Polypharmacy, Antipsychotics in Children and Adolescents

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Nationwide Children’s Hospital
November 14, 2018
Objectives

- Define and recognize polypharmacy in behavioral health management of children and adolescents.
- Conceptualize common reasons and risk factors leading to polypharmacy of psychotropic medications.
- Identify FDA approved antipsychotic medications and their indications for use in youth.
- Integrate monitoring guidelines for antipsychotic medications in children and adolescents.
- Apply strategies for simplification of medication regimens using case examples.
Thank you pediatrics colleagues!

You're Awesome!

...and I'll make sure they don't forget it!
Burden of mental illness

50% of all lifetime mental illness start by age 14

75% of all lifetime mental illness start by age 24

In 2011, **2.1M+ children in Medicaid received psychotropic medications.** The age distribution is as follows:

- **13-18 yrs. old** (850K children): 39%
- **0-5 yrs. old**: 8%
- **6-12 yrs. old** (1.1M children): 52%

From 2005 to 2011, children ages 0-5 receiving these medications increased by 130% — from 78K to 179K

Source: **CHCS Center for Health Care Strategies, Inc.**
Changes in the Number of Children Receiving Psychotropic Medications

Between 2005 and 2011, the number of children covered by Medicaid increased by nearly 12% to 32.4M

During that same period, Medicaid-covered children receiving psychotropic meds increased by 28%

And expenditures for those medications increased by 70% — a $1B increase, from $1.6B to $2.7B
Children Receiving Psychotropic Meds without Behavioral Health Services

Of the 2.1M+ children receiving these medications in 2011, nearly half (47%) did not receive accompanying behavioral health services.

And almost one-third (30%) are getting more than one of these medications — 47% for children in foster care.

CHCS Center for Health Care Strategies, Inc.
Antipsychotic medications

- One of the fastest growing class of psychotropic meds

- Male, disruptive behavior disorders, foster care placement and Medicaid enrollment are associated with higher rates of prescription

- Only a small percentage of visits associated with antipsychotic Rx are for FDA indicated diagnosis and often associated with polypharmacy

- Significant variation in prescribing patterns (2% Hawaii to 22% Texas) and poor adherence to monitoring guidelines.

- Youth of antipsychotics are at a 50% higher risk of long term metabolic issues including DM2
Pre-test
Polypharmacy

• Most common: ≥2 psychotropic medications in the same class

• For ages 0-5 – any antipsychotic (except risperidone in ASD)

• For ages 6-8: ≥3 psychotropic meds

• For ages 9-17: ≥4 psychotropic meds

• For all ages: doses exceeding recommended doses
Polypharmacy is not always irrational…

<table>
<thead>
<tr>
<th>Type</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi class</td>
<td>Stimulant + alpha agonist (ADHD: Concerta + tenex)</td>
</tr>
<tr>
<td>Adjunctive</td>
<td>Antipsychotic + Benztropine (ASD: Risperidone + Cogentin)</td>
</tr>
<tr>
<td>Augmentation</td>
<td>SSRI + mood stabilizer (Trichotillomania: Sertraline + Topiramate)</td>
</tr>
<tr>
<td>Same class</td>
<td>(Anxiety/insomnia: Citalpram + Trazodone)</td>
</tr>
</tbody>
</table>
Case example:
7 year old child recently came to live with father after changes in custody due to abuse allegations towards mother’s boyfriend. Has history of ADHD, ‘mood swings’, aggression. Dad has the medication list provided by mother.
Medications:
- Concerta 54 mg AM, Ritalin 10 mg at 4 pm
- Periactin 2 mg BID
- Clonidine 0.2 mg bedtime
- Risperidone 0.5 mg TID
- Lamotrigine 25 mg BID
- Colace 50 mg daily
- Melatonin 10 mg bedtime
Avoiding polypharmacy pitfalls

- Obtain accurate medication history and reconciliation including OTC medications
- Ensure adherence to medications
- Link each prescribed medication to the diagnosis
- Identify medications for treating side effects
- Consider de-prescribing if the drug causing side effects changed or discontinued
Antipsychotic polypharmacy

• More than 2 antipsychotics used in the same patient for extended period of time

• Excess dose that recommended for age

(Does not include cross taper)
Use of Multiple Concurrent Antipsychotics in Children and Adolescents (APC)

- The percentage of children and adolescents 1–17 years of age who were on two or more concurrent antipsychotic medications for at least 90 consecutive days during the measurement year.
### Antipsychotics: Preview

<table>
<thead>
<tr>
<th>First Generation Antipsychotics (FGA)</th>
<th>Second Generation Antipsychotics (SGA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chlorpromazine</td>
<td>• Aripiprazole</td>
</tr>
<tr>
<td>• Fluphenazine</td>
<td>• Asenapine</td>
</tr>
<tr>
<td>• Haloperidol</td>
<td>• Brexpiprazole</td>
</tr>
<tr>
<td>• Loxapine</td>
<td>• Clozapine</td>
</tr>
<tr>
<td>• Perphenazine</td>
<td>• Iloperidone</td>
</tr>
<tr>
<td>• Pimozide</td>
<td>• Lurasidone</td>
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<tr>
<td>• Thioridazine</td>
<td>• Olanzapine</td>
</tr>
<tr>
<td>• Thiothixene</td>
<td>• Paliperidone</td>
</tr>
<tr>
<td>• Trifluoperazine</td>
<td>• Quetiapine</td>
</tr>
<tr>
<td></td>
<td>• Risperidone</td>
</tr>
<tr>
<td></td>
<td>• Ziprasidone</td>
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</table>
# FGA: approved indications

<table>
<thead>
<tr>
<th></th>
<th>Schizophrenia</th>
<th>Tourette’s</th>
<th>Severe Behavioral Problems</th>
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</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td></td>
<td></td>
<td>6 mo - 12 yrs</td>
</tr>
<tr>
<td>Haloperidol</td>
<td></td>
<td>≥ 3 yrs</td>
<td>“children”</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>≥ 12 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pimozide</td>
<td></td>
<td>≥ 12 yrs</td>
<td></td>
</tr>
<tr>
<td>Thiothixene</td>
<td>≥ 12 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>≥ 12 yrs</td>
<td></td>
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</table>
## SGA: approved indications

<table>
<thead>
<tr>
<th></th>
<th>Schizo</th>
<th>BPD, Mania</th>
<th>BPD, Mixed</th>
<th>BPD, Maint</th>
<th>ASD, Agitation</th>
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</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>13-17 yrs</td>
<td>10-17 yrs</td>
<td>10-17 yrs</td>
<td></td>
<td>6-17 yrs</td>
</tr>
<tr>
<td>Asenapine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lurasidone</td>
<td>13-17 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>13-17 yrs</td>
<td>13-17 yrs</td>
<td>13-17 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paliperidone</td>
<td>12-17 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>13-17 yrs</td>
<td>10-17 yrs</td>
<td></td>
<td>10-17 yrs</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>≥ 13 yrs</td>
<td>≥ 10 yrs</td>
<td>≥ 10 yrs</td>
<td>≥ 10 yrs</td>
<td>≥ 5 yrs</td>
</tr>
</tbody>
</table>
SGA: Side effects to look for...

- Sedation
- Stomach upset
- Nausea
- Constipation
- Prolactin elevation
  - Risperidone
  - Paliperidone
- Cardiovascular
  - QTc prolongation

- Extrapyramidal Symptoms (EPS)
  - Dystonic Reaction
  - Akathisia
  - Tardive Dyskinesia

- Metabolic Effects
  - Weight gain
  - Lipid abnormalities
  - Glucose intolerance
## SGA: nuts and bolts

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Dosage form</th>
<th>Starting dose</th>
<th>Specific comment</th>
</tr>
</thead>
</table>
| Risperidone     | 0.25, 0.5, 1– 4 mg 1mg/ml - liquid | 0.25 mg HS   | EPS ++  
Prolactin increase risk  
Lowers sz threshold                   |
| Aripiprazole    | 2,5, 10, 15, 30 mg 1mg/ml - liquid | 2 mg daily   | Long half life  
Black box - suicide  
Impulsivity, gambling               |
| Olanzapine      | 2.5, 5, 7.5, 10, 15, 20 mg | 2.5 mg HS   | Weight gain highest  
Dyslipidemia risk                   |
| Quetiapine      | 25, 50, 100, 200, 300, 400 mg | 25 mg BID   | Sedation, orthostasis  
Large pills to swallow  
QTc prolongation risk               |
| Ziprasidone**   | 20, 40, 60, 80 mg            | 20 mg HS    | Nausea  
Take with food (500 calories) for absorption  
EKG at baseline for QTc              |

** (off label)
• Children and adolescents appear to be more susceptible to a number of side effects caused by antipsychotic medications
  - Sedation, withdrawal dyskinesia, endocrine abnormalities, age-inappropriate weight gain

• Safety and tolerability data are still sparse fewer long-term safety studies exist to evaluate the risks/benefits
• Aripiprazole
• Lurasidone
• Asenapine
• Risperidone
• Paliperidone
• Quetiapine
• Olanzapine

Increasing Metabolic Side Effects
### ADA Monitoring protocol for patients on SGAs*

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>4 weeks</th>
<th>8 weeks</th>
<th>12 weeks</th>
<th>Quarterly</th>
<th>Annually</th>
<th>Every 5 years</th>
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<tr>
<td>Personal/family history</td>
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<tr>
<td>Weight (BMI)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
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<td></td>
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<tr>
<td>Fasting plasma glucose</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Fasting lipid profile</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

*More frequent assessments may be warranted based on clinical status*
De-prescribing

What is it NOT

- Indication that prescribing provider is doing it wrong

- Need to take children off of individual medications (rather than cumulative risk from multiple drugs)

- Denial of effective treatment for eligible patient

- Abrupt discontinuation without monitoring, consent from patient and collaboration with other providers
De-prescribing

What it IS:

- Part of good prescribing continuum - backing off when doses are too high, or stopping medications that are not longer needed.

- Systematic, patient centered process of identifying and discontinuing medications where existing or potential harms (current and future) outweigh the risks

- In the context of individual patient’s status, goals and preferences
De-prescribing principles

- Review of *diagnosis and rationale* for med regimen
- *Side effects* from medications mistaken as target symptom?
- Establish *stability* of symptoms (remission, no regression) for specified period of time
- Consider *tapering* the medication that:
  - have greatest risk of side effects
  - least evidence of efficacy
  - supratherapeutic dose without justification
  - subtherapeutic dose with limited effectiveness
- Taper one medication at a time
De-prescribing principles

- Intensive therapy and psychosocial supports
- Close monitoring of recurrence or worsening of symptoms
- Some dysregulation and defiance is expected

- If symptoms recur and impair functioning:
  • Restart the last tapered medication or increase the dose to the last effective dose
  • Consider alternative medication
Revisiting 7 y/o Joe....

Medications:
- Concerta 54 mg AM, Ritalin 10 mg at 4 pm (*given at 6 pm by mom*)
- Periactin 2 mg BID
- Clonidine 0.2 mg bedtime
- Risperidone 0.5 mg TID
- Lamotrigine 25 mg BID
- Colace 50 mg daily
- Melatonin 10 mg bedtime

- ADHD: Concerta, Ritalin
- Mood: Risperidone, Lamotrigine
- Side effects: Periactin, Clonidine, Colace
- Primary/sleep: Melatonin
Revisiting 7 y/o Joe

DDx
- ADHD, anxiety related to trauma, possible PTSD
- Referral for trauma informed cognitive behavioral therapy

T0
- 1. Reduced Concerta to 36 mg, moved Ritalin 10 mg from 6 pm to 2 pm
- 2. Stopped Clonidine, Reduced melatonin to 3 mg + sleep hygiene
- 3. Periactin reduced to AM

T1
- 1. Weaned off Lamotrigine
- 2. Tapered Risperidone to 0.5 mg in BID over 2 weeks
- 3. Started Sertraline 12.5 mg and titrated to 25 mg daily

T2
- 1. Decreased Risperidone to 0.5 mg in PM due to continued irritability, aggression.
- 2. Stopped melatonin, stopped Colace

T3
- ADHD – Concerta 36 mg AM, Ritalin 5 mg 2 pm (plan to reassess and d/c trial during holidays)
- PTSD – Zoloft 25 mg AM, Risperidone 0.5 mg PM (plan to d/c Risperidone in future)
Prescribing Optimization

Prescribing Guidelines for Behavioral Health

**Behavioral Health**

**Nationwide Children's**

When your child needs a hospital, everything matters.

**Partners For Kids**

When your child needs a hospital, everything matters.

### Prescribing Guidelines for Behavioral Health

#### Years: 2016 - 2017

Member List - through 2018Q3

<table>
<thead>
<tr>
<th>Prescribing Program - Pharmacy Shared Savings - ADHD</th>
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</thead>
<tbody>
<tr>
<td>PPK Practice:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scripts</td>
<td>Paid</td>
</tr>
<tr>
<td>1398</td>
<td>$144,318.32</td>
</tr>
<tr>
<td>18.4%</td>
<td>20.0%</td>
</tr>
<tr>
<td>656</td>
<td>$19,277.70</td>
</tr>
</tbody>
</table>

#### Drug Summary

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scripts</td>
<td>Paid</td>
</tr>
<tr>
<td>NET ER</td>
<td>711</td>
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<tr>
<td>D-AMPHETAMINE ER</td>
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<td>D-AMPHETAMINE</td>
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<tr>
<td>D-AMPHET</td>
<td>49</td>
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<tr>
<td>D-AMPHETAMINE ER</td>
<td>51</td>
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<td>T-COMBO</td>
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<tr>
<td>D-AMPHETAMINE ER</td>
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<tr>
<td>D-AMPHET</td>
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</tbody>
</table>

*Note: The end of the reporting period was 2 years following the end of the 2-year period. All members were included at the end of the 2nd year. All Prescriptions paid for by PPK for the members are included.*
# Behavioral Health

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<th>Toolkits</th>
<th>Quick Links</th>
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<tr>
<td>Anxiety Disorders</td>
<td>▶</td>
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<tr>
<td>Behavioral Health Webinar Series</td>
<td>▶</td>
</tr>
<tr>
<td>Prescribing for Behavioral Health Overview</td>
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<tr>
<td>Attention Deficit/Hyperactivity Disorder (ADHD)</td>
<td>▶</td>
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<tr>
<td>Long-acting Stimulant Conversion Guide</td>
<td>▶</td>
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<tr>
<td>Disruptive Behavior Disorders (DBD)</td>
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<tr>
<td><strong>Depressive Disorders</strong></td>
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<td>Bipolar Disorder (BPD)</td>
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<tr>
<td>Autism Spectrum Disorder (ASD)</td>
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</tr>
<tr>
<td>Medication List for Ohio Medicaid Plans</td>
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</tbody>
</table>

[Connect with a specialist](#)
Resources


• AACAP: Resources for Primary Care
  https://www.aacap.org/AACAP/Resources_for_Primary_Care/Home.aspx

• Nationwide Children’s Hospital: Physician direct connect
Questions?