

# Pediatric Psychopharmacology for Treatment of ADHD, Depression, and Anxiety

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The pediatric practitioner is often the first point-of-contact for children and adolescents suffering from mental illness. Part of the treatment planning for psychiatric diagnoses includes consideration of medication. Attention-deficit/hyperactivity disorder, one of the most common diagnoses, is very responsive to stimulant medications; for children who are unable to tolerate stimulants or who do not achieve satisfactory symptom management, central  $\alpha$ -agonists and atomoxetine are effective and generally well-tolerated alternative or augmentative agents. Depression and anxiety disorders are also frequently encountered in the pediatric office setting. The use of selective serotonin reuptake inhibitors is considered first-line psychopharmacology for depression and anxiety symptoms. Despite concerns for suicidal ideation related to this medication class, the benefits typically outweigh the risks. This review provides basic clinical pharmacology of stimulant and nonstimulant attention-deficit/hyperactivity disorder medications and selective serotonin reuptake inhibitors intended to serve as a primer for the general pediatrician.

abstract

Approximately 1 in 5 children in the United States suffers from some form of mental illness, yet 80% of these children do not receive treatment.<sup>1,2</sup> It is estimated that 75% of children and adolescents with psychiatric disorders are seen in primary care.<sup>3</sup> Furthermore, 7.5% of children and adolescents are prescribed a psychiatric medication, and 85% of psychopharmacologic prescribing is by pediatric providers.<sup>4,5</sup> Consistent with the American Academy of Pediatrics' (AAP's) mission to enhance pediatric care in a medical home, the AAP charges the following: "Pediatric primary care providers have unique opportunities and a growing sense of responsibility to prevent and address mental health and substance abuse problems in the medical home."<sup>6</sup>

The purpose of this review article is to empower primary care pediatricians as basic psychopharmacologists for the common mental health diagnoses of attention-deficit/hyperactivity disorder

(ADHD), depression, and anxiety. Mental health care involves an array of interventions, including psychological education, and, contingent on the needs of the child, neuropsychological testing to assess for learning and other comorbid disorders, school accommodations, and psychotherapy. These treatment modalities are important aspects of care but are outside the scope of this article.

## ADHD MEDICATIONS

### Case Vignette

Joey, a 6-year-old, 20-kg boy, presents to his pediatrician, Dr Smith, with complaints of significant hyperactivity, impulsivity, and defiance that are problematic in the classroom and at home. Presentation in the office and parent and teacher Vanderbilt rating scale scores\* are consistent with

\*The Vanderbilt ADHD Rating Scale is widely available, including at <http://www.chadd.org/>.

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a diagnosis of ADHD, and other medical, psychiatric, and learning issues are ruled out. Dr Smith provides psychological education about ADHD, refers for parent management training, and recommends school accommodations for classroom symptoms. After ensuring no contraindications, he prescribes dexamethylphenidate extended release (ER) (Focalin XR) 5 mg every morning (qAM).

At subsequent weekly or biweekly follow-ups, the dose is titrated to 10, 15, and 20 mg qAM based on parent and teacher Vanderbilt scores demonstrating little or no improvement. At the fourth follow-up, Dr Smith switches to amphetamine/dextroamphetamine ER (Adderall XR) 20 mg, after which parent and teacher report notable improvement in hyperactivity and impulsivity, although Joey experiences appetite suppression. Dr Smith counsels on high-protein and high-calorie nutrition, but Joey's weight decreases to the point of crossing a weight percentile. The amphetamine/dextroamphetamine ER dose is decreased to 15 mg then to 10 mg over subsequent visits; although Joey's appetite and weight improve toward baseline, Vanderbilt scores demonstrate return of hyperactivity and impulsivity, although not to the degree of severity of initial presentation. Dr Smith augments amphetamine/dextroamphetamine ER 10 mg qAM with guanfacine ER (Intuniv) 1 mg at bedtime (qHS).

Three weeks later, parent and teacher Vanderbilt scores endorse satisfactory ADHD symptom management, which is maintained through the remainder of the school year, and Joey's weight gain follows an age-appropriate trajectory.

## STIMULANTS

### Indications

ADHD diagnosis and stimulant medication prescription have steadily

increased over time.<sup>7-9</sup> The AAP and the American Academy of Child and Adolescent Psychiatry (AACAP) practice guidelines endorse stimulant medications, methylphenidate and amphetamine, as first-line treatment<sup>10-12</sup> (see Table 1 for effect sizes).

Recommendations are robustly evidence based. Specifically, the Multimodal Treatment of ADHD trial showed improvement in inattention, hyperactivity, and impulsivity and amelioration of general disruptive behavior and, to a lesser degree, academic achievement and appropriate peer relations.<sup>13-16</sup> Off-label prescription indications for stimulant medications include defiance, aggression, depression, and narcolepsy.<sup>17-19</sup>

### Prescribing Practice

Before stimulant prescription, the AAP and the American Heart Association recommend careful physical examination and patient and family histories of heart disease, as follows: patient history of palpitations, syncope, or chest pain and family history of sudden death or cardiac disease in children or young adults.<sup>20</sup> Any concerning signs or symptoms warrant cardiac workup before beginning medication. The various formulations of methylphenidates and amphetamines are generally considered to be equally efficacious, although a meta-analysis and more recent randomized controlled trial suggest superiority of lisdexamfetamine over methylphenidates.<sup>21,22</sup>

Amphetamines, however, may have a greater risk of side effects.<sup>23-25</sup> The

Food and Drug Administration (FDA)-approved minimum age for most stimulants is 6 years, with the exception of immediate-release mixed amphetamine salts and dextroamphetamine, both approved to age 3 years. Despite this FDA age approval, methylphenidate was the medication treatment arm selected for use in the landmark Preschool Attention-Deficit/Hyperactivity Disorder Treatment Study, which influenced current clinical practice in preschool-aged children with ADHD.<sup>26</sup> General dosing recommendations favor initiation at the lowest dose and titration as expeditiously as 1-week intervals (see Table 2 for dosing parameters) Long-acting stimulants are generally preferred over short-acting stimulants to minimize dosing frequency. Morning medication should be administered after breakfast. Although some long-acting stimulants claim up to 12 hours of medication effect, some children metabolize the medication more quickly, potentially warranting the addition of a short-acting stimulant dose in the afternoon. The Texas Children's Medication Algorithm Project for pharmacotherapy of ADHD advises prescription of a stimulant medication titrated to effect. If response is unsatisfactory, it is recommended that the clinician trial the other stimulant class at an equivalent dose (2 mg methylphenidate to 1 mg dexamethylphenidate to 1 mg amphetamine) titrated to effect.<sup>27</sup> Of note, it is important for pediatricians to discuss the risks of stimulant recreational abuse and diversion with adolescent patients and their families when initiating stimulant medications (see Table 3 for common and serious side effects).

### NONSTIMULANT ADHD MEDICATIONS

Although stimulants are first-line treatment of ADHD based on established robust efficacy, there are various indications for the use of

TABLE 1 ADHD Medication Effect Size

	Effect Size
Stimulant medications	1.0 <sup>a</sup>
α-Agonist medications, ER	0.7
Atomoxetine	0.7

Data from ref 10. 0.2 = small effect size, 0.5 = moderate effect size, 0.8 = large effect size.

<sup>a</sup> 0.4-0.8 in preschoolers.

**TABLE 2** Stimulant Dosing Parameters

	Dosage Forms	Maximum Recommended Dose	Notes
<b>Methylphenidates</b>			
<b>Long-acting</b>			
Focalin XR (Novartis, East Hanover, NJ)	5-, 10-, 15-, 20-, 25-, 30-, 35-, and 40-mg capsules	1 mg/kg or 30 mg/day	Capsule may be opened and contents dissolved
Methylphenidate ER (Concerta)	18-, 27-, 36-, and 54-mg tablets	2 mg/kg or 72 mg/day	Tablet must be swallowed whole
Ritalin LA (ALZA, Mountain View, CA)	10-, 20-, 30-, and 40-mg capsules	2 mg/kg or 60 mg/day	Capsule may be opened and contents dissolved
Metadate CD (UCB, Rochester, NY)	10-, 20-, 30-, 40-, 50-, and 60-mg capsules	2 mg/kg or 60 mg/day	Capsule may be opened and contents dissolved
Methylin ER (AlliantPhr, Alpharetta, GA)	10- and 20-mg tablets	2 mg/kg or 60 mg/day	
Ritalin SR (Novartis, East Hanover, NJ)	20-mg tablets	2 mg/kg or 60 mg/day	
Daytrana (Shire US, Wayne, PA)	10-, 15-, 20-, and 30-mg patches	30 mg/day	Topical patch applied 2 hours before and removed 9 hours later
Quillivant (Pfizer, New York, NY)	25-mg/5-mL suspension	Initial dose 20 mg QAM titrated by 10- to 20-mg increments Maximum dose 60 mg QAM	Liquid formulation
<b>Short-acting</b>			
Focalin (Novartis, East Hanover, NJ)	2.5-, 5-, and 10-mg tablets	2 mg/kg or 60 mg/day	
Ritalin (Novartis, East Hanover, NJ)	5-, 10-, and 20-mg tablets	2 mg/kg or 60 mg/day	
Methylin (AlliantPhr, Alpharetta, GA)	5-, 10-, and 20-mg tablets or 5-mg/5-mL or 10-mg/5-mL solution	2 mg/kg or 60 mg/day	Liquid formulation available
<b>Amphetamines</b>			
<b>Long-acting</b>			
Vyvanse (Shire US, Wayne, PA)	10-, 20-, 30-, 40-, 50-, 60-, and 70-mg capsules	1 mg/kg or 70 mg/day	Prodrug that may decrease risk of recreational abuse Capsule may be opened and contents dissolved
Adderall XR (Shire US, Wayne, PA)	5-, 10-, 15-, 20-, 25-, and 30-mg capsules	1 mg/kg or 30 mg/day	Capsule may be opened and contents dissolved
Dexedrine (GlaxoSmithKline, Research Triangle Park, NC)	5-, 10-, and 15-mg capsules	1 mg/kg or 30 mg/day	
<b>Short-acting</b>			
Adderall (Shire US, Wayne, PA)	5-, 7.5-, 10-, 12.5-, 15-, 20-, and 30-mg tablets	1 mg/kg or 30 mg/day	
Dextroamphetamine (GlaxoSmithKline, Research Triangle Park, NC)	5- and 10-mg tabs	1 mg/kg or 30 mg/day	
ProCentra (Independence Pharmaceuticals, Newport, KY)	5-mg/5-mL solution	1 mg/kg or 30 mg/day	Liquid formulation available

CD, controlled delivery; LA, long-acting; SR, sustained release; XR, extended release.

FDA-approved nonstimulant medications for children aged  $\geq 6$  years (see Table 1 for effect sizes.) These include failed trials of methylphenidate and amphetamine (secondary to unsatisfactory symptom response at maximum dosage or intolerable side effects), underlying medical conditions lending to greater concern for potential stimulant side effects (including underweight or hypertension), comorbid substance abuse, or family preference. An  $\alpha$ -agonist or atomoxetine may be prescribed as monotherapy or, in cases of partial stimulant response,

ER clonidine and guanfacine are also FDA-approved as augmentative to stimulant medication.

**Indications: Central  $\alpha_2$ -Agonists**

Initially indicated for management of hypertension, the central  $\alpha_2$ -agonist medications guanfacine and clonidine are now formulated as ERs (Intuniv and Kapvay, respectively). These are FDA-approved for ADHD treatment in the pediatric population down to age 6 years, and efficacy has been corroborated by a recent meta-analysis.<sup>28</sup> In addition to reduction in distractibility, hyperactivity, and impulsivity, off-label uses include

defiance and, with clonidine, sleep-onset insomnia.<sup>29</sup>

**Prescribing Practice:  $\alpha_2$ -Agonists**

Because of the antihypertensive effects of guanfacine ER and clonidine ER, strict adherence to prescribing instructions is critical; overdosing could lead to dangerous hypotension and inconsistent dosing might lead to rebound hypertension. Because of potential sedation, it is recommended that dosing initially be at bedtime. Efficacy is observed between 1 and 3 weeks after initiation, and dosing titration may be weekly. Clonidine ER is administered twice daily beginning

**TABLE 3** Stimulant Side Effects

Side Effect	Management
Gastrointestinal distress	Typically self-resolves Symptomatic care
Headache	Typically self-resolves Symptomatic care
Appetite suppression	Counsel on high-protein, high-calorie nutrition and frequent snacks
Insomnia	Counsel on sleep hygiene Consider melatonin as needed
Elevated blood pressure and heart rate	No action if within age-appropriate norms and asymptomatic
Agitation or mood disturbance	Discern direct medication (emotional symptoms correlate with expected time of medication effect) as opposed to rebound effect (emotional symptoms occur later in day as medication expected to wearing off) If medication effect, discontinue medication If rebound effect, may add short-acting stimulant in afternoon
Tics (note: stimulants are not causative but may uncover or exacerbate)	If no impairment, no action If distressing, taper or discontinue stimulant medication and consider guanfacine ER or clonidine ER monotherapy or augmentation
Transient growth effects (ultimate adult height not compromised)	No action
Priapism (rare)	Medical emergency; discontinue medication

If any symptoms are severe, prescriber may decrease medication dose or switch to another ADHD medication (stimulant or nonstimulant)

with the first titration step (see Table 4 for dosing parameters.) When resuming  $\alpha$ -agonist medication administration after a period off of medication ( $\geq 2$  days), the dosing should start at the initiation dose and titrated as before. Because abrupt discontinuation of these  $\alpha$ -agonists can lead to rebound hypertension, these drugs should be tapered in stepwise intervals weekly until complete discontinuation (see Table 5 for common side effects).

### Atomoxetine

#### Indications

Atomoxetine (Strattera) is a norepinephrine reuptake inhibitor medication that is also FDA-approved for use in children and adolescents with ADHD down to age 6 years. A recent positive meta-analysis corroborates efficacy; however, studies suggest that atomoxetine is inferior to stimulants and guanfacine ER.<sup>30</sup> There is evidence for unique benefit in children with comorbid anxiety. As

with the aforementioned ADHD medications, there is some medication benefit for defiance.<sup>31</sup>

#### Prescribing Practice

Atomoxetine is titrated in no sooner than 3 days to the target dose (see Table 4 for dosing parameters.) Twice-daily dosing may be associated with a decrease in defiance and less gastrointestinal side effects.<sup>32,33</sup> Slower titration is indicated when prescribed concurrently with CYP2D6 inhibitors such as fluoxetine. Medication effect is slower-acting than stimulant and  $\alpha$ -agonist medications so families should be advised that it may take 2 to 6 weeks before effects are noticed (see Table 5 for common and serious side effects).

### SSRIs

#### Case Vignette

Emma, a 13-year-old girl, presents to Dr Smith with parent complaints of irritability and withdrawal. Her responses on

the 9-item Patient Health Questionnaire<sup>†</sup> (PHQ-9) screening tool score positive for severe depression, and she describes pervasive and significant mood and neurovegetative symptoms secondary to numerous school and home stressors. After establishing safety as well as screening for bipolar disorder in Emma and her family and other comorbid or confounding conditions, such as substance abuse or trauma, Dr Smith provides psychological education, refers for cognitive behavioral therapy, and discusses initiation of an SSRI. The family agrees to initiate fluoxetine 10 mg daily. One week later, Emma describes mild gastrointestinal distress; Dr Smith recommends symptomatic treatment and continuation of the medication. By week 2, Emma reports resolution of gastrointestinal symptoms and denies any notable positive or negative medication effects. On office follow-up in 4 weeks after medication initiation, Emma's PHQ-9 reveals very mild improvement in depressive symptoms, and she reports scheduled intake with a therapist in 1 week. Dr Smith titrates fluoxetine to 20 mg daily. Thereafter, monthly office follow-ups reveal little change in Emma's PHQ-9 scores. The pediatrician titrates fluoxetine by 10 mg at each monthly visit to a maximum dose of 40 mg daily. At follow-up in another month, there is reported mild improvement, but symptoms remain overall moderate so the pediatrician discontinues fluoxetine and initiates escitalopram 10 mg daily. At primary care follow-up, now 4 months since the initiation of psychopharmacologic intervention, Emma reports marked improvement of symptoms (of mild-moderate severity on the PHQ-9). She graduates out of cognitive behavioral therapy and endorses depressive symptom remission in monthly then in every 3-month follow-ups. Ten months later, Emma, her parents, and Dr Smith

<sup>†</sup>The 9-item Patient Health Questionnaire is widely available, including at <http://PHQscreeners.com>.

**TABLE 4** Nonstimulant ADHD Medication Dosing Parameters

Generic (Brand)	Initial Dose	Titration	Maximum Recommended Dose	Dosage Forms
Guanfacine ER (Intuniv) <sup>a</sup> (Shire US, Wayne, PA)	1 mg qHS	1 mg	27–40.5 kg, 2 mg 40.5–45 kg, 3 mg >45 kg, 4 mg qHS	1-, 2-, 3-, and 4-mg tablets
Clonidine ER (Kapvay) <sup>a</sup> (Concordia Pharmaceuticals Inc, Bridgetown, Barbados)	0.1 mg qHS	0.1 mg	27–40.5 kg, 0.2 mg TDD 40.5–45 kg, 0.3 mg TDD >45 kg, 0.4 mg TDD	0.1-mg tablets
Atomoxetine (Strattera) <sup>a</sup> (Eli Lilly, Indianapolis, IN)	0.5 mg/kg or 40 mg	1.2 mg/kg or 80 mg	1.4 mg/kg or 100 mg TDD	10-, 18-, 25-, 40-, 60-, 80-, and 100-mg tablets

qHS, take at bedtime; TDD, total daily dose.

<sup>a</sup> Tablets must be swallowed whole.

discuss tapering off of escitalopram over summer break, which she does without difficulty.

**Indications**

SSRIs are important treatment tools for moderate- severe depression and anxiety disorders. A review of published and unpublished data on SSRI treatment of pediatric depression suggests that the risks and benefits of SSRI use in pediatrics should be carefully considered within the context of each patient.<sup>34</sup> However, the published literature supports the AAP and AACAP position statements of SSRI efficacy for

pediatric depression and anxiety.<sup>35–42</sup> Three of the most significant trials include the Treatment of Adolescents with Depression Study, the Pediatric Obsessive Compulsive Disorder Treatment Study, and the Child/ Adolescent Anxiety Multimodal Study; these are multisite, placebo-controlled studies that concluded that combination SSRI and psychotherapy is superior to either alone.<sup>43–46</sup> Only a few medications are FDA-approved for use in the pediatric population, so that much of the psychopharmacologic prescribing for pediatric depression and all of the prescribing for non-obsessive-compulsive disorder

anxiety are considered off-label. Although most SSRIs are considered equivalent, paroxetine is disfavored in the pediatric population because of its efficacy and side-effect profile<sup>47–49</sup> Research does not support the use of SSRIs as first-line treatment of symptoms of posttraumatic stress disorder, although, in practice, they are commonly used as an adjunctive therapy.<sup>50,51</sup> Despite the conflicting adult literature and an even smaller pediatric evidence base, some clinicians have found anecdotal success with the use of SSRIs to target core eating disorder symptoms of anorexia or bulimia nervosa.<sup>52</sup>

**Prescribing Practice**

Specific dosing for SSRIs for depression and anxiety can be found in Table 6. Management algorithms for pediatric depression and anxiety exist to further guide providers.<sup>41,42,53,54</sup> When initiating SSRI treatment, early effects may be seen at 1 to 2 weeks, but patients should be advised that efficacy may not be seen for 4 to 8 weeks. Follow-up with the patient in the office or via telephone should be scheduled at 1 and 2 weeks after starting the medication; titration may be made at 3- to 4-week intervals to the effective dose as tolerated or to a maximum dosage. If a patient experiences absent or partial response with the maximum dosage of first SSRI, the pediatrician should discontinue and initiate a different SSRI.<sup>40,55</sup> Failure of a second SSRI at the maximum tolerated or recommended dose constitutes

**TABLE 5** Nonstimulant ADHD Medication Side Effects

	Management
Guanfacine ER and clonidine ER side effects	
Gastrointestinal distress	Typically self-resolves Symptomatic care
Headache	Typically self-resolves Symptomatic care
Decreased blood pressure or heart rate	No action if within age appropriate norms and asymptomatic
Sedation	Typically self-resolves Administration at bedtime
Atomoxetine side effects	
Gastrointestinal distress	Typically self-resolves Symptomatic care
Headache	Typically self-resolves Symptomatic care
Sedation	Administration at bedtime
Suicidal ideation	Rare but warrants reevaluation and potential medication discontinuation
Hepatotoxicity (rare)	Counsel families on warning signs and symptoms with initial prescription; discontinue medication
Transient growth effects	No action
Elevated blood pressure or heart rate	No action if within age appropriate norms and asymptomatic
Priapism (rare)	Medical emergency; discontinue medication

If any symptoms are severe, prescriber may decrease medication dose or switch to another ADHD medication (stimulant or nonstimulant).

**TABLE 6** SSRI Dosing Parameters

Generic (Brand)	FDA Approval for Children and Adolescents	Initial Dose	Titration	Maximum Recommended Dose	Dosage Forms
Citalopram (Celexa) <sup>a</sup> (Forest Laboratories, Parsippany, NJ)		<12 years, 10 mg/day; ≥12 years, 20 mg/day	<12 years, 5 mg; ≥12 years, 10 mg	40 mg/day	10 mg/5 mL; 10-, 20-, and 40-mg tablets
Escitalopram (Lexapro, Forest Laboratories, Parsippany, NJ)	≥12 years old with depression	<12 years, 5 mg/day ≥12 years, 10 mg/day	5 mg 10 mg	20 mg/day	5 mg/5 mL; 5- and 10-mg tablets
Fluoxetine hydrochloride (Prozac, Eli Lilly, Indianapolis, IN)	≥8 years old with depression ≥7 years old with OCD	<12 years, 5 mg/day ≥12 years, 10 mg/day	5 mg 10 mg	40 mg/day	20 mg/5 mL 10-, 20-, and 40-mg capsules 10-, 20-, and 60-mg tablets 90-mg delayed release capsules
Fluvoxamine (Luvox, Actavis, Parsippany, NJ)	≥8 years old with OCD	25 mg/day	25 mg (divide BID for doses >50 mg/day)	<12 years, 200 mg/day ≥12 years, 300 mg/day	25-, 50-, and 100-mg tablets 100- and 150-mg ER capsules
Sertraline (Zoloft, Pfizer, New York, NY)	≥6 years old with OCD	<12 years, 12.5 mg/day ≥12 years, 25 mg/day	25 mg 50 mg	200 mg/day	20 mg/mL 25-, 50-, and 100-mg tablets

OCD, obsessive-compulsive disorder.

<sup>a</sup> Not FDA approved for children and adolescent.

**TABLE 7** SSRI Side Effects

Side Effect	Management
Gastrointestinal distress	Typically self-resolves Symptomatic care
Headache	Typically self-resolves Symptomatic care
Appetite change	Counsel on healthy nutrition
Sedation	Administration at bedtime
Sleep disturbance	Administration in morning Counsel on sleep hygiene Consider melatonin as needed
Diaphoresis	No action if mild
Sexual side effects	Consider medication change
Activation (disinhibition, agitation, irritability, silly)	If persistent and significant, discontinue medication
Platelet dysfunction (rare)	Discontinue medication

If any symptoms are severe, prescriber may decrease medication dose or switch to another.

**TABLE 8** SSRI Benefit to Suicidal Risk Comparison

Diagnosis	Number Needed to Treat	Number Needed to Harm
Depression	10 <sup>a</sup>	112
OCD	6	200
Non-OCD anxiety	3	143

Data from ref 60. OCD, obsessive-compulsive disorder.

<sup>a</sup> High number needed to treat likely secondary to high placebo response rate in pediatric depression studies (30% to 60% compared with 40% to 70% SSRI response rate). SSRI efficacy has been established, but pooled studies and this high number needed to treat underscore the importance of individualizing treatment.

treatment nonresponse to first-line medication and warrants referral to a child psychiatrist. Once remission has been achieved, patients should be monitored every 3 months, and the medication should be continued for at least 6 to 12 months of stability.<sup>53,54</sup> When discontinuing the medication, the clinician should slowly taper over

a minimum of 1 to 2 months.<sup>56,57</sup> Abrupt discontinuation may cause flulike symptoms including agitation, dizziness, feeling “spaced out,” lightheadedness, drowsiness, poor concentration, nausea, headache, and fatigue. These effects can be reversed by resuming the preceding SSRI dose and tapering at a more gradual rate<sup>57</sup>

(see Table 7 for common SSRI side effects).

**Safety Risk**

After the FDA and UK Medicine Healthcare Products Regulatory Agency released warnings about increased suicidal thoughts and suicidal behaviors among children taking antidepressants, the use of these medications decreased worldwide.<sup>58,59</sup> The literature calculates the risk of suicidality in children and adolescents taking an SSRI to be low: 1% to 2% of children experience the emergence of suicidal thoughts and behaviors but not completed suicides.<sup>60,61</sup> The highest risk is seen during the first 9 days of treatment and with higher than usual starting doses.<sup>61–63</sup> There does not appear to be a significant difference between the various antidepressants despite historical data incriminating paroxetine.<sup>64,65</sup> The nature of the association between SSRI use and suicidality is unclear. Pediatricians need to be vigilant of the possibility of increased suicidality among patients for whom they are prescribing SSRIs; however, concerns for suicidal ideation are outweighed by the positive, protective effects of an overall decrease in the burden of

disease morbidity and suicide mortality. Informed consent should include the discussion of the relative risk of increased suicidal thinking with antidepressant medications versus the risk of suicide without psychopharmacologic treatment. Consent also includes discussion of the mutually agreed upon threshold for referral to a psychiatric specialist, such as worsening safety concerns, adverse medication reactions that include emergence of mania or psychosis, and lack of response to first-line treatments (see Table 8 for comparison of benefit to suicidality risk<sup>61</sup>).

## CONCLUSIONS

The management of the common diagnoses of ADHD, depression, and anxiety, by way of psychological education, psychotherapy referral, basic psychopharmacology, and appropriate child psychiatry referral, is within the scope of general pediatric practice. Indications for referral include symptoms refractory to first-line treatment, psychotherapy, and aforementioned medications (whether secondary to limiting adverse side effects or to lack of optimal response to maximum dosage) or severe symptoms, including significant and ongoing suicidal ideation or attempt or symptoms of mania or psychosis. Clinicians are encouraged to develop a practical management algorithm within their practice that includes appropriate referral resources and comfort with the use of stimulants and nonstimulants in treatment of ADHD and of the use of SSRIs for depression and anxiety. The reader is directed to AAP and AACAP practice guidelines for further direction.<sup>41,42,53,54</sup>

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## ABBREVIATIONS

AACAP: American Academy of Child and Adolescent Psychiatry  
 AAP: American Academy of Pediatrics  
 ADHD: attention-deficit/hyperactivity disorder  
 ER: extended release  
 FDA: Food and Drug Administration  
 PHQ-9: 9-item Patient Health Questionnaire  
 qAM: every morning  
 qHS: at bedtime  
 SSRI: selective serotonin reuptake inhibitor

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