Screening, Referral and Treatment for Attention Deficit and Hyperactivity Disorder (ADHD) – Adult – Ambulatory Clinical Practice Guideline

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Release Date: October 2014

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Executive Summary

Guideline Overview

This document has been developed to assist in identifying, treating, and monitoring adult patients with potential or diagnosed ADHD.

Key Practice Recommendations

1. Assess symptoms and functional impairment
2. Complete physical exam and consider comorbid or alternative diagnoses
3. Establish ADHD diagnosis using DSM-5 diagnostic criteria
4. Provide behavioral and/or pharmacotherapy
5. Perform periodic follow-up to confirm treatment efficacy and absence of side effects

Companion Documents

1. Adult ADHD Algorithm
2. Adult ADHD Medication Algorithm
3. Adult Medication Charts

External Resources

1. Wisconsin Prescription Drug Monitoring Program (PDMP)
2. Wisconsin Uniform Controlled Substances Act

Scope

Disease/Condition(s):

Attention deficit and hyperactivity disorder (ADHD)

Clinical Specialty:

Family Medicine, Neurology, Pediatrics, Psychiatry, and Psychology

Intended Users:

Primary Care Physicians, Advanced Practice Providers, Psychiatrists, Psychologists

CPG objective(s):

To provide evidence-based recommendations for the effective diagnosis and treatment of adult patients with ADHD.

Target Population:

Adult patients (age 18 years or older).

Methodology

Methods Used to Collect/Select the Evidence: Evidence was selected using hand searches of published literature and electronic databases.

Methods Used to Assess the Quality and Strength of the Evidence and Recommendations: Recommendations developed during the workgroup meetings used the modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (**Figure 1**) to establish evidence grades for each piece of literature and/or recommendation.

Rating Scheme for the Strength of the Evidence and Recommendations: See Appendix A.

Methods Used to Formulate the Recommendations: Recommendations developed by external organizations were adopted while others were developed via group consensus through discussion of the literature evidence and expert experiences.

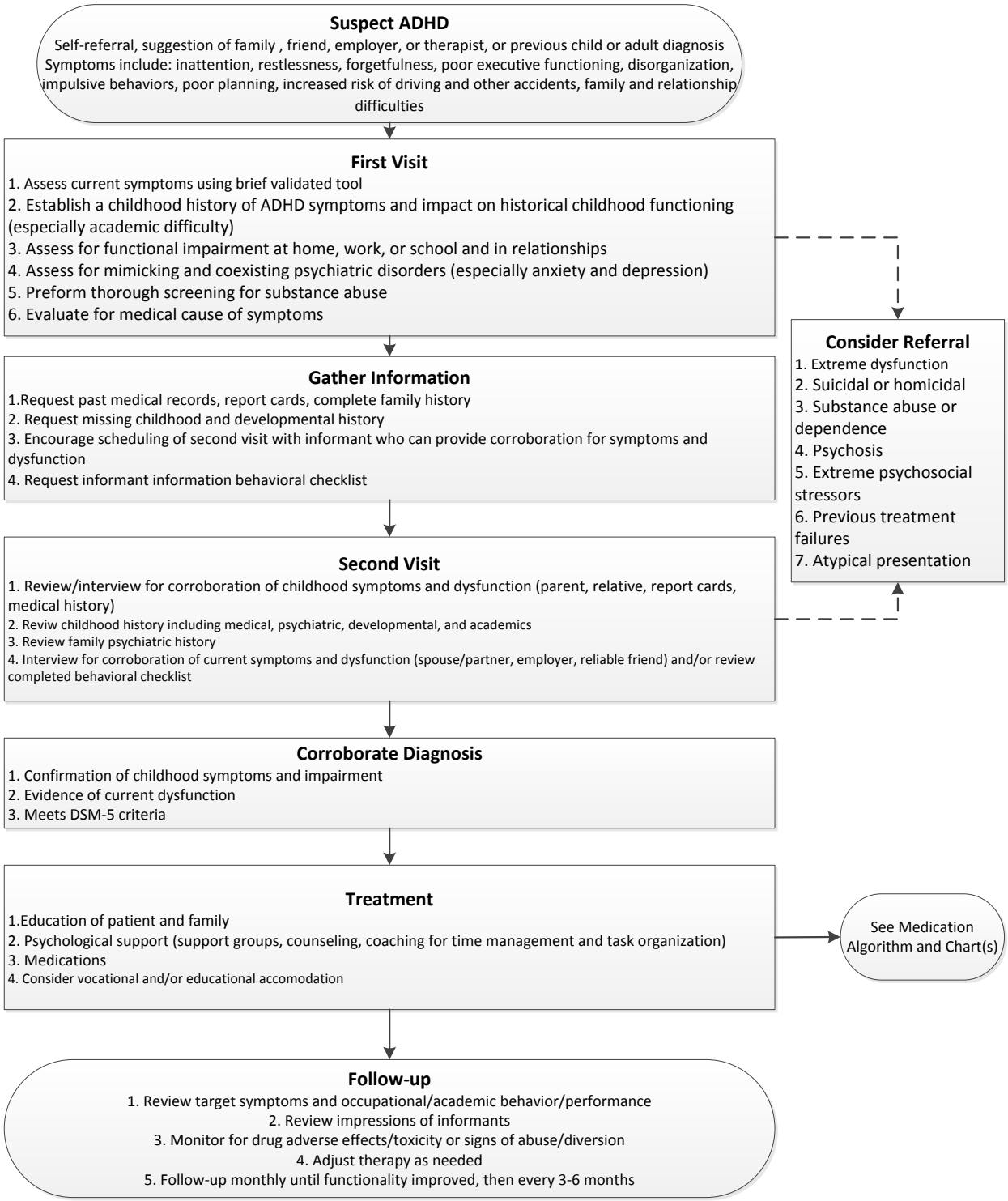
Introduction

Attention Deficit Hyperactivity Disorder, originally thought to occur just in childhood, is now widely understood as persisting into adulthood. Between 50 to 65 percent of adults diagnosed with childhood ADHD will continue to have symptoms of inattention, distractibility and impulsivity causing functional impairment as adults. In addition, adults who were never diagnosed as children may present with a complicated array of behavioral, legal and functional problems requesting diagnosis and treatment.

This guideline is designed to provide primary care clinicians with a structure, tools and referral criteria for diagnosis and treatment of adults 18 and over with symptoms typical of ADHD.

Recommendations

Adult ADHD Algorithm (ages 18 years or older)



1. PRESENTATION AND SCREENING

Adults with potential ADHD may present with a self-diagnosis, at the suggestion of a family member, friend, employer or therapist or with other behavioral or psychological problems. *(Class I, LOE B)* There may or may not be a previous childhood or adult diagnosis of ADHD.

Adult ADHD is commonly characterized by poor executive functioning. Indicators of ADHD and screening symptoms include:

- Inattention
- Restlessness
- Forgetfulness
- Disorganization
- Impulsive behaviors/often impatient
- Poor planning
- Increased risk of driving and other accidents
- Family and relationship difficulties
- Difficulties with parenting

High risk behaviors, failed relationships, legal difficulties, substance abuse and recurrent job loss are common. Physical hyperactivity diminishes in severity with age, but inattentive symptoms become more prominent and may be perceived as incompetence. Some adults compensate by finding a spouse / partner who organizes them or a job which is very active, highly absorbing or stimulating.

2. CLINICAL ASSESSMENT

Evaluation of adults presenting with ADHD symptoms typically requires at least two visits. As well as allowing for a thorough evaluation, two visits allows the clinician to assess motivation for follow up, persistence of symptoms and dysfunction and likelihood for alternative diagnoses. The following components of a complete evaluation are considered during both visits *(Class I, LOE C)*:

- review and corroboration of current symptoms and dysfunction
- determination of a childhood onset
- evaluation for comorbid and /or mimicking psychiatric problems, medical disorders or substance abuse.

First Visit

A. Review Current Symptoms and Functional Impairment *(Class I, LOE C)*

- DSM-5 diagnostic criteria for ADHD should be used and followed. A validated adult ADHD assessment tool (such as the Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist) may be used to adjunctively evaluate an adult patient.
- Adults may present with distractibility, impulsiveness and poor executive functioning. A variety of psychiatric or lifestyle conditions need to be considered when these symptoms are present.

B. Establish Onset *(Class I, LOE C)*

- ADHD is a neurodevelopmental disorder that may persist into adulthood.
- In order to meet diagnostic criteria, symptoms and functional impairment need to have been present in patients prior to age 12.

C. Perform Medical Evaluation *(Class I, LOE C)*

- Screen for medical, psychiatric or substance abuse issues which could explain or exacerbate symptoms of ADHD. *(Class I, LOE C)*
- Screen for medical and psychological conditions which would influence choice of medication. When considering a stimulant in an adult with risk factors for cardiac disease, the provider should consider a cardiovascular evaluation before initiating therapy. *(Class I, LOE C)*
- Establish baseline vital signs: weight, blood pressure, pulse. *(Class I, LOE C)*
- Laboratory testing should be limited to areas of concern. *(Class I, LOE C)*

D. Evaluate for Psychiatric or Lifestyle Conditions

- Adults may present with distractibility, impulsiveness and poor executive functioning. A variety of psychiatric or lifestyle conditions need to be considered when these symptoms are present. *(Class I, LOE C)*

GATHER ADDITIONAL INFORMATION

A. Corroborate Childhood Onset and Impairment

Childhood history can be gathered by review of medical records, review of report cards or other academic materials, and interview with parents or close family member either in person or via a phone call. High activity patterns, difficult temperament, and frequent accidents or risk taking behavior are common childhood characteristics. Review of academic background should reveal areas of impairment or concern. Look for drop outs, failures, learning disability, special evaluations or classes, suspensions / expulsions, and focused problems in areas such as reading, writing, penmanship or math. *(Class I, LOE C)*

Review of report cards often indicates behavior problems, lack of expected achievement, incomplete work, or inadequate effort. If there is no objective evidence of childhood symptoms and impairment, the diagnosis of adult ADHD should be reconsidered.

B. Review Family Psychiatric History

It is common to have a positive family psychiatric history. Inquire particularly about learning disabilities, behavior problems, legal difficulties, ADHD, and substance abuse. *(Class I, LOE B)*

CONSIDER COMORBID OR ALTERNATIVE PSYCHIATRIC DIAGNOSIS

(Class I, LOE B)

Psychiatric disorders can cause inattentive symptoms or can influence the course of treatment. Presence of another psychiatric diagnosis does not preclude a diagnosis of

adult ADHD but it does make diagnosis and treatment more confusing. Significant physical, verbal or emotional abuse / neglect can contribute to symptoms characteristic of ADHD. Depression, Post-Traumatic Stress Disorder (PTSD), bipolar disorder, anxiety disorder, personality disorders, substance abuse and other psychiatric disorders should be considered as a part of the evaluation.

Patients whose psychiatric status is unclear should be referred to a mental health provider. Patients with active substance abuse should be referred to a substance use treatment program. Consider evaluation for drug-seeking behavior with multiple pharmacies or prescribing providers using the Wisconsin Prescription Drug Monitoring Program.

It is important to identify comorbid disorders because they can mimic ADHD.

a. Comorbid or alternative psychiatric conditions should be addressed prior to starting treatment for ADHD.
b. Certain medical conditions (liver disease, seizures, hypertension, glaucoma) are relative contraindications to certain ADHD medications.

CONSIDER REFERRAL *(Class I, LOE C)*
Referral to psychiatrists and additional providers is always at the discretion of the provider. There are several presentations and co-conditions for which referral is recommended:

1. Extreme dysfunction
2. Suicidality or homicidality
3. Substance abuse or dependence
4. Psychosis
5. Extreme psychosocial stressors
6. Previous treatment failures
7. Atypical presentation – if presentation as brand new symptoms this is not ADHD, even if not diagnosed as a child the symptoms must concur

3. ESTABLISH DIAGNOSIS

To diagnose ADHD, the clinician should determine that DSM-5 criteria have been met. *(Class I, LOE B)*

DSM-5 Diagnostic Criteria

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/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 (age 17 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 (e.g., overlooks or misses details, work is inaccurate).
b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).
c. Often does not seem to listen when spoken to directly (e.g., 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 (e.g., starts tasks but quickly loses focus and is easily sidetracked).
e. Often has difficulty organizing tasks and activities (e.g., 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 (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).
g. Often loses things necessary for tasks or activities (e.g., 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 (e.g., 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/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 (age 17 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 (e.g., 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” (e.g., 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 (e.g., completes people’s sentences; cannot wait for turn in conversation).
h. Often has difficulty waiting his or her turn (e.g., while waiting in line).
i. Often interrupts or intrudes on others (e.g., 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 (e.g., 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 (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

DSM-5 Diagnosis
Specify whether: **Combined presentation**: If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past 6 months. **Predominantly inattentive presentation**: If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past 6 months. **Predominately 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.

4. PROVIDE TREATMENT

(Class I, LOE C unless otherwise indicated)

1. Provide or offer referral regarding ADHD symptom management, and psycho-education or effective coping strategies for both the patient and family.

2. Follow medication treatment protocol and medication chart (Appendix B and Appendix C). *(Class I, LOE A)* Specific patient needs or wishes should be considered and therapy should be individualized.
3. Little data is available on the use of therapeutic stimulants in pregnancy, but currently they are not associated with major congenital malformations. Risks of discontinuation of therapy should be considered (e.g., driving, vocational responsibilities) along with the benefits for each individual patient. *(Class IIb, LOE C)*
4. Long term benefit should be assessed for each patient, especially those who continue treatment from a childhood diagnosis. A trial discontinuation of therapy can be considered as children age into adulthood to assess ongoing benefit of therapy.
5. In situations where there is increased risk of substance abuse or diversion, non stimulant preparations or slow release stimulants are preferred and can be used to initiate treatment. When crushed, slow release stimulants resemble immediate release preparations in terms of onset and effect.
6. Adults with ADHD who are also parents may benefit from therapy to assist them with parenting skills.
7. Consider vocational and/or educational accommodation.
8. For patients at high risk of substance abuse, consider establishing a drug contract or conducting periodic drug screens.
9. Adjuvant psychotherapy.

5. COMPLETE FOLLOW-UP CARE

Adults with a new diagnosis, uncontrolled symptoms or change in medication should be seen within 30 days by a clinician who can assess for side effects and adjust medication if needed. Monthly contacts or visits should be routine until functionality is significantly improved. Once functionality is improved, follow-up appointments every 3 to 6 months are recommended. Informants should be included, as available, in follow-up sessions. *(Class I, LOE C)*

At each follow-up visit *(Class I, LOE C)*:

1. Review should specifically include diurnal variation in symptoms, as this informs recommendations for change in timing/formulation of the medications prescribed.
2. Review target symptoms, job/school performance, relationship issues.
3. Monitor for adherence to therapy, drug side effects/toxicity or signs of abuse/diversion. Also monitor vital signs to assess for increases in blood pressure and pulse.
4. Review impressions of informants.
5. Adjust therapy as needed.

Medications must be prescribed in accordance with Wisconsin Chapter 961 for controlled substances:

1. Prescription must be written for legitimate medical indication.
2. Sign/date prescription on date of issue with:
    a. Patient full name/address.

b. Drug name, strength, dosage form, quantity, directions for use.

3. Up to 3 monthly prescriptions may be given to patients.
    a. The date of issue (date of prescription is written) must be on all three prescriptions.
    b. The prescriber writes “fill on or after XX/XX/XXXX” for two prescriptions to be filled at a later date.
    c. A prescription for a CII controlled substance cannot be dispensed more than 60 days after the date of issue on the prescription order.

Disclaimer

CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician’s judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

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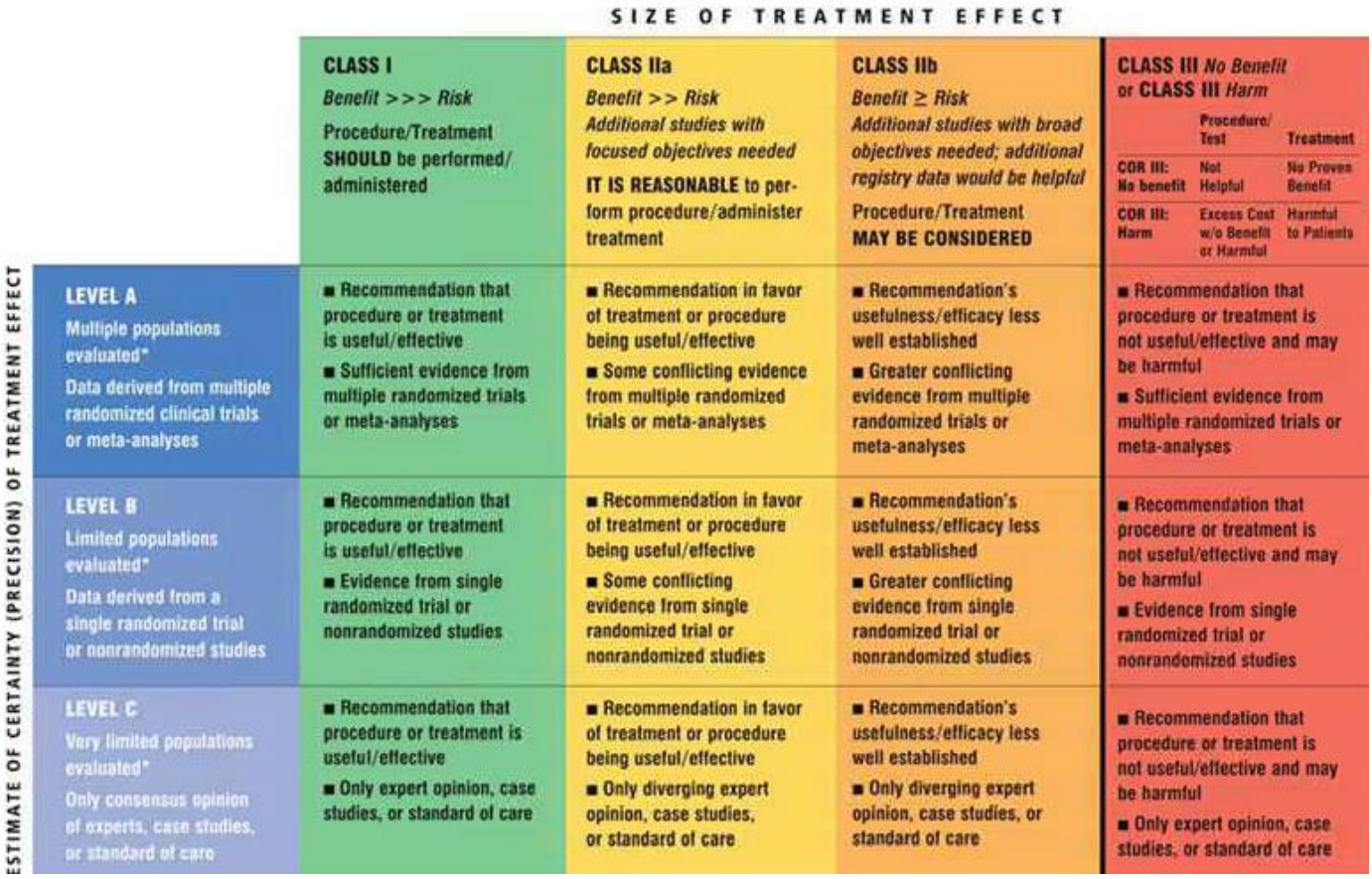
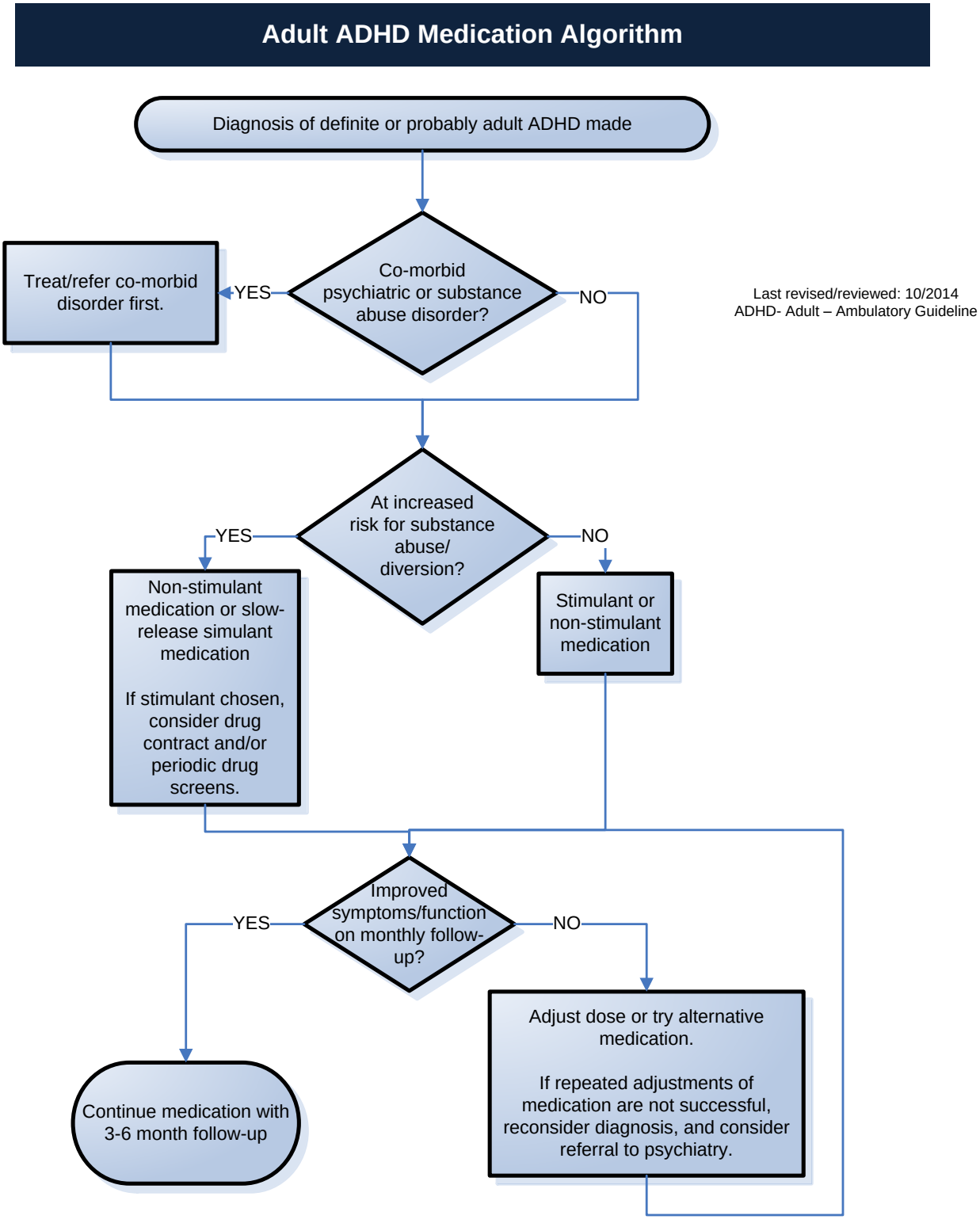
Appendix A

Figure 1. AHA/ACC Modified GRADE Grading Scheme



Appendix B



Last revised/reviewed: 10/2014
ADHD- Adult – Ambulatory Guideline

Appendix C

Medications for Treatment of Attention-Deficit/Hyperactivity Disorder

GENERAL CONSIDERATIONS FOR STIMULANTS

• Consider cardiac risk factors before initiating therapy • Use cautiously if history of tics • Give with/after food and swallow whole with liquids • Longer-acting stimulants may have greater problematic effects on evening appetite and sleep • Use cautiously if history of substance abuse or diversion concern	• Monitor patient weight and vital signs • Pellet/beaded capsule formulation may be opened and sprinkled on soft food • Nonabsorbable tablet shell may be seen in stool (Concerta) • Consider cardiovascular evaluation before initiating therapy

Methylphenidate Products

	Product Names	Strengths Available	Duration of Action	Usual Dosing Adult Titration Dose (titrate every 7 days, unless otherwise indicated)	Maximum Daily Dose
Short acting	methylphenidate tab^* (Ritalin)	5,10, 20 mg tab	≤ 4 hours	5-20 mg given 2-3 times daily Titrate by 5-10 mg every 7-14 days	FDA: 60 mg Off label: 100 mg if over 50 kg
	methylphenidate ^* (Methylin) (equivalent to Ritalin)	2.5, 5, 10mg chew tab 5 mg/5mL, 10mg/5mL solution	≤ 4 hours	5–20 mg given 2-3 times daily Titrate by 5-10 mg every 7-14 days	FDA: 60 mg Off label: 100 mg if over 50 kg
Intermediate acting 4-6 hours	methylphenidate SR tab^* (Ritalin SR) Medadate ER and generics rated AB equivalent	20 mg tab	4 – 6 hours	20–60 mg (divided in 1-2 doses/day) (20-40 mg in morning, 20 mg in early afternoon) Titrate by 20 mg/day	FDA: 60 mg Off label: 100 mg if over 50 kg
	ethylphenidate^* (Methylin ER) (equivalent to Ritalin SR)	10,20 mg tablet	4 – 6 hours	10-60 mg daily	FDA: 60 mg Off label: 100 mg if over 50 kg
	Methylphenidate tab^* (Metadate ER)	20 mg tablet	4 – 6 hours	20-60 mg daily (divided in 1-2 doses/day)	FDA: 60 mg Off label: 100 mg if over 50 kg
	dexmethylphenidate^* (Focalin) cap	2.5, 5, 10 mg tab	4 – 6 hours	2.5–10 mg given twice daily at least 4 hours apart	FDA: 20 mg Off label: 50 mg

	Product Names	Strengths Available	Duration of Action	Usual Dosing Adult Titration Dose (titrate every 7 days, unless otherwise indicated)	Maximum Daily Dose
Intermediate acting 6-8 hours	methylphenidate*^ (Metadate CD) cap (bimodal release with 30% immediate release and 70% delayed release)	10, 20, 30, 40, 50, 60 mg capsule	6 – 8 hours	10-60mg daily Titration 10-20 mg	FDA: 60 mg Off label: 100 mg if over 50 kg
	methylphenidate ER*^§ (Ritalin LA) cap (bimodal release with 50% rapid onset and 50% delayed release)	10, 20, 30, 40 mg capsule	6 – 8 hours	20-60mg daily	FDA: 60 mg Off label: 100 mg if over 50 kg
Long acting	dexmethylphenidate*^§ (Focalin XR) (bimodal release with 50% immediate release and 50% delayed release)	5, 10, 15, 20, 25, 30, 35, 40 mg capsule	10 - 12 hours 5-20 mg once daily	5–40 mg daily	FDA: 40 mg Off label: 50 mg
	methylphenidate ^ (Daytrana) patch apply to hip for 9 hours	10, 15, 20, 30 mg patch	12 hours (with 2 -3 hour delay)	10-30mg patch daily Titrate by next highest strength patch	FDA: 30 mg
	Methylphenidate*^§ (Concerta) tab (bimodal release with immediate onset and delayed release)	18, 27, 36, 54 mg tab	10 hours	18-54mg once daily (titrate by 18 mg)	FDA: 54 mg for children, 72 mg for adolescents and adults Off label: 90 mg adolescents (>40 kg)
^ FDA approved for treatment of ADHD, * Generic product, §Oral long acting methylphenidate products have immediate release and extended release components.					

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Amphetamine Products					
	Product Names	**Strengths Available**	**Duration of action**	**Usual Dosing (titrate every 7 days, unless otherwise noted)**	**Maximum Dose**
Short acting	Dextroamphetamine*	5, 10 mg tablet 1 mg/mL solution	4-6 hours	2.5 -15 mg two to three times Daily Titration 5 mg/week	FDA: 40 mg Off label: 60 mg (>50 kg)
Intermediate acting	dextroamphetamine capsule SR*§ (Dexedrine spansules) (bimodal release with 50% immediate release and 50% delayed release)	5, 10, 15 mg capsule	6-8 hours	5-15mg 2 timestwice daily Titration 5 mg	FDA: 40 mg Off label: 60 mg (>50 kg)
	amphetamine mixed salts tab ^combo* (Adderall) *	5, 7.5, 10, 12.5, 15, 20, 30 mg tab	5-8 hours	52.5-30mg 1-2 times once or twice daily Titration 2.5-5 mg once or twice daily	FDA: 40 mg Off label: 40 mg (≤ 50kg), 60 mg (>50 kg)
Long acting	amphetamine mixed salts capsule^* combo (Adderall XR)*§ (bimodal release with 50% immediate release and 50% delayed release)	5, 10, 15, 20, 25, 30 capsule	10 hours	10-30mg once daily Titration 5-10 mg	FDA: 30 mg Off-label: 30 mg (≤ 50kg), 60 mg (>50 kg)
	lisdexamfetamine (Vyvanse) capsule^	20, 30, 40, 50, 60, 70 mg capsule	10-12 hours	20-70mg once daily Titration 10-20 mg daily	FDA: 70 mg
^ FDA approved for treatment of ADHD, * Generic product, §Oral long acting methylphenidate products have immediate release and extended release components.					

GENERAL CONSIDERATIONS FOR NON-STIMULANTS

• May be used in cases of history of tics worsening from stimulants • Avoid bupropion if history of seizure or eating disorders • Monitor closely for behavioral side effects including suicidal ideation with atomoxetine, tricyclics, and bupropion as identified in FDA Black Box warning for anti-depressants	• Give with/after food and swallow whole with liquids • Medication of choice if concern about abuse or diversion • Consider cardiovascular risk factors before initiating tricyclic therapy and evaluate further if needed • Consider initiation with lower doses to improve tolerability • Guanfacine and clonidine may be used as adjunctive therapy with stimulants.

Non-Stimulant Products					
	Product Names	**Strengths Available**	**Duration of Action**	**Usual Dosing**	**Maximum Dosing**
Anti-depressants	nortriptyline* (Pamelor, Aventyl)	10, 25, 50, 75 mg capsule 10 mg/5 mL solution	8-24 hours	0.5 mg/kg/day (May divide dose to 2-3 times daily)	2 mg/kg or 100 mg (whichever is lowest)
	bupropion* (Wellbutrin)	75, 100 mg tab	4-5 hours	3 -6 mg/kg/day (or 150 mg – 300 mg, whichever is lowest) Divide into 2 or 3 daily doses	6 mg/kg/day (or 300 mg Whichever is lowest) Divide into 2 or 3 daily dose
	bupropion SR* (Wellbutrin SR)	100, 150, 200 mg tab	12 hours	3 -6 mg/kg/day (or 150 mg – 300 mg, whichever is lowest) Divide into 2 daily doses.	6 mg/kg/day (or 300 mg whichever is lowest) Divide into 2 daily doses.
	bupropion XL* (Wellbutrin XL)	150, 300 mg tab	24 hours	3 -6 mg/kg/day (or 150 mg – 300 mg, whichever is lowest)	6 mg/kg/day (or 300 mg whichever is lowest)
Alpha-agonists	clonidine tab ER^ (Kapvay)	0.1, 0.2 mg tab	At least 10-12 hours	0.1-0.4 mg/day Titration: 0.1 mg every 7 days	0.4 mg/day
	clonidine* (Catapres)	0.1, 0.2, 0.3 mg tab	At least 4-6 hours	0.05 mg at bedtime; 01 mg (≥ 45 kg) Titrate by 0.05 mg (<45 kg) or 0.1 mg (≥ 45 kg) increments to twice daily, three times daily, four times daily	0.4 mg (>45 kg)

	Product Names	Strengths Available	Duration of Action	Usual Dosing	Maximum Dosing
Alpha-agonists	guanfacine* (Tenex)	1, 2 mg tab	6-8 hours	0.5 mg at bedtime (<45 kg), 1 mg at bedtime (≥ 45 kg) Titrate by 0.5 mg (<45 kg) or 1 mg (≥ 45 kg) increments to twice daily, three times daily, four times daily	0.4 mg (>45 kg)
	guanfacine tab ER^* (Intuniv)	1, 2, 3, 4 mg tabs	At least 10-12 hours	0.05-0.12 mg/kg daily (or 1-4 mg once daily) Titration: 1 mg every 7 days	4 mg/day
Norepinephrine reuptake inhibitor	atomoxetine^ (Strattera) capsule	10, 18, 25, 40, 60, 80, 100 mg capsule	At least 10-12 hours	Initial dose)40 mg/day) After ≥ 3 days (increase to 80 mg daily)	FDA: 100 mg/day

*Generic product
^ FDA Approved

Potential Harms: Side Effects of Pharmacotherapy

- *Stimulants*: The most common side effects include appetite decrease, weight loss, insomnia, or headache. Less common side effects include tics and emotional lability/irritability, liver toxicity, hypertension, cardiac arrhythmia and psychosis.
- *Atomoxetine*: Side effects of atomoxetine that occurred more often than those with placebo include gastrointestinal distress, sedation, and decreased appetite.
- The U.S. Food and Drug Administration (FDA) and its Pediatric Advisory Committee have reviewed data regarding psychiatric adverse events to medications for the treatment of attention deficit/hyperactivity disorder (ADHD). For each agent examined (all stimulants, atomoxetine, and modafinil), there were reports of rare events of psychotic symptoms, specifically involving visual and tactile hallucinations of insects. Symptoms of aggression, suicidality (but no completed suicides), and cardiovascular issues were also reported.
- *Bupropion* may cause mild insomnia or loss of appetite. The highest recommended dose of bupropion is 450 mg. Higher doses may increase the risk of seizure.
- *Tricyclic Antidepressants (TCAs)* such as nortiptyline - frequently cause anticholinergic side effects such as dry mouth, sedation, constipation, changes in vision, or tachycardia. Among the TCAs, desipramine should be used with extreme caution in children and adolescents because there have been reports of sudden death. For TCAs electrocardiography should be considered for patients at risk and be performed at baseline and after each dose increase. Once the patient is on a stable dose of the TCA, a plasma level should be obtained to ensure the level is not in the toxic range.
- *Alpha- agonists*: Side effects of alpha-agonists include sedation, dizziness, and possible hypotension. Abrupt discontinuations of alpha-agonist are to be avoided.
- *Combinations of Medications*: There have been four deaths reported to the FDA of children taking a combination of methylphenidate and clonidine, but there were many atypical aspects of these cases.