders may benefit from higher doses of stimulant medications.<sup>24</sup> There is also some evidence that adding topiramate to mixed amphetamine salts may confer additional benefits.<sup>26,27</sup>
- Since stimulant medications are controlled substances with the potential for addiction, it is important to monitor carefully for adherence and diversion (ensuring the former will also enhance the potential for efficacy), through various protocols such as treatment agreements, toxicology (to confirm presence of medication), random pill counts, etc. When a patient seems to be benefiting from a medication but the provider is concerned about adherence and/or diversion, the provider could consider providing prescriptions for shorter periods of time, or even referring the patient to a program that can offer closer/daily monitoring, such as an opioid treatment program (for those with co-occurring opioid use disorder). However, it should also be noted that stimulants have been demonstrated to be safe when used to treat cocaine use disorder, with adverse effect rates comparable to placebo.<sup>11</sup>
- While there is evidence that FDA-approved medications for opioid, alcohol, and tobacco use disorders can provide significant benefits without concurrent psychosocial treatment, there is no similar evidence for off-label medications for cocaine or stimulant use disorders. Therefore, off-label medications should be provided along with as robust of a psychosocial treatment plan as individuals are able and willing to engage in. Medications should be discontinued if patients are experiencing no clear benefit after a reasonably adequate trial.

**Summary Table: Non-FDA-Approved Medications with Evidence for Efficacy in Cocaine and/or Stimulant Use Disorders<sup>†</sup>**

Medication	Dose	Evidence for cocaine <sup>#</sup>	Evidence for stimulants <sup>*,#</sup>	Sub-populations that benefit	DEA Schedule	Key adverse effects	Contraindications
Naltrexone	50-100mg PO/d	-	+	Early abstinence, AUD, ?OUD	NS	Mood/anxiety changes, opioid withdrawal, hepatic injury	Severe liver disease, on opioid agonist, OUD for PO
Topiramate	200-300mg PO/d	+	+	AUD, In combination with mixed amphetamine salts for cocaine Low level use for amphetamine	NS	Mood/anxiety changes, cognitive problems, sedation, nephrolithiasis, vision changes, anorexia	N/A but monitor electrolytes and renal function
Bupropion	SR 150mg PO BID, XL 300mg PO/d	+	+	Low-level use for amphetamine, Depression, tobacco use	NS	Mood/anxiety changes, insomnia, seizures, false + test for amphetamines	Seizure disorder, bulimia, bipolar disorder (relative), on MAOI antidepressant or linezolid
Sertraline	200mg PO/d	+	-	Depression, Early abstinence	NS	Mood/anxiety changes, sexual side effects	Bipolar disorder (relative), on MAOI antidepressant or linezolid
Mirtazapine	30mg PO at bedtime	-	+	Depression, insomnia, HIV risk behaviors	NS	Mood/anxiety changes, weight gain, sedation	Bipolar disorder (relative), on MAOI antidepressant or linezolid
Methylphenidate extended/sustained release	Depends on formulation, higher doses for ADHD	-	+	ADHD	II	Mood/anxiety changes, insomnia, psychosis, hypertension, palpitations, arrhythmia, bruxism, anorexia, misuse/addiction	Psychotic disorder, bipolar disorder (relative), severe cardiac disease, glaucoma, tic disorder, on MAOI antidepressant or linezolid
Mixed amphetamine salts – extended release	20-80mg PO/d, higher doses for ADHD	+	+	ADHD, In combination with mixed amphetamine salts for cocaine	II	Mood/anxiety changes, insomnia, psychosis, hypertension, palpitations, arrhythmia, bruxism, anorexia, misuse/addiction	Psychotic disorder, bipolar disorder (relative), severe cardiac disease, glaucoma, tic disorder, on MAOI antidepressant or linezolid
Lisdexamfetamine Dextroamphetamine SR	40-120mg PO/d, higher doses for ADHD	+	+	ADHD, OUD, Binge-eating disorder	II	Mood/anxiety changes, insomnia, psychosis, hypertension, palpitations, arrhythmia, bruxism, anorexia, misuse/addiction	Psychotic disorder, bipolar disorder (relative), severe cardiac disease, glaucoma, tic disorder, on MAOI antidepressant or linezolid
Modafinil	200-400mg PO/d	+	-	No AUD	IV	Mood/anxiety changes, insomnia, anorexia, misuse/addiction	N/A but monitor closely for insomnia

<sup>#</sup>Lack of evidence (-) may indicate lack of studies or only negative studies. NS = Not Scheduled by the US DEA

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### Assessment and Documentation:

- Toxicology panels should include opioids and fentanyl even for individuals who report only using cocaine and/or stimulants\*, to increase knowledge about dangerous substances in the drugs people are using.
- Providers should regularly and carefully assess patients with cocaine or stimulant use disorders for treatment progress, adverse effects, and high-risk behaviors (eg., self-harm, suicidal ideation, high risk drug use, violence risk), particularly when off-label medications are prescribed. All of these domains should be documented in the medical record each time they are assessed.
- When off-label medications are prescribed†, providers should carefully document that they educated patients about risks, benefits, alternatives, the evidence for using the medications, and the fact that the medications have not been FDA-approved to treat the indication for which they are prescribing them. Providers should consider having patients sign treatment agreements detailing this information and the expectations for treatment before starting off-label medications.
- When primary care providers do not feel comfortable that diagnoses of SUDs and/or co-occurring psychiatric conditions are clear or well-established, or when individuals are failing to benefit from treatment, they should have a low threshold for consultation with a specialist, such as an Addiction Psychiatrist or Addiction Medicine provider.
- Assessments should include domains in addition to cessation of drug use/negative toxicology screens, including but not limited to: treatment engagement/retention, decreasing drug use, safer drug use (eg., decreasing or stopping injection, employing overdose prevention skills), mental health, physical health, and social and occupational functioning. Assessments should take a comprehensive and holistic view in determining whether treatment is providing benefit. Improvement or lack thereof should be documented in the medical record. Providers should be familiar with professional guidelines for appropriate use and interpretation of toxicology screening; including revised guidance from NYS OASAS (pending).

### Harm Reduction:

- Reducing the harm of cocaine or stimulant use should be incorporated into treatment goals and plans. These goals should be included in assessing treatment progress. (See “Assessment and Documentation” above.)
- In addition to overdose prevention education and naloxone provision (see “Overdose Prevention” above), providers can consider discussing community drug testing strategies with their patients, such as using fentanyl urine test strips. There is some preliminary evidence that use of fentanyl test strips is associated with safer drug use-related behavior. Some individuals with intentional opioid use could utilize fentanyl test strips to seek out fentanyl, so providers should employ this strategy with caution and in an individualized, person-centered manner. However, it is unlikely that individuals seeking to use only cocaine or stimulants would want fentanyl in their drugs, and could greatly benefit from testing their drugs for fentanyl and analogues. [Here](#) is a video depicting the use of fentanyl urine test strips. Individuals interested in testing methamphetamine (and some other drugs such as MDMA) should be aware that they should dilute drug residue in half a cup of water before testing, rather than testing the drug itself, to avoid false positives. Programs and providers should be aware that [no Federal funds](#) can currently be used to purchase drug testing supplies.

- Persons who inject drugs should be educated on safer injection practices and should be assisted in accessing sterile syringes. [Here](#) is more information on safer injection and syringe access from the NYS Department of Health.
- There are special harm reduction considerations for individuals who use cocaine and other stimulants\* beyond overdose prevention and safer injection drug use, such as strategies to avoid/reduce the psychiatric and physical consequences of over-use and encouraging safer sex practices when drug use is combined with sex. Providers should familiarize themselves with this information and share it with their patients. [Here](#) is an example of stimulant-specific resources from AIDS United.
- Individual or group-based harm reduction counseling should be considered an evidence-based psychosocial treatment approach and should be encouraged for individuals willing to consider participating in them.

### **Key Take-Home Points:**

- Overdose deaths related to use of cocaine and other stimulants\* have recently been rising. This increasing overdose mortality is driven largely – though not entirely – by co-use of opioids including fentanyl and analogs, either intentionally or unintentionally.
- All individuals who use cocaine or other stimulant drugs should be given overdose prevention education and offered naloxone, regardless of whether they also report opioid use.
- Individuals who use cocaine or other stimulant drugs should receive robust and evidence-based treatment for co-morbid substance use disorders, psychiatric conditions, and medical problems.
- While psychosocial treatment is currently the standard of care for cocaine-and-other-stimulant use disorders, some medications have evidence for efficacy, though no medications have received FDA approval to treat cocaine-and-other-stimulant use disorders.<sup>†</sup>
- When using medications for non-FDA-approved indications<sup>†</sup>, clinicians should provide and document careful patient education, should monitor patients closely for adverse effects (including addiction to and diversion of the medication) and clinical response, and should discontinue medications as soon as risks outweigh the benefits.
- Assessment of clinical response/benefit should include domains in addition to abstinence/negative toxicology, such as reduction in use, safer use, improvement in mental or physical health, and gains in functioning.
- Providers should incorporate harm reduction strategies into treatment plans, and should consider harm reduction to be an essential part of evidence-based treatment in people who use cocaine or other stimulants.

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