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IN THIS ISSUE

Evidence-Based Treatment in Child and Adolescent Psychiatry

What Works in Child and Adolescent Psychiatry: A Guide to Evidence-Based Treatments

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Dr. Steuber has no financial relationships with companies related to this material.

When treating kids and teens with psychiatric disorders, it's easy to feel overwhelmed by treatment options. This guide walks you through what works best, based on the evidence, for the most common conditions in child and adolescent psychiatry.

First things first

Give yourself adequate time to complete an initial assessment. Children and teens typically come in with multiple conditions, so developmental, social, and family history (including medication responses) will guide your care.

ADHD: Stimulants reign supreme

Stimulants remain the most effective treatment for ADHD, with effect sizes between 0.8 and 1.0—some of the highest in medicine (Pliszka S et al, *J Am Acad Child Adolesc Psychiatry* 2007;46(7):894–921).

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Highlights From This Issue

Feature Article. Evidence-based treatment in child and adolescent psychiatry is effective. Start with nonpharmacological care when possible, reserve medication for moderate-to-severe cases, and taper gently when you can.

Feature Q&A. Use the PICOT framework to evaluate whether a study's population, comparator, and outcomes are relevant to your practice.

Q&A on page 5. Genetic testing can guide care for children with neurodevelopmental disorders, but it rarely changes management for common conditions.

Article on page 8. Newer antipsychotics may offer metabolic advantages for some youth, but pediatric safety data remain limited.

Q&A With the Expert

Assessing the Evidence in Child and Adolescent Psychiatry
Glen Spielmans, PhD

Professor of Psychology, Metropolitan State University, St. Paul, MN.

Dr. Spielmans has no financial relationships with companies related to this material.

CCPR: Why should clinicians critically evaluate the research studies behind the treatments they use?

Dr. Spielmans: Research can take time and skill to review. Is a study relevant to your patients? Are there biases in the design or the way the results are reported? The results may be overhyped, so clinicians need to evaluate the outcomes for themselves. Leucovorin, for example, is touted as a treatment for autistic symptoms; however, the largest placebo-controlled study to date was recently retracted after alert readers noted major numerical discrepancies in the study (www.tinyurl.com/m4ehh8z3). This leaves little evidence of leucovorin's efficacy.

CCPR: How can clinicians identify good research?

Dr. Spielmans: If a study's results seem too good to be true, they probably are. Look for replicated results, especially from independent research groups. To identify good studies, use the PICOT method: Population, Intervention, Comparison, Outcomes, and Time frame. Starting with Population: Is it relevant? Clinical trials often exclude people with anxiety disorders, eating disorders, substance use problems, or suicidality, but our patients rarely present with a depression-only profile (Blanco C et al, *Pediatrics* 2017;140(6):e20161701). Wouldn't we like to know if a treatment works for our suicidal patients with complex diagnostic pictures? If the population isn't relevant, maybe the study isn't either. Also note that medication trials frequently exclude prior non-responders to the drug or its class, likely inflating efficacy estimates: "This drug works, except for people who didn't respond to it."

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Start with behavioral support

Start with parent and school-based behavioral interventions, regardless of medication use. Younger kids often respond well to behavioral treatment and may have more side effects from medications.

First-line meds: Methylphenidate

Try a methylphenidate-based stimulant first. These tend to cause fewer side effects than amphetamines in kids. If the first one doesn't work or causes problems, try a different formulation. If two trials fail, move to an amphetamine-based stimulant. They can be more effective but have more side effects (eg, appetite suppression, insomnia, irritability).

Second-line options

If stimulants aren't effective or preferred, consider:

- *SNRIs (atomoxetine and viloxazine):* Atomoxetine had an effect size of 0.6–0.7 in some research studies, but is less effective in clinical settings. Viloxazine is still rather new. Start low and titrate slowly. Watch for blood pressure elevation and, rarely, suicidal thoughts.
- *Alpha agonists (guanfacine XR or clonidine XR):* These medications have an effect size of 0.4–0.7. They are less effective for core symptoms but helpful for aggression, tics, or sleep problems. Use them alone or to augment stimulants.

Watch for comorbidities

Treat co-occurring issues like anxiety or depression. These may need their own interventions beyond ADHD meds.

Anxiety: Start with cognitive behavioral therapy (CBT)

Anxiety disorders are the most common psychiatric conditions in kids. Many respond well to therapy alone.

First line: CBT

CBT is your best first step, even in moderate cases. For mild anxiety, CBT alone may be enough. Effect size is around 0.6–0.7 (Walter JH et al, *J Am Acad Child Adolesc Psychiatry* 2020;59(10):1107–1124).

Second line: SSRIs

If CBT isn't available or symptoms are severe, add an SSRI. No SSRI clearly outperforms the others, though escitalopram is FDA approved for pediatric generalized anxiety disorder (GAD). Start low and go slow. Monitor for activation and suicidal thoughts, especially in the first month.

Third line: SNRIs

If the first SSRI doesn't work, try another SSRI. Only consider an SNRI like duloxetine after at least two failed SSRIs. Duloxetine is FDA approved for GAD and has an effect size of 0.5, but its side effect burden is higher (Strawn JR et al, *J Am Acad Child Adolesc Psychiatry* 2015;54(4):283–293).

Avoid benzodiazepines (BZDs)

There's little evidence for BZDs in children, with risks usually outweighing any benefit.

OCD: Use exposure and response prevention (ERP), then add SSRIs

First line: CBT with ERP

For kids with mild or moderate OCD, start with CBT that includes ERP.

Second line: SSRIs

If ERP isn't available or symptoms are severe, add an SSRI. No SSRI is superior to another for OCD, but fluoxetine, sertraline, and fluvoxamine are FDA approved for pediatric OCD. Effect sizes for SSRIs are modest (0.3–0.4; Cohen SE et al, *J Am Acad Child Adolesc Psychiatry* 2025;64(7):775–785; see RU on page 11). Higher dosages are typically necessary for OCD. If monotherapy isn't enough, combine medication and therapy.

Third line: Clomipramine

If 2 robust trials of SSRIs fail after an adequate duration (typically 12 weeks), consider clomipramine. It's more effective (effect size ~0.6) but carries more side effects, notably anticholinergic burden and cardiac risks (Watson HJ and Rees CS, *J Child Psychol Psychiatry* 2008;49(5):489–498).

Depression: Therapy first

Mild to moderate: Start with therapy

Use CBT or interpersonal therapy. Both have effect sizes around 0.6 (Walter HJ et al, *JAACAP* 2023;62(5):479–502; Arnberg A and Ost LG, *Cogn Behav Ther* 2014;43(4):275–288).

Severe or treatment resistant: Add an SSRI

If symptoms are severe, or if there's no improvement after 8–12 weeks of therapy, start medication. Antidepressant effect sizes hover around 0.5, slightly lower than psychotherapy (Walter et al, 2023). Fluoxetine has the best evidence and FDA approval. If it fails, try escitalopram, then

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sertraline. Data for antidepressants with younger kids are sparse, and some evidence points to no benefit at all (Wagner KD et al, *J Am Acad Child Adolesc Psychiatry* 2006;45(3):280–288).

Avoid SNRIs in youth depression; they have more side effects and little evidence of benefit (see *CCPR* Oct/Nov/Dec 2025).

Monitor closely

Check for new suicidal thoughts throughout treatment. The risk is low (~1%) but highest in the first few weeks.

Bipolar disorder: Match the phase

Pediatric bipolar disorder is rare. Choose meds based on the phase: depression, maintenance, or, uncommonly, mania.

- *Acute mania or mixed states:* Stabilize with antipsychotics, then try to decrease/discontinue them. Risperidone and aripiprazole have the best data (effect sizes 1.2 and 0.6). Quetiapine and olanzapine are also FDA approved (effect sizes 0.8 and 0.6; Vita G et al, *J Am Acad Child Adolesc Psychiatry* 2025;64(2):143–157). If partial response, add lithium, which is preferred over valproate in adolescents due to fewer metabolic and reproductive side effects.
- *Bipolar depression:* Try lurasidone or the olanzapine/fluoxetine combo—both FDA approved with effect sizes around 0.5.
- *Maintenance:* Use lithium if possible. It prevents relapse, has the strongest long-term data, and is preferred over valproate, especially in teens. For more, see box at right.
- *Add psychosocial support:* Medication isn't enough. Use family-focused therapy and school coordination to reduce relapse and improve adherence.

Schizophrenia: Focus on engagement and side effects

First line: Atypical antipsychotics

For childhood-onset schizophrenia, start with risperidone (effect size ~0.8). Aripiprazole and olanzapine also have strong support (effect sizes ~0.6–0.7). Aripiprazole, risperidone, olanzapine, quetiapine, paliperidone, and lurasidone all have FDA approval. If two antipsychotics fail, try clozapine. Monitor closely due to risks of neutropenia, seizures, and weight gain.

Monitor side effects

Adjust doses slowly. Discuss and closely track weight, glucose, lipids, and neurological effects, including use of the Abnormal Involuntary Movement Scale (AIMS).

Psychosocial care is key

Help families with communication and psychoeducation. Support school engagement and social functioning early.

Autism: Treat co-occurring conditions

No medication treats the core symptoms of autism, and these patients are more sensitive to side effects.

Developmental relationship-based or naturalistic, parent-mediated approaches should be first line for irritability and aggression. Focus on co-regulation and connection. Next, try complementary treatments (eg, omega-3s, melatonin). Then try alpha agonists, stimulants, SSRIs, or propranolol. If symptoms are severe and persistent, try risperidone (effect size ~0.9) or aripiprazole (effect size ~0.6). Both are FDA approved for irritability in autism (Choi H et al, *Mol Autism* 2024;15(1):7).

The Carlat Guide to Antipsychotic Prescribing

- Closely track for early weight gain in all patients.
- Use metformin early if weight is rising (watch for GI side effects).
- Begin metformin or a GLP-1 agonist with the antipsychotic for patients with BMI ≥ 30.
- Check glucose, lipids, and possibly ECG at baseline, three months, and annually.
- Screen for abnormal involuntary movements at least every six months.
- Antipsychotics have significant neurologic and metabolic side effects: Gently reduce and discontinue them when possible (see *CCPR* Apr/May/Jun 2025 for more).

Effective care: Beyond algorithms

Few kids fit neatly into the categories above. The list of other factors to consider in both assessment and treatment planning is long but includes family conflict, trauma, or stress; sleep, diet, and exercise; peer relationships and bullying; and cultural and familial views on mental health.

CARLAT VERDICT

Use nonpharmacologic approaches first whenever possible. When medications are needed, stick with those that have the strongest evidence. Always personalize care to the child and family's needs and values—and taper when appropriate.

Expert Interview – Assessing the Evidence in Child and Adolescent Psychiatry

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CCPR: What about the Intervention itself?

Dr. Spielmans: Ask yourself whether the intervention represents what you do in practice. Suppose you are a cognitive behavioral therapy (CBT) therapist, and you read a study showing "CBT" was efficacious for depression. Examine what the study therapists did. If they focused on depressive thoughts but you focus on behavioral activation, then the study is not very relevant to your work. Just because you subscribe to a particular "brand" of therapy doesn't mean all studies on that brand are relevant.

CCPR: What about the Comparison part?

Dr. Spielmans: When a study reports that treatment was effective, I ask: "Compared to what?" Doing nothing? It's not very informative when a treatment is better than a waitlist. We hope medications are better than placebo, but clinicians harness the placebo effect. In open-label studies, when half of the people get better, it's probably a placebo effect. So, look for head-to-head comparisons and watch for bias. One cleverly titled study, "Why Olanzapine Beats Risperidone, Risperidone Beats Quetiapine, and Quetiapine Beats Olanzapine," examined head-to-head trials of second-generation antipsychotics, finding that 90% of studies declared victory

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for the sponsored drug (Heres S et al, *Am J Psychiatry* 2006;163(2):185–194).

CCPR: Many autism studies use waitlist controls rather than active comparators. What does the research show, and why should clinicians approach these studies with caution?

Dr. Spielmans: This is the problem with most ABA studies. Parents arrive feeling hopeless after failed interventions, making them primed for what Jerome Frank called "re-moralization." The high-intensity treatment program lifts morale, which can shift how parents perceive and rate their child's behavior. Meanwhile, waitlist controls feel worse for waiting, skewing their ratings in the opposite direction. Compounding this, many ABA studies are single-case or non-experimental, observing changes during treatment without any independent control group. Sandbank's sophisticated meta-analysis excluded such studies when comparing effect sizes across traditional ABA, naturalistic developmental behavioral intervention (NDBI), and developmental relationship-based care (DRBI), finding moderate effect sizes for NDBI and DRBI. Despite ABA's reputation, most ABA studies had poor designs and weaker evidence than developmental approaches for treating autism (Sandbank M et al, *BMJ* 2023;383:e076733).

"Don't get excited about any individual study. If something seems too good to be true, it probably is. Look for replicated results, especially by a different group of researchers."

Glen Spielmans, PhD

CCPR: What are we looking for in the Outcomes of a study?

Dr. Spielmans: Most clinical trials use symptom rating scales. There's more to a person than those scores. We overvalue decades-old rating scales without really thinking (Kazdin AE, *Am Psychol* 2006;61(1):42–49; Fried EI et al, *Nat Rev Psychol* 2022;1(6):358–368). Does a five-point change on a scale mean a person's relationships or school function are better? Most scales don't measure those things. Assessments of quality of life and functioning in important areas (social, school, family, etc) are important but underutilized.

CCPR: We also need to track side effects. Is there an illustrative study on that?

Dr. Spielmans: The infamous Study 329 is a great example (Keller MB et al, *J Am Acad Child Adolesc Psychiatry* 2001;40(7):762–772). This randomized trial reported that paroxetine was efficacious and safe, though it was neither (McHenry LB and Jureidini JN, *Account Res* 2008;15(3):152–167). After years of haranguing, paroxetine's sponsor released detailed safety and efficacy data, which were independently analyzed (Le Noury J et al, *BMJ* 2015;351:h4320). The original *JAACAP* paper reported that 5 of 93 paroxetine patients experienced suicidal/self-injurious behaviors compared to 1 of 87 on placebo, yet these were euphemized as "emotional lability" in the original paper. Re-analysis based on careful review of individual participant records found that 11 of 93 paroxetine patients experienced suicidal/self-injurious behaviors compared to 1 or 2 of 87 on placebo. At least two participants on paroxetine who were hospitalized subsequent to threatening suicide were not even coded as being "emotionally labile."

CCPR: What's the lesson here?

Dr. Spielmans: On one hand, published research is the foundation of evidence-based medicine. On the other, published research often excludes key safety data. Sadly, poor safety data reporting à la Study 329 is common (Hughes S et al, *BMJ Open* 2014;4:e005535). In fall 2025, *JAACAP* finally attached a vague expression of concern for the infamous Study 329 paper—24 years after initial publication—despite major concerns being raised almost immediately after the paper was published. The lesson here is that you need to be extra wary of industry-sponsored research.

CCPR: Are there data reporting standards for clinical trials?

Dr. Spielmans: An internal Eli Lilly document described a goal to "mine existing data to generate and publish findings ... support[ing] the reasons to believe the brand promise of olanzapine" (Spielmans GI and Parry PI, *J Bioeth Inq* 2010;7:13–29), and internal documents from other companies reveal a similar playbook. But what if the data don't support the brand promise? The voluntary Consolidated Standards of Reporting Trials (CONSORT) sets a widely accepted standard for clinical trial reporting. A primary outcome measure must be declared before the trial begins, preventing researchers from analyzing data first and then "picking a winning outcome." All efficacy and safety outcomes should follow a predetermined statistical analysis plan and be fully reported. Most medical journals claim to follow CONSORT, yet many articles fall short, and journals often refuse to publish letters pointing out the discrepancy (Jones CW et al, *BMC Med* 2015;13:282; Goldacre B et al, *Trials* 2019;20(1):118). In practice, CONSORT compliance often provides a veneer of credibility over the same poor reporting that has long plagued clinical trials. This makes critical reading essential. To vet an article, find its National Clinical Trial (NCT) number in the abstract or methods section and enter it at clinicaltrials.gov to review the study protocol and history of changes, checking whether all outcomes were reported. It's extra work, but it can meaningfully raise (or lower) your confidence in a study's results.

CCPR: And, finally, what about the Time frames for studies?

Dr. Spielmans: Depressed people are usually better after a few months if you do nothing. So, when a treatment study reports that most people were better in a few months, I'd say, "They should have been anyway." That will vary with severity, co-occurring problems, and the condition being studied. Look for controlled studies with long (eg, one-year) outcomes. Also, don't assume that improvements made in a short-term clinical trial carry forward to months or years later. Symptoms often recur after a study is completed. Taken together, PICOT gives you a practical five-part checklist you can apply to almost any study before acting on its findings.

CCPR: Which reports catch your attention?

Dr. Spielmans: Positive case studies report innovations that springboard systematic research. But I want to see more case studies that say, "I tried this thing, and it didn't work." One review found that 95% of published case studies found positive results; if only we achieved such outcomes in the real world (Albrecht J et al, *J Clin Epidemiol* 2005;58(12):1227–1232)! Side note: I think clinicians should collect data on patient outcomes, for the sake of accountability and quality improvement. We all want to think we're effective, but this should be tracked objectively. Look for clinical trials whose participants are similar to your patients, report data fully, and use reasonable controls (placebo is nice, but a well-implemented established alternative treatment is better).

CCPR: What about groups of clinical studies, such as meta-analyses?

Dr. Spielmans: People already think of meta-analysis as wizard math, but it's essentially combining averages

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across studies using sophisticated statistical formulas. Start by checking for heterogeneity: If studies are too different, lumping them together may not make sense. For example, one CBT study might focus on challenging negative thoughts while another emphasizes behavioral activation. Combining them inflates the sample and statistical power, making effects easier to find across 30 studies than 3, but quantity doesn't equal quality. Individual studies may have poor outcome assessor blinding, questionable randomization, or other sources of bias.

CCPR: Besides Sandbank, which rocked the autism world, what other important meta-analyses are out there in child psychiatry?

Dr. Spielmans: There are few relevant controlled trials for child psychiatry interventions, limiting the availability and informativeness of meta-analyses. A few positive SSRI trials for youth depression were published in the late 1990s to early 2000s based on highly selective publication, but once researchers accessed unpublished data, meta-analyses found minimal to no effects for SSRIs and SNRIs (Jureidini JN et al, *BMJ* 2004;328(7444):879–883; Whittington CJ et al, *Lancet* 2004;363(9418):1341–1345). While fluoxetine appeared to outperform other SSRIs, subsequent studies have raised questions about that finding (Plöderl M et al, *J Clin Epidemiol* 2026;189:112016). *(Editor's note: At Carlat we recognize that antidepressants have little impact on most kids, and we favor fluoxetine if we are going to try using one.)*

CCPR: How are studies of therapy similar to medication studies?

Dr. Spielmans: Many therapy studies use placebo therapy (reflective listening, no homework, no advice) to hold psychotherapy to the same standard as medication. These studies typically show that real therapy outperforms the placebo, but questions remain about therapist training and supervision quality. More informative are head-to-head comparisons of psychotherapies, designed and implemented by experts in each modality being studied.

CCPR: How does all this lead to umbrella reviews?

Dr. Spielmans: Umbrella reviews are meta-analysis of meta-analyses (or of systematic reviews if it's not easily quantifiable). Say we're looking at prevention of depression, anxiety, and substance use. These are related but separate entities. An umbrella review can combine them to look at prevention of mental health problems in general. Some umbrella reviews combine the biggest or best meta-analysis on a topic, because several meta-analyses on the same topic can have a lot of overlap of individual studies. Another way is to gather the individual studies from all existing meta-analyses, but this is a lot more work.

CCPR: How do we talk with families about research, especially with current challenges to mental health care in public forums?

Dr. Spielmans: Use a PICOT approach and check whether the studies are relevant to the family. Say you've got a kid with autism, ADHD, and depression. That's not unusual. How many clinical trials do we have on this combination? Not many, if any. But consider generalizing from narrower studies. You might interpret such studies as a glass half full or glass half empty—but being explicit with families about that uncertainty and framing it as an evolving evidence base, rather than a failing of science, can build trust instead of undermining it.

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

Editor's note: Keep the following in mind when reviewing research you may want to apply to clinical practice:

- *Abstracts often overstate their findings (Shinohara K et al,* PLoS One *2017;12(9):e0184786).*
- *Effect sizes can help distinguish between statistical and clinical significance.*
- *It's worth differentiating outcomes-based studies that show associations from experimental studies, which aim to establish cause and effect.*
- *The quality of an umbrella review is only as strong as the meta-analyses it draws from—and meta-analytic quality is often poor.*

Q&A With the Expert

Managing Genetic Risk for Psychiatric Conditions in Children and Adolescents

Aaron Besterman, MD, DFAACAP

Medical Director, Laura Rodriguez Research Institute; Child & Adolescent Psychiatrist, Family Health Centers of San Diego; Health Sciences Clinical Associate Professor (non-salaried), UCSD.

Dr. Besterman has no financial relationships with companies related to this material.

CCPR: What's new in psychiatric genetic risk?

Dr. Besterman: In the past 5–10 years, we've identified many genetic risk factors for psychiatric illness. Now we need to interpret all this information to inform care, particularly assessment. That includes trying to describe conditions more specifically, as well as thinking about the risks of psychiatric illness and how to reduce those risks. For kids with neurodevelopmental disorders, there are evidence-based guidelines suggesting genetic testing for rare variants. Previously, chromosomal, microarray, and fragile X testing were the standard of care. In the past few years, whole-exome sequencing has enabled the identification of genetic changes related to increased risk of developmental disorders in up to 40% of individuals.

CCPR: How does the identification of genetic risk help these kids?

Dr. Besterman: You can help the patient based on knowledge of the specific genetic disorder; you can offer reproductive counseling and basic emotional support; in some cases you can enroll in clinical trials; and you can find an online group gathering information about the condition. Communities of families and patients play a leading role in driving therapeutic discovery. Families also identify the biggest needs of the patients, and they support fundraising.

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Expert Interview – Managing Genetic Risk for Psychiatric Conditions in Children and Adolescents

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CCPR: What does informed consent look like with genetic testing? Are there risks? Should we always encourage genetic testing for kids with developmental challenges?

Dr. Besterman: Informed consent and informed assent (for adolescents or dependent adults) is necessary prior to genetic testing. Most labs can use buccal swabs mailed from home to do genetic testing. Risks include detecting non-paternity (ie, dad is not dad) and finding genetic changes completely unrelated to the thing you're testing for (eg, breast cancer risk genes). Usually, the family can decide whether they want unrelated genetic results reported. Also, genetic information can be used by life and disability insurance companies when deciding whether to insure, though they can't use it to deny health coverage because of the Genetic Information Nondiscrimination Act. Families should consider getting insurance before testing if they don't have it already. For most children with neurodevelopmental disorders, parents will decide whether to go ahead with testing, but for those who need minimal support, the likelihood of a clinically important finding is lower, and families may wait to let the person decide when they are older.

CCPR: As part of informed consent, how often does testing change the care plan?

Dr. Besterman: Genetic testing rarely changes the care plan, although I've had cases where we picked up Rett syndrome and started trofinetide, a case where we found PTEN hamartoma syndrome and are now monitoring for cancer, and a patient diagnosed with fragile X whom we are starting on metformin (Gantois I et al, *Annu Rev Med* 2019;70:167–181).

CCPR: How do you manage the potential guilt parents might have that they passed the condition on to their child?

Dr. Besterman: Many single-gene differences, such as Huntington's, always lead to the condition, but in most psychiatric conditions this is not the case. So when genetic changes happen de novo it is bad luck, and when they are passed down from parents it is important to note that the genetics add risk but do not guarantee the person will be affected.

"When genetic changes happen de novo it is bad luck, and when they are passed down from parents it is important to note that the genetics add risk but do not guarantee the person will be affected."

Aaron Besterman, MD, DFAACAP

CCPR: Is whole-exome sequencing covered by insurance?

Dr. Besterman: Whole-exome sequencing is covered by most private insurance companies for assessing neurodevelopmental disorders such as autism, intellectual disability (ID), global developmental delay, cerebral palsy, and epilepsy. Government-based insurance unfortunately does not cover it as consistently. Exome sequencing is a first-line diagnostic test and looks only at the gene-coding regions, the exons. Whole-genome sequencing looks not only at the gene coding regions, but more broadly at the regulatory regions. The real questions for clinicians are how to talk with families about getting the test and what to do if there's a positive result. I encourage folks to reach out to medical geneticists or genetic counselors, clinicians who are genetics experts. A shortage of these specialists means that there are often year-long waitlists. There are also companies that do commercial genetic testing and then offer genetic counseling services free of charge. The best way to make sure that they are reputable is to check if they are officially certified by lab oversight bodies (CLIA certification).

CCPR: Is there a role for exome sequencing in psychotic disorders?

Dr. Besterman: Schizophrenia is in the gray zone between disorders like depression and anxiety, and neurodevelopmental disorders like autism and rare neurodevelopmental syndromes. We're identifying genetic disorders in about 6% of children with psychotic conditions using microarray, exome sequencing, or genome sequencing. And in young kids with psychosis, rates of genetic disorders are approaching 10% (Alkelai A et al, *Schizophr Res* 2023;252:138–145; Ahn K et al, *Mol Psychiatry* 2014;19(5):568–572). The Royal College of Psychiatrists in the UK recommends genetic testing for children and teens with psychotic disorders, but no genetic testing is considered standard of care in the US currently. I suspect that will change at some point.

CCPR: Is genetic testing useful for more common psychiatric disorders in children and teens?

Dr. Besterman: For common childhood disorders like depression, anxiety, and OCD, there is no indication for diagnostic genetic testing. Our current diagnostic genetic testing only detects rare variants with a large effect size, and the genetic changes that underlie these disorders are mostly common genetic changes of small effect size. So diagnostic genetic testing like exome sequencing is not informative or indicated. Parents desperate to find an explanation for their child's psychiatric condition will sometimes ask about genetic testing, and I inform them that even if we were to identify a genetic change, it wouldn't tell us anything about their child's psychiatric condition. There is also the risk of finding unexpected "incidental" genetic changes that confer risk for other health conditions. Where genetics have played a role in these conditions is with pharmacogenetic testing, where it is used to look at genes involved in drug metabolism and to choose the right drug or dosage. There's been controversy for years around whether this improves outcomes. A recent RCT found that kids who got pharmacogenetic testing received less frequent evidence-based treatment than those who did not get tested, which was counterproductive (Vande Voort JL et al, *J Am Acad Child Adolesc Psychiatry* 2022;61(1):46–55).

CCPR: Your recent paper talked about a 40% heritability for depression (Besterman AD et al, *Am J Psychiatry* 2025;182(8):728–741). What do you mean when you say heritability?

Dr. Besterman: The word heritability is used colloquially to refer to the general concept of passing on a trait. But it has a technical genetics definition that refers to the specific genetic contribution to a disease. We're really referring to how much of an observed phenotype, in this case psychiatric phenotype, can be explained through genetics.

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CCPR: Can we talk about the heritability of psychiatric disorders? I have parents who feel guilty about their children's conditions, and I have couples worried about having children who might suffer from their own conditions.

Dr. Besterman: Many parents feel their children are doomed to inherit their conditions. It doesn't work that way. Your child will probably be at an increased risk of developing these conditions compared to the average person, but there are so many ways to minimize that risk—things like avoiding certain drugs, getting good sleep and exercise, and eating well. Lifestyle factors have an enormous protective ability against mental illnesses. I like to share the Jar Model, a tool developed by Jehannine Austin and Holly Peay, with families. In this model, we use the idea of a jar that needs to be filled to the top with risk factors for someone to have a disease. *(Editor's note: See figure below.)* There are different risk factors, both genetic and environmental, that can fill up a person's jar. But there are also ways to make the jar larger (eg, building psychological resilience, good fitness, good health, etc). Or you could put a lid on top to prevent more risk factors from being dumped inside (eg, avoiding substances and toxic situations). Just because you have one genetic risk doesn't mean your whole jar is going to get filled to the top.

CCPR: So, if a child is depressed, his jar is overflowing. Does 34% heritability mean that his jar was already about 34% full?

Dr. Besterman: That's the general idea. But heritability is also not a static measure. How much genetics contributes to a condition may vary over time and depending on the specific individual and context. We might find an average heritability, but even that can vary depending on how you calculate heritability. It can vary widely from twin studies to genome-wide association studies, where we just look for tiny genetic risk factors that are more common in the affected population compared to a control population. These are average ballpark numbers—our best guesses of how much genetics contributes to a specific disease in a population. They don't apply perfectly to specific individuals. Don't fixate on a specific number, but use the concept of genetic risk factors, environmental risk factors, and the interaction between the two to help people protect themselves using resilience factors.

CCPR: In autism we talk about over 90% heritability, which argues against concerns about vaccines.

Dr. Besterman: This is important. Autism is one of the more heritable conditions, compared to depression where there seems to be a much larger environmental component. In autism your brain develops in utero, driven by your specific genetic makeup. That's well established: Many of the critical genes in autism are turned on primarily at early times in stages of development. This is not to say that certain environmental factors couldn't contribute to the development of autism, but it's less of a role than in other psychiatric disorders, and vaccines have been rigorously demonstrated not to be associated with an increased risk of autism (Gabis LV et al, *Eur J Paediatr Neurol* 2022;36:151–158).

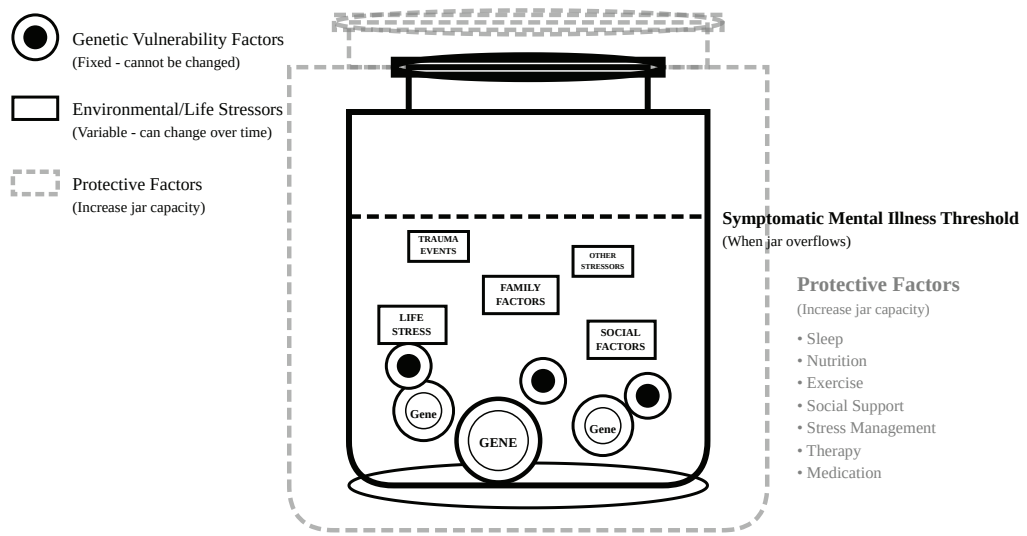
CCPR: Is heritability specific? There's overlap among genes for autism, bipolar disorder, schizophrenia, and ADHD risk.

Dr. Besterman: Historically, neurogenetics and neuropsychiatric genetics focused on monogenic disorders (eg, fragile X syndrome, Angelman syndrome, etc) with some success. But for common psychiatric disorders (depression, schizophrenia, anxiety disorder, eating disorders, basically everything else), we have found that the genetic architecture is polygenic. A change in one individual gene adds a tiny bit of risk. It's the effect of thousands of changes across many genes that cumulatively confers risk for psychiatric disorders. Some of these tiny changes may increase the risk for multiple psychiatric disorders. So, depending on the exact collection of tiny changes, you might be more predisposed to one psychiatric disorder than the other.

CCPR: In summary, saying, "What's in the cats is in the kittens" is not a precise way to address heritability with parents?

Dr. Besterman: Listen to their concerns. If a parent feels they caused their child's condition, spend the session talking about guilt. If their concern is around heritability, a clear understanding of this concept will be very helpful, including whether to recommend diagnostic genetic testing, depending on the specific condition you are talking about. And you need to know whom to reach out to for help and consultation. Have an approach in mind so you can help and support your patients and families the best way possible.

Jar Model



CCPR: How do you help families manage this guilt?

Dr. Besterman: When you can offer an actual genetic diagnosis, mostly for kids with autism and ID, you can say, "I know something important about your child's developmental difficulties. The genetic difference that we have identified in your child was a random event that

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occurred during development that you have no control over, and it was just unlucky." I have had numerous parents break into tears, saying, "This is so relieving. For so many years, I thought I had a sip of wine during pregnancy and that's what caused it." This is where the Jar Model can be helpful, offering parents a general understanding of how genetics, environment, and resilience all interact and contribute to a psychiatric disorder. It gives clarity to families about how these things work—how biology underlies these disorders.

CCPR: Parents often worry that their kids will develop a condition that runs in the family. What can we tell them?

Dr. Besterman: I might say, "Because this disorder runs in your family, your child is at a higher risk than the average person in the population, but for most people who have your child's level of risk, they will not develop it. So there's still a very high chance that your child will be fine even though their risk is elevated compared to the average person in the population." Always taking it back to that reference rate, I think, can be helpful.

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

❖ ❖ ❖

New Antipsychotic Formulations for Children and Adolescents: Caution Prevails

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Dr. Young and Dr. Rosen have no financial relationships with companies related to this material.

Your 16-year-old with schizophrenia has failed several good antipsychotic trials. He's now gained significant weight on risperidone and still struggles with hallucinations, and an extensive medical workup is negative. The family wonders whether "newer antipsychotics" are safer or more effective. Should you consider one of these agents?

Second-generation antipsychotics (SGAs) are mainstays for psychosis and bipolar disorder, but their side effects—weight gain, metabolic changes, neurotoxicity (cortical thinning, several kinds of extrapyramidal symptoms [EPS])—demand great caution. Newer agents are emerging with novel mechanisms of action. In this update, we review what's FDA approved for youth, highlight promising new options, and consider how neuroscience-based nomenclature (NbN) may change how we think about these drugs.

FDA-approved SGAs in youth

Many SGAs are FDA approved in children and adolescents (see table on page 9 for a full list). Aripiprazole and risperidone are the most used, with additional approvals for olanzapine, quetiapine, and others. All carry risks of weight gain, metabolic disturbance, and sedation, though the degree varies.

- *Aripiprazole:* Often chosen first for schizophrenia and bipolar disorder in teens; somewhat less weight gain than risperidone or olanzapine but can cause akathisia and insomnia.
- *Asenapine:* Alternative administration routes by sublingual tablets and transdermal patches; high rates of sedation and metabolic risk.
- *Brexpiprazole:* Approval for schizophrenia was inferred from adult studies, but a pediatric trial has shown reduction in schizophrenia symptoms compared to placebo; however, this may not result in significant clinical differences (Ward C et al, *Lancet Psychiatry* 2025;12(5):345–354).
- *Lurasidone:* Used for schizophrenia and bipolar I depression. Must be taken with at least 350 calories of food for absorption.
- *Olanzapine:* Powerful for acute psychosis and mania but typically avoided in youth because of extreme metabolic risk.
- *Paliperidone:* Has the youngest age range approval for schizophrenia (12 years); however, it carries increased risk of increasing prolactin, like risperidone.
- *Quetiapine:* Useful in acute mania and when sedation is desired (eg, comorbid insomnia) but has limited evidence for schizophrenia in adolescents compared with risperidone or aripiprazole.
- *Risperidone:* Like aripiprazole, has a broad range of approvals, including for autism-related irritability; highly effective but carries significant risk of weight gain, prolactin elevation, and metabolic issues.

NbN drug classification

Traditionally, we've described medications by indication. NbN classifies drugs by mechanism of action, highlighting how receptors map onto symptoms and side effects. This can help clinicians think beyond "first-line SGA" toward mechanism-based choices. Below, we review biochemical pathways relevant to antipsychotics.

- *Dopamine:* Excess mesolimbic dopamine produces hallucinations and delusions; reduced prefrontal dopamine contributes to apathy and impaired executive function (Orzelska-Górka J et al, *Int J Mol Sci* 2022;23(18):10624).
- *Glutamate:* Dysregulation worsens both positive symptoms and cognition (Orzelska-Górka et al, 2022).
- *Serotonin (5-HT):* Modulates dopamine activity and affects both positive and negative symptoms.
- *Muscarinic (M1/M4):* Links to attention, memory, and motivation (Syed YY, *Drugs* 2025;85:103–109).
- *Trace amine associated receptor 1 (TAAR1) agonists:* Regulates dopaminergic and serotonergic activity, with antipsychotic-like and pro-cognitive effects (Achytes ED et al, *Eur Arch Psychiatry Clin Neurosci* 2023;273(7):1543–1556).

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New Antipsychotic Formulations for Children and Adolescents: Caution Prevails
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New meds through the NbN lens

Instead of lumping new drugs together as "antipsychotics," NbN can distinguish a multi-receptor modulator from a muscarinic agonist. A patient with weight gain on risperidone may benefit from a dopamine-sparing mechanism, while someone with apathy might try muscarinic or glutamatergic pathways. Here are some new agents with different mechanisms.

Lumateperone (Caplyta)

- *Mechanism:* Multi-receptor modulator (D2 full antagonist postsynaptic, partial agonist presynaptic; 5-HT2A antagonist; glutamatergic activity).
- *Benefits:* Reduces psychosis with less metabolic burden than risperidone or olanzapine; potential effects on cognition.
- *Adverse effects:* Somnolence, sedation, fatigue, constipation.
- *Status:* FDA approved for adult schizophrenia (Correll CU et al, *JAMA Psychiatry* 2020;77(4):349–358). Pediatric studies are lacking.
- *Clinical pearl:* Consider off-label only when metabolic concerns dominate and established SGAs are poorly tolerated.

Xanomeline/trospium (Cobenfy)

- *Mechanism:* M1/M4 receptor agonist with no D2 activity. Trospium reduces peripheral cholinergic side effects.
- *Benefits:* Improves positive, negative, and cognitive symptoms without weight gain or EPS.
- *Adverse effects:* Constipation, dyspepsia, nausea, vomiting.
- *Status:* FDA approved for adult schizophrenia in 2024 (Syed, 2025). No pediatric data.
- *Clinical pearl:* Promising for patients who are limited by EPS or metabolic burden, but the GI side effects can be significant.

TAAR1 agonists (Ulotaront, Ralmitaront)

- *Mechanism:* TAAR1 agonists reduce presynaptic dopamine synthesis; Ulotaront also has 5-HT1A activity.
- *Benefits:* Early studies suggest small effect sizes (0.2–0.3) in psychosis but minimal metabolic, neurologic, or endocrine side effects.
- *Adverse effects:* Somnolence, agitation, nausea, diarrhea.
- *Status:* Investigational. Ulotaront is in a six-week placebo-controlled trial including adolescents (Achytes et al, 2023; Kane JM, *J Clin Psychopharmacol* 2022;42(5):S1–S13).
- *Clinical pearl:* Not ready for practice, but may one day offer a non-dopamine alternative for psychosis.

Established therapies

Most pediatric antipsychotic use remains off-label, guided by adult trials and clinical judgment, and comparative data between newer agents and standard SGAs in youth are limited. SGAs should be used only when truly indicated—high-dose use carries an 80% increased mortality risk in adolescents and young adults, though lower doses have not been associated with significant risk. Risperidone and aripiprazole remain the most evidence-based choices, particularly as a last resort for autism-related irritability.

Practical considerations for use in youth

Several issues limit the role of these new agents:

- *Lack of pediatric data.* Lumateperone and xanomeline/trospium are approved in adults. Trials in youth are limited or ongoing. Until we have pediatric safety and efficacy data, use should be cautious and highly selective.
- *Formulations.* Long-acting injectables are not yet available for these newer medications.
- *Side effects.* Metabolic and neurologic risks may be lower, but different mechanisms bring challenges, particularly GI effects with muscarinic agents.
- *Access and cost.* High price and limited insurance coverage when compared with generics like risperidone.
- *Monitoring.* Standard monitoring applies (weight, BMI, metabolic labs, Abnormal Involuntary Movement Scale [AIMS]), as does remaining alert for new side effects.

FDA Approvals for Second-Generation Antipsychotics in Children and Adolescents

Medication	Indication	Ages (years)
Aripiprazole	• Schizophrenia • Bipolar disorder (manic/mixed) • Irritability in autism • Tourette's disorder	• 13–17 • 10–17 • 6–17 • 6–18
Asenapine	• Bipolar mania (monotherapy and adjunctive)	• 10–17
Brexpiprazole	• Schizophrenia	• 13–17
Lurasidone	• Schizophrenia • Bipolar I depression	• 13–17 • 10–17
Olanzapine	• Schizophrenia • Bipolar disorder (manic/mixed) • Bipolar I depression (with fluoxetine)	• 13–17 • 13–17 • 10–17
Paliperidone	• Schizophrenia	• 12–17
Quetiapine	• Schizophrenia • Acute mania	• 13–17 • 10–17
Risperidone	• Schizophrenia • Bipolar disorder (manic/mixed) • Irritability in autism	• 13–17 • 10–17 • 5–17

After discussing risks and the lack of pediatric approval, you and the family try lumateperone off-label, given the boy's severe condition. You document your rationale and monitor for sedation, constipation, and symptom response.

CARLAT VERDICT

Newer antipsychotics (lumateperone, xanomeline/trospium, TAAR1 agonists) may offer benefits for carefully selected patients who can't tolerate or don't respond to standard SGAs, though these newer drugs lack pediatric data and are expensive. We recommend caution with all antipsychotics due to metabolic and neurotoxic side effects. Use them if you must, but try other means and (gently) reduce and discontinue antipsychotics when possible.

Research Updates IN PSYCHIATRY

ANTIDEPRESSANTS

A Three-Question Scale Offers a Quick Read on Antidepressant Side Effects in Youth

Joshua Feder, MD. Dr. Feder has no financial relationships with companies related to this material.

REVIEW OF: Hokelekli FO et al, *J Child Adolesc Psychopharmacol* 2025;35(8):463–470

STUDY TYPE: Psychometric validation study (observational cohort)

Side effects are one of the main reasons kids stop antidepressants, yet most monitoring tools take too long for routine visits. Could a three-question scale give clinicians a quick, reliable snapshot of how much medication side effects are actually bothering their patients?

Researchers analyzed data from 746 youth ages 8–20 in the Texas Youth Depression and Suicide Research Network who were taking antidepressants. Participants completed the Frequency, Intensity, Burden of Side Effects Rating—Child (FIBSER-C), a brief self-report tool with three questions: How often do side effects happen? How bad are they? How much do they get in the way of daily life? Each item is scored 0–3, for a total of 0–9.

The three questions held together well statistically and functioned as a single measure of side effect burden. About one-third of youth reported symptoms at least some of the time, 14% said symptoms were "bad" or worse, and about one-quarter said side effects interfered with daily activities. Reassuringly, higher FIBSER-C scores correlated only weakly with depression severity—suggesting the scale captures medication burden rather than just how depressed a patient feels.

CARLAT TAKE

This is exactly the kind of tool that fits real-world practice. The FIBSER-C takes under a minute, requires no clinician training, and can be completed by the patient in the waiting room. Each item uses plain-language response options ("not at all" to "nearly all of the time"), making it accessible even for younger adolescents. If you treat youth on antidepressants, consider adding it to your intake packet or between-visit check-ins. It's a natural conversation starter about specific side effects, tolerability, and adherence, which is where medication management often breaks down.

SSRIs

SSRIs May Slow Height Gain

Joshua Feder, MD.

REVIEW OF: Calarge C et al, *J Clin Psychopharmacol* 2024;44(6):538–544

STUDY TYPE: Prospective cohort study

SSRIs are widely used in children and adolescents, but their effects on physical development are easy to overlook.

Researchers followed 66 youth ages 8–15 who had recently started fluoxetine or sertraline and compared them with 36 healthy, unmedicated controls. All participants were in mid-puberty (Tanner stages 2–4, by report), when growth velocity is highest. Height, weight, and BMI were tracked over six months, along with blood levels of IGF-1, a marker of growth hormone activity.

Youth taking SSRIs grew more slowly than controls, and the effect was dose-related. At typical therapeutic doses, height gain over six months was about 45% lower than expected. Higher SSRI exposure (40 mg fluoxetine or 100 mg sertraline) was linked to progressively smaller increases in height.

Markers of growth hormone signaling told a similar story. Higher SSRI doses were associated with lower IGF-1 levels, suggesting a biologic mechanism for the slowed growth. Weight changes were modest overall for both SSRIs (1.35 +/- 0.42). There were no meaningful differences between the two SSRIs in their effects on height.

CARLAT TAKE

This small, brief, but carefully done study adds to concerns that SSRIs may blunt pubertal growth, especially at higher doses. The effect isn't subtle, and it lines up with changes in growth hormone signaling as a possible mechanism. For some kids, SSRIs are truly helpful. But treat growth like a vital sign, much as we do with stimulant medications. Track height over time, avoid unnecessary dose escalation, and reassess if growth velocity drops off. If growth suppression appears clinically meaningful, consider a dose reduction, an endocrine consult, or a medication switch to another SSRI, since SNRIs have limited value for kids and teens.

SSRIs Help Modestly With Pediatric OCD

Joshua Feder, MD.

REVIEW OF: Cohen SE et al, *J Am Acad Child Adolesc Psychiatry* 2025;64(7):775–785

STUDY TYPE: Individual participant data meta-analysis of RCTs

SSRIs are a mainstay of medication treatment for pediatric OCD, but clinicians often wonder how much improvement they realistically deliver—and for whom.

Investigators analyzed data from 614 children and adolescents ages 6–18 enrolled in four North American trials. Participants received an SSRI or placebo for 10–13 weeks. Outcomes were measured with the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS).

SSRIs led to greater improvement than placebo, but the effect was modest. On average, SSRI treatment reduced CY-BOCS scores by about three points more than placebo. Children receiving SSRIs were nearly twice as likely to meet response criteria (35% reduction of symptoms).

Baseline severity mattered. Children with milder OCD benefited more, while those with more severe symptoms were less likely to respond. Each single point of increase in baseline severity reduced the odds of response by 8%. Severity did not affect partial response rates (25% reduction of symptoms). Age, sex, weight, and illness duration did not meaningfully affect outcomes.

Limitations include short follow-up, high placebo response rates typical in OCD trials, unspecified SSRIs, and a 90% North American sample that may limit generalizability.

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1. Which best describes the relative efficacy of SSRIs versus clomipramine for pediatric OCD?
   [ ] a. SSRIs and clomipramine have equivalent effect sizes
   [ ] b. SSRIs are more effective, with higher effect sizes than clomipramine
   [ ] c. SSRIs have modest effect sizes of 0.3–0.4; clomipramine has an effect size of approximately 0.6
   [ ] d. Clomipramine is first line because SSRIs lack FDA approval for pediatric OCD

2. In head-to-head trials of second-generation antipsychotics, what proportion of studies declared the sponsor's drug the winner?
   [ ] a. Approximately 50% [ ] b. Approximately 65% [ ] c. Approximately 75% [ ] d. Approximately 90%

3. Approximately what percentage of children with psychotic conditions have an identifiable genetic disorder on microarray, exome sequencing, or genome sequencing?
   [ ] a. 1%–2% [ ] b. 6% [ ] c. 15% [ ] d. 25%

4. A pediatric trial of brexpiprazole for adolescent schizophrenia showed which of the following outcomes?
   [ ] a. Superiority over risperidone on symptom measures
   [ ] b. No difference from placebo on any outcome
   [ ] c. Symptom reduction versus placebo, though with possibly limited clinical significance
   [ ] d. Efficacy comparable to aripiprazole with fewer metabolic effects

5. In a validation study of the Frequency, Intensity, Burden of Side Effects Rating—Child scale, scores correlated only weakly with depression severity in youth on antidepressants. Which of the following best characterizes what the scale measures?
   [ ] a. It is too brief to capture meaningful clinical information
   [ ] b. It measures medication side effect burden rather than depressive symptoms
   [ ] c. Depression severity does not predict treatment adherence
   [ ] d. It is most useful for patients with mild depression

6. True or False: For pediatric acute mania, risperidone and aripiprazole have the highest effect sizes among FDA-approved antipsychotics, and lithium is preferred over valproate for maintenance in adolescents due to fewer metabolic and reproductive side effects.
   [ ] a. True [ ] b. False

7. What did researchers find when unpublished trial data on SSRIs for youth depression were incorporated into meta-analyses?
   [ ] a. SSRIs showed strong, consistent efficacy across all agents
   [ ] b. Fluoxetine showed no benefit over placebo
   [ ] c. SSRIs and SNRIs demonstrated very minimal to no effects for youth depression
   [ ] d. Only SNRIs lost statistical significance

8. True or False: An RCT found that pharmacogenetic testing led youth to receive evidence-based psychiatric treatment more frequently than those who were not tested.
   [ ] a. True [ ] b. False

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CARLAT TAKE

SSRIs work for pediatric OCD, but they don't work wonders. A three-point CY-BOCS improvement is real, yet often falls short of what families hope for, especially in moderate-to-severe cases. SSRIs are part of a combined strategy, not a stand-alone fix. For mild OCD, we recommend cognitive behavioral therapy with exposure and response prevention, although medication alone may be reasonable. For more severe presentations, SSRIs play a supporting role. When setting expectations, be honest: SSRIs can help take the edge off, but meaningful recovery usually requires more than medication alone.

EATING DISORDERS

Low-Dose Aripiprazole for Youth With Anorexia

Joshua Feder, MD.

REVIEW OF: Bindseil I et al, *J Child Adolesc Psychopharmacol* 2025;35(8):471–478

STUDY TYPE: Retrospective, matched cohort study

Anorexia nervosa in kids and teens is hard to treat once cognitive rigidity and food avoidance stall family-based therapy. Antipsychotics have been tried, but results are mixed.

Researchers reviewed charts from a comprehensive pediatric eating disorder program and identified 42 patients ages 11–18 who started on aripiprazole for eating disorder cognitions. They were matched 1:2 with 84 controls. Most participants were female with the restricting subtype; the aripiprazole group was somewhat more medically

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Research Updates
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ill at baseline. The medication was typically started midway through treatment.

Patients treated with aripiprazole showed greater improvement in food-avoidant behaviors, with scores improving by about 3.5 points versus less than 1 point in controls on the 42-point, 14-item Ease of Eating Scale. Weight outcomes also favored aripiprazole: Patients gained about 4.8 kg versus 3.1 kg in controls, and 43% reached target weight by discharge compared with 30% of controls. Time to target weight was similar between both groups. Dosing was low: The average starting dose was 1.9 mg/day, with discharge doses around 2.8 mg/day. Side effects were mild, most commonly sedation and dizziness, and over half reported no side effects at all.

CARLAT TAKE

This uncontrolled study isn't definitive, but it may be clinically useful. In youth with anorexia who are stuck (rigid, distressed, and unable to complete meals), low-dose aripiprazole may loosen cognitive rigidity enough to help therapy and weight restoration move forward. Doses stayed well below typical antipsychotic ranges and were mostly well tolerated. No medication has proven benefit for anorexia nervosa, and D2 blockade carries its own risks in this population. We wouldn't use this routinely, but for patients who aren't progressing despite solid family-based treatment, a brief, cautious trial at 1–2 mg/day may be reasonable with thoughtful monitoring.