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Learning Objectives

After reading these articles, you should be able to:

1. Identify and discuss the pros and cons of stimulants for ADHD with patients and caregivers.
2. Describe how the updated AACAP Clinical Practice Guideline impacts the treatment of anxiety disorders in children and adolescents.
3. Summarize some of the findings in the literature regarding psychiatric treatment for children and adolescents.

Talking With Parents About Stimulant Treatment

John C. Raiss, MD. Assistant Clinical Professor of Child and Adolescent Psychiatry, UCLA David Geffen School of Medicine, Los Angeles, CA.

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

After a thorough assessment, you diagnose your 16-year-old patient Alex with ADHD and recommend a trial of stimulant medication. Alex wants to try the medication, but his mother feels he just needs tips and skills to improve his focus and doesn't need to "take pills for the rest of his life."

ADHD is one of the most treatable conditions in psychiatry if patients adhere to medication regimens. Stimulants are widely used in treatment and are usually safe when taken as prescribed; however, parents are often skeptical and concerned about psychotropic medications. In this

Highlights From This Issue

Stimulants are effective for ADHD, but what is the best way to work with skeptical parents? We offer a sensible process for addressing the common challenges that come up in practice.

Should we be trying out the newer ADHD medications, or should we start with the older basic medications? Dr. Anne Buchanan helps us sort through this conundrum.

We have a new way to put together important research into Clinical Practice Guidelines. The first example of an AACAP CPG enlightens us on what works for the usual collection of anxiety disorders.

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Q&A With the Expert

Practical Issues With Prescribing ADHD Meds
Anne Buchanan, DO

Child & Adolescent Psychiatrist with New York City Health and Hospitals, Bellevue, and Maimonides Medical Center in New York, NY.

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

We spoke with Dr. Buchanan about choosing medications for ADHD in 2017, and she is back now with an update. In addition to this interview, check out the table on page 6 for an overview of ADHD medications over the past decade.

CCPR: Thanks for talking with us, Dr. Buchanan. Please help us make sense of the many new ADHD medications.

Dr. Buchanan: Sure. In the amphetamine group, there are four new long-acting options: 1) Mydayis; 2) a chewable Vyvanse; 3) a new liquid formulation, Dyanavel; and lastly 4) Adzenys, which comes in both a liquid and an orally disintegrating tablet. In the long-acting methylphenidate category, there are six new options—Adhansia, Aptensio, Cotempla, Quillivant (which has both liquid and chewable options), and Jornay PM (which is both delayed release and long-acting).

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Expert Interview—Practical Issues With Prescribing ADHD Meds
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CCPR: Wow. And what new short-acting amphetamines do we have?

Dr. Buchanan: The new short-acting amphetamines are Evekeo, which has both a regular tablet and an orally disintegrating option; Zenzedi; and ProCentra, a liquid. Probably the most interesting new medication is Qelbree (viloxazine), which is a non-stimulant selective norepinephrine reuptake inhibitor, just approved a few months ago. But in my personal prescribing habits, I tend to be a bit skeptical and a late adopter of new medication.

CCPR: How did you come to be a late adopter?

Dr. Buchanan: The majority of my clinical work is in the emergency room setting. Working in the emergency room, I evaluate children who are coming from every level of care—from private practices to foster care agencies to residential and juvenile justice facilities. I have the luxury of a bird's-eye view of what my colleagues in the community are prescribing and how children are doing. I tend to wait in my own prescribing until I have a sense of how kids are doing on the newer medicines. Unfortunately, if they're in the emergency room, there's a chance they're not doing so well!

CCPR: So, how do we fit these new medicines into clinical decision-making?

Dr. Buchanan: These new meds are still methylphenidate- or amphetamine-based products, except for Qelbree. I see them as an opportunity to fine-tune symptom coverage and ease of administration, especially for those who struggle to swallow pills, such as small children, or for kids with intellectual or developmental disabilities. We now have more chewable, orally disintegrating, and liquid products in our arsenal. On busy school mornings, it's much easier for parents to give these than to snip capsules and pour beads.

CCPR: Are there other advantages to these new medications?

Dr. Buchanan: Some of them are marketed as lasting much longer, such as 16 hours. This could mean not having to deal with booster doses for children who need additional coverage in the late afternoons or early evenings. I think it's great that there are so many options to fine-tune regimens and make things easier for kids and families. However, keep in mind that these new medications will not revolutionize our ability to treat the core symptoms of ADHD. There aren't new mechanisms of action in terms of their pharmacology.

CCPR: We are all aware that there is so much marketing for new medications, and families often ask us for the newest products. How do you talk with parents who come to you with questions like this?

Dr. Buchanan: Most parents are able to understand the explanation that the active ingredients in the older and newer stimulants are the same. I talk about how some of our medicines have been around for decades. We know they work and they're more affordable for you, for your insurance plan, and the healthcare system in general. I tell them that there's usually no reason to start with the newer medications, but that we'll try different ones until we find the medicine that's the right fit.

CCPR: How soon after prescribing do you suggest we check in with patients and families?

Dr. Buchanan: Ideally, I would have a child come back in one to two weeks after initiating any new medicine, but that's often hard to do in community clinics or busy practices. I think as a field we're pretty good at getting kids back in a month, but some of our primary care colleagues don't have that mindset or availability. I have seen clinical documentation from non-psychiatrists that give directions for titration, with follow-up in three months. Child psychiatrists might recommend going from a half tab to a full tab and see them back in a week, but generally they wouldn't set up a detailed titration plan with a follow-up so far out. I think for primary care colleagues or other non-psychiatrists, seeing patients back as quickly or often as we do is more challenging. Then the question is, is that the right practice setting for that child? But it may be the only option.

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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.

POSTMASTER: Send address changes to *The Carlat Child Psychiatry Report*, P.O. Box 626, Newburyport, MA 01950

Expert Interview—Practical Issues With Prescribing ADHD Meds

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CCPR: You work with families with a range of socioeconomic circumstances. Does that affect prescribing, and if so, can you speak to these differences?

Dr. Buchanan: I think polypharmacy can be a problem in children of lower socioeconomic status. I think at least one reason is lack of access to fellowship-trained child and adolescent psychiatrists, as well as lack of access to quality, evidence-based psychotherapy. Due to high demand, community clinics are often put in the position of utilizing different types of clinicians with different education, training, and experience, sometimes including unlicensed clinicians. A child might benefit from CBT, parent-child interaction therapy, or family therapy with a trained, licensed, and experienced clinician; 30-minute sessions every other week are rarely enough. Many families don't have the time or resources to attend frequent appointments for therapy, and intensive outpatient programs or home-based programs may not be available or may have long waitlists. Clinicians are desperate to help these children and families, and medications may be the only available tool. It's just not possible to do all the things we know that these families would benefit from. It's an insurmountable problem.

CCPR: How good are clinicians at appreciating the clinical complexity of these cases?

Dr. Buchanan: Many of our non-psychiatric colleagues see ADHD as straightforward, and they're comfortable with stimulants. But teasing out ADHD can be complex and incredibly nuanced in many cases. ADHD symptoms are nonspecific, and comorbidities are the rule rather than the exception. Anxiety and atypical depression can look like ADHD, as can autism spectrum disorder, developmental delays, and learning disorders. Trauma, especially complex trauma and its related attachment disruptions, are probably the biggest confounders. Often I review clinical documentation or speak to a clinician only to discover that trauma has not been adequately assessed for. Pediatricians and child neurologists are wonderful at treating ADHD when the diagnosis is straightforward, but I wouldn't expect them to have the training to evaluate for the effects of complex childhood trauma, attachment, and anxiety.

"The newer meds are still methylphenidate- or amphetamine-based products, so I see them as an opportunity to fine-tune symptom coverage and for ease of administration. With more chewable, orally disintegrating, and liquid products in our arsenal, it's much easier for parents to give these medications than to snip capsules or pour beads."

Anne Buchanan, DO

CCPR: With so many kids seeing non-psychiatrists, at least in the first rounds of treatment, how we can better support these colleagues?

Dr. Buchanan: Develop professional relationships with pediatricians, neurologists, or other clinicians in your community who treat children. This helps them know where to turn when a patient starts to feel outside their scope. When a child is failing first-line treatments, that may signal that the child needs an evaluation with an expert. Where child and adolescent psychiatrists are scarce, develop a system through which the child psychiatrist can refer back to the original referring clinician for management, with open communication, once the patient has been stabilized. This frees child psychiatrists to evaluate more patients and allows non-psychiatrists to treat with confidence. New York state offers Project TEACH, a free same-day consultation with a child psychiatrist line for primary care physicians and other clinicians (www.projectteachny.org).

CCPR: When we do encounter a child with straightforward ADHD, how do we help parents decide how to proceed with medication treatment?

Dr. Buchanan: I generally see three types of parents. There are parents who say, "I need help; tell me what to give my kid and I'll fill it today." There are parents who are adamant that their child not take medications, usually because they've heard reports that "these medications make kids into zombies." Finally, there are parents in the middle who want to help their child but are understandably anxious about the idea of their child taking medication.

CCPR: How do you manage these different types of parents?

Dr. Buchanan: For the parents that are on board, we start with the basics and go from there. For parents who have heard negative things about medications, I remind them that we have no idea what happened with that kid down the street who may or may not look like a zombie. We don't know that child's diagnosis, what symptom is being targeted, or why a particular medication is being tried. I tell them that we're going to focus on what's going on with their child and present the evidence-based options that we have. I note that I use these medications all the time and I have a lot of comfort with them. I simply ask that they keep an open mind and work with me, and I stress that I would never ask them to stay with something that their child doesn't feel good on. I also tell them that I will continue to work with them to find whatever combination of medications and therapy is helpful.

CCPR: What if reassurance doesn't work?

Dr. Buchanan: I don't want parents to feel pressured. I want them to want to try medications

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Expert Interview—Practical Issues With Prescribing ADHD Meds

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because they see that their child is suffering, and they want to help their child succeed. But external forces will often do the job for me, whether it's a parent-teacher meeting or frequent calls to come pick up their kid or the after-school program saying, "I'm sorry, your kid can't come any more." *(Editor's note: For strategies to address parents' specific concerns, see "Talking With Parents About Stimulant Treatment" in this issue.)*

CCPR: If they are willing, what's the next step?

Dr. Buchanan: I try to be flexible even if I think a stimulant is the right choice. We can start with therapy, with medication, or with both. If the parent wants to start with something else, I'm happy to do that. If a parent asks what I recommend, I will say what I would start with, but I let them choose. If the child is a little older, I'll let the child weigh in on what they would like to try.

CCPR: How do you get buy-in?

Dr. Buchanan: While academic performance is usually part of the issue, I will focus wherever the parent and child are experiencing the most frustration. For some parents, the child's behavior is more of an issue than their grades. For other families, the child's bedtime routine and poor sleep habits are causing havoc, so maybe instead of a stimulant we start with guanfacine or clonidine at night. If we have success, then I have some parental buy-in to try a stimulant if I think it is still needed.

CCPR: Speaking of other medications, where do you see the role of atomoxetine and viloxazine in comparison to stimulant treatment?

Dr. Buchanan: I consider atomoxetine third line, after stimulants and alpha-agonists, but there are always children who don't tolerate stimulants, and alpha-agonists may not provide the necessary symptom relief or may be too sedating. For these children, atomoxetine can be a good alternative. In an emergency room situation we need prompt symptom control; however, atomoxetine needs titration and time to work. Viloxazine may be similar. Remember that viloxazine is a selective norepinephrine reuptake inhibitor and ideally would not be prescribed to a child who is already on an SSRI for depression or anxiety, as many kids with ADHD are. I have seen one child taking escitalopram and viloxazine in the emergency room with symptoms of activation from both serotonergic agents.

CCPR: Getting back to parents, how do you work with parents who are interested but hesitant to go forward with medication for ADHD?

Dr. Buchanan: I make sure they've been given all the necessary information. Then I tell them, "I understand that you're feeling a little bit ambivalent and aren't sure where to start. Let's try working on sleep and more structure at home. Continue with the therapy for a bit and then we'll have you come back and see how things are going." People respond when they make the decision themselves rather than feeling pushed. Sometimes I say, "I'll just submit the prescription. You don't have to take it. But if you decide as a family that you want to try it, it will be there." This is about giving our patients agency and self-determination. You want people to feel empowered to make their own choice. You're going to be more successful if they're choosing what to start, when to start, where to start—giving parents that level of autonomy feels better for everybody.

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

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Talking With Parents About Stimulant Treatment

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article we'll talk about parental resistance to stimulant medications and how to best work with parents when discussing treatment.

Risks of ineffective therapies or avoiding treatment

Medication nonadherence or avoidance increases the morbidity of psychiatric ADHD conditions as patients are less likely to have their condition respond or remit. Common risks of untreated ADHD include (Biederman J et al, *Psychiatric Services* 2019;70(10):874–880):

- Underachievement at school and work
- Family conflict
- Mood disorders
- Anxiety disorders
- Addiction
- Injuries, including traumatic brain injury
- Accidents
- Premature death
- Suicide

Results from questionnaires show that many parents believe that psychotropic medication can make children more likely to develop later drug addiction (Lazaratou H et al, Ann Gen Psychiatry 2007;6:32). The American Academy of Pediatrics recommends behavioral approaches (CBT) as the first treatment for ADHD for pre-school children, but not school -aged children , in line with the Multimodal Treatment Study of Children with Attention Deficit/ Hyperactivity Disorder (MTA) which demonstrated that stimulant medications are more effective than behavioral

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Talking With Parents About Stimulant Treatment

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treatments for core symptoms of ADHD in school-aged kids. Other reasons often cited by parents range from concern about weight related issues to stigma.

Parents may believe that supplements are natural and less harmful than stimulants, but with the possible exception of saffron, most supplements have little evidence of efficacy in ADHD. Long-chain polyunsaturated fatty acids and minerals have "at best marginal beneficial effects," and zinc, iron, and magnesium lack convincing evidence (Lange KW et al, *Curr Psychiatry Rep* 2017;19(2):8). Micronutrients showed no effect either (Johnstone JM et al, *JAACAP* 2021; in press). Saffron is an exception and may be on par with methylphenidate (Baziar S et al, *J Child Adolesc Psychopharmacol* 2019;29(3):205–212, reviewed in *CCPR* November 2019).

At follow-up two weeks later, Alex reports that he is still unable to focus for even short periods of time. He is drinking products with excessive amounts of caffeine and pulling all-nighters to finish his work. You decide that you need to understand his mother's concerns about stimulants more fully. She confides that she's heard stories of kids misusing their medication. She also doesn't want Alex to be labelled as "an ADHD kid."

Talking with parents

Find out what each parent thinks about medication and what their hesitations or worries might be. A good way to initiate this conversation is to simply state, "Please help me understand your specific concerns." Some parents are truly set against using medication, but most can engage in productive conversation. Once you know what their concerns are, you can take various approaches to encourage parents to partner with you in treating their child or teen. Some helpful tips for talking to medication-hesitant parents include:

- Put medications in context. "Medications are part of an overall plan that includes exercise, structure, nutrition, and sleep."
- Share specifics. "Every medication has its good and bad points. Let's go over them one by one in detail. And remember, we will learn very quickly whether the medication is helpful or not—most likely within a few weeks."
- Destigmatize treatment. "It might be unfair to your child if we don't treat their symptoms. That might make their life unnecessarily difficult. Lots of kids have ADHD and are relieved to get treatment."
- Address family and cultural aspects. "Do you have family members with similar issues? How do people in your family and culture understand and manage ADHD symptoms?"
- Discuss the benefits. "Most kids can focus better when they take these medications. They learn better and get their work done more easily, more like their friends and classmates. Kids often feel a lot better about their abilities, and they have more time for recreation and to enjoy life."
- Talk about the risks of not treating ADHD. "Kids who don't get treatment struggle harder to get their work done. It takes them longer than their friends. They are often criticized for errors, failing to follow instructions, or not turning in assignments."
- Stress that treatment can have other benefits. "Treating ADHD can reduce the risk of accidents, substance use, depression, criminal activity, and teenage pregnancy" (Faraone SV et al, *Neurosci Biobehav Rev* 2021;128:789–818).
- Acknowledge legitimate risks and their management. Be sure to directly address appetite, growth or weight loss issues, height, sleep, blood pressure, and pulse. "Stimulants can reduce appetite, so we will track growth. If your child is not eating enough, we can brainstorm some ideas together. We often use medication holidays during weekends and vacations, as well as other strategies to support growth and minimize the amount of medication you give to your child."
- Discuss sleep challenges. "If issues arise with sleep, we can adjust the timing of the medication to minimize these effects."
- Talk about drug interactions. "ADHD medications can be taken with most other prescriptions, including antidepressants and birth control pills. But we will need to talk about other meds your child is currently taking, including cold medications such as pseudoephedrine. And be sure to keep me updated about future prescribed or over-the-counter meds, as well as supplements."
- Discuss sexual side effects, even if parents and teens do not directly ask about them. "You may have heard that medications have sexual side effects. Stimulants can cause painful erections. This is rare, but you should seek rapid medical attention if that happens."
- Talk about addiction/diversion. "It is important for you to dispense the medication to your child and to keep careful control of it to prevent misuse, but stimulants actually can protect kids against substance misuse."
- Address possible barriers to prescriptions. "Many of these medications are covered by insurance, but some may need a prior authorization." "These medications are more carefully controlled than most to avoid misuse—you may need to show identification when you pick it up."

After talking about her concerns, Alex's mother agrees to a careful one-month trial of stimulants. Alex has a rapid response to 10 mg of extended-release mixed amphetamine salts, and his focus improves. He has mild irritability in the afternoons, which improves with scheduled afternoon snacks. Over the course of the semester, Alex's grades and confidence improve.

CCPR VERDICT: The first three rules for helping parents understand the risks and benefits of ADHD medication are listen, listen, and listen. Address their concerns point by point and be sure they understand that medication can be life changing.

Medications for ADHD: 2012–Present

Brand & Generic Names Year FDA Approved [G]: Generic Availability	Available Strengths (mg except where noted)	Usual Pediatric Dosage Range (starting–max)	Duration of Action	Can It Be Split?	Ages Approved for ADHD (years)	Delivery System/Notes (IR = immediate release, DR = delayed release, ER = extended release)
Short-Acting Amphetamines						
Evekeo (amphetamine) [G] 2012	5, 10	3–5 years: 2.5 mg QAM–20 mg BID 6–17 years: 5 mg QAM–20 mg BID	3–5 hours	Yes	3–17	Scored tablet
Evekeo ODT 2019	2.5, 5, 10, 15, 20	3–5 years: 2.5 mg QD–BID; increase by 2.5 mg weekly 6–17 years: 5 mg QD–BID; increase by 2.5 or 5 mg weekly Max 40 mg daily	4–6 hours	No	3–17	50% dextroamphetamine sulfate and 50% levoamphetamine sulfate
Long-Acting Amphetamines						
Adzenys ER liquid oral suspension 2017	1.25 mg/mL in 450 mg bottles	6.3 mg (5 mL) in the morning; increase by 3.1 mg (2.5 mL) or 6.3 mg (5 mL) weekly Max 18.8 mg (15 mL) daily for ages 6–12 years, 12.5 mg (10 mL) daily for ages 13–17 years	Presumed up to 12 hours	Yes (liquid)	6 and up through adult	50-50 IR and DR mixed amphetamine salts; 1.25 mg (1 mL) solution is equivalent to 2 mg Adderall XR
Adzenys XR-ODT (orally disintegrating tablet) 2016	3.1, 6.3, 9.4, 12.5, 15.7, 18.8	6.3 mg in the morning; increase by 3.1 or 6.3 mg weekly Max 18.8 mg daily for ages 6–12 years, 12.5 mg daily for ages 13–17 years	Onset in 45–60 minutes, duration up to 12 hours	No	6 and up through adult	3.1 mg is equivalent to 5 mg mixed-salts product; increasing dosage preparations correspond to 5, 10, 15, 20, 25, and 30 mg of Adderall XR
Dyanavel XR oral suspension 2015	2.5 mg/mL	2.5 mg (1 mL) or 5 mg (2 mL) in the morning; increase by 2.5 mg (1 mL) to 10 mg (4 mL) every 4–7 days Max 20 mg (8 mL) daily	Onset in 1 hour, duration up to 13 hours	Yes (liquid)	6 and up	Contains dextroamphetamine and levoamphetamine in a 3.2:1 ratio ER oral suspension allows once-daily dosing (must shake well); 2.5 mg = 4 mg mixed amphetamine salts
Mydayis (mixed amphetamine and dextroamphetamine salts) 2017	12.5, 25, 37.5, 50	12.5–25 mg QAM	10–16 hours	Can be sprinkled; do not crush or chew	13–17, adults	pH-dependent ER capsule formulation; may have effect up to 16 hours
Vyvanse (lisdexamfetamine) chewable tablets 2017	10, 20, 30, 40, 50, 60	30 mg in the morning; increase by 10 or 20 mg weekly Max 70 mg daily	Onset in 90 minutes, duration up to 14 hours	No	6 and up	Releases medication at a steady rate for a duration of 2–14 hours; lisdexamfetamine is prodrug of dextroamphetamine
Non-Stimulant NRI						
Qelbree (viloxazine ER) 2021	100, 150, 200	6–11 years: 100 mg daily; increase by 100 mg weekly; max 400 mg 12–17 years: 200 mg daily; increase by 200 mg weekly; max 400 mg	1–3 weeks	Can be sprinkled	6–17	Selective norepinephrine reuptake inhibitor (NRI)
Long-Acting Methylphenidates						
Adhansia XR 2019	25, 35, 45, 55, 70, 85	25 mg daily; increase by 10–15 mg every 5 days or longer Max 85 mg for children, 100 mg for adults	Onset in 1 hour, duration 8–16 hours	Can be sprinkled; do not crush or chew	6 and up, adults	Capsule of 20% IR and 80% DR beads; more adverse reactions for doses over 70 mg in children and 85 mg in adults
Aptensio XR 2015	10, 15, 20, 30, 40, 50, 60	Start 10 mg QAM; increase by 10 mg increments weekly; max 60 mg QAM	8–12 hours	Can be sprinkled; do not crush or chew	6–17, adults	Capsule of 40% IR and 60% DR beads
Cotempla XR-ODT 2017	8.6, 17.3, 25.9	17.3 mg in the morning; can increase weekly by 8.6–17.3 mg increments; max 51.8 mg	Onset in 20 minutes, duration 9–12 hours	No	6–17	Contains 25% IR and 75% ER methylphenidate
Jornay PM 2018	20, 40, 60, 80, 100	Start 20 mg QPM; can increase weekly by 20 mg increments; max 100 mg QPM	8–12 hours, after 10-hour delay in onset	Can be sprinkled; do not crush or chew	6–17, adults	ER capsule of DR beads; taken in evening (6:30–9:30 p.m.)
Quillichew ER 2015	20, 30, 40	Start 20 mg QAM; adjust by 10–20 mg increments weekly; max 60 mg QAM	8–12 hours	Yes	6–17, adults	Chewable ER for those who will not swallow pills or take liquid; 30% IR & 70% ER
Quillivant XR 2012	25 mg/5 mL	Start 20 mg QAM; adjust by 10–20 mg increments weekly; max 60 mg QAM	8–12 hours	Yes (liquid)	6–17, adults	20% IR & 80% ER in oral solution; shake prior to use

Q&A With the Expert

Treating Anxiety Disorders in Children: The New AACAP Clinical Practice Guideline

A. Reese Abright, MD

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

CCPR: Welcome, Dr. Abright. Tell us how the American Academy of Child and Adolescent Psychiatry (AACAP) created the Clinical Practice Guideline on the Assessment and Treatment of Anxiety Disorders in Children and Adolescents (Walter HJ et al, *J Am Acad Child Adolesc Psychiatry* 2020;59(10):1107–1124).

Dr. Abright: The AACAP Committee on Quality Issues (CQI) is responsible for developing what are now called Clinical Practice Guidelines (CPGs). The CPG on anxiety disorders, which was published in *JAACAP* in October 2020, is the product of a dedicated team effort by a writing group comprised of five CQI members led by Dr. Heather Walter and followed by extensive internal and external review from topic experts and relevant stakeholders.

CCPR: How are these CPGs different from the AACAP Practice Parameters from 2007?

Dr. Abright: The Practice Parameters were based on the methodology for guideline development at that time. The new guidelines are updates based on current Institute of Medicine standards for developing professional guidelines. These range from critical review of the literature, with ratings of strength of evidence and graded recommendations for assessment and treatment, to stakeholder participation, external review, and freedom from conflicts of interest and transparency during the guideline development process. The guideline for anxiety disorders is the first AACAP CPG developed through this process. AACAP partnered with the government-funded Agency for Health Research and Quality (AHRQ), which conducted a systematic review of treatment of anxiety disorders in children and adolescents. The review was limited to social anxiety, generalized anxiety, separation anxiety, panic disorder, and specific phobia. It excluded posttraumatic stress disorder and obsessive-compulsive disorder on the basis that treatment approaches for these disorders generally differ from those used in other anxiety disorders.

"The suggestion for use of SNRIs is not as strong as the recommendation for SSRIs, but clinicians must also consider individual factors and patient and family preferences. The goal of the guideline is to offer evidence-based guidance that may assist clinicians in making treatment decisions. It is not meant to limit reasonable treatment options based on clinical assessment, or to serve as a standard of care."

A. Reese Abright, MD

CCPR: How common are anxiety disorders in children and adolescents?

Dr. Abright: Anxiety disorders were the most common condition found in a national comorbidity survey of adolescents, with a lifetime prevalence of 32% and median age of onset at 6 years (Merikangas KR et al, *J Am Acad Child Adolesc Psychiatry* 2010;49(10):980–989). Prevalence for specific anxiety disorders ranges from 20% for specific phobia to 9% for social anxiety disorder and 2% each for agoraphobia, panic disorder, and generalized anxiety disorder (Walter HJ et al, *J Am Acad Child Adolesc Psychiatry* 2020;59(10):1107–1124). Anxiety disorders are highly comorbid with each other as well as with other psychiatric disorders, with chronic physical illnesses such as diabetes and asthma, and with substance use. Any of these things may precede or exacerbate an anxiety disorder.

CCPR: What does the CPG tell us about the natural course of anxiety disorders in children and adolescents?

Dr. Abright: Anxiety disorders wax and wane in intensity but may become chronic and persist into adulthood. They can be homotypic, lasting into adulthood as the same disorder. For example, a child with generalized anxiety disorder may continue to have generalized anxiety disorder as an adult. Disorders can also be heterotypic, meaning that they present one way in childhood and differently in adulthood. For example, separation anxiety disorder in childhood might present as panic disorder or another anxiety disorder in adulthood.

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Expert Interview—Treating Anxiety Disorders in Children: The New AACAP Clinical Practice Guideline

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CCPR: Is this conceptualization of anxiety disorders like the cross-diagnostic concept of anxiety in the NIMH Research and Diagnostic Criteria (RDoC)?

Dr. Abright: RDoC constructs regarding fear, anxiety, and arousal systems may prove useful in addressing issues related to heterogeneity and comorbidity in future studies of anxiety disorders, but they were not a focus in the current review.

CCPR: Do the disorders discussed in the CPG—social anxiety, generalized anxiety, separation anxiety, phobias, and panic disorder—share common characteristics?

Dr. Abright: Yes. Anxiety disorders are characterized by persistent symptoms associated with significant impairments that cut across multiple activities—school, home, athletics, socialization, and many other aspects of a young person's life. These features distinguish anxiety disorders from worries that are expected responses to developmental or other life stressors. DSM-5 includes 11 anxiety disorder diagnoses. Their common symptoms can include hypervigilance, heightened reactivity to emotional and environmental stressors, avoidance of things that are triggering those feelings, and sometimes behavioral outbursts related to the avoidance. An example of these symptoms might be a child who is trying to avoid going to a family event that her parents expect her to attend—she is nervous about going and too embarrassed or ashamed to explain why.

CCPR: How are we doing as a field in identifying and treating anxiety disorders in children and adolescents?

Dr. Abright: Efforts to improve collaboration with pediatricians and other providers are in progress, but much remains to be accomplished. Psychotherapeutic and psychopharmacologic treatments can be effective in the short term for anxiety disorders in children. However, about 50% of patients receiving gold-standard treatments continue to have symptoms, and over half of individuals in this age group do not receive any treatment, while even fewer receive evidence-based treatments (www.childmind.org/2015-childrens-mental-health-report/#gap).

CCPR: What does the CPG tell us about assessment of anxiety disorders?

Dr. Abright: Engage and educate children and parents or other guardians; distinguish transient fears and worries associated with developmental stages from the persistent and impairing symptoms that characterize anxiety disorders; track symptom intensity and frequency and related impairments; treat psychiatric and medical comorbidities; and address traumatic and other stressors. These guideline statements regarding assessment are based on expert consensus as reflected in standard textbooks and other sources (Dulcan MK. *Dulcan's Textbook of Child and Adolescent Psychiatry.* 2nd ed. Washington, DC: American Psychiatric Association Publishing; 2016).

CCPR: What does the CPG say about using scales and questionnaires to help with screening and assessments? Does it mention any specific instruments?

Dr. Abright: The US Preventive Services Task Force recommends universal screening for depression in adolescents but does not have a similar screening recommendation for anxiety disorders. Yet, screening for anxiety is important in specialty and non-specialty clinical settings as well as in schools and community agencies, especially in view of the high prevalence rates and associated distress and impairment in young people. Use rating scales and other measures that are brief, easy to administer and score, freely available, and compatible with electronic medical records. The online version of the CPG includes links to a broad-based and widely used instrument called the Pediatric Symptom Checklist (www.tinyurl.com/pv82dw5j). It can be used for screening for a range of conditions, including anxiety disorders. The CPG also links to anxiety disorder–specific scales such as the Generalized Anxiety Disorder 7 (GAD-7; www.tinyurl.com/yc5fy2f9) or the SCARED (Screen for Child Anxiety Related Emotional Disorders; www.tinyurl.com/vyerrsy7), which can be used to gauge level of anxiety and screen for specific types of anxiety disorders.

CCPR: What does the CPG tell us about treatment?

Dr. Abright: The key take-home messages from the guideline are the recommendations and suggestions for CBT and SSRIs (alone or in combination) as safe and effective treatments for anxiety disorders in children and adolescents, and for SNRIs as additional treatment options. The evidence is limited, so the guideline does not include recommendations for sequencing of treatment based on severity (mild, moderate, severe), preferential use of one SSRI over another, effectiveness of non-CBT psychotherapies, or long-term safety risks of pharmacologic treatments.

CCPR: So, what does this mean for treatment of specific patients?

Dr. Abright: Treatment planning for specific patients should be based on individualized assessment of each patient's symptoms, history, and response to previous treatments; differential diagnosis; collaboration with patients and families in development of patient-specific goals; and consideration of treatment options that take into account available evidence for potential benefits and risks, but also feasibility and acceptability for patients and families.

CCPR: The older Practice Parameters had different levels of confidence in their guidance. Is that true of the CPG?

Dr. Abright: The CPG has two levels of guidance: recommendations and suggestions.

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Recommendations indicate high strength of evidence and confidence that treatment benefits outweigh risks. *Suggestions* indicate lower strength of evidence and less confidence that benefits outweigh risks. The guideline *recommends* CBT and SSRIs for treatment of anxiety and *suggests* SNRIs and combination treatment with CBT and SSRIs as additional options.

CCPR: So, for a child with, say, social anxiety disorder, the family might pick therapy, medication, or both. If medication is part of the plan, what if the family asks for an SNRI, for example if another family member did well with it?

Dr. Abright: The suggestion for use of SNRIs is not as strong as the recommendation for SSRIs, but clinicians must also consider individual factors and patient and family preferences. The goal of the guideline is to offer evidence-based guidance that may assist clinicians in making treatment decisions. The guideline is not meant to limit reasonable treatment options based on clinical assessment, or to serve as a standard of care.

CCPR: We recently reviewed an article that found SSRIs had more side effects (*CCPR*, Jun/Jul/Aug 2021). SNRIs had fewer side effects, but they weren't as effective. What medications were covered in the review?

Dr. Abright: The two medication classes have differing side effect profiles. There is less confidence that the benefits of SNRIs outweigh their risks. For SSRIs, the AHRQ review covered sertraline, citalopram, escitalopram, fluoxetine, fluvoxamine, and paroxetine. For SNRIs, the AHRQ review covered duloxetine, venlafaxine, and the selective NRI atomoxetine. Fluoxetine and escitalopram have FDA approval for treatment of adolescent depression, and fluoxetine has an indication for depression down to age 8, but these medications and other SSRIs do not have an FDA indication for anxiety disorders in this age group. Duloxetine has FDA approval for treatment of generalized anxiety disorder for ages 7–17, but additional factors, including potential risks, are also important considerations in choosing a medication. The AHRQ also looked at benzodiazepines and found insufficient evidence for their effectiveness. The AACAP's *Anxiety Disorders: Parents' Medication Guide* is an excellent information resource for parents and clinicians regarding medications and other treatments (www.tinyurl.com/2p9f9tzc).

CCPR: Does the CPG have anything more to say about combinations of therapy and medications?

Dr. Abright: A major study, the Child/Adolescent Anxiety Multimodal Treatment Study (CAMS), found that combination treatment was superior to sertraline or CBT alone up to 24 weeks, but that this superiority was not maintained at longer-term follow-up (Compton SN et al, *Child Adolesc Psychiatry Ment Health* 2010;4:1). The AHRQ review concluded that there was insufficient evidence to support superior effectiveness of combination treatment over treatment with either CBT or SSRIs alone. The guideline classifies combination treatment as a suggestion rather than a recommendation, but notes that combination treatment may be a good choice for cases with moderate to severe symptoms and impairment or partial response to monotherapy. This topic is the subject of ongoing research and discussion (Hudson JL, *Evid Based Ment Health* 2009;12(3):88).

CCPR: Does the CPG offer additional guidance about specific treatments for specific disorders?

Dr. Abright: The AHRQ review did not find sufficient evidence to support specific treatment recommendations for any of the specific disorders. For example, it did not find evidence that SSRIs are better for generalized anxiety disorder than for panic disorder. This is partly because much of the evidence for treatment of these disorders is based on lumping together different studies and anxiety groupings into a combined analysis. Therefore, clinicians need to rely on their best clinical judgment in treating any individual child or teenager.

CCPR: What does the CPG say about treating anxiety disorders in children and adolescents from underrepresented racial groups or cultural populations?

Dr. Abright: The AHRQ review and the CPG highlight limitations in the current evidence base for treatment of anxiety disorders in minorities and other underrepresented populations as a significant area in need of further research, leaving clinicians to extrapolate results from existing studies without sufficient information about the effectiveness of treatments in these populations. Successfully providing high-quality care to youth from economically disadvantaged and minority backgrounds requires a comprehensive effort that includes partnership with primary care providers, schools, and community agencies; community outreach and education; continued advocacy by AACAP and other major professional organizations; and encouragement of funding for relevant research and clinical programs.

CCPR: This speaks to the interpretation of behaviors as acting out vs driven by anxiety.

Dr. Abright: ADHD and other disorders associated with behavioral problems are frequently comorbid with anxiety disorders, and it is important to address and treat underlying anxiety symptoms when these are identified as triggers for behavioral outbursts.

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

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Research Updates IN PSYCHIATRY

ADHD

Methylphenidate Improves Mood and Boredom in Children With ADHD

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

REVIEW OF: Golubchik P et al, *J Child Adolesc Psychopharmacol* 2021;31(4):310–314

TYPE OF STUDY: Open label, uncontrolled

We are always looking for new angles to understand the conditions we treat. ADHD leads to significant academic and social impairments and is highly comorbid with depression and "boredom." This study examines these associations using the Test of Variables of Attention (TOVA) to see whether methylphenidate (MPH) can help symptoms of depression and boredom in addition to ADHD symptoms.

Researchers enrolled 33 children (24 boys and 9 girls) aged 7–18 years with ADHD and looked at baseline and three-month post-MPH assessments using the parent-rated ADHD Rating Scale (ADHD-RS), the Short Boredom Proneness Scale (SBPS), and the Children's Depression Inventory (CDI-total and its CDI-AS academic and social function subscale). TOVA was administered only at baseline and assessed omission errors, commission errors, and reaction time. MPH was dosed at 10–54 mg based on efficacy and tolerance.

The study found that higher severity of ADHD, depression, and boredom proneness led to worse reaction time (RT) and RT variability on TOVA. Youths with ADHD and low mood had worse attention span than those without low mood. Moreover, MPH treatment was associated with a significant improvement in not only the core ADHD symptoms, but also in academic and social function (CDI-AS) as well as boredom levels.

These results are limited by the study's open-label design, its small sample size, the lack of TOVA after MPH, and the inability in this kind of study to calculate an effect size.

CCPR'S TAKE

Depression and boredom are part of cognitive dysfunction in ADHD, and the role of boredom deserves more investigation. Look for and track these symptoms in patients with ADHD. While more studies are always needed, MPH may be effective beyond core ADHD symptoms of inattention and hyperactivity-impulsivity and help associated depression and boredom.

The Evidence Base for Polypharmacy in ADHD

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

REVIEW OF: Baker M et al, *J Child Adolesc Psychopharmacol* 2021;31(3):148–163

TYPE OF STUDY: Literature review

Psychotropic polypharmacy is increasingly the norm in clinical practice. We use it to address persistent symptoms or to target comorbid conditions, though we do so at the risk of increased side effects, more drug interactions, and worsened patient compliance. This review examines the evidence base for polypharmacy in the treatment of ADHD in children and adolescents.

The authors' literature search found 39 studies and 17 randomized controlled trials (RCTs), a "relatively limited evidence base … to support a practice that occurred in 20% of outpatient visits in 2007 and is likely higher today."

Nearly all trials included a stimulant. The most common additions were alpha-agonists, followed by risperidone and atomoxetine.

Sixteen of the 37 studies combined a stimulant and an alpha-agonist. RCT data showed that for stimulant partial responders, the combination of stimulant and alpha-agonist was superior to alpha-agonist alone in reducing residual ADHD symptoms, and superior to stimulant alone if there was a history of partial response to stimulant monotherapy, with an effect size of about 0.4. Combination treatment was associated with bradycardia, sedation, somnolence, and hypotension.

For ADHD with comorbid aggression and disruptive behavior, RCT data found that stimulants alone had a large effect size. Combination treatment with divalproex or risperidone did improve response beyond stimulant monotherapy, with the greatest support for risperidone; however, there was a price to pay. Despite the short study durations and the low dosages of risperidone (<2 mg/day) in all the studies, significant prolactin elevations and weight gain were seen.

One RCT of atomoxetine found no evidence of improvement with added MPH, with the suggestion that "optimizing dose and allowing adequate duration for response is favorable to adding medications."

For management of comorbid anxiety, depression, and disruptive mood dysregulation disorder, data from four RCTs of SSRIs with stimulants showed this very common combination, while safe, had minimal benefit for anxiety and mood comorbidities.

The authors conclude the data support existing guidelines to start with stimulant monotherapy for ADHD. Still, antipsychotics are worth considering, despite their side effects, when aggression is severe or persistent. The authors recommend using measurement-based care to determine if the benefit of an added medication is worth the risk.

CCPR'S TAKE

Combination treatment for ADHD may be beneficial, though it comes at the cost of more side effects. Adding an alpha-agonist is helpful in partial responders to stimulants, and, in line with clinical lore, adding risperidone can be helpful for aggression. Remember that side effects can differ based on pubertal status.

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1. Which of the following new ADHD medications for children and adolescents is a non-stimulant selective NRI (LO #1)?
   - [ ] a. Quillivant
   - [ ] b. Qelbree
   - [ ] c. Dyanavel
   - [ ] d. ProCentra

2. According to Dr. Abright, in a national comorbidity survey of adolescents, which disorders were most commonly reported (LO #2)?
   - [ ] a. Depressive disorders
   - [ ] b. Bipolar disorders
   - [ ] c. Anxiety disorders
   - [ ] d. Substance use disorders

3. According to a 2021 review of youths with ADHD, which of the following about polypharmacy for ADHD was true (LO #3)?
   - [ ] a. Stimulants alone had a small effect size for ADHD with comorbid aggression and disruptive behaviors
   - [ ] b. Atomoxetine + methylphenidate significantly improved ADHD symptoms compared to atomoxetine alone
   - [ ] c. SSRIs + stimulants improved anxiety and mood comorbidities in ADHD with a large effect size
   - [ ] d. Stimulants + alpha-agonists improved residual ADHD symptoms in stimulant partial responders better than either treatment alone

4. In the Multimodal Treatment of ADHD Study, stimulants were more effective at improving children's core symptoms of ADHD compared to behavioral treatments (LO #1).
   - [ ] a. True
   - [ ] b. False

5. According to Dr. Abright, which of the following treatments for anxiety disorders in children and adolescents is recommended by the Clinical Practice Guideline (LO #2)?
   - [ ] a. Psychodynamic therapy
   - [ ] b. SSRIs
   - [ ] c. SNRIs
   - [ ] d. Benzodiazepines

6. In a recent study of children and adolescents with ADHD, how did methylphenidate (MPH) affect measures of academic and social difficulties, boredom, and ADHD symptoms at three months post-MPH treatment (LO #3)?
   - [ ] a. MPH significantly improved core symptoms of ADHD, boredom levels, and academic and social function
   - [ ] b. MPH significantly improved core symptoms of ADHD and boredom levels but had no effect on academic and social function
   - [ ] c. MPH significantly improved boredom levels but had no effect on core symptoms of ADHD and academic and social function
   - [ ] d. MPH significantly improved core symptoms of ADHD and academic and social function but had no effect on boredom levels

7. According to Dr. Buchanan, what is the role of atomoxetine in the treatment of ADHD, compared to stimulants and alpha-agonists (LO #1)?
   - [ ] a. Atomoxetine should be a second-line treatment after stimulants
   - [ ] b. Atomoxetine should be a third-line treatment after stimulants and alpha-agonists
   - [ ] c. Atomoxetine should be a first-line treatment
   - [ ] d. Atomoxetine does not have a role in the treatment of ADHD

8. In the Child/Adolescent Anxiety Multimodal Treatment Study (CAMS), what was concluded about the efficacy of combination sertraline and CBT, versus each treatment alone, for improving anxiety symptoms in children and adolescents (LO #2)?
   - [ ] a. Sertraline alone was superior to combination treatment and CBT alone at week 23
   - [ ] b. Combination treatment and sertraline alone were superior to CBT alone at week 30
   - [ ] c. CBT alone and sertraline alone were superior to combination treatment at week 19
   - [ ] d. Combination treatment was superior to CBT alone and sertraline alone up to week 24, but this superiority was not maintained at longer follow-up

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Note From the Editor-in-Chief

Masks or no masks, kids with ADHD are struggling. Stimulants are helpful, but how do we choose from all the new preparations? Dr. Anne Buchanan helps us sort that out. Parents are often concerned about giving stimulants to their kids and teens. We have ideas to help you talk with parents and collaborate with them. Anxiety disorders are rampant, and the AACAP featured anxiety for their first Clinical Practice Guideline, a new approach to better consolidated advice. The results offer broad guidance for treatment. This issue also includes research on mood and boredom in ADHD and on the efficacy of combined pharmacotherapy/polypharmacy for ADHD. We planned this ADHD issue long ago, but as we go to press there are more child refugees abroad and, at home, actions targeting parents who support gender-affirming care. Always so much happening—we welcome your thoughts.

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