



It's a Big Deal

Are we overmedicating children and adolescents?

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The issue

- Children and youth are still developing. Little is known about the impact of medications on their development.
- Children & youth are being treated with psychotropic medications that have mostly been approved through clinical trials with adults.
- Many children & youth are taking multiple medications without benefit of positive outcomes. The use of multiple prescriptions increases the likelihood of drug interactions and other adverse effects.
- Medications can prevent the development of psychosocial strategies and interpersonal skills
- Inappropriate use of medications can lead to false expectations from family, school personnel, and other caretakers
- Psychotropic medications produce many serious side effects
- The Monograph: Appropriate Use of Psychotropic Drugs in Children/Adolescents: A Clinical Monograph

Social Context: why discuss this topic?

- There is growing pressure on children to conform to strict behavioral standards in various settings. Behaviors that might have been seen in the past as a product of immaturity – and thus tolerated – are now seen as a problem that must be fixed quickly
- Authorities in schools, the courts and elsewhere often insist on a change in behavior immediately
- Parents, who are busier than in the past, often don't have the time to address issues related to behaviors found to be a problem in various settings. They are desperate to make things ok now.
- Prescribers often have such busy practices that they are not able to balance pharmacotherapy with talking therapy and appropriate psychotherapy and behavioral management therapies are often not available
- All of which leads to the perfect storm: medication management as the primary answer to behavioral issues

Psychotropic medications: Antipsychotics

- First generation vs Second generation antipsychotics
- Mechanism of action:
 - D2 and 5HT2A receptor action; other receptors
 - Circuits: limbic – prefrontal areas
- Evidence supporting use of antipsychotics
 - Psychotic symptoms
 - Schizophrenia, psychosis NOS
 - Bipolar symptoms (irritability?)
 - Aggression and agitation: Instrumental vs impulsive aggression
 - Tourette Syndrome
- FDA approved
 - Schizophrenia, Bipolar Disorder, Special symptoms (disruptive behaviors) associated with Autism

- Side Effects
 - Weight gain, DM, hyperlipidemia
 - Cardio-vascular problems such as prolonged QT, orthostatic hypotension, pericarditis
 - Neutropenia and agranulocytosis
 - Liver dysfunction
 - Increased prolactin levels
 - EEG abnormalities and possible seizures
 - Extra pyramidal symptoms
 - Neuroleptic Malignant Syndrome
 - Cataract formation

Psychotropic medications: mood stabilizers

- Lithium + anti-seizure medications found to be effective with mood problems in adults
- Mechanism of action: Mostly unknown, but these meds increase GABA effects and might inhibit glutamate/NMDA receptor-mediated neuronal excitation. They are metabolized in the liver (P-450 enzymes) and excreted via the kidneys
- Evidence for use in children/adolescents
 - Seizure disorders
 - Disruptive behavioral symptoms/behaviors (Blader et al, 2009)
 - Mood issues: There is no documented evidence to support the use of mood stabilizers for bipolar disorder in children and/or adolescents
- FDA approval
 - Seizures (VPA, Tegretol)
 - Bipolar disorder: Lithium (> 12 years old)

- Side effects
 - Stevens-Johnson Syndrome
 - Agranulocytosis
 - Renal function impairment
 - Tremors
 - Cardio-vascular disease/dysfunction
 - Suicidal ideation

Psychotropic medications: antidepressants

- SSRIs, SNRIs, Tricyclics
- Mechanism of action
 - Block reuptake of serotonin and norepinephrine into the presynaptic ganglion (blocking SERT and NET)
- Evidence supporting use of antidepressants
 - MDD
 - Good response rate (40-70%) but similar to PBO (30-60%) (Birmaher et al, 2007)
 - Use in mild to moderate depression?
 - What about use for suicidal ideation in adolescence?
 - » Lifetime prevalence for suicidal ideation in adolescents is 20-25%
 - » Increased suicide rate in 2004 by 14% (Gibbons et al, 2007)

Psychotropic medications: antidepressants

- Evidence supporting use of antidepressants (continued)
 - MDD (continued)
 - TADS
 - Fluoxetine + CBT = 70% response rate
 - Fluoxetine alone = 60%
 - PBO alone = 34% (Correll et al, 2011)
 - TORIDIA: non-responsive to first SSRI? Switch to another + CBT
 - Anxiety
 - CAMS (non-OCD anxiety disorders; GAD):
 - Sertraline + CBT = 81% response rate
 - CBT alone = 60%
 - Sertraline alone = 53%
 - PBO alone = 24% (Kodish et al, 2011)
 - Treatment of mild to moderate anxiety
 - Overall, SSRIs and SNRIs have a response rate 2x greater than PBO

- Evidence supporting use of antidepressants (continued)
 - Anxiety (continued)
 - OCD
 - Mild to moderate: CBT = first line
 - Moderate to severe: CBT + antidepressant (Walkup et al, 2009)
 - » POTS: (Geller et al, 2012)
 - Clomipramine is superior to SSRIs, but tolerance is an issue
 - Social phobia
 - Little evidence to support pharmacotherapy (Connelly et al, 2007)
 - PTSD
 - TF-CBT: first line; add SSRI for lack of response (Cohen et al, 2010)
 - Alpha-2 adrenergic medications helpful for symptoms
 - ADHD, Bulimia nervosa, chronic pain, premature ejaculation, enuresis
 - Use of Tricyclics for depression and anxiety in children < 15 years of age

- Side effects
 - Manic switching
 - Special precautions for children/adolescents who present with MDE; index episode is usually depression, regardless of ultimate diagnosis (MDD vs Bipolar Disorder)
 - Cardio-vascular problems: QT prolongation
 - Seizures
 - Weight gain and DM
 - Suicidal ideation
 - Priapism
- FDA approval for antidepressants
 - Clomipramine (> 10 years of age for OCD); doxepin (> 12 yr for depression), fluoxetine and fluvoxamine (>8 yr for depression/anxiety), Imipramine (> 6 yr for enuresis); sertraline (>6 yr for depression)

Psychotropic medications: stimulants, etc

- Amphetamines and methylphenidate; Atomoxetine (SNRI); alpha-2 adrenergics
- Mechanism of action: Exact mechanism = ? Block reuptake and increases release of NE and DA
- Evidence: ADHD
 - 75-80% response rate for stimulants; ~60% for atomoxetine; alpha-2 adrenergic agents = ?
- FDA approval: Stimulants approved for ADHD for >6 years of age
- Side effects
 - Sudden death
 - Cardio-vascular problems
 - Manic switching, psychosis
 - Abuse
 - Seizures, HBP, leukopenia, growth suppression (long term use)

- Benzodiazepines and buspirone
- Mechanism of action: Enhances GABA effects; binds to benzodiazepine receptors
- Evidence: not much
 - Panic attacks: strategy of use with SSRIs
- FDA approval
 - Lorazepam (Ativan; > 8 years of age)
- Side effects:
 - Withdrawal potential

Trends in use of psychotropics

- Across age groups, use of psychotropic medications has increased consistently since the early 1980s. In one study, over 8 million youth were found to take 1 or more psychotropic meds (Morris and Stone, 2011)
- **Preschoolers**
 - From 1991 to 1995, prescription rates for Medicaid-enrolled preschoolers doubled, primarily because of increases in atypical antipsychotic and antidepressant use (Zito et al, 2007; Zuvekas et al, 2006)
- **Children and Adolescents**
 - A 2- to 3-fold increase in the percentage of children/adolescents taking any psychotropic med between 1987 and 1996 (Pidano and Honigfeld, 2013)

Trends in use of psychotropics

- **Foster Children**

- In a 2004 study of foster children in Texas, 12,189 out of 32,135 Medicaid recipients (37.9%) were medicated with psychotropic meds; 15.9% received multiple psychotropic meds; antipsychotics were prescribed at a similar rate across 3 diagnostic groups: ADHD, depression, anxiety/adjustment reaction. (Zito, 2008)

- **Public vs Private Payer**

- Medicaid members were twice as likely to receive antipsychotic prescription than privately insured children/adolescents from 2007-2009 in a study by the GAO (2012)

African Americans: underserved



- In the study of psychotropic prescription practices by office-based physicians, African American youths were 2.5 times less likely to receive a prescription for a stimulant medication (Zito et al, 1997)
- African Americans were less likely to receive prescriptions for antidepressants than Caucasians when first diagnosed with depression (Melfi et al, 2000) and are less likely to be treated for mild/moderate depression and anxiety in juvenile justice settings (Dalton et al, 2009)

Who is prescribing psychotropics?

- The majority of psychotropic prescriptions for children and adolescents in the US are written by general practitioners and pediatricians (Shute et al, 2000)
- In a 1999 UNC survey of 600 pediatricians and family physicians, 72% said that they had prescribed antidepressants for children/adolescents, but only 15.6% said they felt “comfortable” doing so, and just 8% said they had adequate training to treat adolescent depression (Shute et al, 2000)
- However, psychiatrists are prescribing also: psychiatrists accounted for more than 80% of prescriptions for antipsychotic medications for Texas youths insured by Medicaid from 1996 to 2001 (Patel et al, 2006)

So, what we know is that...

- There is an increasing use of psychotropic medications across drug classes, age groups, payment sources and prescribers
- There are (at least) three possible explanations that account for the increased use of psychotropic medications
 - **The availability of new classes of drugs**
 - **Change in federal regulations concerning promotion of medications by pharmaceutical companies**
 - **Changing clinical practice**

So, what we know is that....

- **Availability of new classes of drugs**

- **SSRIs:** 9.2% annual growth of antidepressant use from 1998 through 2002 (Delate et al, 2004); **Atypical Antipsychotics:** Rates of use of antipsychotics doubled between 1991 and 1995 (Zito et al, 2007); Long-acting **Stimulants:** Since 1999 prescription rates have increased precipitously for stimulants (Thomas et al, 2006)

- **Changing federal regulations**

- The FDA Modernization Act, which was fully implemented in 1999, loosened restrictions on the promotion to physicians of off-label use of medications (Buck, 2000)
- Overall, spending by the pharmaceutical industry on television advertising increased six-fold to \$1.5 billion between 1996 and 2000 (Rosenthal et al, 2002)

Changing clinical practice

- Psychopharmacotherapy strategy has shifted in recent years to an approach similar to HIV treatment: using low dosages to minimize side effects and choosing meds based on symptoms, neurotransmitters, circuits and receptors (Stalh, 2013)
- This shift has contributed to polypharmacy and to increased use of psychotropic meds

Does this change represent inappropriate clinical practice?

- Walkup (2003) suggested that expanded psychotropic use has been necessary to address child/adolescent mental health problems. Increasingly effective pharmacotherapies are being provided to youths with serious mental health needs
- For example, between 1987 and 1997 the percentage of adolescents taking stimulants grew from 0.5% to 3.0% (Olfson, 2003); however, the prevalence of ADHD in children and adolescents is ~7%

Increased use: good or bad?

- What is the prevalence of child/adolescent behavioral health disorders?

DISORDER (Shafer et al, 1996)	PREVALENCE in childhood and adolescence
Anxiety disorders	13.0%
Mood disorders	7%
Disruptive behavioral disorders	10.3%
ADHD	7%
Substance Use disorders	2.0%
Any disorder	21%

Need vs. Availability

- 70% of children and adolescents who have a need for psychiatric services do not receive them (Burns et al, 1995)

Increased use: good or bad?

- However, as Zito (2003b) noted, the problem with Dr Walkup's argument is that there is no data that supports his view.
 - We do not know if the expanded use of psychotropics has gone to youths who need them
 - Further, little is known about long-term treatment outcome of currently used psychotropics and we simply don't know enough about the benefit/cost ratio of the expanded use of psychotropic medications

Increased use: good or bad?

- One issue in determining if the increased use of psychotropic meds is going to those who need them is that lack of correlation between recorded diagnoses and medication usage
 - 30% of office visits involving prescriptions for psychotropics did not also involve a psychiatric diagnosis (Goodwin et al, 2001)
- The issue is further complicated by the recorded diagnoses, themselves. Angold and colleagues (2000) studied ADHD and medication appropriateness. They found that administrative and clinical survey data provided diagnoses that were generated using non standardized diagnostic procedures. As a result, diagnoses were not reliable.

- **What is actually being treated?**

- Symptoms and behaviors, disconnected from diagnostic categories, have more and more become the focus of clinical decision-making about whether or not to prescribe a psychotropic medication and, if so, which medication, which dose, etc.
- However, most pediatric medication effectiveness studies measure outcome based on symptoms and behaviors **within** the context of specific diagnoses.
- Is impulsivity associated with ADHD treated like impulsivity associated with bipolar disorder? Is aggression associated with conduct disorder treated like aggression associated with affective problems? Is irritability associated with ODD treated like irritability associated with bipolar disorder?

An additional side effect of increased medication management



- The increase use of psychotropic medications appears to be connected to a concomitant decrease in talking therapy
- In a study of commercially-insured adolescents from 1997 to 2000 the results showed a 12.1% growth in medication costs per outpatient with a concomitant decrease in outpatient therapy by 9% (Martin and Leslie, 2003)

Conclusions

- There is ample evidence that use of psychotropic medications has increased consistently since the early 1980s
- The evidence does not clarify whether the increase has helped provide treatment for those who need it but who previously did not receive it. **However, it appears that children and adolescents in the US are both under treated and over treated with psychotropic medications**
- There is data about current psychotropic practices that causes concern and suggests that prescribing practices are sometimes questionable

Suggestions: Providers



1. Conduct an initial psychiatric evaluation (with medical history) utilizing both family and patient clinical interviews and standardized instruments. (Can this type of assessment occur in a primary care office?) (AACAP, 2009)
2. For preschool children, psychosocial treatment should be tried first. For school-age and adolescent youths, pharmacotherapy should not be provided without also providing appropriate psychosocial treatment. (Use psychosocial crisis management techniques before medications during emergencies. Avoid frequent use of emergency medications to control behavior.) (Gleason et al, 2007)

Suggestions: Providers



3. Treatment outcomes should be measured before and after treatment, especially if using a non evidence-based practice
4. Use appropriate treatment for primary disorders as a first-line therapy.
5. Taper and discontinue antipsychotics in patients who show a remission in aggression symptoms for 6 months (Papadopoulos et al, 2003)
6. If a patient is not responding to multiple medications, taper and discontinue one or more medications
7. Use a conservative dosing strategy; use an atypical antipsychotic rather than a typical for aggression

Suggestions: Providers

8. The prescriber is advised to communicate with other professionals involved with the child to obtain collateral history and set the stage for monitoring outcomes and side effects during the medication trial (AACAP, 2009)
9. Complete and document the assent of the child and consent of the parents before initiating medication treatment and at important points during the treatment (AACAP, 2009)
10. The assent and consent discussion focuses on the risks and benefits of the proposed and alternative treatments (AACAP, 2009)

Suggestions: Consumers

- Medication management strategies should be guided by system of care principles: they should be family-driven and youth-guided, among approaches. **Parents/caregivers should have the major voice in directing medication management. They should see prescribers as consultants.**

Suggestions: Consumers



- Parents & caregivers can make sure of the following before medications are tried:
 - A psychiatric evaluation has been completed with their child/adolescent.
 - The evaluation has included a medical history and special circumstances (examples include family issues, school bullying, etc) *ADD psychosocial items here*
 - The process has included all additional appropriate medical evaluations
 - The child/family has been educated about the diagnosis
 - They have tried all other evidence-based/evidence-informed interventions before choosing (non-evidence-based) medication management as a possible solution
 - The medication being suggested has been shown to be at least evidence-informed with children/youth of the same age group as their child
 - They understand the risks and benefits of using this medication
 - They and their child have given consent to try the medication

Suggestions: Consumers

- Parents & caregivers should ask questions about risk/benefit of meds:
 - What is the desired outcome (short-term and long-term) of the use of this med?
 - What are the potential side effects?
 - What will we do if the meds don't work?
 - How long will my child take these meds?
 - What labs will be ordered and with what frequency?
 - Can talking therapy help?
 - Whom do I contact if something goes wrong?

Suggestions: Consumers and CMCs

- Where do families turn when they need help asserting themselves during the treatment planning process?
 - Advocacy groups who can help in ways that run the gamut from coaching to attending treatment planning meetings and treatment sessions with the family/patient
- Families can turn to care managers in CMCs for information on advocacy and to ask for help if dissatisfied with the treatment process

Suggestions: CMCs

- CMCs that manage pharmacy benefits
 - Drug utilization reviews of medication use, especially with vulnerable groups (preschoolers, foster care clients) should be examined thoroughly and frequently
 - Performance Improvement Plans should be developed and implemented in response to DUR findings
 - Evidence-based pharmacotherapy and psychotherapy should be utilized for symptom/diagnosis clusters
- CMCs that do not manage pharmacy benefits
 - Ask that pharmacy management organizations share information about consumer pharmacotherapy to identify troubling trends
 - Medical directors should work directly with pharmacy management organizations to (try to) ensure appropriate use of meds (among ways by serving on P & T committees)

Questions?

Thank You!