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Joshua D. Feder, MD
Editor-in-Chief

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IN THIS ISSUE

Substance Use in Children and Adolescents

Learning Objectives

After reading these articles, you should be able to:

1. Describe the challenges of diagnosing and treating substance use disorders in children and adolescents.
2. Identify the features of a high-quality clinical study.
3. Summarize some of the findings in the literature regarding psychiatric treatment for children and adolescents.

Reading Research: Details Matter

Glen Spielmans, PhD. Professor of Psychology, Metropolitan State University, St. Paul, MN.

Dr. Spielmans has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

When headlines report on positive treatment results from a study, families will come in asking about those results. This article will help you determine what makes a study a good one, and conversely what makes a not-so-great one. With this information, you can be better prepared to talk with families about research studies and results that can affect treatment decisions.

Open-label studies vs randomized controlled trials

In open-label studies, both researchers and patients know what the treatment is, and there is no control group. Positive results in an open-label study can be misleading because the patients may improve due to positive expectations or the natural course of their illness—rather than the treatment. Thus, open-label studies can offer preliminary hope but not solid evidence of efficacy.

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Highlights From This Issue

We need to take alcohol abuse in teens very seriously. Learn why and what we can do in our interview with Dr. Amy Yule.

Performance-enhancing substances are more commonly used than most of us think, and they can be medically dangerous as well as create psychiatric problems.

Our simple guide to reading research can help you efficiently vet studies and make better clinical decisions.

Q&A With the Expert

Teen Drinking: Risks and Responses
Amy Yule, MD

Director of Adolescent Addiction Psychiatry, Boston Medical Center, Boston, MA.

Dr. Yule has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CCPR: Welcome, Dr. Yule. How prevalent is teen drinking?

Dr. Yule: While there has been a decline in alcohol use since the 1980s, alcohol remains the substance most widely used by adolescents. When we look at past-month use by 12th graders in 2019, 5.7% had smoked cigarettes, 22.3% had used cannabis, and 29.3% had used alcohol (www.niaaa.nih.gov/publications/brochures-and-fact-sheets/underage-drinking). It's not just that they're drinking a beer or two; 17.5% of 12th graders had been drunk in the past month.

CCPR: Are they aiming to get drunk?

Dr. Yule: Yes. They may not drink as frequently as some adults, but when they do drink, they're drinking very heavily.

CCPR: Talk to us about the mortality risk associated with youth drinking.

Dr. Yule: The consequences of drinking are striking.

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Expert Interview—Teen Drinking: Risks and Responses
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Between 2006 and 2010, alcohol was a factor in the deaths of 4300 young people under the age of 21. It's frequently a factor in motor vehicle crashes and homicides, alcohol overdoses, falls, burns, and drownings. Alcohol is also often involved in completed suicides in adolescents. And kids die from alcohol overdoses—the term alcohol overdose is an important shift in language from alcohol poisoning. To me, "alcohol poisoning" makes it seem accidental or out of an individual's control. With increased attention to the opioid epidemic, the general public seems to have a greater awareness and understanding that an overdose is dangerous. I think it is helpful to use the same terminology when discussing alcohol.

CCPR: And what about morbidity that falls short of mortality?

Dr. Yule: Alcohol impairs judgment, increasing the risk of physical and sexual assault. I hear so many stories of sexual assaults on young women who've been intoxicated, and physical fights or violence among young men who are intoxicated. It is also important to recognize that a blackout is not a trivial thing—it is a significant neurologic event.

CCPR: What is the risk that kids will develop an alcohol use disorder (AUD)?

Dr. Yule: According to the National Institute of Alcohol Abuse and Alcoholism (NIAAA), people who start drinking before the age of 15 are four times more likely to meet the criteria for alcohol dependence at some point in their life (www.niaaa.nih.gov/publications/brochures-and-fact-sheets/underage-drinking). DSM-IV-TR's "alcohol abuse" translates to a mild substance use disorder (SUD) in the DSM-5, and DSM-IV-TR's "alcohol dependence" is generally equivalent to a moderate or severe SUD in the DSM-5.

CCPR: What current research is there that compels child psychiatrists to intervene?

Dr. Yule: Teens are at high risk for serious consequences associated with heavy alcohol use. Early onset means kids are at even higher risk for an SUD later in life. Kids with psychiatric disorders are at higher risk for an SUD relative to kids who don't have psychiatric disorders (Groenman AP et al, *J Am Acad Child Adolesc Psychiatry* 2017;56(7):556–569).

CCPR: What should child psychiatrists be doing?

Dr. Yule: We may not be able to change the fact that the frontal lobe of an adolescent's brain is still developing and they are more likely to take risks. However, we can be talking with children, adolescents, and their parents about risks associated with alcohol use in adolescence. Other adults in an adolescent's life, like high school teachers or pediatricians, often have less contact with parents and/or less time during an appointment to address these issues. As child psychiatrists, we are well positioned to screen and provide preventative messages about the risks related to alcohol use, especially if kids are transitioning to college. And since the youth we work with are at elevated risk for an AUD, it's our job to address this. We have often been working with children since they were younger through adolescence and have developed a strong relationship with their family.

CCPR: Talk to us about specific screens.

Dr. Yule: The CRAFFT (www.crafft.org) is a great tool to assess for substance use and problems related to substance use. But it is hard in the moment to remember that CRAFFT stands for Car Relax Alone Forget Friends Trouble.

CCPR: Is there something better than the CRAFFT?

Dr. Yule: NIAAA developed two screening questions that I find easy to remember, and they're tailored to the child's developmental age, whether 9 to 11 years old, 11 to 14, or 14 to 18 (www.niaaa.nih.gov/alcohols-effects-health/professional-education-materials/alcohol-screening-and-brief-intervention-youth-practitioners-guide). I like this screener because it sends the message to screen early and often and gives us language that we can use with a 9- to 11-year-old, since they are at a different stage of development than a 14- to 18-year-old. You might see the 9- to 11-year-old with the parents in the room, and it's OK to ask these questions. Ideally, we screen without parents in the room to get the most open and valid answer, but if the parents are present, you're sending a message that alcohol use in a child or an adolescent is not the norm. The media portrays heavy substance use as a rite of passage of adolescence, and it's not.

CCPR: With middle schoolers, I ask, "Do you know kids at school who have already started fooling around with alcohol and other stuff, maybe cigarettes?" If they say yes, I say, "Well, how much have you—not 'if,' but how much *have* you seen that stuff?" And they will or they won't tell me.

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This CME/CE activity is intended for psychiatrists, psychiatric nurses, psychologists, and other health care professionals with an interest in the diagnosis and treatment of psychiatric disorders.

Expert Interview—Teen Drinking: Risks and Responses

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Dr. Yule: That's how the screener works: For middle schoolers, ask about friends' use, then their use: "Do any of your friends drink? How about you? Have you ever had more than a few sips?" For adolescents, it starts with them and then moves to friends. It is also important to ask adolescents how they are accessing alcohol, since kids use what they access. If you're able to access alcohol easily, you're more vulnerable to use alcohol early and develop an AUD.

CCPR: Do you have any tips for sorting out the extent of a substance problem in teens?

Dr. Yule: When I'm working with kids in clinic, one of my first questions is, how are they functioning? How are they doing in school? Are they attending school? These are markers of how much someone's struggling, and sometimes you can use them to engage a kid in being more motivated to make a change. When you have an adolescent who's trying to educate you on how you're "wrong" and that there's no problem with their substance use, try to look at functioning and what's important to them and you can sometimes can find an edge to get them to think a little bit more about it. For instance, they may notice that their athletic performance is impaired when they're hung over or if they're really high on marijuana. They may tell you, "I don't have a problem with alcohol or marijuana," but then they tell you that they never drink heavily before a game or meet. Why is that? These are the edges where you can try to build some insight or build motivation for change.

"When you have an adolescent who's trying to educate you on how you're 'wrong,' look at functioning and what's important to them. They may tell you, 'I don't have a problem with alcohol or marijuana,' but then also say that they never drink heavily or get high before a game or a meet. These are the edges where you can build motivation for change."

Amy Yule, MD

CCPR: The diagnostic criteria can be confusing to apply when working with adolescents.

Dr. Yule: Yes. It's tricky because the diagnostic criteria we use to make the diagnosis of an SUD were designed for adults and don't match youth very well. But any child, adolescent, or young adult who's running into serious consequences related to their substance use would benefit from therapies or interventions addressing that use. So, if someone comes to the emergency room after an alcohol overdose, we want to very closely monitor their substance use in the near future, even if they don't technically meet the criteria for an AUD.

CCPR: How do you approach parents—in particular, those families that traditionally allow youth to have some wine with dinner?

Dr. Yule: With drinking that is part of family culture, it is helpful to think about how half a glass of wine with your family at the table is very different than binge drinking with your friends. And even if alcohol use is part of family culture, if their child is struggling with an AUD, as a family they may need to make the decision not to have alcohol in the house.

CCPR: Teens often listen to peers more than parents.

Dr. Yule: Parents often think that the messages they send don't matter, because it's all about the kid's friends, but authoritative parenting—not authoritarian parenting—is actually very effective in decreasing the risk for heavy alcohol use among adolescents (www.niaaa.nih.gov/publications/brochures-and-fact-sheets/parenting-prevent-childhood-alcohol-use). It involves sending a clear message about the importance of not drinking, avoiding heavy alcohol use. Those things matter and can change an adolescent's drinking patterns.

CCPR: What words does an authoritative parent use?

Dr. Yule: "Our family's expectation is that you're not going to drink before the age of 21, and it's important to us that you make healthy choices that support your growth and development." For kids with mental health challenges who say that other kids use and are doing fine, you need to tell them, "You're working hard and using therapy and medication, and you are at higher risk for making things a lot worse if you use alcohol or other substances." They might respond "you suck" and slam the door, but they hear the message that this is the expectation and the concern.

CCPR: What about teen activities and how they play into drinking?

Dr. Yule: It can be hard for older adolescents or young adults to find activities or access things that don't involve substances. Parents should consider making the extra effort to facilitate their child going to the rock climbing gym on a Friday night, instead of going to a friend's house where the friend's parents might not be there. It's not about saying they can't ever leave the house or have fun anymore. We want to help them connect with other activities that are healthy and fun for them. It often takes quite a bit of problem solving and brainstorming to help them do that.

CCPR: How do you motivate teens to not drink?

Dr. Yule: Motivational interviewing is an important tool. There are a lot of data supporting the use of motivational enhancement therapy paired with cognitive behavioral therapy (CBT) for treating SUDs in adolescents. The challenge is you can't do CBT with someone who's not ready to change yet. You have to develop their motivation to be ready to make a change. Try to understand why the teen might want to drink and what might drive them to drink. Then

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provide them with education about why you're concerned about their substance use, teach them skills, and provide them with structure.

CCPR: Are there specific disparities in risk and treatment among members of Black, Latinx, and LGBTQIA+ communities?

Dr. Yule: Regarding racial and ethnic disparities, access to care is not equal to Caucasians. LGBTQIA+ kids are at higher risk for problems with substance use, and so it's really important to be screening and keeping an eye on that. The other thing to be aware of is gender differences. While there are equal rates of alcohol use disorders among adolescent boys and girls, boys are more likely to receive treatment than girls for all SUDs, including AUD. Substance use, in particular alcohol use, is an equal-opportunity problem across genders, races, and ethnicities. We need to identify it and support teens' access to care in all cases.

CCPR: Why don't girls get treatment? Is their use not as obvious?

Dr. Yule: Unfortunately, there hasn't been a lot of emphasis on looking at why girls with an SUD are less likely to be in treatment than adolescent boys.

CCPR: Do you have a bottom-line message to share with our readers?

Dr. Yule: The kids we work with are at higher risk than other adolescents, and we really need to be screening and identifying alcohol use and sending a message that this is not a normal part of adolescent development. Child psychiatrists often get discouraged that kids are unlikely to change their substance use. But if they're drinking heavily or smoking marijuana all day, it's going to impact how effective your medication and other treatments are, so you can't ignore it. And they do change. They do get better.

CCPR: Thank you for your time, Dr. Yule.

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Reading Research: Details Matter

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Randomized controlled trials (RCTs) are a better way to evaluate a treatment's effects—but they must be examined closely. RCTs are supposed to be double-blind, with participants and clinical raters unaware of who receives which intervention until the study is over. But drug side effects can "unblind" such studies and bias their results. Drugs with more obvious physical or psychological effects can lead to greater unblinding; for instance, a high dose of olanzapine is more likely to cause unblinding than a low dose of fluoxetine. Also, the same clinical raters usually evaluate both efficacy and adverse events. A rater who notes drug-specific adverse events (or a lack of adverse events) may guess which patients are receiving the active treatment, defeating the purpose of the RCT.

Defining success: Effect size is key

Researchers often declare that a treatment "works" if it has a statistically significant benefit over placebo. What does "statistical significance" mean? In an RCT, suppose an antidepressant outperforms placebo by 2 points on a depression rating scale. Based on scores obtained through the rating scale, statistical calculations generate a p-value. The p-value is the probability that the obtained result (the medication outperforming placebo by 2 points) could be explained by the *null hypothesis,* which claims that there is no treatment effect. In other words, if the drug really had no effect (ie, the null hypothesis is true), what are the odds that the study would find at least a 2-point benefit for the drug? If the p-value is less than .05 (5%), the result is deemed statistically significant. However, statistical significance does *not* necessarily mean that the result is important! Among other things, the size of the sample is influential—a very small treatment benefit may be statistically significant in a large study. Statistical significance gives some confidence that there is a treatment effect, so it's an important first step, but it's not the final word on treatment efficacy.

What we really want to know is the *effect size*—the magnitude of the treatment effect. Common convention on effect sizes is that 0.20 = small, 0.50 = medium, and 0.80 = large. In psychiatry, effective treatments nearly always generate small to medium effect sizes (compared to placebo). It is now standard practice to report effect size in treatment studies. A study that fails to report effect size may be trying to downplay a minimal treatment benefit.

Categorical outcomes sound great—but aren't always impressive

Many studies report improvement in symptom scores along a continuous measure. Clinicians often prefer categorical outcomes, like response and remission. However, categories have arbitrary cut-off points. For instance, in autism we can look at a total ADOS score or a change from the severe to moderate range, from the moderate to mild range, etc. But this is tricky—if a patient's score goes from the low end of severe to the very high end of moderate, that shift is not necessarily clinically meaningful. Pay attention to total scores along with any categorical outcomes.

Always check the NNT or NNH

For categorical outcomes, one should examine the number needed to treat (NNT) and number needed to harm (NNH). These values refer to the number of people who would need to receive treatment in order to gain an additional positive (NNT) or negative (NNH) outcome over what would have occurred if all

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participants received placebo. For instance, an NNT of 8 for "response" means 8 patients would need to be treated to gain a response that would not have occurred if all 8 patients had taken placebo. An NNT of 5 is often considered impressive, while an NNT of more than 10 is often considered unimpressive, but there is no firm consensus on this. For NNH, the acceptable range might vary from 10 to 100 depending on the side effect or the likelihood of discontinuation due to a side effect. For severe side effects such as Stevens-Johnson syndrome, you'll want to see a much higher NNH.

Distinguish primary from secondary outcomes

RCTs typically use several outcomes. Researchers declare a single outcome as the *primary outcome* before the study starts. This prevents researchers from cherry-picking a positive outcome after the data have been examined, then declaring it as the primary outcome. When reading a study, you should examine all *secondary outcomes* as well. Patient self-reports, quality of life, levels of functioning in school/work/family life—these measures provide valuable information and should be closely considered along with clinician-rated symptom scales. There may be different results across these outcomes. For instance, antidepressants have been shown to provide small benefits on depression rating scales for youth, but yield no benefits on depression self-reports and quality of life measures compared to placebo (Spielmans GI and Gerwig K, *Psychother Psychosom* 2014;83(3):158–164).

Beware medication discontinuation designs—they may not mean the drug works

Most RCTs last only a few weeks, while child development is measured in years. You cannot assume long-lasting benefit based on a positive short-term RCT. Most studies of long-term drug efficacy inappropriately use a randomized discontinuation design (El-Mallakh RS and Briscoe B, *CNS Drugs* 2012;26(2):97–109). These studies start with only participants who have responded to the drug in the short term. By random assignment, some participants are (usually abruptly) switched to placebo while others continue to take the drug. This conflates drug withdrawal effects among those switched to placebo with treatment efficacy in those who keep taking the drug. The worse the drug discontinuation effects, the worse the placebo group performs after being taken off the medication—and the better those who stay on the medication seem in comparison. A better test of long-term effects is to simply lengthen a short-term placebo-controlled RCT (Khan A et al, *J Psychiatr Res* 2008;42(10):791–796). Longer studies are far more expensive and might reduce the hoped-for positive findings of the researchers, though, so they are rarely done.

Adverse events may be underreported

Ideally, RCTs should accurately detect adverse events. While weight and some lab measures are usually reliably assessed in RCTs, most adverse events are assessed vaguely. For example, until recently, there was little attempt to ask specific questions regarding suicidality in most treatment studies, leading to an underreporting of such events. Adverse events must be systematically assessed, otherwise studies may be unable to detect them. Also, researchers often don't report all recorded adverse events in journal articles (Hughes S et al, *BMJ Open* 2014;4(7):e005535).

Replication of results is crucial

It's easy to get excited about published positive treatment results, but further research may or may not support the initial findings. For industry studies, replication from a non-industry team is important. For therapy studies, you want to see replication of positive results by a separate research group. Two good RCTs of the same treatment for the same indication showing good effect size represent much more powerful evidence than a single trial. How often does this happen in child and adolescent psychopharmacology? Not often. Some treatments have demonstrated consistently poor results; for example, there are multiple studies showing no significant effect of desvenlafaxine or paroxetine on depression in youth.

"Doctor, what about this study?"

How can we help families understand that much popular press coverage of research is misleading, without sounding cynical? Listen respectfully, then calmly and neutrally describe the hope that an open-label study provides, and stress that controlled trials are needed to know whether a treatment is truly helpful. For example, in *CCPR*'s Jan/Feb/March 2021 issue, we talked with Dr. Aaron Besterman about how results from pharmacogenomic testing, while interesting, are unlikely in most cases to lead to changes in good treatment.

CCPR VERDICT: You will hear about and read research your entire career. Pay attention to the quality of the study and effect size. Educate families about how you use your professional judgment to give them truly evidence-based recommendations. We've added a Clinical Research Checklist box below as a guide to help you interpret study results and limitations.

Clinical Research Checklist

Randomized controlled trial (RCT) or open label?

- If open label, then the natural course of illness, placebo effect, and researcher biases may have caused improvement, rather than the treatment itself.
- If RCT, is everyone blind to which treatment the patient received? Note that drug side effects might unblind treatment.

For each efficacy outcome, ask:

- Are results statistically significant?
- What is the effect size of treatment? 0.20 = small, 0.50 = medium, 0.80 = large.

Are there parent reports, self-reports, daily functioning, or quality of life measurements?

Remember that categorical outcomes (eg, remission, response) are usually based on arbitrary cutoff scores. Always consider categorical outcomes in context of rating scale scores and other outcomes.

- What is the number needed to treat (NNT) for these outcomes?

If an adverse event is not systematically measured, it is likely underreported.

- Is a drug effective in the long term? Note that randomly reassigning some patients from drug to placebo may cause drug discontinuation effects and invalidate the comparison.

Q&A With the Expert

Addressing the Hazards of Performance-Enhancing Substances

Kyle T. Ganson, PhD, MSW

Assistant professor at the University of Toronto's Factor-Inwentash Faculty of Social Work.

Dr. Ganson has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CCPR: Welcome, Dr. Ganson. Tell us about your current work.

Dr. Ganson: I'm an assistant professor at Factor-Inwentash Faculty of Social Work at the University of Toronto. I've been focusing my research predominantly on eating disorders and muscle-enhancing behaviors and performance-enhancing substance use among adolescents and young adults.

CCPR: When we talk about performance-enhancing products and substances, what specifically are we referring to?

Dr. Ganson: These products range from readily available over-the-counter creatine monohydrate, whey protein powders, and amino acids to illegal substances like anabolic steroids.

CCPR: What is the scope of the problem?

Dr. Ganson: There are multiple aspects. One is the accessibility factor. Young people can buy many of these legal products at the local pharmacy, grocery store, GNC, or vitamin shop. Another aspect is that similar to vitamins, the FDA doesn't regulate them and ensure that the products are safe or that they are pure or even contain what they say they do. This obviously can create problems for young people who maybe don't have the knowledge or wherewithal to think critically about the substances they put in their bodies. They do not know when not to trust the substances, and this can lead to adverse outcomes.

CCPR: How many kids and adolescents are using these products? And how many in the mental health population?

Dr. Ganson: We published a study in 2020 looking at prevalence and correlates of muscle-enhancing behaviors. We looked at 18- to 26-year-olds in the general population and found that upwards of 16% of males had used legal performance-enhancing substances in the past year, such as creatine. For females, it was only about 1%. We found that nearly a third of teen boys were trying to gain weight. Among the clinical population, we particularly see performance-enhancing substance use in men with eating disorders or muscle dysmorphia (Nagata JM et al, *Int J Adolesc Med Health* 2020. Epub ahead of print).

CCPR: Remind us—what is muscle dysmorphia?

Dr. Ganson: In the DSM-5, it's a type of body dysmorphic disorder in which the person has an overvalued belief that their musculature is imperfectly formed. It's a pathological thinking around their bodies. They attempt to change the body to reach an ideal and become more compulsive and wrapped in psychopathology. Use of muscle-enhancing substances is common in these patients because they align with the pathological aspects of those disorders. For example, studies have suggested that use of steroids occurs at higher prevalence among males with muscle dysmorphia (Olivardia R et al, *Am J Psychiatry* 2000;157(8):1291–1296; Cooper M et al, *Int J Eat Disord* 2020;53(10):1583–1604).

CCPR: Talk to us about the range of motivations that drive this use.

Dr. Ganson: Athletic performance is a major driver in the general population as well as in youth. Young athletes want to improve their performance and decrease recovery time after exertion. Aside from athletic performance, they're predominantly used for achieving muscular strength, attempting to alter the body to look muscular, lean, and cut.

CCPR: This kind of substance use isn't necessarily on the radar of mental health providers.

Dr. Ganson: Correct. Here in Toronto, there was a recent story in the news about the increase in young people calling help lines and needing hospital-level treatment for eating disorders and disordered eating behaviors. For these patients, we have well-researched diagnostic criteria and treatment. However, performance-enhancing substance use is not as well researched or understood. There's an assumption that these products are safe. Clinicians are not aware of how important it is to really inquire about what kind of substances young people are using and how that may impact their functioning. This is particularly true for boys and men who may not "look" like a traditional eating disorder patient.

CCPR: How do we know when it crosses the line into problem use?

Dr. Ganson: It becomes problematic when it is combined with other behaviors, such as alcohol or polysubstance use. Also, it often occurs amidst other disordered eating and weight control behaviors, like excessive exercise, intermittent fasting, restrictive dieting, etc.

CCPR: Do these drugs threaten physical health as well?

Dr. Ganson: We just published a study looking at whether use of legal performance-enhancing substances prospectively increases cardiovascular disease risks, and we didn't find significant associations. However, one recent study showed that young people who use these legal substances have more adverse events like going to the hospital or emergency room or even death—compared, for instance, to use of multivitamins, which are generally

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considered safe (Or F et al, *J Adolesc Health* 2019;65(4):455–461). The problems may arise when these over-the-counter substances are contaminated or don't fully describe the contents of the products.

CCPR: Do you have a sense of how many of these products are problematic?

Dr. Ganson: Studies have shown a range of products that are contaminated with banned and dangerous substances. However, consumers often won't know whether a particular product is toxic at the time of purchase. Another problem is that use of legal performance-enhancing substances can lead to more intense, anabolic-androgenic steroid use, which we found in a recent study. We've also shown that legal performance-enhancing substance use can lead to problematic alcohol behavior, like binge drinking and legal issues due to alcohol. These problematic relationships are particularly common among men (Ganson KT et al, *Pediatrics* 2020;146(3):e20200409).

CCPR: So use of performance enhancers is a gateway process.

Dr. Ganson: Right.

CCPR: Can you talk in more detail about the products that are most commonly used?

Dr. Ganson: Sure—let's begin with protein supplements, which are quite common. Often, they come in the form of whey protein, which comes from dairy. These products can be in powder form or bars. They are meant to build muscle and lean tissue. They also provide the body with more calories, which will help build muscle mass after workouts. The major risk is from contamination of these products.

CCPR: Is there any evidence that these work?

Dr. Ganson: They can help—after all, they contain calories and protein, so they can help you build muscle mass. However, they are likely not needed if one's diet already contains enough protein.

CCPR: What about creatine monohydrate? I understand that your study on cardiovascular disease risk factors didn't find any correlations with use of this product.

Dr. Ganson: Creatine is naturally found in the body. The supplement is meant for increasing muscle mass and improving performance by delaying muscle fatigue. There is science showing it can actually help these things. There is less research on how creatine use impacts young people, but the main concern with creatine is the potential impacts on the kidneys in people with concurrent health problems.

"There's an assumption that performance-enhancing products are safe. Clinicians are not aware of how important it is to really inquire about what kind of substances young people are using and how that may impact their functioning. This is particularly true for boys and men who may not 'look' like a traditional eating disorder patient."

Kyle T. Ganson, PhD, MSW

CCPR: What's Andro?

Dr. Ganson: Andro is short for androstenedione. It is intended to increase the production of testosterone, which of course is meant to increase athletic performance, build muscle, and reduce body fat. This substance is no longer legal and is banned for collegiate and pro athletes.

CCPR: What are the concerns around it?

Dr. Ganson: It can reduce natural testosterone production. Similar to anabolic-androgenic steroids, there are also concerns with cardiovascular, endocrine, psychiatric, and kidney problems (Pope HG et al, *Endocr Rev* 2014;35(3):341–375).

CCPR: And how about anabolic steroids? Even though they're illegal, they seem to be ubiquitous within the world of performance enhancement.

Dr. Ganson: They're probably the most effective means of increasing muscle mass, increasing strength, and increasing muscularity and leanness, though of course they are highly problematic and potentially dangerous. I don't mean to say everybody who uses legal performance-enhancing substances goes on to use steroids. But there's certainly a culture within the muscle-building community and performance-enhancing community that believes using steroids is necessary.

CCPR: Is it easy to obtain steroids?

Dr. Ganson: I can't say yes for sure, but I would assume so—especially in the gym culture of weightlifting and bodybuilding.

CCPR: What amino acids are used?

Dr. Ganson: There are a variety of amino acids, such as hydroxymethyl butyrate (HMB), that are intended to help repair muscle damage or buffer metabolic acidosis resulting from high-intensity workouts. High doses of some amino acids can cause fatty liver disease as well as gout. And again, it may not be only the amino acid that is the problem, but potentially the purity of the contents and an overall constellation of behaviors.

CCPR: Which specific sports communities are more likely to use these substances? And are there are other cultural groups that are more impacted?

Dr. Ganson: Wrestling, football, weightlifting, swimming, and cycling are sports communities where body weight is crucial. You need to have a certain level of strength and/or have a certain body size. Men and boys are more likely to use these substances than women, and sexual minority boys and men are more likely to use these

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substances than heterosexual men.

CCPR: How do you assess a patient's use?

Dr. Ganson: Be specific. Ask: "Do you use substances for building muscle or improving athletic performance or exercise performance?" Ask about whey protein, creatine, amino acids, Andro, and steroids. For each one, ask about frequency, dosing patterns, intensity, and purpose. Paint the picture of how and why this person is using these substances. Next, figure out how this relates to the presenting problem and think about how you want to work with the client about changing behavior. Screen for other problems tied to body image. Talk about body image and eating habits, looking for related disorders.

CCPR: Then what?

Dr. Ganson: Provide psychoeducation about the risks involved in using these. If you're working with minors, parents may need to be involved. Go through the process of getting consent from the youth and provide information to the parent about the substances and the potential hazards. Help parents understand why the teen is using it. What deeper issues need to be addressed?

CCPR: Is there research on such things like motivational interviewing to help these patients? Is there an evidence base?

Dr. Ganson: There's not a lot there, but motivational interviewing would make sense for the substance use aspects and eating disorder approaches, like cognitive behavioral therapy (CBT), for body image problems. You diminish the need to use some of the substances because you're resolving the more root issue, which is the muscle or body dysmorphia or any sort of eating disorder. CBT is one of the main treatment modalities for body dysmorphic disorder, exposure-type therapy as well—trying to help people expose themselves to whatever uncomfortable sort of body aspects they're feeling particularly obsessive about.

CCPR: Tell us more about working with these patients.

Dr. Ganson: Try to get to the crux of why. Why use these substances? What's the need for improving that performance to a certain level that you feel you can't attain otherwise? For high school athletes, that may be tied to things like the pressure of getting scholarships—so who's providing that pressure, and is that pressure necessary? For collegiate athletes, it could be wanting to improve to a certain level to make it into pro sports. Outside of athletics, it could be about body type: Why is it so necessary that you have a certain body type that adheres to a certain ideal? To me, that indicates that there is a larger issue happening that needs to be addressed, whether that be poor self-esteem, not feeling like they fit in, getting bullied, etc. Also, kids in athletics can have a lot of pressure from coaches and parents, and also pressure from themselves to achieve a certain level of status within that sport or within that area.

CCPR: Thank you for your time, Dr. Ganson.

❖ ❖ ❖

Research Updates IN PSYCHIATRY

DMDD

Citalopram Plus Stimulants for Chronic Irritability?

REVIEW OF: Towbin K et al, *J Am Acad Child Adolesc Psychiatry* 2020;59(3):350–361

STUDY TYPE: Randomized controlled trial

Chronic irritability in youth is ever-present in daily practice. Currently called disruptive mood dysregulation disorder (DMDD) in the DSM-5, there is an ever-evolving debate about how to treat this condition, but no definitive conclusion. While there are some encouraging studies of parent management training and cognitive behavioral therapy for DMDD, this small but double-blind placebo-controlled study tried to illuminate possible pharmacological options.

The National Institute of Mental Health (NIMH) conducted an 8-week randomized controlled trial of 53 youth (ages 7–17 years old) with DMDD, in which 25 patients were randomized to stimulants plus adjunctive citalopram (Celexa), and 28 patients were randomized to stimulants plus placebo. The authors argued that since ADHD, anxiety, and depression are often comorbid with DMDD, methylphenidates and citalopram were chosen, although specific reasons for those choices were not noted. There was a 5-week lead-in phase in which all participants received stimulants. Children who remained symptomatic entered the randomized part of the trial. The average dosage of citalopram was 28.33 mg per day. Out of the 53 participants randomized to the trial, 8 did not complete it, 7 of whom withdrew assent during the study.

Citalopram significantly outperformed placebo on the primary outcome of Clinical Global Impression – Improvement (CGI-I): 35% vs 6% with an NNT of 3. However, there was no significant difference in secondary outcomes of Clinical Global Impression – Severity (CGI-S) and functional impairment. Both of these are markers of ongoing severity of condition and arguably more important markers of

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Research Updates
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response, but neither showed statistically significant differences between the two groups.

CCPR'S TAKE

While therapy remains the first-line treatment for DMDD, methylphenidate may be of some help, and if the response is not adequate, citalopram may be a reasonable adjunct to try.

—Eric Robbins, MD. Dr. Robbins has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

ANXIETY

SSRIs vs SNRIs in Pediatric Anxiety Disorders: Which Are More Tolerable?

REVIEW OF: Mills JA and Strawn JR, *J Am Acad Child Adolesc Psychiatry* 2020;59(11):1240–1251

STUDY TYPE: Meta-analysis

For children with anxiety disorders and OCD, SSRIs produce faster and greater improvement than SNRIs (Strawn JR et al, *J Am Acad Child Adolesc Psychiatry* 2018;57(4):235–244.e2). Unfortunately, adverse effects slow down our dose titration and increase the risk of treatment discontinuation, and we lack systematic evaluations of adverse effects in pediatric patients. How can we predict these effects?

The authors analyzed data on 2,631 children or adolescents from 18 prospective, randomized, placebo-controlled studies that evaluated the use of SSRIs (fluoxetine, fluvoxamine, paroxetine, sertraline) or SNRIs (atomoxetine, venlafaxine, duloxetine) in anxiety disorders in children and adolescents. Median duration of acute treatment was 11 weeks. Researchers calculated risk rates of abdominal pain, activation, diarrhea, nausea, insomnia, headache, sedation, discontinuation due to adverse effects, and suicidality. They also looked at disinhibition, increased motor activity, restlessness, fidgetiness, impulsivity, and irritability.

The authors found that SNRIs produced far fewer side effects than SSRIs. Only nausea was higher on SNRIs than on placebo, in contrast to SSRIs, which were associated with more abdominal pain, activation, headaches, and sedation. Adverse effect–related discontinuation was higher than placebo in SSRIs, and no different in SNRIs. Neither SSRIs nor SNRIs caused more treatment-emergent suicidality than placebo, although it is important to remember that this population was characterized by anxiety, not depression. It is also notable that of the 18 studies, 10 were federally funded and 8 were industry funded; however, there was no effort to compare them by category for such things as rates of suicidality.

CCPR'S TAKE

We are left with a conundrum. SSRIs are superior to SNRIs in efficacy and are the treatment of choice for anxiety, but they cause more side effects. If a patient develops activation, would the second choice be a different SSRI or an SNRI with less efficacy but less risk of activation? The authors suggest SNRIs might represent a good second choice, with some demonstrated efficacy in anxiety disorders and OCD and less activation risk. As a reminder, this is not true for depression, where we do not have proven efficacy of SNRIs in children and adolescents.

—John Raiss, MD. Dr. Raiss has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

PARENT TRAINING

Is It Time for an Online Tantrum Tool?

REVIEW OF: Diaz-Stransky A et al, *J Child Adolesc Psychopharmacol* 2020;30(9):558–566

STUDY TYPE: Open pilot study

We often encounter children with disruptive behaviors, but tools to address these issues are few. Although parent management training (PMT) is an effective treatment for disruptive behaviors, access to quality PMT is limited in most places. Online PMT programs exist, but most lack active support from trained clinicians and have poor completion rates among parents. To address this need, the authors of the current study examined the feasibility and utility of a clinician-supported virtual PMT program.

Researchers at the Yale Child Study Center enrolled 15 children (13 boys and 2 girls) aged 3–9 years (mean 5.2 years). They screened participants using semi-structured interviews and DSM-5 criteria. Common diagnoses included oppositional defiant disorder (ODD), disruptive mood dysregulation disorder, and attention deficit hyperactivity disorder.

Parents received PMT via eight 10-minute animated and interactive online modules (see table on page 10), providing practical guidance in everyday scenarios. After the third, sixth, and eighth online module, parents participated in a 45-minute videoconference session to review progress.

After 8 weeks of the intervention, parents reported changes in symptoms via the Disruptive Behavior Rating Scale (DBRS; eight ODD symptoms on a 0–3 scale) and Affective Reactivity Index (ARI; seven irritability questions on a 0–2 scale), and intervention acceptability via the Patient Satisfaction Questionnaire (PSQ; eight acceptability questions on a 1–4 scale).

Remarkably, around 90% of parents completed the online modules and video sessions. Parents who completed the study found the program satisfactory (PSQ score = 26.5) and reported around a 50% reduction in their kids' disruptive behaviors (DBRS score 13.5 > 7.3) as well as irritability (mean ARI score 7.2 > 3.75). The improvements appear to be clinically meaningful and experienced at rates similar to those seen in the regular in-person PMT programs.

The main drawbacks of this study were its very small sample size, lack of control group (which allows for an open label–type bias), lack of clear generalizability since it was conducted in a school setting, and the need for in-person screening for the virtual intervention.

CCPR'S TAKE

Despite the many limitations, this study shows that a brief online program along with just three video sessions by a

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Tantrum Tool Program Modules
• Module 1: Introduction to tantrums
• Module 2: Antecedent > behavior > consequences
• Module 3: Manage triggers
• Videoconference 1: Review concepts and behavior observation chart
• Module 4: Manage child's environment
• Module 5: Learn about effective rewards
• Module 6: Learn appropriate commands
• Videoconference 2: Review progress and identify next goals
• Module 7: Learn to praise
• Module 8: Learn to ignore minor misbehaviors
• Videoconference 3: Review improvement and plan for future

trained clinician shows promise in delivering effective PMT to so many of our patients' families who otherwise do not have access to it. There is a need for such tools as a public health measure, and we hope to see the tool released for general use and independent larger, controlled study by unaffiliated researchers.

—Pavan Madan, MD. Dr. Madan has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

ADHD

ADHD Prevalence in the US Black Population

REVIEW OF: Cénat JM et al, *JAMA Psychiatry* 2021;78(1):21–28

STUDY TYPE: Meta-analysis

In the general population, the reported prevalence of ADHD is about 10%, with estimates varying from around 5% to 15%. Black individuals are typically underrepresented in these studies, and with fewer data, it is no surprise that the estimates are less precise, with an estimated prevalence of 5% to over 20%. This study tried to improve the accuracy of prevalence measures of ADHD among Black individuals as well as identify specific risk factors for ADHD in this population.

The authors found 21 US articles published from 1979 through 2019 with 24 independent samples or subsamples of Black people. Most (13) included both children and adolescents. Eight samples included only children, one included only adolescents, and two included only adults. From these studies, the authors conducted a meta-analysis and computed a pooled ADHD prevalence of 14.5% (95% CI, 10.64%–19.56%). When only the samples of children and adolescents were included, the prevalence was 13.9%, which was not significantly different.

Older children (10–17 years) were more likely to receive an ADHD diagnosis, as were males. Males also received more prescriptions for ADHD than females. In at-risk populations like juvenile offenders, Black youth were less likely to be diagnosed with ADHD. Interestingly, Black parents were less likely to report ADHD symptoms in their children while teachers reported more symptoms. Low socioeconomic status was a risk factor for ADHD in Black individuals, but high socioeconomic status was not a protective factor against ADHD as it is in white individuals.

CCPR'S TAKE

This study shows that Black Americans are more likely to meet diagnostic criteria for ADHD than the general population, with a prevalence of about 14% vs about 10%. It's not clear what drives this disparity, although an increased tendency for teachers to identify ADHD symptoms in Black children, lower socioeconomic status, as well as culturally determined biases in the ADHD construct itself might be factors. These data contradict the DSM-5, which indicates that Blacks have a lower rate of ADHD, and this should encourage us to be more vigilant in screening and treating our Black patients for this condition.

—Thomas Jordan, MD. Dr. Jordan has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CME Post-Test

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1. According to Dr. Yule, what should you address in your first and second NIAAA screening questions, respectively, when inquiring about an adolescent's alcohol use (LO #1)?
   - [ ] a. "Do your friends drink alcohol?" and then "Have you drunk alcohol?"
   - [ ] b. "Have you drunk alcohol with your family?" and then "Have you drunk alcohol without your family?"
   - [ ] c. "Do your friends drink alcohol?" and then "How did they get alcohol?"
   - [ ] d. "Have you drunk alcohol?" and then "Do your friends drink alcohol?"
2. What value of number needed to treat (NNT) is generally considered to be clinically useful for a categorical outcome (LO #2)?
   - [ ] a. Less than 45
   - [ ] b. Less than or equal to 5
   - [ ] c. Greater than or equal to 8
   - [ ] d. Less than 10
3. A recent study compared the risk rates of adverse effects and side effects in SSRIs vs SNRIs for OCD and anxiety disorders in children and found that although SNRIs produced far fewer side effects than SSRIs, SNRIs were less effective (LO #3).
   - [ ] a. True
   - [ ] b. False
4. Which of the following is an accurate statement about the potential adverse physical impacts of legal performance-enhancing substances (LO #1)?
   - [ ] a. Legal performance-enhancing substances are associated with a higher risk of adverse events, compared to multivitamins
   - [ ] b. Creatine increases the risk of cardiovascular disease
   - [ ] c. Anabolic-androgenic steroids can cause gout
   - [ ] d. High doses of some amino acids can cause cardiovascular, endocrine, and psychiatric problems
5. According to a 2020 study of youth with disruptive mood dysregulation disorder, what was concluded about the efficacy of methylphenidate with adjunctive citalopram, compared to stimulants plus placebo (LO #3)?
   - [ ] a. The treatment arm did not significantly differ from placebo on the primary outcome
   - [ ] b. The treatment arm significantly outperformed placebo on the primary outcome
   - [ ] c. The treatment arm significantly outperformed placebo on the secondary outcomes
   - [ ] d. The treatment arm did not significantly differ from placebo on the primary or secondary outcomes
6. Which is the best study design choice for investigating the long-term efficacy of a drug (LO #2)?
   - [ ] a. An open-label design
   - [ ] b. An extended placebo-controlled RCT
   - [ ] c. A randomized discontinuation design
   - [ ] d. A prospective cohort design
7. What effect does early-onset alcohol consumption and/or a history of psychiatric disorders in childhood or adolescence have on the likelihood of developing a substance use disorder (SUD) in adulthood (LO #1)?
   - [ ] a. Neither affect SUD likelihood in adulthood
   - [ ] b. Only early-onset alcohol consumption increases SUD likelihood in adulthood
   - [ ] c. Both increase SUD likelihood in adulthood
   - [ ] d. Only a history of psychiatric disorders increases SUD likelihood in adulthood
8. Which of the following about the risk rates of adverse effects and side effects associated with either SSRI or SNRI therapy for OCD and anxiety disorders in children is true (LO #3)?
   - [ ] a. SSRIs caused more treatment-emergent suicidality than SNRIs and placebo
   - [ ] b. Rates of adverse effect–related discontinuation were higher for SNRIs and SSRIs than placebo
   - [ ] c. SSRIs and SNRIs had equal rates of headaches and sedation, compared to placebo
   - [ ] d. SNRIs were only associated with higher rates of nausea, compared to placebo

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Substance Use in Children and Adolescents
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Next Issue:
Disruptive Moods in Children and Adolescents
Oct/Nov/Dec 2021

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Note From the Editor-in-Chief

Summer of drugs? With rates of substance use in our patients up after a stressful year, we interviewed Dr. Amy Yule on alcohol use in adolescents. Her insights are both frightening and incisive and can help us understand and intervene. We also interviewed Dr. Kyle Ganson to talk about the culture and hazards of performance-enhancing drugs. For summer beach research reading, Dr. Glen Spielmans offers an overview of the important things to look for in journal articles and how not to get caught up in the hype of preliminary studies. In that spirit, we also have research updates on the use of citalopram for irritability in DMDD, the decision between SSRIs and SNRIs for anxiety, an online parent tool to manage tantrums, and disparities in ADHD rates in Black kids. As always, we welcome your feedback.

On another note, we are planning more podcasts related to our content. Pharmacogenetics with Dr. Aaron Besterman went up recently, Qelbree followed soon after, and we plan for the autism research interview with Dr. Micheal Sandbank and our recap of the kinds of autism treatment to follow. If you haven't heard them, our podcasts tend to be more hard hitting than the print versions of these interviews—with people in their own words helping us to uncover important issues in our work. While you will soon get CME for listening, in a world full of advertisements, we currently offer these podcasts free in the spirit of public service. Listen and share them—help us shape a better world!

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