

Improving the Quality of Psychotropic
Prescribing Practices in NYS

PSYCKES CQI Project
**Youth Indicator Set:
Too Young**

March 18th, 2011

Matt Perkins, MD



A Partnership Between Clinic Providers and OMH
to Improve the Outcome of Our Services

Agenda

- PSYCKES Youth Indicator Set
 - Too Young
- Quality Concerns
- Federal Drug Administration (FDA)
Indications for psychotropics in youth
- Recent Clinical Trials, Studies and Guidelines
- General Principles
- Questions and Answers

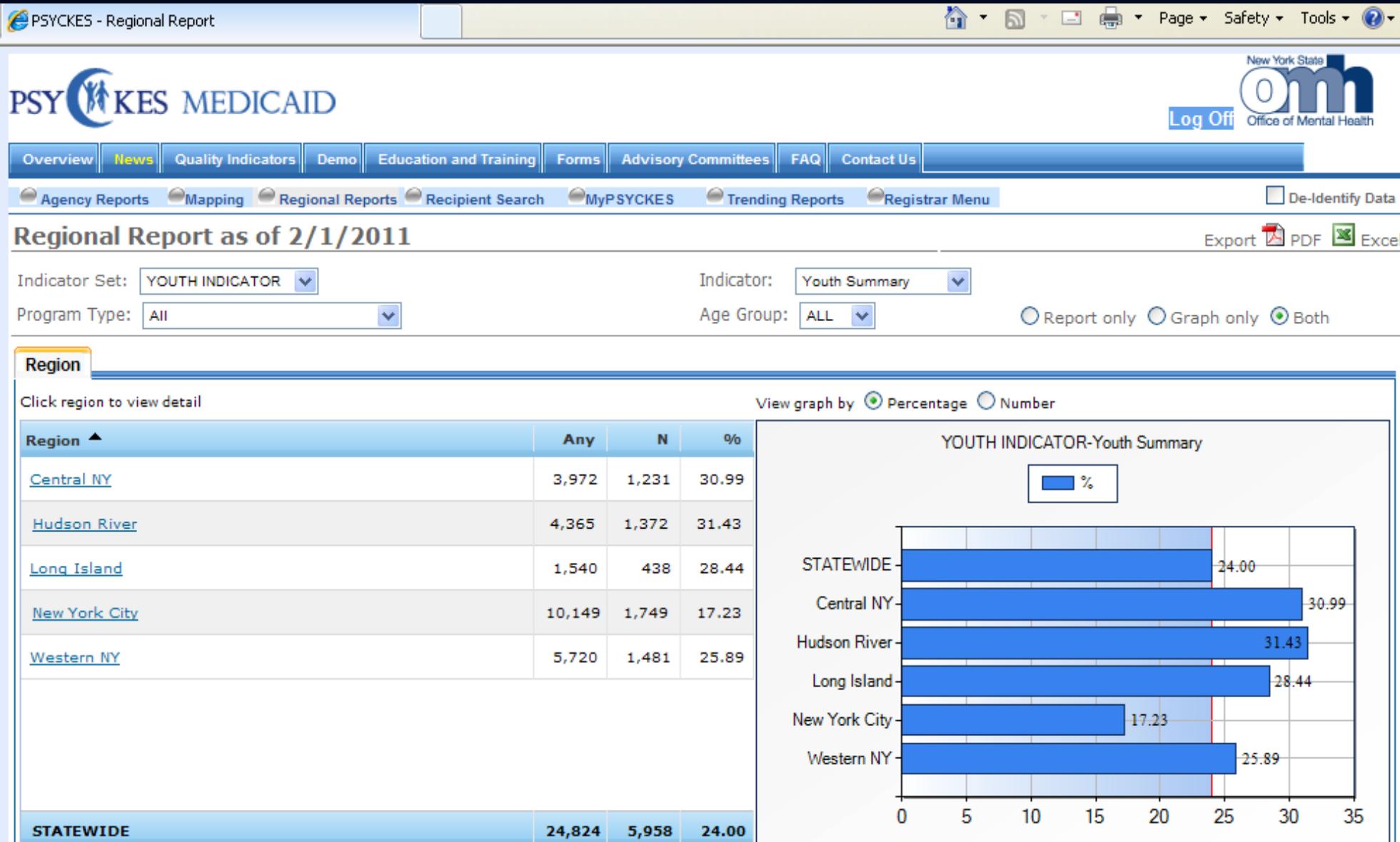
Youth Indicators

< 6	Very young children (less than 6 years old) on a psychotropic medication
Dose(Y)	Individuals under 18 on a higher than recommended dose of a psychotropic
3PP(Y)	Individuals under 18 on three or more psychotropic medications for longer than 90 days

“Too many, too much, too young”

- The rate of polypharmacy in outpatient settings for children on psychotropics. increased from 22%-32% in the past decade.
- The rate of polypharmacy is as high as 70% for children in foster care.
- Rates of antipsychotic use in preschoolers doubled between 1999 and 2007.

PSYCKES Youth Summary



PSYCKES Youth Psychotropic Polypharmacy

Regional Report as of 2/1/2011

Export PDF Excel

Indicator Set: **YOUTH INDICATOR**

Indicator: **Psychotropics Kids**

Program Type: **All**

Age Group: **ALL**

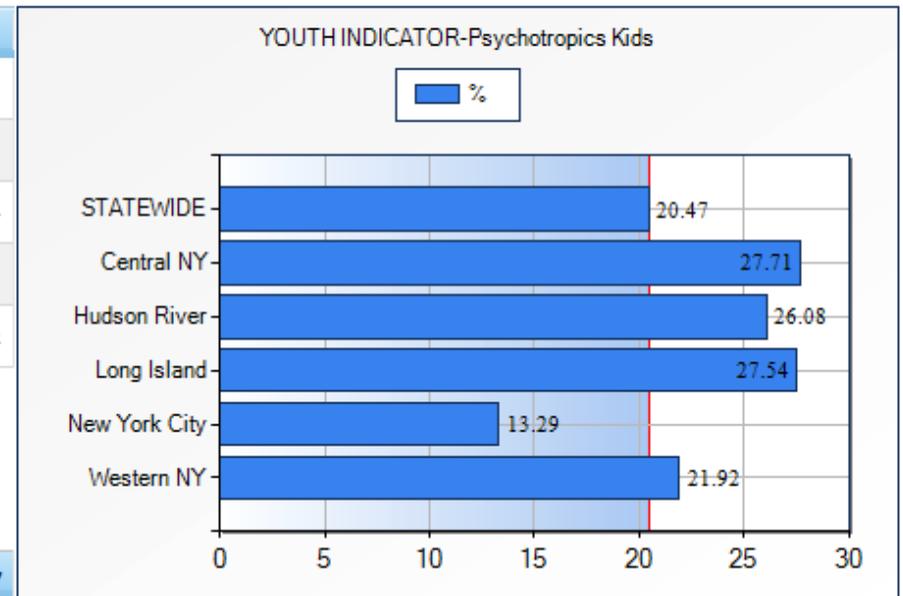
Report only Graph only Both

Region

Click region to view detail

View graph by Percentage Number

Region ^	Any	N	%
Central NY	3,216	891	27.71
Hudson River	3,394	885	26.08
Long Island	1,133	312	27.54
New York City	6,887	915	13.29
Western NY	4,471	980	21.92
STATEWIDE	18,389	3,764	20.47



PSYCKES Very Young Children on Psychotropics

Regional Report as of 2/1/2011

Indicator Set: **YOUTH INDICATOR**

Indicator: **Less than 6 years old**

Program Type: **All**

Age Group: **ALL**

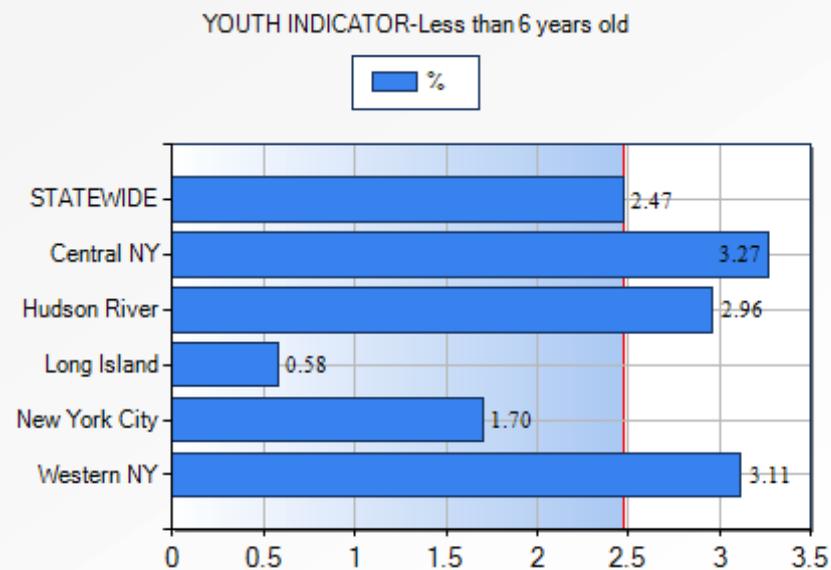
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Region

Click region to view detail

View graph by Percentage Number

Region ▲	Any	N	%
Central NY	3,972	130	3.27
Hudson River	4,365	129	2.96
Long Island	1,540	9	0.58
New York City	10,149	173	1.70
Western NY	5,720	178	3.11
STATEWIDE	24,824	613	2.47



PSYCKES Youth on Higher than Recommended Doses

Regional Report as of 2/1/2011

Indicator Set: **YOUTH INDICATOR**

Indicator: **Dose(Y)**

Program Type: **All**

Age Group: **ALL**

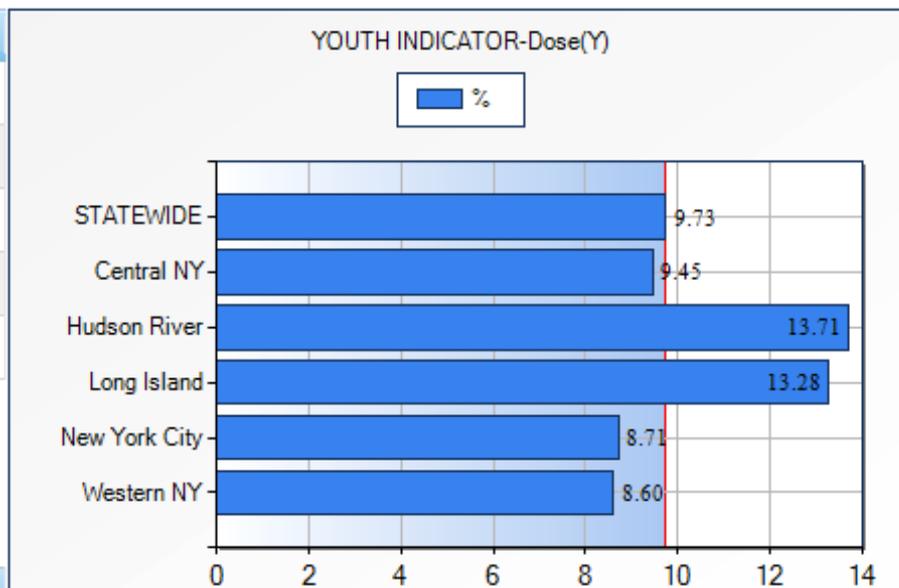
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Region

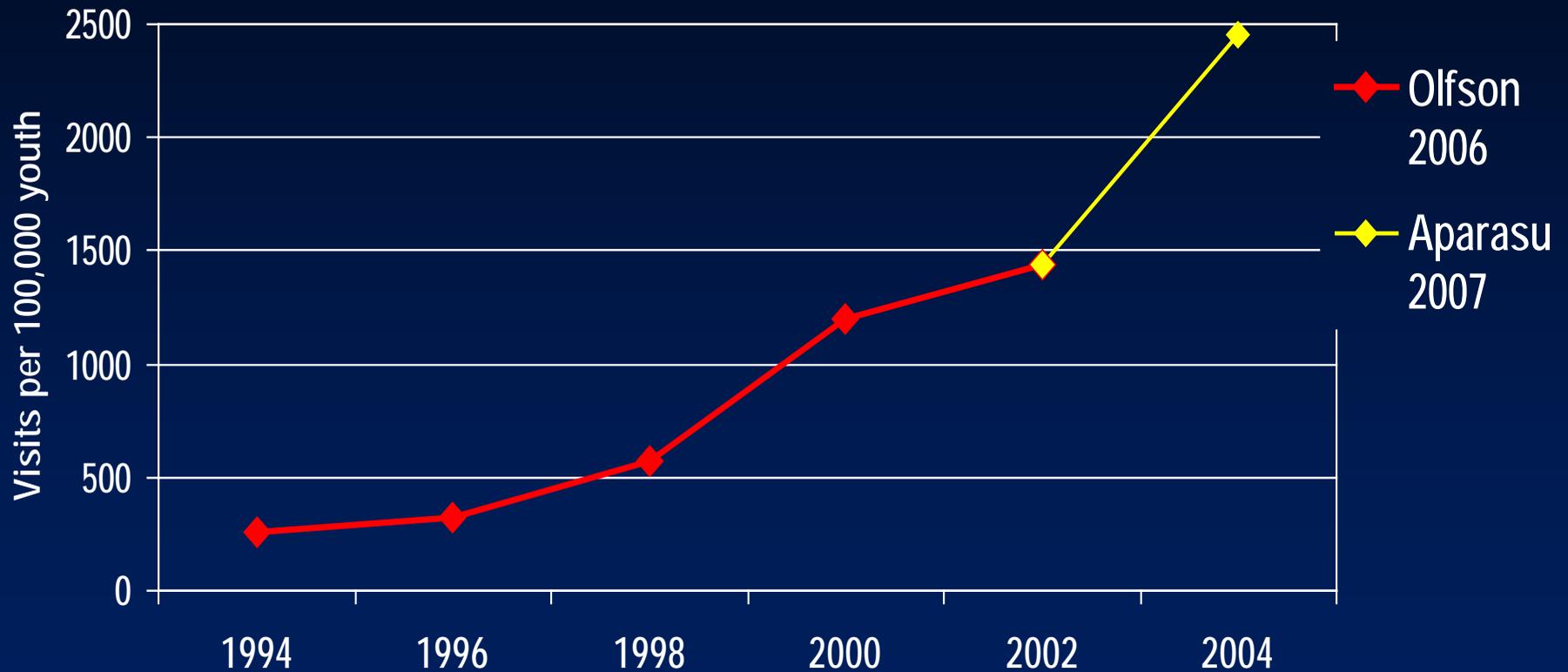
Click region to view detail

View graph by Percentage Number

Region	Any	N	%
Central NY	3,958	374	9.45
Hudson River	4,355	597	13.71
Long Island	1,536	204	13.28
New York City	10,139	883	8.71
Western NY	5,711	491	8.60
STATEWIDE	24,778	2,410	9.73



Atypical Antipsychotic Use Increasing Dramatically in Youth



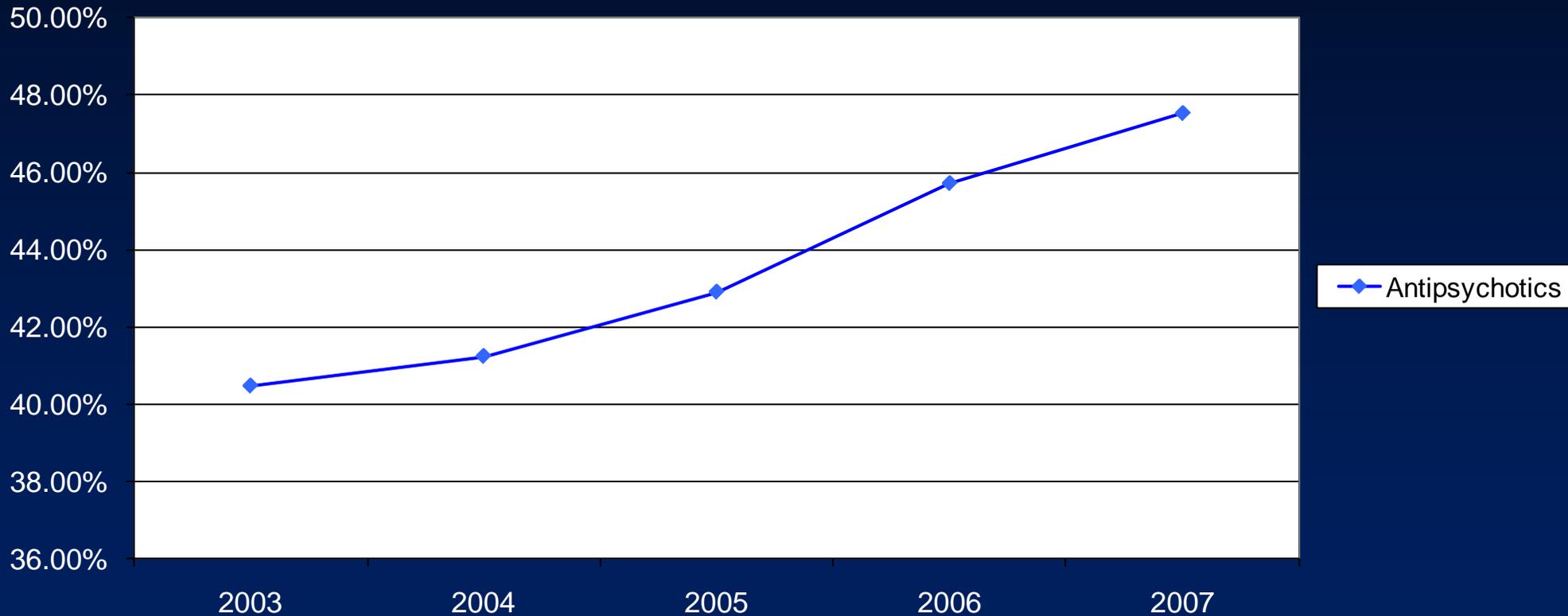
Olfson M et al. Arch Gen Psychiatry. 2006 Jun;63(6):679-85.

Aparasu R and Bhatara V. Curr Med Res Opin. 2007 Jan;23(1):49-56.

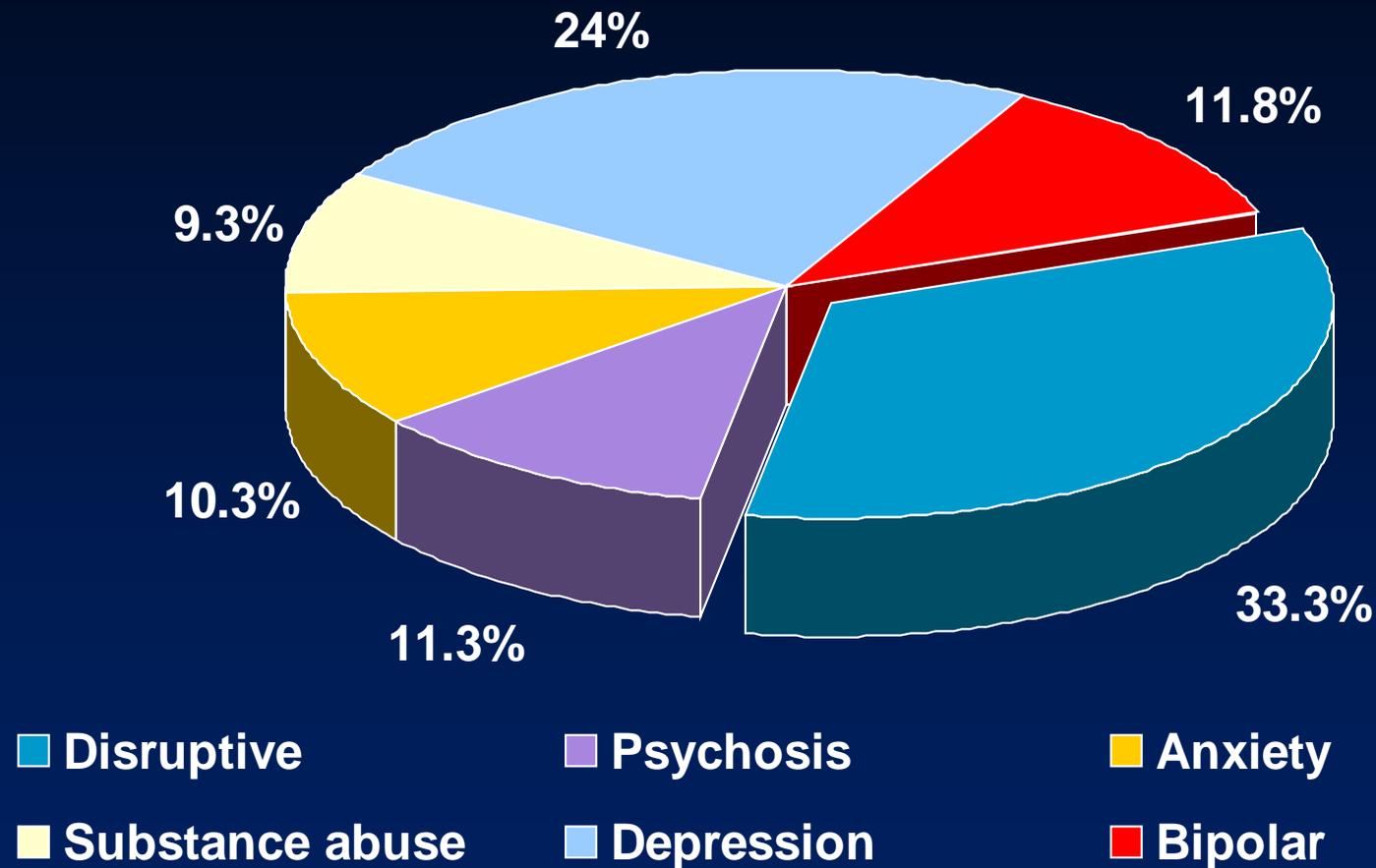
Adapted from Correll, 2008

Increases in Antipsychotic Prescribing

Proportion of Medicaid Recipients (Under 19) on Psychotropics prescribed an Antipsychotic in NYS



Diagnoses of Youths Treated With Antipsychotics



204 diagnoses from a sample of 100 inpatient charts (NYSOMH).
Pappadopoulos EA, Jensen PS, Schur SB, et al (2002). *Schizophr Bull* 28(1):111-121.

NY Times

Bipolar Illness Soars as a Diagnosis for the Young



Nathan Bilow for The New York Times

Brit Simons, 15, and his mother with pets. Drugs have tempered his outbursts, Ms. Simons said, and he is an honor roll student.

National Trends in the Outpatient Diagnosis and Treatment of Bipolar Disorder

- Data from the National Ambulatory Medical Care Survey (NAMCS)
- Between 1994-1995 and 2002-2003
- The number of outpatient visits by children and adolescents that included a bipolar diagnosis increased approximately **forty-fold** while the number of such visits by adults nearly doubled

Quality Concerns in Youth

- Very few randomized clinical trials of psychotropic medications have been conducted in children and adolescents.
- Response rates often decrease in younger children.
- Psychotropic medications are prescribed frequently off label to control behavior.
- As rates of psychotropic prescribing rise, the rates of psychosocial interventions diminish.

Prescribing Risks in Youth

- Youth are more vulnerable to intensity and frequency of side effects, including growth problems, delirium, akathisia and Extrapyramidal Symptoms (EPS), sleep problems, serious behavior changes, and cardiac arrhythmias.
- Youth are more likely to develop cardiometabolic concerns including obesity and type 2 diabetes.

Psychotropic Adverse Events In Children and Adolescents vs. Adults

- Increased risk for acute and intermediate adverse effects:
 - Sedation
 - EPS (except for akathisia)
 - Withdrawal dyskinesia
 - Prolactin-related adverse events (especially postpubertal females)
 - Weight gain and dyslipidemia
 - Suicidal ideas/behavior
- Decreased (or delayed?) risk for events that take many years to develop:
 - Persistent tardive dyskinesia
 - Imminent diabetes mellitus

Psychopharmacological Treatment for Very Young Children: Contexts and Guidelines

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ALICIA F. LIEBERMAN, Ph.D., JOAN L. LUBY, M.D., JUDITH OWENS, M.D.,
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ABSTRACT

Systematic research and practice guidelines addressing preschool psychopharmacological treatment in very young children are limited, despite evidence of increasing clinical use of medications in this population. The Preschool Psychopharmacology Working Group (PPWG) was developed to review existing literature relevant to preschool psychopharmacology treatment and to develop treatment recommendations to guide clinicians considering psychopharmacological treatment in very young children. This article reviews the developmental considerations related to preschool psychopharmacological treatment, presents current evidence bases for specific disorders in early childhood, and describes the recommended algorithms for medication use. The purpose of this effort is to promote responsible treatment of young children, recognizing that this will sometimes involve the use of medications. *J. Am. Acad. Child Adolesc. Psychiatry*, 2007;46(12):1532–1572. **Key Words:** preschool, treatment, psychopharmacology.

Background

- The primary treatment modality for most very young children is psychotherapeutic rather than psychopharmacological
- Studies of preschool psychopharmacological practice suggest that the majority of preschoolers with mental health problems do not receive psychopharmacological treatment
- Comprehensive, developmentally sensitive, and contextually relevant assessment is a prerequisite to consideration of treatment
- The impact of early and/or prolonged exposure to psychotropic medications in the preschool period has not been systematically studied, but research highlights the sensitivity of the developing brain
- Diagnostic, neurodevelopmental, metabolic, and regulatory considerations do not “comprise a universal proscription against the use of medication in young children”

Background (cont.)

- Growing (but still limited) evidence base for psychotherapeutic interventions in preschoolers.
- Evidence-supported models of treatment are effective in decreasing aggression and behavioral problems in young children with
 - Disruptive behavior disorders
 - Reducing child traumatic stress disorder symptoms
- Psychotherapeutic Interventions for preschoolers with Post Traumatic Stress Disorder (PTSD) and mania-like symptoms have also shown promising preliminary outcomes

Preschool Psychiatric Disorders

Can be associated with:

- Child care expulsion
- Inability to participate in family activities
- Impaired peer relationships
- High-risk behaviors
- Future mental health problems

Clinical Recommendations for Reducing Medication Risk in Youth

- Every child deserves a comprehensive psychiatric evaluation prior to the prescription of psychotropics. The primary diagnosis determines the starting point for medication.
- Treatment planning for youth and families should include psychosocial interventions as well as medications.
- “Start low, go slow” when changing doses of **medications**.

Clinical Recommendations for Reducing Medication Risk in Youth (continued)

- Collaborate closely with pediatricians to ensure appropriate monitoring of youth on atypical antipsychotics.
- Consult with a child psychiatrist prior to initiating polypharmacy or antipsychotic medication, or in complex cases.

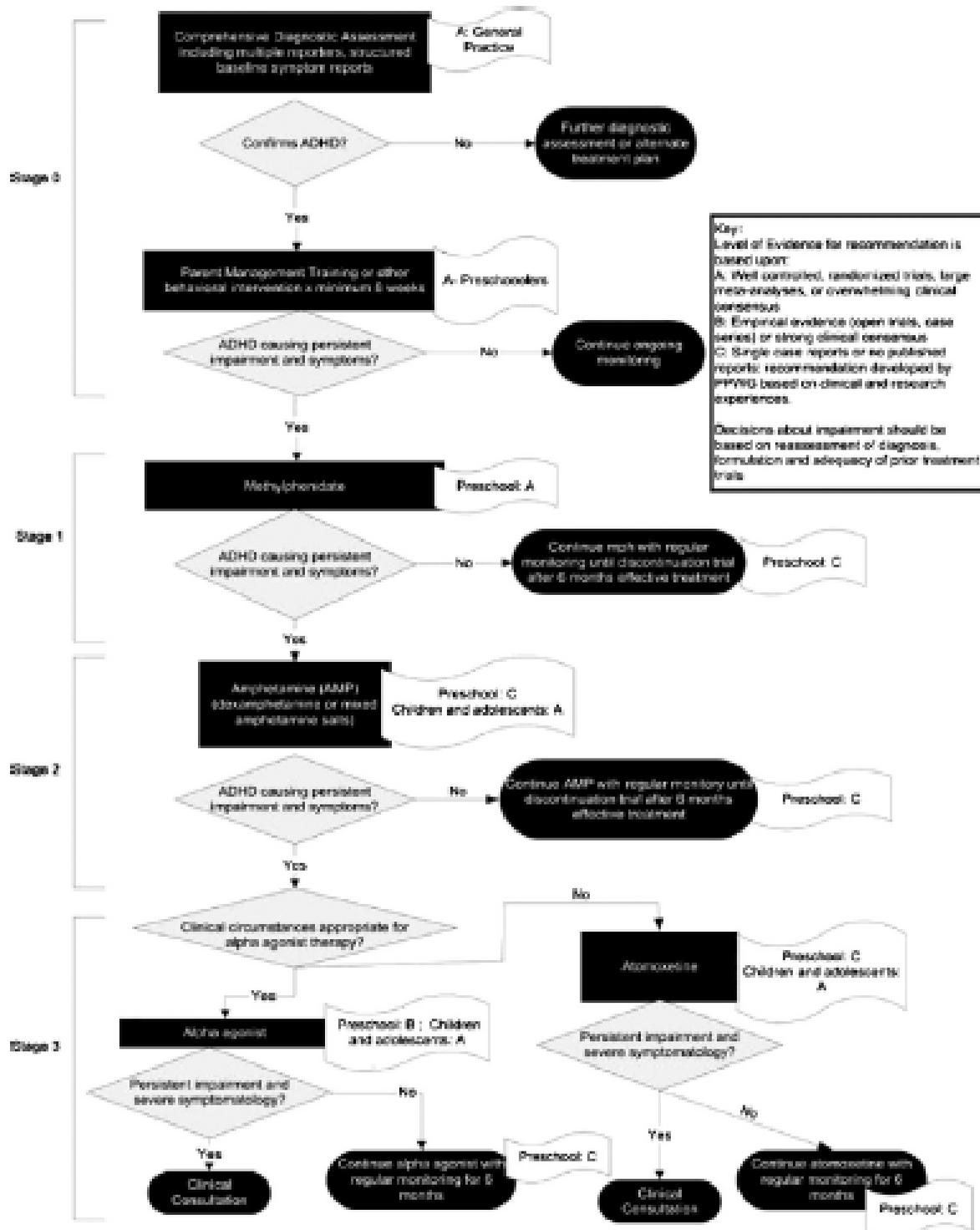


Fig. 1 ADHD algorithm.

Practice Parameter on the Use of Psychotropic Medication in Children and Adolescents

ABSTRACT

The purpose of this practice parameter is to promote the appropriate and safe use of psychotropic medications in children and adolescents with psychiatric disorders by emphasizing the best practice principles that underlie medication prescribing. The evidence base supporting the use of psychotropic medication for children and adolescents with psychiatric disorders has increased for the past 15 to 20 years, as has their use. It is hoped that clinicians who implement the principles outlined in this parameter will be more likely to use medications with the potential for pharmacological benefit in children safely and to reduce the use of ineffective and inappropriate medications or medication combinations. The best practice principles covered in this parameter include completing a psychiatric and medical evaluation, developing a treatment and monitoring plan, educating the patient and family regarding the child's disorder and the treatment and monitoring plan, completing and documenting assent of the child and consent of the parent, conducting an adequate medication treatment trial, managing the patient who does not respond as expected, establishing procedures to implement before using medication combinations, and following principles for the discontinuation of medication. *J. Am. Acad. Child Adolesc. Psychiatry*, 2009;48(9):961–973. **Key Words:** practice parameter, psychopharmacology, multiple medications, treatment.

Practice Parameter on the Use of Psychotropic Medication in Children and Adolescents

Principle 12. The Prescriber Needs a Clear Rationale for Using Medication Combinations.

Principle 12. The Prescriber Needs a Clear Rationale for Using Medication Combinations. Before the use of medication combinations, the prescriber needs to develop a treatment and monitoring plan, educate the patient and family, obtain assent/consent, and then implement the treatment trial as described under the principles above.

Commonly used psychotropic medication combinations include the following: medication combinations used to treat multiple disorders in the same patient (e.g., a stimulant and an SSRI for ADHD and anxiety⁴¹ or an antipsychotic and an SSRI for tics and OCD⁴³), medication combinations that offer unique treatment advantages for a single disorder (e.g., the addition of lithium to ongoing antidepressant treatment⁴⁴), and medication combinations to address side effects of an effective agent (e.g., benztropine for extrapyramidal symptoms secondary to an antipsychotic).

Although it is possible that combining medications from the same class may have empirical support in the future, there is limited support for such approaches at this time. For example, there is limited evidence in children and adolescents for the use of two antidepressants or two antipsychotics as an initial treatment approach or as a specific endpoint for treatment. However, it is not uncommon for patients to be taking two antidepressants or two antipsychotics at the same time when transitioning from one medication to another. For bipolar disorder in adults, data do support the use of two mood stabilizers,⁶⁴ and there is preliminary support for the use of similar strategies in children with bipolar disorder.⁶⁵ In addition, two stimulant formulations (i.e., short and long acting) may be used to “sculpt” dosing for coverage of extended periods of time.¹³

Evidence supporting medication combinations based on a matching medication mechanism of action with a hypothesized underlying central nervous system abnormality is rudimentary at best. For example, there is limited data to support

the use of two antidepressants to cover two neurotransmitter systems (i.e., using a serotonergic and a noradrenergic antidepressant for a certain profile of depressive symptoms). Basing treatment decisions on theories about central nervous system functioning or clinical correlates of hypothesized neurotransmitter abnormalities (e.g., specific symptom profiles, EEG, single-photon emission computed tomography testing) may put patients at risk for unnecessary medication combinations “to cover the neurotransmitter bases” or “to treat the EEG or single-photon emission computed tomography results.”

FDA Indications for Psychotropics in Youth

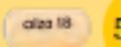
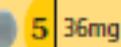
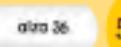
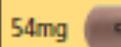
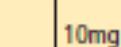
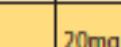
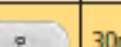
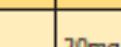
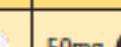
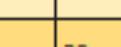
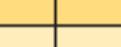
FDA-Approved Medications for ADHD

- Stimulants (ages 6 and up)
 - Methylphenidate (i.e. Ritalin, Concerta, Focalin)
 - Amphetamine (i.e. Dexedrine (ages 3 and up), Adderall, Vyvanse)
- Non-stimulants (ages 6 and up)
 - Atomoxetine (Strattera)
 - Guanfacine XR (Intuniv)
 - Clonidine XR (Kapvay)

ADHD Medication Guide*

Revised: 08/3/10

Methylphenidate Derivatives – Long Acting/Extended Release

	Concerta® †	18mg  5	27mg  5	36mg  5	54mg  5	72mg  +  6	
5	Focalin XR® ‡	5mg 		10mg 	15mg 	20mg 	30mg 
2	Ritalin® LA ‡	10mg 		20mg 	30mg 	40mg 	
3	Metadate® CD ‡	10mg 		20mg 	30mg 	40mg 	50mg  60mg 
2	Methylin® ER	10mg 		20mg 			
4	Ritalin® SR			20mg 			

3 Daytrana®






Daytrana® (methylphenidate transdermal system) 10mg

Daytrana® (methylphenidate transdermal system) 15mg

Daytrana® (methylphenidate transdermal system) 30mg

Daytrana® (methylphenidate transdermal system) 20mg

Methylphenidate Derivatives – Short Acting/Immediate Release

3	Focalin®		2.5mg 	5mg 	10mg 
4	Ritalin®		5mg 	10mg 	20mg 
2	Methylin®		5mg 	10mg 	20mg 
2	Methylin® Chewable §	2.5mg 	5mg 	10mg 	
2	Methylin® Solution (Grape Flavor)		5mg/5ml 	10mg/5ml 	

G indicates a generic formulation is available; generic products are not shown.

*Disclaimer: The North Shore-Long Island Jewish Health System is not affiliated with the owner of any of the brands referenced in this Guide. This Guide should not be used as an exclusive basis for decision-making. The user understands and accepts that if the health system were to accept the risk of harm to the user from use of this Guide, it would not be able to make the Guide available because the cost to cover the risk of harm to all users would be too great. Thus, use of this ADHD Medication Guide is strictly voluntary and at the user's sole risk.

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Amphetamine Derivatives – Long Acting/Extended Release

4	Vyvanse® †	20mg	30mg	40mg	50mg	60mg	70mg
5	Adderall XR® †	5mg	10mg	15mg	20mg	25mg	30mg
7	Dexedrine Spansule®	5mg	10mg	15mg			

For additional or updated copies of the ADHD Medication Guide, contact Dr. Andrew Adesman at ADHDMedGuide@nshs.edu.

Amphetamine Derivatives – Short Acting/Immediate Release

1	Adderall®	5mg	7.5mg	10mg	12.5mg	15mg	20mg	30mg
8	Dextroamphetamine	5mg		10mg				
1	ProCentra™ (Bubblegum Flavor)	5mg/5ml						

Medication Administration Key

- † Must be swallowed whole
- ‡ Can be dissolved in liquid
- § Chewable
- ‡ Capsule can be opened and medication sprinkled on applesauce

Non-Stimulants:

3	Intuniv® † (guanfacine)	1mg	2mg	3mg	4mg			
5	Strattera® † (atomoxetine)	10mg	18mg	25mg	40mg	60mg	80mg	100mg

*Disclaimer: North Shore-Long Island Jewish Health System is not affiliated with the owner of any of the brands referenced in this Guide.

The ADHD Medication Guide is a visual aid for professionals caring for individuals with ADHD. The Guide includes only medications indicated for the treatment of ADHD by the FDA. In clinical practice, this guide may be used to assist patients in identifying medications previously tried, and may allow clinicians to identify ADHD medication options for the future. Medications have been arranged on the card for ease of display and comparison, but dosing equivalence cannot be assumed. Practitioners should refer to the FDA-approved product information to learn more about each medication. Although every effort has been made to depict each medication in its actual size and color, we cannot guarantee that there are not minor distortions in the final image.

AGES FOR WHICH MEDICATIONS HAVE AN FDA INDICATION FOR TREATMENT OF ADHD.

Tab #	3-5 yrs	6-12 yrs	13-16 yrs	17 yrs	Adults
1	✓	✓			
2		✓			
3		✓	✓	✓	
4		✓			✓
5		✓	✓	✓	✓
6			✓	✓	✓
7		✓	✓		
8	✓	✓	✓		



Intuniv (Guanfacine XR)

- FDA approved for use in ages 6 to 17 for treatment of ADHD.
- Approved Sept 2009
- Long acting form of guanfacine
- Must be swallowed whole
- Available in 1,2,3,4 mg dosage strengths
- May take 3-4 weeks to see improvement

Kapvay (clonidine XR)

- FDA approved for use in youth ages 6 to 17 for ADHD as monotherapy and as adjunctive therapy to stimulant medications
- Approved October 2010
- Long acting form of clonidine
- Available in extended-release tablets: 0.1 mg and 0.2 mg, not scored
- Dosing should be initiated with one 0.1 mg tablet at bedtime, and the daily dosage should be adjusted in increments of 0.1 mg/day at weekly intervals until the desired response is achieved. Doses should be taken twice a day, with either an equal or higher split dosage being given at bedtime

Total Daily Dose	Morning Dose	Bedtime Dose
0.1 mg/day		0.1 mg
0.2 mg/day	0.1 mg	0.1 mg
0.3 mg/day	0.1 mg	0.2 mg
0.4 mg/day	0.2 mg	0.2 mg

Stimulant Medications: Efficacy

- Safety and efficacy studies in over 200 controlled studies of ADHD in school-age children
- One of the most robust treatments in psychiatry
- Effective in approximately 70% of children with ADHD—generally equal efficacy across stimulants
- An additional 20% will respond to the next one attempted
- If the 1st and 2nd choices fail, check for wrong diagnosis and/or previously unrecognized comorbidity

Cardiovascular Monitoring and Stimulants

- A thorough patient and family history and physical examination should be performed.
- Treatment without obtaining routine ECGs or routine subspecialty cardiology evaluations is appropriate for most children.
- Acquiring an ECG is not mandatory, but rather is left to the physician's discretion.
- An association between sudden cardiac death and stimulant medication has not been substantiated.

FDA-approved Antidepressants/Anxiolytics

Brand	Generic	Depression	Anxiety
Prozac	fluoxetine	MDD 8-17	OCD 7-17
Lexapro	escitalopram	MDD 12-17	
Zoloft	sertraline		OCD 6-17
Luvox	fluvoxamine		OCD 8-17
Anafranil	clomipramine		OCD 11-17

FDA-Approved Agents for Treatment of Bipolar Disorder

Agents	Manic	Mixed	Maintenance	Depression
ATYPICALS				
Aripiprazole (Abilify®)	+	+	+	- (also adjunctive for MDD)
Olanzapine (Zyprexa®)	+	+	+	-
Quetiapine (SEROQUEL®)	+	-	- (+ adjunctive)	+
Quetiapine XR (SEROQUEL XR®)	+	+	- (+adjunctive)	+ (also adjunctive for MDD)
Risperidone (Risperdal®)	+	+	-	-
Ziprasidone (Geodon®)	+	+	-	-
OTHER				
Carbamazepine ER (Equetro™)	+	+	-	-
Divalproex DR (Depakote®)	+	-	-	-
Divalproex ER (Depakote® ER)	+	+	-	-
Lamotrigine (Lamictal®)	-	-	+	-
Lithium (Lithobid®, Eskalith®)	+	-	+	-
Olanzapine/fluoxetine (Symbyax®)	-	-	-	+

FDA Pediatric Labeling for Bipolar Disorder

Brand name	Generic Name	Indicated Age
Eskalith, Lithobid	lithium carbonate	13 and older (Bipolar Disorder)
Risperdal	risperidone	10 and older (Manic/Mixed)
Abilify	aripiprazole	10 and older (Manic/Mixed)
Seroquel	quetiapine	10 and older (Manic)
Zyprexa	olanzapine	13 and older (Manic/Mixed)

Atypical Antipsychotics

Clozaril '89	clozapine
Risperdal '93	risperidone
Zyprexa '96	olanzapine
Seroquel '97	quetiapine
Geodon '01	ziprasidone
Abilify '02	aripiprazole
Invega '06	paliperidone
Saphris '09	asenapine
Fanapt '09	iloperidone
Latuda '10	lurasidone

FDA Indications for Atypical Antipsychotics in Children and Adolescents

Risperidone (Risperdal)

- Bipolar disorder, Manic/Mixed episodes for children ages 10-17
- Schizophrenia for children ages 13-17
- **Irritability** symptoms of **autistic disorder** in children ages 5-16

Aripiprazole (Abilify)

- Bipolar disorder, Manic/Mixed episodes for children ages 10-17
- Schizophrenia for children ages 13-17
- **Irritability** symptoms of **autistic disorder** in children ages 6-17

Quetiapine (Seroquel)

- Bipolar disorder, Manic episodes for children ages 10-17
- Schizophrenia for children ages 13-17

Olanzapine (Zyprexa)

- Bipolar disorder, Manic/Mixed episodes for children ages 13-17
- Schizophrenia for children ages 13-17

Evidence also for aggression (particularly risperidone) but must weigh side effects and consider general principles (thorough diagnostic evaluation, treat primary disorder, etc)

Safety and Tolerability of Atypical Antipsychotics

	Anticholinergic	Elevated Prolactin	EPS	Orthostasis	QTc Increase	Sedation	Weight Gain
Clozapine	++++	0/+	0/+	+++	+	++++	++++
Risperidone	+	++++	++	++	+	+	+++
Olanzapine	++	++	+	++	+	+++	++++
Quetiapine	+	0/+	0/+	++	+	++	++
Ziprasidone	+	+	+	+	++	+	0/+
Aripiprazole	0/+	0/+	+	+	0	+	0/+

Cardiometabolic Risk of Second-Generation Antipsychotic Medication During First-Time Use in Children and Adolescents

Table 2. Change in Body Composition Parameters Over Time

Outcome Variable	Weeks 0-12	
	Mean (95% CI)	P Value
Weight, kg		
Aripiprazole	4.44 (3.71 to 5.18)	<.001
Olanzapine	8.54 (7.38 to 9.69)	<.001
Quetiapine	6.06 (4.90 to 7.21)	<.001
Risperidone	5.34 (4.81 to 5.87)	<.001
Untreated	0.19 (-1.04 to 1.43)	.77

Significant Changes in Metabolic Parameters Over Time

	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	Non-HDL Cholesterol (mg/dl)	TG:HDL Ratio
Olanzapine	15.58	24.34	16.81	0.59
Quetiapine	9.05	36.96	9.93	1.22
Risperidone	NS	9.74	NS	NS
Aripiprazole	NS	NS	NS	NS

Monitoring for Children and Adolescents on Antipsychotics

Assessments	Frequency
Personal and Family History	Baseline and Annually
Lifestyle monitoring	Every visit
Height, weight, BMI percentile	Every visit
Somnolence/sedation	Every visit
Sexual symptoms/signs	Baseline, during titration and every 3 months
Blood pressure, pulse	Baseline, 3 months and 6-monthly
Fasting glucose, lipids	Baseline, 3 months and 6-monthly
Liver function tests	Baseline, 3 months and 6-monthly
EPS, akathisia	Baseline, titration, 3 months and annually
Dyskinesia/Tardive Dyskinesia	Baseline, 3 months and annually
Electrolytes, blood count, renal function	Baseline and annually (unless on Clozapine)
Prolactin	Only when symptomatic
EKG	If on ZIP, during titration, at max dose

AP SIDE-EFFECTS CHECKLIST

Patient _____

Rater _____

Date _____

INSTRUCTIONS

Rate the severity of the following side effects from 0 (not present) to 3 (severe). Side effects marked with a † should be scored using only 0 (not present) or 1 (present). Refer to the pocket guide for BMI scores and age percentiles.

ANCHORS

0 = None
1 = Mild

2 = Moderate
3 = Severe

N/A = Not Assessed

Life-Threatening

NMS † _____
Decreased ANC _____
Agranulocytosis † _____
Marked increase in LFTs _____

EPS

Akathisia _____
Akinesia _____
Tremor _____
Muscle Rigidity _____
Dystonia † _____
Tardive Dyskinesia _____

Cognitive Effects

Confusion _____
Memory Problems _____
Sedation _____
Hypersomnia _____
Irritability _____
Headache _____

Cardiac

QTc Prolongation _____
Tachycardia _____
Hypotension _____

Weight and Diabetes

Height _____ inches
Baseline Weight _____ lbs.
Current Weight _____ lbs.
Weight Gain _____ lbs.
BMI _____
BMI Percentile _____
Elevated Glucose _____
Elevated Cholesterol _____
Elevated Triglycerides _____

Endocrine

Amenorrhea † _____
Galactorrhea † _____
Gynecomastia † _____

Anticholinergic

Dry Mouth _____
Blurred Vision _____
Constipation _____

Other

Insomnia _____
Nausea/Vomiting _____
Sexual Dysfunction _____
Decreased Libido _____
Dermatological _____
Hypersalivation _____
Enuresis _____

TABLE 7

A 12-Step Healthy Lifestyle Program

Do's	Don'ts
Replace sugar-containing drinks with water	Skip breakfast
Eat 4–5 small meals/day, with no more than 1 meal in the evening or at night	Consume fast food >1/wk
Serve small meal portions	Consume saturated or processed fat-free food (containing high amounts of fast-degradable sugars)
Eat slowly, drink water, take seconds only after delay	Watch TV, play computer games >2 h/day
Eat food with a low glycemic index (<55)	
Consume >25–30 g of soluble fiber per day	
Snack only when hungry and only fruit or vegetables	
Perform moderate physical activity for >30–60 min/day	

Modified from Correll and Carlson.²⁶

Recent Clinical Trials, Studies and Guidelines

Important Child Psychopharmacology Studies

- **Multimodal Treatment Study of ADHD (MTA)**
 - Methylphenidate significantly better than intensive behavioral therapy alone
- **Preschool Attention Deficit Hyperactivity Disorder (ADHD) Treatment Study (PATS)**
 - Preschool study demonstrating efficacy and poorer tolerability of methylphenidate for ADHD
- **Child/Adolescent Anxiety Multimodal Study (CAMS)**
 - Combination of sertraline and Cognitive Behavioral Therapy (CBT) best, monotherapy of either modality also effective
- **Pediatric Obsessive Compulsive Disorder (OCD) Treatment Study (POTS)**
 - OCD treatment should begin with combination of CBT plus a Selective Serotonin Reuptake Inhibitor (SSRI, sertraline) or CBT alone

Important Child Psychopharm Studies—Cont.

- **Treatment of Adolescent Depression Study (TADS)**
 - Combination of fluoxetine and CBT best, fluoxetine monotherapy also effective
- **Treatment of SSRI-Resistant Depression in Adolescents (TORDIA)**
 - If an SSRI doesn't work, either a different SSRI or venlafaxine may be effective and addition of CBT is often beneficial
- **Research Units for Pediatric Psychopharmacology (RUPP)**
 - Risperidone effective for irritability component of Autism
 - Fluvoxamine effective for anxiety
- **Treatment of Early-Onset Schizophrenia Spectrum Disorders (TEOSS)**
 - Molindone as effective as olanzapine and risperidone, but with significantly less cardiometabolic side effect

Recent NIMH Studies

TABLE 1
Recent NIMH-Sponsored Multisite Clinical Trials in Children and Adolescents

Study	Main Aim-Interventions	Psychopathology	Subjects (Randomized)	Design and Duration	Main Findings
TADS	To compare the effectiveness of fluoxetine and CBT, alone and in COMB	Major depressive disorder	<i>N</i> = 439; 12–17 years old	Randomized; parallel groups; placebo-controlled; 12 weeks of acute treatment, followed by a 24-week continuation	Fluoxetine was more effective than CBT alone at accelerating improvement but increased risk for suicidal events. COMB was most effective in accelerating remission and minimizing suicidality. ^{4,5}
TORDIA	To compare the effectiveness of alternative antidepressant medications (SSRI or venlafaxine) alone and in combination with CBT (COMB)	Major depressive disorder nonresponsive to 1 adequate trial of antidepressant medication	<i>N</i> = 326; 12–18 years old	Randomized; parallel groups; factorial with 4 parallel groups; 12 weeks of acute treatment, followed by a 12-week continuation	COMB was better than medication alone at improving depression. No difference in efficacy between types of medication. ⁶
POTS	To test the efficacy of sertraline and CBT, alone and in COMB	Obsessive-compulsive disorder	<i>N</i> = 112; 7–17 years old	Randomized; parallel groups; placebo-controlled; 12 weeks	COMB was most effective; CBT found necessary for optimal effectiveness. ⁷
PATS	To test efficacy and tolerability of methylphenidate	ADHD, hyperactive or combined	<i>N</i> = 165; 3–5 years old	Randomized; placebo-controlled; crossover, with 4 fixed doses plus placebo (1 week for each condition), followed by a 4-week parallel group, and a 10-month naturalistic maintenance	Methylphenidate was efficacious starting at 7.5 mg/day; 12% of children did not tolerate adverse effects; effect on growth with 1-year treatment. ^{8–12}
Treatment of Hyperactivity and Impulsiveness in Children with PDD	To test the efficacy and tolerability of methylphenidate in decreasing ADHD	Autism and other PDDs with impairing hyperactivity and/or impulsivity	<i>N</i> = 72; 5–14 years old	Randomized; placebo-controlled; crossover, with 3 fixed doses plus placebo; 1 week for each condition	Methylphenidate was efficacious in approximately 50% of the patients; 18% of the patients discontinued treatment due to adverse effects. ¹³

Note: NIMH = National Institute of Mental Health; TADS = Treatment for Adolescents with Depression Study; CBT = cognitive-behavioral therapy; COMB = combination; TORDIA = Treatment of Resistant Depression in Adolescents; SSRI = selective serotonin reuptake inhibitor antidepressants; POTS = Pediatric Obsessive-Compulsive Treatment Study; PATS = Preschoolers with ADHD Treatment Study; PDD = pervasive developmental disorder.

Preschool ADHD Treatment Study (PATs)

- 8 phases over 70 weeks
- 6 academic sites
- N=303
- 3 to 5.5 years of age
- Tolerability lower than expected for older kids (11% of patients discontinued)
- Methylphenidate dose of 7.5 to 30 mg/day with mean optimal dose of 14.22 +/- 8.1 mg/day
- MTA—(7-9 year olds) average dose 30.2-41.3 mg/day
- Average adult dosage is 20 mg to 30 mg

Predictors of ADHD later in life

- Preschool expulsion
 - usually caused by
 - aggressive behavior
 - refusal to participate in school activities
 - failure to respect other children's property or boundaries
- Peer rejection
 - parents can easily identify
 - Children with extreme behaviors are avoided by their classmates
 - shunned on the playground
 - Other children are "busy" whenever parents try to arrange playdates

PATS

- Effect size (0.4--0.8) in the PATS was smaller than that seen in older children (0.5--1.3)
- Preschoolers also had higher rates of emotional lability compared with published rates for older children

Child–Adolescent Anxiety Multimodal Study (CAMS)

- Federally funded, multi-site RCT in 488 youth (7-17 yrs) with a primary diagnosis of non-OCD anxiety disorder (separation anxiety disorder, generalized anxiety disorder, or social phobia)
- Randomized to 12 weeks of
 - CBT
 - Sertraline (SER)
 - Combination of CBT + SER (COMB)
 - Placebo (PBO)

Child–Adolescent Anxiety Multimodal Study (CAMS)

Four Treatment Groups
Sertraline for 12 weeks
Cognitive Behavioral Therapy (CBT) for 12 weeks
Combination of sertraline and cognitive behavioral therapy for 12 weeks
Placebo for 12 weeks

COMBINATION > MEDS=CBT > PBO

CAMS

- Efficacy results:
 - CGI-I Response Rates:
 - COMB (81%) > CBT (60%) = SER (55%) > PBO (24%)
 - PARS
 - COMB > SER = CBT > PBO
 - Number Needed to Treat (NNT)
 - COMB 1.7
 - SER 3.2
 - CBT 2.8
- Mean dose of SER/PBO at final visit:
 - SER: 134 mg/day
 - COMB: 146 mg/day

The Treatment for Adolescents With Depression Study (TADS)

- Fluoxetine (FLX) versus FLX and CBT (COMB) versus CBT alone
- Adjusted CGI-I response rates over time :
 - 12 wks: COMB (73%) = FLX (62%) > CBT (48%)
 - 18 wks: COMB (85%) > FLX (69%) = CBT (65%)
 - 24 wks: All three treatments converged
 - 36 wks: COMB (86%) = FLX (81%) = CBT (81%)

The Treatment for Adolescents With Depression Study (TADS)

- Long-term Safety
- Suicidal ideation over time:
 - 12 wks: FLX (19%) > COMB (9%) = CBT (6%)
 - 36 wks: FLX (14%) > CBT (4%) = COMB (3%)
 - No completed suicides

Table 5. ORs and Treatment Contrasts for Suicidal Events

Planned Contrast	ITT Population			OC Population		
	χ^2 Test	<i>P</i> Value ^a	OR (95% CI)	χ^2 Test	<i>P</i> Value ^a	OR (95% CI)
Stage 1						
Combination-CBT ^b	0.0	> .99	1.0 (0.3-3.7)	0.0	> .99	1.0 (0.3-3.7)
FLX-CBT	3.3	.07	2.6 (0.9-7.7)	1.9	.17	2.1 (0.7-6.5)
FLX-combination	3.0	.08	2.5 (0.9-7.4)	1.7	.19	2.1 (0.7-6.2)
Stages 1-3						
Combination-CBT	0.4	.55	1.4 (0.5-3.8)	0.4	.53	1.4 (0.5-4.2)
FLX-CBT	4.1	.04	2.6 (1.0-6.5)	2.3	.13	2.2 (0.8-6.0)
FLX-combination	2.1	.15	1.9 (0.8-4.4)	0.8	.37	1.5 (0.6-3.9)

Abbreviations: CBT, cognitive behavior therapy; CI, confidence interval; FLX, fluoxetine hydrochloride therapy; ITT, intention-to-treat; OCs, observed cases; OR, odds ratio.

^a Unless otherwise indicated, *P* values were calculated using 2×2 χ^2 test results.

^b Fisher exact test was used to calculate the *P* value owing to 25% of the cells having expected counts less than 5.



**TREATMENT OF
MALADAPTIVE
AGGRESSION
IN YOUTH**

T-MAY

The Rutgers CERTs Pocket Reference Guide

For Primary Care Clinicians and Mental Health Specialists

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T-MAY RECOMMENDATIONS

ASSESSMENT + DIAGNOSIS

Engage patients and parents (emphasize need for their on-going participation)
Conduct a thorough initial evaluation and diagnostic work-up before initiating treatment
Define target symptoms and behaviors in partnership with parents and child
Assess target symptoms, treatment effects and outcomes with standardized measures

INITIAL TREATMENT + MANAGEMENT PLANNING

Conduct a risk assessment and if needed, consider referral to mental health specialist or ER
Partner with family in developing an acceptable treatment plan
Provide psychoeducation and help families form realistic expectations about treatment
Help the family to establish community and social supports

PSYCHOSOCIAL INTERVENTIONS

Provide or assist the family in obtaining evidence-based parent and child skills training
Identify, assess and address the child's social, educational and family needs, and set objectives and outcomes with the family
Engage child and family in maintaining consistent psychological/behavioral strategies

MEDICATION TREATMENTS

Select initial medication treatment to target the underlying disorder(s); follow guidelines for primary disorder (when available)
If severe aggression persists following adequate trials of appropriate psychosocial and medication treatments for underlying disorder, add an AP, try a different AP, or augment with a mood stabilizer (MS)
Avoid using more than two psychotropic medications simultaneously
Use the recommended titration schedule and deliver an adequate medication trial before adjusting medication

SIDE-EFFECT MANAGEMENT

Assess side-effects, and do clinically-relevant metabolic studies and laboratory tests based on established guidelines and schedule
Provide accessible information to children and parents about identifying and managing side-effects
Use evidence-based strategies to prevent or reduce side-effects
Collaborate with medical, educational and/or mental health specialists if needed

MEDICATION MAINTENANCE + DISCONTINUATION

If response is favorable, continue treatment for six months.
Taper or discontinue medications in patients who show a remission in aggressive symptoms ≥ 6 months

Note: The order of these recommendations may be tailored to each patient's specific condition and needs.

USUAL MEDICATION DOSING AND TITRATION INTERVALS OF ANTIPSYCHOTICS (APs) *

ANTIPSYCHOTIC	DOSE RANGE (mg)	DOSE STRENGTH (mg)	MEDICATION FORMULATIONS (available for use)	STARTING DOSE (mg)	HALF LIFE (hrs)	TIME TO PEAK (hrs)	TITRATION INTERVALS (days)	PRINCIPAL LIVER ENZYME	LIVER ENZYME INDUCER	LIVER ENZYME INHIBITOR
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SECOND GENERATION ANTIPSYCHOTICS (SGA)

ARIPIPRAZOLE (ARI)	Child: 2.5 - 15 Adol: 5 to 15	2, 5, 10, 15, 20, 30 tbi; 10, 15 diss, liquid 1 (30 mg = 25 mL)	po, im short, diss., liquid	2 to 5	50 to 72	3 to 5	when starting at 2mg, may increase dose every 3rd day; after steady state, increase dose every 7-14 days	2D6 > 3A4	3A4	2D6 3A4
				Chlorpromazine Dose ≈ 7.5mg						
CLOZAPINE (CLO)	Child: 150 - 300 Adol: 200 - 600	25; 100	po	12.5	12	1 to 4	25 mg daily or, every other day	1A2>2C19 2C19>3A4 3A4 > 2C9 2C9 > 2D6	1A2 2C19 3A4	1A2 2C19 3A4 2C9
				Chlorpromazine Dose ≈ 50 mg						
OLANZAPINE (OLA)	N/A	5, 5, 7.5, 10, 15, 20 tb 5, 10, 15, 20 diss; 10im	po, im short, diss.	5 to 10	30	6	increase at intervals > 5 days	1A2 2D6 3A4	1A2 2D6 3A4	1A2 2D6 3A4
				Chlorpromazine Dose ≈ 5 mg						
PALIPERIDONE (PAL)	3 to 12	3, 6, 9	po, ER	3	21 to 30	24	increase at intervals > 5 days	<10% Hepatic Clearance	N/A	N/A
				Chlorpromazine Dose ≈ 3 mg						
QUETIAPINE (QUE)	150 to 750	25, 100, 200	po, XR	50-100 IR 200-300 XR	6 to 7	2	100 mg per day	3A4	3A4	3A4
				Chlorpromazine Dose ≈ 75 mg						
RISPERIDONE (RIS)	Child: 1.5 - 2 Adol: 2 to 4	0.5, 1, 2, 3, 4 tablets; 0.5, 1, 2 diss; liquid 1mg/mL 30ml bottl	po, im long, diss., liquid	0.5 to 1	3	1 to 2	increase at intervals of 0.5-1 per day or > 5 days	2D6 > 3A4	2D6 3A4	2D6 3A4
				Chlorpromazine Dose ≈ 2 mg						
ZIPRASIDONE (ZIP)	80 to 160	20, 40, 60, 80 tablets	po im short	20 to 40			increase at 20- 40 per day	Aldehyde Oxidase > 3A4	3A4	3A4
				Chlorpromazine Dose ≈ 60 mg	7	5				

Modified from: Correll 2008 (Correll CU). Antipsychotics and Adjunctive Medications. In: Textbook of a Child and Adolescent Psychiatry. M Dulcan (ed.), American Psychiatric Publishing, Inc. New York.

Modified from: 2004 .TRAAAY - A Pocket Reference Guide. New York State Office of Mental Health, Research Foundation for Mental Hygiene, Inc. and the Trustees of Columbia University.

TYPICAL MEDICATION DOSING AND TITRATION INTERVALS OF ANTIPSYCHOTICS *

ANTIPSYCHOTIC	DOSE RANGE (mg)	DOSE STRENGTH (mg)	MEDICATION FORMULATIONS (available for use)	STARTING DOSE (mg)	HALF LIFE (hrs)	TIME TO PEAK (hrs)	TITRATION INTERVALS (days)	PRINCIPAL LIVER ENZYME	LIVER ENZYME INDUCER	LIVER ENZYME INHIBITOR
FIRST GENERATION ANTIPSYCHOTICS (FGA)										
HALOPERIDOL (HAL)	1 to 6	0.5, 1, 2, 5, 10, 20 tablets, 2; 10 mg/mL liquid, 5 im	po, im short	0.25-1	3 - 6 po	2-6 po	increase dose by 0.5 kg intervals of 5-7 days	3A4	3A4	3A4
			im long	Chlorpromazine Dose » 2 mg	10-20 im	.05 im				
MOLINDONE (MOL)	20 to 140	5, 10, 25, 50	po	0.5-1 mg/kg/d divided in 3-4 doses	1.5	1.5	N/A	2D6	2D6	2D6
				Chlorpromazine Dose ≈ 10 mg						
PERPHENAZINE (PER)	8 to 32	2, 4, 8, 16	po	TBD; no data available	8 to 12	1 to 3	TBD; no data available	2D6	2D6	2D6
				Chlorpromazine Dose ≈ 10 mg						

Modified from: Correll 2008 (Correll CU). Antipsychotics + Adjunctive Medications. Textbook of a Child + Adolescent Psychiatry. M Dulcan (ed.), American Psychiatric Publishing, Inc. New York.

Treatment of Early-Onset Schizophrenia Spectrum Disorders (TEOSS)

- Double blind, multisite trial, randomized assignment of pediatric patients with early-onset schizophrenia and schizoaffective disorder to:
 - Olanzapine (2.5-20 mg/day)
 - Risperidone (0.5-6 mg/day) OR
 - Molindone (10-140 mg/day, plus 1 mg benztropine)
- No significant differences among treatment groups in response rate
- Olanzapine and risperidone associated with significantly greater risk of weight gain, increased cholesterol, insulin resistance and liver transaminase levels
- Molindone with more self-reports of akathisia (subjective sense of irritability)

AACAP Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficity/Hyperactivity Disorder

SCREENING

Recommendation 1 Screening for ADHD should be part of every patient's mental health assessment.

EVALUATION

Recommendation 2 Evaluation of the preschooler, child or adolescent for ADHD should consist of clinical interviews with the parent and patient, obtaining information about the patient's school or day care functioning, evaluation for comorbid psychiatric disorders, and review of the patient's medical, social, and family histories.

Recommendation 3 If the patient's medical history is unremarkable, laboratory or neurological testing is not indicated.

Recommendation 4 Psychological and neuropsychological tests are not mandatory for the diagnosis of ADHD, but should be performed if the patient's history suggests low general cognitive ability or low achievement in language or mathematics relative to the patient's intellectual ability.

Recommendation 5 The clinician must evaluate the patient with ADHD for the presence of comorbid psychiatric disorders.

TREATMENT

Recommendation 6 A well-thought-out and comprehensive treatment plan should be developed for the patient with ADHD.

Recommendation 7 The initial psychopharmacological treatment of ADHD should be a trial with an agent approved by the Food and Drug Administration (FDA) for the treatment of ADHD.

Recommendation 8 If none of the above agents result in satisfactory treatment of the patient with ADHD, the clinician should undertake a careful review of the diagnosis and then consider behavior therapy and/or the use of medications not approved by the FDA for the treatment of ADHD.

Recommendation 9. During a psychopharmacological intervention for ADHD, the patient should be monitored for treatment-emergent side effects.

Recommendation 10 If a patient with ADHD has a robust response to psychopharmacological treatment and subsequently shows normative functioning in academic, family, and social function, then psychopharmacological treatment of the ADHD alone is satisfactory.

Recommendation 11 If a patient with ADHD has a less than optimal response to medication, has a comorbid disorder, or experiences stressors in family life, then psychosocial treatment in conjunction with medication treatment is often beneficial.

Recommendation 12 Patients should be assessed periodically to determine whether there is continued need for treatment or if symptoms have remitted. Treatment of ADHD should continue as long as symptoms remain present and cause impairment.

Recommendation 13 Patients treated with medication for ADHD should have their height and weight monitored throughout treatment.

General Principles

General Principles Part I

- Children & adolescents are embedded in family and neighborhood networks involving parents/caretakers, siblings, friends, schools, etc.
- Diagnostic systems (DSM and ICD) have limitations (e.g. overlap across diagnoses) in assessing pediatric mental health disorders
 - Diagnoses may unfold over time, and initial symptoms and diagnoses may differ from later adult diagnoses
- Psychiatric medications are generally just one part of a multimodal multidisciplinary treatment plan
 - Medications cannot replace need for therapeutic support, behavioral strategies, problem-solving, etc.

General Principles Part II

- Medication approaches must recognize chronicity of childhood neuropsychiatric disorders, by providing
 - Parental and youth support, empowerment, self-management, and patient activation to promote recovery and hope
 - Sustained therapeutic alliance and problem-solving support
 - Social support
- Children and adolescents developmentally different from adults: learn the differences by medication class for efficacy and side effects
 - e.g., SSRIs, TCAs, stimulants
- Children may require proportionately higher doses: faster metabolism, greater kidney clearance, and greater liver-to-total-body-size ratio

General Principles Part III

- Perform a thorough diagnostic and bio-psychosocial evaluation
- Fully involve the family and child in the medication decision-making process (shared decision making)
 - Inquire about concerns, continue to address their concerns
- Treat primary diagnosis (or the most urgent or impairing problem) with indicated medication first
- Use systematic rating scale to measure symptoms at baseline and throughout treatment
- Whenever possible, use medications supported by double-blind randomized clinical trials (RCTs) for this age group and diagnosis

General Principles Part IV

- Start low, go slow, taper slow (exception: stimulants can be discontinued more quickly)
- Use medications at appropriate dose for adequate duration before changing or augmenting
- Minimize use of multiple medications
- When changing meds:
 - Make only one med change at a time; monitor results
 - Always consider environmental strategies as alternative or complement
 - “Don’t change horses midstream”
 - Use systematic rating method to measure side effects
- Evaluate iatrogenic effects of multiple medications
 - When unclear, consider tapering or discontinuing most worrisome medication or the one with the least amount of RCT evidence

Effective Working Alliance

- Ensure case formulation precedes prescription
- Evoke a sense of understanding in communications with patients and families
- Involve the patient/family in the decision-making process
- Assess the understanding of the mental illness and meaning of medication for the patient and family
- Nurture all professional relationships necessary to sustain child's health
- Visit consumer websites often and help families connect to support groups
- Identify references and books to help patients
- When discussing pharmacotherapy, pause and listen to family's response to the word "medication"
- Provide a small number of choices for medications whenever possible so that past associations with a particular medication do not derail treatment
- Respect the family's right to informed consent and need to know about side effects, without burdening them with so much information they feel overwhelmed
- Practice the 3 C's of good pharmacotherapy:
 - Collaboration (therapists, other providers, families)
 - Conscientiousness (of standard of practice and sociocultural needs)
 - Communication (return phone calls and e-mails promptly, be available, document so others follow pharmacotherapy reasoning)
- Remember all actions have potential meaning for patients and families, from pens, to language, to the way the prescriber provides realistic hope for the future

PSYCKES CQI Project
**Youth Indicator Set:
Too Young**

Questions and Discussion

Matt Perkins, MD