ADHD: TREATMENT OVERVIEW

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SEATTLE CHILDREN’S HOSPITAL
GENERAL DISCLOSURES

The University of Washington School of Medicine also gratefully acknowledges receipt of educational grant support for this activity from the Washington State Legislature through the Safety-Net Hospital Assessment, working to expand access to psychiatric services throughout Washington State.
## DISCLOSURE OF POTENTIAL CONFLICTS

<table>
<thead>
<tr>
<th>Source</th>
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<tr>
<td>Research Funding</td>
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<td>Books, Intellectual Property</td>
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<td>Advisor/ Consultant</td>
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<td>Stock or Equity</td>
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</tr>
<tr>
<td>Honorarium or expenses for this presentation or meeting</td>
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OBJECTIVES

1. After participating in this program, learners will be able to describe common components of a comprehensive treatment plan for ADHD.

2. After participating in this program, learners will be able to describe at least one recommended psychosocial intervention for pre-adolescents, adolescents, and adults with ADHD.

3. After participating in this program, learners will be able to describe commonly used medication classes for ADHD, including side effects associated with each class.
ADHD TREATMENT ACROSS THE DEVELOPMENTAL CONTINUUM
MULTIMODAL TREATMENT OF ADHD

• Psychoeducation
• Medication treatment if indicated
• Behavioral interventions
  – Rewarding desirable behaviors, non-punitive consequences for negative behaviors for youth
  – cBT for adults
• Parent management training for youth
  – Maintain schedule, organize home, set small goals, limit choices, use charts/lists to maintain focus, encourage successful activities, reduce distractions, use calm discipline
    – Incredible Years Parenting Program, New Forest Parenting Program, Parent-Child Interaction Therapy, Positive Parenting Program
• Training in skills deficits
  – Organization and planning for adolescents and adults
  – cBT for adults
PSYCHOEDUCATION ON ADHD SHOULD INCLUDE DISCUSSION OF:

- Nature of disorder (causes, prevalence, clinical course)
- Establishing goals of treatment
- Importance of assessing level of impairment and response to treatment in terms of lowering impairment
- Safety issues (escalating doses, cardiac concerns, etc)
- Importance of having a multimodal approach to treatment
- Role of behavioral interventions (eg, parent management training in for children, cBT for adults)
- Importance of lifestyle modifications (eg, sleep, exercise)
- Medication selection and monitoring of response
- Possible need for referrals (eg, neuropsych testing, specialty providers, vocational services and/or disability)
ADULT PSYCHOEDUCATION EXAMPLES:

- “Adults with ADHD are often trying extremely hard and have the best of intentions, but because their brains have trouble keeping track of time, or remembering what they were in the middle of doing, the result is often failure and disappointment.”
- “A lifetime of ADHD behaviors and problems can lower self-esteem and affect your relationships. Individual counseling, medications and support groups can help.”
- “There are small, strategic changes we can help you make in your daily routine to compensate for these difficulties and help you become more successful at work and at home.”
Figure 1. Functional Outcomes of “Well Established” Psychosocial Treatments for ADHD Throughout Development.

*Treatments to be prioritized for this developmental period
NON-MEDICATION TREATMENT RECOMMENDATIONS FOR YOUTH

• Classroom interventions
  – Homework notebook, extended time for tasks, daily report card, reduced distractions (seat away from window, doors), frequent breaks, physical movement when possible, tutoring, help with creating organizational system, signal from teacher when off task, occupational therapy tools.
  – Classroom interventions effective in improving achievement scores, but benefits sustained only as long as interventions continued

• Training in skills deficits
  – Organization and planning
  – CBT for adolescents (builds organizational and management skill, set up for success to avoid distractibility, adaptive thinking strategies)
ADHD TREATMENT IN ADOLESCENTS

Review

Treatment of Attention-Deficit/Hyperactivity Disorder in Adolescents
A Systematic Review

Eugenia Chan, MD, MPH; Jason M. Fogler, PhD; Paul G. Hammerness, MD

CONCLUSIONS AND RELEVANCE Evidence supports the use of extended-release methylphenidate and amphetamine formulations, atomoxetine, and extended-release guanfacine to improve symptoms of ADHD in adolescents. Psychosocial treatments incorporating behavior contingency management, motivational enhancement, and academic, organizational, and social skills training techniques were associated with inconsistent effects on ADHD symptoms and greater benefit for academic and organizational skills. Additional treatment studies in adolescents, including combined pharmacological and psychosocial treatments, are needed.

CBT FOR ADULT ADHD

cBT emphasizes the interactive role of automatic thoughts, images and belief systems as well as behaviors in perpetuating symptoms of ADHD (small c, capital B to emphasize the behavioral component). Focus on helping the patient lay out specific functional treatment goals. Help the patient improve organizational, time-management, and problem-solving skills by:

• Chunking large tasks into smaller steps
• Introducing a daily planner and emphasizing use of one planner or notebook only
• Manage to-do’s using assistive devices, such as mobile phones
• Starting tasks well in advance of their deadline
• Reducing distraction (i.e. clutter-free desktop, windowless and quiet space to work, etc.)
• List-making and task prioritization
• Self-monitoring with regular completion of behavioral check-lists and logging
• Target behaviors as they come up in session, such as arriving late for appointments or losing homework
MEDICATION TREATMENT FOR ADHD
TREATMENT SEQUENCING

• Starting with behavioral therapy instead of medication therapy may improve treatment outcomes

Behavioral and pharmacological treatments for children with attention deficit/hyperactivity disorder (ADHD) were evaluated to address whether endpoint outcomes are better depending on which treatment is initiated first and, in case of insufficient response to initial treatment, whether increasing dose of initial treatment or adding the other treatment modality is superior.

Children with ADHD (ages 5–12, N = 146, 76% male) were treated for 1 school year. Initially randomized to parent management training or low dose methylphenidate. After 8 weeks insufficient responders were re-randomized to secondary interventions that either increased the dose/intensity of the initial treatment or added the other treatment.

The group beginning with behavioral treatment displayed significantly lower rates of observed classroom rule violations (the primary outcome) at study endpoint and tended to have fewer out-of-class disciplinary events. Further, adding medication secondary to initial behavior modification resulted in better outcomes on the primary outcomes and parent/teacher ratings of oppositional behavior than adding behavior modification to initial medication.

Normalization rates on teacher and parent ratings were generally high. Parents who began treatment with behavioral parent training had substantially better attendance than those assigned to receive training following medication. Beginning treatment with behavioral intervention produced better outcomes overall than beginning treatment with medication.

MULTIMODAL TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER STUDY (MTA)

• 600 children, 7-9 yo

• Treatment modes:
  
  – intensive medication management (methylphenidate tid, other drugs if necessary; algorithmic adjustments; general advice and readings);
  
  – intensive behavioral treatment alone (parent training; structured teacher consultation; full time summer treatment program; half time classroom behavioral specialist);
  
  – a combination of both;
  
  – routine community care (the control group).

The MTA Cooperative Group. A 14-month Randomized Clinical Trial of Treatment Strategies for Attention-Deficit/Hyperactivity Disorder. Arch Gen Psychiatry 1999; 56: 1073-1086.
MTA AT 14 MONTHS

• Combination treatment and medication management are superior to behavior management and community care.

• Combination treatment is better for certain areas of functioning:
  – oppositional/aggressive symptoms, anxiety symptoms, reading achievement, parent-child relations, and social skills.

• 4% of patients stopped medications due to adverse effects.

The MTA Cooperative Group. A 14-month Randomized Clinical Trial of Treatment Strategies for Attention-Deficit/Hyperactivity Disorder. Arch Gen Psychiatry 1999; 56: 1073-1086.
MTA AT 14 MONTHS

- About 1 mg/kg optimal
- Those in combination treatment ended up on lower doses of medication than medication treatment alone group.
  - Medication management 32.3 mg/day
  - Combined care 28.7 mg/day

MTA AT 8 YEARS

• After initial 14 months of treatment, patients returned to community care.
• No outcome differences between original treatment groups at 8 years
• Despite overall maintenance of improvement in functioning relative to pretreatment, the MTA group as a whole was functioning significantly less well than the non-ADHD classmate sample. Sustained improvement is achievable, but not normalization.
• Children with behavioral, socio-economic, or intellect advantage or best response to treatment have the best prognosis.

PRESCHOOL ADHD TREATMENT STUDY (PATS)

- NIMH funded multi-center randomized efficacy trial
- 3-5.5 yo with severe ADHD unresponsive to 10 week psychosocial intervention
- 37/279 patient parents said behavioral treatment resulted in satisfactory improvement.

Outcomes: Stimulants were effective, but
- lower end doses (mean optimal methylphenidate dose 14.2 mg/day or 0.7 mg/kg)
- lower effect sizes
- higher rates of side effects (crabbiness, proneness to crying, irritability)

PATS at 6 years:
- Persistent ADHD diagnoses—89.9% still meeting diagnostic criteria for ADHD.
- Patients with comorbid ODD or conduct disorder had higher rates of ADHD.
- Girls experienced a steeper symptom decline (but girls’ baseline symptoms more severe).
- Hint of positive long-term benefit on parent ratings for those who completed the study.

ADHD: PHARMACOLOGICAL TREATMENT

**Stimulants**
- Methylphenidate
- Dexedrine
- Amphetamine compounds

**FDA Approved**

**Higher effect size than nonstimulant**

**Atomoxetine**

**FDA Approved**

**Alpha agonists**
- Guanfacine
- Clonidine
- Guan/Clon+stimulants

**FDA Approved**

**Pediatric Only**

**Antidepressants**
- Bupropion*
- Tricyclics*

**Weaker evidence**

**Not FDA approved**

**Modafinil**

*Off-label use.
STIMULANTS

• Medications for ADHD are dopaminergic or noradrenergic.

• Evidence exists for the protective effect of stimulants on comorbid disorders.
  – Depressive and anxiety disorders
  – Disruptive behavior
  – Family quality of life
  – Repeating a grade

STIMULANTS

• Can start with either a methylphenidate or an amphetamine product
  – Amphetamines FDA approved ≥ 3 yo
  – Methylphenidates FDA approved ≥ 6 yo
• Similar efficacy
• Side effects may be more pronounced with amphetamine products.
• Push a stimulant dose before moving on to next trial.
  – Avoid unsafe doses.

# IMMEDIATE RELEASE STIMULANTS

<table>
<thead>
<tr>
<th>Name</th>
<th>Duration of Action</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylphenidate (Ritalin, Methylin)</td>
<td>4-6 h</td>
<td></td>
</tr>
<tr>
<td>D-methylphenidate (Focalin)</td>
<td>4-6 h</td>
<td>*2x potency of methylphenidate</td>
</tr>
<tr>
<td>Mixed amphetamine salts (Adderall)</td>
<td>4-6 h</td>
<td></td>
</tr>
<tr>
<td>D-amphetamine (Zenzedi, ProCentra)</td>
<td>4-6 h</td>
<td>Liquid 5 mg/5 ml Approved ages 3-5</td>
</tr>
<tr>
<td>Methamphetamine Desoxyn</td>
<td>4-6 h</td>
<td>FDA-indicated for ADHD and obesity</td>
</tr>
<tr>
<td>Amphetamine (Evekeo)</td>
<td>4-6 h</td>
<td>Approved ages 3-5 FDA-indicated for ADHD, obesity, and narcolepsy</td>
</tr>
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# Long Acting Stimulants

<table>
<thead>
<tr>
<th>Name</th>
<th>Mode of Delivery</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritalin SR, Metadate ER, Methylin ER</td>
<td>Gradual release</td>
<td>4-8 h</td>
</tr>
<tr>
<td>Metadate CD</td>
<td>30% IR, 70% 3 h later</td>
<td>7-9 h</td>
</tr>
<tr>
<td>Ritalin LA</td>
<td>50% IR, 50% 4 h later</td>
<td>7-9 h</td>
</tr>
<tr>
<td>Quillivant XR</td>
<td>20% IR, 80% gradual release</td>
<td>8-10 h</td>
</tr>
<tr>
<td>Focalin XR</td>
<td>50% IR, 50% 4 h later</td>
<td>Up to 12 h</td>
</tr>
<tr>
<td>Concerta</td>
<td>22% IR, pump</td>
<td>Up to 12 h</td>
</tr>
<tr>
<td>Daytrana patch</td>
<td>Gradual release</td>
<td>3-5 h after removal</td>
</tr>
<tr>
<td>Adderall XR</td>
<td>50% IR, 50% 4 h later</td>
<td>8-12 h</td>
</tr>
<tr>
<td>Dexedrine spansule (dextroamphetamine)</td>
<td>50% IR, 50% gradual</td>
<td>10 h</td>
</tr>
<tr>
<td>Vyvanse</td>
<td>Activated in GI tract</td>
<td>10 h</td>
</tr>
<tr>
<td>Aptensio XR (methylphenidiate)</td>
<td>40% IR, 60% ER (may be sprinkled)</td>
<td>12 h</td>
</tr>
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</table>

Epocrates, accessed 3.2.2016
TREATMENT HIERARCHY

- If IR is not tolerated or ineffective, try XR and vice versa.
- If first stimulant class is unsuccessful, try the other class.
- If stimulants are ineffective, revisit diagnosis before proceeding to non-stimulants.
- Use a single medication when possible.
- Consider adding alpha agonists if response is suboptimal but increasing stimulant not possible due to side effects.
- Adding Strattera to stimulant generally not advised but may be useful in certain cases.
VARIABILITY IN ADHD CARE IN COMMUNITY-BASED PEDIATRICS

- 93% received medication, 13% received psychosocial treatment
- Half using rating scales during assessment
- Variability at patient but also practice level
- “Almost no ADHD care follows ADHD consensus guideline recommendations for treatment”
- “the proportion of children receiving psychosocial treatment was miniscule”

MEDICATION ADHERENCE AND CONTINUITY

• ½ of the children experienced their first 30-day gap in medication supply within the first 3 months of treatment
• Fewer than ½ of the parents had contact with their physicians within the first month of medication initiation with the average time being greater than 2 months
• The average time to the first medication change was over 3 months.
• Results indicated that early physician contact and titration were related to greater continuity and medication supply over a period of 1 year

ADHD TREATMENT IN INTEGRATIVE SETTINGS: THE UW INTEGRATED CARE MODEL
# Adverse Effects of ADHD Medications

<table>
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<tr>
<th>Adverse Effect</th>
<th>MPH&lt;sup&gt;1-5&lt;/sup&gt;</th>
<th>Amph.&lt;sup&gt;5-7&lt;/sup&gt;</th>
<th>ATX&lt;sup&gt;8-11&lt;/sup&gt;</th>
<th>Alpha-2 Agonists&lt;sup&gt;12-15&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>↓ Appetite/anorexia</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Abdominal pain</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Irritability</td>
<td>++</td>
<td>++</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Somnolence/asthenia</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Sleep problems/Insomnia</td>
<td>++</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Emotional lability</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tics</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Light-headed/Dizzy</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Increased heart rate</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Increased blood pressure</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
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</table>

SIDE EFFECTS OF STIMULANTS

• Appetite decrease, insomnia, headaches, stomachache, dry mouth, emotional lability/aggression, priapism
• Can cause a slowing in growth velocity for weight and height
• Adrenergic effect on heart rate (5bpm in MTA)
• Obtain baseline levels.
• Options: decrease dose, switch, augment (eg, add clonidine or melatonin for sleep)

SIDE EFFECTS: CARDIAC CONCERNS

- AHA says obtaining ECG reasonable.
- AAP does not recommend routine ECG.
  - Consider ECG when on high dose, combining medications, BP/pulse change from a medication, or any cardiac symptoms.

- ADHD medications do not appear to increase the risk of serious cardiovascular events.
  - 1,200,438 patients with ADHD prescription matched with 2 nonusers; 2,579,104 person years: hazard ratio 0.7.

Cooper at al. ADHD Drugs and Serious Cardiovascular Events in Children and Young Adults. NEJM 2011; 365 (20): 1896-904.
SIDE EFFECTS: CARDIAC CONCERNS

• Physical exam before initiating stimulant treatment
• Ask about palpitations, syncope, chest pain, exercise intolerance, family history of sudden death under age 35 (including drowning and motor vehicle accidents).
• Patients with known cardiac issues should be referred to cardiology before a stimulant trial.
• During treatment, monitor blood pressure and heart rate and ask about development of cardiac symptoms.

SIDE EFFECTS: TICS AND ADHD

• High comorbidity
  – Multi-site international database of 3500 tic disorder patients: 60% also have ADHD

• Stimulants and Tics
  – “Although stimulants have not been shown to worsen tics in most people with tic disorders, they may nonetheless exacerbate tics in individual cases. In these instances, treatment with alpha agonists or atomoxetine may be an alternative.”

--Cochrane Review, 2011

Treatment of Children With Attention-Deficit/Hyperactivity Disorder (ADHD) and Irritability: Results From the Multimodal Treatment Study of Children With ADHD (MTA)

Lorena Fernández de la Cruz, PhD, Emily Simonoff, MD, James J. McGough, MD, Jeffrey M. Halperin, PhD, L. Eugene Arnold, MD, MEd, Argyris Stringaris, MD, PhD, MRCPsych

Objective: Clinically impairing irritability affects 25% to 45% of children with attention-deficit/hyperactivity disorder (ADHD); yet, we know little about what interventions are effective in treating children with ADHD and co-occurring irritability. We used data from the Multimodal Treatment Study of Children With ADHD (MTA) to address 3 aims: to establish whether irritability in children with ADHD can be distinguished from other symptoms of oppositional defiant disorder (ODD); to examine whether ADHD treatment is effective in treating irritability; and to examine how irritability influences ADHD treatment outcomes.

Method: Secondary analyses of data from the MTA included multivariate analyses, and intent-to-treat random-effects regression models were used.

Results: Irritability was separable from other ODD symptoms. For treating irritability, systematic stimulant treatment was superior to behavioral management but not to routine community care; a combination of stimulants and behavioral treatment was superior to community care and to behavioral treatment alone, but not to medication alone. Irritability did not moderate the impact of treatment on parent- and teacher-reported ADHD symptoms in any of the 4 treatment groups.

Conclusion: Treatments targeting ADHD symptoms are helpful for improving irritability in children with ADHD. Moreover, irritability does not appear to influence the response to treatment of ADHD.

Clinical trial registration information—Multimodal Treatment Study of Children With Attention Deficit and Hyperactivity Disorder (MTA); http://www.clinicaltrials.gov; NCT00000388.

Key Words: irritability, attention-deficit/hyperactivity disorder, oppositional defiant disorder, treatment outcomes

SIDE EFFECTS: ADHD AND IRRITABILITY

• Recent publication from the MTA examined irritability (not headstrong oppositional behavior) and treatment outcomes.
  
  – Irritability contributed to impairment and showed longitudinal continuity.

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<tr>
<th>Intervention</th>
<th>Effect Size</th>
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<tr>
<td>Combined treatment</td>
<td>0.82</td>
</tr>
<tr>
<td>Medication management</td>
<td>0.63</td>
</tr>
<tr>
<td>Community comparison</td>
<td>0.48</td>
</tr>
<tr>
<td>Behavioral treatment</td>
<td>0.42</td>
</tr>
</tbody>
</table>

SIDE EFFECTS: ADHD AND SLEEP

Stimulant Medications and Sleep for Youth With ADHD: A Meta-analysis

Katherine M. Kidwell, MA, Tori R. Van Dyk, MA, Alyssa Lundahl, MA, Timothy D. Nelson, PhD

abstract

**CONTEXT:** Mixed findings exist on whether stimulant medications alter youth sleep.

**OBJECTIVE:** To determine the effect of stimulant medications on sleep.

**DATA STUDIES:** Studies published through March 2015 were collected via CINAHL, PsycINFO, and PubMed. References of retrieved articles were reviewed.

**STUDY SELECTION:** Eligibility criteria included studies with children/adolescents who had attention-deficit/hyperactivity disorder (ADHD), random assignment to stimulants, and objective sleep measurement. Studies that did not include information about key variables were excluded.

**DATA EXTRACTION:** Study-level, child-level, and sleep data were extracted by 2 independent coders. Effect sizes were calculated by using random effects models. Potential moderators were examined by using mixed effect models.

**RESULTS:** A total of 9 articles (N = 246) were included. For sleep latency, the adjusted effect size (0.54) was significant, indicating that stimulants produce longer sleep latencies. Frequency of dose per day was a significant moderator. For sleep efficiency, the adjusted effect size (−0.32) was significant. Significant moderators included length of time on medication, number of nights of sleep assessed, polysomnography/actigraphy, and gender. Specifically, the effect of medication was less evident when youth were taking medication longer. For total sleep time, the effect size (−0.59) was significant, such that stimulants led to shorter sleep duration.

**LIMITATIONS:** Limitations include few studies, limited methodologic variability, and lack of unpublished studies.

**CONCLUSIONS:** Stimulant medication led to longer sleep latency, worse sleep efficiency, and shorter sleep duration. Overall, youth had worse sleep on stimulant medications. It is recommended that pediatricians carefully monitor sleep problems and adjust treatment to promote optimal sleep.

ATOMOXETINE

• Brand name: Strattera
• Noradrenergic reuptake inhibitor
• Once daily or twice daily dosing
• Start at 0.5 mg/kg/day for 2 weeks. Increase to 1.2 mg/kg/day.
• Maximum 100 mg or 1.4 mg/kg (whichever is less).
• Metabolized by P450 2D6 pathway
• Approved ≥ 6 yo

ATOMOXETINE

• Can be helpful to anxiety

• Can take up to 6 weeks for benefit
  – Counsel family on delayed effect compared to stimulants.

• Effect size 0.6 (similar to guanfacine)
  – For comparison, effect size of stimulants approximately 0.9
  – For reference, effect size 0.2 is mild, 0.6 is moderate, and 0.8 is high.

Fig. 1 Temporal course of changes in the Attention-Deficit/Hyperactivity Disorder Rating Scale–IV–Parent Version: Investigator Administered and Scored (ADHD-RS total score). Unlike moderate/nonresponders (filled diamonds), much improved responders (filled squares) experienced sharp decreases (i.e., improvements) in the ADHD-RS total score within the first 1 to 4 weeks, with continued divergence at later time points. *p < .001 at each time point across response groups by week.

ATOMOXETINE SIDE EFFECTS

• GI distress, sedation (insomnia in adults)
• Possible suppression in growth velocity
• Not recommended if structural cardiac abnormalities, cardiomyopathy, or rhythm abnormalities
• Warning for liver disease (2 reports; none in 6000 patients in clinical trial)
  – Monitoring of LFTs not recommended.
• Boxed warning for suicidal thinking (risk of 4/1000 in a large controlled study); no completed suicides

ALPHA AGONISTS

- May be more effective for hyperactivity than inattention
- Clonidine more soporific; guanfacine may be better for inattention
- Soporific effect may wane after 2-3 weeks
- May not see full benefit for 4-6 weeks
- Sedation, dizziness, hypotension, bradycardia
- Review personal and family cardiac history
- Review risk of rebound hypertension
<table>
<thead>
<tr>
<th></th>
<th>Starting dose</th>
<th>Maximum dose</th>
<th>Half life</th>
<th>FDA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guanfacine</strong></td>
<td>&lt;45kg, 0.5 mg qhs; &gt;45 kg, 1 mg qhs</td>
<td>2 mg (27-40.5 kg); 3 mg (40.5-45 kg); 4 mg (&gt;45 kg)</td>
<td>14 h</td>
<td>Not approved</td>
</tr>
<tr>
<td><strong>Guanfacine extended release</strong></td>
<td>1 mg daily</td>
<td>From 3 mg (25 kg) to 7 mg (58.5 Kg and above) Alt: 0.05-0.12 mg/kg</td>
<td>16 h</td>
<td>Approved 6-17yo</td>
</tr>
</tbody>
</table>

Wait one week between dose increases.

# CLONIDINE

<table>
<thead>
<tr>
<th></th>
<th>Starting dose</th>
<th>Maximum dose</th>
<th>Half life</th>
<th>FDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonidine</td>
<td>&lt;45kg, 0.05 mg qhs</td>
<td>0.2 mg (27-40 kg);</td>
<td>12 h</td>
<td>Not approved</td>
</tr>
<tr>
<td></td>
<td>&gt;45 kg, 0.1 mg qhs</td>
<td>0.3 mg (40-45 kg);</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4 mg (&gt;45 kg).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonidine extended release (Kapvay)</td>
<td>0.1 mg qhs; doses greater than 0.1 mg should be bid</td>
<td>0.4 mg</td>
<td>12-16 h</td>
<td>Approved 6-17yo</td>
</tr>
</tbody>
</table>

Wait one week between dose increases.

BUPROPION

• Brand name: Wellbutrin
• Not FDA approved for pediatric use
• Combined dopaminergic/noradrenergic mechanism of action
• Consider when primary treatments have failed or in patients with co-occurring mood disorders, substance abuse, or smoking.

BUPROPION

• Side effects: insomnia, appetite decrease, less commonly tics, seizures
• Risk of drug induced seizures increases 10x at doses > 450 mg/day
• Starting dose less than 150 mg/day or 3mg/kg/day
• Maximum dose less than 300 mg/day or 6 mg/kg/day
• No single dose greater than 150 mg

ALTERNATIVE TREATMENTS

• Omega-3s: some evidence for benefit based upon meta-analyses (effect size: 0.31)

• Dietary: Elimination of food dye may provide small benefit in sensitive patients

• Neurofeedback and computer training: Some evidence but not well-established; remains controversial

• Physical exercise: evidence for benefit for executive functioning and behavioral disturbances