Practical Tips on Psychopharmacology

Behavioral Health Symposium

May 20, 2017

Sponsored by the 1998 Society and the Children’s Healthcare of Atlanta Behavioral Health Initiative

Jennifer Holton, MD
Assistant Professor
Department of Psychiatry and Behavioral Sciences
Emory University School of Medicine
Common Questions

How do I know which medication to prescribe?

What doses do I use?

What should I be on the lookout for?

  Side effects (black box warning)

  Medication interactions

  Monitoring

When should I refer?
Overview

ADHD medications
Antidepressants
Anxiolytics
Mood Stabilizers
Antipsychotics
ADHD Medications

Stimulants
Non-Stimulants
ADHD Treatment

What is the recommended treatment for ADHD in pediatric patients?

Preschool-Aged Children (4-5)

– Behavior therapy / parent-training program
  • If not available, consider risks of medication vs harm of delaying treatment
  • If insufficient, may prescribe Methylphenidate per the 2011 American Academy of Pediatrics Clinical Practice Guideline on ADHD (based on PATS); Adderall, Evekeo, ProCentra, and Zenzedi are FDA-Approved for > 3 yr olds

School-Aged Children (6-18)

– Medication that is FDA-Approved for ADHD +/- Therapy
  • Stimulants (Effect Size 1.0)
  • Atomoxetine, Extended Release Guanfacine/Clonidine (Effect Size 0.7)
ADHD Medications

Before Starting ADHD Medications

• Physical Exam including vital signs (height, weight, BP, pulse)

• Review Medical & Family History (particularly personal/family cardiovascular hx)
  – Preexisting cardiac/vascular disease, cardiac symptoms (chest pain, palpitations, dyspnea, near syncope, syncope), arrhythmias, structural cardiac abnormalities, sudden death of young family members, cardiac murmurs, hypertrophic cardiomyopathy, Wolf-Parkinson-White syndrome, long QT syndrome, QT prolonging medications, Marfan syndrome, etc
  – If present, further evaluation is warranted (ECG; consider cardiology referral)

Monitoring on ADHD Medications

• Height, weight, blood pressure, pulse
  – For alpha 2 agonists, if baseline pulse <60 or BP is > or < 2 standard deviations from age and gender adjusted means on 2 repeated evaluations, more detailed evaluation is needed

• Monitor symptoms and potential side effects
  – Can use scales [ie: Conners ($) or Vanderbilt (free)] to track symptoms
  – Further evaluation if cardiovascular symptoms arise
ADHD Medications – Stimulants

First-Line / Strongest Evidence for Effectiveness

• Effect Size 1.0 (0.4-0.8 in preschoolers)

Two Classes

• Methylphenidate Derivatives or Amphetamine Derivatives

With multiple formulations and delivery options

• Short, Intermediate, and Long-acting formulations

• Patch, Liquid, Tablets, Capsules (some that can be opened and sprinkled or dissolved; some that must be swallowed whole)
# ADHD Medications – Stimulants

## Methylphenidate Derivatives

### ADHD Medication Guide*

**Revised: December 2016**

<table>
<thead>
<tr>
<th>Methylphenidate Derivatives – Long Acting/Extended Release*</th>
</tr>
</thead>
</table>
| **Ritalin® La**  
8.5mg  
10mg |
| **Methylphenidate CD**  
20mg |
| **Methylphenidate ER**  
20mg |

### Methylphenidate Derivatives – Short Acting/Immediate Release*

<table>
<thead>
<tr>
<th>Methylphenidate Derivatives</th>
</tr>
</thead>
</table>
| **Focalin®**  
2.5mg |
| **Ritalin®**  
5mg  
10mg |
| **Methylphenidate Chewable**  
2.5mg  
5mg  
10mg |
| **Methyl® Solution**  
5mg  
10mg |

*Indicates a generic formulation is available; generic products are not shown.

---

http://www.adhdmedicationguide.com/  
developed by Dr. Andrew Adesman at Cohen Children's Medical Center of New York
# ADHD Medications – Stimulants

**Amphetamine Derivatives**

<table>
<thead>
<tr>
<th>Amphetamine Derivatives – Long Acting/Extended Release**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dyrenium® XR</strong> (controlled release)</td>
</tr>
<tr>
<td><strong>Adderall XR</strong> (immediate release)</td>
</tr>
<tr>
<td><strong>Vyvanse®</strong> (oral suspension)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Amphetamine Derivatives – Short Acting/Immediate Release**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Express®</strong> (2.5 mg amphetamine sulfate)</td>
</tr>
<tr>
<td><strong>Focalin®</strong> (5 mg amphetamine sulfate)</td>
</tr>
<tr>
<td><strong>Adderall®</strong> (immediate release)</td>
</tr>
<tr>
<td><strong>ProCentra®</strong> (dextroamphetamine aspartate)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-Stimulants**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intuniv®</strong> (guanfacine extended release)</td>
</tr>
<tr>
<td><strong>Capvay®</strong> (capsules, extended release)</td>
</tr>
<tr>
<td><strong>Strattera®</strong> (atomoxetine)</td>
</tr>
</tbody>
</table>

**Important:** Medications have been arranged on the card for ease of display and comparison; dosing equivalences cannot be ascertained. Practitioners should refer to the FDA-approved product information to learn more about each medication.

**Administration Key:**
- Chewable
- Must be swallowed whole
- Slowly disintegrating tablet
- Can be mixed with yogurt, orange juice, or orangeade
- Can open capsule and sprinkle medication on applesauce

http://www.adhdmedicationguide.com/
developed by Dr. Andrew Adesman at Cohen Children's Medical Center of New York
ADHD Medications – Stimulants

How do I choose a stimulant?

Similar efficacy regardless of class/formulation

Can start with either class

Choose based on what type of formulation might be best

i.e.: can the child swallow pills, how long does the medication need to last, has the patient or a family member had a positive/adverse response, concern for possible substance use d/o, cost/insurance coverage, etc.

What if the first stimulant doesn’t work?

Non-responders to one class will often respond to the other class

Switch to other class
ADHD Medications – Stimulants

Side effects / risks include:

• Decreased appetite
• Abdominal pain, stomach upset
• Headaches
• Insomnia
• Decreased growth velocity (1-2cm)
• Weight loss
• Increase in blood pressure / pulse
• Sudden cardiac death (in those with structural abnormalities or other serious cardiovascular issues)
• Tics
• Mood changes (lability, irritability, dysphoria, blunted affect, worsened anxiety)
• Psychosis
• Risk of misuse/abuse/diversion
ADHD Medications – Atomoxetine

Benefits

• Not a controlled substance; low abuse potential
• Doesn’t share some of stimulant SE (ie: less insomnia/weight loss)
• May also have some benefit on anxiety, mood, behavior in addition to ADHD

Risks / Side Effects / Potential Negatives include:

• Has to be taken daily; requires titration; can take 2-6 weeks to become effective
• Metabolized by 2D6; careful with 2D6 inhibitors (ie: fluoxetine, paroxetine)
• Side effects include: somnolence, GI distress, decreased appetite, mild increase in BP/pulse, increased suicidal thoughts (rare), hepatotoxicity (rare)
• Typically once daily dosing, but divided dosing (BID) can help with tolerability
ADHD Medications – Alpha 2 agonists
(Guanfacine/Intuniv and Clonidine/Kapvay)

Benefits

• Useful when stimulants cannot be tolerated or are ineffective
• May be used as monotherapy or as adjunctive therapy with stimulants
• May also help with tics, aggression, sleep, and overarousal in addition to ADHD symptoms

Side effects / risks include:

• Sedation, dry mouth, dizziness, hypotension, decreased pulse, rebound hypertension, depression/irritability, sleep disruption, dermatitis with patch
• Guanfacine tends to cause less sedation and fewer CV side effects than Clonidine
• Extended release formulations have less effect on blood pressure and pulse than immediate release formulations
• All should be tapered to discontinue rather than stopping abruptly
<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Initial Titration Dose</th>
<th>Frequency</th>
<th>Time to Initial Effect</th>
<th>Duration, h</th>
<th>Maximum Dose</th>
<th>Available Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed amphetamine</td>
<td>Adderall&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.5–5.0 mg</td>
<td>QD–BID</td>
<td>20–60 min</td>
<td>6</td>
<td>40 mg</td>
<td>5.0-, 7.5-, 10.0-, 12.5-, 15.0-, 20.0-, and 30.0-mg tablets</td>
</tr>
<tr>
<td>salts</td>
<td>Adderall XR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>10</td>
<td>40 mg</td>
<td>5-, 10-, 15-, 20-, 25-, and 30-mg capsules</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>Dextrostat</td>
<td>2.5 mg</td>
<td>BID–TID</td>
<td>20–60 min</td>
<td>4–6</td>
<td>40 mg</td>
<td>5- and 10-mg (Dextrostat only) tablets</td>
</tr>
<tr>
<td></td>
<td>Dextedrine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 mg</td>
<td>QD–BID</td>
<td>≥60 min</td>
<td>≥6</td>
<td>40 mg</td>
<td>5-, 10-, and 15-mg capsules</td>
</tr>
<tr>
<td>Lisdexamfetamine</td>
<td>Vyvanse</td>
<td>20 mg</td>
<td>QD</td>
<td>60 min</td>
<td>10–12</td>
<td>70 mg</td>
<td>20-, 30-, 40-, 50-, 60-, and 70-mg capsules</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>Concerta</td>
<td>18 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>12</td>
<td>54 mg (&lt;13 y); 72 mg (≥13 y)</td>
<td>18-, 27-, 36-, and 54-mg capsules</td>
</tr>
<tr>
<td></td>
<td>Methyl ER</td>
<td>10 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>8</td>
<td>60 mg</td>
<td>10- and 20-mg tablets</td>
</tr>
<tr>
<td></td>
<td>Methylin</td>
<td>5 mg</td>
<td>BID–TID</td>
<td>20–60 min</td>
<td>3–5</td>
<td>60 mg</td>
<td>5-, 10-, and 20-mg tablets and liquid and chewable forms</td>
</tr>
<tr>
<td></td>
<td>Daytrana</td>
<td>10 mg&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Apply for 9 h</td>
<td>60 min</td>
<td>11–12</td>
<td>30 mg</td>
<td>10-, 15-, 20-, and 30-mg patches</td>
</tr>
<tr>
<td></td>
<td>Ritalin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 mg</td>
<td>BID–TID</td>
<td>20–60 min</td>
<td>3–5</td>
<td>60 mg</td>
<td>5-, 10-, and 20-mg tablets</td>
</tr>
<tr>
<td></td>
<td>Ritalin LA</td>
<td>20 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>6–8</td>
<td>60 mg</td>
<td>20-, 30-, and 40-mg capsules</td>
</tr>
<tr>
<td></td>
<td>Ritalin SR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20 mg</td>
<td>QD–BID</td>
<td>1–3 h</td>
<td>2–6</td>
<td>60 mg</td>
<td>20-mg capsules</td>
</tr>
<tr>
<td></td>
<td>Metadate CD</td>
<td>20 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>6–8</td>
<td>60 mg</td>
<td>10-, 20-, 30-, 40-, 50-, and 60-mg capsules</td>
</tr>
<tr>
<td></td>
<td>Dexamphetamine</td>
<td>2.5 mg</td>
<td>BID</td>
<td>20–60 min</td>
<td>3–5</td>
<td>20 mg</td>
<td>2.5-, 5-, and 10.0-mg tablets</td>
</tr>
<tr>
<td></td>
<td>Focalin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.5 mg</td>
<td>QD–BID</td>
<td>20–60 min</td>
<td>1–2 wk</td>
<td>At least 10–12 h</td>
<td>1.4 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Focalin XR</td>
<td>5 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>8–12</td>
<td>30 mg</td>
<td>10-, 18-, 25-, 40-, 60-, 80-, and 100-mg capsules</td>
</tr>
<tr>
<td></td>
<td>Atomoxetine</td>
<td>0.5 mg/kg per d, then increase to 1.2 mg/kg per d; 40 mg/d for adults and children at &gt;154 lb, up to 100 mg/d</td>
<td>QD–BID</td>
<td>1–2 wk</td>
<td>At least 10–12 h</td>
<td>1.4 mg/kg</td>
<td>10-, 18-, 25-, 40-, 60-, 80-, and 100-mg capsules</td>
</tr>
<tr>
<td></td>
<td>Strattera</td>
<td>1 mg/d</td>
<td>QD</td>
<td>1–2 wk</td>
<td>At least 10–12 h</td>
<td>4 mg/d</td>
<td>1-, 2-, 3-, and 4-mg tablets</td>
</tr>
<tr>
<td></td>
<td>Intuniv</td>
<td>0.1 mg/d</td>
<td>QD</td>
<td>1–2 wk</td>
<td>At least 10–12 h</td>
<td>0.4 mg/d</td>
<td>0.1- and 0.2-mg tablets</td>
</tr>
</tbody>
</table>

QD indicates daily; BID, twice daily; TID, three times daily.  
<sup>a</sup> Available in a generic form.  
<sup>b</sup> Dosages for the dermal patch are not equivalent to those of the oral preparations.  

## ADHD Medications – Dosing for Additional Newer FDA-Approved Stimulant Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Initial Dose</th>
<th>Titration</th>
<th>Max Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>Evekeo (tabs – shortacting)</td>
<td>2.5 or 5mg qd-BID(^1)</td>
<td>2.5 or 5mg q wk</td>
<td>40mg/d</td>
</tr>
<tr>
<td></td>
<td>Dyanavel XR (liquid 2.5mg/mL)</td>
<td>2.5-5mg qAM</td>
<td>2.5-10mg q 4-7 d</td>
<td>20mg/d</td>
</tr>
<tr>
<td></td>
<td>Adzenys XR-ODT (ODT)</td>
<td>6.3mg qAM</td>
<td>3.1 or 6.3mg q wk</td>
<td>18.8mg/d (6-12 yrs) 12.5mg/d (13-17 yrs)</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>Zenzedi (tabs – shortacting)</td>
<td>2.5 or 5mg qd-BID(^1)</td>
<td>2.5 or 5mg q wk</td>
<td>40mg/d</td>
</tr>
<tr>
<td></td>
<td>ProCentra (liquid 5mg/5mL - short)</td>
<td>2.5 or 5mg qd-BID(^1)</td>
<td>2.5 or 5mg q wk</td>
<td>40mg/d</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>Aptensio XR (cap 40 IR / 60 ER)</td>
<td>10mg qAM</td>
<td>10mg q wk</td>
<td>60mg/d</td>
</tr>
<tr>
<td></td>
<td>Quillivant XR (liquid 25mg/5mL)</td>
<td>20mg qAM</td>
<td>10-20mg q wk</td>
<td>60mg/d</td>
</tr>
<tr>
<td></td>
<td>Qullichew ER (chewable 30 IR / 70 ER)</td>
<td>20mg qAM</td>
<td>10-20mg q wk</td>
<td>60mg/d</td>
</tr>
</tbody>
</table>

\(^1\) 2.5mg for 3-5 yr olds and 5mg for 6+ yr olds
Antidepressant Medications

SSRIs
SNRIs
Others
Antidepressants

When should I use antidepressants for pediatric depression/anxiety?

- Depression / Anxiety
  - Mild: Therapy
  - Moderate-Severe: Therapy (CBT or IPT) and Medication (SSRI)
Antidepressants – SSRIs

What should I consider before starting an SSRI?

• Any personal or family history of mania, hypomania, or bipolar disorder; antidepressants can induce mania
• Any suicidality (past or present); document and follow closely
• Any current somatic/physical symptoms, especially ones that could later be mistaken for medication side effects
• Other medications – think about cytochrome P450 inhibition and potential drug-drug interactions
Antidepressants – SSRIs

How do I choose which SSRI to prescribe?

• FDA-Indications
• Evidence Base
• Other Factors:
  – side effect profiles
  – drug-drug interactions
  – duration of action and patient compliance
  – positive/negative response by a first degree relative
  – patient/family preference
# Antidepressants – SSRIs

## Pediatric Depression

**FDA-Approval:**
- **Escitalopram** (12+), **Fluoxetine** (8+)

**Evidence Base:**
- Positive RCTs for Citalopram, Escitalopram, Fluoxetine, Sertraline
- Negative trials for Paroxetine

## Pediatric Anxiety

**FDA-Approval:**
- Only for OCD: **Fluoxetine** (7+), Fluvoxamine (8+), Sertraline (6+)
- No FDA-Approved SSRIs for non-OCD anxiety disorders (SNRI Duloxetine is FDA-approved for GAD)

**Evidence Base:**
- Positive RCTs for **Fluoxetine**, Fluvoxamine, Paroxetine, **Sertraline**
- Open label and retrospective studies also support Citalopram / Escitalopram
Antidepressants – SSRIs

When starting an SSRI, discuss and document the following:

Risks, benefits, alternatives
FDA approval status
Black Box Warning for suicidality

2004 review of all pediatric randomized placebo-controlled trials of antidepressant medications found an increased incidence of suicidal thoughts/behaviors in the medication group (4%) vs the placebo group (2%); no one committed suicide; FDA issued black-box warning that antidepressants may increase suicidal thinking/behaviors in youth (up to age 24)

Emergency services / safety plan

Start with a low dose
Monitor frequently in the beginning
Antidepressants – SSRIs

FDA Recommended Monitoring Schedule:

<table>
<thead>
<tr>
<th>1st Month</th>
<th>2nd Month</th>
<th>3rd Month</th>
<th>Thereafter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly</td>
<td>Q 2 weeks</td>
<td>Monthly</td>
<td>As clinically indicated</td>
</tr>
</tbody>
</table>

At these visits:

Assess response and tolerability

Assess and document any suicidal thoughts, intent, or plan; respond with your treatment plan accordingly (ie: continued outpatient treatment versus need for a higher level of care)
Antidepressants – SSRIs

Side Effects / Risks Include:

- **GI side effects** (nausea, vomiting, diarrhea, dyspepsia), change in appetite, weight gain/loss, sweating, dry mouth, bruxism, headaches, dizziness, irritability, insomnia, hypersomnia, fatigue, restlessness, tremor, akathisia, skin rashes, increased bruising/bleeding, mania, hyperactivity, vivid/strange dreams, sexual side effects, **suicidality** (black box warning)

- **Serotonin syndrome**
  - agitation, restlessness, confusion/delirium, diaphoresis, tachycardia, hypertension, hyperthermia, vomiting, diarrhea, dilated pupils, tremor, muscle rigidity, myoclonus, hyperreflexia, loss of muscle coordination, ataxia, headache, shivering, seizures, dilated pupils

- **Activation/Disinhibition**
  - hyperactivity, agitation, defiance, irritability, angry outbursts, heightened emotional reactivity, nervousness

- **Discontinuation Syndrome if stopped abruptly**
  - Flu-like symptoms (headache, diarrhea, nausea, vomiting, chills, dizziness, fatigue), irritability, agitation, electrical / shock-like sensations
Antidepressants – SSRIs

How do I start and titrate SSRIs?

• Starting dose can vary depending on several factors including age, prior medication exposure/experience, and concern for side effects
• Titration can vary depending on several factors including symptom severity, time to steady state, effectiveness, tolerability/side effects
• Starting low and titrating up gradually improves tolerability and minimizes adverse events
• Therapeutic effects can take from 2-8 weeks
  – Need 1-2 months at max tolerated dose for adequate trial (longer in OCD)
• Taper to discontinue
## Antidepressants – SSRIs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Formulations</th>
<th>Initial dose</th>
<th>Target Dose in Children</th>
<th>Target Dose in Adolescents</th>
<th>Max dose</th>
<th>FDA Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>Tablet: 10 mg, 20 mg, 40 mg Solution: 10 mg/5 mL</td>
<td>10</td>
<td>20–40</td>
<td>20–40</td>
<td>40</td>
<td>Depression (Adult)</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Tablet: 5 mg, 10 mg, 20 mg Solution: 5 mg/5 mL</td>
<td>2.5-5-10</td>
<td>10–20</td>
<td>10–20</td>
<td>20</td>
<td>Depression (12+) GAD (Adult)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Capsule: 10 mg, 20 mg, 40 mg Tablet: 10 mg Solution: 20 mg/5 mL</td>
<td>5-10</td>
<td>10–20</td>
<td>20–40</td>
<td>60</td>
<td>Bulimia (Adult) Depression (8+) OCD (7+) PD (Adult)</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Tablet: 25 mg, 50 mg, 100 mg</td>
<td>25</td>
<td>50–200</td>
<td>50–200</td>
<td>200</td>
<td>OCD (8+)</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Tablet: 10, 20, 30, 40 mg Tablet CR: 12.5, 25, 37.5 mg Suspension: 10 mg/5 mL</td>
<td>10</td>
<td>10–20</td>
<td>20–40</td>
<td>30 50</td>
<td>Depression (Adult) GAD (Adult) OCD (Adult) PD (Adult) PMDD (Adult) PTSD (Adult) SOC (Adult)</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Tablet: 25 mg, 50 mg, 100 mg Solution: 20 mg/mL</td>
<td>12.5–25</td>
<td>25–150</td>
<td>50–200</td>
<td>200</td>
<td>Depression (Adult) OCD (6+) PD (Adult) PMDD (Adult) PTSD (Adult) SOC (Adult)</td>
</tr>
</tbody>
</table>

Dosing in mg
Antidepressants – SSRIs:

Example Titration Schedules:

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting Dose</th>
<th>Titration Schedule</th>
<th>Final Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escitalopram</td>
<td>2.5-5-10mg</td>
<td>Increase by 5mg q 1-4 weeks to a max of 20mg/d</td>
<td>Titrate until symptoms significantly improved / resolved, side effects emerge, or maximum recommended dose reached</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>5-10-20mg</td>
<td>Increase by 5-10mg q 1-2 weeks (or 20mg q month) to a max of 60mg/d</td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td>12.5-25-50mg</td>
<td>Increase by 25-50mg q week to a max of 150-200mg/d</td>
<td></td>
</tr>
</tbody>
</table>
Antidepressants – SSRIs

What if the SSRI doesn’t work?

No Response
- Assess adherence and adequacy of dose/duration
- Increase to max dose if tolerated
- Switch to different medication (SSRI>SNRI) if at maximum dose
- Add/increase therapy
- Reevaluate diagnosis/comorbidities

Partial Response
- Assess adherence and adequacy of dose/duration
- Increase to max dose if tolerated
- Switch to different medication (SSRI>SNRI) if at maximum dose
  OR augment
- Add/increase therapy

Can refer to a child and adolescent psychiatrist at any point
Antidepressants – SSRIs

How long do I continue the SSRI if it is working well?

• Continue for 1 year
• Then reassess continued need
• Consider gradual taper/discontinuation during a period of low stress
• CBT may decrease risk of relapse
Antidepressants – SNRIs

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)
Duloxetine, Venlafaxine XR

Evidence to support efficacy but may have more side effects than SSRIs in pediatric population

Typically considered after two failed SSRI trials

Duloxetine is FDA-approved for GAD in those >7

Have to monitor blood pressure and pulse
Antidepressants – Others

Bupropion
Some evidence in pediatric depression (open-label) but no RCTs

Mirtazapine
No real evidence to support its efficacy in pediatric population

Tricyclic Antidepressants (TCAs)
Amitriptyline, Clomipramine, Doxepin, Imipramine, Nortriptyline
Evidence for Clomipramine in pediatric OCD; mixed evidence for treatment of pediatric anxiety disorders; negative trials in pediatric depression
Potentially dangerous (QTc prolongation); requires monitoring (EKG, labs)
Not often used given limited evidence and concerning risks; DO NOT use for pediatric depression
Anxiolytics

Benzodiazepines
Buspirone
Hydroxyzine
Beta Blockers
Anxiolytics

Benzodiazepines
Evidence base in children/adolescents is limited; some benefit but generally not statistically significant; use should be short-term

Buspirone
Some case reports and open-label studies in children/adolescents have shown benefit but RCTs have not found significant differences from placebo

Hydroxyzine
Evidence base is limited but used for short-term treatment of anxiety/insomnia

Beta Blockers
Evidence base limited but sometimes used for performance anxiety, somatic symptoms of anxiety
Summary
Summary

ADHD:
Stimulants are first-line for those ≥6 yrs old; choose from one family (methylphenidate or amphetamine based); if ineffective, try the other family, or if not tolerated, try Atomoxetine or extended-release Guanfacine or Clonidine

Depression/Anxiety:
SSRIs are first-line for moderate-severe; if first SSRI is ineffective, try a 2nd one (and add psychotherapy if not already engaged in psychotherapy)

When to Refer:
If the symptoms are severe or the child is having poor response to first-line treatments, consider referral to a child psychiatrist
References
Primary References


Cheung A, Zuckerbrot RA, Jensen PS, et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): part II—treatment and ongoing management. Pediatrics. 2007;120(5). Available at: [www.pediatrics.org/cgi/content/full/120/5/e1313](www.pediatrics.org/cgi/content/full/120/5/e1313)


Zuckerbrot RA, Cheung AH, Jensen PS, Stein REK, Laraque D; GLAD PC Steering Group. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): part I—identification, assessment, and initial management. Pediatrics. 2007;120(5). Available at: [www.pediatrics.org/cgi/content/full/120/5/e1299](www.pediatrics.org/cgi/content/full/120/5/e1299)
Additional Materials for Reference
ADHD Medications – Stimulants

Cardiovascular Monitoring
American Academy of Pediatrics
2008 Policy Statement on Cardiovascular Monitoring and Stimulant Drugs for ADHD

FIGURE 1
Cardiac evaluation of children and adolescents receiving or being considered for stimulant medications.

Found at http://pediatrics.aappublications.org/content/pediatrics/122/2/451.full.pdf
# Antidepressants – SNRIs

<table>
<thead>
<tr>
<th></th>
<th>Duloxetine (Cymbalta)</th>
<th>Venlafaxine XR (Effexor XR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA Approval</td>
<td>GAD ≥7</td>
<td>No (but + studies in GAD, SOC, MDD)</td>
</tr>
<tr>
<td>Initial Dose</td>
<td>30mg daily or 20mg BID</td>
<td>37.5mg</td>
</tr>
<tr>
<td>Target Dose</td>
<td>40-60mg</td>
<td>150-225mg</td>
</tr>
<tr>
<td>Max Dose</td>
<td>120mg</td>
<td>300mg</td>
</tr>
<tr>
<td>Half-Life</td>
<td>12.5 hrs</td>
<td>10.3 hrs</td>
</tr>
<tr>
<td>Time to Steady State</td>
<td>3 days</td>
<td>3 days</td>
</tr>
<tr>
<td>CYP450 Inhibition</td>
<td>1A2, 2D6</td>
<td>Weak 2D6 &amp; 3A4</td>
</tr>
<tr>
<td>Special Considerations</td>
<td>Avoid in renal/liver failure; caution in epilepsy; may help with pain</td>
<td>Has caused EKG changes and blood pressure elevations; treatment-emergent SI/agitation may be more common; may work better for adolescents than for younger children</td>
</tr>
<tr>
<td>Side Effects</td>
<td>GI side effects (nausea/vomiting), headache, fatigue, hypersomnia, insomnia, decreased appetite, weight loss, weight gain, irritability, dizziness, palpitations, elevated blood pressure, increased heart rate, sweating, dry mouth, SI</td>
<td></td>
</tr>
<tr>
<td>Monitoring</td>
<td>Monitor blood pressure and heart rate</td>
<td></td>
</tr>
</tbody>
</table>
Antidepressants – Bupropion

Bupropion

Pharmacology:
• Comes in immediate, sustained, and extended release forms
• Half Life: 20 hours
• Sample dosing for Bupropion XL: start at 150mg daily; can increase to 300mg after 1-2 weeks; max 450mg daily
• CYP2D6 inhibitor so careful for drug-drug interactions

Evidence Base:
• Some evidence in pediatric ADHD (effect size half that of stimulants)
• Some evidence in pediatric depression (open-label) but no RCTs
Antidepressants – Bupropion

Bupropion

Side Effects / Risks include:
seizures (do not use in those with seizure disorders or eating disorders; caution if taking other meds which also lower the seizure threshold), hypertension, tachycardia, arrhythmias, dizziness, headache, insomnia, itching, rash, sweating, constipation, dry mouth, nausea/vomiting, weight loss, agitation, anxiety, blurred vision, pruritus, rash, activation of mania or psychosis, increased SI

Monitor: blood pressure, SI
Antidepressants – Mirtazapine

Mirtazapine

Pharmacology:
• Starting Dose: 7.5-15mg
• Titration Schedule: may titrate up by 15mg q 1-2 weeks
• Total Daily Dose: 15-45mg
• Half Life: 20-40 hours
• Time to reach steady state: 4 days

Evidence Base: no real evidence to support its efficacy in pediatric population

Side Effects / Risks include: weight gain, sedation, hypotension, elevated liver enzymes, leukopenia with a flu-like syndrome
Antidepressants – TCAs

Tricyclic Antidepressants (TCAs)
   ie: Amitriptyline, Clomipramine, Doxepin, Imipramine, Nortriptyline

Evidence:
   • Evidence for Clomipramine in pediatric OCD
   • Mixed evidence for treatment of pediatric anxiety disorders
   • Negative trials in pediatric depression
   • Evidence in ADHD

Potentially dangerous
   • QTc prolongation – complete heart block or other fatal arrhythmias
   • Requires EKG monitoring and blood draws for monitoring levels
   • Can be fatal in overdose

Not often used given limited evidence and concerning risks;
DO NOT use for pediatric depression
Anxiolytics – Benzodiazepines

Evidence base in children/adolescents is limited

Some benefit but generally not statistically significant

Use should be short-term (ie: acute stressor, before medical procedure, as an adjunctive short-term treatment for acute reduction in severe anxiety symptoms while an SSRI is titrated)

Have different onset of action, duration of effect, and potencies
# Anxiolytics – Benzodiazepines

<table>
<thead>
<tr>
<th></th>
<th>Alprazolam (Xanax)</th>
<th>Clonazepam (Klonopin)</th>
<th>Lorazepam (Ativan)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Starting Dose</strong></td>
<td>0.25mg (or 0.125mg)</td>
<td>0.25-0.5mg (&lt;10 or &lt;30kg: 0.01-0.03 mg/kg/d)</td>
<td>0.25-0.5mg</td>
</tr>
<tr>
<td><strong>Daily Dose Range</strong></td>
<td>0.25-4mg</td>
<td>0.25-4mg (&lt;10 or &lt;30kg: 0.1-0.2 mg/kg/d)</td>
<td>0.25-8mg (0.05mg/kg q4-8hrs)</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>TID</td>
<td>QD-BID</td>
<td>BID-TID</td>
</tr>
<tr>
<td><strong>Max</strong></td>
<td>4mg/day</td>
<td>4mg/day</td>
<td>2mg/dose, 8mg/day</td>
</tr>
<tr>
<td><strong>Side Effects</strong></td>
<td>-- Sedation, drowsiness, decreased alertness/cognitive performance (can impede learning), decreased psychomotor speed/coordination, disinhibition (aggression, irritability, behavioral disinhibition).</td>
<td>-- Decrease REM &amp; Stage 4 sleep (hence effect on night terrors/sleepwalking)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-- Regular use may cause tolerance/dependence; taper to discontinue (abrupt d/c can cause insomnia, anxiety, GI upset, seizures).</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-- Avoid in those with substance abuse history, pregnant, breastfeeding.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Equivalencies:** Clonazepam 0.25mg = Alprazolam 0.5mg = Lorazepam 1mg
Anxiolytics – Buspirone

Evidence Base is limited
Some case reports and open-label studies in children/adolescents have shown benefit but RCTs have not found significant differences from placebo.

Dosing:

<table>
<thead>
<tr>
<th></th>
<th>Children</th>
<th>Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting dose</td>
<td>2.5-5mg BID</td>
<td>5-10mg BID</td>
</tr>
<tr>
<td>Titrate q3-4 days by</td>
<td>2.5-5mg</td>
<td>5-10mg</td>
</tr>
<tr>
<td>Typical dose</td>
<td>5-7.5mg BID</td>
<td>5-30mg BID</td>
</tr>
<tr>
<td>Max daily dose (divided 2-3 times/day)</td>
<td>20-40mg</td>
<td>60mg</td>
</tr>
<tr>
<td>mg/kg dosing: 0.2-0.6 mg/kg (BID-TID)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Side effects / risks include:
Lightheadedness, dizziness, headache, dyspepsia, nausea, sedation/fatigue, nervousness
Anxiolytics – Antihistamines: Hydroxyzine

Evidence Base is limited
• Unable to find RCTs in children/adolescents
• Some evidence in adults with GAD

Typical Uses: short-term treatment of anxiety/insomnia

Dosing: start 10-25mg/d (depending on age, day vs night use, etc); titrate up to 50-100mg/d (or 2mg/kg/d) as needed divided q6-8h prn

Pharmacology: rapid onset of action (15-30 min); 4-6 hour duration of effect

Side effects include: sedation, dizziness, hypotension, dry mouth, constipation, urinary retention, tremor, headaches, tinnitus; QT prolongation is possible
Anxiolytics – Beta Blockers

Evidence Base is limited: Unable to find RCTs in children/adolescents for anxiety disorders

Typical Uses: performance anxiety, somatic symptoms of anxiety

Before Starting:
• Obtain medical history (esp. cardiovascular, pulmonary, Raynaud’s, pregnancy)
• Obtain baseline blood pressure and pulse; t/c EKG if indicated
  – Hold if BP < 90/60 or if pulse <50 in adolescents or < 60 in young children

Dosing examples:
Propranolol (Beta-1,2): start 10-20mg; may need to titrate; max 120-240mg/d
Atenolol (Beta-1): start 25mg; may need to titrate; max 50-100mg/day

Side effects include: Bradycardia, hypotension, weakness/lethargy, fatigue/sedation, clouded sensorium, GI upset, bronchospasm, impotence, depression