The Rational Use of Psychotropic Medications

Trends, Concerns, and Recommendations

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Associate Professor
ACRC Public Policy Co-Chair
Introduction

• My background

Who is in the audience?

• Administrators?
• Direct Care staff?
• Clinical Staff?
• Nursing Staff?
• Educational Staff?
Scope of the Problem

• In Ontario, Canada, psychotropic drugs are prescribed to nearly half of the state wards accounting for drug prescriptions at a rate three times that of children in the general population. Globe and Mail, 9 June 2007

• The number of U.S. preschoolers diagnosed with attention-deficit hyperactivity disorder (ADHD) jumped 56 percent between 2007–08 and 2011–12, according to data from the National Survey of Children's Health.

• Perhaps even more stunning: The number of children ages 2 to 5 taking a psychoactive medication to treat ADHD doubled, the survey found (APA, 2015)

• In 2010, Columbia University research found that the rates of antipsychotic use among privately insured young children (2–5 y/o) more than doubled from 1999 to 2007, but fewer than half of these children received a mental health assessment, had a psychotherapy visit or visited a psychiatrist.

• Comer's own research (2011) found that from 1996 to 2007, the use of antipsychotic drugs for anxiety disorders more than doubled among adults and children age 6 and up, with the most pronounced increases among new patients.
• A study in the *Journal of Child and Adolescent Psychopharmacology* found that from 2001 to 2010, rates of **antipsychotic use** in children younger than 6 years old more than tripled.

• In addition, use in teens is also rising... (Olfson, King and Schoenbaum, 2015).

• **Psychiatric Diagnoses In Youth**
  - **20%** of America’s Youth have a Psychiatric Disorder in any given year (50%+ of all of us will have a diagnosable condition at some point in our lives)
  - **50%** of all diagnoses occur by the age of 14
  - **75%** of all diagnoses occur by the age of 24
• The use of psychotropic drugs by adult Americans increased 22% from 2001 to 2010.²

• One in five adults currently takes at least one psychotropic medication

• More than 8 million U.S. kids take one or more psych med – a rate higher than any other country in the world

• Expenditures have skyrocketed. In 2010 the U.S. spent:
  o $16 billion on antipsychotics
  o $11 billion on antidepressants
  o $7 billion on ADHD meds
    • “Seroquel, antipsychotic drug — $4.4 billion”
    • “Abilify, antipsychotic drug — $4.6 billion” in 2011
So how have Antipsychotics become so prominent in the “treatment” of troubled youth?

$453$ million in advertising translated to $12.6$ billion in sales

1:27 ratio
“Use of 'behaviour-altering' drugs widespread in foster, group homes”

“Top CAS (Children’s Aid Society) officials describe the high number on “psychotropic or behaviour-altering medication” as a crisis.”

“Drugs can ease disruptive behaviour. But doctors and CAS officials are concerned that mental-health issues caused by trauma aren’t being addressed. Dosages at times are too high and long-term side effects, according to some experts, are poorly studied. A Star investigation in 2012 found 600 cases, reported to Health Canada during a 10-year period, of children and youth suffering serious side effects while on ADHD medication, including amnesia and suicide.”
**DRUGGED:** Children in group-home settings are taking psychotropic or behavioural drugs at higher rates than children in other settings. Many are diagnosed with ADHD. Studies suggest some of these children may have suffered trauma and are exhibiting symptoms that mimic those of ADHD. Customary care is specialized placement for young Aboriginal children.

<table>
<thead>
<tr>
<th>Young people taking psychotropic or behaviour-altering medications</th>
<th>AGE</th>
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<tbody>
<tr>
<td></td>
<td>0-4</td>
</tr>
<tr>
<td>Foster home</td>
<td>2%</td>
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<tr>
<td>Customary care</td>
<td>0%</td>
</tr>
<tr>
<td>Kinship</td>
<td>0%</td>
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<tr>
<td>Group home</td>
<td>58%</td>
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<tr>
<td>Independent living</td>
<td></td>
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<tr>
<td><strong>Overall</strong></td>
<td>2%</td>
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</table>
Guided by Science?

What are we told about these disorders?

• Are they chemical imbalances?
• Are they genetic?
• Are they brain disorders?
• Over 100 Billion neurons
• Each neuron can have up to 10,000 connections with other cells...some 100 trillion synapses
• Neurons can have multiple neurotransmitters
• 500 Billion - 1 Trillion glial cells
• The most complex part of the brain is the cortex where 50% of all neurons in the brain are within the outer 1/4 inch of the surface of the cortex
### Research versus Naturalistic Settings

- Youth in care are often on medications for years.
- How long should medications be studied (on their target population) before being approved by the FDA?

<table>
<thead>
<tr>
<th>Medication</th>
<th>Study Duration</th>
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<tbody>
<tr>
<td>Concerta</td>
<td>3 &amp; 4 week studies</td>
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<tr>
<td>Adderall XR</td>
<td>3 weeks</td>
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<tr>
<td>Focalin</td>
<td>4 weeks</td>
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<tr>
<td>Strattera</td>
<td>6, 8, 9 weeks</td>
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<tr>
<td>Abilify</td>
<td>4 and 6 weeks (with Sz)</td>
</tr>
<tr>
<td>Geodon</td>
<td>4, 6 and 52 weeks (with Sz)</td>
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<tr>
<td>Zyprexa</td>
<td>6 weeks (with Sz)</td>
</tr>
<tr>
<td>Seroquel</td>
<td>6 weeks (with Sz)</td>
</tr>
<tr>
<td>Zoloft</td>
<td>6 and 8 weeks</td>
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</table>
Understanding Our Troubled Youth

- **The DSM-5**
  - DMDD
  - Conduct Disorder Limited Prosocial
  - Attenuated Psychosis

- **The ICD-10**

- **Interrater Reliability**

- **The NIMH**
  - RDoC
Reliable Diagnosing?

- Reliability:

  - “any kappa below 0.60 indicates inadequate agreement among the raters and little confidence should be placed in the study results”
Thinking Critically

Doesn’t Require Thinking Negatively

• We are medicating more youth, with more medications, than any other country

• Our use of multiple medications extends dramatically beyond the established science

• Practice Guidelines require ongoing revisions due to emerging research
Medicating Foster Youth
Rational Use of Psychotropics

- Assessment, Diagnosis & Treatment Planning
- Medication Management, Monitoring & Quality Improvement
- Developmental Context & Discharge Planning
- Collaboration & Innovation
- Overcoming Barriers
• The “reason for referral” may appear quite different once the child is in a therapeutic milieu.

• Trauma **MUST** be considered in the clinical conceptualization. A trauma assessment (ACEs?) must be an integral part of the diagnostic process.

• Developmental considerations are essential in the diagnostic formulation. A diagnosis of Bipolar disorder in an 8 year old may look quite differently in a 14 year old.

• Youth and families should be fully involved in making and supporting both pharmacological and non-pharmacological treatment decisions. It is critical that youth and families are provided psychoeducation regarding medication, that their attitudes towards and beliefs about medications are respected, and that open dialog is encouraged. Youth responses to medication will be variable (Foltz & Huefner, 2013).
Wherever possible, minimizing medication use to the **lowest effective dose** and **fewest number** of medications should be the goal.

Rational use of medication also must **attend to duration of psychotropic treatment**. Longer term treatment regimens are sometimes utilized based on research of short-term outcomes, despite emerging evidence of potential risks of such sustained usage on the developing brain and body, for example increased risk of obesity and cardiovascular and endocrine abnormalities in chronic antipsychotic usage.

**Careful monitoring** of the impact of medication trials will improve outcomes.

**Information has to be communicated** across treatment providers about the benefits, drawbacks, and responses to medications in the child’s care and treatment, and the concomitant risk of communication breakdowns.
• Training regarding psychotropic medication for employees at all levels, youth, families, advocates, funders, and external stakeholders will develop understanding of both reasonable expectations and limitations to psychotropic medication use, as well as the range of potential adverse effects, and will elevate the perceived and actual importance of monitoring and communicating regarding medication response, drug interactions, etc.
Developmental Context & Discharge Planning

• **Youth change in response to their ongoing experience.** Development of resiliency, executive functions, and coping abilities will result from treatment or simply maturation, and medications that are “necessary” early in an episode of care may need to be reconsidered periodically.

• **Discharge and transition planning must minimize post-discharge instability in medication...** It is critical to collaborate actively with youth, family, caregivers, and community providers while also building new partnerships and improving effectiveness of communication between settings, in order to reduce adverse events and the potential need for readmission.
Psychiatrists and other prescribing practitioners who work in youth residential treatment settings should not operate in a “vacuum.” **Reliable communication strategies** must be established for efficient collaboration with psychiatrists & prescribers and residential providers.

Collaborations with research institution partners can develop or enhance an evidence base for psychototropic medication use in residential treatment, and improve diagnostic and clinical understanding.

This level of collaboration will enhance the dissemination of valuable information, research, outcomes, and advocacy for children & families.
Overcoming Barriers

• Dialogue with Team members. Examine the assumptions of the strengths & limitations of medication. Recognize that psychiatrists & medications are one piece of the overall treatment approach.

• The treatment team must recognize that health is not the absence of symptoms.

• Promote increased use of family-driven & youth-guided practice and facilitate youth and families in becoming much more able to see themselves as agents of their own change as opposed to their relatively passive role in the traditional medication compliance regimen.
Conclusions

• ACRC urges its members as well as other practitioners in the field to implement the rational approach to psychotropic medication described in this paper and the specific practices identified, and to be active consumers of the evidence basis for psychotropic medication.

• Judicious use of these medications alongside other therapies will allow for the children and families we serve and support to grow and thrive to the best of their ability.
Conclusions

• The goal of our efforts has to stay focused on the engagement, success, and happiness of youth & families.

• Establishing standards of care must be examined, practiced, and re-examined. The youth in residential care are often not the subjects of common research.

• While the challenges within residential care are often under-estimated, the outcomes will be enhanced through careful monitoring, collaboration, and participation of providers, youth & families.
Examining the Evidence

Bipolar Disorder

ADHD
### Summary of Levels of Evidence

<table>
<thead>
<tr>
<th></th>
<th>Bipolar I Disorder, Manic or Mixed, Without Psychosis</th>
<th>Bipolar I Disorder, Manic or Mixed, With Psychosis</th>
<th>Bipolar Depressive Episode</th>
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<tbody>
<tr>
<td>Lithium</td>
<td>A &amp; B</td>
<td>A &amp; B</td>
<td>B &amp; C</td>
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<tr>
<td>Divalproex</td>
<td>B &amp; C</td>
<td>B &amp; C</td>
<td>C</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>B</td>
<td>B</td>
<td>ND</td>
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<tr>
<td>Oxcarbazepine</td>
<td>D</td>
<td>D</td>
<td>ND</td>
</tr>
<tr>
<td>Topiramate</td>
<td>C</td>
<td>C</td>
<td>ND</td>
</tr>
<tr>
<td>Clozapine</td>
<td>C</td>
<td>C</td>
<td>ND</td>
</tr>
<tr>
<td>Risperidone</td>
<td>B &amp; C</td>
<td>B &amp; C</td>
<td>ND</td>
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<tr>
<td>Olanzapine</td>
<td>B &amp; C</td>
<td>B &amp; C</td>
<td>B</td>
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<tr>
<td>Quetiapine</td>
<td>B &amp; C</td>
<td>B &amp; C</td>
<td>B</td>
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<td>Ziprasidone</td>
<td>B &amp; C</td>
<td>B &amp; C</td>
<td>ND</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>B &amp; C</td>
<td>B &amp; C</td>
<td>ND</td>
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<tr>
<td>Selective serotonin reuptake inhibitors</td>
<td>NA</td>
<td>NA</td>
<td>ND</td>
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<tr>
<td>Bupropion</td>
<td>NA</td>
<td>NA</td>
<td>ND</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>C</td>
<td>C</td>
<td>B &amp; D</td>
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**Note:** Level A data consist of child/adolescent placebo-controlled, randomized clinical trials. Level B data consist of adult randomized clinical trials. Level C data consist of open child/adolescent trials and retrospective analysis. Level D data consist of child/adolescent case reports or the panel consensus as to recommend current clinical practices. ND = no data; NA = not applicable.

* May be mood destabilizing.
Bipolar I Disorder, Manic or Mixed, without Psychosis

**Stage 1**
- Monotherapy with Mood Stabilizer or Atypical Antipsychotic (Li, VAL, CBZ, OLZ, QUE, RISP)
- Total Nonresponse/Not Tolerated
- Switch Monotherapy Agent (Li, VAL, CBZ, OLZ, QUE, RISP) (drug class not tried in Stage 1)
- Partial Response

**Stage 2**
- No Response
- Partial Response

**Stage 3A**
- Monotherapy (Li, VAL, CBZ, OLZ, QUE, RISP) (drug class not tried in Stage 1 and 2)
- No Response or Partial Response

**Stage 3B**
- Combination Treatment
  - Li + VAL
  - Li + OLZ
  - Li + QUE
  - Li + RISP
  - VAL + OLZ
  - VAL + QUE
  - VAL + RISP
  - CBZ + OLZ
  - CBZ + QUE
  - CBZ + RISP

**Stage 4A**
- Combination Treatment
  - Li + VAL
  - Li + OLZ
  - Li + QUE
  - Li + RISP
  - VAL + OLZ
  - VAL + QUE
  - VAL + RISP
  - CBZ + OLZ
  - CBZ + QUE
  - CBZ + RISP

**Stage 4B**
- Combination 2 Mood Stabilizer + Atypical
  - Li + VAL + OLZ
  - Li + VAL + QUE
  - Li + VAL + RISP
  - Li + CBZ + OLZ
  - Li + CBZ + QUE
  - Li + CBZ + RISP

**Stage 5**
- Alternate Monotherapy
  - OXC, ZIP, ARI

**Stage 6**
- Stage 6A
  - ECT (Adolescents)
- Stage 6B
  - Clozapine
How Good *IS* the Evidence?

- As lithium is indicated with the best evidence, how many youth should have been studied to establish this foundation of evidence-based care?
<table>
<thead>
<tr>
<th>Date</th>
<th>Sample</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1977</td>
<td>This study included 6 children...3 had to discontinue because of significant worsening of symptoms. One developed EEG abnormalities.</td>
<td>6</td>
</tr>
<tr>
<td>1998</td>
<td>25 youth diagnosed with Bipolar Disorder &amp; secondary substance abuse. 13 were receiving lithium, 12 placebo. Only 4 in the lithium group were diagnosed with Bipolar I</td>
<td>13</td>
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<tr>
<td>1972</td>
<td>18 youth diagnosed with psychosis.</td>
<td>18</td>
</tr>
<tr>
<td>1981</td>
<td>6 children selected for research because their parents were responders to lithium. Authors noted there were 2 &quot;clear cut responders&quot;</td>
<td>6</td>
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<tr>
<td>1990, 1978</td>
<td>Two studies also cited, but I could not access these studies through academic resources.</td>
<td>43</td>
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</tbody>
</table>
2009 Depakote Study

• Dbl blind, placebo-controlled
• 150 youth, 10 – 17 y/o
• Multicenter
• Once daily placebo or Depakote ER
• 28 days
Outcomes

- There was no statistically significant difference between divalproex ER and placebo in the YMRS total score mean change from baseline to final evaluation.
Conclusion

• The YMRS scores decreased for both the divalproex ER and placebo groups but not of a magnitude that would be considered clinically significant.

• …a treatment effect was not observed for any of the other secondary efficacy measures, including C-GAS, CGI-S, CGI-I, CDRS-R, CGSQ, and ADHD Rating Scale-IV

• **Conclusions:** The results of the study do not provide support for the use of divalproex ER in the treatment of youths with bipolar I disorder, mixed or manic state.
“In addition to the current study, recent double-blind placebo-controlled trials of anticonvulsants for pediatric bipolar disorder have failed to show statistically significant superiority to placebo.”
Lancet Summary of Adult Trials on Anticonvulsants (and Antipsychotics)

68 randomised controlled trials included in the multiple treatment meta-analysis*

7 aripiprazole vs other antimanic drugs or placebo
48 placebo vs antimanic drugs
18 lithium vs other antimanic drugs or placebo
13 haloperidol vs other antimanic drugs or placebo
7 quetiapine vs other antimanic drugs or placebo
6 ziprasidone vs other antimanic drugs or placebo
17 olanzapine vs other antimanic drugs or placebo
3 lamotrigine vs other antimanic drugs or placebo
10 valproate vs other antimanic drugs or placebo
10 risperidone vs other antimanic drugs or placebo
2 asenapine vs other antimanic drugs or placebo
8 carbamazepine vs other antimanic drugs or placebo
5 topiramate vs other antimanic drugs or placebo
1 gabapentin vs other antimanic drugs or placebo
• In head-to-head comparisons, **Haldol** had the highest number of significant differences compared with other antimanic drugs. It was significantly more effective than Lithium, Seroquel, Abilify, Tegretol, Depakote, Geodon, Lamictal, Topamax, and Neurontin.

• Risperdal and Zyprexa had a very similar profile of comparative efficacy, being more effective than Depakote, Geodon, Lamictal, Topamax, and Neurontin.
“Exact mechanism of action unknown – primary action has been attributed to D2 blockade, although the receptor profiles of SGAs suggest a possible role for antagonism of a combination of dopamine receptors (eg D3, D4) and other neurotransmitters (eg serotonin & glutamate).

SGAs and TGA have greater affinity for 5HT2a vs D2 receptors. The TGA, Abilify, is a partial agonist at D2 and 5HT1a receptors and an antagonist at 5HT2a receptors. It also binds to D3 and D4 receptors.”

Clinical Handbook of Psychotropic Drugs
The ‘off label’ use of antipsychotics

• Many of these medications are being used for symptoms / conditions well beyond their ‘indications.’

• Your experiences?

• Do they “work?”
Controlling aggression

**Haldol v. Risperdal v. Placebo**

- Controlling aggression in adults with intellectual disability
- “Analysis...showed greater change for placebo than for the other two active drugs combined after baseline differences were accounted for.”
- “Although we noted a reduction in aggression with all treatments after 4 weeks, the greatest was with placebo.
- Furthermore, we recorded no differences between groups in terms of aberrant behavior, quality of life, general improvement, effect on carers, and adverse drug effects.”
The popular Atypical Antipsychotics compared to Haldol

<table>
<thead>
<tr>
<th></th>
<th>Clozapine</th>
<th>Risperidone</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Ziprasidone</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
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<tbody>
<tr>
<td>D₁ blockade</td>
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<td>+++</td>
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<td>D₂ blockade</td>
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<td>D₃ blockade</td>
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<td>D₄ blockade</td>
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<td>H₁ blockade</td>
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“HALDOL is clearly neurotoxic. Should it be banned?”
Current Psychiatry, July 2013

This summary is based on 28 published studies highlighting the neurotoxic effects of typical antipsychotics.

The molecular mechanisms of neurotoxicity of older-generation antipsychotics, including haloperidol, fall into several major categories:
- apoptosis
- necrosis
- decreased cell viability
- inhibition of cell growth
- increased caspase activity (the “death spiral”)
- impaired glutamate transport
- mitochondrial damage.
Stimulants for ADHD

- Stimulants are some of the most commonly prescribed psychotropic medications.
- The U.S. uses 80% of the world’s Ritalin, 60%+ of the world’s amphetamine supply.
- Why are they used?
MTA Study

- **579 Children, 7 to 9 years old, randomly assigned to 4 tx groups**
  - Behavior Modification
  - Medication Management
  - Combined treatment
  - Community Control (tx as usual)

- **Six sites**

- **Treatment continued for the 14 months of the study**
  - However, therapist contact in Beh Mod condition faded after 7 to 10 months
The MTA Study – Long Term

Fig. 1  Average ADHD and ODD Symptoms and Columbia Impairment Scale scores through 36 months. Comb = combination of medication management and behavior therapy; Med = medication management; Beh = behavior therapy; CC = usual community care.
The MTA – Longer Term

• At 8-year follow-up:
• The MTA group as a whole was functioning significantly less well than the non-ADHD classmate sample recruited at 24 months.

• “Our results suggest that the initial clinical presentation in childhood, including severity of ADHD symptoms, conduct problems, intellect, and social advantage, and strength of ADHD symptom response to any treatment, are better predictors of later adolescent functioning than the type of treatment received in childhood for 14 months.”
• “Type or intensity of 14 months of treatment for ADHD in childhood (at age 7.0-9.9 years) does not predict functioning 6 to 8 years later.”

• “We found poorer performance for the MTA children as a group versus LNCG children for 91% of the variables.”
“Ritalin could best be described as a dopamine reuptake inhibitor.

At the therapeutic dose, it blocks 70% of the ‘transporters’ that remove dopamine from the synaptic cleft and bring it back into the presynaptic neuron.”

Cocaine works in a very similar way, but Ritalin clears from the brain much more slowly, so it blocks dopamine reuptake for hours.
Academic Success?

Most ADHD youth are engaged in treatment to improve their academic performance, it is important to note that “stimulants have no effect on academic achievement in the short-term. No long-term effects have been reliably reported on any outcome measure” (APA Working Group, 2006, p. 43).
A 2010 study found: “that medication effects are more likely to be found on subjective measures than objective measures, especially if other factors such as IQ and baseline performance are not controlled for in the analyses; neither medication (current or cumulative) nor in-school academic supports significantly predict academic achievement over and above the covariates of baseline performance and IQ.

Based on the correlational analyses a disassociation was found between the impact of medication on objective (i.e., standardized assessment) and subjective (i.e., questionnaire) measures of academic achievement. The results indicate that teacher and parent ratings of children’s academic achievement were more positive when the child was receiving medication. However, there was no significant improvement found in the performance of these same children on a standardized measure of achievement.

These results are consistent with the conclusions of previous research, which indicated that medication has little to no impact on long-term academic achievement (Raggi & Chronis, 2006; Schachar et al., 2002).”
Vayarin — new ADHD medication!

Vayarin
For the dietary management of ADHD

SAFE. WITH VIRTUALLY NO SIDE EFFECTS.

Vayarin has been clinically shown to manage ADHD symptoms with virtually no side effects. Vayarin takes a longer-lasting approach to gradually build in the system to balance lipid levels, so there are no “comedowns.” Without negative side effects, your child will not need to take a break from Vayarin.

BREAK FREE FROM SIDE EFFECTS

USES WHAT THE BODY KNOWS TO MAKE THE BODY BETTER.
Antidepressants
In 2004, the FDA established a Black Box warning for antidepressants in young people.

**WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS**

*See full prescribing information for complete boxed warning.*

Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for Major Depressive Disorder (MDD) and other psychiatric disorders (5.1).

*When using PROZAC and olanzapine in combination, also refer to Boxed Warning section of the package insert for Symbyax.*
Suicide

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<td>5–14</td>
<td>0.2</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
<td>0.8</td>
<td>0.7</td>
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<td>8.8</td>
<td>12.3</td>
<td>13.2</td>
<td>10.2</td>
<td>10.3</td>
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<td>9.9</td>
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Per 100,000, from the U.S. Center for Disease Control
TADS is randomized, controlled trial designed to evaluate the effectiveness of three active treatments:

- Fluoxetine (Prozac)
- Cognitive Behavioral Treatment (CBT)
- Combined Treatment

Also offered Placebo control during the acute phase
Study Demographics

- 439 adolescents
- 12 – 17 years old
  - Fluoxetine (N = 109)
  - CBT (N = 111)
  - COMB (N = 107)
  - Placebo (N = 112)
FIGURE 1. Depression Scores From Baseline to End of Naturalistic Follow-Up for 327 Adolescents With Major Depressive Disorder Treated With Fluoxetine, Cognitive-Behavioral Therapy (CBT), or a Combination

- Combination treatment
- Fluoxetine
- CBT

Adjusted Predicted Mean Score on Children’s Depression Rating Scale—Revised (intention-to-treat analysis)

- Baseline
- Week of Study Treatment
- Month of Naturalistic Follow-Up

Derived from the random coefficients regression model with adjustments for fixed and random effects.
“Given the high levels of reorganization, growth and pruning occurring during adolescence both within and between brain systems, perturbations of the balance between these processes can have profound and lasting consequences.”
• “Antidepressants cause neuronal damage and mature neurons to revert to an immature state, both of which may explain why antidepressants also cause neurons to undergo apoptosis (programmed death)”

• Because of the ‘push back’ compensator mechanisms of the brain after exposure to antidepressants, “antidepressant use appears to increase susceptibility to depression.”
I have recently seen more adolescent clients prescribed Cymbalta

- It functions as an SNRI
- Does it work?
Cymbalta vs Prozac vs Placebo

• A Double-Blind Efficacy and Safety Study of Duloxetine Fixed Doses in Children and Adolescents with Major Depressive Disorder, May 2014
• 463 children & adolescents
• 36 weeks (10 weeks of treatment)
  • 2 doses of Cymbalta (60mg & 30mg)...224 youth
  • 20mg of Prozac...117 youth, considered active controls
  • Placebo...122 youth
• Outcome Measures: Childrens Depression Rating Scale, Adverse Events, Columbia Suicide Severity Rating Scale
• Authors note that the results are “inconclusive” because neither the drug (Cymbalta), nor the active control (Prozac), “separated from placebo” at study endpoint.
If that’s not enough

- The Cymbalta Package Insert (information provided within the Physician’s Desk Reference)

8.4 Pediatric Use

Efficacy was not demonstrated in two 10-week, placebo-controlled trials with 800 pediatric patients with MDD, age 7-17. Neither Cymbalta nor the active control (indicated for treatment of pediatric depression) statistically separated from placebo. Duloxetine steady state plasma concentration was comparable in children (7 - 12 years), adolescents (13 - 17 years) and adults. Cymbalta has not been studied in patients under the age of 7. Thus, safety and effectiveness in the pediatric population has not been established [see Boxed Warning and Warnings and Precautions (5.1)].

Decreased appetite and weight loss have been observed in association with the use of SSRIs and SNRIs. Pediatric patients treated with Cymbalta in MDD clinical trials experienced a 0.2 kg mean decrease in weight at 10-weeks, compared with a mean weight gain of approximately 0.6 kg in placebo-treated patients. The proportion of patients who experienced a clinically significant decrease in weight (≥3.5%) was greater in the Cymbalta group than in the placebo group (11% and 6%, respectively). Subsequently, over the six-month uncontrolled extension period, most Cymbalta-treated patients trended toward recovery to their expected baseline weight percentile based on population data from age- and gender-matched peers. Perform regular monitoring of weight and growth in children and adolescents treated with an SNRI such as Cymbalta.
• Two placebo-controlled trials in 766 pediatric patients with MDD and two placebo-controlled trials in 793 pediatric patients with GAD have been conducted with Effexor XR, and the data were not sufficient to support a claim for use in pediatric patients.

• Anyone considering the use of Effexor XR in a child or adolescent must balance the potential risks with the clinical need.
A Final Word on Antidepressants

- A prestigious journal, The Lancet, recently published a meta-analysis of antidepressants in youth. (June 8th, 2016)

- Their review included over 5,000 study subjects across 14 medications.

- Study durations ranged from 5 to 12 weeks.
Study Conclusions

• “When considering the risk–benefit profile of antidepressants in the acute treatment of major depressive disorder, these drugs do not seem to offer a clear advantage for children and adolescents.

• **Fluoxetine** is probably the best option to consider when a pharmacological treatment is indicated.

• According to GRADE, the quality of evidence for primary outcomes was rated as very low for most comparisons (appendix p 77–86). **Quality of evidence was very low for overall ranking of treatment in terms of efficacy and low for tolerability.**”
Using Medications in a Strength-Based Setting

• What do we believe medications can accomplish, that relationships cannot?
Questions? Comments?

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