American Academy of Pediatrics Ohio Chapter

BUILDING Mental Wellness LEARNING COLLABORATIVE

Module 5 – Evidence-Informed Pharmacotherapy

Supported by the Ohio Colleges of Medicine Government Resource Center with funding from the Ohio Department of Health and the Ohio Department of Medicaid

Draft 10-15-2013

MedTAPP Medicaid Technical Assistance and Policy Program

Best Evidence for Advancing Childhealth in Ohio NOW B.E.A.C.O.N

Objectives

- Review evidence-informed recommendations for medication management of ADHD, depression, anxiety, and disruptive behavior
- Discuss common adverse effects and contraindications/precautions
- Highlight tools and resources for effective prescribing

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Guide to 8 Medications for Prescribing

Within the four drug classes, eight specific medications met each of the effectiveness, dosing and monitoring, and safety criteria. The table below gives more information about each medication and its proposed use in pediatric populations: ADHD, anxiety, or major depressive disorder (MDD). The table also notes whether the proposed use matches the FDA indication for the medication in youth. For example, the FDA has not officially approved any medication for anxiety in pediatric patients, but prescribing SSRIs for certain forms of childhood anxiety is considered community standard. Each medication listed below will be available in generic form by 2012.

Psychiatric medications for use by pediatric primary care clinicians.

Drug (class)	Trade names	Proposed use in primary care	FDA indication?
Methylphenidate (stimulant)	Ritalin, Concerta and others	ADHD	Yes
Amphetamines (stimulants)	Dexedrine, Adderall and others	ADHD	Yes
Guanfacine (alpha-2A adrenergic agonist)	Tenex, Intuniv	ADHD	Yes
Clonidine (alpha-2 adrenergic agonist)	Catapres, Kapvay	ADHD	Yes
Atomoxetine (SNRI)	Strattera	ADHD	Yes
Fluoxetine (SSRI)	Prozac	Anxiety* MDD	No Yes
Sertraline (SSRI)	Zoloft	Anxiety* MDD**	No No
Escitalopram (SSRI)	Lexapro	Anxiety MDD	No Yes

**Though the FDA has not officially approved fluoxetine and sertraline for treating anxiety disorders such as social phobia, separation anxiety, or generalized anxiety disorders, there is convincing evidence for using these medications for these disorders.*

*** Sertraline has some evidence supporting its use in MDD, but not enough evidence to support an FDA indication.*

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Ashley is an 8 year old girl referred for an ADHD evaluation. Her mother describes problems with inattention both at home and at school. She is in 2nd grade and is struggling in school. Her teacher notes that “she just doesn’t pay attention.” She has trouble sitting still and often disrupts the classroom. Her family is concerned that these issues are interfering with her school performance.

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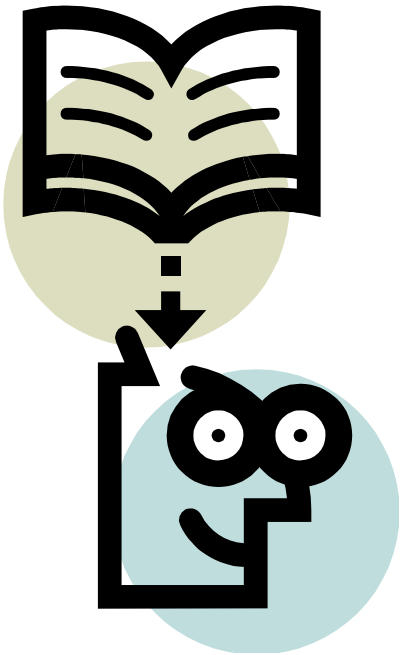
Ashley has also missed several days of school this year for stomach pains and headaches. Her mother has recently taken a new job, and these absences have been difficult for her family to manage. They would like to get Ashley started on ADHD medication to help her in school and reduce family stress.

Assessment Process

- Presence of DSM-IV Criteria
- Evidence of Impairment
- Behavioral rating scales



Clinician judgment

AAP. Pediatrics. 2011.

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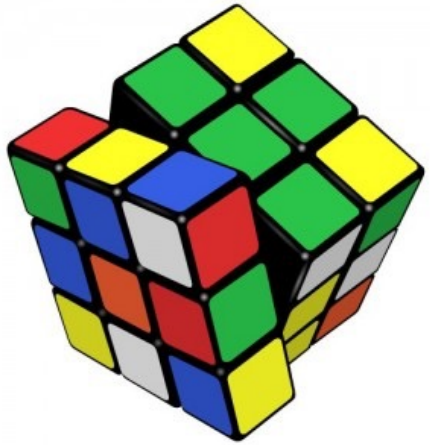
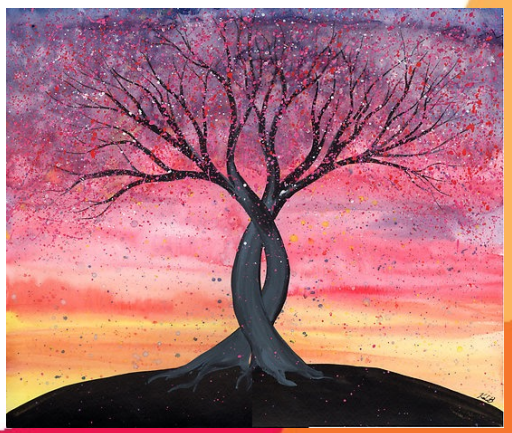
Assessment Process

Importance of accurate diagnosis

1. Many conditions can masquerade as “attention problems”
2. There is a high degree of comorbidity in children with ADHD





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Vanderbilt Rating Scales

	Parent	Teacher
Inattention	✓	✓
Hyperactivity/Impulsivity	✓	✓
Total symptom score	46	36
ODD Screen		
Conduct Disorder Screen		
Anxiety/Depression Screen	✓	
# Areas with Impairment	3	2
Average Performance Score	3.5	3

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ADHD First or Depression First?

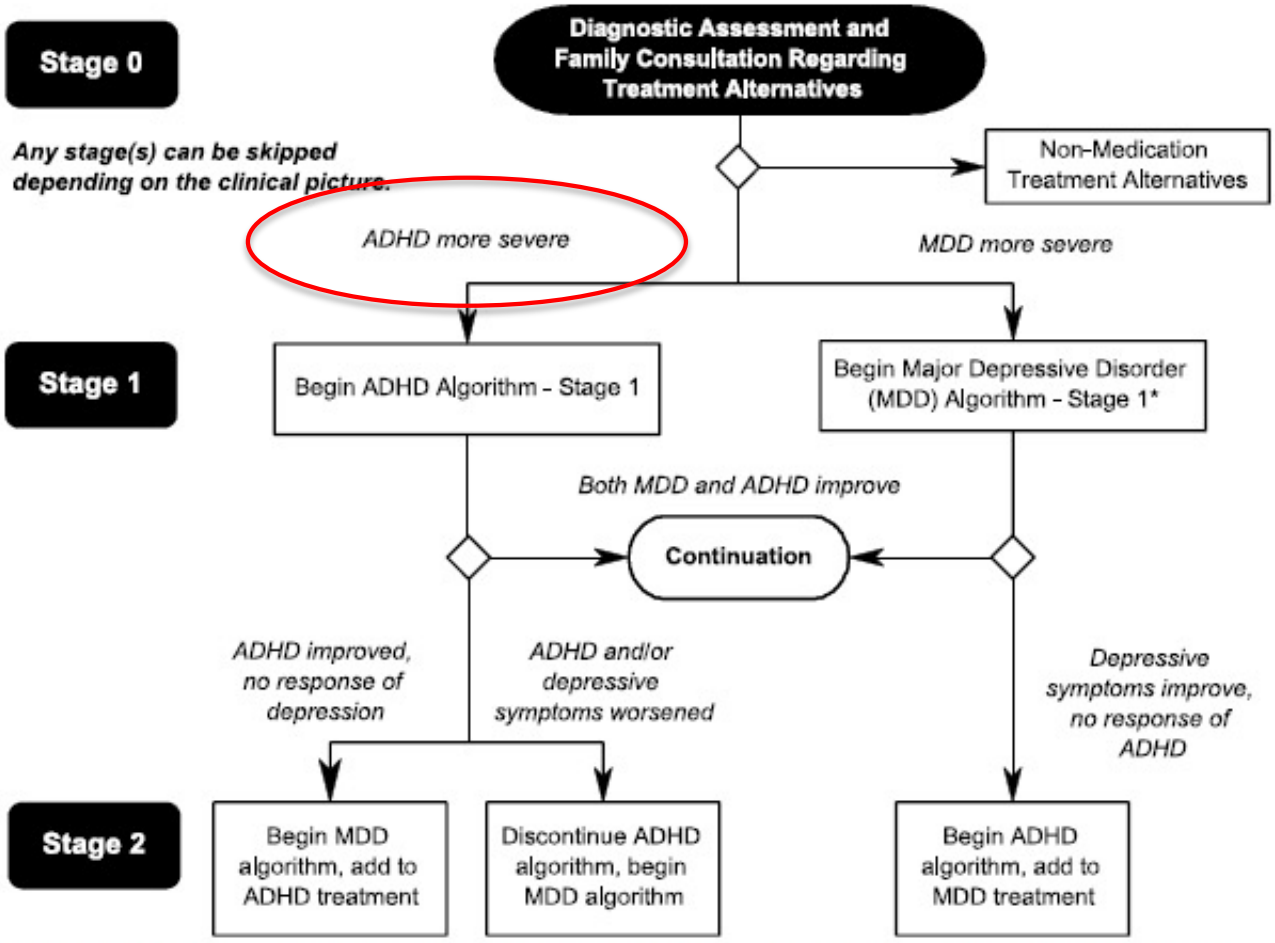

Fig. 2 Algorithm for the psychopharmacological treatment of ADHD and comorbid depressive disorder. (*See Hughes et al., unpublished, 2005.)

Pliska et al. J Am Acad Child Adolesc Psychiatr. 2006;45:642-657.

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Interventions

- Define ADHD as a chronic condition
- Identify target outcomes
- Use stimulant medications and behavioral therapy as indicated
- Monitor treatment response systematically

AAP. Pediatrics. 2011;128:1007-1022.
AACAP. J Am Acad Child Adolesc Psychiatr. 2007;46:894-921.

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ADHD Medications

- Most recent guidance based on strength of evidence:

Methylphenidate ~ Amphetamine

> Atomoxetine

> Long acting Guanfacine

> Long acting Clonidine

AAP. Pediatrics. 2011;128:1007-22.

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Methylphenidate

- Start low, reassess, and adjust if needed
  - Start at 10mg/day
  - Increase 5-10mg/day every 1-2 weeks if limited benefits and adverse effects
  - Consider short acting afternoon dose if needed

Minds Matter
Ohio Psychotropic Medication Quality Improvement Collaborative

www.ohiomindsmatter.org

AACAP. J Am Acad Child Adolesc Psychiatr. 2007;46;89-921.

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Methylphenidate

- Maximum FDA dosing per day (off-label)
  - Ritalin®, Methylin®, Methylin ER®, Metadate ER®, Ritalin SR®, Metadate CD®, Ritalin LA® 60mg (100mg for >50kg)
  - Concerta® 72mg (108mg)
  - Focalin® 20mg (50mg); Focalin XR® 30mg (50mg)
  - Daytrana® 30mg (?)

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AACAP. J Am Acad Child Adolesc Psychiatr. 2007;46;89-921.

Methylphenidate

- Other considerations
  - Many long acting forms can be opened and sprinkled on applesauce or pudding
    - Metadate CD®, Ritalin LA®, Focalin XR®
  - Concerta® capsule cannot be opened due to delivery system
  - Daytrana®
    - Patch is applied at the hip; may cause skin irritation
  - Quillivant® is a new extended release liquid preparation

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Amphetamine

- Start low, reassess, and adjust if needed
  - Start at 5-10mg/day
  - Increase 5-10mg/day every 1-2 weeks if limited benefits and adverse effects

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Adapted from AACAP. J Am Acad Child Adolesc Psychiatr. 2007;46;89-921.

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Amphetamine

- Maximum FDA dosing per day (off-label)
  - Dexedrine,® Dextrostat,® Adderall,® and Dexedrine spansule® 40mg/day (60mg if >50kg)
  - Adderall XR® 30mg (60mg if >50kg)
  - Vyvanse® 70mg (?)

Adapted from AACAP. J Am Acad Child Adolesc Psychiatr. 2007;46;89-921.

Amphetamine

- Other considerations
  - Adderall XR® and Dexedrine spansule® can be opened and sprinkled
  - Vyvanse® capsule can be opened and contents dissolved in small amount of water (1-2 tsp)
  - Vyvanse® may have decreased abuse potential due to pro-drug delivery system

Atomoxetine

- Mechanism of action
  - Selective norepinephrine reuptake inhibitor
  - May take up to 12 weeks for full effect
  - Dosing is weight based (unlike other ADHD medications)

Stahl SM. *The Prescriber's Guide*. 3rd ed. New York, NY: Cambridge Press; 2009:329.

Atomoxetine

- Dosing recommendations
  - For <70kg: start with 0.5mg/kg/day, then increase to 1.2mg/kg/day after 4-7 days
    - Max dose 1.4mg/kg/day or 100mg (lesser of 1.8mg/kd/day or 100mg)
  - For >70kg: 40mg/day, then increase to 80mg/day after 7 days
    - Max dose 100mg (increase after 2-4 weeks if needed)

AACAP. J Am Acad Child Adoles Psychiatr. 2007;46;89-921.
Stahl SM. *The Prescriber's Guide*. 3rd ed. New York, NY: Cambridge Press; 2009:51-52.

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Atomoxetine

- Other considerations
  - Pills cannot be opened or split
  - Can divide dose BID to minimize side effects
  - Must give daily
  - Dose adjustment in patients with impaired liver function

Alpha Agonists

- Dosing recommendations
  - Guanfacine (Intuniv®)
    - Long acting: start at 1mg qd; increase weekly to 4mg maximum dose
  - Clonidine (Kapvay®)
    - Long acting: start at 0.1mg qHS; increase weekly by 0.1mg divided BID to 0.4mg/day maximum dose

Adverse Effects

- Contraindication
  - Mania
  - Psychosis
- Precautions
  - Anxiety
  - Parental substance abuse
- Considerations
  - Tics

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Adverse Effects

- Stimulants
  - Aggression
  - Irritability
  - Social withdrawal
  - Hypertension, tachycardia
  - Appetite suppression
  - Sleep disturbance

Adverse Effects

- Atomoxetine
  - Suicidal ideation
  - Hypertension, tachycardia
  - GI upset
  - Behavioral activation
- Alpha agonists
  - Hypotension, bradycardia
  - Sedation

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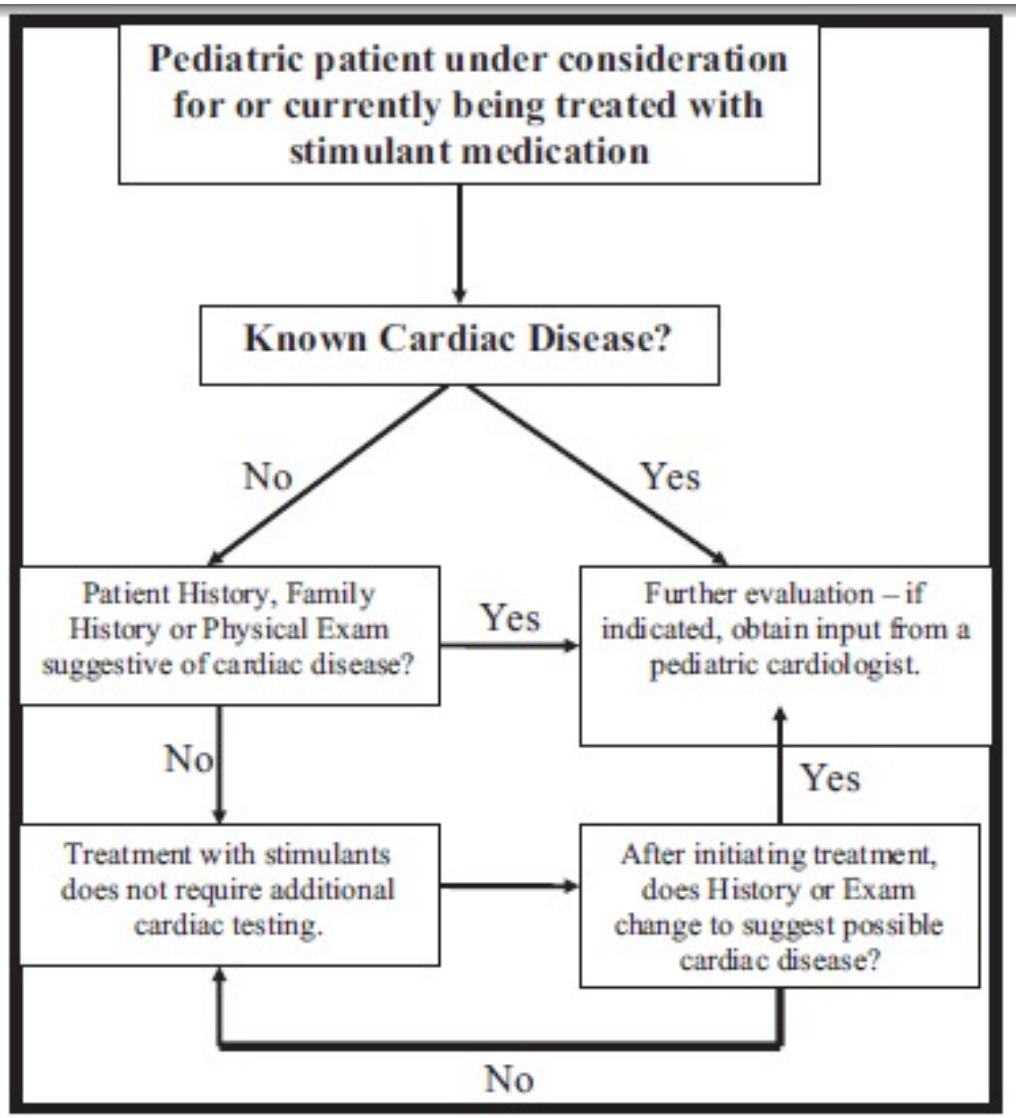

POLICY STATEMENT

Cardiovascular Monitoring and Stimulant Drugs for Attention-Deficit/Hyperactivity Disorder

Perrin et al. Pediatrics. 2008;122:451-453.

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Update on Ashley

- Ashley is prescribed Concerta® 18mg each morning. At one week, no side effects are noted, but no benefits are seen. Concerta® is increased to 27mg.
- At one month, Ashley is seen for a follow up visit. She is now taking 36mg each morning after another dose increase.
- Vanderbilt questionnaires are available for your review.

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Vanderbilt Rating Scales

	Parent	Teacher
Inattention		
Hyperactivity/Impulsivity		
Total symptom score	46→ 38	36→20
ODD Screen		
Conduct Disorder Screen		
Anxiety/Depression Screen		
# Areas with Impairment		
Average Performance Score		

Consider afternoon short acting dose

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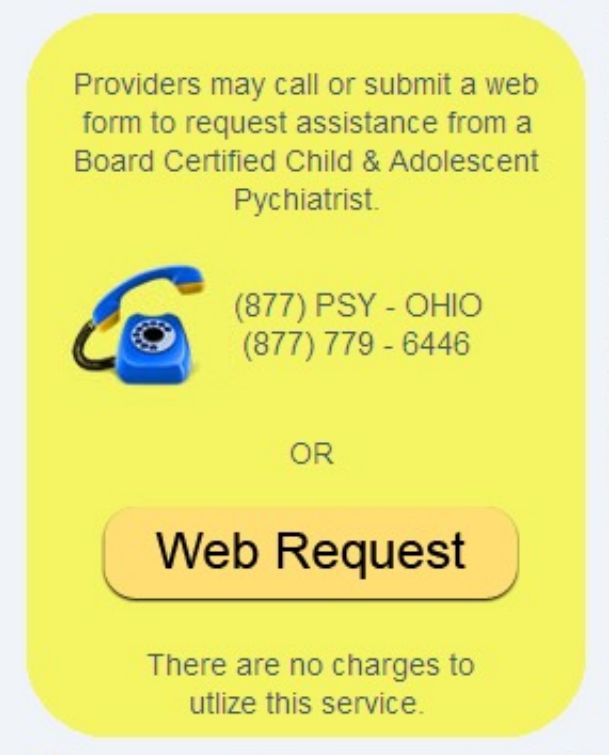
What if…

- She doesn't tolerate Concerta?
  - Consider switch to amphetamine product
- Symptoms improve but persist at the top of the dosing interval?
  - Consider switch to amphetamine product
  - If previous medications unsuccessful, consider adjunctive therapy with non-stimulant



http://ppn.mh.ohio.gov

Pediatric Psychiatry Network
A Clinical Decision Support Service for Ohio Physicians

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ADHD First or Depression First?

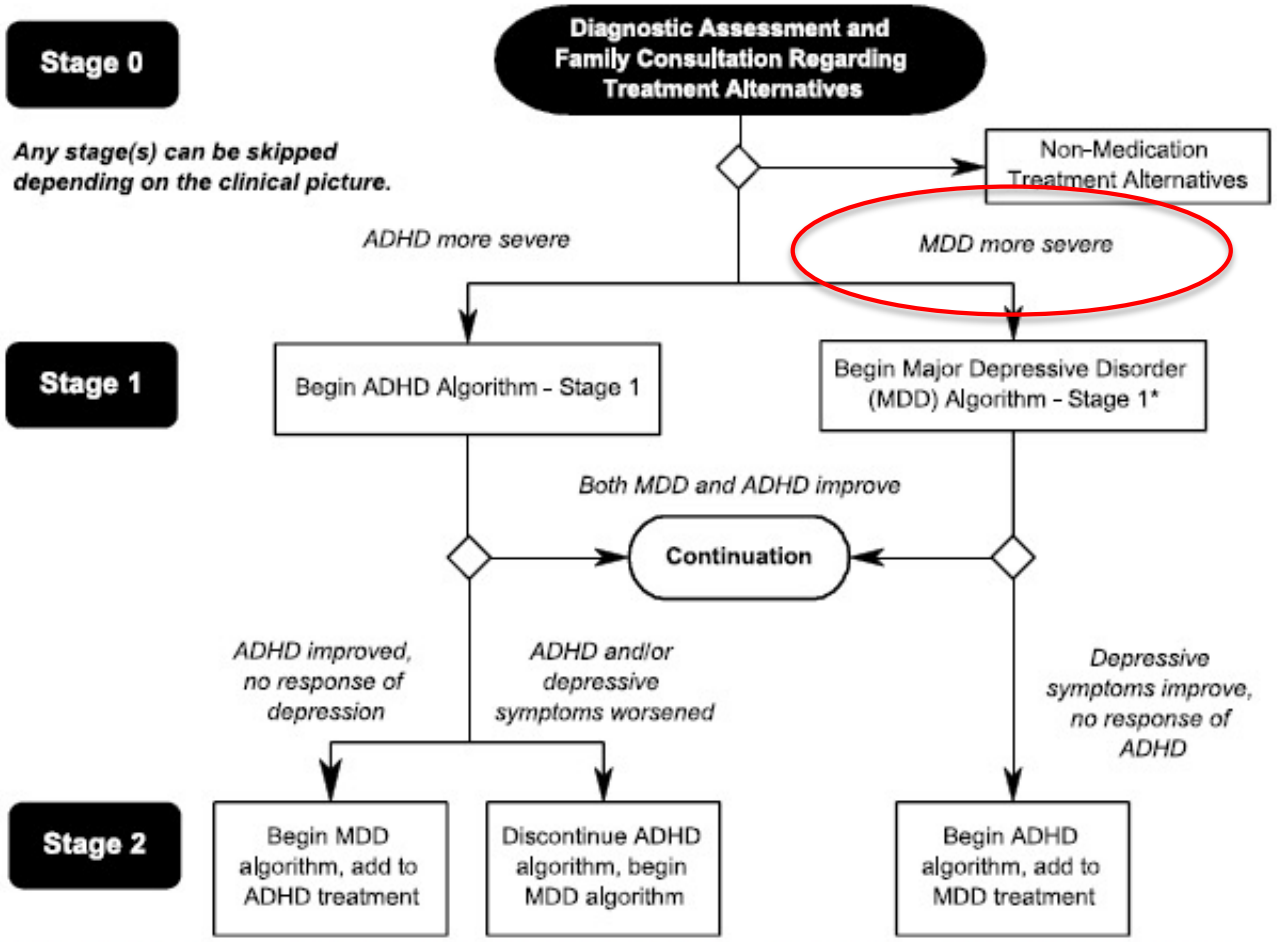

Fig. 2 Algorithm for the psychopharmacological treatment of ADHD and comorbid depressive disorder. (*See Hughes et al., unpublished, 2005.)

Pliska et al. J Am Acad Child Adolesc Psychiatr. 2006;45:642-657.

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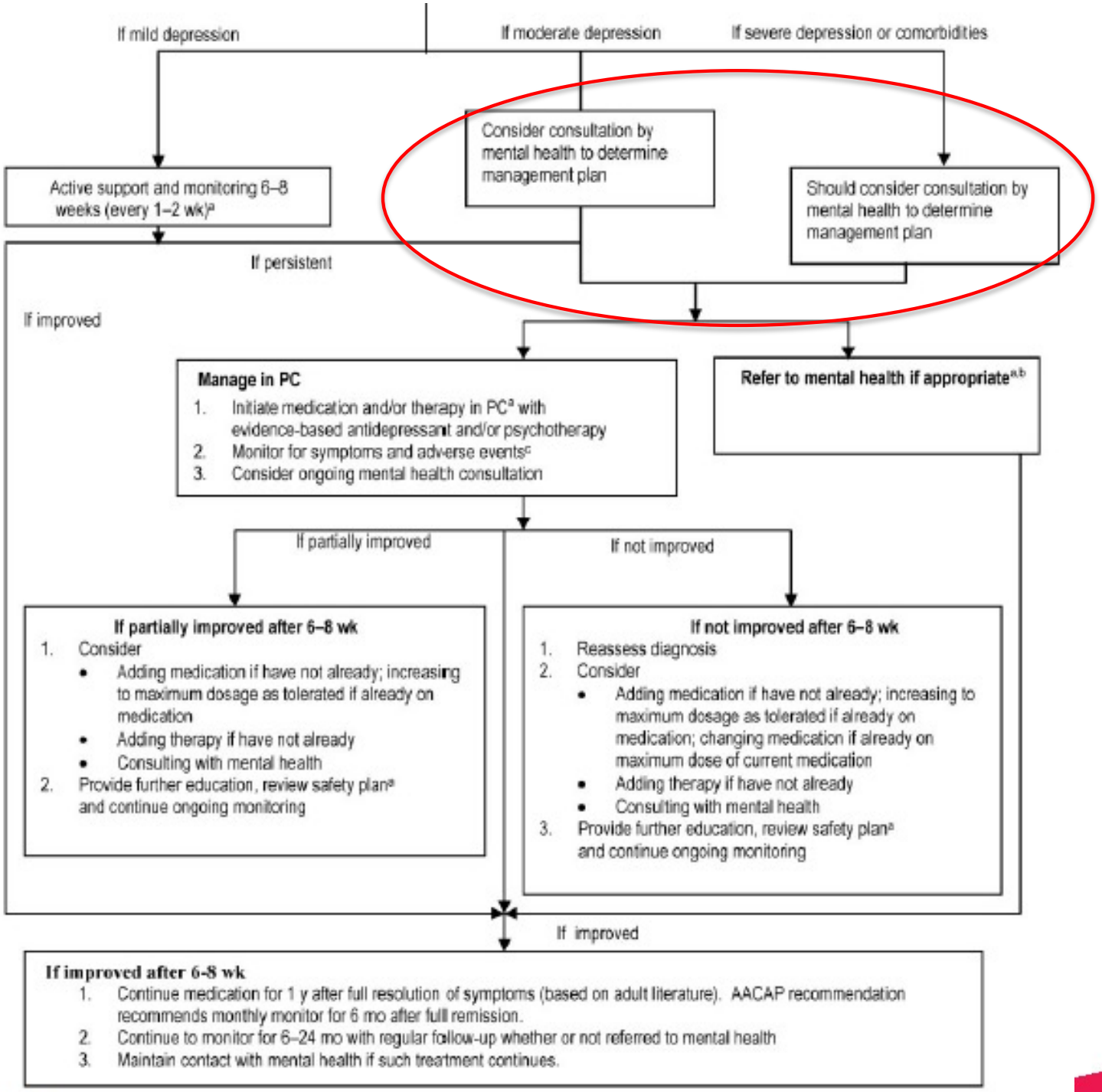

Cheung et al. Pediatrics. 2007;120(5):1313-1326.

SSRI's

- Indications
  - Anxiety Disorders
    - **Sertraline (Zoloft®):** FDA indicated age 6 and up for OCD
    - **Fluoxetine (Prozac®):** FDA indicated OCD age 7 and up
  - Depression
    - **Fluoxetine (Prozac®):** FDA indicated age 8 and up
    - **Escitalopram (Lexapro®):** FDA indicated age 12 and up

When moderate to severe impairment is present

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Selective Serotonin Reuptake Inhibitors (SSRI's)

SSRI	Starting Dose, mg	Increments, mg	Effective Dose, mg	Maximum Dose, mg
Fluoxetine (Prozac®)	10	10-20	20	60
Sertraline (Zoloft®)	25	12.5-25	50	200
Escitalopram (Lexapro®)	5	5	10	20

Adapted from Cheung et al. Pediatrics. 2007;120(5):e1313-1326.

SSRI's

- Start low, reassess, and adjust as needed
  - Increase dose after 1-2 weeks, then monitor
  - Maximal effectiveness after 4-6 weeks
  - Continue for 6-12 months after symptoms resolve
  - Taper when discontinuing to avoid withdrawal effects

Medication for depression and anxiety disorders can be approached similarly

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SSRI's

- Contraindications
  - Bipolar disorder
  - Psychosis
- Interactions/precautions
  - Use with caution in other serotonergic medications
  - Serotonin syndrome
    - Mental status changes
    - Autonomic instability
    - Tremor, myoclonus

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Adverse Effects

- SSRI's
  - Nausea
  - Headaches
  - Dizziness
  - Insomnia
  - Activation
  - Bipolar switching
  - Sexual dysfunction
  - Suicidal thinking

http://www.glad-pc.org/

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Adverse Effects

- Black box warning:
  - Issued in 2004 after concerns about an increase in suicidal thinking in children prescribed SSRI's
    - 24 clinical trials reviewed; over 4000 children
    - No completed suicides
    - Prevalence of suicidal thoughts/actions 2X higher in those taking SSRIs (2% vs. 4%)
  - Close monitoring for suicidal thinking is recommended, especially during titration phase

http://www.fda.gov/ohrms/dockets/ac/04/briefing/2004-4065b1-10-TAB08-Hammads-Review.pdf

Summary

- Consider the risks and benefits of medication
- Discuss openly with patients and families
- Develop a process for monitoring
- Respond promptly to concerns

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Ashley's 6 year old brother, Antwon, has also been diagnosed with ADHD. He is taking Adderall XR®, and symptoms have improved. He continues to have problems with refusing to follow directions. He tends to get angry easily. He often tries to get back at people and can be spiteful. When his mother tries to set limits, he has tantrums that last for several minutes. His mother notes that things at home have been very stressful because of his behavior.

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Antwon has also been diagnosed with Oppositional Defiant Disorder. His mother doesn't know if more medication is the right choice, but she doesn't know what else to do. She feels that they are "at the end of their rope."

Is medication appropriate for the treatment of Oppositional Defiant Disorder?

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Oppositional Defiant Disorder

- Behavioral interventions are first line treatment
  - Office based interventions
  - Parent training programs
    - Incredible Years
    - Parent Child Interaction Training
    - Triple P Positive Parenting Program

AACAP. J Am Acad Child Adolesc Psychiatr. 2007;46:126-141.

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Oppositional Defiant Disorder

- Medications can be considered as adjunctive treatment but are NOT curative
  - Maximally treat underlying ADHD symptoms first, if present
  - Use is off-label and not well studied
    - Alpha-agonists
    - Atypical antipsychotic medications
  - Consider consultation with PPN

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Atypical Antipsychotic Medications

- Dramatic increase in prescribing
  - Children in foster care
  - Children with Severe Emotional Disturbance (SED)
  - Children with ADHD
- Concerns
  - Safety
  - Questionable efficacy
  - Cost

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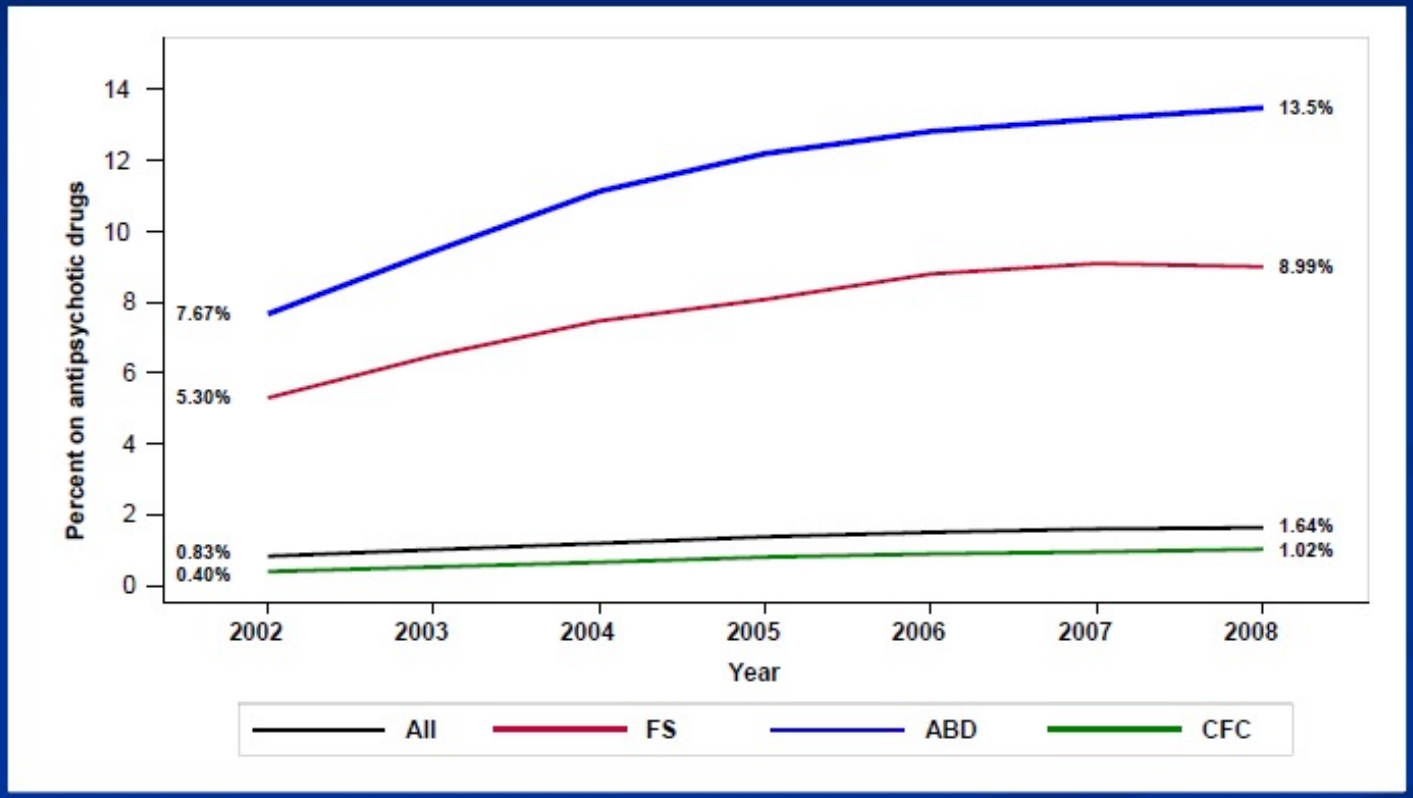
Trends in Antipsychotic Use Among Youth Enrolled in Ohio Medicaid by Eligibility Group, 2002-2008



Note: FC = Foster care. ABD = Aged, Blind, and Disabled. CFC = Covered Families and Children. Percentages are based on the month of October for youth who were continuously enrolled in Medicaid during each fiscal year. Trend test for all three groups were significant ($p < 0.001$)

Slide courtesy of the Government Resource Center.

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www.ohiomindsmatter.org

Minds Matter
Ohio Psychotropic Medication Quality Improvement Collaborative

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Update on Antwon

- Antwon's mother participates in a parent training program for children with disruptive behavior
- Antwon receives additional school supports designed to increase desirable behavior
- You work with Anton's family to maximize treatment of ADHD symptoms

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Summary

- Medications can be an effective component of a comprehensive treatment plan
- Evidence-informed resources are available to guide care
- Resources including the Pediatric Psychiatry Network and Ohio Minds Matter are useful guides as questions arise

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References

- American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with Attention-Deficit Hyperactivity Disorder. J Am Acad Child Adolesc Psychiatr. 2007;46:894-921.
- American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with oppositional defiant disorder. J Am Acad Child Adolesc Psychiatr. 2007;46:126-141.
- Cheung AH, Zuckerbrot RA, Jensen PS et al. Guidelines for the Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and Ongoing Management. Pediatrics. 2007;120:e1313-e326.
- Gibbons RD, Brown CH, Hur K, et al. Early Evidence on the Effects of Regulators' Suicidality Warnings on SSRI Prescriptions and Suicide in Children and Adolescents. Am J Psychiatry 2007; 164:1356–1363**.**
- Hammad TA. Review and evaluation of clinical data. Washington, DC, Food and Drug Administration, Aug 16, 2004 (http://www.fda.gov/ohrms/dockets/ac/04/briefing/2004-4065b1-10-TAB08-Hammads-Review.pdf). Accessed October 22, 2012.
- Pappadopulos E, MacIntyre JC, Crismon ML et al. Treatment recommendations for the use of antipsychotics for aggressive youth (TRAAY). Part II. J Am Acad Child Adolesc Psychiatr. 2003;42:145-161.
- Pliszka SR, Crismon ML, Hughes CW, et al. The Texas Children's Medication Algorithm Project: Revision of the algorithm for pharmacotherapy of Attention-Deficit-Hyperactivity Disorder. J Am Acad Child Adolesc Psychiatr. 2006;46:642-657.
- Subcommittee on Attention-Deficit/Hyperactivity Disorder and the Committee on Quality Improvement. Clinical practice guideline: treatment of the school-aged child with Attention-Deficit/Hyperactivity Disorder. Pediatrics. 2001;108(4):1033-1044.
- Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management. ADHD: Clinical practice guideline for the diagnosis, evaluation, and treatment of Attention-Deficit/Hyperactivity Disorder in children and adolescents. Pediatrics. 2011;128:1007-1022.