Patients with attention-deficit/hyperactivity disorder (ADHD), especially adolescents and young adults, commonly have comorbid conditions, including substance use disorder (SUD), which can complicate the treatment and management of both illnesses. Patients with ADHD and SUD have an earlier age at onset of SUD, may take longer to achieve remission than those with only SUD, and are likely to have a longer course, poorer outcome, and higher rates of other psychiatric comorbidities. There is evidence of misuse and diversion with stimulant medications, which raises several safety concerns. Studies of pharmacotherapy for ADHD and comorbid SUD are limited but have shown that stimulant medications probably do not exacerbate the SUD. Nonstimulant medications for ADHD and extended-release stimulant formulations are available and may be less likely to be misused or diverted. Understanding the motives for drug use and misuse is important in treating patients with ADHD and comorbid SUD. A number of tools are available to the clinician to detect substance use problems in patients with ADHD, including drug and alcohol screening questionnaires and toxicology screens. Clinical recommendations for treating this dual diagnosis include using nonstimulant agents or extended-release stimulant formulations in conjunction with psychosocial therapies to treat both the ADHD and the SUD.
all classes of substances, but abuse and dependence diagnoses are the most commonly used. For a diagnosis of abuse, a person must meet 1 or more of the following criteria in a 12-month period: have recurrent impairment as manifested by role impairment or inability to fulfill major obligations at home, work, or school; have recurrent legal problems related to substance use; repeatedly use substances in potentially hazardous situations such as driving or operating machinery; and have recurrent substance use despite related social or interpersonal problems. A diagnosis of substance dependence requires that, at any time within a 12-month period, a patient meet 3 of the following 7 criteria: tolerance; withdrawal; loss of control; attempting to quit or cut down; spending significant time obtaining, using, or recovering from the effects of a drug; impairment of regular activities; and psychological or physical problems caused or exacerbated by substance use.

**Attention-deficit/hyperactivity disorder.** For a diagnosis of ADHD, a patient has to meet 6 or more symptoms of inattention and/or hyperactivity/impulsivity for at least 6 months and to a degree that is disruptive and inappropriate for the patient’s developmental level. For example, parents may mistake toddlers’ behavior to be an indication for the patient's developmental level. Additionally, the DSM-IV requires that the impairing symptoms of hyperactivity-impulsivity or inattention present before 7 years of age and in 2 or more settings, such as school, work, home, and social settings. In clinical settings, it is important to identify this distinction. For example, the clinician may need to focus on helping parents improve their parenting skills rather than treating the child for ADHD if the impairment is solely at home. The final criterion for a diagnosis of ADHD includes symptoms that cannot be better accounted for by the presence of another disorder, such as a pervasive developmental disorder, psychotic disorder, or mood disorder.

### Populations at Risk for Substance Use Disorder

The 2004 Substance Abuse and Mental Health Services Administration’s National Survey on Drug Use and Health (NSDUH) reported a prevalence rate for current (i.e., past month) illicit drug use of 3.8% for those aged 12 to 13 years, which steadily rose during the teen years to a high of 22.3% in those aged 18 to 20 years. The rate dropped with subsequent ages. The prevalence of SUD is equivalent in boys and girls aged 12 to 17 years. However, at 18 years and older, the prevalence of SUD is twice as high in men as in women. The data highlight the need for prevention and treatment efforts relating to SUD focused on adolescents and young adults.

### Commonly Abused Substances

The Monitoring the Future survey, which is sponsored by the National Institute on Drug Abuse, reported patterns and trends of drug use in 8th, 10th, and 12th grade students, as well as college students and adults aged 19 to 45 years. In the sample of 8th, 10th, and 12th grade students, alcohol was the most frequently used substance in the past 30 days (Figure 1). Similar prevalence rates were reported among the 3 grade levels for tobacco use in the form of cigarettes, marijuana use, and other illicit drug use. However, tobacco was the most commonly used substance on a daily basis, whereas marijuana was the most commonly used illicit drug overall. The Monitoring the Future survey and the NSDUH both reported trends and patterns of use for other illicit drugs such as methamphetamine, club drugs (e.g., ketamine, lysergic acid diethylamide [LSD], and methylenedioxymethamphetamine [ecstasy]), and prescription medications. Illicit drug use among adolescents has decreased over the past several years with the exception of prescription medications.

### OVERLAP AND COMORBIDITIES

#### Substance Use Disorder in Adults With ADHD

People with ADHD commonly have comorbid disorders such as antisocial disorders, mood disorders, anxiety disorders, and SUDs. Biederman found that almost 30% of adults with ADHD also met the DSM-IV criteria for alcohol and drug dependency. More men than women met the criteria for alcohol and drug dependency, which supports the gender discrepancies found in the NSDUH. An earlier study by Biederman and colleagues compared the prevalence of lifetime psychopathology in adults with and without ADHD (Figure 2). The rates of drug abuse and dependence increased almost 4-fold in adults with ADHD compared with adults without ADHD.

The presence of ADHD may affect the age at onset for SUD. Wilens and colleagues examined the age at onset for SUD in adult patients with untreated ADHD and found that adults with ADHD had a significantly
ADHD in Adults With Substance Use Disorders

While SUDs are highly prevalent in adults with ADHD, ADHD is conversely overrepresented in patients with SUDs. Wilens16 reviewed studies of polydrug use, opiate use, cocaine use, and alcohol use and found that, depending on the sample, the rate of ADHD in people with SUDs ranged from 10% to 71%. Kessler and colleagues17 showed results of the National Comorbidity Survey Replication, which reported that the average prevalence rate of ADHD in patients with SUDs was 10.8% versus only 3.6% in patients without any comorbid disorder.

Several studies18–21 have examined the influence of ADHD on the severity of SUD. Adults with SUD and comorbid ADHD are more likely than those without comorbid ADHD to continue to have problematic abuse,18 and they take longer to achieve remission from SUD.20 Further, adults with SUD and comorbid ADHD have poorer outcomes than those without ADHD despite more treatment exposure,18,19,21 suggesting that the presence of ADHD worsens the prognosis for SUD treatment. Patients with SUD and comorbid ADHD also have higher rates of other comorbid disorders than patients with SUD alone.18,19,21

SUBSTANCE MISUSE AND DIVERSION

Medication misuse occurs when the medication is used in a manner in which it was not prescribed. Performance enhancement and recreational use of medication are forms of misuse. However, in order for recreational use to be considered abuse, it must meet the DSM-IV10 threshold for abuse. The one-time recreational use of a medication to get high does not qualify as abuse. Diversion is the transfer of medication from the patient to another person for any purpose, such as performance enhancement or recreational use. The term nonmedical use is often used as a blanket term for misuse, abuse, and diversion.

Misuse of Stimulants in the General Population

McCabe and colleagues have published several studies22–24 on medication diversion and misuse among high school and college students, which showed that the misuse of stimulants in the general population of high school students nearly doubled from 8th grade to 12th grade. A student’s academic performance was inversely linked to the misuse of prescription stimulants.22 Students who made A grades on average had substantially lower misuse of prescription stimulant medications compared with those who were making poorer grades. These data are consistent with reports from the Monitoring the Future survey,12 which found that the overall use of drugs was lower among high school students who had plans to go to college, which suggests that goal-oriented, long-term plans may be an important protective factor for preventing drug use.

McCabe et al.23 published a later study of stimulant misuse in college students and found rates similar to those of the high school students in their earlier study.22 Another important finding from the later study was that universities or colleges with more competitive admissions policies had a higher misuse of stimulant medications than the less competitive schools, which would suggest that these students may be using stimulants for performance enhancement.

Misuse and Diversion in the ADHD Population

Students misuse stimulant medications for various reasons. My colleagues and I25 found that 22% of college students prescribed stimulants misused their medication for recreational reasons. In a study conducted by McCabe and colleagues,24 a substantial minority (5.4%) of students prescribed stimulant medication reported illicitly using their medication. Students who were prescribed stimulant medications were approached to divert their medication at twice the rate (54%) compared with students overall (27%) and students prescribed pain medication (26%) and almost 3 times more (54%) than those prescribed sedatives or anxiety agents (19%) or sleeping medications (14%). Hence, stimulant medications are
desired among college students, perhaps more than analgesics or anxiolytics.

Teter and colleagues found that, of more than 9000 surveyed college students, lifetime prevalence of prescription stimulants was 5.4%. The most frequently reported reasons for stimulant misuse were related to performance enhancement (“helps me concentrate” [58%], “increases my alertness” [43%]). Recreational use was the second most common reason (43%) for illicit use of prescription medication.

Misuse and diversion of stimulant medications arouse safety concerns primarily because there is little or no physician oversight. Without oversight, patients and other stimulant users are at an increased risk for overdose, especially if they are misusing their stimulant medications with other stimulant drugs, such as cocaine. Interactions with nonstimulants may also exist, but without physician oversight, users are often not aware of the contraindications or warnings, including cardiovascular risks in some patients, particularly those with congenital cardiac anomalies.

### Misuse of Immediate-Release Versus Extended-Release Stimulants

Many clinicians report that, according to their patients, extended-release preparations of stimulant medications are more difficult to misuse than immediate-release stimulant medications. Additionally, a recent study found that patients reported that they liked the drug effect more with an immediate-release preparation than the extended-release stimulant, indicating that immediate-release preparations may have greater abuse potential.

Spencer and colleagues randomly assigned 12 patients to comparable oral therapeutic doses of either immediate-release methylphenidate or extended-release methylphenidate. On 2 separate occasions, the patients were questioned on the likeability of the drug. The immediate-release formula was associated with a greater likeability than the osmotic-release formula from 1 to 5 hours after administration. These findings suggest that the extended-release formula of methylphenidate is associated with a lower abuse potential because of its lower likeability ratings, although these results cannot be generalized to other stimulant products.

### TREATMENT OF ADHD IN PATIENTS WITH SUBSTANCE USE DISORDERS

The dilemma that many psychiatrists and primary care physicians face is that the most effective treatments for ADHD—stimulants—also have abuse potential. Treating patients with ADHD and comorbid SUD can be challenging. Unfortunately, not many studies on the treatment of comorbid ADHD and SUD exist (Table 1), and initial studies in this area were mainly case reports and case series. However, more recent studies have more subjects and examine a wider range of medications.

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Drug of Abuse</th>
<th>Study Method</th>
<th>Medication Used</th>
<th>Results</th>
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<td>1</td>
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<td>+</td>
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<td>DB</td>
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</tr>
<tr>
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<td>Methylphenidate/dextroamphetamine</td>
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<tr>
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<tr>
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<td>Bupropion</td>
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<tr>
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<td>CR</td>
<td>Moclobemide</td>
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<td>DB</td>
<td>Pemoline</td>
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<td>Bupropion</td>
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<tr>
<td>Levin et al</td>
<td>106</td>
<td>Cocaine</td>
<td>DB</td>
<td>Methylphenidate</td>
<td>±</td>
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</table>

Abbreviations: CR = case report, DB = double-blind, THC = tetrahydrocannabinol.
Symbols: + = improvements in both attention-deficit/hyperactivity disorder and substance use disorder symptoms, – = no improvement, and ± = mixed results.
associated with a reduction in ADHD symptoms only on the clinician-rated measure. No evidence of ADHD symptom reduction was found on combined measures in this study. Similarly, Riggs and colleagues\(^4\) found significant improvement (p = .05) on the Clinician’s Global Impressions-Improvement (CGI-I) for the intent-to-treat sample but no significant improvement (p = .13) on the parent-rated Conners’ Hyperactivity-Impulsivity (CHI) scale. In the completer sample the improvement was reversed. Those who finished the 12-week trial had significant improvement (p = .01) on the CHI but not on the CGI-I (p = .24). None of the studies found serious adverse events as a result of treatment, nor did the substance use disorder worsen because of use of a stimulant product. Although none of the studies specifically inquired about diversion behaviors in the samples, none of them reported evidence of diversion.

Several studies\(^4\) examined the treatment of cocaine addiction with dextroamphetamine, hypothesizing that substituting a stimulant medication for an illicit stimulant drug could reduce cocaine use. All 4 double-blind, randomized, placebo-controlled trials found that dextroamphetamine treatment reduced cocaine use in the study. However, 2 studies\(^4\) found that only higher doses of dextroamphetamine treatment (30–60 mg compared with 15–30 mg) were effective in reducing cocaine dependence. None of the studies reported serious adverse events from amphetamine treatment, and none reported evidence of diversion or misuse of prescribed stimulants. The fact that only the higher doses of dextroamphetamine were able to reduce cocaine use may suggest that the stimulant medications used at lower doses for the treatment of ADHD may be less likely to have cocaine-like effects.

Wilens and colleagues\(^5\) analyzed the literature on whether stimulant treatment for ADHD can lead to SUD in later life. The authors concluded that stimulant medication does not increase the odds of a patient with ADHD having SUD later in life and suggested that stimulant treatment may even have a protective effect.

**CLINICAL CONSIDERATIONS AND RECOMMENDATIONS**

Clinicians should approach the treatment of patients with SUD and comorbid ADHD by making a careful assessment using DSM-IV criteria when diagnosing ADHD in patients with SUD. An adequate assessment can help to minimize common problems of overdiagnosis and underdiagnosis of ADHD in patients with SUD.

**Factors Leading to Underdiagnosis of ADHD in Patients With Substance Use Disorder**

One factor that may lead to underdiagnosis is that some clinicians assume that other psychiatric disorders, such as bipolar disorder or major depressive disorder, preclude the diagnosis of ADHD, and that is not true. For example, a patient can have both bipolar affective disorder and ADHD, but the diagnosis of ADHD becomes harder because of an overlap of symptoms. In addition, the clinician may not use the DSM-IV criteria or a rating scale for diagnosis and instead try to rely on memory to do an assessment for ADHD. Clinicians often do not recognize that in adults, symptoms of ADHD may be fewer or less obvious than in children. Adults with ADHD often compensate for their ADHD symptoms. For example, college students with ADHD may make good grades, but they may have to study much longer compared with students without ADHD.

**Factors Leading to Overdiagnosis of ADHD in Patients With Substance Use Disorder**

Overdiagnosis of ADHD in adult patients with SUD could be avoided if clinicians obtained an adequate longitudinal history. ADHD does not occur de novo in adulthood. It is a developmental disorder, and onset occurs during childhood. A longitudinal history could uncover which patients have a greater likelihood of adult ADHD. Relying on screening instruments alone may also lead to overdiagnosis. ADHD is a clinical diagnosis, and screening instruments can be used as an adjunct tool in the diagnostic process, but the clinician should not substitute these instruments for the valuable diagnostic tool of face-to-face interviews with the patient. Clinicians may fail to ensure that a patient’s ADHD symptoms occur in more than 1 setting. ADHD is not a disorder that only occurs at a particular time of day or in a particular setting; it occurs across different settings and throughout the day. Not ensuring that symptoms cause impairment can also lead to the overdiagnosis of ADHD in patients with SUD.

Patients may intentionally exaggerate their symptoms of ADHD in order to mislead their clinician to obtain secondary gains. Exaggerating symptoms can lead to overdiagnosis. Some patients, particularly high school students or college students, may desire special consideration at school, such as extra time on tests, or they may want stimulant medications for misuse or diversion. Keeping in mind what a patient has to gain from an ADHD diagnosis can help to minimize common problems of overdiagnosis and underdiagnosis of ADHD in patients with SUD.

**Evaluating ADHD and Substance Use Disorder in Clinical Practice**

Distinguishing between current or past SUD is important when evaluating individuals with ADHD and

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comorbid SUD. These 2 groups may require different treatments, so assessing which group the patient fits into is important before prescribing medication for ADHD. If the patient has a history of drug use, establish the patient’s period of abstinence from drug use as well as the details of the patient’s treatment. If the patient has current SUD, determine whether the patient is currently involved in substance abuse treatment. Before prescribing stimulants for ADHD treatment, find out if the patient has a history of stimulant or amphetamine use or abuse. Patients who have used stimulant medication for performance enhancement may not necessarily need to be excluded from stimulant medication treatment, but those who have used stimulants recreationally should probably not be prescribed stimulant medication first line. Addressing any additional comorbid disorders that may be present is also important because these disorders may require additional medication or treatment.

**Screening tools.** Many tools are available for screening SUDs in adults as well as adolescents (Table 2). The CAGE59 questionnaire (see Table 2 for definition of acronym) is a commonly used screening tool. It is a 4-item questionnaire asking if the patient has ever felt the need to cut down on drinking, been annoyed by others’ criticism of your drinking, felt guilty about drinking, needed an eye-opener drink first thing in the morning? The AUDIT50 Alcohol Use Disorders Identification Test (AUDIT) is recommended screening tool. The CRAFFT53 questionnaire is the CRAFFT (see Table 2) questionnaire asking if the patient has ever felt the need to get drunk first thing in the morning? For adolescents, the CRAFFT53 questionnaire (see Table 2) is the recommended screening tool. The CRAFFT questionnaire has good sensitivity (92.3%) and specificity (82.1%) for identifying adolescents needing alcohol and other drug treatment.

**Toxicology tests.** Toxicology tests are a key component of assessment and treatment of substance use disorders. Toxicology tests that show ranges of detection of various drugs in the urine can be used to determine the length of time between ingesting a drug and when the drug can be detected in the urine. Toxicology tests can be helpful in detecting substance use or abuse in patients. If a clinician suspects that a patient is using illicit drugs during treatment, the frequency of urine tests can be determined by gauging the amount of time it would take for the suspected drug of use to be eliminated from the patient’s system.

**Clinical Recommendations for Treating ADHD in Patients With Substance Use Disorder**

The use of stimulant medication in substance-abusing patients is complex and controversial. If possible, clinicians should include family members or close non–substance-using friends in the treatment plan to monitor the patient and to provide useful information. Inform the patient and family of potential risks involved in using stimulants. For patients actively using drugs or for those who are only recently abstinent, consider using nonstimulants as first-line treatment. Each one of the nonstimulants should be considered individually for treatment based on its benefits to the patient. For example, because of its antianxiety properties, atomoxetine may be a preferred product if a patient has a comorbid anxiety disorder. Precautionary steps can be taken in clinical settings when using medications with abuse potential in patients with ADHD and comorbid SUD. The first precautionary step is to limit and keep track of pills by having the patient bring the pill bottle at each visit. Second, obtain urine toxicology screens at regular patient visits to monitor substance use in general. Frequent visits are important; seeing a patient with ADHD once a month is not unusual, and tracking prescription medication improves patient compliance. Third, prescribing long-acting preparations of stimulant medications, such as osmotic release oral system methylphenidate and lisdexamfetamine dimesylate, which is an amphetamine-prodrug, may be desirable. The methylphenidate transdermal patch also has properties that make it harder to abuse. Nonpharmacologic approaches for ADHD may also be explored in adults, such as cognitive remediation and cognitive-behavioral therapy. Fourth, emphasize the importance of taking medications regularly, not on an as-needed basis. Some patients do not take their medications daily and then divert or misuse the leftover medication. Finally, discuss with patients how to store the medication safely and avoid letting others know that they are taking a stimulant medication.

Red flags for diversion or misuse include patients demanding immediate-release products, having repeatedly discordant pill counts, frequently losing prescriptions and calling for another one, and frequently asking to escalate the dose. Symptoms of psychosis can be a red flag for misuse, but they can also mean that patients are having side effects from the medication. Symptoms associated with
heavier-than-prescribed use include palpitations, syncope, and shortness of breath.

Having an intervention plan for patients with ADHD and comorbid SUD is an important part of managing the comorbidity. Be aware of the resources for SUD treatment in the community, know the risks of stimulant medication use, and warn patients about the consequences of misuse and diversion. Frequently monitor the patient’s ADHD response with rating scales, schedule more frequent office visits to monitor medication usage and drug abuse, and involve the family in the treatment process. Consider using a stimulant medication for a patient who has a documented history of sobriety, but if the patient is actively using a drug, consider delaying the use of stimulant medication until the SUD is in remission. Office-based or laboratory toxicology testing can be used as indicated. Assess the family for SUD and refer them for treatment if necessary. Optimally, efficacious treatment strategies for SUD should be used in an integrated fashion with ADHD treatment to treat patients with both ADHD and SUD. Efficacious psychosocial treatment strategies for SUD include cognitive-behavioral therapy, contingency management, the 12-step Minnesota model, motivational interviewing, family therapies, and combination therapies, such as integrative psychosocial therapy. Pharmacotherapy for specific substances (e.g., naltrexone for alcohol dependence) should be considered.

CONCLUSION

ADHD is present in a substantial proportion of substance-abusing people seeking treatment, and ADHD is an independent risk factor for SUD. Additional psychiatric comorbidities are common in individuals with ADHD and should be considered when developing a plan to treat not only the ADHD symptoms but comorbid SUD as well. The treatment of individuals with ADHD and comorbid SUD requires management of both the SUD and ADHD symptoms in an integrated fashion, not as separate entities.

Drug names: atomoxetine (Strattera), bromocriptine (Parlodel and others), bupropion (Wellbutrin and others), dextroamphetamine (Dextrostat, Dexedrine, and others), lisodexametamine (Vyvanse), methylphenidate (Methylin, Ritalin, and others), naltrexone (ReVia and others), osmotic release oral system methylphenidate (Concerta), transdermal methylphenidate (Daytrana), venlafaxine (Effexor and others).

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, bromocriptine and dextroamphetamine are not approved by the U.S. Food and Drug Administration for the treatment of cocaine use disorder and bupropion and venlafaxine are not approved for the treatment of attention-deficit/hyperactivity disorder. If you have questions, contact the medical affairs department of the manufacturer for the most recent prescribing information.

REFERENCES