What’s New in Psychotropic Prescribing for Children: Trends, Guidelines & Practice

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What’s New in Psychotropic Prescribing for Children: Trends, Guidelines & Practice

Gail Edelsohn, MD, MSPH
Senior Medical Director, Community Care
Exton, PA
Objectives

• Understand recent pediatric psychotropic prescribing trends

• Identify the sources re: pressures to prescribe

• Review guidelines for assessment and treatment

• Become familiar with updated psychopharmacological evidence base for select disorders

• Resources - guidelines, practice parameters
Question

• National outpatient data for youth < 21 yr. looking at trends across 1995-2010 reported which type of medication to be most frequently prescribed?
  a) Antipsychotics
  b) Antidepressants
  c) Anxiolytics
  d) ADHD medications
  e) Mood stabilizers
Question

• Which class of psychotropic had the highest likelihood of being prescribed in 2007-2010 compared to being prescribed in 1995-1998?
  
  a) ADHD medications  
  b) Antipsychotics  
  c) Antidepressants  
  d) Mood stabilizers  
  e) Anxiolytics
Trends in Office-Based Medical Visits

Figure 2. Trends in Office-Based Medical Visits by Young People With Psychotropic Medications, 1995-2010

The attention-deficit/hyperactivity disorder (ADHD) medications include stimulants, atomoxetine hydrochloride, guanfacine hydrochloride, and clonidine hydrochloride. The odds ratios (ORs) and 95% CIs for the study period are for ADHD medications (OR, 4.13 [95% CI, 3.04-5.61]), anxiolytics (OR, 1.28 [95% CI, 0.91-1.79]), antidepressants (OR, 1.60 [95% CI, 1.21-2.11]), antipsychotics (OR, 6.01 [95% CI, 3.90-9.26]), and mood stabilizers (OR, 1.92 [95% CI, 1.29-2.84]). Data are from the National Ambulatory Medical Care Survey.
• Describe antipsychotic patterns focused on age and sex

• Retrospective analysis, using large prescription database from retail pharmacies

• Ages < 24 yrs.

• Calendar yrs. 2006, 2008, 2010

• Age groups 1-6 (young children); 7-12 (older children); 13-18 (adolescents); 19-24 (young adults)
Antipsychotic Medication Treatment

Figure. Percentage of Male and Female Population With Antipsychotic Medication Use by Sex and Age, United States, 2010

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Antipsychotic Use Among Children

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Stephen Crystal et al. Health Aff 2016;35:974-982
Antipsychotics: Children w/ Medicaid

• 3% of Medicaid-insured children in foster care accounted for 15% of those treated with antipsychotics in 2010

• In 2010, antipsychotic use was higher among non-Hispanic white children than African American or Hispanic children both in foster care and non-foster care Medicaid

• Nearly 2/3 of foster children on antipsychotics also received psychosocial interventions compared to fewer than 1/3 of other Medicaid-insured children on antipsychotics

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# Pediatric Antipsychotic Trends: Community Care

<table>
<thead>
<tr>
<th>Year</th>
<th>Youth on antipsychotics</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008 (n=216,479)</td>
<td>10,721 (4.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2009 (n=230,052)</td>
<td>11,080 (4.82)</td>
<td></td>
</tr>
<tr>
<td>2010 (n=244,381)</td>
<td>10,867 (4.49)</td>
<td></td>
</tr>
<tr>
<td>2011 (n=272,645)</td>
<td>11,016 (4.04)</td>
<td></td>
</tr>
<tr>
<td>2012 (n=270,077)</td>
<td>9,544 (3.53)</td>
<td></td>
</tr>
<tr>
<td>2013 (n=286,996)</td>
<td>8,764 (3.05)</td>
<td></td>
</tr>
</tbody>
</table>

*Note: p-value indicates statistical significance.*
Pediatric Antipsychotic Trends

• Community Care Data 2008 – 2013
  – Downward trend for 0-5 yrs. and 6-12 yrs.
  – Increase in use for adolescents 13-17 yrs.
  – No difference in rates by gender or race
  – Use of antipsychotics gradually decreased for children in out-of-home placement

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## Pediatric Polypharmacy Trends: Community Care

<table>
<thead>
<tr>
<th>Measure Description - year</th>
<th># Children (Num)</th>
<th>% Children based on number filling at least 1 psychotropic</th>
<th>% Children based on total number enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td># Children with 3 meds for at least 90 days - 2011</td>
<td>2552</td>
<td>7.233%</td>
<td>0.940%</td>
</tr>
<tr>
<td># Children with 3 meds for at least 90 days - 2012</td>
<td>2281</td>
<td>6.293%</td>
<td>0.848%</td>
</tr>
<tr>
<td># Children with 3 meds for at least 90 days - 2013</td>
<td>2367</td>
<td>6.236%</td>
<td>0.827%</td>
</tr>
<tr>
<td># Children with 3 meds for at least 90 days - 2014</td>
<td>2894</td>
<td>7.608%</td>
<td>0.985%</td>
</tr>
<tr>
<td># Children with 3 meds for at least 90 days - 2015</td>
<td>2995</td>
<td>7.42%</td>
<td>0.95%</td>
</tr>
</tbody>
</table>
Facts, Trends, and Concerns

• While pediatric antipsychotic rates are not increasing, the “new normal” is much higher than rates prior to 2000

• Evidence base: child/adolescent bipolar mania, adolescent schizophrenia, irritability in ASD

• Most outpatient visits in youth for antipsychotics are not prescribed for these diagnoses; vary by age

• Risk of cardiovascular and metabolic effects

• Less than optimal rates of metabolic monitoring

• Antipsychotics prescribed with other psychotropics

• Long-term safety issues
Parent Pressure: For and Against

• “I don’t want my child to be a zombie on meds; he’s just being a boy...”

• Overwhelmed and chaotic homes

• Child at risk for OOH placement

• “My son/daughter is about to get kicked out of school.”

• “My child runs away from the school bus, is too nervous to go, now being called truant; isn’t there some medication to help?”
Best Practice & Prescribing Dilemmas

• Medication is but one component of a comprehensive treatment plan

• Benefits:
  – Remain in school
  – Stay at home and take advantage of community-based treatment and supports

• Medication evaluation should identify the behavioral issues best addressed by psychosocial interventions
  – What if medication is the only treatment option available?
Guidelines for Assessment

• History and MSE for a thorough assessment of:
  – Presenting symptoms
  – Child’s functioning at
    • Home, school, and community
  – Comorbid psychiatric disorders
  – Past history
  – Developmental history
  – Medical history & any lab workup needed
  – Social/peer relationship & school history
  – Family history
  – Target Sxs
  – Rating scales and questionnaires
    • Parents and teachers
Psychoeducation

• Misperceptions about mental illness
  – **Legitimate** diagnosis
  – Causes
  – How it should be treated

• Clarify **misperceptions** and explore caregivers’ concerns and expectations for treatment
  – Encouraging parents to actively participate
    • **Decision making process** is important
    • In formulating an acceptable treatment plan in line with the parents’ **personal values**
Before Prescribing

• Informed Consent
  – Side effects
  – Black box warnings
  – **Off-label use**
  – **Situations** for which the treatment contract could be **terminated**
  – Requirements for **baseline workup, frequency** of appointments, and **regular monitoring** for height, weight, blood pressure, and pulse

• **Disagreements** between family members/guardians
Monitoring Response

• **Symptom reduction** and **functional** improvement
  – Home, school, peers, community

• **Start low and go slow & stop slowly**

• Adequate trial

• Manage side effects

• Inadequate response
  – Switch class
  – Avoid using more than 2 medications simultaneously
ADHD: Guidelines

• Texas Children’s Algorithm Program (2006)

• AACAP Practice Parameters (2007)

• AAP ADHD Guidelines: preschool – adolescence (2011)

• The Medical Letter, Drugs for ADHD (2015)
ADHD Pharmacotherapy: Stimulants

• Start lower doses of stimulants in females

• Pharmacogenomics testing only useful when not responding to stimulants

• Re-challenge with stimulants if tics experienced on stimulants, especially if ADHD sx worsen off meds

• 20% of children with ADHD will get tics regardless of the medication

• If a child presents with ADHD and tics before treatment, pick a time that is free of stress or excitement to start stimulants
Stimulant Treatment Monitoring

• Baseline history of syncope, family sudden cardiac death, cardiac abnormalities

• Do not use stimulants if patient has history of aortic stenosis, Wolf Parkinson White, arrhythmogenic right ventricular dysplasia (ARVD)

• See ADHD patients every three months, check pulse and BP at baseline and every six months

• Obtain ADHD checklist from both parent(s) and teachers to guide medication adjustment

• No need for routine EKG but refer to cardiology if persistent tachycardia or hypertension (> 95 percentile)
Other Stimulant Hints

• Select stimulant based on proportion of immediate-release component

• Greater immediate release: reduces symptoms early in the day
  – Metadate CD, Methylphenidate ER, Methylphenidate LA, mixed salts amphetamine extended release, dexmethylphenidate extended release

• Lesser immediate release: reduces symptoms later in the day
  – Methylphenidate (Quillivant, Quillichew), Amphetamine XR solution (Dynavel), OROS MPH (Concerta), Daytrana, lisdexamfetamine mesylate
Non-Stimulant Medications ADHD

• Atomoxetine Moderate Effect Size (ES)
  – Concerta > Atomoxetine > placebo
  – Target dose of atomoxetine 1.2 mg/kg/day
  – Serious adverse events or suicidality not different from placebo
  – 40% of those on atomoxetine continue significant symptoms

• Long Acting Alpha 2 Agonists Moderate ES
  – Better than placebo for ADHD, ODD
  – A2As higher incidence of hypotension, bradycardia, fatigue, somnolence, and sedation
  – Monitoring needed; average loss of 7 mm/Hg of systolic BP
  – Studies needed
    • Dose response tolerability, efficacy, compare with stimulants, utility with aggression, tics
Stimulants for Preschoolers

• PATS (2006), children 3.5-5 yrs.
  – Determined best MPH dose, roughly ½ dose for school-age MTA study
  – MPH side effects higher than for school-age (11% vs 2%)
  – MPH effect size for preschoolers with ADHD lower than for school-age children
  – PATS 6-year follow-up
    • 63% have persistence of ADHD up to age 10 yrs.; 64% on medications but symptomatic

• CDC urging parents of preschoolers to try behavior therapy before medication (2016)
  – Less than half receive behavioral tx; 75% receive medication
ADHD Summary

• Non-pharmacological treatments have lower effect sizes but can boost response rates to medications

• Combination of drug classes tested in RCTs to treat ADHD with co-morbidities

• No proof yet that long-term treatment with stimulants reduces ADHD symptoms

• Growth suppression of height can persist in minority of children who consistently take stimulants throughout development

• Infrequent week-long drug holidays may help growth
Depression Quiz

1. Which antidepressant is FDA approved for the acute treatment of major depressive disorder in a 9-yr.-old child?

   a) Escitalopram
   b) Fluoxetine
   c) Sertraline
   d) Venlafaxine

2. What is the average response rate to antidepressant treatment?

   a) 10%
   b) 30%
   c) 60%
   d) 90%
Screening for Adolescent Depression

• PHQ-9 vs PHQ-2
  – PHQ-9 items: interest or pleasure, depressed, sleep, fatigue, appetite, psychomotor retardation/agitation, concentration, self-esteem, suicidality
  – PHQ-9 was more valid (AUC 93% vs 87%)

• Screening items for adolescents
  – History of concussion
    • 3.3-fold increased risk for depression
  – Parental job loss
    • 2-3% increase in suicide-related behaviors
  – Parental suicide attempt
    • 5-fold increased risk for suicide attempts in offspring
Depression Medications

• Two FDA-approved choices
  – Fluoxetine for children and adolescents 8-17 yrs.
  – Escitalopram for adolescent depression 12-17 yrs.

• From TADS we know that antidepressants alone or with CBT lead to earlier symptom reduction than treatment with CBT alone

• From the TORDIA study we know for antidepressant non-responders switching to a second SSRI or SNRI lead to 40% improvement
  – Adding in CBT increases the improvement rate to approximately 55%
Suicidal Risk of Antidepressants

• Meta-analysis of suicidal risk of antidepressants in pediatric patients
  – 27 trials of pediatric depression

  – Antidepressants: 3% suicidal ideation/attempts

  – Placebo: 2% suicidal ideation/attempts
Suicide Attempt Risk Among Children

### TABLE 2

|                    | Person-Years of Current Use | Events | Rate/1000 Person-Years | Adjusted RR (95% Confidence Interval)
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>3070</td>
<td>76</td>
<td>24.8</td>
<td>1</td>
</tr>
<tr>
<td>Sertraline</td>
<td>4208</td>
<td>104</td>
<td>24.7</td>
<td>0.97 (0.66–1.45)</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>2056</td>
<td>71</td>
<td>24.0</td>
<td>0.80 (0.52–1.21)</td>
</tr>
<tr>
<td>Citalopram</td>
<td>1271</td>
<td>37</td>
<td>29.1</td>
<td>0.92 (0.57–1.50)</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>1066</td>
<td>27</td>
<td>25.3</td>
<td>0.80 (0.45–1.43)</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>721</td>
<td>21</td>
<td>29.1</td>
<td>0.80 (0.43–1.51)</td>
</tr>
<tr>
<td>Multiple SSRIs only</td>
<td>1354</td>
<td>83</td>
<td>61.3</td>
<td>1.70 (1.10–2.62)</td>
</tr>
</tbody>
</table>

*Relative risks (RRs) were estimated with generalized estimate equation regression models with Poisson distribution and were weighted by the inverse of a propensity score for each medication, age, calendar year, psychiatric conditions (use of psychotropic medications and diagnoses for serious psychiatric disorders), and utilization of health care (psychiatric and medical hospitalizations, and unintentional injuries). Inverse propensity score weights were trimmed at the 99th percentile due to a few large, influential weights.*
Psychosocial Treatment of Depression

• CBT

• Study of family-based interpersonal psychotherapy for depressed children (7-12 yrs.) vs. client-centered therapy
  – Small study, FB-IT > CCT

• Adolescents’ Assessments of Depression Tx
  – National survey of adolescents with major depressive episode; what’s helpful
  – Counselling alone: extremely + a lot= 32%
  – Medication + counselling: extremely + a lot= 47%
Bipolar Disorder & DMDD

• Mania/bipolar criteria revisions
  – DSM 5 changes for mania/hypomania
  – One week of abnormally and persistently elevated, expansive, or irritable mood and
    • **Persistent and abnormal activity/energy level**
    • **Occurring most days and most of the day**
    • **These symptoms are concurrent with the B symptoms and represent a change from “usual self”**
    • **Children with chronic severe irritability (explosive outbursts) have been given Disruptive Mood Dysregulation Disorder diagnosis**
    • **“Mixed” is no longer an episode; is a specifier, 3 symptoms of depression during mania, or 3 symptoms of mania during depression, can be noted as a specifier**
## Trials, FDA Approval for Acute Mania

<table>
<thead>
<tr>
<th>Drug</th>
<th>Age $\geq 18$</th>
<th>Age $&lt; 18$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>+</td>
<td>Approved $\geq 12$</td>
</tr>
<tr>
<td>Divalproex</td>
<td>+</td>
<td>FDA required study, (-), another (+)</td>
</tr>
<tr>
<td>Carbamazepine ER</td>
<td>+</td>
<td>Trial suspended</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Not studied</td>
<td>Negative</td>
</tr>
<tr>
<td>Risperidone</td>
<td>+</td>
<td>Approved $\geq 10$</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>+</td>
<td>Approved $\geq 10$</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>+</td>
<td>Positive, but no FDA approval in children</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>+</td>
<td>Approved $\geq 10$</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>+</td>
<td>Approved $\geq 13$</td>
</tr>
<tr>
<td>Asenapine</td>
<td>+</td>
<td>Approved $\geq 10$</td>
</tr>
</tbody>
</table>
Bipolar Disorder

• Antipsychotics as monotherapy risperidone, olanzapine, aripiprazole, quetiapine, asenapine all FDA-approved

• TEAM risperidone>lithium>valproic acid

• COLT lithium clinically superior to placebo

• Lamotrigine add on trial in 12 yrs. and up superior to placebo in a discontinuation trial
Comorbidity – ADHD

• Rates 25-50% in teens; 75-98% in children

• Comorbidity lengthens a manic episode, worsens bipolar treatment response

• If unclear which it is, treat ADHD first after discussion with family

• If true bipolar +ADHD, stabilize the mania and then treat the ADHD; no evidence that it hurts and definite evidence that it helps
Poor Quality of Evidence

- Meds used for bipolar disorder:
  - Gabapentin (Neurontin)
    - Off-label for children & adults
  - Levetiracetam (Keppra)
    - No pediatric or adult bipolar indication
  - Topiramate (Topamax)
    - Off-label for pediatric bipolar, off-label for weight gain associated medication side effects
Disruptive Mood Dysregulation Ds

- Severe recurrent verbal or physical temper outbursts out of proportion to situation or provocation and inconsistent with developmental level

- Diagnosis not made < 6 yrs. or > 18 yrs.

- Behaviors not exclusively during MDD and not better explained by autism, PTSD, separation anxiety, dysthymia

- Trumps oppositional defiant disorder (ODD)

- Can occur with ADHD, Conduct Ds, and Substance Use Ds

- Differential from Intermittent Explosive Ds is absence of irritable mood between episodes
  - So both diagnoses cannot be made in the same child
DMDD

• Too new to have treatment studies

• Many conditions have irritability and explosive outbursts

• “Not better accounted for by” in the criteria means should look for other conditions first because they have treatments

• Important to really understand the explosive episode
  – Parent and child interviews, chronicity of irritable mood, triggers for outbursts, where the problems occur
Question

• T-MAY stands for:
  – Trauma-informed approach for multiply abused youth
  – Treatment for multiply addicted youth
  – Treatment of maladaptive aggression in youth
  – Time limited medication algorithm for youth
  – Translational medicine for abused youth
T-MAY Guide

The Rutgers CERTs Pocket Reference Guide
For Primary Care Clinicians and Mental Health Specialists

TREATMENT OF MALADAPTIVE AGGRESSION IN YOUTH

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Assess and Define Target Symptoms

- **B** – BEHAVIOR: In what ways does the child exhibit aggression?
- **O** – ONSET: When does it happen? What triggers it, and why?
- **L** – LOCATION: Where do the symptoms occur – home/school?
- **D** – DURATION: How long does it last?
- **E** – EXACERBANTS: What makes it worse?
- **R** – RELIEF: What makes it better?
Resources

• AACAP Involvement with Child Welfare System

• AACAP Psychotropics in Children and Adolescents

• AACAP Facts for Families Table of Contents
Resources

- **T-MAY**

- **AAP ADHD**
  [http://pediatrics.aappublications.org/content/early/2011/10/14/peds.2011-2654](http://pediatrics.aappublications.org/content/early/2011/10/14/peds.2011-2654)

- **AACAP Atypical Antipsychotics**

- **AACAP ASD**
Resources

• Texas Department of Family and Protective Services, 2016 Psychotropic medication utilization parameters for children and youth in foster care, 5th version
  http://www.dfps.state.tx.us/Child_Protection/Medical_Services/guide-psychotropic.asp

• PA DHS Guidelines for Psychotropic Medication Prescribing in Primary Care for Children and Adolescents in Foster Care
  http://www.dhs.pa.gov/searchresults/index.htm?q=psychotropic+prescribing
Contact Information

Gail A. Edelsohn, MD, MSPH
edelsohnga@ccbh.com

Thank you