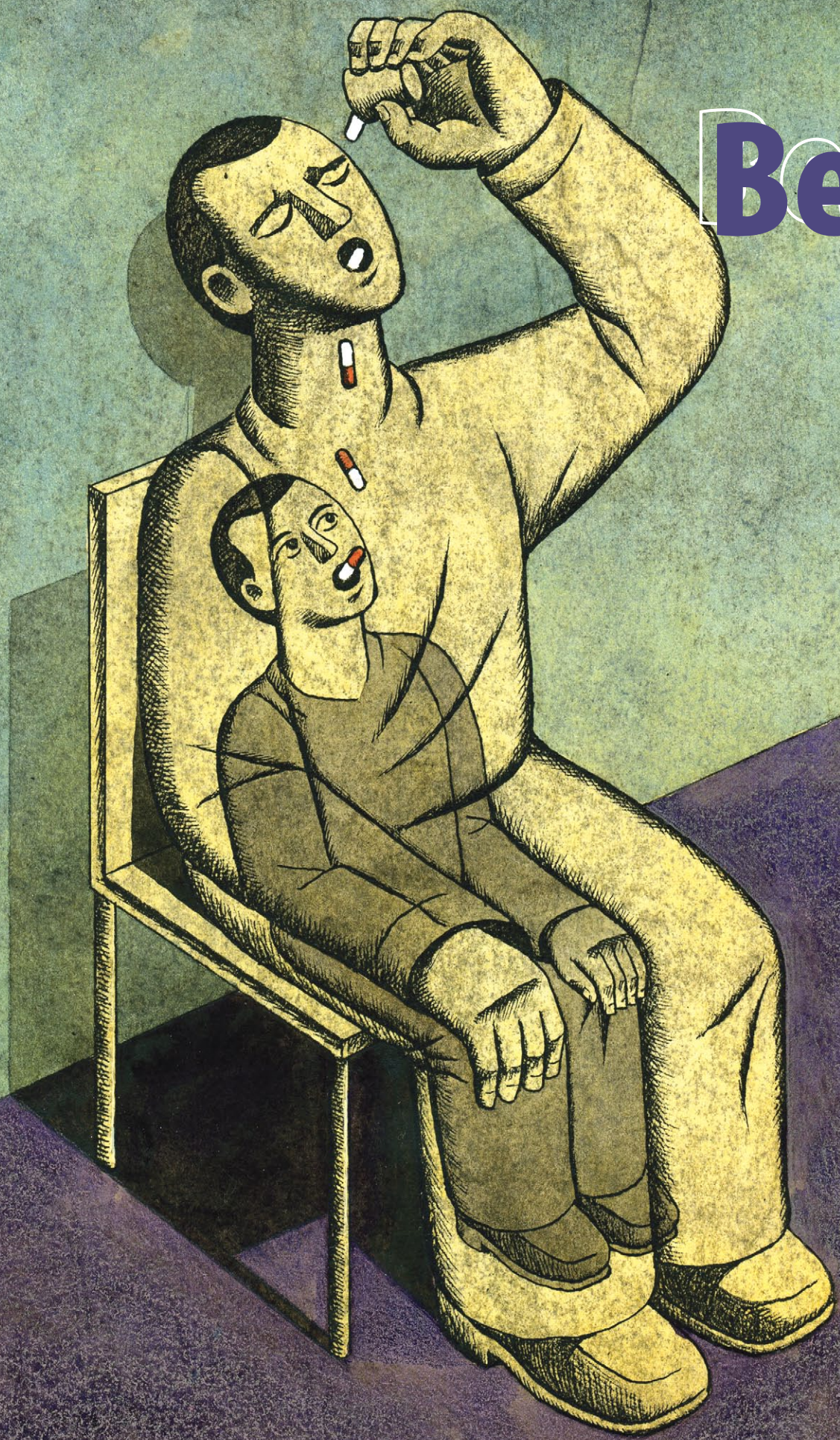


Ben





benzodiazepines and stimulants for patients with substance use disorders

Careful assessment, close monitoring are essential
when prescribing drugs with abuse potential

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Although benzodiazepines and stimulants have well-documented efficacy for numerous psychiatric disorders, psychiatrists hesitate to prescribe these medications to patients with substance use disorders (SUDs)—even to those with a comorbid condition that likely would respond to a benzodiazepine or stimulant—because of risk of abuse or dependence. Conventional practice typically has focused on treating active substance use first rather than using simultaneous treatments. Prejudice, fear, and misinformation can influence this decision.

We believe these cases lie on a continuum. At one extreme, ignoring a past or present SUD may lead a remitted patient toward relapse, or further delay recovery for an active user. At the other end, psychiatrists who overreact to a remote history of substance use may deprive patients of legitimate pharmacologic symptom relief. Most cases lie somewhere in the middle.

A literature review does not support the assertion that the use of these medications leads to future substance use or worsens active use, especially for stimulants. In fact, stepwise—as opposed to concurrent—treatment for both conditions actually may delay recovery and increase patients' risk for morbidity.

We outline issues involved in these complex clinical situations, point out controversies, review relevant research data, and offer guidelines for treatment.

continued



Benzodiazepines and stimulants

Clinical Point

It often is difficult to tell whether a patient truly has an anxiety disorder or has anxiety symptoms secondary to substance use or withdrawal

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Table 1

Clinical uses of benzodiazepines

Insomnia
Anxiety disorders (eg, generalized anxiety disorder, panic disorder, posttraumatic stress disorder, social phobia, and obsessive-compulsive disorder)
Side effects of other psychiatric medications (eg, akathisia with antipsychotics or tremor with lithium)
Alcohol or benzodiazepine withdrawal
Acute agitation states, either as monotherapy or as adjuncts to antipsychotics or mood stabilizers
Catatonia
Source: Reference 1

CASE 1

Panic disorder in sobriety

Since he was a teen, Mr. A, age 51, drank heavily, which cost him jobs and relationships. After being convicted for driving under the influence, he was court-ordered to attend a rehabilitation facility, where, as he describes it, he “finally turned [his] life around.” He followed up residential treatment with regular attendance at Alcoholics Anonymous meetings.

After 1 year of sobriety, Mr. A develops increasingly frequent episodes of intense anxiety with sweating, nausea, chest pain, and hyperventilation and is diagnosed with panic disorder. His internist prescribes alprazolam, 0.5 mg 3 times a day, which provides some symptom relief, and refers him for follow-up psychiatric care. At his first visit, Mr. A confides to his psychiatrist that he is taking much more than the prescribed dosage of alprazolam, even when he is not experiencing anxiety, and is contemplating “buying it on the street” if his dosage is not raised to “at least 3 mg 3 times a day.”

CASE 2

Anxiety in controlled psychosis

Ms. B, age 40, had her first psychotic break at age 18 and was diagnosed with schizophrenia. Since then, she has had multiple psychiatric hospitalizations, usually presenting with auditory hallucinations and a recurring delusion that the person who calls herself Ms. B’s mother is really an actress “playing”

her mother. At times this delusion has led Ms. B to attack her “imposter” mother. Over several years Ms. B began to drink heavily, but recently achieved a few months of sobriety by attending dual-diagnosis groups at her local community mental health center and individual psychotherapy sessions with her case manager. Fortunately, Ms. B’s psychosis has been stabilized with risperidone long-acting injection, 25 mg every 2 weeks, which she tolerates well.

When her beloved calico cat passes away, Ms. B experiences intense anxiety. Ms. B’s friend tells her she “needs some Valium,” but her psychiatrist, case manager, and the other patients in her dual-diagnosis group are not sure this is a good idea.

Benzodiazepines

Pros. There are multiple legitimate uses of benzodiazepines in general medicine and psychiatric practice, based upon their considerable sedative/hypnotic, anxiolytic, anticonvulsant, and muscle-relaxant properties (*Table 1*).¹

Recommendations regarding benzodiazepine use for anxious patients with a history of SUD are not clear-cut. First, it often is difficult to determine whether the patient truly has an anxiety disorder or is suffering anxiety symptoms secondary to substance use and/or withdrawal. In addition, even if a diagnosis of a separate anxiety disorder is established, psychiatrists debate how to treat such patients. Some clinicians maintain that benzodiazepines should be used only for acute detoxification, and that ongoing benzodiazepine use will lead to relapse or benzodiazepine dependence. However, in a prospective study of 545 alcohol use disorder (AUD) patients receiving benzodiazepines for anxiety disorders, Mueller et al² found no association—at 12 months or at 12 years—between benzodiazepine use and AUD recurrence. Furthermore, there was no difference in benzodiazepine usage when comparing patients with and without an AUD.³

Cons. Although widely prescribed—and despite their efficacy in numerous conditions—both acute or long-term benzodiazepine use

frequently causes adverse effects.⁴ Patients may develop tolerance, which can lead to escalating dosages and/or to withdrawal symptoms when patients attempt to cut back. Benzodiazepines eventually become ineffective for sleep, and continued use can cause rebound insomnia. Also, with many patients taking benzodiazepines long-term, clinicians struggle to differentiate between “real” anxiety symptoms and subtle states of withdrawal from fluctuating benzodiazepine blood levels.⁵

Geriatric patients who take benzodiazepines are at risk for falls and hip fractures.⁴ Although older dementia patients are at particular risk for cognitive problems—including frank delirium—secondary to benzodiazepine use, patients of all ages are susceptible to these medications’ deleterious neurocognitive effects.

Benzodiazepines can lead to excessive sedation, thereby impairing performance at work or school, and have been implicated as a cause of motor vehicle accidents.⁶ Finally, a serious drawback to benzodiazepine use is possible lethality in overdose, especially when combined with alcohol.

Benzodiazepine prescribing should not be taken lightly. Always analyze the difference between benzodiazepines’ well-documented efficacy and their adverse effect profile. This risk-benefit analysis becomes much more complex for patients with SUDs.

Special considerations. Patients at higher risk for benzodiazepine abuse include those with:

- severe alcohol dependence (ie, long-term use, drinking since a young age [“Type II”])
- intravenous drug use
- comorbid alcoholism and antisocial personality disorder.^{7,8}

Exercise special caution when considering benzodiazepines for patients with severe psychiatric illness such as schizophrenia-spectrum disorders, bipolar disorder, or severe depression. Patients with schizophrenia have high rates of alcohol, cocaine, cannabis, and benzodiazepine abuse.^{9,10} Bipolar disorder patients show similar vulnerability—up to 56% of patients screen positive for sub-

stance abuse or dependence.¹¹ Vulnerability to addiction in severely ill psychiatric patients is thought to be related to several factors, including:

- use of drugs as self-medication
- genetic predisposition
- environment/lifestyle that supports substance abuse
- neurobiologic deficits that lead to lack of inhibition of reward-seeking behaviors.¹¹

Bipolar disorder patients in particular score high on measures of sensation seeking, which leaves them vulnerable to abusing all classes of substances.¹²

In a 6-year study of 203 patients with severe psychiatric illnesses and SUDs, Brunette et al¹³ found that these patients were 2.5 times more likely than patients with severe psychiatric illness alone to abuse prescribed benzodiazepines. In an analysis of Medicaid records, Clark et al¹⁴ found similar vulnerability in patients with major depressive disorder (MDD) and SUD. Not only did these patients show a higher rate of benzodiazepine use than patients with MDD without SUD, but the dual-diagnosis group also gravitated toward more addictive high-potency/fast-acting benzodiazepines, such as alprazolam, estazolam, or triazolam.

Case discussion/suggestions. Initially, Mr. A may seem to be an appropriate candidate for closely monitored benzodiazepine use. However, he shows a pattern of misuse, likely related to his history of severe alcohol dependence and alprazolam use. This benzodiazepine is fast-acting and has a short half-life, and thus is highly reinforcing.

Similarly, Ms. B might benefit from benzodiazepine treatment. However, her history of schizophrenia and alcohol abuse makes her a risky candidate, and alternative treatments for anxiety symptoms should be considered. If prescribed at all, a benzodiazepine should be used only short-term (eg, 1 to 2 weeks).

In general, avoid prescribing benzodiazepines to most patients who have an ongoing or past SUD.¹⁵ Consider making an exception for SUD patients with comorbid anxiety disorders, with close monitoring of their benzodiazepine use. Clonazepam,

Clinical Point

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Benzodiazepines and stimulants

Clinical Point

In general, avoid prescribing benzodiazepines to most patients who have a past or ongoing substance use disorder

Table 2

Alternatives to benzodiazepines for anxiety and/or insomnia

Treatment option	Comments
CBT, relaxation techniques, sleep hygiene counseling	Many advantages to nonpharmacologic interventions (eg, fewer side effects, no risk of substance dependence)
Antihistamines (eg, diphenhydramine, 25 to 50 mg at bedtime* for sleep, or 2 to 3 times a day for anxiety)	Can be used for anxiety or insomnia; can cause confusion in older patients
Atypical antipsychotics	Off-label use; many agents in this class have metabolic side effects
SSRIs/SNRIs	First-line for many anxiety disorders, including panic disorder, GAD; possible weight gain and sexual side effects
Mirtazapine (7.5 to 30 mg at bedtime*)	Sedation side effect helps with sleep; weight gain and oversedation limit use
Trazodone (25 to 100 mg at bedtime*)	Commonly used off-label as a sleep aid
Monoamine oxidase inhibitors	May be useful for social phobia; dietary restrictions and side effects limit use
Doxepin (3 to 6 mg at bedtime)	Minimal anticholinergic and alpha-blockade side effects at this dose; FDA-approved for insomnia
Gabapentin (300 to 2,000 mg/d* in divided doses)	Off-label use, mild anxiolytic and sedative properties, relatively weight neutral
Beta blockers (eg, propranolol, 20 to 80 mg twice a day*)	Useful for peripheral manifestations of anxiety; may be effective for social phobias
Pregabalin (50 to 200 mg 3 times a day*)	Off-label use; industry-sponsored studies show comparable to SNRIs for anxiety
Non-benzodiazepine GABA _A receptor modulators	Short-term option for primary insomnia, some abuse potential
Melatonin (1 to 3 mg at bedtime*)	Mild and 'natural' but not always an effective sleep aid

*Off-label approximate doses based on the authors' clinical experience and consensus of the literature; agents listed may require slow titration and close monitoring for adverse effects

CBT: cognitive-behavioral therapy; GABA: gamma-aminobutyric acid; GAD: generalized anxiety disorder; SNRI: serotonin-norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor

Source: Reference 17

chlordiazepoxide, clorazepate, and oxazepam may be less reinforcing for SUD patients than diazepam, lorazepam, alprazolam, estazolam, or triazolam.^{7,16} The drawbacks of benzodiazepines, especially in the situations described above, point to the need to find alternative treatments (Table 2).¹⁷ Keep in mind nonpharmacologic options, which completely avoid the risks of medication misuse and diversion. Cognitive-behavioral therapy (CBT), for instance, has well-documented efficacy in treating insomnia and anxiety disorders.^{18,19}

CASE 3

Adult ADHD and marijuana use

Mr. C, age 30, presents to a psychiatrist with ongoing complaints of inattention, fatigue, and difficulty staying organized. A self-report

screen yields symptoms consistent with adult attention-deficit/hyperactivity disorder (ADHD). Mr. C's school and job history and collateral history from his wife appear to corroborate his assertion that his symptoms have been lifelong. He later admits to regular marijuana use. After further discussion and full evaluation of his substance use, Mr. C is started on bupropion, titrated to 300 mg/d. After 2 months, despite faithful attendance at appointments and openness about his continued marijuana use, Mr. C's symptoms remain unchanged. He asks about atomoxetine.

Stimulants

Pros. Despite many clinicians' hesitance to prescribe controlled substances to patients with SUDs, psychostimulants should be considered in a variety of sce-

continued on page 64



Benzodiazepines and stimulants

Clinical Point

Withholding ADHD treatment based on concerns about future or increased current substance abuse is unfounded

narios. Although nonstimulant options are available, stimulants consistently have demonstrated superior efficacy over other treatments and remain first-line agents for adult ADHD.²⁰ Methylphenidate, mixed amphetamine salts, lisdexamfetamine, and atomoxetine are FDA-approved for adult ADHD. Both stimulant classes (methylphenidate and amphetamine-based products) are equally effective for ADHD. In addition, stimulants are used to treat narcolepsy, cognitive disorders such as traumatic brain injury, and as augmentation to antidepressants for MDD.

ADHD affects 5% to 12% of children, and >60% of patients remain symptomatic into adulthood and require continued treatment.²¹ In particular, problematic inattention may persist throughout adulthood. ADHD does not appear to be an independent risk factor for SUDs in children and adolescents.²² However, substance use increases sharply as ADHD patients enter late adolescence and adulthood, and eventually becomes a problem for 20% of adolescents and adults with ADHD. Conversely, 17% to 50% of patients with alcohol, cocaine, or opioid dependence have co-occurring ADHD.²³

Withholding ADHD treatment based on concerns about future or increased current substance abuse is unfounded. A meta-analysis of 6 studies that included 674 medicated and 360 unmedicated patients with ADHD who were followed at least 4 years demonstrated that childhood treatment of ADHD with stimulants reduces the risk of developing alcohol and other drug disorders in adulthood.²⁴ Regarding the effect stimulants have on active substance use, a 12-week, double-blind, randomized controlled trial of 48 cocaine-dependent adults with ADHD showed methylphenidate did not change cocaine abuse or craving, but did improve ADHD symptoms.²⁵

Clinicians also must assess whether untreated ADHD symptoms impair patients' work or other activities. Driving is a particular concern because ADHD is associated with risky driving habits, motor vehicle accidents, traffic violations, and driving license suspensions.²⁶ In a study that administered cognitive tests to 27 adults

with ADHD, methylphenidate treatment improved cognitive performance related to driving (eg, better visual-motor coordination under high-stress conditions, improved visual orientation, and sustained visual attention).²⁷ It is likely this effect could be generalized to other activities where safety is important. Finally, appropriate stimulant treatment may improve participation in rehabilitative programs.

Cons. Despite their positive effects, stimulants can have adverse effects and consequences.²⁸ In routinely prescribed dosages, methylphenidate and amphetamines can cause symptoms related to sympathetic activation, including anxiety, tics, anorexia/weight loss, and sleep disturbance. A 5-year study of 79 school-age children prescribed methylphenidate, dextroamphetamine, or pemoline, which is no longer available in the United States, showed a significant association between adherence to stimulants and persistence of physiological (eg, headaches, insomnia, anorexia) and mood-related (eg, irritability, dysphoria) side effects.²⁹ Stimulants' sympathomimetic properties also can lead to dangerous drug-drug interactions with monoamine oxidase inhibitors. For both methylphenidate and amphetamines, overdose can lead to seizures, cardiac toxicity, dysrhythmias, and hyperthermia. All stimulants carry an FDA "black-box" warning that lists increased risk of cardiac complications, sudden death, and psychiatric complications such as psychosis or mania.³⁰

Special considerations. All stimulants have potential for diversion or abuse. Pay close attention to these issues, especially in vulnerable populations and situations where rates of abuse and diversion are elevated. Among college students, white patients, fraternity/sorority members, and individuals with lower grade point averages may be at higher risk for nonmedical stimulant use.³¹ Adults who misuse or divert stimulants commonly have a history of substance abuse and conduct disorder.³² Short-acting stimulants are abused 4 times more often than extended-release preparations.³³

Table 3

Alternatives to stimulants for ADHD

Treatment option	Comments
Atomoxetine	Effectiveness may be limited to inattentive type
Modafinil	Well-tolerated but expensive, limited evidence, no FDA indication; may be a consideration in ADHD + SUD
α2-adrenergic agonist (eg, clonidine or guanfacine)	Useful when hyperactivity/impulsivity symptoms predominate, or when stimulant-induced insomnia occurs
Bupropion	Some evidence of mild efficacy, especially useful if nicotine dependence also is a target for treatment
Psychotherapy	Can be useful as adjunctive treatment, but as monotherapy it is of little benefit in ADHD

ADHD: attention-deficit/hyperactivity disorder; SUD: substance abuse disorder
Source: Reference 35

If your ADHD patient has active substance use, be clear that continued substance use is likely to limit stimulants' effectiveness. In patients who are actively using substances, it will be difficult to disentangle apparent nonresponse to stimulants from the negative cognitive effects of substance use.

Case discussion/suggestions. As Mr. C's case illustrates, there are alternatives to stimulants for ADHD. For example, atomoxetine, a selective norepinephrine reuptake inhibitor, may be considered a first-line agent in patients with mostly inattentive ADHD symptoms and comorbid stimulant abuse, or for those in whom stimulants cause adverse effects such as mood lability or tics.³⁴ Other alternatives to stimulants are listed in *Table 3*.³⁵

Because Mr. C did not respond to bupropion, which presumably was tried first because of his ongoing substance use, he asked about atomoxetine. This agent is not addictive and there is no evidence that it leads to or exacerbates substance use. Depending on Mr. C's symptom profile, atomoxetine might be a good choice. Continued monitoring of his marijuana use and frequent assessment of his motivation to quit are necessary. Psychoeducation about the cognitive effects of marijuana, including inattention and poor concentration, is important.

If Mr. C does not respond to atomoxetine, his psychiatrist will face a difficult decision. Setting Mr. C's marijuana use aside, symp-

toms that do not respond to atomoxetine or a second-line agent are likely to respond to a stimulant. However, several issues must be addressed. If Mr. C's motivation to stop using marijuana is low, how motivated is he to improve his ADHD symptoms? Next, would marijuana's depressive/blunting effects counteract the anticipated benefit of a stimulant? Also, what is the risk that Mr. C might sell or exchange his stimulants to obtain marijuana? Assessing these complicated questions is key. Another important factor in Mr. C's case is his wife's involvement. Does she monitor his marijuana use? Would she be willing to supervise Mr. C's stimulant use, and would he allow it?

Past or present SUDs are not an absolute contraindication to stimulant use. You should affirm the diagnosis and identify target symptoms. Consider nonstimulant alternatives if appropriate.

Legal liabilities

Being aware of the medicolegal issues of benzodiazepine and/or stimulant prescribing is crucial because a court may find a psychiatrist liable for negative outcomes (eg, suicide) when controlled substances are prescribed to a patient with a history of addiction.³⁶ The most prudent course is to weigh the pros and cons for each patient individually, taking into consideration the factors described above.⁸ This is consistent with guidelines from the American Psychiatric Association and the British Association for

Clinical Point

Short-acting stimulants are abused 4 times more often than extended-release formulations



Benzodiazepines and stimulants

Clinical Point

Provide and document explicit instructions that the patient will receive stimulants from only a single provider

Related Resources

- National Institute on Drug Abuse. Prescription drugs: abuse and addiction. Research Report Series, 2005. <http://drugabuse.gov/ResearchReports/Prescription/Prescription.html>.
- Galanter M, Kleber HD. The American Psychiatric Publishing textbook of substance abuse treatment. 4th ed. Arlington, VA: American Psychiatric Publishing, Inc; 2008.

Drug Brand Names

Alprazolam • Xanax	Gabapentin • Neurontin
Atomoxetine • Strattera	Guanfacine • Tenex, Intuniv
Bupropion • Wellbutrin, others	Lisdexamfetamine • Vyvanse
Chlordiazepoxide	Lithium • Eskalith, Lithobid
• Librium	Lorazepam • Ativan
Clonazepam • Klonopin	Methylphenidate • Ritalin, Concerta, others
Clonidine • Catapres	Mirtazapine • Remeron
Clorazepate • Tranxene	Mixed amphetamine salts
Dextroamphetamine	• Adderall
• Dexedrine	Modafinil • Provigil
Diazepam • Valium	Oxazepam • Serax
Diphenhydramine	Pemoline • Cylert
• Benadryl, others	Propranolol • Inderal
Doxepin • Silenor	Trazodone • Desyrel, Olepro
Estazolam • ProSom	Triazolam • Halcion

Disclosures

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Psychopharmacology,³⁷ both of which call for extreme caution in these cases.

Educate patients and caregivers about the risks of taking a controlled substance, including misuse, diversion, and theft. Provide and document explicit instructions that the patient will receive stimulants from only a single provider. Remind patients that state and federal authorities closely track controlled medications. Finally, a “stimulant contract” or “benzodiazepine contract,” similar to a pain or narcotic contract, may be useful to formally document discussions about appropriate medication use.

References

1. Ashton H. Guidelines for the rational use of benzodiazepines. When and what to use. *Drugs*. 1994; 48(1):25.
2. Mueller TI, Pagano ME, Rodriguez BF, et al. Long-term use of benzodiazepines in participants with comorbid anxiety and alcohol use disorders. *Alcohol Clin Exp Res*. 2005; 29(8):1411-1418.
3. Mueller TI, Goldenberg IM, Gordon AL, et al. Benzodiazepine use in anxiety disordered patients with and without a history of alcoholism. *J Clin Psychiatry*. 1996; 57(2):83-89.
4. Ashton H. The diagnosis and management of benzodiazepine dependence. *Curr Opin Psychiatry*. 2005;18(2):249-255.
5. Back SE, Brady KT. Anxiety disorders with comorbid substance use disorders: diagnostic and treatment considerations. *Psychiatric Annals*. 2008;38(11):724-729.
6. Walsh JM, Flegel R, Cangianelli LA, et al. Epidemiology of alcohol and other drug use among motor vehicle crash victims admitted to a trauma center. *Traffic Inj Prev*. 2004;5(3):254-260.
7. Ciraulo DA, Nace EP. Benzodiazepine treatment of anxiety or insomnia in substance abuse patients. *Am J Addict*. 2000;9(4):276-279; discussion 280-284.
8. Sattar S, Bhatia S. Benzodiazepines for substance abusers. *Current Psychiatry*. 2003;2(5):25-34.
9. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA*. 1990;264(19):2511-2518.
10. Kendler KS, Gallagher TJ, Abelson JM, et al. Lifetime prevalence, demographic risk factors, and diagnostic validity of nonaffective psychosis as assessed in a US community sample. The National Comorbidity Survey. *Arch Gen Psychiatry*. 1996;53(11):1022-1031.
11. Buckley PF. Prevalence and consequences of the dual diagnosis of substance abuse and severe mental illness. *J Clin Psychiatry*. 2006;67(suppl 7):5-9.
12. Bizzarri JV, Sbrana A, Rucci P, et al. The spectrum of substance abuse in bipolar disorder: reasons for use, sensation seeking and substance sensitivity. *Bipolar Disord*. 2007;9(3):213-220.
13. Brunette MF, Noordsy DL, Xie H, et al. Benzodiazepine use and abuse among patients with severe mental illness and co-occurring substance use disorders. *Psychiatr Serv*. 2003;54(10):1395-1401.
14. Clark RE, Xie H, Brunette MF, et al. Benzodiazepine prescription practices and substance abuse in persons with severe mental illness. *J Clin Psychiatry*. 2004;65(2):151-155.
15. Longo LP. Addiction: part I. Benzodiazepines—side effects, abuse risk and alternatives. *Am Fam Physician*. 2000;61(7):2121-2128.
16. Ciraulo DA, Barnhill JG, Ciraulo AM, et al. Alterations in pharmacodynamics of anxiolytics in abstinent alcoholic men: subjective responses, abuse liability, and electroencephalographic effects of alprazolam, diazepam, and buspirone. *J Clin Pharmacol*. 1997;37(1):64-73.
17. Casher MI, Bess JD. Manual of inpatient psychiatry. Cambridge, United Kingdom: Cambridge University Press; 2010.
18. Hofmann S, Smits JA. Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. *J Clin Psychiatry*. 2008;69(4):621-632.
19. Morgenthaler T, Kramer M, Alessi C, et al. Practice parameters for the psychological and behavioral treatment of insomnia: an update. An American Academy of Sleep Medicine report. *Sleep*. 2006;29(11):1415-1419.

Bottom Line

Patients with substance use disorders commonly have psychiatric comorbidities for which the best pharmacologic treatment carries abuse potential. Considering possible risks and benefits of prescribing a controlled substance and closely examining alternatives leads to the best possible treatment.

20. Wilens TE. Drug therapy for adults with attention-deficit hyperactivity disorder. *Drugs*. 2003;63(22):2395-2411.
21. Faraone SV, Biederman J, Mick E. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. *Psychol Med*. 2006; 36(2):159-165.
22. Biederman J, Wilens T, Mick E, et al. Is ADHD a risk factor for psychoactive substance use disorders? Findings from a four-year prospective follow-up study. *J Am Acad Child Adolesc Psychiatry*. 1997;36(1):21-29.
23. Waid L, Johnson D, Anton R. Attention-deficit hyperactivity disorder and substance abuse. In: Kranzler HR, Rounsaville BJ, eds. *Dual diagnosis and treatment: substance abuse and comorbid medical and psychiatric disorders*. vol 8. New York, NY: Marcel Dekker; 1998:393-425.
24. Wilens TE, Faraone SV, Biederman J, et al. Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics*. 2003;111(1):179-185.
25. Schubiner H, Saules KK, Arfken CL, et al. Double-blind placebo-controlled trial of methylphenidate in the treatment of adult ADHD patients with comorbid cocaine dependence. *Exp Clin Psychopharmacol*. 2002;10(3):286-294.
26. Barkley RA, Murphy KR, Kwasnik D. Motor vehicle driving competencies and risks in teens and young adults with attention deficit hyperactivity disorder. *Pediatrics*. 1996;98(6 Pt 1):1089-1095.
27. Sobanski E, Sabljic D, Alm B, et al. Driving-related risks and impact of methylphenidate treatment on driving in adults with attention-deficit/hyperactivity disorder (ADHD). *J Neural Transm*. 2008;115(2):347-356.
28. Leonard BE, McCartan D, White J, et al. Methylphenidate: a review of its neuropharmacological, neuropsychological and adverse clinical effects. *Hum Psychopharmacol*. 2004;19(3):151-180.
29. Charach A, Ickowicz A, Schachar R. Stimulant treatment over five years: adherence, effectiveness, and adverse effects. *J Am Acad Child Adolesc Psychiatry*. 2004;43(5):559-567.
30. Schatzberg AF, Nemeroff CB. *The American Psychiatric Publishing textbook of psychopharmacology*. 4th ed. Arlington, VA: American Psychiatric Publishing, Inc; 2009.
31. Wilens TE, Adler LA, Adams J, et al. Misuse and diversion of stimulants prescribed for ADHD: a systematic review of the literature. *J Am Acad Child Adolesc Psychiatry*. 2008;47(1):21-31.
32. Wilens TE, Gignac M, Swezey A, et al. Characteristics of adolescents and young adults with ADHD who divert or misuse their prescribed medications. *J Am Acad Child Adolesc Psychiatry*. 2006;45(4):408-414.
33. Bright GM. Abuse of medications employed for the treatment of ADHD: results from a large-scale community survey. *Medscape J Med*. 2008;10(5):111.
34. Biederman J, Spencer T, Wilens T. Evidence-based pharmacotherapy for attention-deficit hyperactivity disorder. *Int J Neuropsychopharmacol*. 2004;7(1):77-97.
35. Mann N, Bitsios P. Modafinil treatment of amphetamine abuse in adult ADHD. *J Psychopharmacol*. 2009;23(4): 468-471.
36. Grant JE. Prudent prescribing for patients with addictions. *Current Psychiatry*. 2006;5(10):99-102.
37. Lingford-Hughes AR, Welch S, Nutt DJ, and the British Association for Psychopharmacology. Evidence-based guidelines for the pharmacological management of substance misuse, addiction and comorbidity: recommendations from the British Association for Psychopharmacology. *J Psychopharmacol*. 2004;18(3):293-335.

This month's instant poll



Mr. D, age 62, has been taking trazodone, 25 mg/d, which relieves his insomnia. After his grandchild suddenly passes away, trazodone is no longer effective and he asks you to prescribe a different medication. Mr. D has a remote history of alcohol abuse, but has been sober for 20 years. **What would you do?**

- Prescribe diazepam, 5 mg at bedtime
- Prescribe zolpidem, 10 mg at bedtime
- Prescribe an antihistamine, such as diphenhydramine, 25 mg/d at bedtime
- Recommend cognitive-behavioral therapy or sleep hygiene counseling

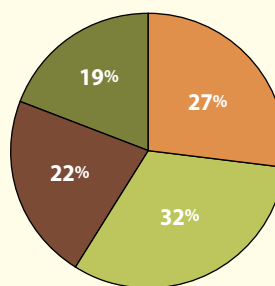
See "Benzodiazepines and stimulants for patients with substance use disorders" page 58-67



Visit CurrentPsychiatry.com to answer the Instant Poll and see how your colleagues responded. **Click on "Have more to say!"** to comment.

MARCH POLL RESULTS

You've been successfully treating Mrs. K, age 31, for major depressive disorder with sertraline, 100 mg/d, and for prescription opioid addiction with buprenorphine and naloxone, 12 mg/d. She has responded well to each medication. At her next visit, Mrs. K reveals that she is pregnant. **Which treatment option would you choose?**



27% Initiate tapering to discontinue buprenorphine and naloxone

32% Switch Mrs. K to buprenorphine, 12 mg/d

22% Refer her to a facility that can provide methadone maintenance treatment

19% Continue buprenorphine and naloxone, 12 mg/d



▲ Data obtained via CurrentPsychiatry.com, March 2011

SUGGESTED READING:

Miller SC, Fernandez L, Soria R. *CURRENT PSYCHIATRY*. 2011;10(3):34-45.