**The ASAM/AAAP Clinical Practice Guideline**

**on the Management of Stimulant Use Disorder**

**Appendices**

**Appendix A: Glossary of Terms**

# Appendix B. Abbreviations and Acronyms

# ****Appendix C. Differential Diagnosis for Agitation and Psychosis****

# Appendix D. Disclosures of Interest

# Appendix E. Clinical Questions

# Appendix F. Topics with Insufficient or Negative Evidence

# Appendix G. Additional Resources

# Appendix H. ****Substance Use Disorder Biopsychosocial Assessment****

# Appendix I. ****Baseline Laboratory Testing****

# Appendix J. Principles of Drug Testing During Withdrawal Management

# Appendix K. Medication Dosing in Clinical Trials

# Appendix L. Acute Issues and Complications of Stimulant Intoxication and Withdrawal

# Appendix M. ****Non-acute Issues and Complications**** of Stimulant Use

# Appendix N. Medications for Managing Intoxication

# Appendix A. Glossary of Terms

**addiction:** A treatable chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual’s life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences. Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

**addiction medicine:** A medical subspecialty concerned with the prevention, evaluation, diagnosis, treatment, and recovery of people with the disease of addiction and substance-related health conditions, as well as people who use substances—including nicotine, alcohol, prescription medications, and other licit and illicit drugs—in an unhealthy manner (see **addiction**, **substance use disorder**). Addiction medicine is recognized as a distinct medical subspecialty within preventive medicine by the American Board of Medical Specialties (ABMS; see **addiction specialist physician**).

**addiction medication:** Medications that are specifically indicated for and prescribed to treat substance use disorders (SUDs) as an initial lifesaving measure, motivational engagement strategy (i.e., withdrawal management), and as part of a long-term treatment plan similar to medications used to treat other chronic diseases such as bipolar disorder or diabetes (see **substance use disorder**).

**addiction psychiatry:** A psychiatric subspecialty concerned with the evaluation and treatment of individuals with alcohol, drug, or other substance-related disorders and of individuals with co-occurring substance-related and other psychiatric disorders (see **addiction**, **substance use disorder**). Addiction psychiatry is recognized as a distinct medical subspecialty within psychiatry by the American Board of Medical Specialties (ABMS; see **addiction specialist physician**).327

**addiction specialist physician:** A licensed physician who has specialty board certification in addiction medicine or addiction psychiatry (see **addiction medicine**, **addiction psychiatry**).

**adolescent:** A person who is 12 to 17 years of age.

**cultural humility:** A process of entering a relationship with another person with the intention of honoring their beliefs, customs, and values. It entails an ongoing self-exploration and self-critique combined with a willingness to learn from others.328 One component of trauma-sensitive practices (TSP; see **trauma-sensitive practices**).

**drug testing:** The process of analyzing a biological specimen to check for the presence of chemicals that indicate exposure to selected substances.

**patient:** An individual receiving substance use disorder treatment. Interchangeable with client, which is used more commonly in nonmedical settings.

**psychosocial services** (as treatment)**:** Interventions that seek to enhance a patient’s social and mental functioning, including psychotherapy, counseling, contingency management (CM), psychoeducation, and mental health services.329

**recovery:** A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential.330

**recovery support services (RSS):** The collection of services that provide emotional and practical support for continuing recovery, as well as daily structure and rewarding alternatives to substance use (see **recovery**).331

**recurrence:** A return of substance use disorder (SUD) symptoms, including substance use, after a period of remission from SUD (see **recovery**, **substance use disorder**).329

**social determinants of health (SDOH):** The conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks.332

**substance use disorder (SUD):** A medical illness consisting of a cluster of cognitive, behavioral, and physiological symptoms caused by repeated misuse of a substance or substances. Characterized by clinically significant impairments in health, social function, and impaired control over substance use (see **addiction**).331

**substance-induced disorders:** Illnesses or conditions that are directly caused by substance use. Distinct from independently co‑occurring mental disorders in that all or most of the psychiatric signs and symptoms are the direct result of substance use (see **substance use disorder**).18

**telehealth:** The use of electronic information and telecommunications technologies to support delivery of health care, health-related education, and other health-related services and functions, including but not limited to electronic health records, mobile applications, telemedicine, and web-based tools (see **telemedicine**).333

**telemedicine:** Services that utilize telecommunication platforms to perform direct (i.e., synchronous) patient services when healthcare providers are located at a distance from patients (see **telehealth**).

**toxicology testing:** Also called toxicology screening, this term refers to the process of testing for the presence of toxins or poisons (see **drug testing**).

**trauma-informed care (TIC):** The process of engaging in trauma-based educational training, including gathering information on the various types of traumas, the physiological and emotional impact of surviving trauma, and healing modalities to prevent disruptive aftereffects.

**trauma-responsive care (TRC):** An ongoing process that furthers trauma-based education through information embodiment by asking treatment providers to understand and comprehend information through self-exploration, self-awareness, and reflective practices to develop a concrete understanding of their own emotional literacy and how this impacts the care that they provide. One component of trauma-sensitive practices (TSP; see **trauma-sensitive practices**).

**trauma-sensitive practices (TSP):** A system of care that facilitates opportunities that advance clinician knowledge, expand clinician attitudes, and offer therapeutic practices designed around each patient’s unique culture, life experiences, and present circumstances. Comprised of trauma-informed care (TIC), trauma-specific care (TSC), trauma-responsive care (TRC), and cultural humility (see **cultural humility**, **trauma-informed care**, **trauma-responsive care**, **trauma-specific care**)

**trauma-specific care (TSC):** An ongoing process where treatment providers engage with trauma knowledge and information to impact, refine, and improve the ways in which healthcare services are provided to support better patient outcomes. One component of trauma-sensitive practices (TSP; see **trauma-sensitive practices**).

**warm handoff:** A care transition in which the referring clinician facilitates a direct (i.e., face-to-face) introduction of the patient to the receiving clinician at their next level of care.

**young adult:** A person who is 18 to 25 years of age.

# Appendix B. Abbreviations and Acronyms

AAAP American Academy of Addiction Psychiatry

AACAP American Academy of Child and Adolescent Psychiatry

AAFP American Association of Family Physicians

AAP American Academy of Pediatrics

ABMS American Board of Medical Specialties

ACE adverse childhood event

ACEP American College of Emergency Physicians

ACLS advanced cardiac life support

A‑CRA adolescent community reinforcement approach

ACS acute coronary syndrome

ADHD attention-deficit/hyperactivity disorder

AMA American Medical Association

APA American Psychiatric Association

ASAM American Society of Addiction Medicine

ATS amphetamine-type stimulant

ATTC Addiction Technology Transfer Center Network

AUD alcohol use disorder

BCR blood urea nitrogen/creatinine ratio

BMI body mass index

BUN blood urea nitrogen

BZD benzodiazepine

CBC complete blood count

CBT cognitive behavioral therapy

CBT4CBT Computer Based Training for Cognitive Behavioral Therapy

CDC US Centers for Disease Control and Prevention

CDC WONDER US Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiological Research

CFR US Code of Federal Regulations

CGC Clinical Guideline Committee

CK creatine kinase

CLIA Clinical Laboratory Improvement Amendments of 1988

CM contingency management

CMP comprehensive metabolic panel

CMS Centers for Medicare & Medicaid Services

COVID‑19 coronavirus disease 2019

CPG clinical practice guideline

CPK creatine phosphokinase

CRA community reinforcement approach

CSSA Cocaine Selective Severity Assessment

C‑SSRS Columbia–Suicide Severity Rating Scale

CT computed tomography

d‑AMP dextroamphetamine

DEA US Drug Enforcement Administration

*DSM* *Diagnostic and Statistical Manual of Mental Disorders*

*DSM‑5‑TR* *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, Text Revision

EBI evidence-based intervention

ECG electrocardiogram

ED emergency department

EEG electroencephalogram

EtD Evidence to Decision

FAVOR Faces & Voices of Recovery

FDA US Food and Drug Administration

FTIR Fourier-transform infrared spectroscopy

GABA gamma-aminobutyric acid

GABA‑A gamma-aminobutyric acid A

GRADE Grading of Recommendations Assessment, Development, and Evaluation

HAV hepatitis A virus

HBV hepatitis B virus

HCV hepatitis C virus

HIV human immunodeficiency virus

HUD US Department of Housing and Urban Development

*ICD‑10 International Classification of Diseases*, 10th Revision

IM intramuscular

IPV intimate partner violence

IRETA Institute for Research, Education and Training in Addictions

IV intravenous

LDX lisdexamfetamine

LFT liver function test

MAS‑ER extended-release mixed amphetamine salts

MATCH Matching Alcoholism Treatments to Client Heterogeneity

MDD major depressive disorder

MDMA 3,4-methylenedioxymethamphetamine

MET motivational enhancement therapy

MI motivational interviewing

MI myocardial infarction

MPH methylphenidate

MSK musculoskeletal

MSM men who have sex with men

NAM National Academy of Medicine

NIDA National Institute on Drug Abuse

NMDA N-methyl-D-aspartate

NMS neuroleptic malignant syndrome

NSDUH National Survey on Drug Use and Health

OCCS Obsessive Compulsive Cocaine Scale

OIG Office of the Inspector General

OROS osmotic-controlled release oral delivery system

OTC over the counter

OUD opioid use disorder

PBO phenobarbital

PDMP prescription drug monitoring program

PEP postexposure prophylaxis

PrEP preexposure prophylaxis

Project BETA Best Practices in the Evaluation and Treatment of Agitation

PSS Poisoning Severity Score

PTSD post-traumatic stress disorder

QIC ASAM’s Quality Improvement Council

RCT randomized controlled trial

RoB 2 revised Cochrane Risk of Bias tool

ROBINS‑I Cochrane Risk of Bias in Non-randomized Studies – of Interventions tool

RSS recovery support services

SAMHSA Substance Abuse and Mental Health Services Administration

SBIRT screening, brief intervention, and referral to treatment

SCS supervised consumption sites

SDOH social determinants of health

SGM sexual and gender minorities

SSP syringe service program

SSSA Stimulant Selective Severity Assessment

STI sexually transmitted infection

StUD stimulant use disorder

SUD substance use disorder

TB tuberculosis

TBI traumatic brain injury

TES Therapeutic Education System

TIP Treatment Improvement Protocol

TUD tobacco use disorder

UNODC United Nations Office on Drugs and Crime

USC Code of Laws of the United States of America

USPSTF US Preventive Services Task Force

VA US Department of Veterans Affairs

WHO World Health Organization

WIC Special Supplemental Nutrition Program for Women, Infants, and Children

YPR Young People in Recovery

# ****Appendix C. Differential Diagnosis for Agitation and Psychosis****

The differential diagnosis for agitation and psychosis is very broad. Comprehensive discussion of this topic is addressed well elsewhere. The following highlights common conditions to consider in the differential diagnosis of agitation or psychosis in patients with stimulant intoxication and is not meant to be an exhaustive list. ACEP’s Project BETA provides a helpful and comprehensive resource.

Indications to perform head CT include:

* altered mental status;
* neurologic symptoms;
* signs of physical trauma (e.g., TBI);
* found unconscious or comatose, which can be the result of trauma or stroke, including stimulant-induced stroke; and
* anoxic injury.

Indications to perform lumbar puncture and blood tests for encephalitis include:

* unexplained fever, and
* meningeal signs and symptoms (e.g., stiff neck, photophobia, back pain).

Indications for EEG include:

* seizure not well explained,
* neurologic signs and symptoms not well explained, and
* persistent encephalopathy.

Additional causes of agitation and psychosis include (but are not limited to):

* nutritional deficiencies (e.g., Wernicke encephalopathy),
* neurologic disorders (e.g., Parkinson’s disease, dementia),
* brain tumors,
* infections,
* endocrine dysfunction,
* thyroid toxicity (e.g., thyrotoxicosis),
* hormonal abnormalities (e.g., steroid-induced psychosis),
* autoimmune diseases,
* N‑methyl‑D‑aspartate (NMDA) receptor encephalitis, and
* medication reactions that cause neuropsychiatric symptoms.

# Appendix D. Disclosures of Interest

## Clinical Guideline Committee Members

| **Clinical Guideline Committee Member** | **Employment** | **Consulting** | **Research** | **Investments and Proprietary Interests** | **Healthcare-Related Organizations** | **Advocacy/ Lobbying** |
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| Timothy J. Wiegand, MD, FACMT, FAACT, DFASAM | University of Rochester Medical Center (Director, Program Director) | None | None | None | None | None |

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## ASAM Quality Improvement Council Members

| **Quality Improvement Council Member** | **Salary** | **Consulting** | **Research** | **Investments and Proprietary Interests** | **Healthcare-Related Organizations** | **Advocacy/ Lobbying** |
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| R. Jeffrey Goldsmith, MD, DLFAPA, DFASAM | None | None | None | Merck and Co (Stockholder)\*; Pfizer Inc (Stockholder)\*; Amgen Inc (Stockholder)\*; Gilead Sciences Inc (Stockholder)\* | None | None |
| Margaret A. E. Jarvis, MD, DFASAM | Geisinger (Chief, Addiction Medicine Division) | Expert Witness\*\* | None | None | American Board of Preventive Medicine (Exam Committee Member) | None |
| Navdeep Kang, PsyD, HSP | Acadia Healthcare (Chief Quality Officer) | Everest Health (Advisor) | None | Brightview Health/Shore Capital Partners (Equity Shareholder)\*\* | Talbert House (Board Member) | None |
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| **ASAM Board Member** | **Salary** | **Consulting** | **Research** | **Investments and Proprietary Interests** | **Healthcare-Related Organizations** | **Advocacy/ Lobbying** |
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| Shawn Ryan, MD, MBA, FASAM | BrightView Health (Owner) | Dynamicare (Advisor) | None | Dynamicare (Shareholder) | None | None |
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| Emily Brunner, MD, DFASAM | Hazelden Betty Ford Foundation, Gateway Recovery Center | None | None | None | None | None |
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## AAAP Executive Committee

| **AAAP Executive Committee** | **Salary** | **Consulting** | **Research** | **Investments and Proprietary Interests** | **Healthcare-Related Organizations** | **Advocacy/** **Lobbying** |
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| Kevin Gray, MD | Medical University of South Carolina (Professor and Director of Addiction Sciences) | Jazz Pharmaceuticals (Consulting) | Aelis Farma | None | None | None |
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| John Mariani, MD | Columbia University, New York State Psychiatric Institute (Directors of STARS) | None | None | None | None | None |
| Larissa Mooney, MD | University of California Los Angeles (Professor of Clinical Psychiatry) | Expert Witness | Aelis Farma | None | American Academy of Addiction Psychiatry (President) | None |
| Rebecca Payne, MD | University of South Carolina (Assistant professor of Neuropsychiatry and Behavioral Science) | None | None | None | None | None |
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# Appendix E. Clinical Questions

This appendix presents the clinical questions posed for each topic as outlined in the supplementary EtD document. If a clinical question resulted in a recommendation based only on clinical consensus, there is no corresponding table in the EtD document.

## Treatment of Stimulant Use Disorder

Assessment

1. Initial assessment:
   1. What components should be included in the initial assessment for patients presenting with StUD?
2. Comprehensive assessment:
   1. What components should be included in the comprehensive assessment for patients with StUD?
3. Baseline laboratory testing:
   1. Should baseline laboratory testing be conducted for all patients with StUD or based on clinical assessment of risk factors?
   2. What is the effect of conducting baseline laboratory testing when assessing patients with StUD?
   3. What contextual factors and implementation strategies may influence the effects of baseline laboratory testing?
   4. What are the most impactful and appropriate baseline laboratory tests to conduct when assessing patients who misuse use stimulants?
4. Cardiac evaluation:
   1. Should clinicians routinely request or refer patients for a cardiac evaluation or ECG?
      1. Patients with stimulant intoxication or withdrawal
      2. Patients with StUD
   2. What is the effect of routine screening for cardiac disorders in patients with StUD?
   3. What contextual factors and implementation strategies may influence the effects of screening for cardiac disorders?
   4. Is there a subpopulation that would particularly benefit from routine ECG?
5. Renal evaluation:
   1. For patients diagnosed with stimulant intoxication or withdrawal, should clinicians routinely request or refer patients for an evaluation of renal function?
   2. For patients diagnosed with StUD, should clinicians routinely request or refer patients for an evaluation of renal function?
   3. Is there a subpopulation who would benefit from an evaluation of renal function?

Behavioral Treatment

1. Contingency Management (Table 1):
   1. Is CM an effective and appropriate treatment for StUD?
   2. Does the addition of another treatment to CM improve outcomes for StUD?
   3. What contextual factors and implementation strategies may influence the effects of CM?
2. Community Reinforcement Approach (Table 2):
   1. Is CRA (with or without background treatment) an effective and appropriate treatment for StUD?
   2. Is CRA more effective than other behavioral treatments for StUD?
   3. Does adding CM to CRA improve outcomes for StUD?
   4. What additional considerations and implementation strategies may influence the effects of CRA?
3. Cognitive Behavioral Therapy (Table 3):
   1. Is CBT (with or without background treatment) effective at reducing stimulant use and increasing treatment retention in patients in treatment for StUD?
   2. Is CBT more effective than other behavioral treatments for StUD?
   3. Does adding CM to CBT improve outcomes for StUD?
   4. What additional considerations and implementation strategies may influence the effects of CBT?
4. Matrix Model (Table 4):
   1. Is the Matrix Model an effective and appropriate treatment for StUD?
   2. Is the Matrix Model more effective than other behavioral treatments for StUD?
   3. Does adding CM to the Matrix Model improve outcomes for StUD?
   4. What additional considerations and implementation strategies may influence the effects of the Matrix Model?

Technology-Based Interventions

1. Computer-Delivered Treatment (Table 5):
   1. What is the effect of computer-delivered treatment for StUD?
   2. What contextual factors and implementation strategies may influence the effects of computer-delivered treatment?
2. Telehealth (Table 6):
   1. What is the effect of telehealth-delivered treatment for StUD?
   2. What contextual factors and implementation strategies may influence the effects of telehealth-delivered treatment?

Pharmacotherapy

1. Bupropion for Cocaine Use Disorder (Table 7):
   1. Is bupropion safe and effective at reducing stimulant use and increasing treatment retention in patients with cocaine use disorder?
2. Topiramate for Cocaine Use Disorder (Table 8):
   1. Is topiramate safe and effective at reducing stimulant use and increasing treatment retention in patients with cocaine use disorder?
3. Bupropion for Amphetamine-Type Stimulant Use Disorder (Table 9):
   1. Is bupropion safe and effective at reducing stimulant use and increasing treatment retention in patients with ATS use disorder?
4. Bupropion + Naltrexone for Amphetamine-Type Stimulant Use Disorder (Table 10):
   1. Is the combination pharmacotherapy of bupropion and naltrexone safe and effective at reducing stimulant use and increasing treatment retention in patients with ATS use disorder?
   2. What contextual factors and implementation strategies may influence the effects of bupropion + naltrexone?
5. Topiramate for Amphetamine-Type Stimulant Use Disorder (Table 11):
   1. Is topiramate safe and effective at reducing stimulant use and increasing treatment retention in patients with ATS use disorder?
6. Mirtazapine for Amphetamine-Type Stimulant Use Disorder (Table 12):
   1. Is mirtazapine a safe and effective treatment for ATS use disorder?
7. Modafinil for Cocaine Use Disorder (Table 13):
   1. Is modafinil a safe and effective treatment for patients with cocaine use disorder?
8. Topiramate + Extended-Release Mixed Amphetamine Salts for Cocaine Use Disorder (Table 14):
   1. Is the combination pharmacotherapy of topiramate and MAS‑ER safe and effective treatment for patients with cocaine use disorder?
   2. What contextual factors and implementation strategies may influence the effects of topiramate + MAS-ER?
9. Psychostimulant Amphetamines for Cocaine Use Disorder (Table 15):
   1. Are long-acting amphetamine formulations of prescription psychostimulants safe and effective at reducing stimulant use and increasing treatment retention in patients with cocaine use disorder?
10. Psychostimulant Methylphenidate for Amphetamine-Type Stimulant Use Disorder (Table 16):
    1. Are long-acting MPH formulations or prescription psychostimulants safe and effective at reducing stimulant use and increasing treatment retention in patients with ATS use disorder?

Co-occurring Disorders

1. Integrated Care (Table 17):
   1. What are the most effective and appropriate behavioral interventions for the treatment of StUD in patients with co‑occurring psychiatric disorders?
   2. What contextual factors and implementation strategies may influence the effects of behavioral interventions?
2. Psychosis (Table 18):
   1. Should clinicians use pharmacotherapy to treat psychosis or mania if it is unclear whether the condition is preexisting or stimulant-induced?
   2. What contextual factors and implementation strategies may influence the decision to use pharmacotherapy?
   3. What are the most effective and appropriate interventions for treating psychosis in patients with StUD?
3. Psychosis taper (Table 19):
   1. What is the optimal duration of antipsychotic treatment for persons who are presumed to be experiencing stimulant-induced psychosis or mania?
   2. What is the clinical effectiveness of different antipsychotic tapering strategies?
4. Other Symptoms (Table 20):
   1. Should clinicians use pharmacotherapy to treat depression, anxiety, insomnia, and/or attentional problems in patients with StUD if it is unclear whether the condition is preexisting or stimulant-induced?
   2. What contextual factors and implementation strategies may influence the decision to use pharmacotherapy?
   3. What are the most effective and appropriate pharmacotherapies for treating depression, anxiety, insomnia, and/or attentional problems in patients with StUD?
5. Preexisting diagnosis:
   1. Should patients change or discontinue treatment for a co‑occurring disorder when initiating treatment for StUD?
   2. What contextual factors and implementation strategies may influence the decision to modify the existing treatment plan?
6. Attention-Deficit/Hyperactivity Disorder (Table 21):
   1. What are the most effective and appropriate interventions to treat ADHD in patients with StUD?
   2. Are stimulant medications safe and effective to treat ADHD in patients with StUD?
   3. What contextual factors and implementation strategies may influence the safety and effectiveness of ADHD treatment?
7. Prevention of prescription stimulant misuse:
   1. When prescribing stimulant medications to a patient with co‑occurring StUD and ADHD, what implementation strategies may influence the effect and appropriateness of treatment?
8. Prevention of prescription stimulant misuse in adolescents and young adults:
   1. When prescribing stimulant medications to an adolescent or young adult patient with co‑occurring StUD and ADHD, what implementation strategies may influence the effect and appropriateness of treatment?

Adolescents and Young Adults

1. Toxicology:
   1. What is the most effective and appropriate use of toxicology testing for the treatment of StUD, stimulant intoxication, and stimulant withdrawal in adolescent and young adult patients?
   2. What contextual factors and implementation strategies may influence the effects of toxicology testing?
2. Screening – other:
   1. What is the effect of screening for other co‑occurring conditions when assessing adolescent and young adult patients for StUD?
      1. StUD outcomes
      2. Other outcomes
   2. What contextual factors and implementation strategies may influence the effects of screening for other co‑occurring conditions?
3. Specific support:
   1. Should adolescent patients be referred to adolescent-specific support services or are adult services effective and appropriate?
   2. Do young adult-specific social supports services exist?
   3. What contextual factors and implementation strategies may influence the effectiveness of a support service referral?
4. Contingency Management (Table 22):
   1. Is CM for patients with StUD as effective and appropriate for adolescents and young adults as it is for adults?
   2. What contextual factors and implementation strategies may influence the effects of CM for adolescents and young adults?
   3. What modifications should be made so that CM is delivered in a developmentally appropriate manner?
5. Other Psychotherapy (Table 23):
   1. What are the most effective and appropriate psychotherapy interventions for the treatment of StUD in adolescent and young adult patients?
   2. What contextual factors and implementation strategies may influence the effects of psychotherapy interventions?
6. Family Therapy (Table 24):
   1. Is family therapy effective in treating adolescents and young adults with StUD?
   2. What contextual factors and implementation strategies may influence the effects of family therapy?
7. Specific Treatment (Table 25):
   1. Are adolescent-specific behavioral treatment models (e.g., A-CRA) effective and appropriate treatment for StUD in adolescents and young adults?
   2. Should adolescents be referred to adolescent-specific behavioral treatment models (e.g., A-CRA) or are adult treatment models effective and appropriate?
   3. What modifications should be made so that behavioral treatment is delivered in a developmentally appropriate manner?
8. Group Treatment (Table 26):
   1. Are there modifications that should be made to behavioral treatment so that it is delivered in a developmentally appropriate manner to adolescent and young adult patients?
   2. Should adolescents and young adults who use stimulants be referred to adolescent- and young adult-specific group-based treatment or is adult group-based treatment as effective and appropriate?
9. Pharmacotherapy (Table 27):
   1. What are the most effective and appropriate pharmacotherapies for the treatment of StUD in adolescent and young adult patients?
   2. What contextual factors and implementation strategies may influence the effects of pharmacotherapy?
10. Home drug testing:
    1. What are the potential benefits and harms of home drug testing?
11. Family involvement:
    1. Are there modifications that should be made to behavioral treatment so that it is delivered in a developmentally appropriate manner to adolescent and young adult patients?
    2. Is family involvement in the treatment of StUD in adolescent and young adult patients effective and appropriate?
12. Minor consent:
    1. What considerations should be included regarding consent for treatment for minor patients?

Pregnant and Postpartum Patients

1. Prenatal Care Referral (Table 28):
   1. What additional considerations should clinicians have when evaluating StUD in persons who are pregnant?
   2. What additional considerations should be included when establishing a treatment plan for StUD in persons who are pregnant?
2. Screen Social Services – Pregnancy and Postpartum (Table 29):
   1. Are there additional social service needs that should be addressed when assessing persons who are pregnant or is the standard assessment for StUD appropriate and effective?
3. Screen Factors Pregnancy (Table 30):
   1. Are there additional health conditions that should be evaluated in persons who are pregnant or is the standard assessment for StUD appropriate and effective?
4. Toxicology – pregnancy and postpartum:
   1. Are there additional considerations when conducting toxicology testing in persons who are pregnant or are standard considerations for StUD appropriate and effective?
5. Pharmacotherapy – Pregnancy and Postpartum (Table 31):
   1. What additional considerations should be included when considering pharmacotherapy for StUD, stimulant intoxication, or stimulant withdrawal in persons who are pregnant or breastfeeding?
6. Psychosocial additions – pregnancy and postpartum:
   1. Are there additional treatment needs that should be addressed with pregnant patients or is standard treatment for StUD appropriate and effective?
7. Prenatal Care Incentives (Table 32):
   1. What are the most effective and appropriate interventions for increasing prenatal care access and attendance in patients being treated for StUD?
8. Postpartum Care (Table 33):
   1. Are there additional treatment needs for patients with StUD in the postpartum period? For patients with any level of stimulant use?
9. Breastfeeding (Table 34):
   1. Should patients with StUD breastfeed?
   2. When can a patient who uses stimulants safely breastfeed?
   3. Can clinicians increase the rate of safe breastfeeding in patients with a StUD? With any stimulant use?

Additional Population-Specific Considerations

1. Sexual and Gender Minoritized individuals (Table 35):
   1. What are the most effective and appropriate interventions for the treatment of StUD in SGM patients?
   2. Should SGM patients with StUD be referred to SGM-focused programs?
   3. What additional consideration should clinicians have when evaluating and treating StUD in SGM patients?
2. Disability:
   1. What are the most effective and appropriate interventions for the treatment of StUD in patients with disabilities?
   2. What additional considerations should clinicians have when evaluating and treating StUD in persons with disabilities?
3. Criminal/legal system:
   1. What are the most effective and appropriate interventions for the treatment of StUD in patients with criminal/legal system involvement?
   2. What additional considerations should clinicians have when evaluating and treating StUD in patients with criminal/legal system involvement?
4. Homelessness/unstable housing:
   1. What are the most effective and appropriate interventions for the treatment of StUD in patients with unstable housing or who are experiencing homelessness?
   2. Should patients with unstable housing or who are experiencing homelessness be referred specialized StUD programs or is general StUD treatment effective and appropriate?
   3. What additional considerations should clinicians have when evaluating and treating StUD in persons with unstable housing or who are experiencing homelessness?

## Stimulant Intoxication and Withdrawal

Assessment and Diagnosis

1. Initial assessment – intoxication and withdrawal:
   1. For patients with suspected stimulant intoxication or withdrawal, should an initial assessment for acute issues and complications related to stimulant intoxication and withdrawal be part of routine assessment or only as needed?
   2. What is the appropriate medical workup when evaluating a patient with suspected stimulant intoxication or withdrawal?
2. Comprehensive assessment – intoxication and withdrawal:
   1. For patients with a diagnosis of stimulant intoxication or withdrawal, should comprehensive assessment for acute issues and complications related to stimulant intoxication and withdrawal be part of routine assessment or only as needed?
   2. What is the appropriate medical workup when evaluating a patient with stimulant intoxication or withdrawal?
   3. Should laboratory testing be ordered (or a referral for testing be provided) routinely or as needed according to clinical judgment and based on symptomatology and presence of risk factors?
3. Baseline laboratory testing – intoxication and withdrawal:
   1. Should laboratory testing be ordered (or a referral for testing be provided) for all patients with stimulant intoxication or withdrawal or based on clinical assessment of risk factors?
   2. What is the effect of conducting baseline laboratory testing when assessing patients?
   3. What contextual factors and implementation strategies may influence the effects of baseline laboratory testing?
   4. What are the most appropriate baseline laboratory tests to conduct when assessing patients who use stimulants?
4. Intoxication toxicology:
   1. For patients with suspected stimulant intoxication or withdrawal, should toxicology testing for stimulants be a routine part of diagnostics?
      1. Does this depend on the setting?
   2. If toxicology testing is done as needed, what are the indications?
5. Intoxication setting:
   1. In what setting should patients with stimulant intoxication and withdrawal be managed?
   2. Can suspected stimulant intoxication be managed safely in lower acuity clinical settings?
   3. Which patients with stimulant intoxication be managed safely in lower acuity clinical settings?

Managing Stimulant Intoxication and Withdrawal

1. Agitation–psychosis differential diagnosis:
2. What are indications of different or additional causes of agitation and psychosis?
3. Agitation–psychosis de-escalation:
4. What is the effectiveness of de-escalation techniques for managing stimulant-induced aggression, agitation, or toxic psychosis?
5. Agitation Medication (Table 36):
   1. What are the most effective and appropriate interventions for the treatment of agitation in patients experiencing stimulant intoxication?
   2. What contextual factors and implementation strategies may influence the effects of the intervention for agitation?
6. Psychosis Medication (Table 37):
   1. What are the most effective and appropriate interventions for the treatment of psychosis in patients experiencing stimulant intoxication?
   2. Should clinicians treat stimulant-induced psychotic symptoms with antipsychotics?
7. Agitation–psychosis evaluation:
   1. What are the indications for an immediate need for acute care management in a hospital or ED?
8. Agitation–psychosis transfer:
   1. What factors should be considered when determining whether to transfer a patient presenting with agitation or psychosis to a more intensive level of care?
9. Psychiatric monitoring:
   1. What are the most effective and appropriate strategies to monitor psychiatric symptoms when treating patients experiencing stimulant intoxication or withdrawal?
   2. For patients diagnosed with stimulant intoxication or withdrawal, should clinicians routinely assess fortrauma-related problems or only as needed?
   3. What should the frequency of reassessment be during monitoring?
10. Hyperadrenergic monitoring: No clinical questions in the EtD document.
    1. What are the most effective and appropriate strategies to monitor hyperadrenergic signs and symptoms when treating patients experiencing stimulant intoxication or withdrawal?
    2. What should the frequency of reassessment be during monitoring?
11. Hyperadrenergic Medications (Table 38):
    1. What are the most effective and appropriate interventions for the treatment of hyperadrenergic symptoms that typically accompany stimulant intoxication?
12. Hyperadrenergic Adjunct (Table 39):
    1. What adjunctive treatments can be considered for managing hyperadrenergic symptoms that typically accompany stimulant intoxication?
13. Hypertensive Emergency (Table 40):
    1. What are effective interventions for hypertensive emergencies accompanying stimulant intoxication?
14. Chest Pain Medication (Table 41):
    1. What are the most effective and appropriate interventions for the treatment of chest pain in patients experiencing stimulant intoxication?
15. Chest Pain Beta Blockers (Table 42):
    1. What is the effectiveness of beta blockers for managing the cardiac consequences of stimulant intoxication?
    2. Can beta blockers be used safely to treat chest pain in patients experiencing stimulant intoxication?
16. Chest Pain Evaluation (Table 43):
    1. Should the presence of stimulant intoxication impact the standard evaluation of chest pain?
17. QRS Widening (Table 44):
    1. What are the most effective and appropriate interventions for the treatment of QRS widening following cocaine use?
18. Seizure workup:
    1. Should a full neurological workup be ordered for all patients presenting to the ED with a seizure following stimulant use?
19. Seizure Medication (Table 45):
    1. What are the most effective and appropriate interventions for the treatment of seizure following stimulant use?
20. Screening, Brief Intervention, and Referral to Treatment (SBIRT; Table 46):
    1. How accurate are drug use screening instruments for risky stimulant use?
    2. Does screening for stimulant use reduce stimulant use or improve other risky behaviors?
    3. What are the harms of screening for risky stimulant use?
    4. Do brief counseling interventions to reduce stimulant use, with or without referral, reduce stimulant use or improve other risky behaviors in patients with a positive screen?
    5. What are the harms of brief interventions to reduce stimulant use in patients with a positive screen?

## Secondary and Tertiary Prevention

Screening

1. Screening for Stimulants (Table 47):

1. How accurate are drug use screening instruments for risky stimulant use?
2. Does screening for stimulant use reduce stimulant use or improve other risky behaviors?
3. What are the harms of screening for risky stimulant use?
4. Screening for Prescription Psychostimulants (Table 48):
5. What additional considerations should be applied when screening for prescription psychostimulant misuse?
6. Check Prescription Drug Monitoring Program (Table 49):
   1. What are the benefits and harms of checking PDMPs for patients with StUD?

Assessment

1. Assessing Route Complications – Prevention (Table 50):
   1. What are effective strategies for assessing route of administration and related history of complications?
2. Assessing Risky Patterns – Prevention (Table 51):
   1. What are effective strategies for assessing risky patterns of stimulant use?
3. Assessing Risky Sex – Prevention (Table 52):
   1. What are effective strategies for assessing risky sexual behaviors in patients with SUD/StUD?
4. Assessing context of stimulant use – prevention:
5. What are effective strategies for assessing the context of a patient’s stimulant use?
6. Assessing trauma – prevention:
7. What are effective strategies for assessing trauma in patients with SUD/StUD?
8. Assessing baseline laboratory testing – prevention:
9. What are the most effective and appropriate baseline laboratory tests to conduct when assessing patients who misuse or use stimulants?
10. What is the effect of conducting baseline laboratory testing when assessing patients who misuse stimulants?
    * 1. For StUD outcomes
      2. For other outcomes
11. Should baseline laboratory testing be conducted for all patients who misuse or use stimulants or based on clinical assessment of risk factors?
12. What contextual factors and implementation strategies may influence the effects of baseline laboratory testing?
13. Assessing ADHD – prevention:
14. Should all patients who misuse or use stimulants be assessed for ADHD?
15. What factors should be considered when determining which patients to assess for ADHD?

Early Intervention for Risky Stimulant Use

1. Early Intervention – Screening and Brief Intervention (Table 53):
   1. Do brief counseling interventions to reduce stimulant use, with or without referral, reduce stimulant use or improve other risky behaviors in patients with a positive screen?
   2. What are the harms of brief interventions to reduce stimulant use in patients with a positive screen?
2. Early Intervention Refer to Treatment (Table 54):
   1. Does referral to treatment reduce stimulant use or improve risky behaviors in patients with a positive screen?
   2. What are effective strategies for referral to treatment for StUD?
3. Early Intervention Peer Navigation (Table 55):
   1. Does peer navigation improve referral for treatment in patients with a positive screen?

Harm Reduction

1. Education Stimulants (Table 56):
   1. What are effective educational strategies for reducing harms related to stimulant use or StUD-related behaviors?
2. Prevention – Refer to Harm Reduction (Table 57):
   1. Does referral for harm reduction services reduce harms related to stimulant use or StUD-related behaviors?
3. Education – Overdose (Table 58):
   1. What are effective strategies for preventing overdose in patients with StUD?
4. Education – Sex (Table 59):
   1. What are effective strategies for preventing risky sex-related harms in patients with StUD?
5. Prevention – Condoms:
   1. What are effective strategies for increasing condom use in patients with StUD?
6. Prevention – Routine Sexually Transmitted Infection Testing:
   1. How often should STI testing be conducted in patients with StUD and other StUD-related risk factors?
7. Prevention – Naloxone (Table 60):
   1. What are effective strategies for distributing naloxone to patients with StUD?
8. Prevention – Drug Checking (Table 61):
   1. Is drug checking an effective strategy for reducing harms related to StUD?
9. Prevention – Supervised Consumption (Table 62):
   1. Is referral to SCS effective for reducing harms related to StUD?
10. Prevention – Routine Sexually Transmitted Infection Testing (Table 63):
    1. How often should STI testing be conducted in patients with StUD and other StUD-related risk factors?
11. Education – Injection Drug Use (Table 64):
    1. What educational interventions are effective for reducing harms related to injection drug use?
12. Prevention – Injection Drug Use Kits (Table 65):
    1. Are injection drug use kits effective for reducing harms related to injection drug use?
13. Prevention – HIV Preexposure Prophylaxis (PrEP) (Table 66):
    1. What factors should be considered when determining the appropriateness of HIV PrEP for patients with StUD?
14. Prevention – Oral Health (Table 67):
    1. What interventions are effective for preventing oral health-related harms in patients with StUD?
15. Prevention – Nutrition:
16. What interventions are effective for preventing nutrition-related harms in patients with StUD?

# Appendix F. Topics with Insufficient or Negative Evidence

The following table presents interventions for which the evidence considered by the CGC was determined to be insufficient or not supportive.

|  |  |
| --- | --- |
| **Intervention Type** | **Intervention** |
| Technology-based interventions | Text messaging interventions for StUD |
| Technology-based interventions | Noninvasive brain stimulation for StUD |
| Alternative interventions | Exercise as standalone or add-on treatment for StUD |
| Alternative interventions | Auricular acupuncture for ATS use disorder |
| Pharmacotherapy | Topiramate and mixed amphetamine salts for ATS use disorder |
| Pharmacotherapy | Bupropion and naltrexone for cocaine use disorder |
| Pharmacotherapy | Modafinil for ATS use disorder |
| Pharmacotherapy | Mirtazapine for cocaine use disorder |
| Pharmacotherapy | Disulfiram |
| Pharmacotherapy | Naltrexone |
| Pharmacotherapy | Naltrexone and N-acetylcysteine |

ATS, amphetamine-type stimulants; StUD, stimulant use disorder

# Appendix G. Additional Resources

## Stimulant Use Disorder: General Information and Guidelines

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## Other Topics

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# Appendix H. ****Substance Use Disorder Biopsychosocial Assessment****

In developing this Guideline, the CGC sought to include recommendations that were specific to StUD or of increased importance in the treatment of this illness. However, it is important for clinicians to deliver the full standard of care that should be provided to any patient with SUD, including a full biopsychosocial assessment that evaluates:

* substance use-related risks (e.g., risks associated with current patterns of substance use);
* social and environmental factors, including SDOH, that may impact access to or efficacy of care, such as housing, transportation, and childcare needs, among others;
* trauma-related concerns using trauma-sensitive screening practices;
* biomedical comorbidities;
* post-acute symptoms of withdrawal;
* psychiatric comorbidities and psychiatric disorder history;
* risk factors for infectious diseases, such as HIV and viral hepatitis (e.g., HAV, HBV, HCV), including:
  + sexual practice history to screen for risky sexual behaviors in accordance with current guidance,
    - When taking a sexual history and addressing risk factors for STI, clinicians should pay particular attention to patient comfort, seek to maximize rapport, and be responsive to the patient's readiness to discuss their sexual practices.
  + injection drug use, and
  + sharing drug preparation supplies;
* co-occurring behavioral addictions and/or compulsions (e.g., gambling disorder, internet use, gaming, sex);
* family and/or household substance use, SUDs, and psychiatric histories; and
* contraceptive practices and related needs.

# Appendix I. ****Baseline Laboratory Testing****

In developing this Guideline, the CGC sought to include recommendations that were specific to StUD or of increased importance in the treatment of this illness. However, it is important for clinicians to deliver the full standard of care that should be provided to any patient with SUD, including routinely ordering baseline laboratory testing for patients with a newly diagnosed SUD or psychiatric disorder.

In non-acute care settings, clinicians should order the following clinical tests for most patients:

* CBC,
* CMP (e.g., renal panel, LFTs),
* screening for infectious diseases in accordance with current guidance,
* HIV and HCV for all patients,
* HBV for patients at increased risk for infection,
* screening for STIs (e.g., gonorrhea, chlamydia, syphilis), and
* pregnancy testing for all patients with childbearing potential.

Clinicians can also consider ordering the following clinical tests:

* tuberculosis (TB) for patients at increased risk for infection;
* HAV for patients at increased risk for infection; and
* other clinical tests as necessary based on clinical assessment, such as CK if signs of rhabdomyolysis are present (e.g., increased muscle tone/rigidity, elevated temperature).

# Appendix J. Principles of Drug Testing During Withdrawal Management

This appendix outlines the major principles in ASAM’s *Appropriate Use of Drug Testing in Clinical Addiction Medicine* consensus statement. For additional guidance, please refer to the full statement.

1. Drug testing can be used to help inform clinical decision-making for patients with SUD or at risk for substance withdrawal.
2. Drug testing can neither diagnose nor rule out SUD.
3. Drug test results should be used in combination with patient history, physical exam, and psychosocial assessment to determine the patient’s care plan.
4. Drug testing can be an important supplement to patient self-report because patients may not be aware of the composition of the substances they have used.
5. Drug test selection should be individualized based on specific patients and clinical scenarios. Before choosing the type of test and matrix, the clinician should determine the questions they are seeking to answer and consider the benefits and limitations of each test and matrix (e.g., urine, blood, saliva, hair). The methods used will impact interpretation of the results:
   1. Each matrix has advantages and disadvantages (e.g., ease of collection, window of detection, susceptibility to tampering).
   2. Tests are designed to measure if specific substances have been used within particular windows of time.
   3. Selection of a drug testing panel should be based on the patient’s self-reported use, prescribed medications, and substances commonly used in the geographic area and by the patient’s peer group.
      1. Note that many drug test panels do not detect fentanyl and fentanyl analogs.
   4. It is important to understand the difference between presumptive drug tests, which are routinely used for point-of-care testing, versus definitive tests, which are used to confirm the results of presumptive tests and rule out false positives.
      1. Definitive testing is done by CLIA-certified laboratories.
6. Definitive testing should be used when the results inform clinical decisions with major clinical or nonclinical implications for the patient (e.g., changes in medications or legal status).
7. Drug test results should be interpreted by a clinician whose scope of practice includes ordering drug tests and interpreting drug test results and who will consider the limitations of the specific test used.
8. Discrepancies between patient self-report and drug tests should be discussed with the patient.
9. Clinicians should keep drug test results confidential to the extent permitted by law.
10. Providers should be aware of the adverse legal and social consequences of detecting substance use via drug testing in pregnant patients. The patient should be made aware of local and state reporting requirements before drug tests are conducted.

# Appendix K. Medication Dosing in Clinical Trials

This appendix presents a summary of dosing strategies used in the clinical trials reviewed but is not intended as a dosing guide.

*Table 1. Medication Dosing: Psychostimulant*

| **Study** | **Drug** | **Dose** | **SUD** |
| --- | --- | --- | --- |
| Modafinil | | | |
| Anderson et al, 2009334 | Modafinil | 200 mg or 400 mg/day | Cocaine |
| Anderson et al, 2012335 | Modafinil | 200 mg or 400 mg/day | Cocaine, ATS |
| Dackis et al, 2005336 | Modafinil | 400 mg/day | Cocaine |
| Dackis et al, 2012337 | Modafinil | 200 mg or 400 mg/day | Cocaine |
| Heinzerling, 2010338 | Modafinil | 400 mg/day | Cocaine, ATS |
| Kampman et al, 2015339 | Modafinil | 300 mg/day | Cocaine |
| Kampman, 2018340 | Modafinil | 300 mg/day | Cocaine |
| Kampman, 2020341 | Modafinil | 400 mg/day | Cocaine |
| Karila et al, 2016342 | Modafinil | 200–400 mg/day | Cocaine |
| Morgan et al, 2010343 | Modafinil | 200–400 mg/day | Cocaine |
| Morgan et al, 2016344 | Modafinil | 100–400 mg/day | Cocaine |
| Schmitz et al, 2012345 | Modafinil | 400 mg/day | Cocaine |
| Schmitz et al, 2014346 | Modafinil | 200 mg BID | Cocaine |
| Shearer et al, 2009347 | Modafinil | Max 200 mg/day | ATS |
| Topiramate | | | |
| Levin et al, 2020137 | Topiramate + MAS-ER | Topiramate max 100 mg BID + MAS-ER max 60 mg/day | Cocaine |
| Mariani et al, 2012348 | Topiramate + MAS-ER | Topiramate max 150 mg BID + MAS-ER max 60 mg/day | Cocaine |
| MAS-ER | | | |
| Levin et al, 2015349 | MAS-ER | 60 or 80 mg/day | Cocaine |
| Dextroamphetamine/Lisdexamfetamine | | | |
| Charnaud and Griffiths, 1998350 | Dextroamphetamine (d-AMP) | Individualized | ATS |
| Galloway et al, 2011351 | Dextroamphetamine (d-AMP-SR) | 30 mg BID | ATS |
| Grabowski et al, 2001352 | Dextroamphetamine (d-AMP-SR) | Max 60 mg/day | Cocaine |
| Grabowski et al, 2004353 | Dextroamphetamine (d-AMP-SR) | Max 60 mg/day | Cocaine |
| Longo et al, 2010354 | Dextroamphetamine (d-AMP-SR) | Max 110 mg/day | ATS |
| Merrill et al, 2005355 | Dextroamphetamine (d-AMP) | Max 100 mg/day | ATS |
| Mooney et al, 2015356 | Lisdexamfetamine (LDX) | 70 mg/day | Cocaine |
| Nuijten et al, 2016357 | Dexamphetamine (d-AMP-SR) | 60 mg/day | Cocaine |
| Schmitz et al, 2012345 | Dextroamphetamine (d-AMP-SR) + modafinil | d-AMP-SR 15 mg BID + modafinil 200 mg/day | Cocaine |
| Shearer et al, 2001358 | Dexamphetamine (d-AMP) | Max 60 mg/day | ATS |
| Shearer et al, 2003359 | Dexamphetamine (d-AMP-SR) | Max 60 mg/day | Cocaine |
| White, 2000360 | Dexamphetamine (d-AMP) | Max 90 mg/day | ATS |
| White et al, 2006361 | Dexamphetamine (d-AMP) | 30–60 mg/day | ATS |
| Selegiline transdermal system patch | | | |
| Elkashef et al, 2006362 | Selegiline transdermal system patch | Continuous release 6 mg/24h | Cocaine |
| Methylphenidate | | | |
| Dürsteler-MacFarland et al, 2013363 | Methylphenidate | 30 mg BID | Cocaine |
| Grabowski et al, 1994364 | Methylphenidate | 20–25 mg BID | Cocaine |
| Grabowski et al, 1997365 | Methylphenidate SR | Max 45 mg/day | Cocaine |
| Konstenius et al, 2010366 | Methylphenidate ER | 18–72 mg/day | ATS |
| Konstenius et al, 2014367 | Methylphenidate ER | Max 180 mg/day | Cocaine, ATS |
| Levin et al, 2006368 | Methylphenidate SR | 20–40 mg BID | Cocaine |
| Levin et al, 2007369 | Methylphenidate SR | 20–40 mg BID | Cocaine |
| Ling et al, 2014370 | Methylphenidate SR | 54 mg/day | ATS |
| Miles et al, 2013371 | Methylphenidate ER | 54 mg/day | ATS |
| Minařík et al, 2016372 | Methylphenidate short acting | Mean 37.6 mg/day | ATS |
| Rezaei et al, 2015373 | Methylphenidate SR | 54 mg/day | ATS |
| Schubiner et al, 2002374 | Methylphenidate | 30 mg TID | Cocaine |
| Solhi et al, 2014375 | Methylphenidate | Max 10 mg/day | ATS |
| Tiihonen et al, 2007376 | Methylphenidate SR | 54 mg/day | ATS |
| Mazindol | | | |
| Stine et al, 1995377 | Mazindol | 2 mg/day | Cocaine |
| Margolin et al, 1995378 | Mazindol | 1 mg/day | Cocaine |
| Margolin et al, 1997379 | Mazindol | 1 or 8 mg/day | Cocaine |
| Perry et al, 2005380 | Mazindol | 2 mg TID | Cocaine |
| Oral methamphetamine | | | |
| Mooney et al, 2009381 | Oral methamphetamine | Immediate release 5 mg six times daily  SR 30 mg/day | Cocaine |

ATS, amphetamine-type stimulant; BID, two times per day; d‑AMP, dextroamphetamine; d‑AMP‑SR, sustained-release dextroamphetamine; ER, extended release; LDX, lisdexamfetamine; MAS‑ER, extended-release mixed amphetamine salts; SR, sustained release; TID, three times per day

*Table 2. Medication Dosing: Non-Psychostimulant*

|  |  |  |  |
| --- | --- | --- | --- |
| **Study** | **Drug** | **Dose** | **SUD** |
| Bupropion | | | |
| Anderson et al., 2015382 | Bupropion SR | 150 mg bid | Methamphetamine |
| Das et al., 2010383 | Bupropion XL | 300 mg | Methamphetamine |
| Elkashef et al., 2008384 | Bupropion SR | 150 mg bid | Methamphetamine |
| Heinzerling et al., 2014385 | Bupropion SR | 150 mg bid | Methamphetamine |
| Margolin et al., 1995386 | Bupropion HCL | 100 mg bid or tid | Cocaine/ Opioid |
| McCann and Li 2012387 | Bupropion SR | 150 mg bid | Methamphetamine |
| Poling et al., 2006107 | Bupropion hydrochloride SR | 300 mg/d | Cocaine/ Opioid |
| Shoptaw et al., 2008108 | Bupropion hydrochloride | 150 mg bid | Cocaine |
| Shoptaw et al., 2008388 | Bupropion SR | 150 mg bid | Methamphetamine |
| Winhusen et al., 2014389 | Bupropion hydrochloride XL+ Nicotine inhaler | 300 mg/d  6-16 cartridges/d (ad libitum) | Cocaine/ Methamphetamine |
| Bupropion and Naltrexone | |  |  |
| Mooney et al., 2016120 | Bupropion (ER) and Naltrexone (ER, injectable) | 450 mg/d and 380 mg (Once/month) | Methamphetamine |
| Trivedi et al., 2021121 | Bupropion (ER) and Naltrexone (ER, injectable) | 450 mg/d and 380 mg (every 3 weeks) | Methamphetamine |
| Mirtazapine | |  |  |
| Coffin et al., 2020126 | Mirtazapine | 30 mg/d | Methamphetamine |
| Colfax et al., 2011127 | Mirtazapine | 30 mg/d | Methamphetamine |
| Cruickshank et al., 2008390 | Mirtazapine | 30 mg/d | Methamphetamine |
| Kongsakon et al., 2005391 | Mirtazapine | 15-60 mg/d | Amphetamine |
| McGregor et al., 2008289 | Mirtazapine | 60 mg/d | Methamphetamine |
| Topiramate | | | |
| Baldacara et al., 2016392 | Topiramate | 200 mg/d | Cocaine |
| Elkashef et al., 2012123 | Topiramate | 200 mg/d | Methamphetamine |
| Johnson et al., 2013393 | Topiramate | 100-150 mg bid | Cocaine |
| Kampman et al., 2004394 | Topiramate | 200 mg/d | Cocaine |
| Kampman et al., 2013395 | Topiramate | 150 mg bid | Cocaine/ Alcohol |
| Nuijten et al., 2014396 | Topiramate | 200 mg/d | Cocaine |
| Rezaei et al, 2016397 | Topiramate | 200 mg/d | Methamphetamine |
| Umbricht et al., 2014398 | Topiramate | 150 mg bid | Cocaine/ Opioid |

Bid, twice a day; ER, extended-release; SR, sustained release; tid, three times a day; XL extended-release

# Appendix L. Acute Issues and Complications of Stimulant Intoxication and Withdrawal

**Acute issues and complications of stimulant intoxication and withdrawal include but are not limited to:**

* electrolyte and fluid imbalances (e.g., dehydration, acidosis, hyperkalemia, hyponatremia);
* hyperthermia;
* agitation;
* psychosis;
* cardiovascular dysfunction such as cardiac arrhythmias, hypertensive emergency, acute decompensated heart failure, and takotsubo cardiomyopathy;
* acute neurologic complications such as seizures and cerebrovascular accidents;
* serious infections such as infective endocarditis, osteomyelitis, epidural abscesses, septic arthritis, serious skin infections, bacteremia, and sepsis;
* rhabdomyolysis;
* movement disorders;
* gastrointestinal perforation;
* trauma and trauma-related complications; and
* risk for harm to self or others.

# Appendix M. ****Non-acute Issues and Complications**** of Stimulant Use

Patients with stimulant intoxication should be routinely assessed for complications and sequalae of stimulant use and factors that impact treatment planning. Assess or refer for an assessment of these relevant conditions and issues and treat or refer for treatment in an appropriate medical or psychiatric setting when these conditions and issues are identified. Non-acute issues and complications of stimulant use include but are not limited to:

* general complications, including weight change (e.g., body mass index [BMI]) and deficits in hygiene;
* cardiovascular complications, such as hypertension, arrhythmia, ischemia, pulmonary hypertension, and heart failure;
* dental complications, such as poor dentition, dental caries, and abscesses;
* dermatologic complications, such as picking, neurodermatitis, cellulitis, abscesses, and other skin or soft tissue infections;
* hepatic complications, such as drug-induced hepatitis;
* infectious complications, including STIs (e.g., HIV, HCV);
* neurologic complications, such as involuntary movement disorders, rigidity, tremor, seizures, stroke, and cognitive impairment (e.g., deficits in memory and/or attention);
* nutritional deficits, such as malnutrition, cachexia, and sequalae involving specific vitamin deficiencies;
* oropharyngeal complications, such as teeth grinding and jaw clenching, earache, headache, and facial pain;
* renal complications, such as acute kidney injury and chronic kidney disease;
* rhinologic complications such as rhinitis, mucosal atrophy, rhinorrhea, anosmia, oronasal fistula, and septum perforation; and
* sexual dysfunction (use trauma-sensitive screening practices).

# Appendix N. Medications for Managing Intoxication

The information in this table is intended to guide management of stimulant intoxication in a variety of settings. The choice of medication, medication dosing (including initial and redosing), and route of administration should be guided by the patient’s signs and symptoms, degree of intoxication, the level of care, and the resources of the setting. This does not represent a comprehensive list but rather provides illustrative examples of medications discussed in the narrative.

| **Agent/Class** | **Mechanism** | **Example dosing** | **Indications** | **Other considerations** |
| --- | --- | --- | --- | --- |
| ***Sedatives*** | | | | |
| Benzodiazepines (BZDs) (first line) | GABAergic | Initial dosing:  Lorazepam 1–2 mg IV based on clinical signs and symptoms and duration of effects  Diazepam 5–10 mg PO for less severe symptoms based on patient parameters  Midazolam 5 mg IM or 0.01-0.05 mg/kg IV for acute agitation in adult patients  Redosing frequency and dose should be guided by the degree and duration of the clinical effects of the initial dose | Excitatory symptoms  Anxiety/Agitation  Neuromuscular excitation  Seizures | Parenteral vs. PO administration based on signs and symptom severity and drug availability (e.g., parenteral BZD shortages). IM administration allows for administration in agitated patients without IV access.  Lorazepam has very slow IM onset (15–30 min)  Midazolam has very rapid IV onset, allowing for easy titration, and a relatively fast IM onset  If psychosis is primary symptom, antipsychotics should be considered primarily or adjunctively |
| Phenobarbital (PBO) | GABAergic | Incremental 130–260 mg parenteral/IV/PO based on symptoms and patient parameters  Loading strategy (e.g., 5-10 mg/kg)  Titrate based on clinical effects | BZD shortages or contraindications  Patient not responding to escalating doses of BZDs  Severe sympathomimetic intoxication | High oral bioavailability; PO dosing can be similar to parenteral dosing  Onset of effects, while slower than IV, is still fairly quick compared to other PO medications |
| Propofol | GABAergic + NMDA receptor antagonism | 10–50 µg/kg/min based on symptoms and patient parameters | For critically ill patients in the ICU  Severe sympathomimetic intoxication not responding to other agents | Patients can be administered BZDs, PBO, and/or propofol concomitantly  Intubation is almost always required for propofol administration |
| ***Sympatholytics*** | | | | |
| Clonidine | Alpha‑2 agonism +/- other | 0.1–0.2 mg PO every 4 hours as needed | Anxiety | Useful medication adjunct to BZDs  Maintain hydration to avoid orthostatic symptoms |
| Dexmedetomidine | Alpha‑2 agonism | Start at 0.2–0.4 µg/kg/hr and titrate every 30 min up to maximum of 1.5 µg/kg/hr | For critically ill patients in the ED or ICU as primary or secondary medication for sedation | Useful medication adjunct to BZDs or other sedation agents  Onset of effects generally  30–60 min  Sedation without impairments in ventilation |
| ***Antipsychotics*** | | | | |
| Butyrophenones (2nd gen) | Dopamine antagonism | Haloperidol or droperidol 5 mg IM | Acute agitation with psychosis  Agitation not responding to BZDs  Toxic psychosis | Consider atypical or newer generation antipsychotics as alternatives  Consider risk of QT prolongation |
| Atypical | Dopamine antagonism +/- other | Olanzapine 5 mg PO  Quetiapine 50–100 mg PO at night | Anxiety or agitation with psychotic features  Stimulant-induced psychosis  Stimulant-induced sleep derangements | Consider risk of QT prolongation  For olanzapine, degree of symptoms to balance needs for PO vs. IM |
| ***Other*** | | | | |
| Ketamine | NMDA receptor antagonism | 1–5 mg/kg IM depending on degree of agitation | For severe agitation as primary or secondary agent | Rapid IM onset of action compared to other agents |

BZD, benzodiazepine; ED, emergency department; ICU, intensive care unit; IM, intramuscular; IV, intravenous; NMDA, N-methyl-D-aspartate; PBO, phenobarbital; PO, *per os* (by mouth/oral)