



Attention-Deficit Hyperactivity Disorder

ADHD

Guideline Team

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Patient population. Children and young adults ages 3-30 years. Considerations for preschool children (ages 3-5) and adults (ages 18-30) are discussed (see Special Populations).

Objectives. 1. Recognize and treat ADHD early in the primary care setting. 2. Identify appropriate treatment options and drug adverse effects. 3. Identify common comorbidities and indications for referral. 4. Identify appropriate support resources for patients and their families.

Key Points

Epidemiology

Common. ADHD is the most common behavioral disorder in school-age children, with a US community prevalence of 7-11% in 4-17 year-olds. It is more common in boys [C]. About 2.5-5% of adults meet criteria for ADHD [C]. The rate of ADHD continuation from childhood into adulthood is being studied; various reports have suggested rates ranging from 5-76%.

Primary care. Most children with ADHD receive care through their primary care clinicians.

Diagnosis

Types. Diagnosis is based on the DSM-5 criteria (see Table 1) [D]. The three main types are predominately hyperactive, predominately inattentive, and combined.

Multiple sources. No specific test can make the diagnosis. Input from both parents and teachers or other source is required. Some psychological rating tools are useful but are not diagnostic (eg, Vanderbilt, Conners; see Figure 1, Tables 1 & 2, and Appendix A1). If a learning problem is suspected, consider a neuropsychological evaluation to assess for learning disorders.

Diagnosis is complicated by overlapping symptoms and co-occurrence of other disorders (eg, anxiety disorders, autism spectrum disorders, bipolar disorder, fetal alcohol spectrum disorders, learning disorders, major depressive disorders, obstructive sleep apnea, oppositional defiant disorder, post-traumatic stress disorder, reactive attachment disorder; see Appendices B1 & B2).

Treatment (See Table 4)

Drug treatment (See Tables 5-7)

- Stimulants are first-line treatment and will benefit most patients with ADHD. If one stimulant class fails or has unacceptable adverse effects, then another should be tried [IA*].
- Atomoxetine is a secondary choice [IA].
- Other medications may be used alone or in combination, depending upon the ADHD type, response to therapy, or comorbidity profile: eg, alpha-2 agonists (clonidine, guanfacine) in patients with hyperactivity or impulsivity; bupropion (over age 8) with comorbid depression; risperidone (atypical antipsychotic) for aggression (see Table 6) [IIIA].
- Comorbid conditions may require additional treatment (eg, for depression, or sleep disorder) and consideration of referral to a specialist (eg, mental health or sleep medicine).

Non-pharmacologic interventions

- Age-appropriate behavioral interventions at home: education and support [IB]; routines, clear limits, and positive reinforcement for child target behaviors; consider referral for other therapies for older children and adults [IIB] (see Table 8 and Appendix A2).
- School interventions: children with ADHD may qualify for a Section 504 education plan or special education services with an individualized education plan (IEP) [IID] (see Appendices A3 & A4).

Special Populations or Circumstances

Special considerations apply to: 3-5 year olds, adolescents and adults, head-injured patients, intellectually disabled patients, and those with fetal alcohol spectrum disorders, autism spectrum disorders, or substance use disorders (see Appendix B3).

Controversial Areas

Common myths. Several common beliefs related to ADHD are untrue: eg, that it is not a real disorder, it is an over-diagnosed disorder, children with ADHD are over-medicated.

Diets. Although a few studies suggest that dietary modification may have promise, reviews demonstrate no or mixed evidence of efficacy (eg, individually tailored hypoallergenic diets, essential fatty acids, flax seed) [IIB]; studies have shown the Feingold diet and modifying sugar consumption have no effect [IIIB].

Complementary and Alternative Medicine. Use is controversial, but common (see Appendix B4).

* Strength of recommendation:

I = generally should be performed; II = may be reasonable to perform; III = generally should not be performed.

Level of evidence supporting a diagnostic method or an intervention: A = randomized controlled trials; B = controlled trials, no randomization; C = observational trials; D = opinion of expert panel.

Table 1. DSM-5 Diagnostic Criteria for ADHD

- A. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):
1. **Inattention:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic or occupational activities:
Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (ages 17 years and older), at least five symptoms are required.
 - a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (eg, overlooks or misses details, work is inaccurate).
 - b. Often has difficulty sustaining attention in tasks or play activities (eg, has difficulty remaining focused during lectures, conversations, or lengthy reading).
 - c. Often does not seem to listen when spoken to directly (eg, mind seems elsewhere, even in the absence of any obvious distraction).
 - d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (eg, starts tasks but quickly loses focus and is easily sidetracked).
 - e. Often has difficulty organizing tasks and activities (eg, difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).
 - f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (eg, schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).
 - g. Often loses things necessary for tasks or activities (eg, school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
 - h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).
 - i. Is often forgetful in daily activities (eg, doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).
 2. **Hyperactivity and impulsivity:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic or occupational activities:
Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (ages 17 years and older), at least five symptoms are required.
 - a. Often fidgets with or taps hands or feet or squirms in seat.
 - b. Often leaves seat in situations when remaining seated is expected (eg, leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).
 - c. Often runs about or climbs in situations where it is inappropriate. (**Note:** In adolescents or adults, may be limited to feeling restless.)
 - d. Often unable to play or engage in leisure activities quietly.
 - e. Is often "on the go," acting as if "driven by a motor" (eg, is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).
 - f. Often talks excessively.
 - g. Often blurts out an answer before a question has been completed (eg, completes people's sentences; cannot wait for turn in conversation).
 - h. Often has difficulty waiting his or her turn (eg, while waiting in line).
 - i. Often interrupts or intrudes on others (eg, butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).
- B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.
- C. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (eg, at home, school, or work; with friends or relatives; in other activities).
- D. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.
- E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (eg, mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

(Table continued on next page)

Table 1. DSM-5 Diagnostic Criteria for ADHD, continued

Specify whether:

(F90.2) Combined presentation: If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past 6 months.

(F90.0) Predominantly inattentive presentation: If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past 6 months.

(F90.1) Predominantly hyperactive/impulsive presentation: If Criterion A2 (hyperactivity-impulsivity) is met and Criterion A1 (inattention) is not met for the past 6 months.

Specify if:

In partial remission: When full criteria were previously met, fewer than the full criteria have been met for the past 6 months, and the symptoms still result in impairment in social, academic, or occupational functioning.

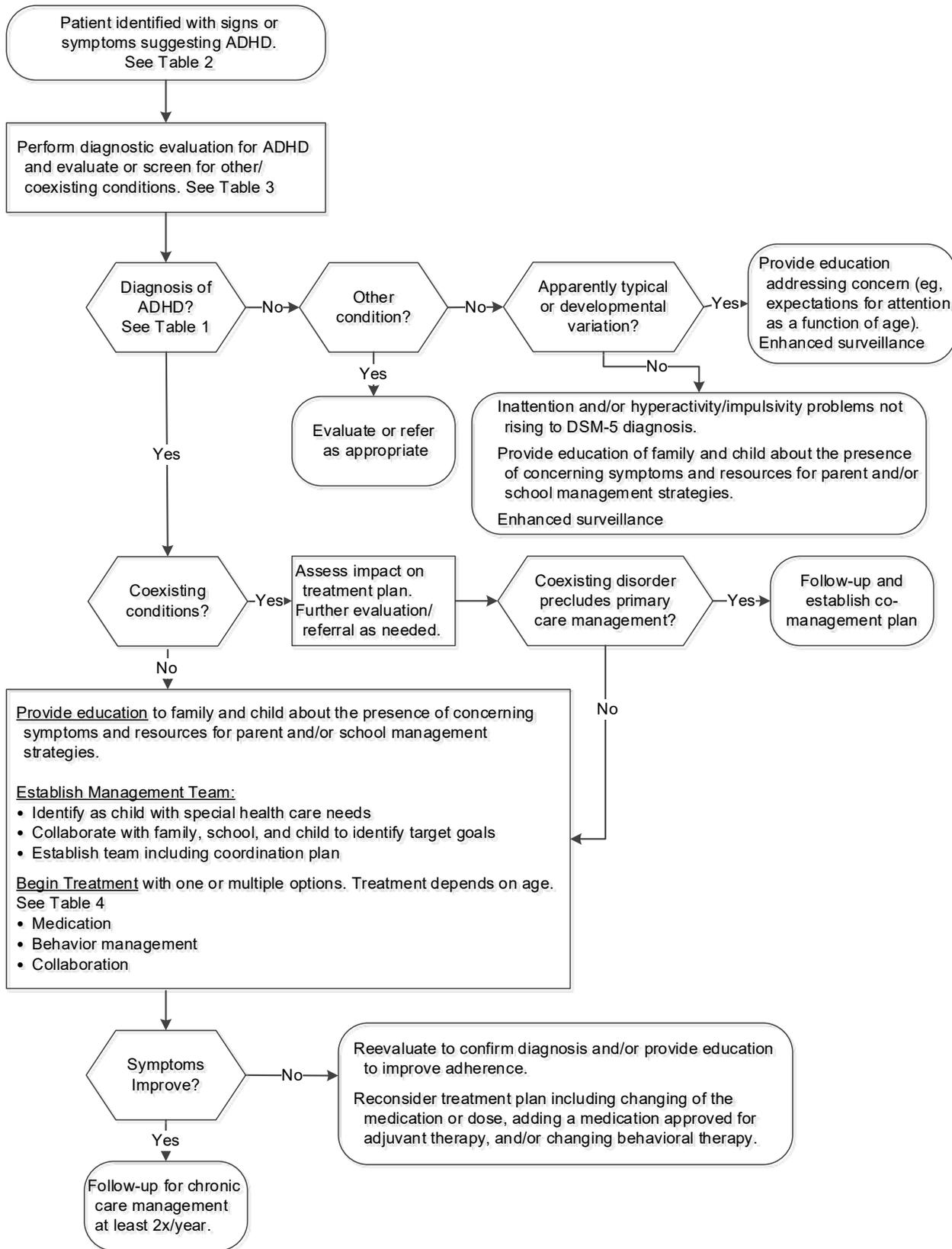
Specify current severity:

Mild: Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning.

Moderate: Symptoms or functional impairment between “mild” and “severe” are present.

Severe: Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

Figure 1. Overview of Diagnosis and Treatment of ADHD in Patients Ages 4-18 years *



* The overall sequence of evaluation and treatment for adults is similar, see the text details specific to adults. Note: Adapted from American Academy of Pediatrics, Implementing the key action statements: An algorithm and explanation for process of care for the evaluation, diagnosis, treatment, and monitoring of ADHD in children and adults. Pediatrics, 2011; 128(5): S1 1-S119

Table 2. Screen for ADHD

<p>Screening Questions:</p> <p>How is the patient functioning at school and other community settings?</p> <p>Are there any concerns about learning?</p> <p>Are there problems completing class work or homework?</p> <p>Are there behavior concerns at home, school, or work, or when playing/interacting with others?</p> <p>Consider ADHD if the patient presents with:</p> <p>Hyperactivity; cannot sit still; feeling generally restless</p> <p>A lack of attention; easily distracted; does not listen; daydreaming</p> <p>Acting without thinking; impulsive in conversation</p> <p>Behavior problems</p> <p>Academic underachievement</p>
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Table 3. Information Sources for Evaluation for ADHD

Family (parents, guardian, other frequent caregivers)	School (and other important community informants):	Child/Adolescent/Young Adult (as appropriate for patient's age and developmental status)
Chief concerns	Concerns	Interview, including concerns regarding behavior, family relationships, peers, school
History of symptoms (eg, age of onset and course over time)	Validated ADHD instrument	
Family history	Evaluation of coexisting conditions	
Past medical history	Report on how well patient functions in academic, work, and social interactions	For adolescents/young adults: validated self-report instrument of ADHD and coexisting conditions
Psychosocial history		
Review of systems	Academic records (eg, report cards, standardized testing, psychoeducational evaluations)	Report of patient's self-identified impression of function, both strengths and weaknesses
Validated ADHD instrument	Administrative reports (eg, disciplinary actions)	Clinician's observations of patient's behavior
Evaluation of coexisting conditions		Physical and neurologic examination
Report of function, both strengths and weaknesses		

Note: From ADHD: Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents, American Academy of Pediatrics, Nov. 2011

Table 4. Treatment Options for ADHD

<p>Preschool age children: first-line treatment is behavior therapy. If not significantly improved, consider methylphenidate.</p> <p>Elementary school age children and adolescents (age ≥ 6 years): first-line treatment is methylphenidate. Pharmacological treatment improves symptoms. Behavioral management techniques help modify behavior.</p> <p>Medication</p> <ul style="list-style-type: none"> Assess for any past medical or family history of cardiovascular disease Initiate medication treatment Titrate to maximize benefit and minimize adverse effects Monitor target outcomes <p>Behavior management</p> <ul style="list-style-type: none"> Identify service or approach, and support adherence Consider developmental variation, and address other developmental or mental health problems, in addition to ADHD Monitor target outcomes <p>Collaboration</p> <ul style="list-style-type: none"> Work with school to enhance supports and services, either informally with the teacher, or via a Section 504 plan or IEP Identify changes Consider developmental variation, and address other developmental or mental health problems in addition to ADHD Monitor target outcomes and maintenance of the intervention(s) by the school
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Note: Adapted from ADHD: Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents, American Academy of Pediatrics, Nov. 2011.

Table 5. First-Line Drug Therapy for ADHD

Generic Name, Brand Name, Dosages and Dosage Form	Time to Max Serum Concentration (hours)	Duration of Effect on Behavior (hours)	Recommended Prescribing: Starting Dose Increasing/Maximum Dose	30-Day Cost ¹	Comments/ Dose Conversions
Stimulants: Short-Acting (Immediate-Release) Amphetamine and Methylphenidate Based Products²					
Notes:					
Recommend taking stimulant medications 30 minutes after a meal to minimize appetite suppression.					
Recommend first dose upon awakening and second dose 4-6 hours later with second dose no later than 4 PM to avoid insomnia					
Methylphenidate/dexmethylphenidate absorption is increased 25% when taken after a meal.					
Amphetamine-based product absorption is increased when taken with acidic products (eg, vitamin C, orange juice, citric acid).					
All immediate-release tablets may be crushed.					
Medications are approved for 6 years of age and older unless otherwise specified.					
See Table 7 for common warnings.					
Methylphenidate³ Ritalin 5, 10, 20 mg tablets Methylin oral solution 5 mg/5 mL, 10 mg/5 mL	0.5-2	3-6	5-20 mg 2-3 times/day. May increase dose by 5-10 mg/day weekly, max 60 mg/day	\$29-50 \$13-25	Oral solution grape flavored
Dexmethylphenidate³ Focalin 2.5, 5, 10 mg tablets	0.5-2	3-6	2.5-10 mg 2-3 times/day. May increase dose by 2.5-5 mg/day weekly, max 30 mg/day	\$25	2.5 mg dexmethylphenidate = 5 mg methylphenidate
Mixed Amphetamine Salts Adderall 5, 7.5, 10, 12.5, 15, 20, 30 mg tablets (dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine sulfate, amphetamine aspartate)	0.5-3	5-7	[The following statements apply to mixed amphetamine salts, amphetamine sulfate, and dextroamphetamine] 5-15 mg 2 times/day or 5-10 mg 3 times/day. (For patients ages 3-5 years, begin with 2.5 mg daily). May increase dose by 2.5 mg/day (ages 3-5 years) or 5 mg/day (age > 6 years) weekly, max 40 mg/day	\$20-35	
Amphetamine Sulfate Evekeo 5, 10 mg tablets Evekeo ODT 5, 10 mg	0.5-3	5-7		\$125	Tablets also FDA approved for narcolepsy and exogenous obesity (only for ≥ 12 years of age) with alternate dosing Orally disintegrating tablets. Sweetened but not flavored, may be bitter
Dextroamphetamine Zenzedi 2.5, 5, 7.5, 10, 15, 20, 30 mg tablets ProCentra 5 mg/5 mL oral solution	0.5-3	5-7		\$20-30 \$100	Solution is clear, colorless, bubblegum flavor and dispensed in multi-dose bottles Solution requires oral dosing syringe for administration
<i>(Table continued on next page)</i>					

Table 5. First-Line Drug Therapy for ADHD, continued

Generic Name, Brand Name, Dosages and Dosage Form	Time to Max Serum Concentration (hours)	Duration of Effect on Behavior (hours)	Recommended Prescribing: Starting Dose Increasing/Maximum Dose	30-Day Cost ¹	Comments/ Dose Conversions
Stimulants: Long-Acting Amphetamine-Based Products²					
<p>Notes: Dosed once daily in the morning consistently either with or without food. Taking with acidic products (eg, vitamin C, orange juice, citric acid) may increase levels. May require supplemental afternoon dosing. Medications are approved for 6 years of age and older unless otherwise specified. Most products have both immediate (IR) and controlled release (CR) combined to result in 2 peak concentrations. See Table 7 for common warnings.</p>			<p>Capsules may be sprinkled on applesauce or yogurt. Entire mixture should be consumed immediately after mixing, without chewing beads. Do not crush, chew, or divide solid dosage forms. Liquid products must be measured and dosed with an oral syringe. ODT should not be chewed. ODTs should be taken immediately after removing from blister pack. Decrease dose 30% with renal impairment (eGFR 15-30 ml/min/1.73m²).</p>		
Dextroamphetamine					
Dexedrine 5, 10, 15 mg spansules	8	6-10	5 mg 1-2x daily May increase dose weekly by 5 mg/day to max 40 mg/day	\$30-50	Usually can be dosed once daily Absorption and duration of effect is variable
Lisdexamfetamine					
Prodrug of dextroamphetamine – requires conversion to dextroamphetamine in the bloodstream after absorption					
Vyvanse 10, 20, 30, 40, 50, 60, 70 mg capsule	3 (fasted) 5 (high fat)	12	30 mg daily May increase weekly by 20 mg to max 70 mg daily	\$325	70 mg Vyvanse is similar to 30 mg Adderall XR Time to peak is based on dextroamphetamine levels after the prodrug is converted
Vyvanse 10, 20, 30, 40, 50, 60 mg chewable tablet					
Mixed Amphetamine Salts					
Mixed salts of dextroamphetamine and levoamphetamine; products may have different ratios of dextro- and levo- isomers. These differences have not demonstrated significant differences in efficacy.					
Adderall XR 5, 10, 12.5, 15, 20, 30 mg capsules	7	8-12	10 mg once daily (20 mg adult). May increase weekly by 5-10 mg/day to max 30 mg/day	\$50-75	Both IR and CR beads (% not specified), but one peak level 1:1 conversion from IR total daily dose
Adzenys ER suspension 1.25 mg/mL	5	11-15	[The following statements apply to ER suspension and XR]	\$525-700	50% IR and 50 % CR Orange flavor
Adzenys XR ODT 3.1, 6.3, 9.4, 12.5, 15.7, 18.8 mg (6-count blister cards)	5-7	11-15		6.3 mg (6-17 years) or 12.5 mg (adult) once daily May increase weekly by 3.1-6.3 mg to max 18.8 (6-12 years); 12.5 mg (13-17 years and adults)	\$350-400
Dyanavel XR suspension 2.5 mg/mL	4	10-12	2.5 or 5 mg once daily May increase weekly by 2.5-10 mg/day to max 20 mg daily	\$300	Mix of IR and CR (% not specified) Bubblegum flavor Shake well before each dose
Mydayis 12.5, 25, 37.5, 50 mg capsules	7	16	12.5 mg once daily (13+ years) May increase weekly by 12.5 mg to max 25 mg (13-17 years) or 50 mg (adult)	\$300	37.5 mg = 25 mg Adderall XR + 12.5 mg Adderall IR 8 hours later
<i>(Table continued on next page)</i>					

Table 5. First-Line Drug Therapy for ADHD, continued

Generic Name, Brand Name, Dosages and Dosage Form	Time to Max Serum Concentration (hours)	Duration of Effect on Behavior (hours)	Recommended Prescribing: Starting Dose Increasing/Maximum Dose	30-Day Cost ¹	Comments/ Dose Conversions
Stimulants: Long-Acting Methylphenidate Products^{2, 3}					
Notes:	<p>Dosed once daily in the morning, consistently either with or without food. (Taking with food may increase absorption 25% but delay peak levels.) May require supplemental afternoon dosing. Medications are approved for 6 years of age and older unless otherwise specified. Most products have both immediate (IR) and controlled release (CR) combined to result in 2 peak concentrations. See Table 7 for common warnings.</p>			<p>Capsules may be sprinkled on applesauce or yogurt. Entire mixture should be consumed immediately after mixing without chewing beads. Do not crush, chew, or divide solid dosage forms. Liquid products must be measured and dosed with an oral syringe. Orally disintegrating tablets (ODT) should not be chewed. ODTs should be taken immediately after removing from blister pack.</p>	
Adhansia XR 25, 35, 45, 55, 70, 85 mg capsules	1.5 and 12	14-16	25 mg once daily in morning. May increase dose by 10-15 mg weekly to daily max 70 mg (< 18 years) or 85 mg (adults)	\$350	20% IR and 80% CR Dose conversion from other methylphenidate products not available
Aptensio XR 10, 15, 20, 30, 40, 50, 60 mg capsules	2 and 8	10-12	10 mg once daily in morning. May increase dose by 10 mg weekly to max 60 mg/day	\$250	40% IR and 60% CR
Concerta 5, 18, 27, 36, 54 mg tablets	1-2 and 6-8	8-12	18 mg (18-36 mg adults) daily May increase dose by 18 mg/day weekly to daily max 54 mg (6-12 years); 72 mg (or <2 mg/kg/day for 13-17 years); 72 mg adults	\$100-150	Conversion from IR methylphenidate: 5 mg BID-TID = 18 mg 10 mg BID-TID = 36 mg 15 mg BID-TID = 54 mg 20 mg BID-TID = 72 mg
Cotempla XR-ODT 8.6, 17.3, 25.9 mg tablets	5	8-10	17.3 mg once daily in morning. May increase dose by 8.6-17.3 mg weekly to max of 51.8 mg/day	\$375	25% IR and 75% CR: does not have two distinct peak levels Dispensed in blister packs with 6 tablets in each Grape flavor Only approved for 6-17 years of age
Daytrana 10, 15, 20, 30 mg patch (sizes 12.5, 18.75, 25, 37.5 cm ² respectively)	7	10-12	10 mg to skin of hip 2 hours prior to desired initial effect. May increase by patch size increment weekly to max 30 mg/day	\$375	Do not apply near waistband Remove 9 hours after application No direct conversion, however 10 mg patch similar to 36 mg Concerta and 30 mg patch similar to 54 mg Concerta
Focalin XR (dexmethylphenidate) 5, 10, 15, 20, 25, 30, 35, 40 mg capsules	1.5 and 6.5	10-12	5 mg (< 18 years) or 10 mg (adults) once daily May increase dose weekly by 5 mg (<18 years) or 10 mg (adults) to max of 30 mg (< 18 years) or 40 mg (adults)	\$80	50% IR and 50% CR 1:1 dose conversion from IR dexmethylphenidate Dose 50% lower than IR methylphenidate

(Table continued on next page)

Table 5. First-Line Drug Therapy for ADHD, continued

Generic Name, Brand Name, Dosages and Dosage Form	Time to Max Serum Concentration (hours)	Duration of Effect on Behavior (hours)	Recommended Prescribing: Starting Dose Increasing/Maximum Dose	30-Day Cost ¹	Comments/ Dose Conversions	
Stimulants: Long-Acting Methylphenidate Products^{2, 3}, continued						
Jornay PM 20, 40, 60, 80, 100 mg capsules	14	20-24	20 mg once in evening at 8 PM May increase dose weekly by 20 mg to max 100 mg/day	\$375	Dose conversion from other methylphenidate products not available Must be dosed in evening due to 10-12 hour delay in onset of action	
Metadate CD 10, 20, 30, 40, 50, 60 mg capsules	1-2 and 4-5	8-10	<i>[The following statements apply to Metadate CD, Metadate ER, Quillichew, Quillivant, and Ritalin]</i> 20 mg daily May increase dose weekly by 10-20 mg/day to max 60 mg/day	\$65-100	30% IR and 70% CR	
Metadate ER 20 mg tablets	5	8		\$30	Slow, sustained release. Does not have multiple peak levels	
QuilliChew ER 20, 30, 40 mg tablets	5	8-12		\$300	30% IR and 70% CR Dose conversion from other methylphenidate products not available Cherry flavor	
Quillivant XR 25 mg/5 mL suspension	4-5	8-12		\$275	20% IR and 80% CR 1:1 conversion from IR total daily dose Available in 60, 120, 150, 180 mL bottles Must be reconstituted by pharmacy and dispensed as a full bottle Banana flavor. Shake well before each dose.	
Ritalin LA 10, 20, 30, 40, 60 mg capsules	2 and 6	8-10		\$125	50% IR and 50% CR 1:1 conversion to IR total daily dose	
Relexxii 72 mg tablet	1-2 and 6-8	8-12		Only to be used in patients who have titrated to 72 mg of Concerta and desire single tablet option	\$500	Conversion from IR methylphenidate: 20 mg twice daily or three times daily = 72 mg

Note: For children younger than 5 years, consider referral to child psychiatry for drug therapy.

¹ Cost = Average cash price including available discounts per GoodRx.com accessed 11/2019.

² Stimulants are not recommended for children younger than 3 years.

³ May in rare instances cause prolonged and sometimes painful erections known as priapism. Healthcare professionals should talk to male patients and their caregivers to make sure they know the signs and symptoms of priapism and stress the need for immediate medical treatment should it occur. Younger males, especially those who have not yet reached puberty, may not recognize the problem or may be embarrassed to tell anyone if priapism occurs.

Table 6. Second-Line Medications for Treatment of ADHD

Medication	Indications	Recommended Prescribing: Starting Dose Increasing/Maximum Dose	Range	Cost ¹	Drug Class Adverse Effects and Comments
Alpha-2 Central Agonists					
Notes: May cause sedation, dizziness, nausea, orthostatic hypotension, insomnia, agitation, headaches, stomach aches, enuresis, constipation. Sedation tends to decrease over time. Maximum effect may take weeks. Consider referral to child psychiatry for use in children younger than 5 years.				Rebound hypertension and/or rebound insomnia may occur if stopped abruptly. Taper over at least 1-2 weeks to discontinue. Monitor blood pressure at baseline, after dose adjustment, and at follow up. Obtaining a baseline EKG is advisable.	
Parent counseling: Do not give as needed. Do not make up missed doses and do not give supplemental doses due to the risk of severe hypotension.					
Clonidine Catapres 0.1, 0.2, 0.3 mg tablets Also available as 0.1, 0.2, 0.3 mg per 24 hr patches Kapvay 0.1 mg 12-hour extended release tablet	ADHD + tics ADHD + Post traumatic stress disorder (PTSD) PTSD Insomnia, oppositionality Hyperarousal, aggression	0.05 mg at bedtime Increase 0.05 mg every 3-7 days Frequency: 2-4 doses/day for ADHD, but may be given just at bedtime for PTSD, insomnia 0.1 mg at bedtime May increase weekly by 0.1 mg/day Frequency: 2 doses per day for ADHD (either split equally or with the higher split dosage given at bedtime); maximum: 0.4 mg/day	0.05-0.2 mg/d	\$5-7 tab \$70 -100 patch \$100	4 cases of sudden death have been reported with combination treatment of clonidine + methylphenidate Immediate release (IR) total daily dose is similar to extended release (ER) total daily dose. Clearance of clonidine is up to 44% lower in patients receiving amphetamine. May require lower starting dose for patients on amphetamines, or dose reduction if amphetamines are added.
Guanfacine 1, 2 mg tablets (limited data available) Intuniv (long-acting) 1, 2, 3, 4 mg tablets	ADHD + tics ADHD + PTSD PTSD Insomnia, oppositionality Hyperarousal, aggression	0.5 mg at bedtime Increase 0.5 mg/week Give as 1-2 doses/day 1 mg in AM Increase by 1 mg/week, max 4 mg/day	0.5-3 mg/day 1-4 mg/day	\$10-25 \$45	Somnolence/sedation less common compared to clonidine Long-acting should be taken consistently with or without food. High fat breakfast increases absorption from 60% to 80%. Immediate release (IR) absorption is not impacted by food. Long-acting dose approximately 20-40% lower than IR. Specific dose conversion not available. Manufacturer recommends titrating from starting dose when transitioning products. Primarily metabolized via CYP3A4. Consider dose reduction with strong inhibitors of CYP3A4 (eg, fluvoxamine, fluconazole), and consider dose increase with strong inducers (eg, carbamazepine, phenytoin, rifampin).
<i>(Table continued on next page)</i>					

Table 6. Second-Line Medications for Treatment of ADHD, continued

Medication	Indications	Recommended Prescribing: Starting Dose Increasing/Maximum Dose	Range	Cost ¹	Drug Class Adverse Effects and Comments
Selective Norepinephrine Reuptake Inhibitor					
Atomoxetine (Strattera) ² 10, 18, 25, 40, 60, 80, 100 mg capsules	Slow onset	<p>≤ 70 kg 0.5 mg/kg/day Increase after a minimum of 3 days to 1.2 mg/kg/day, max 1.4 mg/kg/day or 100 mg, whichever is less</p> <p>> 70 kg 40 mg/day Increase after a minimum of 3 days to 80 mg/day, max 100 mg/day</p>	<p>18-100 mg/day</p> <p>40-100 mg/day</p>	\$92	<p>When transitioning from stimulants to atomoxetine, cross-taper (ie, decrease stimulant gradually while increasing dose of atomoxetine)</p> <p>Dosage adjustments are required for patients concurrently taking CYP2D6 inhibitors and those with hepatic insufficiency³</p> <p>1.6-1.8 mg/kg/day may be warranted in some pts.</p> <p>Not recommended for children younger than 6 years</p> <p>Capsules should not be opened. Contents can be irritating to oral mucosa and have a very bitter taste. Some compounding pharmacies may be able to make a suspension formulation; however, it will be in an oil base due to lack of stability in an aqueous environment.</p>

1 Cost = Average cash price including available discounts per GoodRx.com accessed 11/2019

2 May in rare instances cause prolonged and sometimes painful erections known as priapism. Healthcare professionals should talk to male patients and their caregivers to make sure they know the signs and symptoms of priapism and stress the need for immediate medical treatment should it occur. Younger males, especially those who have not yet reached puberty, may not recognize the problem or may be embarrassed to tell anyone if priapism occurs.

3 For patients concurrently taking CYP2D6 inhibitors (eg, bupropion, duloxetine, fluoxetine, paroxetine) the dose should be increased only if symptoms fail to improve after 4 weeks and the initial dose is well-tolerated. For patients with moderate hepatic insufficiency (Child-Pugh Class B), initial and target doses should be reduced to 50% of the normal dose. For patients with severe hepatic insufficiency (Child-Pugh Class C), initial and target doses of atomoxetine should be reduced to 25% of the normal dose.

Table 7. Precautions for Stimulants and Atomoxetine in Treatment of ADHD

Drug Class Adverse Effects and Monitoring Parameters
Stimulants
<p>Black Box Warning: Stimulants have high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy.</p> <p>Cardiovascular risk: Prior to prescribing stimulants, screen all patients for history of syncope with exercise, history of structural or congenital heart defects, and any family history of sudden unexpected cardiovascular death. Patients with a positive screen to one of these 3 questions should be considered for further evaluation, such as an electrocardiogram (EKG), before beginning stimulant therapy.</p> <p>Common adverse effects (>10%): Upset stomach/abdominal pain, decreased appetite, dry mouth, headache, insomnia, anxiety.</p> <p>Less common adverse effects (1-10%): irritability, weight loss, dizziness, flattened affect, social withdrawal, sweating, mood lability, agitation, tics, tremor, reduced growth velocity.</p> <p>Rare adverse effects: auditory/visual hallucinations, seizures.</p> <p>Monitor: height, weight, blood pressure, and pulse.</p> <p>Avoid concomitant use of decongestants due to increased risk of adverse effects.</p> <p>FDA Medication Guide warnings for patients and/or parents (dispensed by pharmacy with prescriptions):</p> <ul style="list-style-type: none"> • Heart related problems – risk of sudden death, stroke, heart attack, increased blood pressure and heart rate • Psychiatric problems – new or worse behaviors, thought problems, bipolar illness, aggressive behavior, hostility, psychotic symptoms or manic symptoms • Circulation problems – fingers or toes feel numb, painful or change from pale to blue to red (Raynaud’s phenomenon) • Methylphenidate based products only: May cause prolonged and sometimes painful erections (priapism).
Atomoxetine (Strattera)
<p>Black Box Warning: Increased risk of suicidal ideation early in treatment compared to placebo (0.4%).</p> <p>Common adverse effects (>10%): Abdominal pain, decrease in appetite, vomiting, headaches, insomnia, somnolence, fatigue, dizziness, irritability, increase in heart rate and blood pressure.</p> <p>Less common adverse effects (1-10%): Decreased weight, dizziness, constipation, feeling jittery, urinary hesitation, sweating.</p> <p>Rare but serious adverse effects: seizures, priapism; liver injury (discontinue in patients with elevated liver enzymes); sudden cardiac death (avoid in patients with known serious structural cardiac abnormalities, cardiomyopathy, or arrhythmias).</p> <p>Monitor: blood pressure, pulse, suicidal thinking/behavior, unusual changes in behavior.</p> <p>Important information for patients and/or parents: Atomoxetine takes weeks to months for full effect. Delay in onset should not be confused with lack of efficacy, especially for patients who have previously been on stimulants, which can provide benefit immediately upon initiation.</p>

Table 8. Types of Intervention for ADHD

Pharmacotherapy	See above.
Psychoeducation and Support	Clinicians can give patients, families, and schools materials or links to websites such as Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD) regarding diagnosis, medications, and treatment and support services.
Parent Skills Training	Parent-Child Interaction Therapy (PCIT) and other parent management training may help the child learn appropriate expectations and responses.
Family Therapy	Family therapy may be particularly useful when working with children with more disruptive behaviors. It also may be helpful for adults who suffer from ADHD or have complicated psychosocial circumstances.
School-based Interventions	Schools can provide tutoring, resource room periods, modifications or accommodations in the classroom, and behavioral interventions. Accommodations might include strategic seating, extended time to complete work, or a private signal from the teacher to come back on task. Behavioral interventions might include a Daily Report Card, whereby the teacher communicates to parents about behaviors at school and progress can be monitored. A Section 504 plan may be implemented in the school to provide a formal plan for accommodations. If the patient is eligible, an IEP (Individualized Education Plan) can provide special education services. The CHADD website and others provide information about such interventions. The clinician may be called upon to provide evidence of ADHD or co-occurring conditions, and clinicians can help advocate for school services.
ADHD Support Groups	These groups may be available in your local area through CHADD or other local organizations identified by community mental health or your local Intermediate School District (ISD).
Advocacy Groups	These groups help parents learn about the legal rights their children have with regard to educational settings and special education services. One such group is PACER Center – Champions for Children with Disabilities (Parent Advocacy for Children’s Educational Rights).
Social Skills Training	Using role-playing, modeling, and group feedback, children and teens can practice interpersonal skills in a safe setting (eg, maintaining eye contact, initiating and maintaining conversations, how to read facial expressions and judge an appropriate response, etc.).
Cognitive Behavioral Therapy	This work focuses on thought patterns and may be useful if there is a co-existing condition such as anxiety, or mood disorder.
Complementary and Alternative Medicine (CAM)	See below.

Clinical Background

Clinical Problem and Current Dilemma

Prevalence and Impact

Attention deficit hyperactivity disorder (ADHD) is the most commonly diagnosed behavioral disorder of childhood. The estimated prevalence of ADHD in children is 7-11%. [C] It is more commonly diagnosed among boys. The combined subtype is the most common. Observational studies show some gender differences in subtypes: in girls the inattentive subtype is more common. The rate of ADHD continuation from childhood into adulthood is a current area of research; studies have suggested variable rates ranging from 5-76%. Some researchers suggest that childhood and adult ADHD may be different conditions. Current estimates indicate that approximately 2.5-5% of adults meet diagnostic criteria for ADHD. Factors that predict persistence to adulthood include coexisting mental health problems, more severe initial symptoms, and parental mental health problems.

The core symptoms of ADHD include developmentally inappropriate levels of attention, concentration, activity, distractibility, and impulsivity that persist over a period of at least six months. Children with ADHD usually have functional impairment across multiple settings, including home, school, and peer relationships. These children experience long-term adverse effects on their academic performance, vocational success, and social-emotional development [B]. They experience peer rejection, engage in disruptive behavior, and are frustrated learners. They have higher injury rates. Untreated, they have higher rates of motor vehicle accidents, substance use disorders, and school dropout [B]. These patterns are also true for adults with untreated ADHD, including effects on educational attainment, and impairment in work performance, social functioning, emotional and marital adjustment, driving record, and financial management.

Some children with ADHD qualify for accommodations under Section 504 of the Rehabilitation Act. Others with more significant symptoms or co-existing conditions that affect academic functioning may qualify for special education services. Information about school support is

available at the U.S. Department of Education, <https://www2.ed.gov/about/offices/list/osers/osep/index.html>. Eligibility designations for Michigan Special Education are available at: <https://www.michigan.gov/mde/0,4615,7-140-6598---,00.html>. All children benefit from teacher awareness and educational support [D].

International statistics are difficult to compare due to varying clinical definitions of the disorder, use of different assessment tools, and differing cultural definitions of acceptable childhood behavior. For instance, Hyperkinetic disorder (ICD-10) uses a stricter definition than the DSM-5 definition of ADHD. Overall, ADHD is thought to affect 7.2% of children worldwide [C].

Primary Care Role

Most patients will present to their primary care clinician, generally with concerns about performance at school or work, and/or behavioral problems. Depending upon the presentation and potential comorbidities, the primary care clinician will often be able to establish the diagnosis, institute appropriate therapy, and provide follow up. Screening questions are useful in identifying potential patients with this disorder. The most common therapy is stimulant medication. These schedule II controlled substances must be prescribed monthly. This is most conveniently done by the primary clinician. Primary care clinicians will need to arrange for subspecialist consultations in more complex diagnostic or management situations. Lack of insurance coverage is a barrier to specialty care. There are no documented strategies for the prevention of ADHD. Currently there is no cure.

Diagnostic Concerns

Some experts see ADHD as underdiagnosed. The high prevalence of comorbidities is often confusing. Diagnosis requires a more extensive evaluation than is usually possible in one primary care office visit. Evaluation of children requires observational information from classroom teacher and parents. Evaluation of adults may include information from another person who knows the individual well; parental information and school documentation from childhood is often helpful. Currently, ADHD is a behaviorally-based diagnosis without clinically useful biologic measurements.

Treatment Concerns

Concern has been expressed by some that clinicians are too quick to label patients with ADHD and prescribe medication. However, ADHD is a chronic condition of childhood for which medication has been shown to be the most effective therapy [A], and there are accepted standards for diagnosis and treatment. Long-term use of stimulant therapy in children has been associated with effects on linear growth in one study but not others. Effect on linear growth may be related to cumulative dose exposure [C]. Drug holidays can be used, but the benefits of this strategy in mitigating growth delays have not been demonstrated in a controlled setting.

Failure to treat could result in sub-optimal learning with long-term adverse developmental and physical outcomes. Drug diversion of stimulant medication is an important problem for which the clinician must be alert. Stimulant treatment of ADHD has been associated with decreased rates of substance use disorder [C]. The majority of studies do not find that stimulants increase risk for later substance misuse.

Rationale for Recommendations

Etiology & Natural History

While the etiology of ADHD is unknown, evidence supports a neurological basis for the disorder. ADHD is characterized by disturbances of executive functioning (eg, deficits in working memory; inability to plan, organize, and integrate information). At least three brain regions have been implicated in the disorder. MRI studies have correlated severity of ADHD symptoms with smaller frontal and temporal gray matter, caudate, and cerebellar volumes [B]. More than 20 genetic studies support the tendency for inheritability of ADHD. Specifically, genetic studies have shown increased prevalence of ADHD in children of affected persons.

ADHD appears to be a chronic condition that often persists into adulthood. Symptoms tend to improve with age, although this may be due in part to improved coping skills. Synaptogenesis and myelination continue into adolescence and young adulthood (especially in the frontal lobes), which may also explain improvement of symptoms with age. As previously stated, some experts propose that adult ADHD may be distinct from childhood ADHD for some individuals.

Diagnosis

Diagnostic criteria and evaluation. The criteria for ADHD in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) were established for children. (See Table 1.) For teens 17 years and older and adults, 5 (rather than 6) symptoms are required to be present for at least 6 months and inappropriate for developmental level, for both inattentive and hyperactive-impulsive categories. The symptoms may present differently for adults (eg, feelings of general restlessness rather than observable hyperactivity). In addition, several symptoms should have been apparent before age 12 years.

An overview of evaluation and diagnosis of children and adolescents is presented in the top half of Figure 1 and in Tables 2 and 3. The overall sequence is similar for adults.

Children and adolescents. Any child age 4-18 years who presents to their primary care clinician with inattention, hyperactivity, impulsivity, academic underachievement, or behavior problems (Table 2) should undergo an evaluation for ADHD. The DSM-5 criteria (Table 1) are used to make the diagnosis.

The following information must be obtained from both family and educational settings to derive the diagnosis of ADHD: presence and duration of core symptoms (Table 1); degree of functional impairment; and any associated conditions. The evaluation process usually requires multiple visits.

Review the social and medical history of the patient's family. For children and adolescents, review the patient's growth and development history.

Perform a complete physical exam to detect alternate diagnoses or comorbidities. Screen for other medical problems. Screen for sensory impairments. Usually the physical exam is normal. The patient's attention span, amount of fidgeting, and (for children) parental interactions can all be observed over several visits. Absence of hyperactivity in the office does not rule out the diagnosis.

For children, use of standardized rating scales for parent and teacher reports is strongly recommended. A variety of rating scales are available. Some are free of charge, but many are copyrighted and must be purchased, such as the Conners Rating Scales (see Appendix A1). Note that for teenagers, teacher rating scales may be less reliable due to lack of prolonged observation. Consider obtaining ratings from more than one teacher or other adult who works with the teen.

Teens with ADHD present a special challenge. During these years, academic and organizational demands increase. Adolescents also face other challenges related to normal development: discovering their identity, establishing independence, dealing with peer pressure, exposure to drugs and alcohol, learning to drive, and emerging sexuality.

No specific diagnostic test is necessary or sufficient to establish the diagnosis of ADHD. Tests such as blood lead levels, thyroid function tests, brain imaging, and electroencephalogram have no discriminative ability in establishing the diagnosis of ADHD.

Adults. Many adult patients had ADHD symptoms during childhood, but they may not have been identified and diagnosed. Adult ADHD patients may have graduated from high school, but are having a difficult time with more demanding activities in adulthood, eg, studies in college, holding on to a job, or managing other tasks and relationships. Often adult patients become aware of their own symptoms when their child is first diagnosed.

Requesting ADHD medication for "performance enhancement" in college or the workforce does not meet criteria for prescribing medication. Adult patients need to demonstrate that their symptoms are causing them functional impairment in some aspect of their life.

For adults, only five core symptoms in one or both ADHD domains are necessary in DSM-5, rather than six (see Table

1). Adult diagnosis of ADHD is also supported by having some symptoms of the condition present before age 12.

Adults with ADHD may be easily distracted, have difficulty sustaining attention and concentrating, are often impulsive and impatient, and may have mood swings or low frustration tolerance. They may be disorganized and have difficulty planning ahead. Although frank hyperactivity is much less common in adults, they may be fidgety or feel internally restless. Adults may experience career difficulties. They may lose jobs due to poor performance (lack of attention, poor task completion, disorganization), or interpersonal problems.

A new diagnosis of adult ADHD should be based on having some core symptoms that were present during childhood and are persisting. Assessment of areas of functioning that are impacted should include work, daily activities, social relationships, and psychological and physical well-being. Comorbidities (ie, substance use disorders, depression, hearing impairment, sleep apnea, thyroid disease) are common and often complicate the diagnosis. Timing of the onset of symptoms is important; eg, inattentiveness that occurs after the onset of depression is less likely due to ADHD as the primary factor. A familial pattern is frequently present. Self-assessment instruments are often used.

Some primary care clinicians may be comfortable making a new ADHD diagnosis in an adult if there is a strong history of positive core symptoms during childhood. However, referral to a psychologist or psychiatrist with experience diagnosing ADHD anew in adulthood is recommended.

Commonly confused and associated conditions. ADHD is a common disorder of childhood, but the symptoms of ADHD are non-specific and occur in a wide variety of developmental, psychiatric, and medical disorders. Concerns about over- or under-diagnosis of ADHD may relate in part to the presence of conditions that are commonly confused with ADHD, such as developmental disorders (learning disorders, intellectual disorders, autism spectrum disorders), psychiatric disorders (oppositional defiant disorder, anxiety disorders, mood disorders), environmental factors (stress, child neglect or abuse, toxins), and medical disorders (post-traumatic encephalopathy, post-infectious encephalopathy, chronic illness, seizures, sleep disorders, sensory disorders, drug-induced changes). Sleep disorders can include sleep disordered breathing (eg obstructive sleep apnea), restless legs syndrome, periodic limb movement disorder, or other medical problems that affect sleep continuity and duration.

Specific diagnostic criteria have been developed and published for ADHD (see DSM-5; some relevant definitions are reproduced in Appendix B1). However, if an individual displays symptoms atypical for uncomplicated ADHD, or if the individual does not respond to treatment as expected, the primary care clinician should strongly consider an additional or alternate diagnosis and consult with an appropriate specialist.

ADHD may co-occur with other disorders. About two-thirds of children with ADHD have at least one other comorbid disorder, according to the 1999 MTA study. Learning disorders, depressive disorders, anxiety disorders, sleep disorders, and tic disorders are more prevalent in patients diagnosed with ADHD. When comorbid conditions exist, academic and behavioral problems may be more complex and difficult to treat. One reason for (apparent) treatment failure is unrecognized comorbidity. Conversely, patients with untreated or inadequately treated ADHD are at higher risk for psychiatric and behavioral comorbidity. See Appendix B2 for selected psychiatric disorders that may be confused with or co-occur with ADHD, as well as suggestions for distinguishing between disorders.

Treatment

An overview of treatment is presented in the bottom half of Figure 1 and Table 4. The goals of treatment are to improve symptoms and maintain school performance, social interaction, self-worth and self-esteem, and an opportunity for successful learning. Treatment may be considered successful when it improves school and work performance and relationships, decreases struggles, and relieves frustration.

Preschool children (younger than 6 years). Behavior therapy is the first line of treatment [A]. If behavioral interventions do not provide significant improvement, and moderate-to-severe functional disturbances continue, methylphenidate may be prescribed. Consultation with child psychiatry or a developmental behavioral pediatrician is recommended when considering medication treatment. If evidence-based behavioral treatments are not available, clinicians need to weigh the risks of starting medication at an early age against the harm of delaying diagnosis and treatment.

School age children, adolescents, and adults (age ≥ 6 years). A treatment plan for ADHD should include both pharmacologic and behavioral components. Pharmacologic treatment improves core symptoms [A]. Behavioral management techniques can address and modify behavior, which is helpful for all children, particularly those with challenging behavior in circumstances such as:

- During periods poorly covered by medications (eg, later in the day for those on stimulants)
- Patients requiring lower doses due to adverse effects
- The 10-30% of patients who do not respond to medication approaches or who have intolerable adverse effects.

Pharmacologic treatment. The treating clinician must decide the strategy of pharmacologic treatment based on the circumstances of the individual patient, with input from the family and patient if appropriate, keeping in mind the patient's activities and goals. Typically, the first-line agents are stimulants (methylphenidate, dextroamphetamines, and mixed amphetamine salts). Atomoxetine, guanfacine, and clonidine are non-stimulant medications approved by the FDA for treatment of ADHD. Other non-stimulant medications used for ADHD are some antidepressants (eg,

bupropion, trazodone) and occasionally atypical antipsychotics (eg, risperidone, aripiprazole) or mood stabilizers (eg, carbamazepine). These are not approved by the FDA for treatment of ADHD. A few controlled studies have shown them to be useful when stimulants are ineffective or comorbidities are present. Tables 5-7 provide an overview of dosing, cost, adverse effects, and other information for first-line and second-line agents.

Costs and cost reduction. All first-line and second-line medication classes have products available as low-cost generic medications (< \$20 for a 30-day supply). Specific extended-release products may require prior authorization from insurers prior to use due to high cost (up to 20-fold more than generic products) and lack of comparative efficacy to support benefit. For patients who are paying cash for medications, multiple websites help predict medication costs and discounts. The site www.goodrx.com provides price estimates for local pharmacies and coupon discounts for many pharmacy chains. For patients with low income, <http://www.rxoutreach.com/> is a mail order pharmacy with discounted prices on medications for those who meet income requirements. This site requires that patients fill out an application with income attestation. Prescriptions for stimulants have to be physically mailed to the [rxoutreach](http://www.rxoutreach.com/) pharmacy due to their Schedule II controlled substance status.

Stimulants are the best-researched [A], safest, and most effective medications for ADHD pharmacologic management. Stimulants improve the core symptoms of inattention, impulsivity and hyperactivity. They also improve the individual's ability to follow rules, decrease emotional over-reactivity, and improve relationships with peers and family members, thereby improving self-control, social interactions, and self-esteem. However, long-term outcomes in educational and occupational achievement and behavior have not been demonstrated. Studies have shown that stimulants do not change underlying cognitive ability, although academic performance may improve.

Stimulants are categorized as Schedule II controlled substances because they have the potential for abuse and dependence. Multiple studies have shown that children taking stimulants to treat ADHD do not develop dependence or signs of addiction [B]. Multiple studies also suggest that children taking stimulants to treat their ADHD may reduce their risk for illicit drug use. However, these medications do carry a black box warning about abuse potential.

The mechanism of action of stimulants is not fully known, but is predominantly attributed to binding of the dopamine transporter and subsequent inhibition of dopamine reuptake, resulting in increased levels of extracellular dopamine.

The two major categories of stimulants available for the treatment of ADHD are methylphenidate and amphetamine salts (and their isomers and pro-drugs). Both are considered first-line agents, and both are available in various short-, intermediate-, and long-acting formulations (see Table 5).

The decision regarding which agent a clinician first prescribes is often made on the basis of individual preferences, including clinician or previous family member experience. Some guidelines suggest beginning with methylphenidate agents due to a greater number of studies of efficacy.

The choice of a short-acting or long-acting preparation will vary depending on patient age and clinician preference. Most individuals do well with stimulant medications and have few significant adverse effects. However, monitoring during the trial period is necessary, and changes in medication group or brand-name may be needed. The patient should be informed that some long-acting preparations have to be swallowed whole. Time of onset of action and duration of action varies by preparation and by product.

Treatment is generally initiated with a methylphenidate agent. Among the long-acting options are products such as Ritalin LA and Metadate CD, which use a bead delivery system. A portion of the beads are released initially to provide immediate coverage, and a second portion is released about four hours later. Concerta has 3 layers. The central core is surrounded by a semi-permeable membrane, which is then surrounded by an immediate release coating. When the tablet reaches the GI tract, the outer layer dissolves, providing the initial dose of methylphenidate. Water then permeates through the semi-permeable membrane (which is the second layer) into the central core of the tablet and helps release the rest of the drug to provide a longer coverage period.

Daytrana is a transdermal (patch) delivery system applied to the hip area for 9 hours. It can cause skin irritation and loss of pigmentation at the site of application. It is useful for those who cannot take oral medication. This delivery system also allows for early removal of the patch in patients who have insomnia due to the medication.

The intermediate-acting forms of methylphenidate (Ritalin-SR, Methylin ER, Metadate ER) are formulated in a wax matrix core, which may result in unpredictable release of active methylphenidate. Therefore, the durations of action of these formulations are more variable.

Supplementation with a single small dose of an immediate-release methylphenidate product may be necessary, even when using long-acting products. Supplementation can be either in the morning (eg, with Concerta – to provide faster onset of action), or in the afternoon (eg, with Ritalin LA, Metadate CD, or Concerta – to extend the coverage).

Mixed amphetamine salts are the second choice for therapy. Adderall XR has a bead delivery system with a portion released initially and the rest about four hours later. The Dexedrine Spansule preparation delivers the initial dextroamphetamine dose immediately; the remaining medication is released slowly over time so that the therapeutic levels last from 6 to 8 hours.

Lisdexamfetamine (Vyvanse) is a pro-drug is converted to dextroamphetamine by hydrolysis in the bloodstream after absorption. Its theoretical advantage is less potential for abuse or overdose toxicity.

Starting stimulant therapy. It is helpful to define behavioral targets for the individual patient, taking into account their age, school or work environments, home environment, educational and athletic expectations, and specific after-school or work activities. Cultural factors that affect the patient's health care also need to be considered. Goals should be realistic and achievable. These behavioral targets can then be monitored for improvement during the trial period. It may be helpful to choose targets that parents can monitor on the weekends, because by the time a child is home from school, the medication effects have waned for many.

Unlike many other medications, the beneficial dosage of stimulants is generally not considered to be weight dependent. Start with the lowest dose. Increase the dose on a weekly interval until the desired improvements in behavioral and academic performance targets are achieved or the patient develops undesirable adverse effects. Suboptimal doses of stimulant medication may result in inconsistent or incomplete coverage through the day and inadequate control of symptoms. Management of these medications is complex, and failures are often due to improper dosing rather than ineffectiveness of the medication.

During the first month of treatment, titration may involve weekly or biweekly follow-up, either by in-person visits or by phone calls or video visits, with the first follow up within 4 weeks of starting the medication trial. Patients can be instructed to start with a low dose and then to increase the dose after one week if no adverse effects have been observed. They can call into the office to notify the prescriber how the change went. It is not uncommon to make 2-3 changes in one month's time when initiating therapy.

The timing and dose of medication are best determined using feedback from the patient as well as their parents and teachers. For adults, other family members can provide helpful feedback, and family members should be advised about potential adverse effects and the expected duration of effectiveness of the medication. Behavioral rating scales may be helpful (See Appendix A1.) After the dose has been established, the patient may be seen for follow-up 2-3 times per year.

Studies have shown that about 70–75% of patients respond to the first stimulant medication. This number increases to 90–95% when a second stimulant is tried. If the patient does not respond to or develops adverse effects with one stimulant, try a different stimulant. Adverse effects are mostly due to adrenergic activity and are dose dependent. Most adverse effects can be managed by changing the form of the stimulant or adjusting the dose and timing.

Maintaining stimulant therapy. As noted previously, a booster dose of short-acting stimulant medication may help with completing homework or other work later in the day, participation in extracurricular activities, and interactions with peers and family members. Many patients choose to continue the medication on weekends and holidays (if effects on growth are not a consideration) as it helps them across community pursuits as well as school.

Several studies have found that adolescents and young adults with ADHD have more traffic violations, motor vehicle accidents, and suspended licenses than those without the diagnosis. Some studies demonstrate that appropriate treatment of the ADHD with stimulant medication can decrease these risks. Anticipatory guidance should be given to parents with teenagers and to young adults regarding their disease, its treatment, and safe driving (eg, avoiding driving without medication).

Adverse effects of stimulants. A common adverse effect of stimulants is appetite suppression, which may result in transient weight loss. Administering the stimulant with or after meals may minimize this adverse effect. Abdominal pain, headache, irritability and sleep problems may also occur. Difficulty in initiation of sleep may be associated with increased hyperactivity and irritability as the effect of the medication wears off. In some patients a small dose of a short-acting stimulant may help alleviate this symptom. If the problem is insomnia due to duration of action of the stimulant, try giving the medication earlier, or try a shorter acting agent. Sometimes, the addition of a medication to help sleep initiation (eg, melatonin) or a second-line ADHD agent may be necessary.

Before starting the medication, it is important to obtain a history of the patient's eating and sleeping patterns (so that the clinician can document if the medication causes a change from baseline), ask about any family history of tics or Tourette syndrome, and assess for any signs of depression and social withdrawal. Tics may appear in some patients when they are on stimulant medication, and for some, tics decline with discontinuation of medication. Presence of tics is not a contraindication for taking stimulants. The decision to stop or modify the stimulant dose needs to be individualized.

Rare patients may appear to develop Tourette syndrome when on stimulants, but in actuality 50% of patients with Tourette syndrome also have ADHD, which may present 2 to 3 years before the tics appear. It is believed that stimulant therapy does not cause Tourette syndrome, which is an inherited disorder, but simply unmask the condition. This usually occurs in elementary school age or adolescence.

Controversies about suppression of growth in patients on stimulants have still not been resolved. Long-term use of stimulant therapy in children has been associated with effects on linear growth in one study but not others. Effect on linear growth may be related to cumulative dose exposure. Elevated heart rate and blood pressure have been observed in

children undergoing therapy with stimulants. These effects are generally considered clinically insignificant and dose related.

Concerns have been raised about the risk of sudden cardiac death in patients on stimulants. The American Academy of Pediatrics (AAP) in collaboration with the American Heart Association (AHA) put out a statement regarding careful screening of pediatric patients for any family history of sudden cardiac death, hypertrophic cardiomyopathy or long QT syndrome, or any personal history of heart disease, palpitations, syncope, or seizures [B]. The screening evaluation should include a thorough cardiovascular examination. An electrocardiogram (EKG) is not mandatory but should be left to the discretion of the treating physician [D].

Methylphenidate products may in rare instances cause prolonged and sometimes painful erections known as priapism. If not treated right away, priapism can lead to permanent damage to the penis. Priapism can occur in males of any age and happens when blood in the penis becomes trapped, leading to an abnormally long-lasting and sometimes painful erection.

Atomoxetine (Strattera) has also been associated with priapism in children, teens, and adults. Priapism appears to be more common in patients taking atomoxetine than in those taking methylphenidate products.

While many patients with seizure disorders safely use stimulant medications for ADHD management, stimulants reduce the seizure threshold. Consider consultation with the patient's neurologist before initiating stimulant medication.

Long-term management of stimulants. There is not consensus regarding visit frequency. However, a reasonable approach might be: visits every month until optimal response is consistent; visits every 3 months during the first year of treatment; then visits every 6 months once stable to monitor course, growth, and to watch for emerging co-morbid concerns.

Laboratory tests are not necessary except for patients on multiple psychotropic medications (eg, liver function tests for patients on divalproex sodium; fasting glucose and A1c among other labs for patients on risperidone). At each visit, the clinician should check height, weight, heart rate, blood pressure, and the dosage and timing of medications. The clinician should talk to older children alone to obtain a reliable report from their point of view regarding relationship issues (eg, problems with peers or family), and to screen for comorbid issues (eg, sleep problems, depression, substance use disorders, sexual activity).

The duration of treatment is individualized. Ambivalence about medication is common and can cause poor compliance, even when benefits are obvious. The prescribed medication is often discontinued without consulting the prescriber. To prevent this, trial periods off medication and the potential

effects on targeted symptoms should be discussed. Trials off medication often demonstrate the true utility of the medication. To improve reliability of a trial off medications, avoid doing so at the beginning of the school year or when there are other changes imminent (eg, change in school or job, divorce or remarriage). Termination of medication can be planned if missed dosages do not result in behavior or academic problems. If symptoms do not recur, the patient can remain off the medication.

Misuse of stimulants. Misuse is using the medication without a prescription. This does not imply abuse. Stimulants are misused by 5-35% of college-age individuals. Many of these individuals are likely using these medications for the purpose of increasing their concentration and attentiveness rather than for getting high. Studies report 25% or more patients with ADHD have been asked by a peer to trade, sell, or give them their stimulant medication. Explain to adolescents and young adults that they may be asked to share their medication and inform them that sharing or “dealing” their medications is a felony. Role playing or discussing strategies to deal with this situation may be helpful. Stimulants are controlled substances. Patients suspected of trading, selling, or abusing them should undergo the same monitoring procedures used for patients on more frequently abused prescription drugs. Procedures are detailed in the UMHS clinical guideline “[Managing Chronic Non-Terminal Pain in Adults, Including Prescribing Controlled Substances.](#)” Some key aspects are summarized below.

- Watch for signs of overuse or diversion. Watch for patterns of early refills, multiple contacts about stimulants, multiple sources of stimulants, and young adults not previously diagnosed who are seeking stimulants. People seeking to abuse these medications are more likely to request short-acting Ritalin or Adderall. It is harder to abuse the long-acting preparations due to their formulation (eg, Concerta) or activation (eg, Vyvanse).
- Pill counts. Schedule follow-up visits before refills are due to check that medication use over time matches prescribing.
- Check actual use with urine testing. If diversion is suspected, check for the presence or absence of stimulants in urine. A standard urine drug screen will only detect amphetamine based products, not methylphenidate.
- Check for other controlled substance prescriptions. Search local state prescription monitoring programs (eg, MAPS in Michigan, <https://michigan.pmpaware.net/login>) for stimulant and other controlled substance prescriptions.
- Establish and enforce conditions for continued prescribing. Discuss conditions that patients must meet in order to continue prescribing stimulants, and formalize them in a “Controlled Substance Treatment Agreement.”

Non-stimulants: In general, non-stimulants are less effective than stimulants but are an important FDA-approved option.

Non-stimulants have an effect size of about 0.7 compared to an effect size of about 1.0 for stimulants. Second-line agents may be considered if there are concerns about adverse side effects with stimulants, a co-occurring condition that would benefit from the addition of or sole use of a second-line agent, or if there is stimulant drug diversion.

Atomoxetine (Strattera). Atomoxetine is a non-stimulant drug approved by the FDA for treatment of ADHD. Atomoxetine is believed to work by increasing norepinephrine levels via inhibition of norepinephrine reuptake at neuronal synapses. Atomoxetine can be given once a day and works for 24 hours. Start with 0.5 mg/kg daily to avoid adverse effects (abdominal discomfort, nausea, somnolence). After a week, advance to the therapeutic dose, typically 1.0-1.2mg/kg/day. Rarely some children may need to go up to 1.6-1.8 mg /kg/day. It takes about 4 weeks to note the benefits of atomoxetine.

The FDA recommends that children and adolescents being treated with atomoxetine be closely monitored for clinical worsening, such as agitation, irritability, suicidal thinking or behaviors, and unusual changes in behavior, especially during the initial few months of therapy or when the dose is changed. A black box warning regarding suicidal ideation was added in 2005. Giving the medication in the evening can help if sleepiness due to the medication is persistent. Other reported adverse effects include liver damage, which is reversible with medication discontinuation. Liver function tests should be obtained at the first symptom or sign of liver dysfunction. Atomoxetine should be discontinued in patients with clinical evidence of liver injury (eg, jaundice, right upper quadrant abdominal tenderness) or laboratory evidence of liver injury, and should not be restarted.

Antihypertensives. The alpha-2 adrenergic agonists, clonidine (Catapres, Kapvay) and guanfacine (Tenex, Intuniv) are also non-stimulants approved by the FDA for treatment of ADHD. They may be beneficial as alternatives or adjuncts to stimulants, but they have been studied in very few clinical trials as compared to stimulants.

Clonidine has been reported to be effective in 50% of patients [B], especially those who are over aroused, easily frustrated, very hyperactive, impulsive, or aggressive. Potential advantages of guanfacine over clonidine include greater selectivity for the alpha-2 receptor, a longer half-life, and fewer sedative and hypotensive effects.

Antihypertensives are useful in combination with stimulants for patients who have ADHD-related sleep problems, or problematic behaviors later in the day when the stimulant benefit has waned (eg, aggression and excessive hyperactivity). These agents are also valuable as monotherapy or in combination with stimulants for children with tics or Tourette syndrome.

Start antihypertensives at low doses and titrate slowly to avoid hypotension and dizziness. When discontinuing antihypertensives, avoid the risk of rebound hypertension by

tapering over 1-2 weeks. Counsel parents not to give supplemental doses (eg as needed or to make up for missed doses) due to the risk of severe hypotension.

Other agents. Additional medications are used off-label to treat ADHD symptoms refractory to standard treatment or as non-stimulant alternatives. Reserve these agents for patients with refractory symptoms under the care of a psychiatrist.

Bupropion. This is an antidepressant that increases norepinephrine and dopamine activity to a lesser degree than stimulants. A few placebo-controlled trials with small numbers of patients (mainly adolescents with comorbid disorders, such as nicotine dependence or substance use disorders) demonstrated that bupropion improves hyperactivity and aggressive behavior. Bupropion decreases the seizure threshold and should not be prescribed in patients with pre-existing seizure disorders. The seizure risk increases with escalation of the bupropion dose. Bupropion should be avoided in patients with bulimia or anorexia nervosa; there is a higher reported incidence of seizures in this group with bupropion use.

Desipramine. This tricyclic antidepressant acts as a norepinephrine reuptake inhibitor, similar to atomoxetine. With the introduction of atomoxetine, use of desipramine declined due to its anticholinergic and hypotensive side effects. For patients with problematic enuresis, consider it as an adjunctive agent.

Antipsychotics. Risperidone (Risperdal) in combination with stimulants has been shown to be useful in managing treatment-resistant aggression in children with ADHD. Adverse effects include hyperglycemia, weight gain, metabolic syndrome, and prolactin elevation (with potential for gynecomastia, lactation, menstrual abnormalities, and sexual dysfunction). Aripiprazole (Abilify) is another agent in this group. While it has a lower risk of metabolic syndrome and hyperprolactinemia than risperidone, it carries a high rate of restlessness and akathisia, which may complicate assessment of hyperactive symptoms. It is reasonable to consider using either one in patients with comorbid bipolar disorder, but they should not be used as primary treatment for ADHD.

Behavioral management. Behavioral management should be considered as a part of the treatment plan for ADHD at all ages, with a focus on parent and patient education, social skills and organizational training, and home and classroom interventions to differentially reinforce positive behaviors and teach skills needed to accomplish goals. Psychological interventions may be beneficial for co-morbid conditions but have not demonstrated efficacy for ADHD symptoms alone.

The Multimodal Treatment of ADHD (MTA) study of children sought to assess the impacts of medication, behavior, and combination treatment. Overall, combined medication and behavioral interventions were not superior to medication alone. However, the results suggest that the addition of behavioral interventions allows effective management at lower medication doses, better adherence to

recommendations, improved parent-child interactions and greater improvement in symptoms related to co-morbid conditions.

Parents, teachers and individuals with ADHD need adequate education about the condition so they can understand its medical basis and how the diagnosis explains many of the affected individual's behavioral difficulties and needs. This education will help them view behavioral interventions as step-wise approaches to building skills that will help improve function at school, home, or on the job. In addition, behavioral interventions facilitate families working together with educators and doctors for long-term treatment success.

Behavioral targets for intervention depend on the individual's age and needs. Parents and teachers of children and adolescents should expect that new intervention and training needs will emerge with increasing age and educational level or demands. Social skills, developing methods for self-monitoring, and learning how to keep track of time should be included for all age groups. In general, interventions should target behaviors one at a time with a positive approach. Limitations of behavioral therapy are that it needs to be continued for long periods and can be costly.

Recommendations for behavioral management are available through the following and other sources:

- CHADD (Children and Adults with Attention Deficit Disorder) Fact Sheets <http://www.chadd.org/>
- NICHQ ADHD Tool Kit http://www.nichq.org/resources/adhd_toolkit.html
- AAP Parent Pages <http://www.healthychildren.org/>
- American Academy of Child & Adolescent Psychiatry https://www.aacap.org/AACAP/Families_and_Youth/Resource_Centers/ADHD_Resource_Center/Home.aspx
- NIMH: Attention Deficit Hyperactivity Disorder www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml

Many sites provide helpful handouts for parents, teachers, and young adults with ADHD. See Appendix A2 for a brief review of tips for home and school for children and young adults.

As with medication choices, it is important to recognize when other conditions may co-occur with ADHD. Regular screening for comorbid conditions is important over time. If comorbid conditions are found, consultation with a psychologist, child psychiatrist, or developmental behavioral pediatrician may be helpful.

Two Federal laws, Section 504 of the Rehabilitation Act of 1973 and the Individuals with Disabilities Education Act (IDEA) safeguard the rights of individuals with disabilities, including ADHD, to a free and appropriate public education. These laws provide an opportunity for accommodations within the school setting if a medical condition is found to be severe enough to affect learning. Parents or individuals with ADHD can request an assessment by the school district but should do so in writing. The extent of the evaluation, accommodations, and safeguards are determined by law. See

Appendix A3 for further information about these laws and Appendix A4 for a list of special education terms.

It is also important to recognize that individuals with ADHD have problems with executive functioning that are not currently recognized under traditional special education rules. Problems with executive functioning include inconsistent performance, poor organizational skills, trouble knowing how to break down tasks, and a poor sense of time. Such areas should be included as goals in the IEP or for accommodations in the Section 504 plan.

Special Populations

Primary care clinicians should consider specialist consultation to assist in the diagnosis and treatment of ADHD in the following populations:

- Preschool age (younger than 6 years)
- Head-injured patients
- Intellectually disabled patients or those with autism spectrum disorders
- Fetal Alcohol Spectrum Disorders (FASD)
- Patients with substance use disorders
- Older adult patients (age \geq 31 years)

Additional information about each of these populations is presented in Appendix B3.

Controversial Areas

Common Myths

Some of the common myths about ADHD are listed below along with explanations regarding them.

ADHD is not a real disorder. The US Surgeon General's Report of 2001 and subsequent documentation reflects the consensus that ADHD is a medical disorder with lifelong consequences.

ADHD is a disorder of childhood. Long-term studies suggest that children with ADHD have significant symptoms into adolescence and as adults.

ADHD is over-diagnosed. Current prevalence rates reflect changes in the last decades, adjusted diagnostic criteria by age in the DSM-5, changes in special education legislation, improved recognition by clinicians, and changes in how the prevalence data is ascertained. However, national prevalence rates have been relatively stable (7-11%) and are consistent with global estimates. ADHD remains under-diagnosed in some communities.

Children with ADHD are over-medicated. Families may report over-medication experiences for previously treated family members, even decades ago. Fortunately, current medication monitoring practices reduce this risk by assessing response for targeted behaviors.

Poor parenting causes ADHD. Evidence from twin studies suggests that genetics accounts for about 80% of the

variance for children with ADHD who share the same environment.

Minority children are over-diagnosed with ADHD and are over-medicated. In fact, African-American children are unfortunately less likely to receive appropriate access to mental health services and are 2-2.5 times less likely to be appropriately diagnosed and managed for ADHD.

Girls have lower rates and less severe ADHD than boys. In fact, girls with ADHD are less likely to be recognized due to lower rates of externalizing behaviors. However, girls with ADHD have higher rates of internalizing behaviors, with more mood and anxiety disorders and problems with social functioning.

Diet and Dyes

Parents should not rely upon dietary changes to the exclusion of other more effective therapies for ADHD.

The Feingold Diet (Kaiser-Permanente diet) requires children to eliminate all foods containing artificial colors, flavors and salicylates. This eliminates nearly all processed foods. Rigorous dietary studies have failed to duplicate Dr. Feingold's clinical observations. Children with atopic disease may have a higher response rate to diets that eliminate artificial colorings and preservatives.

Meta-analyses of elimination diets suggest some children may benefit, but there are discrepancies between parent and teacher reports regarding improvements. Long-term benefits in those that improve are unknown. Current clinical guidelines do not routinely recommend this strategy, but short-term open-label trials might be reasonable to consider on a case-by-case basis. When implementing an elimination diet, a symptom diary is maintained and foods are re-introduced one at a time. Compliance with these strict diets is challenging. A dietician can help in monitoring sufficient nutrient intake during such trials and can provide appropriate nutrition education.

Essential omega-6 and omega-3 fatty acids must be obtained from the diet to form long-chain fatty acids known as eicosanoids. Meta-analyses have not provided clear evidence that essential fatty acid supplementation has benefits for ADHD, but their addition is unlikely to be harmful.

Complementary and Alternative Medicine

Appendix B4 lists common Complementary and Alternative Medicine (CAM) therapies used by families for ADHD and related problems. The use of CAM for ADHD is controversial yet commonly reported by adults and children. Studies suggest that less than 40% of parents of CAM users discuss it with their child's doctor. The primary care clinician should be aware of CAM and inquire about CAM use as a primary or secondary therapy.

Regarding some specific CAM therapies:

- Homeopathy – a Cochrane review of homeopathy found this treatment had no significant impact on the severity,

core symptoms, or related outcomes for children with ADHD.

- Chamomile or lavender teas or baths have not been studied but are used.
- Supplements vary in purity and potency. St. John's wort, Echinacea, Valerian root, Ginkgo biloba, and pycnogenol are the most commonly tried herbals. Contamination with heavy metals has been reported, as has a 10- to 1000-fold variability in potency by lot. Contamination is a greater problem for supplements that are not US made and not under the jurisdiction of the USDA. Additional information can be found in the Cochrane Database and the Natural Medicines Comprehensive Database.
- Mind-body techniques, including diaphragmatic breathing, progressive relaxation, journaling, or meditation are used as an alternate energy outlet and might assist focus and attention.

Strategy for Literature Search

The literature search for this update began with results of the literature search performed in 2002 to develop the initial guideline released in 2005. The literature search for this update used keywords that were very similar to those used in the previous search. However, instead of beginning the search with literature in 2002, the guideline team accepted the search strategy and results for the search performed through April 2006 for the AACAP Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder.

The search for this update was conducted prospectively using the major keywords of: attention deficit disorder with hyperactivity, humans age 3-30, clinical guidelines, controlled clinical trials, cohort studies, English language, and published 1/1/2007 to 1/1/2010 on Medline. Additional key words for specific searches included: symptoms (academic underachievement, behavior problems, classroom behavior, classroom interventions, degree of functional impairment, evidence of school work, frequent disciplinary events, hyperactivity, impulsivity, inattention, learning patterns, poor concentration, poor task completion, social adjustment), commonly associated/coexisting conditions (learning/language disorder, child abuse, medication side effects, oppositional defiant disorder, conduct disorder, anxiety, depression), commonly confused conditions/differential diagnosis (learning disorder, intellectual disability, mood/anxiety disorder, abuse, developmental delay, static encephalopathy, pervasive development disorder, autism spectrum, absence seizures, sleep disorder, substance abuse) evaluation and testing (vision exam, hearing exam, growth chart, developmental review, neurological exam, chronic physical or mental disorders), rating scales for ADHD, qualitative EEG and functional MRI, other EEG, cognitive behavioral therapy, behavioral interventions (set limits, establish routines, provide positive reinforcement), parental intervention (parenting class, family therapy), alpha-II agonists (clonidine, tenex), antidepressants – wellbutrin, effexor, tricyclics (imipramine, nortriptyline, desipramine),

stimulants (adderall, concerta, daytrana, dexedrine, dextro-amphetamine, focalin, lisdexamfetamine, metadate, methylphenidate, ritalin, vyvanse), modafanil, strattera, transitional and longitudinal care for adults (since 10/1/2002), and nutritional supplements and diet (since 10/1/2002).

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle. Conclusions were based on prospective randomized controlled trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Related National Guidelines

The UMHS Clinical Guideline on ADHD is consistent with: American Academy of Child and Adolescent Psychiatry – Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder, 2007.

American Academy of Pediatrics – ADHD: Clinical practice guideline for the diagnosis, evaluation, and treatment of Attention-Deficit/Hyperactivity Disorder in children and adolescents, 2011.

Measures of Clinical Performance

At this time no major national programs have clinical performance measures specifically for ADHD diagnosis and treatment.

Regional programs that have clinical performance measures for treating ADHD include the following.

- Blue Cross Blue Shield of Michigan (BCBSM)
- Blue Care Network [HMO]: clinical performance measures (BCN)

The measures are summarized below

Follow-up after initiating ADHD medication. Percentage of patients ages 6-12 years (and 13-17 years) with a starting ambulatory prescription dispensed for ADHD medication who had a follow-up visit with a practitioner with prescribing authority during the 30-day initiation phase. (BCBSM, BCN)

Follow-up during continuation and maintenance phase. Percentage of patients ages 6-12 and 13-17 years at the time that ambulatory prescription for ADHD medication was started, who remained on the medication for at least 9 months and who, after the 30-day initiation period, had at least two additional follow-up visits in the following 9 months (ie, months 2-10 following treatment initiation). (BCBSM, BCN)

Disclosures

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Review and Endorsement

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Child and Behavioral Health, Family Medicine, General Pediatrics, and Child and Adolescent Psychiatry. The Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers endorsed the final version.

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2005 John M. O'Brien, MD, Family Medicine; Barbara T. Felt, MD, Developmental Behavioral Pediatrics; R. Van Harrison, PhD, Medical Education; Paramjeet K. Kochhar, MD, Pediatrics; Stephanie A. Riolo, MD, MPH, Child and Adolescent Psychiatry. Consultant: Nadine Shehab, PharmD, College of Pharmacy.

Annotated References

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Schelleman H, Bilker WB, Kimmel SE, et al. Methylphenidate and risk of serious cardiovascular events in adults. *American Journal of Psychiatry*, 2012; 169(2):178-185

These reviews examine the risk of cardiovascular events in children and adults taking ADHD drugs (particularly stimulants) and found no evidence that these drugs increase cardiovascular risk.

**University of Michigan Health System
Guidelines for Clinical Care**

Attention-Deficit Hyperactivity Disorder

APPENDICES

Appendix A Management Tools

- A1 Behavioral Rating Scales
- A2 Tips for Parents of Children with ADHD
- A3 ADHD and Educational Rights
- A4 Special Education and Evaluation Terms

Appendix B Differential Diagnosis and Treatment Resources

- B1 Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria
- B2 Conditions That May Be Confused with ADHD
- B3 Special Patient Populations
- B4 Overview of Complementary and Alternative Medicine Associated with ADHD

Appendix A1. Behavioral Rating Scales

Tool	Psychometrics	Company	Cost	Comments
<u>Scales for Children and Adolescents</u>				
Conners 3 Conners-EC (Early Childhood)	Good Sensitivity and specificity	Multi-Health Systems, Inc. http://www.mhs.com	Kit \$400-500 Forms \$70/25	On-line (-3 and -EC) or paper forms available (all). Normed by age and gender, for ages 2-18 years. Available in English, Spanish, French (Canadian). On all scales, behavior is rated from 0-3 based on strength of endorsement for a particular behavior. Separate tests are given for parents, teachers, or self- report (12-18).
ACTers (ADD-H) Comprehensive Teacher's Rating Scale Parent Teacher Self-report	Good	WPS <a href="https://www.wpspub
lish.com/acters-add-
h-comprehensive-
teachers-rating-
scale-second-
edition/">https://www.wpspub lish.com/acters-add- h-comprehensive- teachers-rating- scale-second- edition/	Kits \$75 Forms \$55/50	Standardized K-8 grade. Not age normed.
Child Behavior Checklist (CBCL) Parent Report (ages 6- 18 years) Teacher Report Form (ages 6-18 years) Preschool Form (ages 1 - 5 years) Youth Self-Report (YSR; ages 11-18 years)	Good Demonstrated reliability and validity. Non-Specific to ADHD, but allows assessment of comorbid problems. Widely used.	Achenbach System of Empirically Based Assessment 1 South Prospect St. Burlington, VT 05401-3456 www.aseba.org Order online: https://store.aseba.org/	Available in many forms so costs vary; forms & manuals \$35-55; software module \$400; starter kit \$500	112 items. Behavior is rated from 0-3 based on strength of endorsement for a particular behavior. Available in Spanish. Can be scored with hand- scored profiles and templates or with computer programs. Eight behavioral domains: Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior. Normative data from large, representative US sample (N=1,753, ages 6-18 years, 40 states, all race & income). Normed by gender and age (4-11 and 12-18 years).
Vanderbilt Assessment Scale Parent Informant Teacher Informant	Good sensitivity and specificity	Bright Futures – <a href="http://www.brightfut
ures.org/mentalhealt
h/pdf/professionals/
bridges/adhd.pdf">http://www.brightfut ures.org/mentalhealt h/pdf/professionals/ bridges/adhd.pdf	Free	Scales are part of an ADHD Tool Kit developed by the AAP for primary care clinicians to use for children. Separate forms for evaluation and follow-up. Not age or gender normed.
ADDES-4 (Attention Deficit Disorders Evaluation Scale)	Good sensitivity and specificity	Hawthorne Educational Systems, Inc. www.hes-inc.com/	Kits \$367 Forms, manuals, CD, or online: \$50	ADDES-4: provides separate norms for male and female students 4-18 years of age

(Continued on next page)

Appendix A1. Behavioral Rating Scales (continued)

Tool	Psychometrics	Company	Cost	Comments
<u>Scales for Adults</u>				
ASRS (Adult ADHD Self-Report Scale)	Good specificity Moderate sensitivity	https://www.hcp.med.harvard.edu/ncs/asrs.php	free	Official instrument of World Health Organization 18-item questionnaire for patients at risk for ADHD Quick 6-item version also available. Available in multiple languages.
Brown Adult ADD Scale	Good sensitivity Low specificity	https://www.pearsonassessments.com/store/usassessments/en/Store/Professional-Assessments/Behavior/Attention-ADHD/Brown-Attention-Deficit-Disorder-Scales/p/100000456.html	\$90	Asks about clinical history, early schooling, family history, sleep, health, substance use. Requests data from an observer/ significant other. Contains 40 items. Primarily concerned with inattention
Conners Adult ADHD Rating Scales (CAARS)	Good sensitivity and specificity	Multi-Health Systems, Inc. http://www.mhs.com	Kit \$420 Forms \$70/25	Adult scales for either self-report or observer ratings. Various versions available. Asks about childhood and adult histories. DSM-5 criteria plus items about emotional lability.
Wender Utah Rating Scale	Good sensitivity and specificity	www.neurotransmitter.net/Wender_Utah.doc https://www.mdapp.co/wender-utah-adhd-rating-scale-calculator-182/	Free	Measures severity of symptoms in adults with ADHD using Utah criteria. Useful to assess mood lability symptoms. An on-line version that scores automatically.

Note: Standardized rating scales provide useful information and behavioral descriptions but are not diagnostic. Comparison of parent and teacher report using rating scales can reveal discrepancies which may have clinical importance. For example, if a child has more difficulties with a particular caretaker, situation, or environment, this may suggest intervention strategies or may lead to concerns regarding comorbidity.

Appendix A2. Tips for Individuals with ADHD

General Tips for Parents of Children

- Become educated about ADHD. Resources include your child's or your own clinician and evidence-based websites including:
 - Children and Adults with ADHD (CHADD);
 - American Academy of Pediatrics (AAP);
 - American Academy of Child and Adolescent Psychiatry (AACAP);
 - National Institutes of Mental Health (NIMH);
 - Centers for Disease Control (CDC).
- Help your child become educated about ADHD at a level appropriate to age and developmental stage in order to promote adherence to treatment recommendations and self-advocacy.
- Remember, parents are the best teachers; schedule one-on-one time with your child every day.
- Keep schedules and routines stable day to day; including eating and sleeping.
- Be a model of calm and respectful interactions.
- Ask your child's doctor to summarize the care plan for your child including targeted academic and behavioral goals.
- Discuss behavioral targets with other family members to improve uniform approaches.
 - Use frequent positive reinforcement for appropriate behaviors.
 - Selectively ignore minor negative behaviors.
 - Provide immediate, constructive feedback for the targeted inappropriate behaviors.
 - Monitor frequency of targeted behaviors at baseline and in response to intervention.
- If behavioral areas remain a struggle, seek out parent-child interaction training or other behavioral resources.

Younger Children

- Routines are very important.
- Balance higher energy and quieter activities through the day.
- Choose your battles; ignore minor misbehaviors.
- Give choices, but limit the number.
- Avoid harder demands during high-risk situations and times of day. Review the "rules" (hands to self, inside voices) immediately before venturing into a community setting.
- Consider taking "practice trips" that will allow you to implement a consequence (leaving if the rules are not followed) without disturbing your planned and needed shopping trip.

School-Age Child at Home

- Invite peers one at a time to reduce stimulation, encourage friendship and allow you to provide feedback. Include homework time as a part of the family routine.
- Organize a non-distracting place for homework.
- Check your child's backpack every day and help organize homework into manageable chunks.
- Suggest brief breaks between the chunks of homework.
- Use activities your child enjoys as incentives for getting work done (eg, homework and chores). This can be called "work first, then fun."
- Help your child use a system (eg, labeled folders for each subject) to get the homework back to school and turned in.
- Many children benefit from working with a tutor or educational coach.
- Be aware of long-term assignments; discuss and frequently monitor the timeline for completion.

Child and Adolescent at School

- The following approaches can be helpful at school:
 - An orderly and predictable classroom setting
 - Consistent rules and expectations
 - Regular breaks
 - Quiet work areas
 - Seating near where the teacher does the teaching.
- Include a curriculum about time management and study skills.
- Teach self-monitoring and self-reinforcement skills.
- Establish a system of daily communication – Daily Report Card (DRC) between school and home.
- Communicate regularly with your child's teacher and/or team about homework, grades, and behavior.
- If your child is struggling, consider requesting an evaluation for a Section 504 plan or IDEA, especially if there is concern about a possible learning disorder or other disability.

Older Adolescent and Young Adult

- Work on organization, time management and self-motivation strategies.
- Maximize supportive assistive technologies.
- Obtain further self-education on ADHD to assist in self-advocacy for accommodations in college and on the job
- Consider cognitive behavioral therapy and other counseling.

Appendix A3. ADHD and Educational Rights

Section 504

Section 504 of the National Rehabilitation Act of 1973 is a civil rights law with the intent to protect the rights of individuals with disabilities. Section 504 is not within the Special Education designation, but it generally provides “reasonable” accommodations and services such as reduced assignments, adjusting testing conditions, and meeting transportation needs.

IDEA

The Individuals with Disabilities Education Act (IDEA) (originally Public Law 94-142, amended in 1997 – Public Law 105-17, and reauthorized in 2004), provides legal safeguards for children and adults ages 3-21 with disabilities (including significant ADHD). In most cases, the assistance provided and the legal safeguards from IDEA are greater than Section 504.

- The parent must submit a written request for the evaluation.
- The evaluation is multidisciplinary in nature.
- Children and teens with ADHD may be eligible for Special Education categorization under Other Health Impairment (OHI). During the evaluation process, a team that includes the parent, (the child if older or the teen), school psychologist, teacher and other evaluators determines the individual’s eligibility for special education categorization, documents the child’s specific needs, targets specific outcomes, and determines the needed interventions.
- The results of the psychoeducational evaluation are shared with the parent at an Individualized Education Plan Committee (IEPC) meeting.
- If a learning disability (LD) or other co-morbid eligibility is determined to be present (eg, speech and language impairment, emotional impairment), the child may be eligible for services for both the ADHD and the co-morbid diagnosis.

Individualized Education Plan (IEP)

An IEP is a written agreement between the parents and the school about what the child/teen needs and what will be done to address those needs. An IEP is a legal document under IDEA that must be drawn up by the educational team and signed by the student’s parents before implementation.

REED and RTI

Many school districts provide a review and intervention approach before entering into an evaluation under an IEP. School teams will conduct a Review of Existing Educational Data, termed REED, and provide targeted support over a defined period. A Response to Intervention, termed RTI, will then determine if the need has been addressed or if further evaluation for special education services is needed. It is important for parents to monitor this process so that the planned reviews occur and that further determination of needs is not delayed.

Appendix A4. Special Education and Evaluation Terms

Special Education Terms		Intelligence Tests	
BIP	Behavioral Intervention Plan	K-ABC	Kaufman Assessment Battery for Children
EI	Emotionally Impaired	SB	Stanford-Binet
IDEA	Individuals with Disabilities Act (1997)	WISC	Wechsler Intelligence Scale for Children
IEP	Individualized Education Plan	WJ-R	Woodcock Johnson Psychoeducational Battery, Tests of Cognitive Ability
IEPC	Individualized Education Plan Committee		
OHI	Other Health Impairment		
REED	Review of Existing Evaluation Data	Achievement Tests	
RTI	Response to Intervention	PIAT-R	Peabody Individual Achievement Test
Section 504	National Rehabilitation Act (1973)	WIAT	Weschler Individual Achievement Test
SLD	Specific Learning Disability	WJ-R	Woodcock Johnson Psychoeducational Battery, Revised, Tests of Cognitive Ability
SST	Student Study Team	WRAT-R	Wide Range Achievement Test, Revised

Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria

Anxiety Disorders

Generalized Anxiety Disorder (GAD) (ICD-10: F41.1)

- A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
- B. The individual finds it difficult to control the worry.
- C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months):
Note: Only one item is required in children.
 1. Restlessness or feeling keyed up or on edge.
 2. Being easily fatigued.
 3. Difficulty concentrating or mind going blank.
 4. Irritability.
 5. Muscle tension.
 6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).
- D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- E. The disturbance is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication) or another medical condition (eg, hyperthyroidism).
- F. The disturbance is not better explained by another mental disorder (eg, anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).

Panic Attacks Specifier

Note: Symptoms are presented for the purpose of identifying a panic attack; however, panic attack is not a mental disorder and cannot be coded. Panic attacks can occur in the context of any anxiety disorder as well as other mental disorders (eg, depressive disorders, posttraumatic stress disorder, substance use disorders) and some medical conditions (eg, cardiac, respiratory, vestibular, gastrointestinal). When the presence of a panic attack is identified, it should be noted as a specifier (eg, “posttraumatic stress disorder with panic attacks”). For panic disorder, the presence of panic attack is contained within the criteria for the disorder and panic attack is not used as a specifier.

An abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur:

Note: The abrupt surge can occur from a calm state or an anxious state.

1. Palpitations, pounding heart, or accelerated heart rate.
2. Sweating.
3. Trembling or shaking.
4. Sensations of shortness of breath or smothering.
5. Feelings of choking.
6. Chest pain or discomfort.
7. Nausea or abdominal distress.
8. Feeling dizzy, unsteady, light-headed, or faint.
9. Chills or heat sensations.
10. Paresthesias (numbness or tingling sensations).
11. Derealization (feelings of unreality) or depersonalization (being detached from oneself).
12. Fear of losing control or “going crazy.”
13. Fear of dying.

Note: Culture-specific symptoms (eg, tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms.

Obsessive-Compulsive Disorder (F42.9)

- A. Presence of obsessions, compulsions, or both:

Obsessions are defined by (1) and (2):

1. Recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.
2. The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (ie, by performing a compulsion).

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

Compulsions are defined by (1) and (2):

1. Repetitive behaviors (eg, hand washing, ordering, checking) or mental acts (eg, praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.
2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive.

Note: Young children may not be able to articulate the aims of these behaviors or mental acts.

- B. The obsessions or compulsions are time-consuming (eg, take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication) or another medical condition.
- D. The disturbance is not better explained by the symptoms of another mental disorder (eg, excessive worries, as in generalized anxiety disorder; preoccupation with appearance, as in body dysmorphic disorder; difficulty discarding or parting with possessions, as in hoarding disorder; hair pulling, as in trichotillomania [hair-pulling disorder]; skin picking, as in excoriation disorder; stereotypies, as in stereotypic movement disorder; ritualized eating behavior, as in eating disorders; preoccupation with substances or gambling, as in substance-related and addictive disorders; preoccupation with having an illness, as in illness anxiety disorder; sexual urges or fantasies, as in paraphilic disorders; impulses, as in disruptive, impulse-control, and conduct disorders; guilty ruminations, as in major depressive disorder; thought insertion or delusional preoccupations, as in schizophrenia spectrum and other psychotic disorders; or repetitive patterns of behavior, as in autism spectrum disorder).

Specify if:

- **With good or fair insight:** The individual recognizes that obsessive-compulsive disorder beliefs are definitely or probably not true or that they may or may not be true.
- **With poor insight:** The individual thinks obsessive-compulsive disorder beliefs are probably true.
- **With absent insight or delusional beliefs:** The individual is completely convinced that obsessive-compulsive disorder beliefs are true.

Specify if:

- **Tic-related:** The individual has a current or past history of a tic disorder.

Separation Anxiety Disorder (F93.0)

- A. Developmentally inappropriate and excessive fear or anxiety concerning separation from those to whom the individual is attached, as evidenced by at least three of the following:
 1. Recurrent excessive distress when anticipating or experiencing separation from home or from major attachment figures.
 2. Persistent and excessive worry about losing major attachment figures or about possible harm to them, such as illness, injury, disasters, or death.
 3. Persistent and excessive worry about experiencing an untoward event (eg, getting lost, being kidnapped, having an accident, becoming ill) that causes separation from a major attachment figure.
 4. Persistent reluctance or refusal to go out, away from home, to school, to work, or elsewhere because of fear of separation.
 5. Persistent and excessive fear of or reluctance about being alone or without major attachment figures at home or in other settings.
 6. Persistent reluctance or refusal to sleep away from home or to go to sleep without being near a major attachment figure.
 7. Repeated nightmares involving the theme of separation.
 8. Repeated complaints of physical symptoms (eg, headaches, stomachaches, nausea, vomiting) when separation from major attachment figures occurs or is anticipated.
- B. The fear, anxiety, or avoidance is persistent, lasting at least 4 weeks in children and adolescents and typically 6 months or more in adults.
- C. The disturbance causes clinically significant distress or impairment in social, academic, occupational, or other important areas of functioning.
- D. The disturbance is not better explained by another mental disorder, such as refusing to leave home because of excessive resistance to change in autism spectrum disorder; delusions or hallucinations concerning separation in psychotic disorders; refusal to go outside without a trusted companion in agoraphobia; worries about ill health or other harm befalling significant others in generalized anxiety disorder; or concerns about having an illness in illness anxiety disorder

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

Anxiety Disorder Not Otherwise Specified (F41.9)

This category applies to presentations in which symptoms characteristic of an anxiety disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for any of the disorders in the anxiety disorders diagnostic class. The unspecified anxiety disorder category is used in situations in which the clinician chooses not to specify the reason that the criteria are not met for a specific anxiety disorder, and includes presentations in which there is insufficient information to make a more specific diagnosis (eg, in emergency room settings).

Bipolar Disorders

For a diagnosis of bipolar I disorder, it is necessary to meet the following criteria for a manic episode. The manic episode may have been preceded by and may be followed by hypomanic or major depressive episodes.

Manic Episode

- A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased goal-directed activity or energy, lasting at least 1 week and present most of the day, nearly every day (or any duration if hospitalization is necessary).
- B. During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:
 1. Inflated self-esteem or grandiosity.
 2. Decreased need for sleep (eg, feels rested after only 3 hours of sleep).
 3. More talkative than usual or pressure to keep talking.
 4. Flight of ideas or subjective experience that thoughts are racing.
 5. Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
 6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (ie, purposeless non-goal-directed activity).
 7. Excessive involvement in activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).
- C. The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.
- D. The episode is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication, other treatment) or to another medical condition.

Note: A full manic episode that emerges during antidepressant treatment (eg, medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a manic episode and, therefore, a bipolar I diagnosis.

Note: Criteria A–D constitute a manic episode. At least one lifetime manic episode is required for the diagnosis of bipolar I disorder.

Hypomanic Episode

- A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 4 consecutive days and present most of the day, nearly every day.
- B. During the period of mood disturbance and increased energy and activity, three (or more) of the following symptoms (four if the mood is only irritable) have persisted, represent a noticeable change from usual behavior, and have been present to a significant degree:
 1. Inflated self-esteem or grandiosity.
 2. Decreased need for sleep (eg, feels rested after only 3 hours of sleep).
 3. More talkative than usual or pressure to keep talking.
 4. Flight of ideas or subjective experience that thoughts are racing.
 5. Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
 6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.
 7. Excessive involvement in activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

- C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic.
- D. The disturbance in mood and the change in functioning are observable by others.
- E. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization. If there are psychotic features, the episode is, by definition, manic.
- F. The episode is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication, other treatment).

Note: A full hypomanic episode that emerges during antidepressant treatment (eg, medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a hypomanic episode diagnosis. However, caution is indicated so that one or two symptoms (particularly increased irritability, edginess, or agitation following antidepressant use) are not taken as sufficient for diagnosis of a hypomanic episode, nor necessarily indicative of a bipolar diathesis.

Note: Criteria A–F constitute a hypomanic episode. Hypomanic episodes are common in bipolar I disorder but are not required for the diagnosis of bipolar I disorder.

Major Depressive Episode

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad, empty, or hopeless) or observation made by others (eg, appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others; not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

- C. The episode is not attributable to the physiological effects of a substance or another medical condition.

Note: Criteria A–C constitute a major depressive episode. Major depressive episodes are common in bipolar I disorder but are not required for the diagnosis of bipolar I disorder.

Note: Responses to a significant loss (eg, bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

In distinguishing grief from a major depressive episode (MDE), it is useful to consider that in grief the predominant affect is feelings of emptiness and loss, while in MDE it is persistent depressed mood and the inability to anticipate happiness or pleasure. The dysphoria in grief is likely to decrease in intensity over days to weeks and occurs in waves, the so-called pangs of grief. These waves tend to be associated with thoughts or reminders of the deceased. The depressed mood of a MDE is more persistent and not tied to specific thoughts or preoccupations. The pain of grief may be accompanied by positive emotions and humor that are uncharacteristic of the pervasive unhappiness and misery characteristic of a major depressive episode. The thought content associated with grief generally features a preoccupation with thoughts and memories of the deceased, rather than the self-critical or pessimistic ruminations seen in a MDE. In grief, self-esteem is generally preserved, whereas in a MDE, feelings of worthlessness and self-loathing are common. If self-derogatory ideation is present in grief, it typically involves perceived failings vis-à-vis the deceased (eg, not visiting frequently enough, not telling the deceased how much he or she was loved). If a bereaved individual thinks about death and dying, such thoughts are generally focused on the deceased and possibly about “joining” the deceased, whereas in a major depressive episode such thoughts are focused on ending one’s own life because of feeling worthless, undeserving of life, or unable to cope with the pain of depression.

Bipolar I Disorder

- A. Criteria have been met for at least one manic episode (Criteria A–D under “Manic Episode” above).
- B. The occurrence of the manic and major depressive episode(s) is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.

Major Depressive Disorder

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad, empty, hopeless) or observation made by others (eg, appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A–C represent a major depressive episode.

Note: Responses to a significant loss (eg, bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual’s history and the cultural norms for the expression of distress in the context of loss.

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

In distinguishing grief from a major depressive episode (MDE), it is useful to consider that in grief the predominant affect is feelings of emptiness and loss, while in MDE it is persistent depressed mood and the inability to anticipate happiness or pleasure. The dysphoria in grief is likely to decrease in intensity over days to weeks and occurs in waves, the so-called pangs of grief. These waves tend to be associated with thoughts or reminders of the deceased. The depressed mood of MDE is more persistent and not tied to specific thoughts or preoccupations. The pain of grief may be accompanied by positive emotions and humor that are uncharacteristic of the pervasive unhappiness and misery characteristic of MDE. The thought content associated with grief generally features a preoccupation with thoughts and memories of the deceased, rather than the self-critical or pessimistic ruminations seen in MDE. In grief, self-esteem is generally preserved, whereas in MDE feelings of worthlessness and self-loathing are common. If self-derogatory ideation is present in grief, it typically involves perceived failings vis-à-vis the deceased (eg, not visiting frequently enough, not telling the deceased how much he or she was loved). If a bereaved individual thinks about death and dying, such thoughts are generally focused on the deceased and possibly about “joining” the deceased, whereas in MDE such thoughts are focused on ending one’s own life because of feeling worthless, undeserving of life, or unable to cope with the pain of depression.

1. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
2. There has never been a manic episode or a hypomanic episode.

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition

Fetal Alcohol Spectrum Disorders (FASD)

The teratogenic effects of alcohol produce a range of outcomes extending from full Fetal Alcohol Syndrome to a milder appearing disorder in which there are no characteristic facial features, but there are clinically significant learning and behavioral problems. Individuals with full FAS have a distinct pattern of facial abnormalities, growth deficiency and evidence of central nervous system dysfunction. In addition to learning, and attention problems, individuals with FAS may have other neurological deficits such as poor motor skills and hand-eye coordination. They may also have a complex pattern of behavioral and learning problems, including difficulties with memory, communication and judgment. Individuals without full facial features of FAS, but who have clinically significant learning and behavioral problems are diagnosed with Alcohol-Related Neurobehavioral Disorder (ARND). Alcohol-related birth defects (ARBD) describe affected organs or functions including heart, kidney, bone or hearing problems. Neurobehavioral Disorder with Prenatal Alcohol Exposure (ND-PAE) describes children with history of prenatal exposure and problems in 3 areas including cognition, behavior and adaptive functioning.

Fragile X Syndrome

Fragile X syndrome is the second most common 'chromosomal' cause of mental impairment after trisomy 21. It is characterized by moderate to severe intellectual disability, macroorchidism, large ears, prominent jaw, and high-pitched jocular speech. Patients typically have flat feet and finger joint hypermobility. Mitral valve prolapse may be present. Many males have relative macrocephaly. Patients may also have tactile defensiveness. This condition accounts for about one-half of X-linked intellectual disability. Frequency estimates vary, but it occurs in about 1 in 7,000 males and 1 in 11,000 females.

Cognitive and behavioral profile: Hyperkinetic behavior and a problem with concentration are present in most affected males; therefore, this condition can be easily confused with ADHD. Longitudinal observations indicate a deterioration of IQ with age; intellectual disability may, for example, be moderate at age 12 and severe at age 25. Patients frequently may have autistic-like behavior and apparent speech and language deficits, making it easily confused with Autistic Disorder. Psychiatric comorbidity is high, with increased risk of ADHD, oppositional defiant disorder, enuresis, and encopresis. Fragile X syndrome may also be difficult to distinguish from Prader-Willi Syndrome, except that patients with Fragile X Syndrome lack the neonatal hypotonia and infantile feeding problems followed by hyperphagia during toddlerhood seen in Prader-Willi.

Inheritance: Fragile X Syndrome is associated with mutations in the FMR1 gene. All mothers of males with the fragile X have been found to be carriers; the mutation must occur either at a low rate or only in males. Twenty percent of males who carry a fragile X chromosome are phenotypically normal; their daughters, to whom they transmit the fragile X chromosome, are likewise normal, but their grandsons are often affected. The brothers of the clinically normal, transmitting males have a low risk, while grandsons and great-grandsons have much higher risks.

Diagnosis: is made by immunofluorescence studies and is quite reliable. The most efficient and cost effective methodology for diagnosis is cytogenetic analysis, followed by molecular studies only when the fra(X) is seen or suspected.

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

Learning Disorders (LD)

Learning Disorder or Disability (LD) is a broad term that covers a pool of possible causes, symptoms, treatments, and outcomes. Learning Disabilities can be divided up into three broad categories:

- (1) Developmental speech and language disorders
- (2) Academic skills disorders
- (3) "Other" disorders- includes certain coordination disorders and learning handicaps not covered by the other terms.

Specific Learning Disability

- A. Difficulties learning and using academic skills, as indicated by the presence of at least one of the following symptoms that have persisted for at least 6 months, despite the provision of interventions that target those difficulties:
1. Inaccurate or slow and effortful word reading (eg, reads single words aloud incorrectly or slowly and hesitantly, frequently guesses words, has difficulty sounding out words).
 2. Difficulty understanding the meaning of what is read (eg, may read text accurately but not understand the sequence, relationships, inferences, or deeper meanings of what is read).
 3. Difficulties with spelling (eg, may add, omit, or substitute vowels or consonants).
 4. Difficulties with written expression (eg, makes multiple grammatical or punctuation errors within sentences; employs poor paragraph organization; written expression of ideas lacks clarity).
 5. Difficulties mastering number sense, number facts, or calculation (eg, has poor understanding of numbers, their magnitude, and relationships; counts on fingers to add single-digit numbers instead of recalling the math fact as peers do; gets lost in the midst of arithmetic computation and may switch procedures).
 6. Difficulties with mathematical reasoning (eg, has severe difficulty applying mathematical concepts, facts, or procedures to solve quantitative problems).
- B. The affected academic skills are substantially and quantifiably below those expected for the individual's chronological age, and cause significant interference with academic or occupational performance, or with activities of daily living, as confirmed by individually administered standardized achievement measures and comprehensive clinical assessment. For individuals ages 17 years and older, a documented history of impairing learning difficulties may be substituted for the standardized assessment.
- C. The learning difficulties begin during school-age years but may not become fully manifest until the demands for those affected academic skills exceed the individual's limited capacities (eg, as in timed tests, reading or writing lengthy complex reports for a tight deadline, excessively heavy academic loads).
- D. The learning difficulties are not better accounted for by intellectual disabilities, uncorrected visual or auditory acuity, other mental or neurological disorders, psychosocial adversity, lack of proficiency in the language of academic instruction, or inadequate educational instruction.

Note: The four diagnostic criteria are to be met based on a clinical synthesis of the individual's history (developmental, medical, family, educational), school reports, and psychoeducational assessment.

Coding note: Specify all academic domains and subskills that are impaired. When more than one domain is impaired, each one should be coded individually according to the following specifiers.

Specify if:

(F81.0) With impairment in reading:

Word reading accuracy
Reading rate or fluency
Reading comprehension

Note: *Dyslexia* is an alternative term used to refer to a pattern of learning difficulties characterized by problems with accurate or fluent word recognition, poor decoding, and poor spelling abilities. If dyslexia is used to specify this particular pattern of difficulties, it is important also to specify any additional difficulties that are present, such as difficulties with reading comprehension or math reasoning.

(F81.81) With impairment in written expression:

Spelling accuracy
Grammar and punctuation accuracy
Clarity or organization of written expression

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

(F81.2) **With impairment in mathematics:**

- Number sense
- Memorization of arithmetic facts
- Accurate or fluent calculation
- Accurate math reasoning

Note: *Dyscalculia* is an alternative term used to refer to a pattern of difficulties characterized by problems processing numerical information, learning arithmetic facts, and performing accurate or fluent calculations. If dyscalculia is used to specify this particular pattern of mathematic difficulties, it is important also to specify any additional difficulties that are present, such as difficulties with math reasoning or word reasoning accuracy.

Specify current severity:

Mild: Some difficulties learning skills in one or two academic domains, but of mild enough severity that the individual may be able to compensate or function well when provided with appropriate accommodations or support services, especially during the school years.

Moderate: Marked difficulties learning skills in one or more academic domains, so that the individual is unlikely to become proficient without some intervals of intensive and specialized teaching during the school years. Some accommodations or supportive services at least part of the day at school, in the workplace, or at home may be needed to complete activities accurately and efficiently.

Severe: Severe difficulties learning skills, affecting several academic domains, so that the individual is unlikely to learn those skills without ongoing intensive individualized and specialized teaching for most of the school years. Even with an array of appropriate accommodations or services at home, at school, or in the workplace, the individual may not be able to complete all activities efficiently.

Unspecified Neurodevelopmental Disorder (F81.9)

This category applies to presentations in which symptoms characteristic of a neurodevelopmental disorder that cause impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for any of the disorders in the neurodevelopmental disorders diagnostic class. The unspecified neurodevelopmental disorder category is used in situations in which the clinician chooses *not* to specify the reason that the criteria are not met for a specific neurodevelopmental disorder, and includes presentations in which there is insufficient information to make a more specific diagnosis (eg, in emergency room settings).

Oppositional Defiant Disorder (F91.3)

- A. A pattern of angry or irritable mood, argumentative or defiant behavior, or vindictiveness lasting at least 6 months as evidenced by at least four symptoms from any of the following categories, and exhibited during interaction with at least one individual who is not a sibling.

Angry or Irritable Mood

1. Often loses temper.
2. Is often touchy or easily annoyed.
3. Is often angry and resentful.

Argumentative or Defiant Behavior

4. Often argues with authority figures or, for children and adolescents, with adults.
5. Often actively defies or refuses to comply with requests from authority figures or with rules.
6. Often deliberately annoys others.
7. Often blames others for his or her mistakes or misbehavior.

Vindictiveness

8. Has been spiteful or vindictive at least twice within the past 6 months.

Note: The persistence and frequency of these behaviors should be used to distinguish a behavior that is within normal limits from a behavior that is symptomatic. For children younger than 5 years, the behavior should occur on most days for a period of at least 6 months unless otherwise noted (Criterion A8). For individuals 5 years or older, the behavior should occur at least once per week for at least 6 months, unless otherwise noted (Criterion A8). While these frequency criteria provide guidance on a minimal level of frequency to define symptoms, other factors should also be considered, such as whether the frequency and intensity of the behaviors are outside a range that is normative for the individual's developmental level, gender, and culture.

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

- B. The disturbance in behavior is associated with distress in the individual or others in his or her immediate social context (eg, family, peer group, work colleagues), or it impacts negatively on social, educational, occupational, or other important areas of functioning.
- C. The behaviors do not occur exclusively during the course of a psychotic, substance use, depressive, or bipolar disorder. Also, the criteria are not met for disruptive mood dysregulation disorder.

Specify current severity:

- **Mild:** Symptoms are confined to only one setting (eg, at home, at school, at work, with peers).
- **Moderate:** Some symptoms are present in at least two settings.
- **Severe:** Some symptoms are present in three or more settings.

Post-Traumatic Stress Disorder (PTSD; F43.10)

Note: The following criteria apply to adults, adolescents, and children older than 6 years. For children ages 6 years and younger, see corresponding criteria below.

- A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:
1. Directly experiencing the traumatic event(s).
 2. Witnessing, in person, the event(s) as it occurred to others.
 3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
 4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (eg, first responders collecting human remains; police officers repeatedly exposed to details of child abuse).
 - **Note:** Criterion A4 does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related.
- B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:
1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
 - **Note:** In children older than 6 years, repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed.
 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).
 - **Note:** In children, there may be frightening dreams without recognizable content.
 3. Dissociative reactions (eg, flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings).
 - **Note:** In children, trauma-specific reenactment may occur in play.
 4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
 5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
- C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:
1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
 2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
- D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
1. Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs).
 2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (eg, “I am bad,” “No one can be trusted,” “The world is completely dangerous,” “My whole nervous system is permanently ruined”).
 3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame self or others.
 4. Persistent negative emotional state (eg, fear, horror, anger, guilt, or shame).
 5. Markedly diminished interest or participation in significant activities.
 6. Feelings of detachment or estrangement from others.
 7. Persistent inability to experience positive emotions (eg, inability to experience happiness, satisfaction, or loving feelings).

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

- E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects.
 2. Reckless or self-destructive behavior.
 3. Hypervigilance.
 4. Exaggerated startle response.
 5. Problems with concentration.
 6. Sleep disturbance (eg, difficulty falling or staying asleep or restless sleep).
- F. Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.
- G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- H. The disturbance is not attributable to the physiological effects of a substance (eg, medication, alcohol) or another medical condition.

Specify whether:

- **With dissociative symptoms:** The individual's symptoms meet the criteria for posttraumatic stress disorder, and in addition, in response to the stressor, the individual experiences persistent or recurrent symptoms of either of the following:
 1. **Depersonalization:** Persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body (eg, feeling as though one were in a dream; feeling a sense of unreality of self or body or of time moving slowly).
 2. **Derealization:** Persistent or recurrent experiences of unreality of surroundings (eg, the world around the individual is experienced as unreal, dreamlike, distant, or distorted).

Note: To use this subtype, the dissociative symptoms must not be attributable to the physiological effects of a substance (eg, blackouts, behavior during alcohol intoxication) or another medical condition (eg, complex partial seizures).

Specify if:

With delayed expression: If the full diagnostic criteria are not met until at least 6 months after the event (although the onset and expression of some symptoms may be immediate).

Posttraumatic Stress Disorder for Children Ages 6 Years and Younger

- A. In children ages 6 years and younger, exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:
1. Directly experiencing the traumatic event(s).
 2. Witnessing, in person, the event(s) as it occurred to others, especially primary caregivers.
Note: Witnessing does not include events that are witnessed only in electronic media, television, movies, or pictures.
 3. Learning that the traumatic event(s) occurred to a parent or caregiving figure.
- B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:
1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
Note: Spontaneous and intrusive memories may not necessarily appear distressing and may be expressed as play reenactment.
 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).
Note: It may not be possible to ascertain that the frightening content is related to the traumatic event.
 3. Dissociative reactions (eg, flashbacks) in which the child feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.) Such trauma-specific reenactment may occur in play.
 4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
 5. Marked physiological reactions to reminders of the traumatic event(s).

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

- C. One (or more) of the following symptoms, representing either persistent avoidance of stimuli associated with the traumatic event(s) or negative alterations in cognitions and mood associated with the traumatic event(s), must be present, beginning after the event(s) or worsening after the event(s):
- Persistent Avoidance of Stimuli
1. Avoidance of or efforts to avoid activities, places, or physical reminders that arouse recollections of the traumatic event(s).
 2. Avoidance of or efforts to avoid people, conversations, or interpersonal situations that arouse recollections of the traumatic event(s).
 3. Negative Alterations in Cognitions
 3. Substantially increased frequency of negative emotional states (eg, fear, guilt, sadness, shame, confusion).
 4. Markedly diminished interest or participation in significant activities, including constriction of play.
 5. Socially withdrawn behavior.
 6. Persistent reduction in expression of positive emotions.
- D. Alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects (including extreme temper tantrums).
 2. Hypervigilance.
 3. Exaggerated startle response.
 4. Problems with concentration.
 5. Sleep disturbance (eg, difficulty falling or staying asleep or restless sleep).
- E. The duration of the disturbance is more than 1 month.
- F. The disturbance causes clinically significant distress or impairment in relationships with parents, siblings, peers, or other caregivers or with school behavior.
- G. The disturbance is not attributable to the physiological effects of a substance (eg, medication or alcohol) or another medical condition.

Specify whether:

- **With dissociative symptoms:** The individual's symptoms meet the criteria for posttraumatic stress disorder, and the individual experiences persistent or recurrent symptoms of either of the following:
 1. **Depersonalization:** Persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body (eg, feeling as though one were in a dream; feeling a sense of unreality of self or body or of time moving slowly).
 2. **Derealization:** Persistent or recurrent experiences of unreality of surroundings (eg, the world around the individual is experienced as unreal, dreamlike, distant, or distorted).

Note: To use this subtype, the dissociative symptoms must not be attributable to the physiological effects of a substance (eg, blackouts) or another medical condition (eg, complex partial seizures).

Specify if:

With delayed expression: If the full diagnostic criteria are not met until at least 6 months after the event (although the onset and expression of some symptoms may be immediate).

Reactive Attachment Disorder (F94.1)

1. A consistent pattern of inhibited, emotionally withdrawn behavior toward adult caregivers, manifested by both of the following:
 1. The child rarely or minimally seeks comfort when distressed.
 2. The child rarely or minimally responds to comfort when distressed.
2. A persistent social and emotional disturbance characterized by at least two of the following:
 1. Minimal social and emotional responsiveness to others.
 2. Limited positive affect.
 3. Episodes of unexplained irritability, sadness, or fearfulness that are evident even during nonthreatening interactions with adult caregivers.

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Appendix B1. Definitions of Selected Psychiatric Disorders: DSM-5 Diagnostic Criteria (Continued)

3. The child has experienced a pattern of extremes of insufficient care as evidenced by at least one of the following:
 1. Social neglect or deprivation in the form of persistent lack of having basic emotional needs for comfort, stimulation, and affection met by caregiving adults.
 2. Repeated changes of primary caregivers that limit opportunities to form stable attachments (eg, frequent changes in foster care).
 3. Rearing in unusual settings that severely limit opportunities to form selective attachments (eg, institutions with high child-to-caregiver ratios).
4. The care in Criterion C is presumed to be responsible for the disturbed behavior in Criterion A (eg, the disturbances in Criterion A began following the lack of adequate care in Criterion C).
5. The criteria are not met for autism spectrum disorder.
6. The disturbance is evident before age 5 years.
7. The child has a developmental age of at least 9 months.

Specify if:

- **Persistent:** The disorder has been present for more than 12 months.

Specify current severity:

- Reactive attachment disorder is specified as **severe** when a child exhibits all symptoms of the disorder, with each symptom manifesting at relatively high levels.

Appendix B2. Conditions That May Be Confused with ADHD

Note: For confused or comorbid conditions, referral to a specialist in these disorders is recommended. See Appendix B for DSM-5 diagnostic criteria for conditions.

Anxiety Disorders	
Prevalence	26% (CI: 18%, 35%)
Overlapping Symptoms	<ul style="list-style-type: none"> • Poor concentration • Appears fidgety and/or agitated • Difficulty settling to sleep, with or without insomnia • Jumps from task to task • Both may have poor appetite
Distinguishing Symptoms of This Disorder	<ul style="list-style-type: none"> • School avoidance • Excessive performance or test-taking anxiety • Reluctance to participate in age-appropriate activities (sleep-overs, outings) • Excessive worry (eg, school work, illness) • Over-concern about adult matters (eg, finances, parental relationships, parental welfare) • Catastrophic thoughts (eg, car accidents, kidnapping, break-ins) • Compulsive behaviors (eg, hoarding, counting, ordering) • Nightmares, excessive worries or fears at bedtime • Physiological symptoms: racing heartbeat, difficulty breathing, chest pain • Patient becomes anxious or has visual hallucinations in response to stimulants
Distinguishing Symptoms of ADHD	<ul style="list-style-type: none"> • Should not see significant symptoms of anxiety in uncomplicated ADHD.
Bipolar Disorder	
Prevalence	Diagnosis of Bipolar Disorder in children and adolescents is highly controversial; therefore, rates are unreliable. Lewinsohn et al. (1995) reported a lifetime prevalence of 1% for Bipolar Disorders in a large community sample of older adolescents.
Overlapping Symptoms	<ul style="list-style-type: none"> • Inattention, easily distracted • Motor activity • Sleep disturbance • Accident prone • Disruptive behavior • Hypertalkativeness
Distinguishing Symptoms of This Disorder	<p>Highly controversial diagnosis in children. Always refer to child psychiatrist if suspected.</p> <ul style="list-style-type: none"> • Mood swings; behavior is cyclical or erratic • Being kicked out of multiple daycare programs is a red flag. • Parents report the child has “no control” over behavior • Grandiosity (Exaggerated ideas of ability and importance). For example, the child may think they can teach the class better than the teacher, despite failing in school. • Severe aggression (especially toward adults); rage attacks • Hypersexuality - sexual jokes or language, inappropriately touching adults • Hallucinations • Severe insomnia • Extreme changes in energy levels and behavior • Rage attacks • Irrational ideas • Tangential speech, rapid or pressured speech • Extremely impulsive, with or without self-endangering behavior • Extreme hyperactivity, especially if climbs excessively or seems to be “fearless” • Intrusive behavior • Suicidal behavior in children under 13 is concerning and warrants urgent psychiatric evaluation
<i>(Continued on next page)</i>	

Appendix B2. Conditions That May Be Confused with ADHD (Continued)

	Bipolar Disorder (continued)
Distinguishing Symptoms of ADHD	<ul style="list-style-type: none"> • ADHD symptoms should be present since childhood, whereas, Bipolar Disorder typically occurs later (most commonly around puberty) • Problems are chronic and more consistent in ADHD rather than cyclical in Bipolar disorder • Aggression, if it occurs, is usually not severe in uncomplicated ADHD & generally related to frustration • Grandiosity, hypersexuality, and psychosis are NOT typical in ADHD • Sleep problems are generally not severe and rarely are cyclical in ADHD • In samples of prepubertal patients with Bipolar Disorder, almost 100% have comorbid ADHD. In adolescent Bipolar sample, rates of comorbid ADHD and Bipolar Disorder are 30-50%
	Fetal Alcohol Spectrum Disorders
Prevalence	<p>Fetal Alcohol Syndrome (FAS): 0.33 cases per 1,000 live births.</p> <p>Alcohol-Related Neurobehavioral Disorder (ARND): Several times the magnitude of FAS cases.</p>
Overlapping Symptoms	<ul style="list-style-type: none"> • Poor academic performance. • Inattention. • Hyperactivity. • Poor growth (not on stimulants). • Disruptive behavior.
Distinguishing Symptoms of This Disorder	<ul style="list-style-type: none"> • Must have proven or strong suspicion of exposure to alcohol in utero • ± Growth deficiencies. • ± Skeletal deformities (especially microcephaly). • ± Facial abnormalities (short palpebral fissures, long or flat philtrum, thin upper lip; flat midface, ptosis; nearsightedness; strabismus; short upturned nose; cleft palate; micrognathia; low-set or poorly formed ears. • ± Organ deformities (heart, genitourinary). • CNS: intellectual disorders; learning disorders; short attention span. • May preferentially respond to Dexedrine or Adderall versus Ritalin. May require high stimulant dose and/or multiple psychotropic medication (including antipsychotics or mood stabilizer) at high doses to control symptoms. • Often needs special education services.
Distinguishing Symptoms of ADHD	<ul style="list-style-type: none"> • Characteristic facial features of FAS are not present in ADHD or ARND. • Aggression, if it occurs, usually is not severe in uncomplicated ADHD; however, may be more severe in some patients with FAS or ARND. • Most patients have average (or higher) IQ; whereas, many patients with FAS have mental retardation. • Appetite and growth problems are less severe. • Most children with uncomplicated ADHD are otherwise healthy; whereas, children with severe FAS often have many medical problems and often appear unhealthy.
	Learning disorders: Reading, Mathematics, Language, Articulation disorders, Written and/or Receptive
Prevalence	Not known; however, the CDC (1987) estimated 5-10%.
Overlapping Symptoms	<ul style="list-style-type: none"> • Both have a higher prevalence in males: 3-5:1. • Both can have very poor handwriting and poor reading comprehension. • Poor school performance, may not be evident immediately. • Often dislike and/or avoid school.
Distinguishing Symptoms of This Disorder	<ul style="list-style-type: none"> • Look for specific areas of academic difficulty. • Definitive diagnosis made by psychoeducational testing (neuropsychological testing may be beneficial).
Distinguishing Symptoms of ADHD	<ul style="list-style-type: none"> • Although children with either condition may have variable performance ability, children with ADHD more obviously perform better at tasks they enjoy.
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Appendix B2. Conditions That May Be Confused with ADHD (Continued)

Major Depressive Disorder	
Prevalence	Preadolescence: 1-5%, Adolescence: 5-10% Prior to puberty the gender ratio for depressive disorders is 1:1. After puberty the ratio is 2:1 ratio for females to males, which continues into adulthood.
Overlapping Symptoms	<ul style="list-style-type: none"> • Poor concentration • Difficulty settling to sleep, with or without insomnia • Poor self-esteem • Indecision • May appear fidgety or agitated • ± Poor appetite
Distinguishing Symptoms of This Disorder	<ul style="list-style-type: none"> • Frequent or excessive sadness, with or without tearfulness • Irritability, agitation, hostility, anger, moodiness • Lack of enthusiasm, poor motivation, constant boredom • Extreme sensitivity to rejection, poor self-esteem • Suicidal ideation or self-injurious behavior • Sad themes in play or drawings • Feelings of hopelessness, worthlessness, or excessive guilt • Change in school performance or behavior: decreased grades, change in pattern of socialization, withdrawal from activities • Neuro-vegetative changes: (1) sleep (2) appetite (3) energy • ± life stressors: relationship break-up, parental divorce, bereavement, chronic illness, etc. • Frequent physical complaints (eg, headaches, stomachaches) • Suicidal behavior in children under 13 (a concerning symptom that warrants psychiatric evaluation)
Distinguishing Symptoms of ADHD	<ul style="list-style-type: none"> • ADHD symptoms should be present since childhood before onset of depression. • Symptoms of ADHD are consistent and chronic; although there may be a gradual increase in symptoms with increasing expectations at school or work • There may be poor self-esteem in children with untreated ADHD. However, if sadness and tearfulness are daily or if there is self-injurious behavior or suicidal ideation think about depression. • Depression may be comorbid with ADHD • Sleep difficulty is generally characterized by trouble settling to sleep and early awakening rather than severe initial insomnia or middle awakening • Poor oral intake can be related to inattention and hyperactivity at meals
Oppositional Defiant Disorder	
Prevalence	35% (CI: 27%, 44%)
Overlapping Symptoms	<ul style="list-style-type: none"> • Fail to follow directions • May appear to ignore others • Disruptive behavior
Distinguishing Symptoms of This Disorder	<ul style="list-style-type: none"> • Pattern of negativistic, hostile, and defiant behavior: angry, argumentative • Refuses to comply with adults' requests • Blames others, vindictive • Especially has difficulty interacting with parents and authority figures • Family and social history are very important (eg, depression, abuse)
Distinguishing Symptoms of ADHD	<ul style="list-style-type: none"> • ADHD symptoms should be present since childhood. • Children with ADHD often do not follow directions well; however, this is due to forgetfulness, distractibility, rather than refusal. • Over time, children with untreated or residual ADHD symptoms may dislike or avoid school and other tasks and situations that require sustained attention or sustained sitting.
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Appendix B2. Conditions That May Be Confused with ADHD (Continued)

Post-Traumatic Stress Disorder (PTSD)	
Prevalence	15%– 40% of children have experienced at least one traumatic event in their lifetime. Of these, 5-10% have PTSD.
Overlapping Symptoms	<ul style="list-style-type: none"> • Hyperactivity or agitation • Memory and attentional difficulties • Difficulty settling to sleep ± Insomnia
Distinguishing Symptoms of This Disorder	<ul style="list-style-type: none"> • Must have history of trauma • Hypervigilance • Nightmares • Flashbacks • Feeling detached or estranged • Reenactment of trauma in play, drawings, or verbalizations. • May see speech disturbances, poor sleep, poor appetite and other physiologic symptoms
Distinguishing Symptoms of ADHD	<ul style="list-style-type: none"> • ADHD symptoms should be present since early childhood. • Note that children with ADHD often have parents with ADHD who may have had difficult and chaotic lives (unwanted pregnancies, substance use, motor vehicle accidents) because of untreated or poorly treated ADHD. Think about the possibility of primary PTSD, or comorbid ADHD + PTSD.
Reactive Attachment Disorder (RAD)	
Prevalence	Experts in RAD estimate that this disorder has been misdiagnosed as Bipolar Disorder or Attention Deficit Disorder in 40-70 percent of cases.
Overlapping Symptoms	<ul style="list-style-type: none"> • Both may be overly sociable and/or hypertalkative • Difficulty sleeping • Poor growth • Disruptive behavior • Poor social skills
Distinguishing Symptoms of This Disorder	<ul style="list-style-type: none"> • History of neglect, abuse, separation from parents, early severe chronic illness, multiple caretakers • Either: Indiscriminate friendliness with strangers, eg, hugs strangers • Or: Withdrawal or aloofness with others with extreme mistrust of nearly everyone. • Hoarding food or belongings is a red flag • May see night-time wandering with or without night-time binge eating • May have a wasted or pale appearance, waif-like • Often are emotionally detached and may have restricted or superficial expression of emotions • These children may be quite needy of attention and tend to tire out caretakers
Distinguishing Symptoms of ADHD	<ul style="list-style-type: none"> • ADHD symptoms should be present since early childhood. • Note that children with ADHD often have parents with ADHD who may have had difficult and chaotic lives (unwanted pregnancies, substance use, motor vehicle accidents) because of untreated or poorly treated ADHD. Therefore, children with RAD are also potentially at increased risk of ADHD by heredity. RAD may look like ADHD, but there may also be comorbid ADHD + RAD.

Appendix B3. Special Patient Populations

Preschool age (3-5 year olds)	<u>Diagnosis</u> <ul style="list-style-type: none">• May be difficult to determine whether hyperactivity, impulsivity, and inattention are due to normal developmental variation. <u>Treatment and referral</u> <ul style="list-style-type: none">• Some patients with severe symptoms may require medication.• Parent education and training is important• Referral to clinicians with expertise in developmental pediatrics or child psychiatric disorders is recommended for diagnosis and treatment.
Closed head injury	<u>Diagnosis</u> <ul style="list-style-type: none">• Patients with head injury (and static encephalopathy from other etiologies) are at increased risk for impulsivity and inattention.• There are reported cases of young children that developed (permanent) symptoms consistent with ADHD after severe head injury, encephalitis, or brain tumor. <u>Comorbidity</u> <ul style="list-style-type: none">• Watch for comorbid seizures.• Watch for aggression, personality changes, mood and anxiety symptoms. <u>Treatment and referral</u> <ul style="list-style-type: none">• Patients may respond to stimulant treatment only or may require other medications, eg, antipsychotic medication (risperidone) or mood stabilizers (carbamazepine).• Referral to clinicians with expertise in physical medicine & rehabilitation, developmental pediatrics, child psychiatric disorders, or neurologic disorders is recommended for assistance with diagnosis and treatment.• Encourage special education services and IEP development
Intellectually disabled patients	<u>Diagnosis</u> <ul style="list-style-type: none">• Data are limited regarding the diagnosis and treatment of ADHD in intellectually disabled patients.• Diagnosis must take into account the maturity and developmental challenges of the patient. ADHD may be easier to evaluated in individuals with mild-moderate intellectual disability and more difficult to diagnose in individuals with severe to profound intellectual disability. <u>Comorbidity</u> <ul style="list-style-type: none">• Consider evaluation by Genetics for all individuals with intellectual disability• Watch for comorbid seizures.• Watch for personality changes, mood and anxiety symptoms.• Watch for aggression, irritability, hypomania, and hallucinations <u>Treatment and Referral</u> <ul style="list-style-type: none">• Intellectually disabled patients with ADHD may respond well to stimulant treatment, however, as will other patients, watch for irritability.• Clonidine (Catapres) and guanfacine (Tenex) may be helpful as primary or adjunctive therapy.• All intellectually disabled patients should have an IEP to facilitate appropriate educational curriculum and services.• Referral to practitioners with expertise in neuropsychology, developmental pediatrics and/or child psychiatric disorders is recommended.
Fetal Alcohol Syndrome (FAS) and Alcohol-Related Neurobehavioral Disorder (ARND)	<u>Diagnosis</u> <ul style="list-style-type: none">• Fetal Alcohol Spectrum Disorders (FASD) are thought to affect 2-5% of children in the US with higher prevalence in children in foster care and adoption.• A genetics referral may be helpful in diagnosis.• Some centers have multidisciplinary clinics for diagnosis and treatment. <u>Comorbidity</u> <ul style="list-style-type: none">• It is estimated that up to 48% of patients with FASD have symptoms consistent with ADHD.• Learning problems particularly in math are common.• Mood symptoms are common.• Poor judgement and problems with the law are a risk <u>Treatment and Referral</u> <p>FAS and ARND patients with ADHD may respond to stimulant treatment but they may require more monitoring and consideration of other medication classes to address co-morbid diagnoses.</p>

[Note: ARND is also called Fetal Alcohol Effects (FAE) or partial FAS]

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Appendix B3. Special Patient Populations (continued)

FAS and ARND (continued)

- Patients often require psychoeducational testing and an IEP. They may require special education services due to math and/or language learning disorders or intellectual disability.
- FAS is a *static* encephalopathy: cognitive deficits usually do *not* substantially improve with time; however, interventions that build on skill areas and bridge other more challenging areas are helpful.
- Referral to a practitioner with expertise in genetics, developmental pediatrics, neurology, or child psychiatric disorders is recommended for assistance with diagnosis and treatment.

13 years – Adult

Diagnosis

- ADHD is a chronic condition. Symptoms may persist into adulthood, or an apparently new ADHD diagnosis may be a consideration.
- Factors that predict persistence to adulthood include coexisting mental health problems, more severe symptoms, and parent mental health.
- Evaluation with a neuropsychologist and/or psychiatrist may be helpful for complex cases.

Comorbidity

- Diagnosis is adulthood is often confounded by comorbid diagnoses (eg, mood disorders, substance use disorders).

Treatment and Referral

- No specific guidelines are available regarding medication discontinuation, however, many persons with ADHD benefit from continuing medication throughout high school and into adulthood.
- For most stimulants, data is not available to assess safety or harm during pregnancy.

Substance Abusing Patients Treatment

- Medication treatment for ADHD has been demonstrated to reduce the risk of subsequent substance use disorders.
- Medication treatment of comorbid ADHD and substance use disorders is possible but patients require careful monitoring. Non-controlled substances may be useful (eg, bupropion, atomoxetine).
- Stimulant medications can be abused, therefore, most are schedule II medications. True physiological dependence is rare.
- Discuss substances of abuse and risks of diversion with patients.

Appendix B4. Overview of Complementary and Alternative Medicine Associated with ADHD

Therapy	Use	Dose	Adverse Effects	Evidence
General				
Expressive (sensory integration, occupational therapy, music, dance, art)	ADHD and neurodevelopmental disorders		None	Anecdotal
Exercise	ADHD	Not determined	None	Small studies suggest benefit
Diet restriction (Feingold, red dye, sugars)	ADHD			Most controlled studies show no benefits or limited benefits for small groups of children
Megavitamins				
Neurofeedback (EEG biofeedback)	ADHD, Tics, Seizures	20-40 sessions	None	Small studies suggest some benefit
Optometric vision training	ADHD		None	No systematic data
Supplements: ADHD				
Ginkgo biloba	Antioxidant Improves blood flow. Small benefit to adult cognitive function.	120-240 mg/day (Adult)	Headache, dizziness, arrhythmias, hypotension, GI upset (nausea, vomiting, diarrhea), restlessness, cutaneous hyper-sensitivity. Avoid in bleeding disorders.	Some evidence in open-label trials but limited.
Fish oil (omega-3, EPA, DHA)	hyperlipidemia, hypertriglyceridemia, hypertension	500-1000 mg/day (Adult)	Flatus, halitosis, heartburn, (high doses): nausea, loose stools, (doses > 3 g/d): Avoid in bleeding disorders, (long-term) weight gain	Meta-analyses have not demonstrated clear evidence of benefit but unlikely to be harmful.
Evening primrose oil (linolenic, gamma linoenic acid)		500 mg 3-6x/day (Adult)	High dose or chronic use: Nausea, diarrhea, headache	Two blinded placebo control crossover studies suggest some behavioral improvement
Supplements: Sleep disorder				
Melatonin (N-acetyl-5-methoxytryptamine)	Sleep disorders	Melatonin (ages 6-12 years): 1-6 mg by mouth 30-120 minutes before sleep onset time Melatonin (age > 12 years): 1-6 mg by mouth 30-120 minutes before sleep onset time	Sleepiness, fatigue, headache. Possible proconvulsant with multiple neurologic disabilities. May suppress puberty.	Support in limited RCTs and open label trials of benefit for insomnia management.