Psychiatric Medications in young children: lots of questions and some answers

J. Rebecca Weis, MD
October 28, 2019
Who We Are

New York Center for Child Development

- NYCCD has been a major provider of early childhood mental health services through federal, state, city and philanthropic funded programs in New York.
- NYCCD has a long history of providing system-level expertise to inform policy and support the field of Early Childhood Mental Health through training and direct practice.

Training and Technical Assistance Center (TTAC)

- NYCCD was selected by the New York City Department of Health and Mental Hygiene under Thrive NYC to develop a citywide Early Childhood Mental Health Training and Technical Assistance Center (TTAC).
- NYCCD’s Subcontractor in the TTAC Center is New York University McSilver Institute for Poverty Policy & Research which offers clinic, business, and system transformation supports statewide to all behavioral healthcare providers.
  
  http://www.TTACny.org
Learning Objectives

• How common is psychiatric medication use in young children?
• How do mental health professionals approach treatment decisions with young children, including for medication?
• What are some basic categories of psychiatric medications used in young children and what is important to know about each of these?
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Figure 1 Prevalence of psychiatric disorders in preschoolers, children and adolescents, and adults. Data abstracted from: Angold, Egger, Erkanli, & Keeler, submitted; Costello, Egger, & Angold, 2005; Kessler, Chiu, Demler, & Walters, 2005b.

- Used information from the National Ambulatory and National Hospital Ambulatory Medical Care Surveys
- 1.00% of children in sample on a psychotropic medication from 2006-2009
- Some disparities – groups more likely to be on psychotropic medication
  - Boys
  - Older children (4-5 year olds vs 2-3 year olds)
  - White children
  - Those lacking private insurance
- ADHD most common diagnosis
- Stimulants most common medication used
- Psychotropic prescription rates higher for those with co-morbid diagnosis ADHD & mood disorder

(Chirdkiatgumchai, 2013)
Psycototropic medication in child and adolescents in the United States in the year 2004 vs 2014

- Compared 2004 to 2014 using claims data from Medicare and Medicaid
- Broke prevalence into age groups

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2004</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 2-4</td>
<td>3.08%</td>
<td>2.63%</td>
</tr>
<tr>
<td>Age 5-12</td>
<td>8.74%</td>
<td>8.73%</td>
</tr>
<tr>
<td>Age 13-18</td>
<td>10.89%</td>
<td>12.11%</td>
</tr>
</tbody>
</table>

(Lopez-Leon, 2014)
Trends in Psychotropic Medication Use for Medicaid-Enrolled Preschool Children

- Tracked psychotropic medication prescriptions between 2002 and 2008 in Ohio
- One in ten children had a mental health diagnosis
- Overall rate in 2008 – 1.9%
- Most common medications
  - Stimulants (0.8%)
  - Alpha agonists (0.7%)
  - Anxiolytics (0.5%)
  - Antipsychotics (0.5%)
  - Polymedication (three or more medications) (0.9%)
- Similar stats for those most likely to be receiving meds: 4-5 years, male, white, living in poverty, living in urban area
- More on this study a little later…

(Fontanella, 2014)
Learning Objectives

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• What are some basic categories of psychiatric medications used in young children and what is important to know about each of these?
How are treatment decisions made in the medical field?

- Thorough assessment
- Diagnosis
- Treatment options
- Weighing risks and benefits
- Treatment plan
Attention Deficit Hyperactive Disorder

Must meet **at least 6** of the criteria within A1 and/or A2, and have experienced for at least the past 6 months.

### A1: Inattention

- 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).
- Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or reading lengthy writings).
- Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).
- 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; fails to finish schoolwork, household chores, or tasks in the workplace).
- Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized, work; poor time management; tends to fail to meet deadlines).
- 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, or reviewing lengthy papers).
- Often loses things necessary for tasks or activities (e.g., school materials, pencil, books, tools, wallets, keys, paperwork, eyeglasses, or mobile telephones).
- Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).
- Is often forgetful in daily activities (e.g., chores, running errands, for older adolescents and adults, returning calls, paying bills, keeping appointments).

### A2: Hyperactivity and Impulsivity

- Often fidgets with or taps hands or feet or squirms in seat.
- Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, office or other workplace, or in other situations that require remaining seated).
- Often runs about or climbs in situations where it is inappropriate. (In adolescents or adults, may be limited to feeling restless).
- Often unable to play or engage in leisure activities quietly.
- Is often “on the go,” acting as if “driven by a motor” (e.g., is unable or uncomfortable being still for an extended time, as in restaurants, meetings, etc; may be experienced by others as being restless and difficult to keep up with).
- Often talks excessively.
- Often blurts out an answer before a question has been completed (e.g., completes people’s sentences and “jumps the gun” in conversations, cannot wait for next turn in conversation).
- Often has difficulty waiting his or her turn (e.g., while waiting in line).
- 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, adolescents or adults may intrude into or take over what others are doing).

B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12.
C. Criteria for the disorder are met in two or more settings (e.g., at home, school or work, with friends or relatives, or in other activities).
D. There must be 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 accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).
• System for social-emotional diagnoses in young children
• Focuses on incorporating developmental issues that may affect how symptoms present in young children
Overactivity Disorder of Toddlerhood (OADT)

- Describes a syndrome of pervasive, persistent, extreme, developmentally inappropriate hyperactivity and impulsivity
- Must have both high activity and experience impairment
- Must meet full ADHD criteria for hyperactive type (at least 6/9 symptoms)
- Based on
  - High stability in children with extremes of hyperactivity starting at 18 months old
  - Clinical awareness of children with extreme impairment
- Age: Older than 24 months and younger than 36 months (6 months duration)
- Importance of differential diagnosis

ZERO TO THREE, 2016, pp. 30-34
OADT Considerations

- Potential benefits of this new disorder: Access to early intervention to young children with clinically impairing disorders
- Concerns raised:
  - Potential for pathologizing typical behavior patterns
  - Medication exposure
- Safeguards
  - “Excessive when compared to developmentally and culturally expected norms”
  - Cause impairment
How are treatment decisions made in the medical field?

1. Thorough assessment
2. Diagnosis
3. Treatment options
4. Treatment plan
5. Weighing risks and benefits
General approach to treatment in young kids

- Therapy/psychosocial interventions should be first choice
  - The evidence base supports the efficacy of psychotherapy, sometimes more solidly than for meds
  - ADHD might be an exception to this as kids age
- Address parental issues
  - Parent management training or other coaching
  - Treatment of parental psychopathology
- When meds are indicated, usually should also be combined with therapy
General approach to psychopharmacology in young kids

- Less research for essentially EVERY type of medication in children and adolescents
- Very few medications are actually FDA approved for children
  - This includes non-psychiatric medications as well
  - So there is a lot of “off-label” prescribing
- Essentially no long term follow-up data available for anything other than stimulants
## FDA approvals

- Very few medications are FDA approved below age 6

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<thead>
<tr>
<th>Medication</th>
<th>Age Range</th>
<th>Indications</th>
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<tr>
<td>Haloperidol</td>
<td>age 3-12</td>
<td>Tourette’s, hyperactive behavior after failure to respond to non-antipsychotic and psychotherapy, psychotic disorder, schizophrenia</td>
</tr>
<tr>
<td>Dextroamphetamine IR</td>
<td>age 3-16</td>
<td>for ADHD</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>age 1-12</td>
<td>Severe behavioral problems marked by combativeness and/or explosive hyperexcitable behavior (out of proportion to immediate provocations) &amp; short-term treatment of hyperactive children who show excessive activity with accompanying conduct disorders</td>
</tr>
<tr>
<td>Risperidone</td>
<td>age 5-16</td>
<td>Irritability associated with autism</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>adults and children &gt;2 years and &gt;20 pounds</td>
<td>Schizophrenia</td>
</tr>
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How are treatment decisions made in the medical field?

Thorough assessment

Diagnosis

Treatment options

Weighing risks and benefits

Treatment plan

Recommend psychotropic medication in preschoolers only

1) After a trial of evidence-based psychosocial treatment has failed OR is inaccessible

2) In instances of moderate to severe symptoms and functional impairment when there is a high risk of injury to self/others or worsening family dysfunction

Gleason, 2007

- Algorithms for treatment for common disorders
  - Based in available evidence
  - Stages of assessment and treatment
    - Thorough diagnostic assessment
    - Implementation of evidence-based psychosocial treatment
    - Treatment of parental psychopathology if it is impacting childhood symptoms
    - Initiation medication treatment for a 6-month trial with consistent monitoring if prior interventions did not alleviate symptoms

Gleason, 2007
## Risk/benefit & risk/risk concept

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Risk</th>
<th>Benefit</th>
<th>Risk of untreated problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>aspirin</td>
<td>Stomach upset, increased bleeding</td>
<td>Decreased pain and inflammation</td>
<td>Continued pain and inflammation</td>
</tr>
<tr>
<td>dextromethorphan-phenidate (Ritalin)</td>
<td>Stomach upset, headaches, changes in sleep &amp; appetite, rarely significant cardiovascular symptoms</td>
<td>Significant decrease in hyperactivity and impulsivity, improved learning</td>
<td>Continued impairment due to symptoms, possibly fall behind academically, preschool expulsion</td>
</tr>
<tr>
<td>Parent Management Training</td>
<td>Weekly sessions mean missing out on other activities, challenges for parents in implementing</td>
<td>Significant decrease in behavioral issues</td>
<td>Continued impairment due to symptoms, child internalizes idea of self as “bad”</td>
</tr>
</tbody>
</table>
In very young children…

<table>
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<tr>
<th>Risks</th>
<th>Benefits</th>
<th>Risk of untreated problem</th>
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<tbody>
<tr>
<td>Short-term</td>
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<td>Short-term</td>
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<tr>
<td>Long-term?</td>
<td>Long-term?</td>
<td>Long-term?</td>
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How do you know if it’s a side effect?

• In FDA studies for medications, any reported negative event or symptom occurring while taking the medication is required to be reported
  – Sometimes random events get associated with the medication
• In reality, there should be patterns with side effects
  – Timeline of new or increased event/symptom should match either starting the medication (at least within a few days) or increasing the dose of the medication
  – Side effects unlikely to fluctuate dramatically day-to-day if patient is taking medication consistently
  – Side effect should disappear if stop medication
• More meds, more chance of side effects!
Generic versus brand name

- When the FDA approves a new medication (or new delivery mechanism), the company that developed the medication gets a period of exclusivity during which only that company can bring that medication to market.
  - When that time period expires, the market is usually open for other companies to make generic copies of the medication.
    - The FDA requires data that the generic medication is bioequivalent to the brand name medication.
    - The cost of generic medication is usually 80-85% less because the company is not trying to re-coup the development costs and initial marketing costs.
- BOTTOM LINE – generic is usually just as good!
How are treatment decisions made in the medical field?

- **Thorough assessment**
- **Diagnosis**
- **Treatment options**
- **Weighing risks and benefits**
- **Treatment plan**
General approach to psychopharmacology in young kids

- Dosing for children and adolescents sometimes needs to be adjusted - more so for younger children than adolescents
  - The “start low and go slow” rule often applies
  - Conversely, young children may be rapid metabolizers due to great liver and kidney function
Are there ways you can help make sure medication goes well for kids you see?

• Importance of ongoing communication
  — Prescribers (and therapists) are generally very interested in feedback from people who are interacting with kids they treat

• What might help you effectively communicate with the prescriber
  — Pick a designated team member who can gather info from all sources
  — Consider communicating in writing when it’s hard to coordinate phone calls
  — Standardized questionnaires and rating scales

• Support parents
  • Encourage parents to talk to doctor honestly
    — before stopping meds or changing doses,
    — about worries they may be having
    — In preparation for visits, write down questions
Pill boxes – they’re not just for “old people”

- Many psychiatric medications need to be taken on a daily basis to be effective, but according to studies 30-50% of patients with a psychiatric disorder are non-adherent to medication
- If symptoms seem to vary a lot day-to-day, consider talking to parents
  - They aren’t in trouble – you want to help them find ways to remember
  - Pill boxes
  - Putting the medication somewhere that helps them remember (for instance, beside toothbrush assuming the patient always brushes teeth)
  - Setting an alarm on phone for each day
- For younger children parents should always administer
- Consider whether it may work better to administer at school
When kids can’t swallow pills

• Limits options quite a lot
  – Liquid option
  – Chewable tablet or disintegrating tablet form
  – Transdermal patch
Plan for re-evaluating medications

• When starting meds
  — Have specific target symptoms
    • Is the medicine helping?
  — Have a timeline to re-evaluate
    • Is the medicine still helping?
  — Consider trial off medication
    • Have symptoms changed?
    • Is it possible to discontinue the medication?
Summary of General Approach

• Good assessment crucial
• Psychosocial and parental interventions should be first-line treatment
  — Medication second-line
• Non-psychiatrist professionals can really help with assessment and monitoring of treatment
• Strategies to support parents
  — Encouraging communication
  — Remembering medication
• Importance of clear plan for re-evaluation
Learning Objectives

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The Great Pretenders

• All treatments can have side effects
• A number of medications can cause side effects that mimic social-emotional symptoms
  — Particularly common in young children
• Common examples:
  — Benadryl can cause disinhibition in young children
  — Asthma medications can cause a variety of issues
    • Albuterol: hyperactivity, difficulty sleeping
    • Steroids: mood changes, hyperactivity, difficulty sleeping
Stimulants and other medicines for ADHD: The PATS Study

- Preschool ADHD Treatment Study
- Funded by NIMH, randomized controlled trial
- Children age 36-65 months (n=303)
- Study conducted in phases
- Parent management training - If symptoms were markedly improved after parent training, patient did not continue in study
- Dose range methylphenidate (MPH) 1.25-7.5 mg 3 X per day (TDD 3.75 mg – 22.5 mg)
  - Parents and teachers completed rating scales at each dose
- In phase 6, 114 children, half MPH/half placebo
  - Trend toward improvement of ADHD
  - Teachers noted improvement in social competence in MPH group
  - MPH group slightly more moody
  - Results probably skewed by the fact that 45% of the placebo group dropped out during phase 6 because of behavioral deterioration when off MPH
Stimulants and other medicines for ADHD: The PATS Study

- At least 14 publications out of this ongoing study so far
- During phase 7: 10 month long open-label continuation trial (n=140)
  - Maintained improvements that were seen during prior MPH treatment
  - 11% had adverse effects that caused discontinuation at some point
    - Emotionality/irritability was most common reason for discontinuation
    - Appetite loss also relatively common
- 6 year follow-up
  - 89% of the kids still met criteria for ADHD (so diagnosis was pretty reliable)
  - 1 in 4 of the children was on medication at that point (not only MPH though)

**Summary**
ADHD could be effectively diagnosed in preschool children,
There were differences in side effects compared to older children but many children were able to tolerate the medication,
There were improvements in ADHD symptoms and associated functional outcomes (like social competence) but not as robust as in older children
Stimulants and other medicines for ADHD: Stimulants

- Methylphenidate vs. Amphetamine
  - Methylphenidate blocks the reuptake of DA and NE but has little effect on presynaptic release of dopamine
  - Amphetamine blocks reuptake of DA and NE & increases release of DA and NE

- Enhancement of dopamine and norepinephrine in different parts of the brain may improve
  - concentration, attention, executive functioning and wakefulness
  - Hyperactivity
  - depressive symptoms, fatigue and sleepiness.
Stimulants and other medicines for ADHD: Stimulant dosing

- Stimulants come in short- and long-acting versions
  - Short acting have 2-4 hour duration of action
  - Long acting have 8-12 hour duration of action

- Long Acting Forms - 3 delivery options:
  - SODAS/DIFFUCAPS: combination of immediate and extended release beads
  - OROS: capsule with H₂O permeable holes which release medication depending on osmotic pressure
  - Prodrug: Lisdexamfetamine, a prodrug bound to L-lysine which uses GI tract to metabolize → dextroamphetamine
  - Also, liquid and patches – multiple dosing options

- Sometimes long- and short-acting meds are “layered”
Stimulants and other medicines for ADHD: Stimulant dosing

TAKE HOME POINTS:
• Although there are really only two stimulants (methylphenidate and amphetamine), there are a lot of different formulations
• Because the delivery of the medicine varies by formulation, some kids do better on one versus another
• So you will often seem some dosage as well as formulation adjustments happening
Stimulants and other medicines for ADHD: Stimulant dosing

• **Start low and go sort of slow**
  - Too often, kids are kept on ineffective doses for way too long – see parameters below
  - Use of standardized rating scales like the SNAP or Vanderbilt can significantly improve titration practices

• Can see effects almost immediately – helps to average a few days to assess therapeutic benefit

• If no improvement or only partial improvement after 3-7 days
  - Increase dose
  - If current medication is already maximized, consider changing medication
  - If current medication is not well tolerated, consider changing medication

• Many children take medication “holidays”
  - Administer only on schools days/days child needs to be more attentive and composed
  - Allows for chance to catch up on calories for those with appetite suppression and catch up on growth if needed (especially over the summer)
Stimulants and other medicines for ADHD: Stimulant side effects

• Common (10-50%): nausea, stomach upset, decreased appetite, insomnia, headache
  — Some will decrease after child takes for a few weeks
  — Practical management – eat before taking, last dose several hours before bedtime
• Uncommon: motor tics (resolve when stop med), dysphoria, irritability, hallucinations, “zombie”
• Cardiac: rare cases of cardiac problems, associated with pre-existing cardiac problems
• Growth: still under study – MTA showed 1cm/year decrease in height over 1-3 years of continuous treatment, but other studies showed no difference – prospective studies under way
  — Update 2017 – children treated may be 1-2 cm shorter as adults (Swanson)
• Rebound: As stimulants wear off, an increase of symptoms sometimes even above the baseline symptoms
Stimulants and other medicines for ADHD: Alpha agonists – 2\textsuperscript{nd} line for ADHD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual starting dose</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>clonidine (Kapvay)</td>
<td>0.05 mg at bedtime</td>
<td>0.4 mg/day (may be divided)</td>
</tr>
<tr>
<td>guanfacine (Tenex)</td>
<td>0.5 mg at bedtime</td>
<td>4 mg/day (usually divided bid)</td>
</tr>
</tbody>
</table>

- clonidine tends to cause more sedation than guanfacine
- guanfacine is also available in a long-acting version (brand name Intuniv)
- Alpha agonists are sometimes carefully combined with stimulants to address hyperactivity that hasn’t responded to stimulant
- Not really helpful with inattentive symptoms
- Alpha agonists are also very helpful sometimes for other types of symptoms in young children – PTSD dysregulation, irritability, sleep problems not helped with other interventions
Stimulants and other medicines for ADHD: Dosing alpha agonists

• Start **low** and go **slow**!
• Not fast acting like stimulants
  — Take a few weeks of consistent dosing to take effect
• Monitor condition routinely to evaluate for side effects and to see if you have reached a dose that will give desired response
  — Monitor blood pressure and heart rate
  — Although it’s relatively rare, warn parents and adolescents about risk of rebound hypertension if they suddenly stop the medication, especially from a higher dose
• If no improvement (after 2 weeks – 2 months) increase dose
  — Frequency of dose increases is often determined in part by side effects
    • At each dose, you may need to wait for patient’s **blood pressure** to accommodate and for any **daytime sleepiness** to resolve (the two main side effects)
  — If current medication dose is already maximized, consider changing medication
  — If current medication is not well tolerated, consider changing medication
Stimulants and other medicines for ADHD: Non-Stimulant Treatment of ADHD

• atomoxetine (brand name Strattera):
  — Selective NE reuptake inhibitor
  — Advantages: low abuse potential, less insomnia/growth problems
  — Disadvantages: delayed onset of effect (2-4 wks), lower efficacy than stimulants
  — Dose based on weight: 0.5mg/kg/day, up to 1.2mg/kg/day as tolerated
  — Adverse effects: nausea, stomach pain, moodiness, increased heart rate, Black Box – suicidality
Summary of Stimulants and other meds for ADHD

• In young children, usually important to try other interventions first
• Medicines fall into three categories
  — Stimulants – two types of these
    • Methylphenidates
    • Amphetamines
    • Lots of different brand names
  — Alpha agonists
  — Other - atomoxetine
• Best evidence: methylphenidate
• Also some recent evidence: atomoxetine
• FDA approved: dextro-amphetamine
• Your involvement in measuring effectiveness
Antipsychotics – why use these in young children?: Dopamine Hypothesis

• Symptoms of psychosis are the by-product of dysfunction of dopamine neurotransmission.
  o Came from the discovery that chlorpromazine (the first antipsychotic) treated symptoms
  o D2 receptor sub-type most closely linked to symptom control for psychosis

• However, antipsychotics also act on lots of other receptors/neurotransmitters
  o Efficacy for treatment of other issues
  o Side effects
Trends in Psychotropic Medication Use for Medicaid-Enrolled Preschool Children (cont’d from earlier)

• Although antipsychotics are used overall at low rates, concern that use has been increasing in preschoolers
• Diagnoses in this study associated with antipsychotics included ADHD, disruptive behavior disorders, mental retardation, and bipolar disorder
• Concerns raised:
  – Only 33% had a mental health assessment
  – Only 27.9% received psychotherapy
  – Only 11.4% had a psychiatrist visit
  – 75.1% of children were treated by nonspecialists

(Fontanella, 2014)
Antipsychotics – why use these in young children?: List of antipsychotic medications

<table>
<thead>
<tr>
<th>First generation (Typical)</th>
<th>Second Generation (Atypical)</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlorpromazine (Thorazine)</td>
<td>aripiprazole (Abiify)</td>
</tr>
<tr>
<td>haloperidol (Haldol)</td>
<td>asenapine (Saphris)</td>
</tr>
<tr>
<td>others are rarely used now</td>
<td>clozapine (Clozaril)</td>
</tr>
<tr>
<td></td>
<td>lurasidone (Latuda)</td>
</tr>
<tr>
<td></td>
<td>olanzapine (Zyprexa)</td>
</tr>
<tr>
<td></td>
<td>paliperidone (Invega)</td>
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<tr>
<td></td>
<td>quetiapine (Seroquel)</td>
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<tr>
<td></td>
<td>risperidone (Risperdal)</td>
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<td></td>
<td>ziprasidone (Geodon)</td>
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Antipsychotics – why use these in young children?: FDA approvals for antipsychotics in children/adolescents

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<th>Diagnosis/condition</th>
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<tr>
<td>aripiprazole</td>
<td>Psychosis in schizophrenia</td>
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</tr>
<tr>
<td></td>
<td>Mania in bipolar</td>
<td>10-17</td>
</tr>
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<td></td>
<td>Irritability in autism</td>
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<tr>
<td>risperidone</td>
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<tr>
<td></td>
<td>Irritability in autism</td>
<td>6-17</td>
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<td>13-17</td>
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<tr>
<td>paliperidone</td>
<td>Psychosis in schizophrenia</td>
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Commonly also used for impulsive aggression, mood lability/irritability without bipolar diagnosis, augmentation of antidepressants, PTSD dysregulation, and tic disorders.
Antipsychotics – why use these in young children?: FDA approvals for antipsychotics in children/adolescents

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<td>5-17</td>
</tr>
<tr>
<td>risperidone</td>
<td>Psychosis in schizophrenia</td>
<td>13-17</td>
</tr>
<tr>
<td></td>
<td>Mania in bipolar</td>
<td>10-17</td>
</tr>
<tr>
<td></td>
<td>Irritability in autism</td>
<td>6-17</td>
</tr>
<tr>
<td>quetiapine</td>
<td>Psychosis in schizophrenia</td>
<td>13-17</td>
</tr>
<tr>
<td></td>
<td>Mania in bipolar</td>
<td>10-17</td>
</tr>
<tr>
<td>olanzapine</td>
<td>Psychosis in schizophrenia</td>
<td>13-17</td>
</tr>
<tr>
<td></td>
<td>Mania in bipolar</td>
<td>13-17</td>
</tr>
<tr>
<td>paliperidone</td>
<td>Psychosis in schizophrenia</td>
<td>12-17</td>
</tr>
</tbody>
</table>

Commonly also used for impulsive aggression, mood lability/irritability without bipolar diagnosis, augmentation of antidepressants, PTSD dysregulation, and tic disorder.
Antipsychotics – why use these in young children?: Studies supporting use of antipsychotics in preschoolers

• Open-label and one randomized controlled trial support use in autism
  — Masi et al, 2001 age 3-6 (open-label)
  — Masi et al, 2003 age 3-6 (open-label)
  — Luby et al, 2006 age 2-6 (RTC)

• Lack of high-quality research for use in ADHD and disruptive behavior disorders
Antipsychotics – why use these in young children?: Antipsychotic side effects

- Sedation
- Anticholinergic effects (dry mouth, constipation, blurry vision, etc)
- **Weight gain*** (younger children especially!)
- Elevated glucose
- Insulin resistance
- Elevated triglyceride and cholesterol levels
- Extrapyramidal symptoms (not common in young children)
- Irreversible involuntary movements (tardive dyskinesia) (usually only with long-term use)
- Increased prolactin
  - Gynecomastia
  - Galactorrhea
  - Impact on bone density?
- Cardiac rhythm/conduction effects

**Antipsychotics require blood draws for monitoring blood sugar and lipids**
Antipsychotics – why use these in young children?: Summary of antipsychotics in preschoolers

• Concern that use could have risen without proper assessments and other services being completed first
• Second or third (or fourth) line - try psychosocial and parent interventions first
• Some evidence for irritability in autism
• Often used for other indications
  — Impulsive aggression
  — Irritability
  — ADHD?
• Complicated list of side effects
  — Weight gain
  — Need for blood monitoring
What other medicines might you see used with young kids?: Antidepressants

<table>
<thead>
<tr>
<th>Selective Serotonin Reuptake Inhibitors</th>
<th>Selective Serotonin Norepinephrine Reuptake Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>generic name</strong></td>
<td><strong>Brand name</strong></td>
</tr>
<tr>
<td>fluoxetine</td>
<td>Prozac</td>
</tr>
<tr>
<td>paroxetine</td>
<td>Paxil</td>
</tr>
<tr>
<td>sertraline</td>
<td>Zoloft</td>
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<td>fluvoxamine</td>
<td>Luvox</td>
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<tr>
<td>citalopram</td>
<td>Celexa</td>
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<td>escitalopram</td>
<td>Lexapro</td>
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<tr>
<td>venlafaxine</td>
<td>Effexor</td>
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<td>desvenlafaxine</td>
<td>Pristiq</td>
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<tr>
<td>duloxetine</td>
<td>Cymbalta</td>
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<tr>
<td>bupropion</td>
<td>Wellbutrin</td>
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<tr>
<td>mirtazepine</td>
<td>Remeron</td>
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<tr>
<td>Clomipramine</td>
<td>Anafranil</td>
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<td>Imipramine</td>
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</table>
What other medicines might you see used with young kids?: Antidepressants

<table>
<thead>
<tr>
<th>Class</th>
<th>Medication</th>
<th>FDA indication</th>
<th>Age range (years)</th>
<th>Target dose (mg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI</td>
<td>Fluoxetine</td>
<td>Major depressive disorder</td>
<td>8–17</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obsessive compulsive disorder</td>
<td>7–17</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Fluvoxamine</td>
<td>Obsessive compulsive disorder</td>
<td>8–17</td>
<td>150</td>
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<tr>
<td></td>
<td>Sertraline</td>
<td>Obsessive compulsive disorder</td>
<td>6–17</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>Escitalopram</td>
<td>Major depressive disorder</td>
<td>12–17</td>
<td>&gt;10</td>
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<tr>
<td>SSNRI</td>
<td>Duloxetine</td>
<td>Generalized anxiety disorder</td>
<td>7–17</td>
<td>60–90</td>
</tr>
</tbody>
</table>

Dose looks higher but therapeutically no difference – calorie example
What other medicines might you see used with young kids?: Antidepressants specifically SSRI’s

- Most evidence for children and adolescents
  - Fluoxetine (Prozac)
  - Escitalopram (Lexapro)
  - Sertraline (Zoloft)

- Only case studies and quasi-experimental studies for young children (Barterian, 2014)
  - Fluoxetine ($n=8$) and sertraline ($n=2$) most published studies
  - Anxiety syndromes – selective mutism, OCD, specific phobia/feeding anxiety
    - Improvements, but behavioral disinhibition and other side effects prompted discontinuation in some
  - No studies looking at treatment of depression in preschool age group
  - One open-label study in 1998 suggested benefit in autism
Common Side Effects for SSRI/SNRI's

**Long term:**
- Sexual dysfunction (up to 33%)
- Weight gain (5 – 10%)

**Short term:**
- GI upset / nausea
- Jitteriness / restlessness / insomnia
- Sedation / fatigue

* Treatment emergent suicidal ideation

From AIMS Center presentation “Treating Depression in Primary Care”
What other medicines might you see used with young kids?: Summary of antidepressants

- Only evidence is for SSRI’s (selective serotonin reuptake inhibitors)
- Little evidence for depression/mood disorders
- Some evidence for treatment of anxiety disorders in combination with therapy
- Possible efficacy in autism but limited research

- Use of tricyclics (an older type of antidepressant) for enuresis is very rare now
  - Behavioral interventions
  - Desmopressin
What other medicines might you see used with young kids?: mood stabilizers (very briefly)

- Classically used for treatment of bipolar disorder
  - Does this exist in young children?
    - DC:0-5 does not include this disorder
    - Area of controversy overall – good overview by Luby, Tandon, and Belden in 2009 “Preschool Bipolar Disorder”
    - For pediatric mania, more studies support use of antipsychotics

- Often used to address emotional lability or impulsive aggression without bipolar diagnosis in older children

- Lithium (Eskalith, Lithobid)

- Anti-seizure meds we have borrowed
  - Valproic acid (Depakote, Depakene)
  - Lamotrigine (Lamictal)
  - Children with seizure disorders are at higher risk for mental health issues
What other medicines might you see used with young kids?: Antihistamines

- diphenhydramine (Benadryl)
  - Allergy medication – used for its side effect of sedation/calming effect in children
  - Use with caution in young children as can see disinhibition and agitation (paradoxical effect)
And what about sleep?

- First of all, careful assessment if the problem is persistent
  - Anxiety, ADHD, etc.
- Sleep hygiene should always be the first step
  - Sleep schedule/routine before going to bed
  - Limit screen time 2 hours before bedtime (and this is a whole other topic for young kids!)
  - Quiet activities before bedtime
  - Behavioral reinforcement and reward prevention
- Commonly used for insomnia
  - Melatonin
  - Clonidine especially in the context of ADHD
  - Benadryl
QUESTIONS/COMMENTS/DISCUSSION

Thank you!
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Thank you!