BEST PRACTICE ADHERENCE WITH ANTIPSYCHOTIC MEDICATION TREATMENT

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Director, Child Psychiatry Fellowship
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## Disclosures of Potential Conflicts

<table>
<thead>
<tr>
<th>Source</th>
<th>Research Funding</th>
<th>Advisor/Consultant</th>
<th>Employee</th>
<th>Speakers' Bureau</th>
<th>Books, Intellectual Property</th>
<th>In-kind Services (example: travel)</th>
<th>Stock or Equity</th>
<th>Honorarium or expenses for this presentation or meeting</th>
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<tr>
<td>Norton &amp; Norton</td>
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<td>Psychology Today</td>
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Acknowledgements

- Jeanne E. Greenblatt, MD, MPH
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- Bill McMains, MD

- Also to all clinicians who completed the survey
What Are Antipsychotics?

- Also called in the past neuroleptics or major tranquilizers
- Class of medications developed to treat schizophrenia and other psychotic disorders
- First appeared in 1950s
- Second generation or “atypical” medications began to be used in 1990s
  - Thought to be less likely to cause certain side effects related to movement problems

### Risperidone

![Risperidone Chemical Structure](image-url)
## FDA Approved Antipsychotic Uses

### Table 3. Antipsychotics and FDA-Approved Indications for Pediatric Use

<table>
<thead>
<tr>
<th>FGAs</th>
<th>Approved Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Schizophrenia</strong></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine*</td>
<td>1 to 12 years</td>
</tr>
<tr>
<td>Loxapine</td>
<td>Children ≥12 years</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>Children ≥12 years</td>
</tr>
<tr>
<td>Thiothixene</td>
<td>Children ≥12 years</td>
</tr>
</tbody>
</table>

*Also approved for hyperactivity and severe behavioral problems.
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### FGAs (Continued)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Approved Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Schizophrenia (Continued)</strong></td>
<td></td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Children ≥2 years</td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>Children ≥6 years</td>
</tr>
</tbody>
</table>

### Bipolar Disorder

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Approved Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>1–12 years (mania)</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Children &gt;2 years and &gt;20 pounds</td>
</tr>
</tbody>
</table>

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### Table 3. Antipsychotics and FDA-Approved Indications for Pediatric Use (Continued)

<table>
<thead>
<tr>
<th>SGAs</th>
<th>Approved Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Schizophrenia</strong></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>13–17 years</td>
</tr>
<tr>
<td>Olanzapine</td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td></td>
</tr>
</tbody>
</table>

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### SGAs (Continued)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Approved Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bipolar Disorder</strong></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>10–17 years (manic/mixed)</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>13–17 years (manic/mixed)</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>10–17 years (manic)</td>
</tr>
<tr>
<td>Risperidone</td>
<td>10–17 years (manic/mixed)</td>
</tr>
</tbody>
</table>

### Irritability Associated With Autism

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Approved Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>6–17 years</td>
</tr>
<tr>
<td>Risperidone</td>
<td>5–16 years</td>
</tr>
</tbody>
</table>
Soaring Numbers of Children on Powerful Adult Psychiatric Drugs

DEAD WRONG: HOW PSYCHIATRIC DRUGS CAN KILL YOUR CHILD

From the makers of the award-winning documentaries Making a Killing: The Untold Story of Psychotropic Drugging and The Marketing of Madness: Are We All Insane? comes this
Changes in Antipsychotic use

• Olfson et al., JAMA Psychiatry, 2015
Antipsychotic Usage by Age

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

- Olfson et al., JAMA Psychiatry, 2015
Changes in Youth Medication Usage


**Figure 1.** Trends in the Use of Psychotropic Medications.

*Olfson et al., NEJM, 2015*
National Trends in the Office-Based Treatment of Children, Adolescents, and Adults With Antipsychotics

Mark Olfson, MD, MPH; Carlos Blanco, MD, PhD; Shang-Min Liu, MS; Shuai Wang, PhD; Christoph U. Correll, MD

• Survey and not claims based
• Dramatic increase in antipsychotic usage in children and adolescence from mid 1990s to mid 2000s
• Disruptive Behavioral Diagnosis most common diagnostic category
• Often no diagnosis given
• Risperidone most common antipsychotic medication

Olfson et al, Arch Gen Psych, 2012
Factors Related to Increase

• Rise in diagnosis of Bipolar Disorder and Autism Spectrum Disorders
  • “True” increase versus changes in diagnostic threshold and better detection
• New FDA indications in youth
• Reduced stigma of mental health disorders
• Influence of pharmaceutical industry
• Insurance and access limitations to psychotherapy
Medication Under-treatment?

- Community sample of 10,000 adolescents from National Comorbidity Study – Adolescence
- 14.2% of individuals with a psychiatric diagnosis were taking a medication
- 1.7% of those with bipolar disorder taking an antipsychotic medication
- Challenged perception of medication overuse

Table 2. Prevalence Rates of Specific Classes of Medication Among Participants With 12-Month Diagnostic Groups

<table>
<thead>
<tr>
<th>Primary Diagnosis</th>
<th>% (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>11.8 (2.1)</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>16.0 (4.9)</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>4.5 (0.9)</td>
</tr>
<tr>
<td>Other 12-mo disorder</td>
<td>7.6 (1.4)</td>
</tr>
<tr>
<td>None of above</td>
<td>1.3 (0.2)</td>
</tr>
<tr>
<td>Stimulants</td>
<td></td>
</tr>
<tr>
<td>ADHD</td>
<td>20.4 (3.8)</td>
</tr>
<tr>
<td>Conduct or ODD</td>
<td>6.6 (2.1)</td>
</tr>
<tr>
<td>Other 12-mo disorder</td>
<td>2.0 (0.5)</td>
</tr>
<tr>
<td>None of above</td>
<td>0.8 (0.2)</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td></td>
</tr>
<tr>
<td>Neurodevelopmental disorders</td>
<td>2.0 (1.0)</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>1.7 (1.1)</td>
</tr>
<tr>
<td>ADHD/conduct/ODD</td>
<td>1.8 (0.7)</td>
</tr>
<tr>
<td>Depression</td>
<td>0.6 (0.3)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.1 (0.1)</td>
</tr>
<tr>
<td>Other 12-mo disorder</td>
<td>0.5 (0.5)</td>
</tr>
<tr>
<td>None of above</td>
<td>0.1 (0.0)</td>
</tr>
</tbody>
</table>
Antipsychotics and Weight Gain

Kowatch et al., Current Psychiatry, 2009

Mean weight gain with atypical antipsychotics in pediatric bipolar trials

Weight gain in children and adolescents with bipolar disorder varied among atypical antipsychotics used in 5 recent randomized controlled trials. Treatment duration was 3 weeks with olanzapine, risperidone, and quetiapine and 4 weeks with aripiprazole and ziprasidone. Dosages were olanzapine, 10.4 ± 4.5 mg/d; risperidone, 0.5 to 2.5 mg/d or 3 to 6 mg/d; aripiprazole, 10 or 30 mg/d; quetiapine, 400 or 600 mg/d; and ziprasidone, 80 to 160 mg/d.

Source: References 3-7
### ADA Screening Guidelines for Patients on Second-Generation Antipsychotics

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>4 Weeks</th>
<th>8 Weeks</th>
<th>12 Weeks</th>
<th>Annually</th>
</tr>
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<tbody>
<tr>
<td><strong>Personal family history</strong></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
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<tr>
<td><strong>Weight (BMI)</strong></td>
<td></td>
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<tr>
<td>Overweight (25.0-29.9)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Obese (≥30.0)</td>
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<tr>
<td><strong>Waist circumference</strong></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>(&lt;40&quot; in males, &lt;35&quot; in females)</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td><strong>Blood pressure</strong></td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>Fasting plasma glucose</strong></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
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<tr>
<td>IFG (100-125 mg/dL)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Diabetes (≥126 mg/dL)</td>
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<tr>
<td><strong>Fasting lipid profile</strong></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Total cholesterol (&lt;200 mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>HDL (&gt;40)</td>
<td></td>
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<tr>
<td>LDL (&lt;100)</td>
<td></td>
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<tr>
<td>TG (&lt;150)</td>
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</table>

Normal values (in parentheses) based on 2007 ADA Guidelines and National Cholesterol Education Program (NCEP) Guidelines. More frequent assessments may be warranted based on patient results and the monitoring recommendations in the package inserts for individual antipsychotic drugs used. LDL=low density lipoprotein.

2. ADA. Diabetes Care. 2007;30(suppl 1):S4-S41.
Lack of Metabolic Screening

- Recommendations for regular monitoring of weight, BMI, lipids, glucose with antipsychotic use
- Studies show lack of regular monitoring, especially laboratory measures

Morrato et al, 2010
Antipsychotic Medication Prescribing in Children Enrolled in Medicaid

David C. Retlew, MD, Jeanne Greenblatt, MD, MPH, Jody Kamon, PhD, Diane Neal, RPh, Valerie Harder, MHS, PhD, Richard Wasserman, MD, Patricia Berry, MPH, RN, Charles D. MacLean, MD, Nancy Hogue, BS, PharmD, and William McMains, MD

+ Author Affiliations
Psychiatric Medications for Children and Adolescence Trends Monitoring Workgroup

- Diverse group of professionals
- Medical Director – Bill McMains, MD
- Meet regularly
Limitations of Existing Research

• Mostly insurance claim data
• Contradictory information about over and under-treatment of medication
• Can’t answer about appropriateness of medication treatment
• What we really want to know….Are the RIGHT kids getting the RIGHT medication at the RIGHT time in their treatment????
Antipsychotic Survey

• Came from Vermont Department of Health Access (VDVA) in collaboration with the Drug Utilization Review (DUR) Board of the DVHA, the Department of Mental Health (DMH) and the Department for Children and Families (DCF) with guidance from the Child and Adolescent Psychiatric Medications Trend Monitoring Group

• Sent to all prescribers of antipsychotics to Vermont children using Medicaid (total 978)

• Completion in two months required as a prior authorization

• Survey per medication not per patient

• Occurred around Fall 2012
Survey Completion

- Return rate 80% (n=778)
  - 56 not completed due to stopping medication
  - 34 not completed due to physician no longer seeing them
  - 3 not usable
  - Final N=685 survey of 647 children and 148 prescribers
- Extensions given to those who had trouble completing them
- Some anger and concern raised about survey and especially using a prior authorization process
- Child sample 71% male, 13.3 years of age (min 3.5)
Summary Variables

• Combined multiple variables to form broader measures of quality

• FDA Indication
• Clinical Indication
  • Second-line usage requiring using other medications and non-pharmacological treatments first

• Best Practice Adherence
  • Clinical Indication
  • Age
  • Just one antipsychotic medication
  • Dosing
  • Monitoring
Prescribers

- Most prescribers of antipsychotic medications not psychiatrists
- 2/3rds of prescriptions from psychiatrists
Who started the medication?

- 43% of respondents reported that they were not the ones who started the antipsychotic medication
- Started in inpatient setting in 24% of cases when known
- Primary care clinician starting medication without consultation: 27%
5% of Clinicians Wrote 36% of RXs

Number of Patients per Prescribing Physician

Number of Patients

Number of Prescribers
Which Medications

- Risperidone (Risperdal) preparations: 46%
- Quetiapine (Seroquel) preparations: 29%
- Aripiprazole (Abilify) preparations: 16%
- Ziprasidone (Geodon) preparations: 7%
- Olanzapine (Zyprexa) preparations: 1%

- Girls more likely to be prescribed quetiapine relative to others ($X^2=12.73, p<.001$)
- Greater proportion of patients under the age of 13 were prescribed risperidone ($X^2(3)=56.1, p<.001$)
- 5% of sample taking 2 antipsychotic medications (but could be a cross taper)
• In 79% of cases, Aggression, Mania, Psychosis, Mood Instability, or Tics listed as one of target symptoms
In 69% of cases, Psychotic, Bipolar, Tic, Mood NOS, Intermitt Explos, Devel, or Autistic Disorder listed as a target DX.
Previously Tried Medications

Rare for antipsychotics to be first type of medication tried, although significant minority of “unknown”
Current Medications

• Average number of 2.8 addition medications concurrently if taking an antipsychotic
• Most common antidepressants, stimulants, and alpha agent
• Antipsychotic agent only psychiatric medication: 8.3%
Nonpharmacological Treatment

- Most children getting other types of treatment but not evidence-based therapy
• Weights common but labs done in only about 60%
Broader Measures

- FDA Indication: 27.3%
- Overall Best Practice Guidelines: 51.9%
  - Psychiatrists: 58.9%
  - Non-psychiatrists: 37.9% (difference significant)
- Clinical Indication: 91.7%

<table>
<thead>
<tr>
<th>Reason for Best Practice Nonadherence</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of laboratory evaluations for metabolic monitoring</td>
<td>216 (84.4)</td>
</tr>
<tr>
<td>(For non-first-line indications) previous psychotherapy not tried first</td>
<td>110 (66.3)</td>
</tr>
<tr>
<td>(For non-first-line indications) other type of medication not tried first</td>
<td>43 (26.1)</td>
</tr>
<tr>
<td>Not a first- or second-line indication</td>
<td>47 (16.3)</td>
</tr>
<tr>
<td>&gt;1 antipsychotic used</td>
<td>25 (9.5)</td>
</tr>
<tr>
<td>Age of patient &lt;5 years</td>
<td>2 (0.8)</td>
</tr>
</tbody>
</table>

For individuals taking >1 antipsychotic medication, best practice guidelines were counted as adherent if principles were followed for all antipsychotic medications. More than 1 reason could apply per case and denominator changes according to item.
Qualification of Data

- Generous with regard to literal best practice adherence
- Reliance on report of prescribing clinician
- Some indication that Vermont may be more conservative than other states
  - No subjects with excessive dosing
  - Very few young children prescribed antipsychotic medications
- Medicaid only
Action Plans

• **What we now know**
  - Lots of kids are having their antipsychotic medication managed by someone other than the person who started it

• **What we might do**
  - Help prescribers know when and how to taper
  - Check places and people where medications originate
Action Plans

• What we now know
  - A small number of prescribers are responsible for a large share of the prescriptions

• What we might do
  - Ensure that these folks are following best practice guidelines
  - If not, consider various actions
Action Plans

• What we now know
  ➢ Few children taking antipsychotics are also receiving evidence-based therapy

• What we might do
  ➢ Improve access and training to evidence-based therapy
Action Plans

- **What we now know**
  - Metabolic monitoring is relatively low

- **What we might do**
  - Design efforts to improve monitoring (electronic alerts, letters) which may decrease amount of suboptimal use
Action Plans

• What we now know
  ➢ Many clinicians don’t know the treatment history of their patients

• What we might do
  ➢ Improve information flow of medication information across settings
Follow Up

- Media, legislative, and clinical session to present data
- Follow-up meeting with committee
- Specific action plans based on findings
- New program to help DCF caseworkers do informed consent
Other State Actions

• Making voluntary consultation to a child psychiatrist as easy as possible (MA, VT)
• Having required consultation with a mental health professional (MD, IL)
• Peer to peer phone calls for prescribers of antipsychotics to youth less than 5 (AL)
• Prior authorization required for use (PA, VT, others)
• Review of medical records by public health nurses (CA)
• Child passport of information (NY)
• Creation of “watch list” (IL)
• Mandated clinical reviews (OR)
• Improving medication knowledge and informed consent process for social workers of children in state custody (CA, VT)
Final Thoughts

• Key Findings
  • Relatively low rate of best practice prescribing (50%) for antipsychotic medications
  • Some reassurance that clinicians are not using antipsychotic medications in knee-jerk fashion
  • Illumination of specific areas that might improve best practice adherence
• Should regulation come more from professional and licensing agencies and less from insurance companies?
• Importance to keep discussion and keep in mind challenges of working with some of the most impaired children and families
THANK YOU

QUESTIONS?