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To: Buprenorphine prescriber and pharmacy communities

The Maine Opioid Response Clinical Advisory Committee consists of approximately 30 leaders in substance use disorder prevention, treatment and harm reduction in Maine including both prescribers and pharmacists. As part of our efforts, we have been working on developing clinical protocols to assist other clinicians who care for patients with substance use disorders. One of the common challenges clinicians encounter is managing co-occurring stimulant use disorder in patients prescribed buprenorphine for opioid use disorder. In an effort to assist you as you care for patients prescribed buprenorphine, we have attached some proposed treatment recommendations. These recommendations are intended to enhance your care and should not replace your own clinical judgement. We recognize that, depending upon insurance type, some of the treatment options may not be readily available, particularly those in behavioral health, and there are ongoing discussions on this topic. If you have any questions, please do not hesitate to contact us.

Sincerely,
Maine Opioid Response Clinical Advisory Committee

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Maine Clinical Opioid Advisory Committee: Treatment of Co-Occurring Stimulant Use Disorder in Patients with Opioid Use Disorder (OUD)

Maine has recently seen a dramatic increase in overdose deaths involving illicit stimulants, typically combined with non-pharmaceutical opioids. Cocaine involved deaths increased from 90 to 110 from 2018 to 2019 (22%) and methamphetamine involved deaths from 26 to 47 (81%).[1] In clinical practice, we have noted a rise in the presence of stimulants cut into illicit fentanyl and vice versa so that, for people with active opioid use disorder (OUD) in Maine, unknown exposure to other illicit drugs is now common. Patients with stimulant use disorders may rapidly develop tolerance to the drug's effects, leading them to progress relatively quickly to higher and more frequent doses.[2] The effect of stimulants at higher and repeated doses include anxiety, agitation, aggression and even delusions and hallucinations. The withdrawal phase can cause dysphoria and suicidality. Use of stimulants can therefore require immediate emergency care and/or psychiatric hospitalization.[2] Though the sequelae of stimulant use are far reaching in terms of mental health, functional impact and injection related harms, the major cause of death in stimulant use disorder remains opioid-related overdose.[1,3]

When evaluating a patient for substance use disorder (SUD) treatment, determining whether a co-occurring stimulant use disorder is present (using DSM V) will aid in risk stratification and treatment planning. Clinicians should obtain information pertaining to the severity of use including frequency, duration, route and perceived consequences of use. Patients are often ambivalent about their stimulant use disorder due, perhaps in part, to the lack of available treatment options. After diagnosing stimulant use disorder, the clinician may consider potential treatment options specific to this condition which are discussed in more detail below. It is critical to make every effort to retain these patients in OUD treatment while treating their stimulant use disorder. The patient should be continued on medications for OUD if efficacy of OUD treatment persists, if the patient is making progress toward some treatment goals, and if continuing to prescribe buprenorphine does not present a safety risk to the patient or community (due to diversion). Treatment centers must determine how they can design care to balance provision of responsible treatment and financial viability with barriers to care for patients with this condition. This is an ongoing challenge. Clinicians can also consider referral to a higher level of SUD treatment but should make every effort to continue the patient's OUD treatment during this transition given the increased risk of overdose following the discontinuation of buprenorphine.[4] It is also important to address any underlying co-occurring mental health disorders that may be present. Posttraumatic stress disorder, depression, bipolar disorder, anxiety disorder, ADHD, learning disabilities, and personality disorders are all associated with an increased risk of stimulant use disorder.[2,5]

Pharmacotherapy: There are many studies exploring, yet few quality studies supporting, the use of pharmacotherapy for the treatment of stimulant use disorder. The quality of the data are generally low (i.e., limited by small power, attrition).[6-11] The use of pharmacotherapy for the treatment of stimulant use disorder remains off-label through the FDA. While some medications have been studied in the treatment of cocaine use disorder and others in methamphetamine use disorder, it is reasonable to try any of the medications below when treating stimulant use disorder.

- Recent reviews found low strength evidence that bupropion (300 mg daily) and topiramate (200 mg daily) were more effective than placebo in achieving abstinence for two or more weeks.[6-7] The use of long-acting bupropion is preferred to the short-acting formulation.
- Mirtazapine (30 mg nightly) has been associated with a reduction in methamphetamine use[9] and baclofen (20 mg TID) with a reduction in cocaine use.[10]
- Evidence supporting the efficacy of prescription stimulants in the treatment of stimulant use disorder is low quality and does not show a consistently positive effect.[6-7,11] The use of prescription stimulants to treat stimulant use disorder is not recommended based on current evidence as the risks often outweigh the benefits.
- Consideration and evidence regarding the role of prescription stimulants in treating ADHD in the setting of stimulant and other substance use disorders will be addressed in a future document.

Behavioral Interventions: Behavioral interventions including contingency management are presently the most effective evidence-based treatment for stimulant use disorders.[12] Strength of the evidence regarding the effectiveness of behavioral interventions on stimulant use disorders is moderate for contingency management (CM) and low to moderate for other behavioral interventions, though benefits likely outweigh risks. Clinicians can engage in shared decision making around patient preferences and goals.

- Contingency Management (CM) is a behavioral health treatment option that emphasizes operant conditioning and provides "rewards" to patients as a means to incentivize either engagement in treatment or negative drug screens.[13] CM provides competing reinforcement to the brain's reward system which has been impaired by ongoing drug use. As federal and state law have annual limits on patient incentives, it is critical to recognize CM as evidence-based treatment rather than financial incentives,[14] and it is being used successfully within the Veterans Administration.[15] The FDA has approved Reset-O, a phone-based CM digital platform. However, access is limited due to the burden of related fees.
- Cognitive Behavioral Therapy (CBT), drug-related counseling, and recovery-focused behavioral therapy may also be effective for the treatment of stimulant use disorder. The Matrix Model (manual available at SAMHSA.gov) is evidence-based though evaluation was limited to a relatively uniform population.[16] CBT4CBT is computer based training for CBT that may help patients stop or reduce stimulant and other drug use when used as part of a comprehensive treatment plan.
- Community Reinforcement Approach (CRA) is a more comprehensive intervention that often combines CM, CBT, other recovery-oriented counseling, and job training.
- For patients with co-occurring PTSD and stimulant disorder, behavioral interventions specially targeted to PTSD can be employed (i.e., Seeking Safety, exposure-based therapies) as they are associated with improvements in both conditions.[17]

Harm reduction interventions: Patients with stimulant use disorder are at higher risk of unsafe sex and drug use behavior.[2] Safer sex and injection practices, overdose response training, infectious disease screening and risk reduction are all evidence based and improve health outcomes.[8] These are recommended as a part of all care for

patients with SUD including stimulant use disorder. Naloxone should be provided to all patients with stimulant use disorder regardless of whether they have known co-occurring OUD.

Treatment Recommendations – Stimulant Use Disorder:

For patients with stimulant use disorder, we recommend:

- Contingency management or CRA as first line, if possible. If CM-based approaches are not available, we recommend CBT programs that have demonstrated efficacy for stimulant use disorder. General recovery-focused counseling enhancing the motivation for treatment engagement, crisis assessment and planning, and addressing related social determinant of health needs is a third option.
- Pharmacotherapy may be employed with or without behavioral therapy however this may not provide meaningful benefit based on evidence to date.
- Harm reduction interventions, appropriate for risk group, are always indicated.

References

1. Sorg, M. Maine drug death report for 2019. Margaret Chase Smith Policy Center, University of Maine.
2. United Nations Office on Drugs and Crime. Treatment of stimulant use disorders: Current practices and promising perspectives. 2019. https://www.unodc.org/documents/drug-prevention-and-treatment/Treatment_of_PSUD_for_website_24.05.19.pdf
3. Kariisa M, Scholl L, Wilson N, et al. Drug Overdose Deaths Involving Cocaine and Psychostimulants with Abuse Potential — United States, 2003–2017. MMWR Morb Mortal Wkly Rep 2019;68:388–395.
4. Williams AR, Samples H, Crystal S, Olfson M. Acute care, prescription opioid use, and overdose following the discontinuation of long-term buprenorphine treatment for opioid use disorder. Am J Psychiatry. 2020 Feb; 177(2): 117-124.
5. Saunders EC, Lambert-Harris C, McGovern MP, et al. The prevalence of posttraumatic stress disorder symptoms among addiction treatment patients with cocaine use disorders. J Psychoactive Drugs. 2015; 47(1): 42-50.
6. Chan B, Freeman M, Kondo K, et al. Pharmacotherapy for methamphetamine/amphetamine use disorder-a systematic review and meta-analysis. Addiction. 2019 Dec;114(12):2122-2136.
7. Chan B, Kondo K, Freeman M, et al. Pharmacotherapy for cocaine use disorder: A systematic review and meta-analysis. J Gen Intern Med. 2019 Dec;34(12):2858-2873.
8. Farrell M, Martin NK, Stockings E, et al. Responding to global stimulant use: challenges and opportunities. Lancet. 2019 Nov 2;394(10209):1652-1667.
9. Colfax GN, Santos GM, Das, M, et al. Mirtazapine to reduce methamphetamine use. Arch Gen Psychiatry. 2001; 68(11): 1168-1175.
10. Shoptaw S, Yang X, Rotheram-Fuller EJ, et al. Randomized placebo-controlled trial of baclofen for cocaine dependence: Preliminary effects for individuals with chronic patters of cocaine use. J Clin Psychiatry 2003; 64: 1440-1448.
11. Castells X, Cunill R, Perez-Mana C, Vidal X, Capella D. Psychostimulant drugs for cocaine dependence. Cochrane Database Syst Rev. 2016 Sept 27;9(9).
12. De Crescenzo F, Ciabattini M, D'Alò GL, et al. Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: A systematic review and network meta-analysis. PLoS Med. 2018 Dec; 15(12): e1002715.
13. Kellog, S et al., Foundations and principles of CM, 2008. http://www.bettertxoutcomes.org/bettertxoutcomes/PDF/Kellog-Stitzer.pdf.
14. Glass JE, Nunes EV, Bradley KA. Contingency management: A highly effective treatment for substance use disorders and the legal barriers that stand in its way. Health Affairs Blog 3/11/20 https://www.healthaffairs.org/do/10.1377/hblog20200305.965186/full/
15. Petry NM, DePhilippis D, Rash CJ, et al. Nationwide dissemination of contingency management: The veterans administration initiative. Am J Addict. 2014; 23(3): 205–210.
16. Rawson, R. Addiction Technology Transfer Center Network. Stimulant Use Disorder Webinar Series, Part 1 Strategies to Address Cocaine and Methamphetamine, June 2019. Northwest ATTC Webinar Series | Addiction Technology Transfer Center (ATTC) Network
17. Hien D, Kropp F, Wells EA, et.al. The women and trauma study and its national impact on advancing trauma-specific approaches in community substance abuse treatment and research. J Subst Abuse Treat. 2020; March 1125:12-17.