Treatment of ADHD in Adults

Diagnostic Principles

ADHD is a **diagnosis of exclusion** requiring a **comprehensive, longitudinal assessment** over **2–3 visits** (See Assessment of ADHD in Adults).

- Allows time to gather information from multiple sources, assess persistence of symptoms and function, motivation for follow-up and rule out alternative diagnoses.

Treatment begins **only after a confident diagnosis** to ensure appropriate stimulant use.

Treatment Efficacy

Medication [1-5]

- Stimulants and non-stimulants **moderately reduce symptoms of ADHD** (moderate-quality evidence).
- Long-term safety data are limited; trials often exclude psychiatric comorbidities.
- Medication is associated with **lower rates of self-harm, injury, traffic crashes, and crime**, though associations have recently weakened (low quality evidence).

Cognitive Behavioral Therapy (CBT) [4,6-10]

- When available, CBT reduces symptoms and improves quality of life with or without medication (low quality evidence).
- Combined CBT + medication may be more effective than medication alone (low quality evidence).
- CBT can be tailored to improve comorbid depression, anxiety and dysfunctional behaviors.
- Skills training can help with time management, distraction delay techniques, emotion regulation, problem solving, and social communication.

Medication Selection

Stimulants [2,11]

Stimulant Type	
ER Amphetamine (e.g., Adderall XR, Vyvanse)	Preferred first-line; may provide better symptom improvement in adults than methylphenidate.
ER Methylphenidate (e.g., Concerta, Ritalin LA)	Use if amphetamine not tolerated or ineffective.
IR Stimulant	Add if ER dose wears off too early.

Abbreviations: ER = extended-release formulations; IR = immediate-release formulations

Non-Stimulants [1,2,6,13]

Medication	
Atomoxetine (Strattera) **Viloxazine** (Qelbree)	Long-acting; useful when ER stimulants fail.
Bupropion	Effective but best used to address cooccurring indications (e.g., depression, smoking cessation, etc.).
Guanfacine / Clonidine	Insufficient evidence.
Modafinil	Unlikely to be effective.

Duration of effect should be considered when starting a stimulant or switching between stimulants. Do not substitute on a mg-per-mg basis.

The ADHD Medication Calculator may be a helpful reference aid when switching medications: https://www.adhdmedcalc.com/.

Approximate durations of effect for formulations approved for adults are highlighted below.

Amphetamine-based Formulations	Duration (hr)	Methylphenidate-based Formulations	Duration (hr)
Adderall	4-6	Ritalin, Methylin	3-4
Adderall XR, Adzenys XR, Dyanavel XR	8-13	Ritalin SR, Ritalin LA, Methylin ER, Metadate CD, Metadate ER, QuilliChew ER	6-8
Mydayis	16	Concerta, Aptensio XR, Quillivant XR, Jornay PM	8-12
Evekeo, Evekeo ODT	9	Focalin XR	12
Vyvanse	8-14	Aztarys	6-11
Xelstrym	9		

Recommended Treatment Algorithm

Step	
1	**Discuss Treatment Options** ⟶ Medication ⟶ Cognitive Behavioral Therapy (CBT) ⟶ Combination therapy (often most effective)
2	**Start** with an **ER amphetamine** formulation ⟶ Titrate weekly for up to 6 weeks ⟶ Consider adding **IR amphetamine** formulation if afternoon symptoms return
3	If ER amphetamine not tolerated or ineffective, **switch to ER methylphenidate** ⟶ Titrate weekly for 6 weeks ⟶ Consider adding **IR methylphenidate** if afternoon symptoms return
4	If stimulants not tolerated or ineffective, **switch to non-stimulant** ⟶ **Atomoxetine preferred** due to lower cost ⟶ Expect response in **2–4 weeks**, sometimes longer ⟶ Non-stimulants may be preferred in some patients with: • Anxiety • Tics • Insomnia • Eating disorder • Substance use disorder (SUD) • Poor stimulant tolerance ⟶ If not tolerated or ineffective → consider **bupropion** or **consult OPAL** • OPAL (Oregon Psychiatric Access Line) provides free consultations to registered Oregon providers
5	**When to refer to psychiatry** ⟶ No response after: • **Two 6-week stimulant trials** (amphetamine + methylphenidate) **AND** • **One 6-week non-stimulant trial** ⟶ Diagnostic uncertainty ⟶ Complex comorbidities (bipolar disorder, severe SUD, psychosis)

Step	
	⟶ Pregnancy with significant functional impairment
6	**Offer CBT, psychosocial interventions** ⟶ At any stage if patient prefers ⟶ When medication is not tolerated ⟶ As augmentation for partial response ⟶ For ADHD + depression/anxiety ⟶ For skills training (time management, emotion regulation, organization)
7	**General Monitoring Parameters** Before Starting Medication: ⟶ Blood pressure (BP), heart rate (HR) ⟶ Cardiac history ⟶ Psychiatric history ⟶ Substance use screening ⟶ Sleep assessment During Treatment (every 3-6 months with maintenance; 1-2 weeks after stimulant dose increase; 3-4 weeks after non-stimulant dose increase): ⟶ BP, HR and weight at each visit ⟶ Appetite and sleep ⟶ Mood symptoms (mania, psychosis) ⟶ Misuse/diversion risk (stimulants) ⟶ Symptom reduction and functional outcomes (work, relationships, daily tasks) ⟶ Treatment adherence ⟶ New stressors that may hinder treatment response

Dose Response

	Key Points [12,14]
Titration	Weekly titration; stimulants may take up to 6 weeks to optimize.
Dose-response	Amphetamine dose-response unclear; start low. Current life stressors and traumatic events can hinder response.
Plateau	Improvement plateaus beyond **30–35 mg/day (amphetamines)** and **35–40 mg/day (methylphenidate)** (moderate quality evidence).
ED50/ED95	Amphetamine ED50 ~12.5 mg/day; ED95 ~30 mg/day. Methylphenidate ED50 ~25 mg/day; ED95 ~72.5 mg/day.

Abbreviations: ED50 = median effective dose in 50% of population; ED95 = median effective dose in 95% of population.

Special Populations with Co-occurring Disorders

See Assessment of ADHD in Adults before treating ADHD symptoms in individuals with co-occurring disorders.[6] Treat the most functionally impairing or destabilizing disorder first.

Psychiatric and Neurodevelopmental Disorders [1,15]

Bipolar disorder	Treat bipolar first; stimulants are safe if mood stabilized. Methylphenidate may be preferred.
Autism Intellectual disability	Increased sensitivity to stimulants; use lower doses and slow titration.

Substance Use Disorders [16-18]

- Integrate ADHD + SUD treatment with care coordination.
- ER stimulants, atomoxetine, or bupropion are recommended (low-quality evidence).
- Patients with stimulant use disorder and ADHD may need higher stimulant doses. Careful monitoring, consultation with OPAL or specialist recommended.

- Stimulants should not be prescribed to treat stimulant use disorder (without ADHD) except by a practitioner specialized in addiction medicine or addiction psychiatry.

Sleep Disorders

- Treat sleep disorder first and then reassess ADHD symptoms.
- Healthy sleep hygiene is particularly important in people with ADHD.

Eating Disorders [19,20]

- Patients may have complex risk factors, treatment requires close monitoring.
- Lisdexamfetamine is FDA-approved for both ADHD and binge-eating disorder.
- Bupropion is contraindicated in anorexia nervosa and bulimia nervosa.
- Medication + CBT may be more effective than medication alone (low quality evidence).

Seizure Disorders [21]

- Stimulants likely safe with close monitoring (low-quality evidence).
- Bupropion is contraindicated.

Perinatal Considerations [22-25]

- Stimulants cross placenta, may present small increased risk for: preeclampsia, preterm birth, low birth weight (amphetamines); fetal cardiac malformations (methylphenidate) (low quality evidence).
- Stimulants transfer into human milk in low levels; no short-term effects but long-term effects unknown (insufficient evidence). Monitor infant for weight gain, fussiness, sleep issues.
- Unknown if atomoxetine or bupropion provide lower risk (insufficient evidence).
- Consider CBT or self-management in mild to moderate ADHD.
- Individualized shared decision-making process essential.

Perimenopausal Considerations

- Stimulants remain first-line; dose adjustments may be needed during low estrogen periods premenstrually (1-2 weeks before period).
- Adjunct hormone therapy, particulary transdermal estradiol, may help improve cognitive and mood symptoms but impact on core ADHD symptoms is not well studied.

Medication Safety

Common Adverse Effects

- Appetite reduction
- Delayed sleep onset
- Adults tolerate ADHD medications less well than children.[2]

Cardiovascular Risks [2,26-29]

- Stimulants and non-stimulants increase BP and pulse, may increase risk for cardiovascular disease (low quality evidence).
- Avoid in structural heart abnormalities or heart disease, sudden death has been reported.

Psychosis and Manic Symptoms [30-31]

- Risk with stimulants and non-stimulants is inconclusive in adults, even with history of psychosis (low quality evidence).
- Symptoms may resolve after stopping medication.

Misuse and Abuse of Stimulants [32-34]

- Misuse of prescribed stimulants has been consistently reported in a minority of adults, most in younger adults and college students (moderate-quality evidence).
- Individuals who meet criteria for prescription stimulant use disorder most commonly use amphetamines. High rates of concurrent substance use is also common.
- No clear association between stimulant use and developing long-term dependence or new SUD.

National Stimulant Shortages

- Stimulant supply chain disruptions and increased demand have created drug shortages.[35]
- If preferred stimulant unavailable:
    - Switch to another ER stimulant.
    - Use IR formulation temporarily.
    - Consider non-stimulant.
    - The ADHD Medication Calculator may be a helpful resource when switching medications: https://www.adhdmedcalc.com/.

Disposal

- Do not flush unused medications down the toilet or drain.
- Find collection boxes to dispose of medications properly at medtakebackoregon.org.

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