

State-of-the-Art Management of ADHD in Children, Adolescents, and Adults: Best Practices and Emerging Strategies

Barbara J. Coffey, MD, MS

Division Chief, Child and Adolescent Psychiatry
Director, UHealth Tics, OCD and Related Problems
Professor, Department of Psychiatry and Behavioral
Sciences
University of Miami, Miller School of Medicine
Miami, FL



Learning Objective 1

Apply *DSM-5* criteria and validated rating scales in the assessment ADHD in children, adolescents, and adults.



Learning Objective 2

Apply best practices for minimizing side effects associated with traditional stimulants used to treat ADHD.

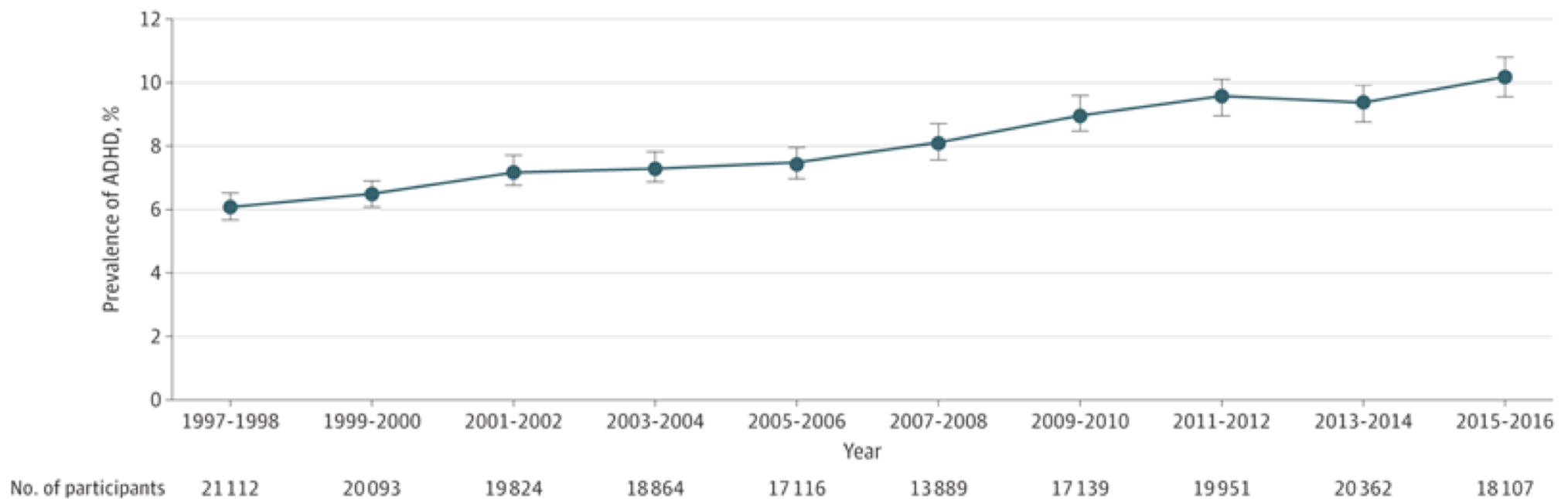


Learning Objective 3

Evaluate clinical trial data for new or emerging agents with novel MOAs to treat ADHD in children, adolescents, and adults.

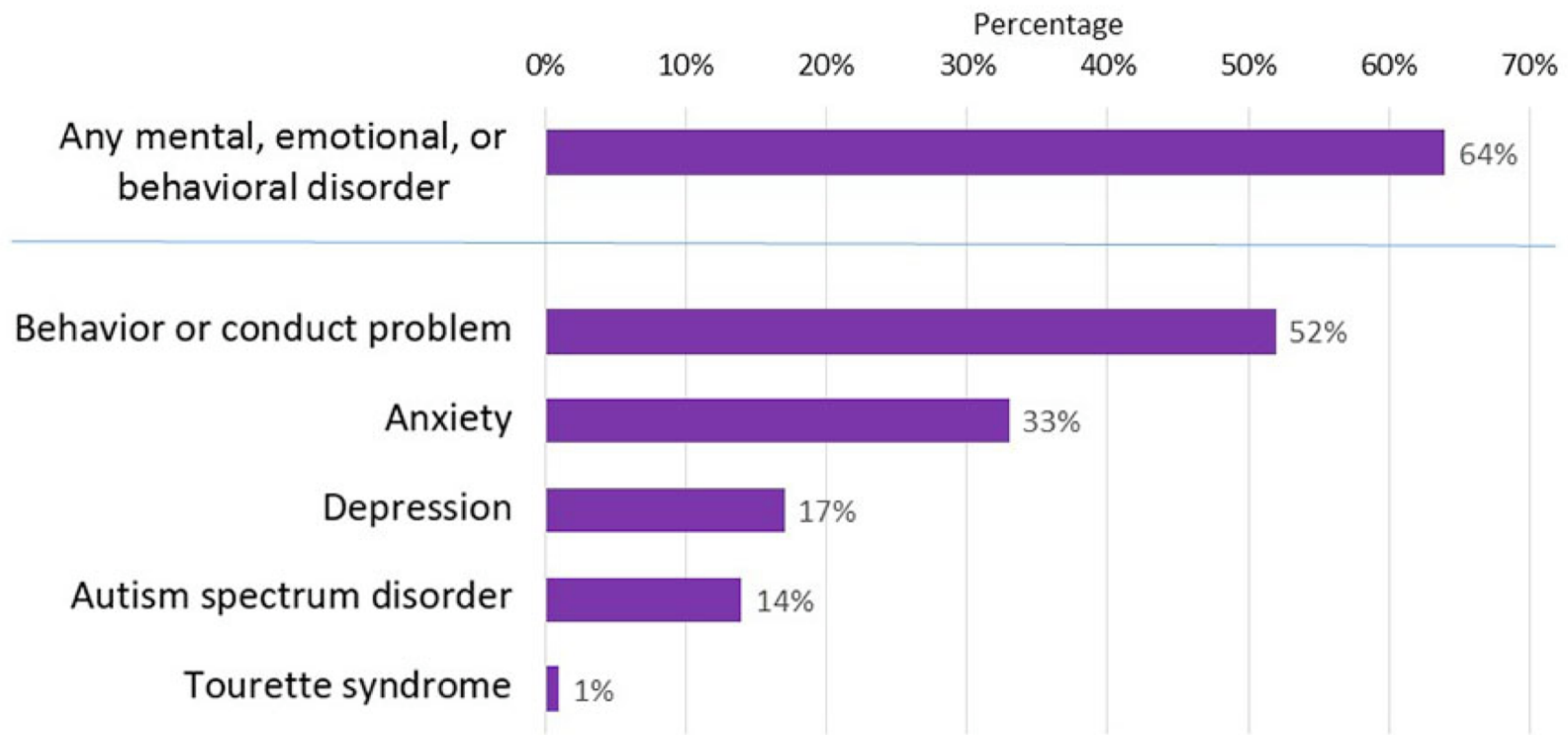


Rising Prevalence of ADHD Among Children and Adolescents in the United States



Xu G, et al. *JAMA Network Open*. 2018;1(4):e181471.

Psychiatric Comorbidities: Common Among Children with ADHD



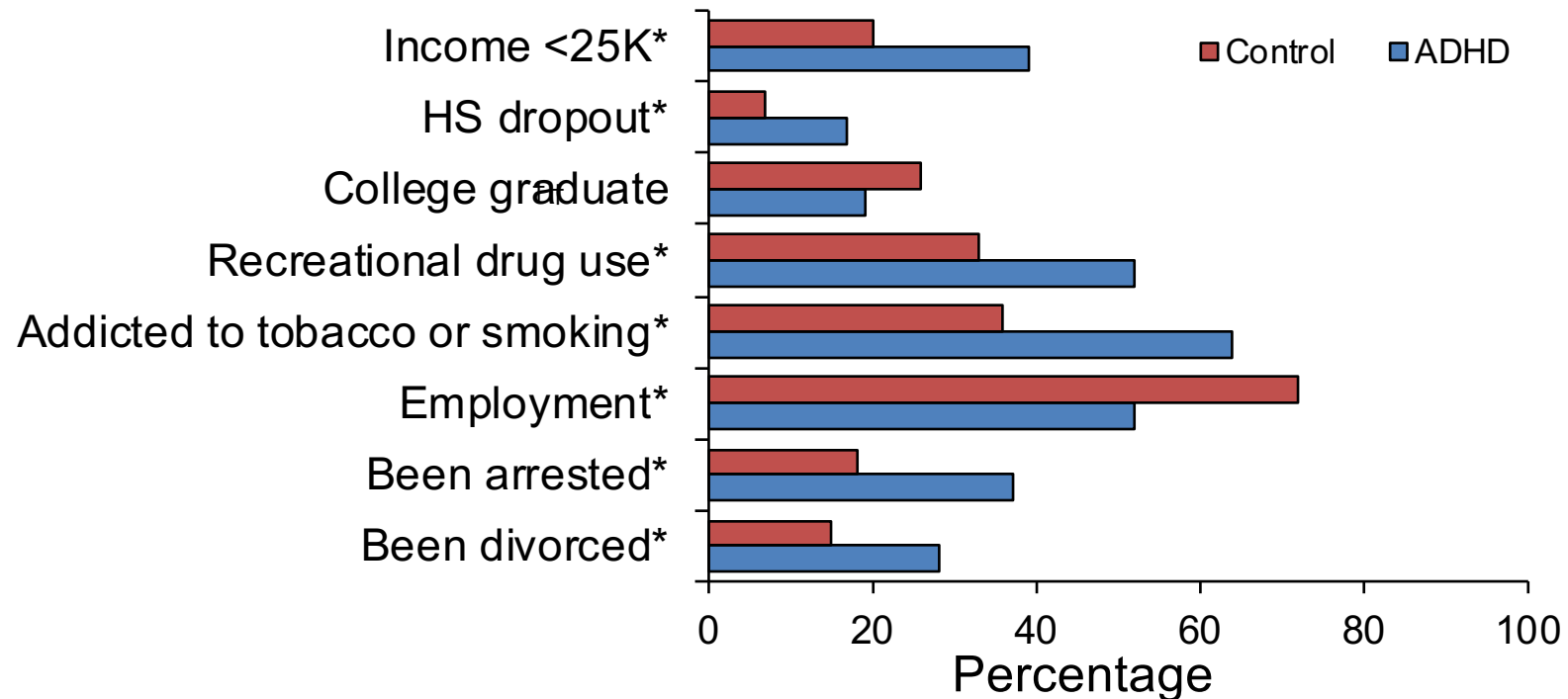
Because the 2016 NSCH survey used different methods, estimates are not directly comparable with estimates based on previous NSCH data. Because of an increased focus on ADHD in younger children, age ranges were expanded to include children age 2-17.
Danielson ML, et al. *J Clin Child Adolesc Psychol*. 2018;47(2):199-212. CDC, 2018.

ADHD in Adults

- Estimated 4.4% of the adult US population, but less than 20% have been diagnosed
- Of these, 41.3% of adult ADHD cases are considered severe
- Diagnosis more common in men (12.9%) compared to women (4.9%)
- About 30% to 60% of children diagnosed with ADHD continue to be affected into adulthood
- Adults with ADHD are prone to traffic violations and accidents
 - 5x more likely to speed
 - 50% more likely to be in a serious car crash
- Increased mortality risk
- Anxiety disorders occur in 50% of cases

Kessler RC, et al. *Am J Psychiatry*. 2006;163(4):716-723.

Real-Life Consequences of ADHD



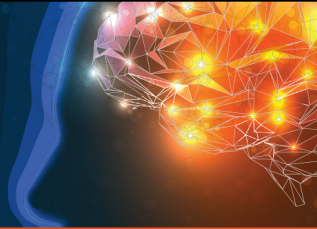
Survey of 500 community adults with ADHD compared with 501 age- and gender-matched controls; 36% of ADHD patients reported medication use.

* $p \leq .001$; † $p < .01$

Biederman J, et al. *J Clin Psychiatry*. 2006;67(4):524-540.; Biederman J, et al. *MedGenMed*. 2006;8(3):12.

DSM-5 Criteria for ADHD:

Symptoms (6/9 age < 16; 5/9 > 17)



Inattentive Symptoms:

- Fails to give close attention to details
- Has difficulty sustaining attention
- Does not seem to listen
- Does not follow through on instructions
- Has difficulty organizing tasks or activities
- Avoids tasks requiring sustained mental effort
- Loses things necessary for tasks
- Is easily distracted
- Is forgetful in daily activities

Hyperactive/Impulsive Symptoms:

- Fidgets with hands or feet or squirms in seat
- Leaves seat in classroom inappropriately
- Runs about or climbs excessively (or internal restlessness)
- Has difficulty playing quietly
- Is “on the go” or acts as if “driven by a motor”
- Talks excessively
- Blurts out answers before questions are completed
- Has difficulty awaiting turn
- Interrupts or intrudes on others

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. 2013.

ADHD Diagnosis: Developmental Considerations



- **Preschool Age**
 - More prominent hyperactivity/impulsivity
 - May be difficult to distinguish from typical development
- **School Age**
 - Emergence of school difficulties
 - Modal age for diagnosis
- **Adolescents**
 - Unique impairments emerge – driving, risky sexual behavior, drug use
 - Challenge – adolescents neither “old kids” nor “young adults”
- **Adults**
 - Might be challenging to obtain reliable history; may have long history of compensatory behaviors. It is helpful to get supporting childhood history of parents are available.
 - Comorbidities and variability in vocational/family settings can confound diagnosis

ADHD Assessment



- Life history (with information from parents and teachers or school records, if available for adolescents)
- Self report for adults
- Mental status exam
- Rating scales – measuring core and broad features; provide quantitative information on symptom severity
- Medical history review; cardiac and neurologic status, blood pressure/pulse
- Detailed review of cardiovascular history is necessary for patients; inquire about significant history in close relatives
- If medical history is unremarkable, laboratory or neurological testing is not indicated
- Evaluate comorbidity (psychiatric, cognitive, psychosocial, medical)

Source of Clinical Data for Diagnosis Dependent on Development Level

7	12	18	25
Child	Adolescent	Adult	
Teacher	Self	Self	
Parent	Teacher	Spouse/Partner	
Self	Parent	Sibling	
Grandparent	Grandparent	Friend	
Other Adult	Other Adult	Co-worker	
Behavioral Observation		Self-Report	

Representative ADHD Rating Scale



- Adult Diagnostic Scales
- Conners' Adult ADHD Diagnostic Interview for DSM-IV (CAADID)
- Barkley's Current Symptoms Scale (CSS)
- Adult ADHD Clinical Diagnostic Scale (ACDS)
- Brown ADD Rating Scales
- Symptom Assessment
- Adult ADHD Investigator Symptom Rating Scale (AISRS)
- 18-question Adult ADHD Self-Report Scale (ASRS) Symptom Checklist and 6-question Screener v1.1
- Conners' Adult ADHD Rating Scales (CAARS)

Adler LA, et al. *Attention-Deficit Hyperactivity Disorder in Adults and Children*. 2015.

Medications

Pharmacological Treatment

Stimulants

Methylphenidate
Amphetamines

← FDA Approved

Atomoxetine

← FDA Approved

Alpha Agonists

Guanfacine (XR)
Clonidine (XR)

← FDA Approved

Guan XR or Clon XR + stimulants

← FDA Approved

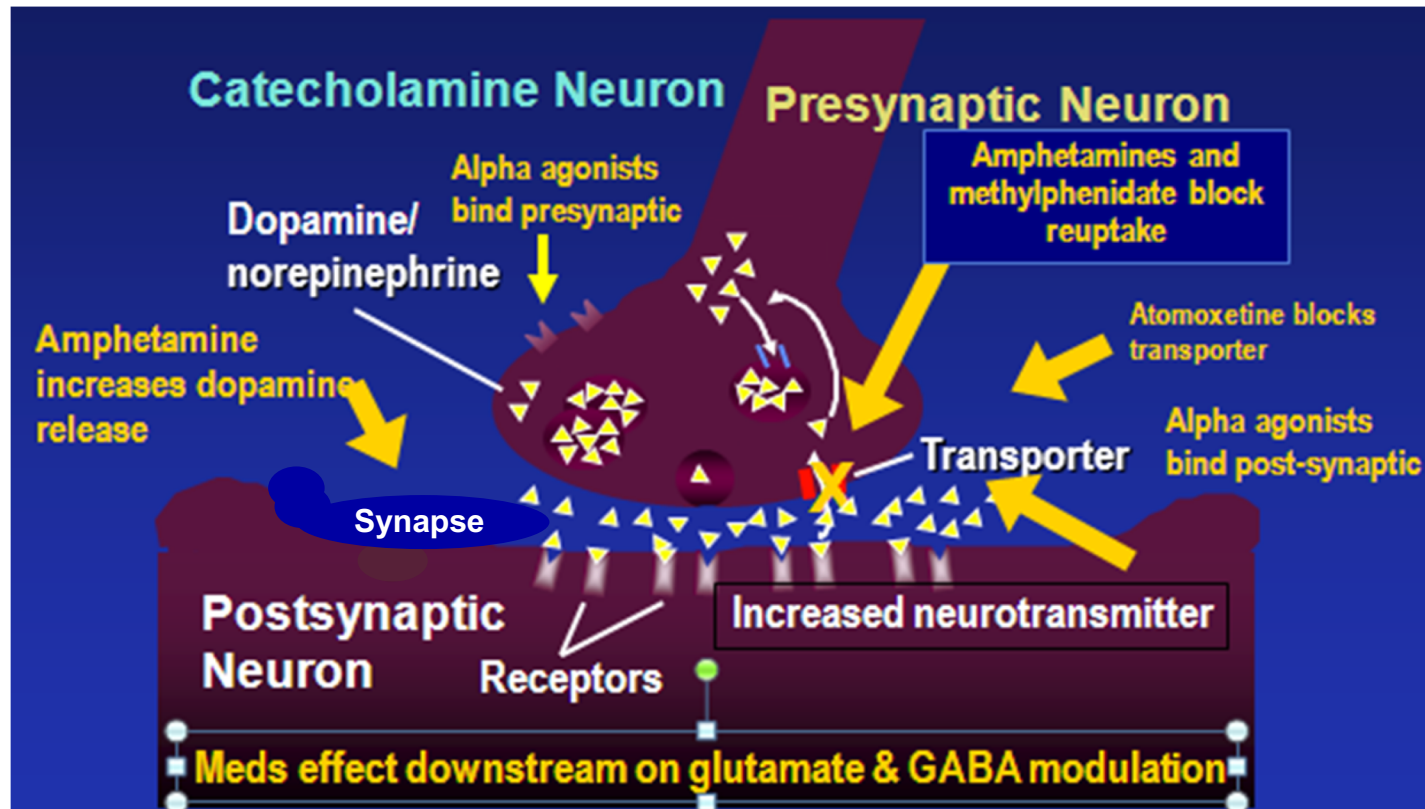
Antidepressants

Bupropion
Tricyclics

Modafinil



Suspected Mechanism of Action of Medications for ADHD



Wilens, TE. *J Clin Psychopharmacol*. 2008;28(3 Suppl 2):S46-S53.

ADHD Medication Effect Size



Effect Size	
Stimulant medications	1.0*
α -agonist medications, extended release	0.7
Atomoxetine	0.7
0.2 = small effect size, 0.5 = moderate effect size, 0.8 = large effect size.	

*0.4 - 0.8 in preschoolers.

The Guideline of Diagnosis and Treatment of Attention-Deficit Hyperactivity Disorder: Developed by ADHD Translational Research Center - Scientific Figure on ResearchGate. Available at: https://www.researchgate.net/figure/ADHD-medication-effect-size-204_tbl2_312221770 [accessed 3 Feb, 2019].

Stimulants for the Treatment of ADHD



Amphetamine-based Formulations	Duration of Effect
Mixed Amphetamine Salts Extended Release	~12 hours
Lisdexamfetamine	~12 hours
Methylphenidate-based Formulations	
OROS Methylphenidate	~12 hours
Dexmethylphenidate XR	10-12 hours

[Package Inserts]. Drugs@FDA Website.

Methylphenidate (MPH) in ADHD: Optimizing Dosing

Generic Name	Brand Name	Starting Dose	Maximum Dose*	Duration
MPH	Ritalin IR®	5 mg QD/BID	2 mg/kg/day	4 hr /BID
D-MPH	Focalin®	2.5 mg QD/BID	1 mg/kg/day	4-5 hr / BID-TID
D-MPH	Focalin XR®	5 mg QD	1 mg/kg/day	10-12 hr QD
MPH	Daytrana®	10 mg		6-16 hr
MPH	Concerta®	18 mg QD	2 mg/kg/day	12 hr / once
MPH	Metadate CD®	20 mg QD		8 hr / once
MPH	Ritalin LA®	20 mg QD		8 hr /once
MPH	Quillivant®	< 10 mg QD		12 hr /once
MPH	Quillichew™	< 10 mg QD		8 hr /once
MPH	Cotempla XR (disintegrating tab)	8.6 mg QD	51.8 mg	12 hr/once
MPH	Aptensio XR (40% IR)	10 mg QD	2 mg/kg/day	12 hr/once

*May exceed FDA approved dose. Wilens TE, et al. *Postgrad Med.* 2010;122(5):97-109. www.drugs.com.

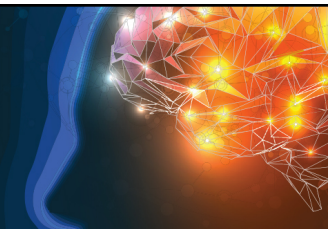
Amphetamine (AMPH) in ADHD: Optimizing Dosing

Generic Name	Brand Name	Starting Dose	Maximum Dose* Usual Dosing	Duration
AMPH,D-AMPH mixed salts	Adderall®	2.5-5 mg QD	1.5 mg/kg/day	6 hr / BID
AMPH,D-AMPH mixed salts	Adderall XR®	2.5-5 mg QD		12 hr / QD
Lisdexamfetamine	Vyvanse®	30 mg QD		12-14 hr / QD
AMPH mixed salts	Mydayis®	12.5 mg QD	50/25 mg (adults/adol)	To 16 hr/QD
D-AMPH	Dexedrine Tablets®	2.5-5 mg BID	1.5 mg/kg/day	3-5 hr / BID-QID
AMPH sulfate	Evekeo®	2.5-5 mg BID		3-5 hr / BID-QID
D-AMPH	Dexedrine Spansule®	5 mg QD		6 hr / QD-BID
AMPH	Dyanavel XR™ (suspension)	2.5-5 mg QD	1.5 mg/kg/day	12 hr / QD
AMPH	Adzenys XR™ (disintegrating tab)	6.3-12.5 mg QD	12.5 mg (adolescents)	12 hr / QD

*May exceed FDA approved dose (e.g., > 20 to 30 mg/day).

Wilens, TE, et al. *CNS News*. 2007.; Wilens TE, et al. *Postgrad Med*. 2010;122(5):97-109.; www.drugs.com.

Extended Release MPH Solution and Chewable Preparations



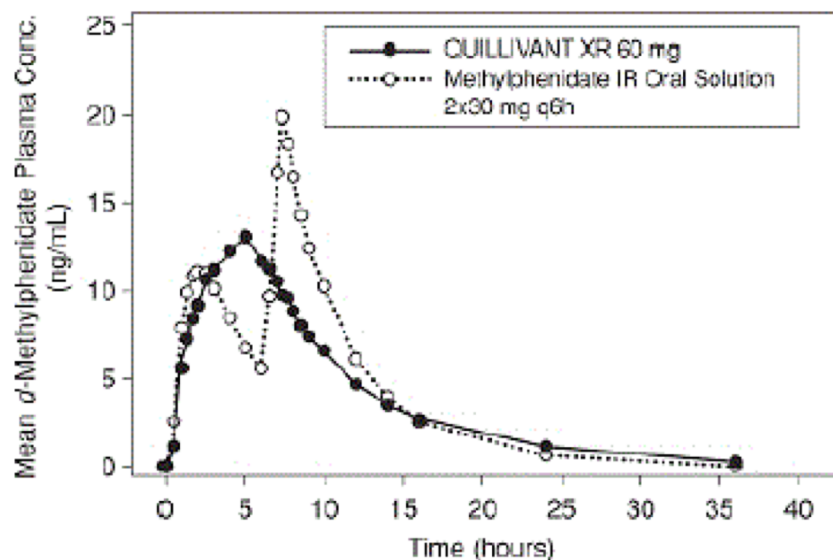
Quillivant XR

Suspension

12 hour duration

25 mg/5 cc (tsp)

Dosing to 60 mg daily



QuilliChew ER

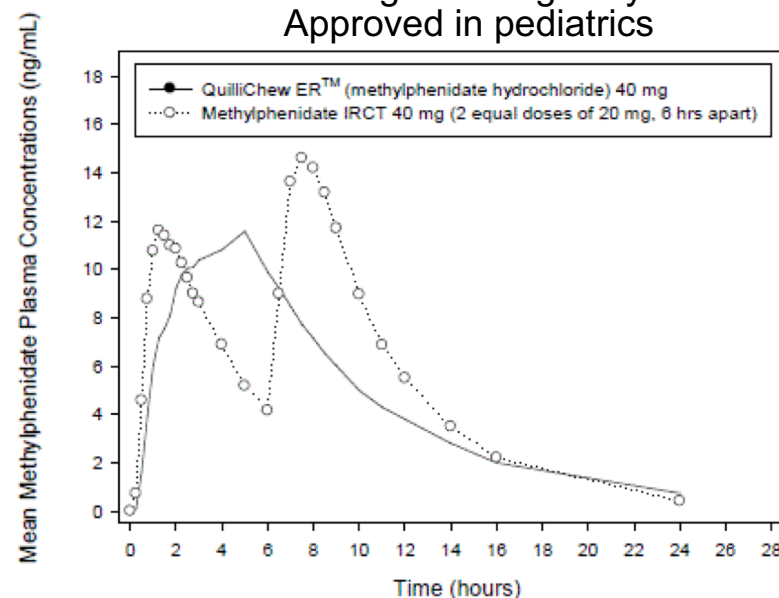
Chewable tablet

8 hour duration

20, 30, 40 mg tablets

Dosing to 60 mg daily

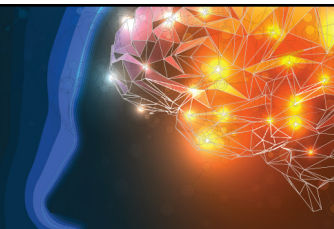
Approved in pediatrics



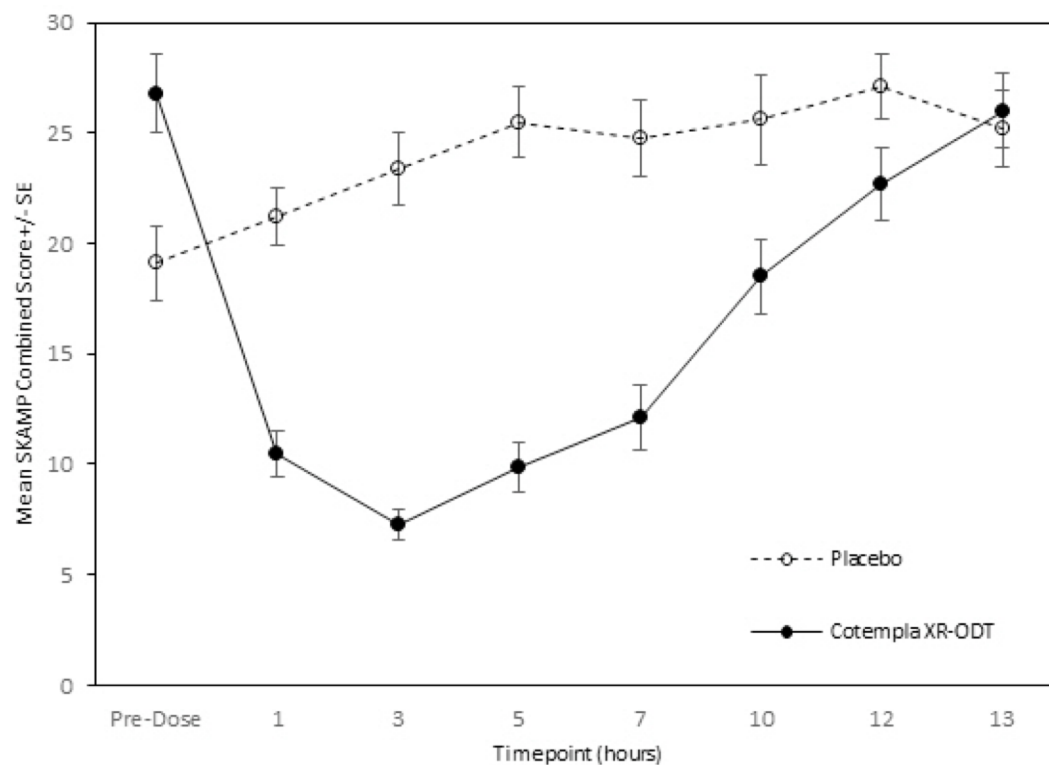
Rx List. <https://www.rxlist.com/quillichew-er-drug.htm>; <https://www.rxlist.com/quillivant-xr-drug.htm>.

US Food and Drug Administration. <https://www.accessdata.fda.gov/scripts/cder/daf/>

Extended-Release Oral Disintegrating Methylphenidate

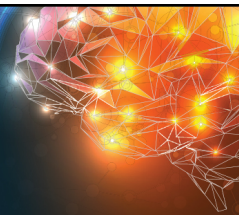


- Extended-release methylphenidate
- 25% IR; 75% XR
- Formulation: Oral disintegrating tablets: grape flavored
- Dosing: 8.6 mg to 25.9 mg QD
- Capsules: 8.6, 17.3, 25.9 mg
- Duration of action: 12 hours



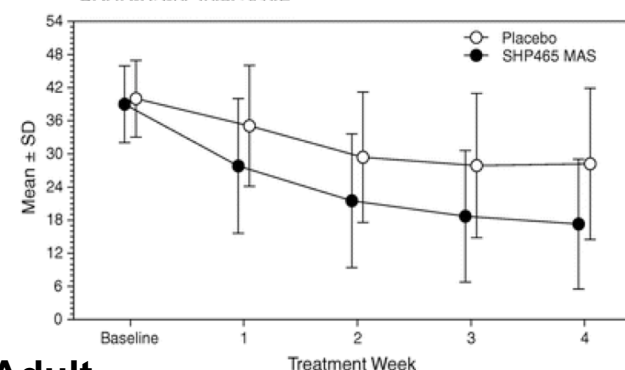
Drugs.com. Cotelma XR-ODT. <https://www.drugs.com/pro/cotelma-xr-odt.html#s-34090-1>

Amphetamine Extended-Extended Release for Adult/Adolescent ADHD

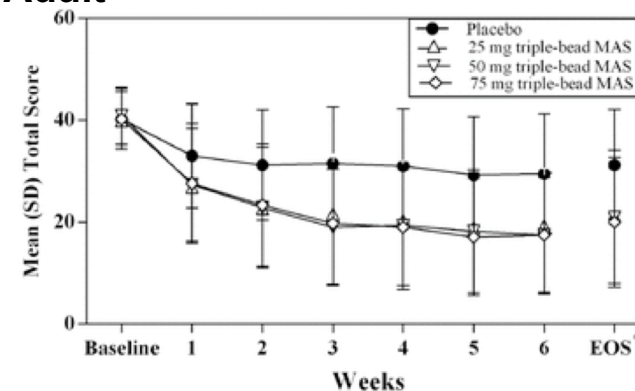


- “Very” extended mixed amphetamine (e.g., XR²)
- 3 types of beads: immediate, two delayed
- For adolescents and adults only
- Composition: mixed-amphetamine salts
- Dosing: 12.5 to 25 mg QD (≥ 13) or 50 mg (adults)
- Capsules: 12.5, 25, 37.5, 50 mg
- Duration of action: 16 hours (onset at 2-4 hours)

Pediatric/Adolescent

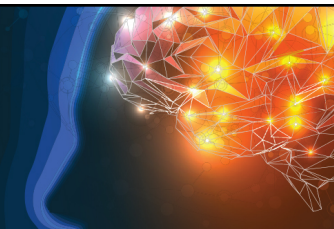


Adult



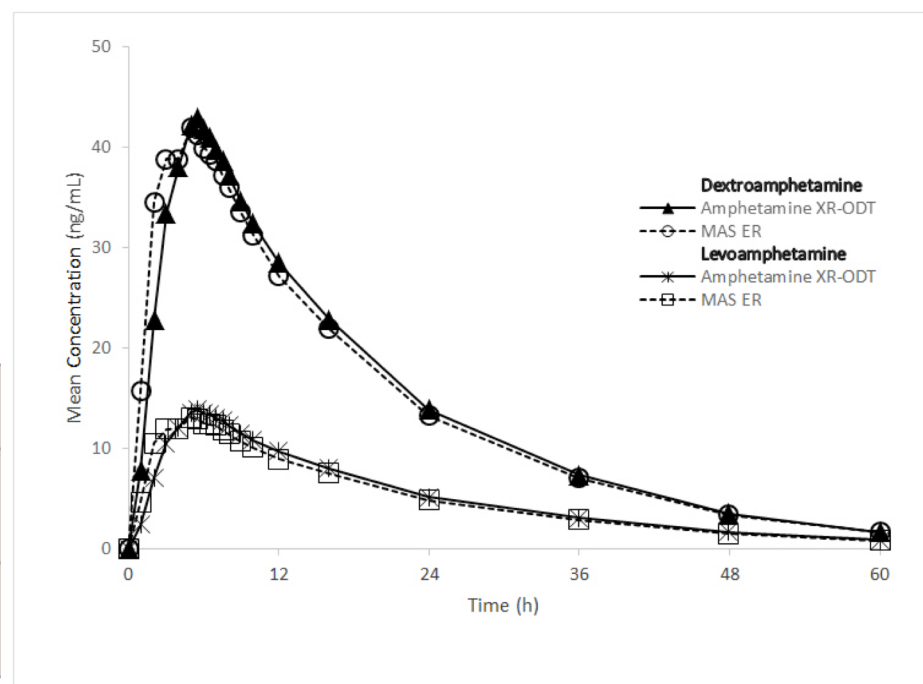
Drugs.com; Frick G, et al. J Atten Disord. 2017 Apr 1;1087054717696771. doi: 10.1177/1087054717696771.
Brams M, et al. *Journal of Child and Adolescent Psychopharmacology*. 2018;28:1

Amphetamine Oral Disintegrating Tabs for Pediatric ADHD

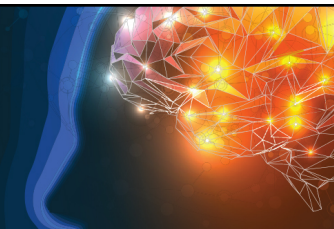


- Mixed amphetamine formulation; dissolves quickly
- Orange flavored; 50% IR; 50% XR
- (3 to 1 ratio of d- to l-amphetamine)
- Duration of action to 12 hours

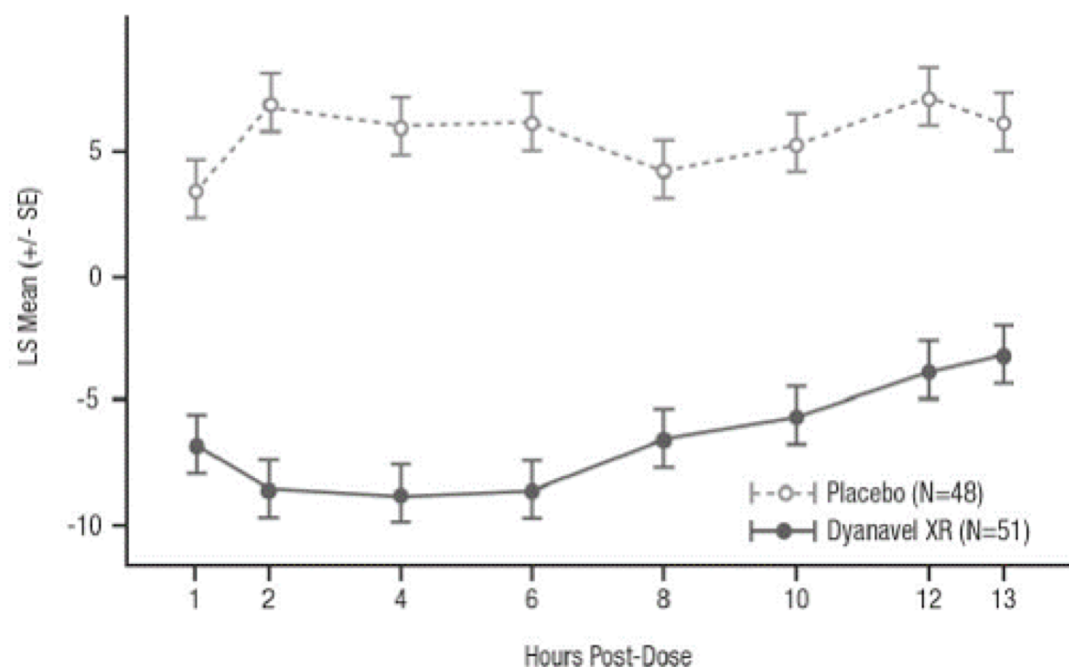
Equivalent Dosing						
AMPH ER disintegrating	3.1 mg	3.1 mg	9.4 mg	12.5 mg	15.7 mg	18.8 mg
Mixed AMPH Salts ER	5 mg	10 mg	15 mg	20 mg	25 mg	30 mg



Amphetamine Suspension XR for Pediatric ADHD



- Amphetamine suspension
- Composition: 3.2 to 1 ratio of d- to l-amphetamine
- Dosing: 2.5 to 5 mg QD
- Duration of action: 12 hours



Rx List. <https://www.rxlist.com/dyanavel-xr-drug.htm#cinpharm>. US Food and Drug Administration.
<https://www.accessdata.fda.gov/scripts/cder/daf/>

Managing Adverse Effects of Stimulants (1)



Adverse Effect	Management Strategies
Appetite Decrease/Weight Loss	<ul style="list-style-type: none">• Time meals when effect is wearing off• Calorie dense foods• Cyproheptadine
Growth Suppression	<ul style="list-style-type: none">• Increase monitoring of height• Consider drug holiday• Change medication or dose• Weight risk/benefit
Insomnia	<ul style="list-style-type: none">• Change formulation• Add alpha 2 agonist• Add melatonin• Add antihistamine

Managing Adverse Effects of Stimulants (2)



Adverse Effect	Management Strategies
Headache	<ul style="list-style-type: none">• Monitor• Adjust dose• Alternate therapy (stimulant or non-stimulant)
Tics*	<ul style="list-style-type: none">• Monitor• Adjust dose if necessary• Alternative treatment
Emotional Lability/Irritability*	<ul style="list-style-type: none">• Adjust dose• Correlate behavior change with time when stimulant active (“rebound”)• Discontinue stimulant and trial alpha 2 agonist

*Less common side effects.

Patient/Parent Counseling



- Provide psycho-education on known course and outcomes
- Referral to support groups is helpful (e.g., CHADD)
- Discuss risks/benefits of treatment
- Monitor side effects
- Discuss strategies to manage side effects

Emerging Therapies for ADHD



- Wide range of both pharmacological and non-pharmacological treatments under investigation
 - Medications with novel mechanisms of action
 - Devices, including therapeutic software
 - Novel approaches to behavior therapy

Optimizing Outcomes Through Adherence and Engagement: Developing an Individualized Treatment Plan

- Cognitive-behavioral therapy is typically recommended initially for children and adolescents
- Parent Child Interaction therapy (PCIT) is evidence based treatment in younger children with ADHD+ behavioral problems
- Pharmacotherapy is typically considered among first-line options if symptoms are at least moderate, causing significant distress and/or impairment
- Once treatment is established, practitioner's role may also include:
 - Coordinating with team health service regarding ADHD treatment and continuity between settings
 - Working with schools and providing educational recommendations
 - Therapeutic use exemptions
 - Preparing the patient (and family) for major transitions

Pliszka S. *J Am Acad Child Adolesc Psychiatry*. 2007;46(7):894-921.

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely



- Increase your recognition and diagnosis of ADHD in children, adolescents, and adults
- Monitor and manage side effects of traditional stimulants
- Stay up-to-date with the latest clinical evidence on emerging therapies

Questions & Answers

Don't forget to fill out your evaluations to collect your credit.

