Practical Pearls in Managing ADHD in Primary Care

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No disclosures

- I will be discussing off label medication use.

Learning Objectives

- Identify presentations of ADHD in the pediatric population
- Create a treatment plan for ADHD, including off label treatment options.
- Evaluate patients with ADHD and other comorbidities, including Autism Spectrum Disorder
- Discuss long term impacts of ADHD pharmacotherapy

ADHD by the numbers

- Affects 7-17 % of Children in the US
- 7 million ambulatory visits in 2006/ > 3 billion US cost
- 2:1 Male: Female Ratio in general population
- Childhood ADHD symptoms persists in 50% at age 25: Lifelong implications

Age of Onset of Pediatric Mental Health Disorders

Toddler/Preschool (0-3 Years)	Early School Age (4-7 years)	School Age-prepuberty (6-12 years)	Adolescent (13-16 years)	Late Teen/Young Adult
ASD	ADHD	Anxiety	Depression	Bipolar/Psychosis Panic Disorder

ADHD: Presenting concerns

- Inattention/short attention span
- Motor hyperactivity
- Impulsivity, risk taking
- Aggression, irritability, defiance
- Poor school performance

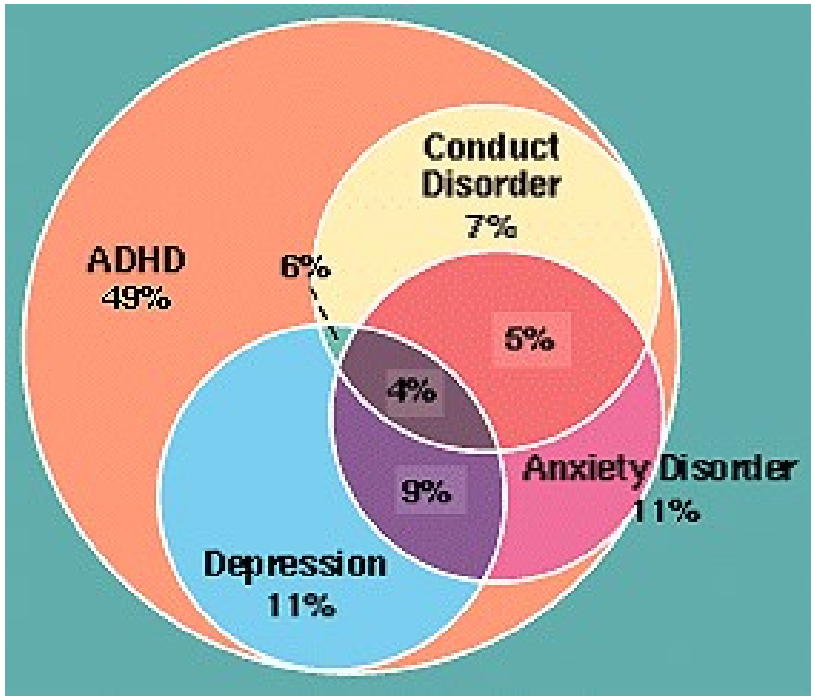
ADHD Differential Diagnosis

- Conduct and oppositional defiant disorder
- Learning and developmental disorders
- Sensory Processing Disorder
- Autism Spectrum Disorder
- Hearing, vision problems
- Anxiety disorders (PTSD, panic, OCD)
- Depressive disorders
- Toxins (Pb)
- Medication side effects (asthma, anti-seizure)
- Abuse, neglect, deprivation
- Parenting problems (limits, structure, consistency)
- S/p head injury
- Seizure disorder- absence, focal seizures with altered awareness

Comorbidities are high in ADHD

Rates of Comorbidities with ADHD

- Conduct disorder/oppositional defiant disorder: 30-50%
  - Parent training
- Depression: 29-45%
  - Therapy +/- SSRI
- Bipolar disorder: 10-30%
- Anxiety: 25%
  - Therapy +/- SSRI
- Learning disorder: 25-45%
  - Support with a 504/IEP
- Tic Disorder: 20-30%
- Obsessive Compulsive Disorder: 10%



ADHD Hyperactive/Impulsivity Presentation

- Hyperactive:
  - Squirms and fidgets
  - Cannot stay seated
  - Runs/Climbs excessively
  - On the go/driven by a motor
  - Talks excessively
  - Cannot perform leisure activities quietly
- Impulsive
  - Blurts out answer
  - Cannot wait turn
  - Intrusive/Interrupts other

Must have 6 or more symptoms for a period of 6 months to a degree that is maladaptive and inconsistent with developmental level

ADHD Inattentive Presentation

- Carelessness
- Difficulty sustaining attention during activity
- Trouble following through
- Avoids tasks requiring sustained mental effort
- Difficulty organizing
- Loses important items
- Easily distracted
- Forgetful in daily activities
- Does not appear to be listening when spoken to directly

Must have 6 or more symptoms for a period of 6 months to a degree that is maladaptive and inconsistent with developmental level

Other criteria for diagnosis

- Symptoms must be present for at least 6 months
- Some symptoms must be present < 12 years old
- Some impairment from symptoms in 2 or more settings
  - School, home, friends/peers, sports, work
- Significant impairment
- Excluded other mental disorders as the primary disorder

ADHD Evaluation

- Rating Scales
  - Vanderbilt Rating Scales (free) (Age 6-12) About 50 questions
  - Connors ($$)- long and short versions. Ages 3-17
- Patient's Report- clinical interview
- Guardian's Report- clinical interview
- History
  - Developmental history
  - Medical history
  - Family History
- Current and past academic functioning
- Peer relationships
- Labs- Lead, Vitamin D, TSH/FT4, Ferritin

Vanderbilt Assessment Scale

- AAP ToolKit includes
  - Assessment Scales for Parent & Teachers
  - Follow-up Scales for Parent & Teachers
- Two Components:
  - Symptom assessment: higher scores = greater symptom frequency. Positive is a score of 2 or 3
  - Performance impairment: higher scores = greater degree of impairment. Positive is a score of 4 or 5
- Includes ODD, Conduct Disorder, Anxiety and Depression screening questions
- Free!
- Validated ages 6-12

- Questions 1-9: Inattentive: Positive 6 out of 9
- Questions 10-18: Hyperactive/Impulsive: Positive 6 out of 9
- Questions 19-26: Oppositional Defiance: Positive is 4 out of 8
- Questions 27-40: Conduct Disorder: Positive is 3 out of 14
- Questions 41-47: Anxiety/Depression Screen: Positive is 3 out of 7
- Questions 48-55: Performance Questions- requires at least one positive

NICHQ Vanderbilt Assessment Scale—PARENT Informant

Today's Date: _____ Child's Name: _____ Date of Birth: _____

Parent's Name: _____ Parent's Phone Number: _____

Directions: Each rating should be considered in the context of what is appropriate for the age of your child. When completing this form, please think about your child's behaviors in the past 6 months.

Is this evaluation based on a time when the child ☐ **was on medication** ☐ **was not on medication** ☐ **not sure?**

Symptoms	Never	Occasionally	Often	Very Often
1. Does not pay attention to details or makes careless mistakes with, for example, homework	0	1	2	3
2. Has difficulty keeping attention to what needs to be done	0	1	2	3
3. Does not seem to listen when spoken to directly	0	1	2	3
4. Does not follow through when given directions and fails to finish activities (not due to refusal or failure to understand)	0	1	2	3
5. Has difficulty organizing tasks and activities	0	1	2	3
6. Avoids, dislikes, or does not want to start tasks that require ongoing mental effort	0	1	2	3
7. Loses things necessary for tasks or activities (toys, assignments, pencils, or books)	0	1	2	3
8. Is easily distracted by noises or other stimuli	0	1	2	3
9. Is forgetful in daily activities	0	1	2	3
10. Fidgets with hands or feet or squirms in seat	0	1	2	3
11. Leaves seat when remaining seated is expected	0	1	2	3
12. Runs about or climbs too much when remaining seated is expected	0	1	2	3
13. Has difficulty playing or beginning quiet play activities	0	1	2	3
14. Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15. Talks too much	0	1	2	3
16. Blurts out answers before questions have been completed	0	1	2	3
17. Has difficulty waiting his or her turn	0	1	2	3
18. Interrupts or intrudes in on others' conversations and/or activities	0	1	2	3
19. Argues with adults	0	1	2	3
20. Loses temper	0	1	2	3
21. Actively defies or refuses to go along with adults' requests or rules	0	1	2	3
22. Deliberately annoys people	0	1	2	3
23. Blames others for his or her mistakes or misbehaviors	0	1	2	3
24. Is touchy or easily annoyed by others	0	1	2	3
25. Is angry or resentful	0	1	2	3

NICHQ Vanderbilt Assessment Scale—TEACHER Informant, continued

Teacher's Name: _____ Class Time: _____ Class Name/Period: _____

Today's Date: _____ Child's Name: _____ Grade Level: _____

Symptoms (continued)	Never	Occasionally	Often	Very Often
32. Feels worthless or inferior	0	1	2	3
33. Blames self for problems; feels guilty	0	1	2	3
34. Feels lonely, unwanted, or unloved; complains that "no one loves him or her"	0	1	2	3
35. Is sad, unhappy, or depressed	0	1	2	3

Performance *Academic Performance*	Excellent	Above Average	Average	Somewhat of a Problem	Problematic
36. Reading	1	2	3	4	5
37. Mathematics	1	2	3	4	5
38. Written expression	1	2	3	4	5

Classroom Behavioral Performance	Excellent	Above Average	Average	Somewhat of a Problem	Problematic
39. Relationship with peers	1	2	3	4	5
40. Following directions	1	2	3	4	5
41. Disrupting class	1	2	3	4	5
42. Assignment completion	1	2	3	4	5
43. Organizational skills	1	2	3	4	5

Comments:

D5 NICHQ Vanderbilt Assessment Follow-up—PARENT Informant

Today's Date: _____ Child's Name: _____ Date of Birth: _____

Parent's Name: _____ Parent's Phone Number: _____

Directions: **Each rating should be considered in the context of what is appropriate for the age of your child. Please think about your child's behaviors since the last assessment scale was filled out when rating his/her behaviors.**

Is this evaluation based on a time when the child ☐ **was on medication** ☐ **was not on medication** ☐ **not sure?**

Symptoms	Never	Occasionally	Often	Very Often
1. Does not pay attention to details or makes careless mistakes with, for example, homework	0	1	2	3
2. Has difficulty keeping attention to what needs to be done	0	1	2	3
3. Does not seem to listen when spoken to directly	0	1	2	3
4. Does not follow through when given directions and fails to finish activities (not due to refusal or failure to understand)	0	1	2	3
5. Has difficulty organizing tasks and activities	0	1	2	3
6. Avoids, dislikes, or does not want to start tasks that require ongoing mental effort	0	1	2	3
7. Loses things necessary for tasks or activities (toys, assignments, pencils, or books)	0	1	2	3
8. Is easily distracted by noises or other stimuli	0	1	2	3
9. Is forgetful in daily activities	0	1	2	3
10. Fidgets with hands or feet or squirms in seat	0	1	2	3
11. Leaves seat when remaining seated is expected	0	1	2	3
12. Runs about or climbs too much when remaining seated is expected	0	1	2	3
13. Has difficulty playing or beginning quiet play activities	0	1	2	3
14. Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15. Talks too much	0	1	2	3
16. Blurts out answers before questions have been completed	0	1	2	3
17. Has difficulty waiting his or her turn	0	1	2	3
18. Interrupts or intrudes in on others' conversations and/or activities	0	1	2	3

D5 NICHQ Vanderbilt Assessment Follow-up—PARENT Informant, continued

Today's Date: _____ Child's Name: _____ Date of Birth: _____

Parent's Name: _____ Parent's Phone Number: _____

Side Effects: Has your child experienced any of the following side effects or problems in the past week?	Are these side effects currently a problem?			
	None	Mild	Moderate	Severe
Headache				
Stomachache				
Change of appetite—explain below				
Trouble sleeping				
Irritability in the late morning, late afternoon, or evening—explain below				
Socially withdrawn—decreased interaction with others				
Extreme sadness or unusual crying				
Dull, tired, listless behavior				
Tremors/feeling shaky				
Repetitive movements, tics, jerking, twitching, eye blinking—explain below				
Picking at skin or fingers, nail biting, lip or cheek chewing—explain below				
Sees or hears things that aren't there				

Explain/Comments:

Conner's Scales

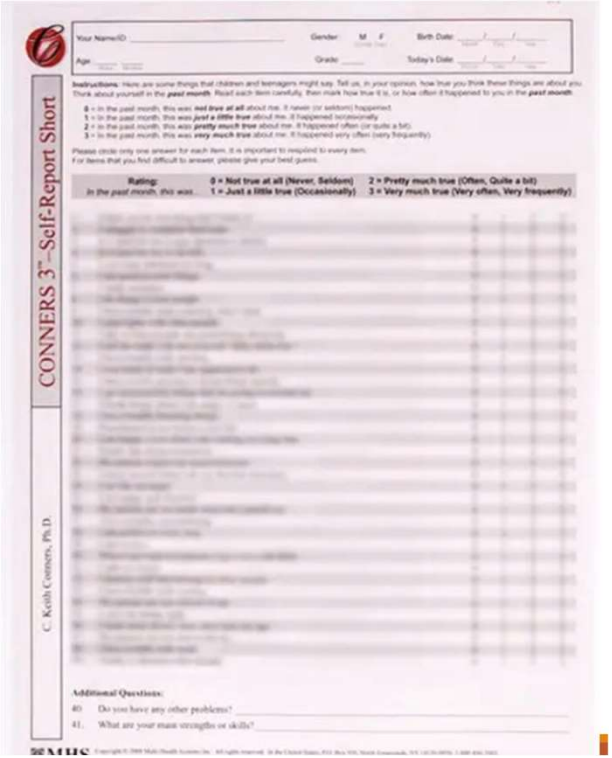
- Symptom Scales:
  - ADHD (18 items)
  - ODD/CD
  - Learning problems
  - Executive functioning problems
  - Peer/Family Relations
  - Anxiety and Depression
- Full length and short version
- Validated for Ages 6-18
- Early Childhood Conners Ages 2-6
  - Inattention/Hyperactivity
  - Oppositional/Aggressive
  - Social Functioning/Atypical Behaviors
  - Anxiety, Mood and Affect
  - Developmental Milestones

- Excellent reliability and validity
- Easy administration, scoring and interpretation with the manual
- Costly (pack of 25 $100)

Conners Scales

Available Tools:

- Conners' Parent Rating Scale-Revised for parents/caregivers
- Conners' Teacher Rating Scale-Revised for teachers
- Conners-Wells' Adolescent Self-Report Scale for teenagers
- 3rd edition- contains parent, teacher, and self-report both full and short forms
- https://www.wpspublish.com $162 for full manual/forms



Answering the Tough Questions

- ADHD is not real
- Johnny can play Fortnight all day, but when it comes to math homework, he is just lazy
  - Attention is different for different tasks- exciting stimuli may draw attention
- What or who caused my child to have ADHD?
- Will my child ever grow out of their ADHD?
- Isn’t ADHD just a school-based problem?

Why treat it? ADHD complications

- Prone to accidents: 50% higher bike accidents, 33% more ER visits
- Increase likelihood of Depressive disorder, Anxiety disorder, Alcohol and drug abuse
- Poor team performance
- Academic failure
- Social struggles- peer rejection, self esteem
- Missed development of life long good work habits and attitude
- Adult impairment
  - Reduced post secondary education
  - Increase number of times fired/quit a job
  - More receive public assistance
  - Greater emotional lability and risky sexual behavior

Treatment options for ADHD

- Psychoeducation
  - AACAP: Parents Medication Guide. www.parentsmedguide.org
- School based accommodations
- Psychotherapy
- Medication
  - ADHD medications are the most successful intervention for ADHD and are the most studied medication treatments in all of pediatrics.
  - Stimulants
    - Stimulants are effective in 70% of children with ADHD (no matter which medication you choose)
  - Non Stimulants
  - Second line Non Stimulants

Major Studies in ADHD

- MTA study
  - Age 7-10, 14 month RCT, with 14 years of follow up data
  - **Behavioral modification + medication (stimulant)** > meds alone > BM alone > community care
  - Stimulants effective in 70% of children with ADHD (no matter which medication you choose)
  - An additional 20% will respond to the next medication attempted

- PATS study
  - Preschool children (3 – 5½)
  - First line Treatment: Parent training/Behavioral training evidence is strong
  - Stimulants have lower efficacy than older children (MTA) but still better than placebo
  - More adverse effects in younger kids
  - Small doses used: Methylphenidate 1.25mg-7.5mg

Pharmacotherapy for ADHD- FDA approved

- **Stimulants**
  - **Methylphenidate**
  - **Amphetamine compounds**
- **Non-Stimulants: Alpha Agonists**
  - **Guanfacine extended release**
  - **Clonidine extended release**
- **Non-Stimulants: Norepinephrine modulators**
  - **Atomoxetine (Straterra)**
  - **Viloxazine (Qelebree)**
- **Combination: Alpha agonists + stimulants**
- Combination: NE modulator + Stimulant (NON FDA-Approved)
- Antidepressants (NON FDA-Approved)
  - Bupropion
  - TCAs
- Modafinil (NON FDA Approved)

Psychotherapy for ADHD

- Behavior management training for parents of younger children
- Behavior based and CBT for school aged youth
- Positive Parenting Program (efficacious in ADHD symptoms)
- Parent Child Interaction Therapy (efficacy in kids ages 2-7)

ADHD and School-Based Accommodations

	IEP	504
Origin	Special Education Law (IDEA)	Civil Rights Law (Section 504 of Rehab Act)
What it does?	Provides individualized specialized education/instruction apart from general education	Provides services and changes to the general education learning environment to meet the needs of the child as adequately as other students.
Who is eligible?	A child's school performance must be "adversely affected" by one of the 13 conditions: learning disability, intellectual disability, ASD, emotional, "other health impairment- ADHD"	A child has any disability, which can include many learning or attention issues and the disability must interfere with the child's ability to learn in a general education classroom. Broader definition of disability
The plan	Sets learning goals for a child and describes the services the school will give her. It's a written document/standardized -reading small group, ST/OT, counseling, accommodations in general education classroom	Doesn't have to be written Ideally lists accommodation and who will provide them and ensure implementation. Can vary by school -Test time/setting, breaks, homework organization, teacher education
Team Members	Strict	Less Specific
Parents' Rights/Roles	"prior written notice" and consent for evaluation, any changes and meetings. Review IEP yearly, Re-evaluate every 3 years	Consent to evaluate, frequency of meetings is not standard

ADHD Treatment algorithm ≥ 6 yrs

Partial Response

- Increase dose of current LA medication by smallest increment
- Use adequate dose and duration before switching
- Consider adding afternoon Short Acting booster of same stimulant class
- If still no improvement, follow algorithm

Data driven

Start Stimulant- Either methylphenidate class or Amphetamine class

Pick based on formulary and available form

Consider family medication history /stigma

Alternate class of stimulant

Switch to AMP or MPH

Check formulary and drug form

Reconsider diagnosis and rule out psuedo-resistance

Medical condition, substance use, sleep dysfunction, non adherence

No data

Long acting alpha-2 agonist plus stimulant

Guanfacine (Intuniv)

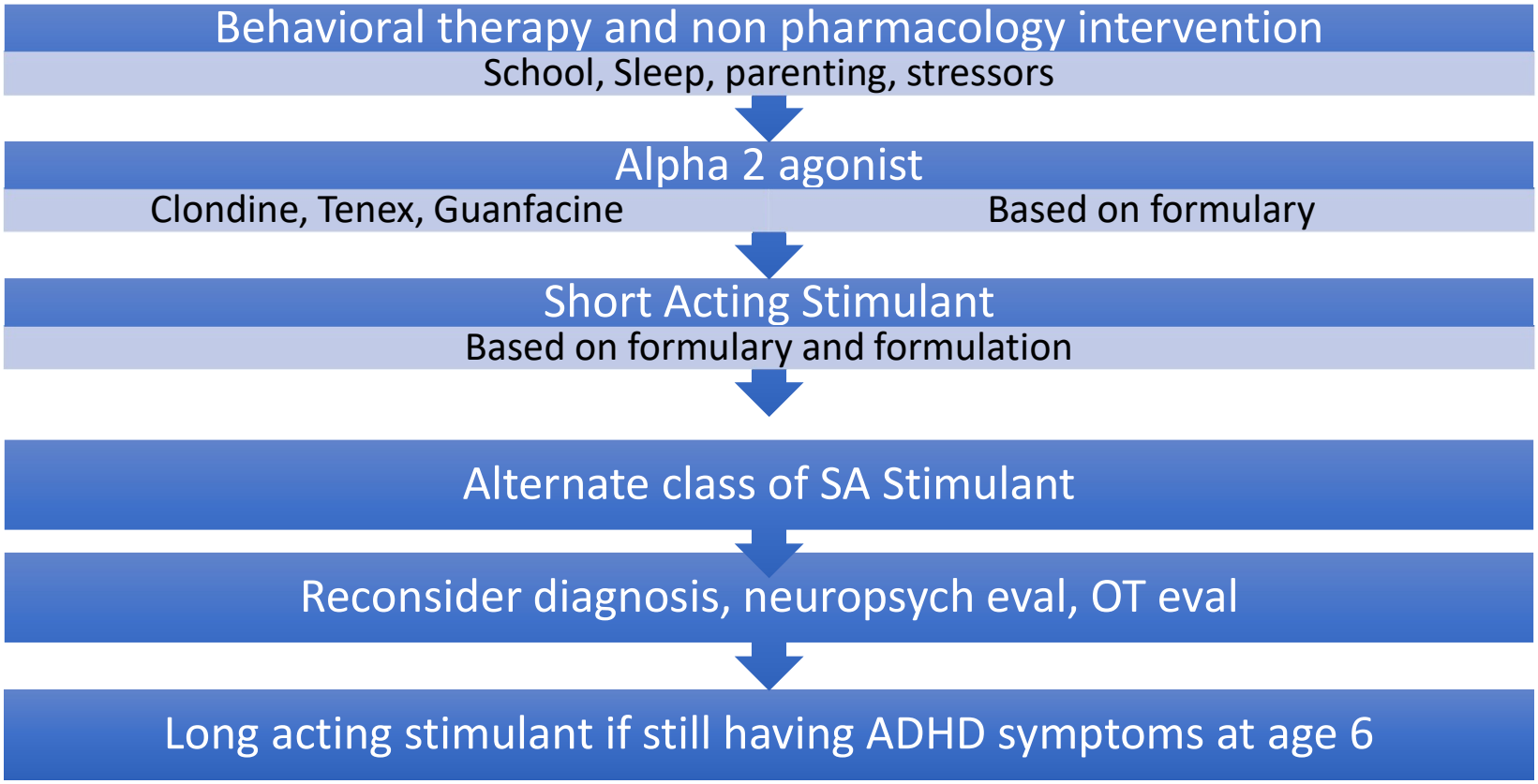
Clonidine (Kapvay)

Long acting alpha-2 agonist alone

Second Line non stimulant: Atomoxetine, Viloxazine

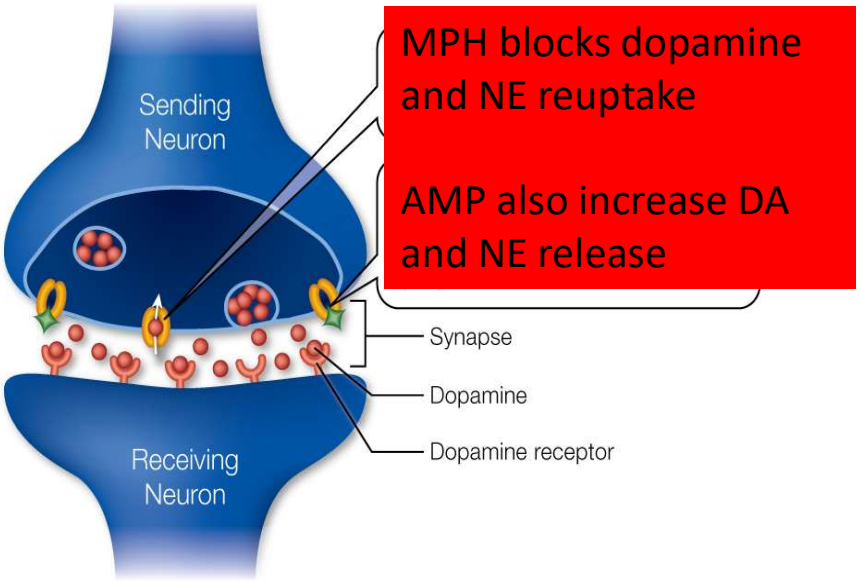
Reconsider diagnosis, further evaluation

ADHD Treatment Algorithm <6 YEARS



The Stimulants- how do they work?

- Dopamine (D) and norepinephrine (NE) play a key role in the areas of the brain responsible for regulating attention and executive function (prefrontal cortex)
- D and NE are deficient in ADHD brains
- Medications ”stimulate” neurons to make increased levels of D and NE.
- The prefrontal cortex appear more active and “turned on” to cognitive tasks and attention when neurotransmitter levels are elevated. (Medication is active)
- Stimulants don't cure ADHD- help to alleviate or reduce symptoms while the stimulant is active in your system.
  - Glasses vs antibiotics analogy



Stimulant Dosing Guidelines

- Weight/age does not predict dose
- Start low and go slow
- Treat to best effect without side effect
- Sum of the IR doses = XR dose
- Will see an immediate effect
- D enantiomer is more active pharmacologically
  - Dexmethylphenidate (Focalin)
  - Dextroamphetamine (Dexedrine)
- Amphetamines stronger than methylphenidates

Screen Shot from the AACAP Parent Medication Guide

MPH Dosing Guide

Methylphenidate (MPH) for ADHD					
Medication	**Starting Dose**	**How Supplied**	**Dosage Form**	**Duration of Medication Effects**	**Given how many times a day?**
Adhansia XR	25 mg	25, 35, 45, 55, 70, 85 mg	capsules	Up to 16 hours	Once
Aptensio XR	10 mg	10, 15, 20, 30, 40, 50, 60 mg	capsules	12 hours	Once
Azstarys XR	26.1/5.2 mg	26.1/5.2, 39.2/7.8, 52.3/10.4 mg	capsules	12 hours	Once
Concerta	18 mg	18, 27, 36, 54 mg	capsules	12 hours	Once
Contempla XR	8.6 mg	8.6, 17.3, 25.9 mg	disintegrating tablets	12 hours	Once
Daytrana	10 mg	10, 15, 20, 30 mg	patch	6–16 hours	Once
Focalin	2.5 mg	2.5, 5, 10 mg	tablets	4–5 hours	Two to three times
Focalin XR	5 mg	5, 10, 15, 20 mg	capsules	10–12 hours	Once
Jornay PM	20 mg	20, 40, 60, 80, 100 mg	delayed-release capsules	12 hours	Once
Metadate CD	20 mg	10, 20, 30, 40, 50, 60 mg	capsules	8 hours	Once
Quillivant	<10 mg	25 mg	suspension	12 hours	Once
Quillichew	<10 mg	20, 30, 40 mg	chewable tablets	8 hours	Once
Ritalin IR	5 mg	5, 10, 20 mg	tablets	3–4 hours	Two to four times
Ritalin LA	20 mg	10, 20, 30, 40 mg	capsules	8 hours	Once

Screen Shot from the AACAP Parent Medication Guide

AMP Dosing Guide

Amphetamine (AMPH) for ADHD					
Medication	**Starting Dose**	**How Supplied**	**Dosage Form**	**Duration of Medication Effects**	**Given how many times a day?**
Adderall	2.5–5 mg	5–30 mg	tablets	6 hours	Once to twice
Adderall XR	2.5–5 mg	5, 10, 15, 20, 25, 30 mg	capsules	12 hours	Once
Adzenys XR	6.3–12.5 mg	3.1, 6.3, 9.4, 12.5, 15.7, 18.8 mg	disintegrating tablets	12 hours	Once
Dexedrine Spansule	5 mg	5, 10, 15 mg	spansules	6 hours	Once to twice
Dexedrine Tablets	2.5–5 mg	5, 10, 15, 20 mg	capsules	3–5 hours	Two to three
Dyanavel XR	2.5–5 mg	2.5 mg	suspension	13 hours	Once
Evekeo	2.5–5 mg	5, 10 mg	tablets	3–5 hours	Two to three
Mydayis	12.5 mg	25, 50 mg	capsules	Up to 16 hours	Once
Vyvanse	30 mg	20, 30, 40, 50, 60, 70 mg	capsules	12–14 hours	Once

Methylphenidate Products

Short Acting (3-5 hours) **Onset: 20-60 minutes** **Duration: 3-5 hours**	**Medium Acting** **Onset: 1-3 hours** **Durations 3-8 hours**	**Long Acting** **Onset: 1 hour** **Durations: 8-12+ hours**

• Ritalin (Methylphenidate IR)
  • 30 minutes until effect, 90 min peak concentration. ½ life of 3 hours
• Methylin (Solution or chewable)
• Focalin (Dexmethylphenidate IR)
  • 5-6 hours
  • D enantiomer is more active pharmacologically
  • Focalin doses 50% lower than Ritalin (mixed d, L enantiomer) doses
	• Ritalin SR (3-8 hours)
	• Ritalin LA (6-8 hours) [50IR/50ER]
	• Metadate ER (3-8 hours)
	• Metadate CD (6-8 hours) [30IR/70ER]
	• Methylin ER (3-8 hours)
	• Quillichew ER (8 hour) [30IR/70ER]
		• Focalin XR (lower doses needed)
		• Concerta
		• Daytrana
		  • Transdermal patch
		  • Higher rates of adverse effects
		• Quillivant XR (12 hr)- liquid suspension [20IR/80ER]
		• Aptensio XR (12hr) [40IR/60ER]
		• Contempla XR-ODT (10-12 hr) [25IR/75ER]
		• Jornay PM (starts to release 10 hours after taken, can last up to 10-12 hours)

Amphetamine Products

Short Acting **Onset: 20-60 minutes** **Duration: 6 hours**	**Medium Acting** **Onset: 60-90 minutes** **Duration: 5-8 hours**	**Long Acting** **Onset: 1 hour** **Duration: 8-12+ hours**
• Dexedrine Tablets • Evekeo	• Adderall IR (4-6 hours • Dexedrine IR (4-6 hours) • DEXtroamphetamine: d enantiomer- more active pharmacologically- lower doses needed	• Adderall XR (10-12 hr) [50IR/50ER] • Dexedrine SR (6-10 hr) • Adenzys-XR-ODT (mixed) [50IR/50ER] • Dyanavel XR (suspension) (mixed) • Lisdexamfetatamine “Vyvanse” (12+ hr) • Mydayis (16 hour) (mixed)

Long Acting Delivery Options

- Single Pulse/first generation uses a wax matrix- Metadate ER, Ritalin SR
  - Can be inconsistent, lower serum concentrations
  - Slower onset of action- may require an IR dose in the AM
- Dual Pulse: SODAS (Spheroidal Oral Drug Absorption System): combination of immediate and delayed release beads: Ritalin LA, Focalin XR, Adderall XR, Dexedrine SR, Adenzys, Contempla and Metadate CD
  - Ritalin LA and Focalin XR are 50 % IR / 50 % ER
  - Two distinct peaks approximately 4 hours apart
  - Metadate CD: 30% IR/70% ER
  - Mimics twice daily dosing of Ritalin IR
- OROS (Osmotic Release Oral System) capsule with H2O permeable holes which release medication depending on osmotic pressure (Concerta)
  - 22 % IR / 78% ER
  - Up to 12 hours
  - Mimics three times/day dosing of Ritalin IR
- Lisdexamfetamine (Vyvanse), a prodrug (inactive) bound to L-lysine which uses GI tract to metabolize → dextroamphetamine (active medication)
  - Onset: 2 hours, lasts up to 13 hours
  - Less risk for abuse

Selecting an XR Medication: When does it Peak?

- Earlier peak for morning symptoms (more immediate release in their prep)
  - Metadate CD: 30% IR
  - Aptensio XR: 37% IR
  - Methylphenidate LA: 50% IR
  - Dexmethylphenidate extended release: 50% IR
  - Mixed Salts Amphetamine extended release (Adderall XR, Adzenys ODT/suspension): 50% IR
- Later peak for afternoon symptoms (more delayed release in their prep)
  - Quillivant/Quillichew: 20% IR, Peaks later
  - Dynavel XR solution 20%, peaks later
  - OROS MPH (Concerta): 22% IR
  - Transdermal methylphenidate (Daytrana): peaks 6-9 hours
  - Lisdexamfetamine (Vyvanse): peaks 6-8 hours

Stimulant Side Effects and Strategies

Loss of Appetite, Nausea, Stomach Upset	• **Monitor weight closely** • **Usually improve within 4-6 months** • **Give medication with meals** • **Add calorie enhanced snacks- instant breakfast, yogurt, cheese, nut products** • **Reduce dose if possible**
Difficulty falling asleep	• Sleep hygiene: waking up at the same time, no caffeine, limiting naps, limit screens • Medication side effect? Give medication earlier, change to shorter acting forms, reduce last dose of the day • Continued hyperactivity? Add on melatonin, low dose clonidine or guanfacine at bedtime, consider IR stimulant in the evening, mirtazapine or periactin QHS
Headache	• Divide dose • Give with food

Stimulant Side Effects: Strategies

Rebound phenomena (more irritable and show an increase in over-activity, impulsivity, and inattention when medication wears off)	• **Change to extended release, consider patch** • **Add short acting stimulant 30 min before rebound** • **Add on low dose clonidine or guanfacine** • **Anticipatory guidance** • **Parent/child behavioral training**

Irritability, sadness, moodiness, agitation	• Evaluate when it occurs:
	  • Peak medication time (may be too much medication)
	  • Rebound time?
	• Reduce dose
	• Change stimulant class or formulation
	• Assess for another problem, such as depression

Stimulant Side Effects and Strategies

Dizziness	• **Hold next dose** • **Check BP and heart rate** • **Increase fluid intake** • **Change to extended release form**
Mild increases in BP and HR	• HR 5 point increase normal • Monitor BP- if persistent, consider regular BP screening labs • If HR and BP > 95% consistently (and a change from baseline) refer to cardiology
Concerning Heart symptoms: (palpitations, almost passing out, chest discomfort/pain, significantly increased heart rate or BP)	• Stop medication • Review patient and family cardiac history (syncope, family sudden cardiac death, cardiac abnormalities) • Cardiac exam- vital signs, murmur, marfanoid • Obtain EKG, cardiology referral

Uncommon Adverse effects of Stimulants

- Motor tics (high comorbidity), dysphoria, irritability, hallucinations, “zombie”
- Cardiac: 25 cases of sudden death; risk is 0.7-1.5/100K children <16
- Myths:
  - Treatment Emergent Mania–stimulants don’t cause mania: higher risk of mania in patients with bipolar who are not on a mood stabilizer
  - Substance abuse: early/long term treatment of ADHD with stimulants lower the risk of later cigarette or illegal drug use

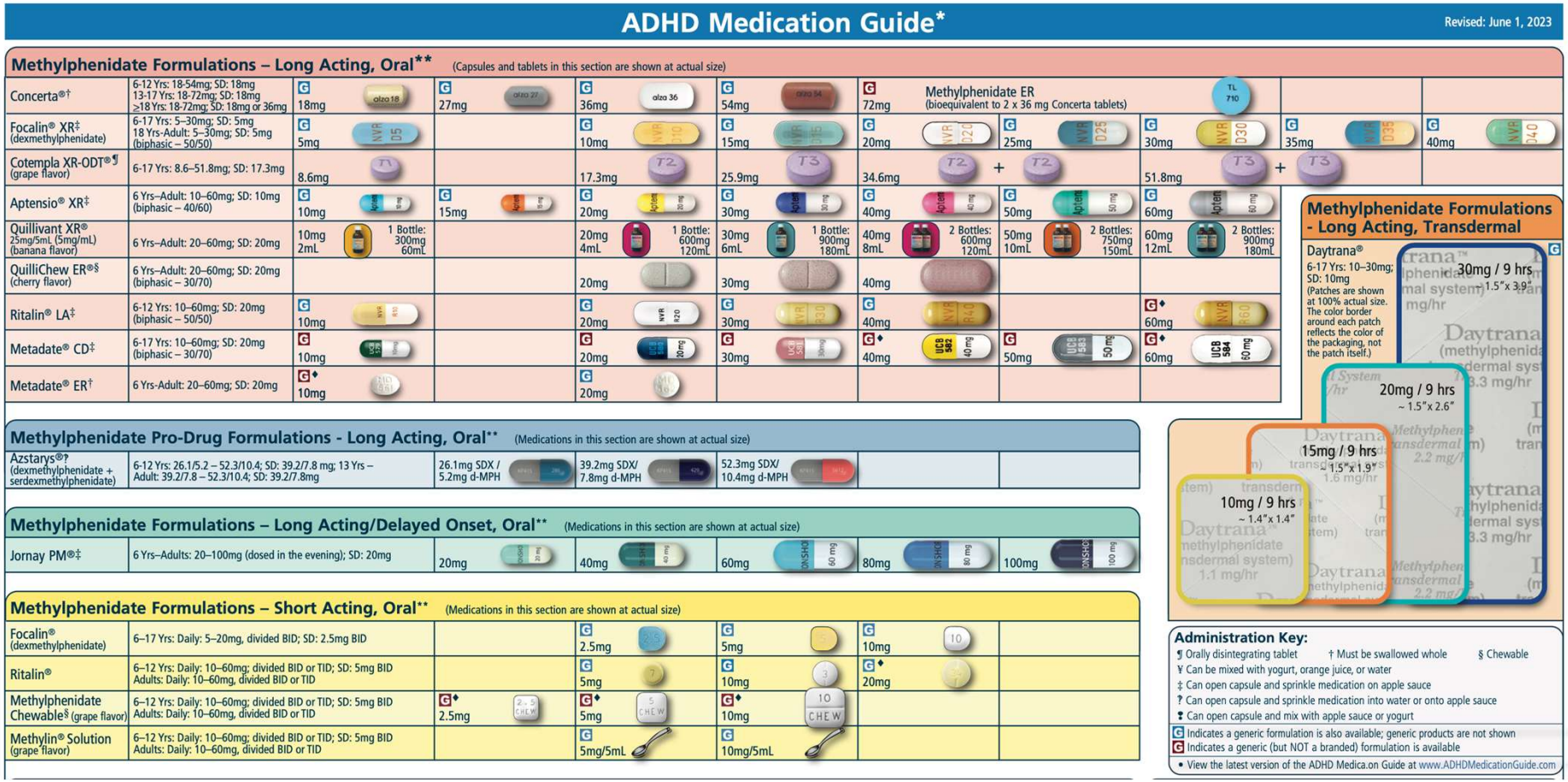
Long Term Use considerations of Stimulants

- Growth:
  - 1cm/year decrease in height over 1-3 yrs of continuous treatment, but other studies show no difference
  - Inconsistently medicated: 1 cm shorter than controls at age 25
  - Consistently medicated: 4cm shorter than controls at age 25
  - **Strategies:**
    - **Monitor height**
    - **Compare with parental height history**
    - **Weekend and vacation holidays, off or on lower dose**
    - **Change to non-stimulant treatment**

- Cardiac
  - Increased baseline heart rate: monitor BP, HR every 3 months
  - Long term risks are unknown, monitor symptoms

http://www.adhdmedicationguide.com

Only includes FDA approved medications



ADHD Treatment algorithm ≥ 6 yrs

Partial Response

- Increase dose of current LA medication by smallest increment
- Use adequate dose and duration before switching
- Consider adding afternoon Short Acting booster of same stimulant class
- If still no improvement, follow algorithm

Data driven

Start Stimulant- Either methylphenidate class or Amphetamine class

Pick based on formulary and available form

Consider family medication history /stigma

Alternate class of stimulant

Switch to AMP or MPH

Check formulary and drug form

Reconsider diagnosis and rule out psuedo-resistance

Medical condition, substance use, sleep dysfunction, non adherence

No data

Long acting alpha-2 agonist plus stimulant

Guanfacine (Intuniv)

Clonidine (Kapvay)

Long acting alpha-2 agonist alone

Second Line non stimulant: Atomoxetine, Viloxazine

Reconsider diagnosis, further evaluation

ADHD treatment: Assessing Response

- Use Vanderbilt Rating scale as objective tool to track symptom control
- Follow school performance
- Therapy progress
- Focus on timing of symptoms (night, school times, specific setting- split households/sports/homework, weekends)
- Sleep issues
- Non adherence
- Drug interactions (luckily very few)
- Dosing Guidelines
  - Increase by smallest increment available of the current medication
  - Booster afternoon doses- younger kids 2.5-5mg. Older kids 5mg-10mg

ADHD Treatment algorithm ≥ 6 yrs

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Non-Stimulant Treatment in ADHD: Alpha Agonist

- **They do work? Yes- evidence based data! FDA approved**
  - Showed Improvement in ADHD and ODD compared to placebo
  - **Combination with stimulant > stimulant alone > alpha agonist alone**
  - Long Acting Alpha 2 Agonists- Guanfacine XR and Clonidine XR
- Mechanism of action
  - Exert their effects primarily through Norepinephrine activity- true mechanism is not known
  - Up to 2 weeks in long-acting forms to see effect
- **Helps with associated motor/vocal tics, aggression, sleep and behavioral dysregulation**
- **Adjunct for ASD**

Guanfacine

- More selective for α_{2a} receptor
- XR Formulation (Intuniv):
  - Dosing: 1-4 mg/day: with effect between 2-4 weeks. One study went up to 7mg/day
  - AM or PM administration show similar efficacy for ADHD scores
- Guanfacine short acting (Tenex)
  - Requires up to 3 times/day dosing
- Side Effects: some sedation/dizziness (less than clonidine), decreased heart rate, rebound hypertension
  - Start low, go slow, don't miss doses.

Clonidine

- Alpha agonist
- **Potential use in Insomnia and ADHD/anxiety,** including daytime doses.
- Short Acting Dosing
  - 0.05mg-0.2mg QHS, increase dose weekly
  - Max Dose 0.4mg qday divided TID/QID
  - **Half life is 3 hours- possible night-time awakening**
- Extended-Release Dosing (Kapvay):
  - Start at 0.1mg QHS, increase dose weekly. Max dose 0.4mg divided BID
- Side effects: bradycardia, dizziness, sedation, hypotension

Atomoxetine (Straterra)

- SNRI: Selective NE reuptake inhibitor, increased NE and Dopamine
- **Advantages: low abuse potential, less insomnia/growth problems, FDA approved**
- **Disadvantages: delayed onset of effect (2-6 wks), lower efficacy than stimulants**
- Dose based on weight: 0.5mg/kg/day, up to 1.2mg/kg/day as tolerated
- Adverse effects: nausea, stomach pain, headache, tired moodiness, increased heart rate, priapism, Black Box – suicidality
  - Start low and slow
  - BID dosing can help with physical side effects
- When to use:
  - Uncomplicated ADHD, refractory ADHD or Comorbid ADHD
  - Anxiety, Depression, Tic Disorders, Disruptive Disorders, Substance Use disorders

Viloxazine (Qelbree)

- SNRI modulator- increases norepinephrine and serotonin
- **Newly FDA approved for ADHD**. Used for depression treatment in Europe for years
- Dosing:
  - 6 to 11 years of age: Start at 100 mg once daily. May titrate in increments of 100 mg weekly to the maximum recommended dosage of 400 mg once daily
  - 12 to 17 years of age: Start at 200 mg once daily. May titrate after 1 week, by an increment of 200mg, to the maximum recommended dosage of 400 mg once daily
- **Cons: Takes weeks to see improvement in ADHD symptoms**
- Side effects: tired, decrease appetite, nausea, insomnia, irritability, suicidal behavior
  - Start low/go slow
  - Food/snack supplements

Buproprion

- Inhibits reuptake of dopamine and norepinephrine
- **FDA approved for adult depression, smoking cessation. Off label use ADHD**
- Dosing:
  - Immediate release (BID dosing: start 37.5mg BID, dose range 100-300mg/day
  - 12-hour sustained release (2mg/kg once daily, qAM, up to 100mg, 3mg/kg qAM, 3mg/kg qAM-2mg/kg qPM, 3mg/kg BID)
  - 24- hour extended release (start 150mg qAM, titrate to 300mg after 2 weeks)
- Side effects: “out of control” behaviors, irritability, insomnia, seizures

Tricyclic Antidepressants (TCAs)

- Serotonin and Norepinephrine Reuptake Inhibitors
- **Some data showing improvement in ADHD symptoms, but not strong evidence**
- Desipramine, nortriptyline used in the studies
- High side effect profile/serotonin syndrome
- High lethality in overdose
- Clomipramine- FDA approved for OCD 10+, not for ADHD
- Low doses can be used as an adjunct for sleep, OCD

Modafinil (Provigil)

- ”Stimulant”- increases dopamine levels
- **Not approved by the FDA for children due to risk for Stevens Johnson syndrome and risk for psychiatric reactions**
  - Consider use in refractory, severe ADHD
- Dosing:
  - <30kg: 200-340mg daily
  - >30kg: 300-425mg daily
- FDA approved for sleep disorders like narcolepsy in adults only

Combining Stimulants and Non-Stimulants

- **Works well in refractory ADHD**
- **Stimulant + Alpha agonist- FDA approved approach**
- Stimulant + Atypical antipsychotic
  - Treatment of Severe Childhood Aggression (TOSCA)
    - Medication Used: Risperidone
    - Wait one month after stimulants and parent training to add on an SGA

ADHD and Sleep

- Sleep hygiene
- Screen Time- blue light wavelength simulates daytime
  - Turn off 1 hour prior to sleep
- Continued hyperactivity/break through ADHD symptoms at night or medication side effects?
  - Consider afternoon stimulant, consider non stimulant, consider your dose formulation- the extended release component
- Clonidine (0.1mg tab)
  - ¼ tab starting dose (0.025mg)
  - Increase by ¼ to ½ tab
  - Max dose: 0.2mg

Melatonin in ADHD

- Study looked at ADHD patients, 40% on stimulants
- 5mg dose of melatonin vs placebo
- Sleep onset and latency improved
- Sleep questionaries showed improvement
- Well tolerated

Other Treatments for ADHD

- Neurofeedback: promote self regulation of brain activity- improved cognitive/behavioral controls
  - Blinded studies showed no effect, $$$
- Omega-3 Fatty Acids
  - Small improvement in ADHD. Improves mood. Ratio of EPA >DHA
- Caffeine
  - Non- prescription stimulant that has been used for ADHD. Some research suggests that caffeine alone might modestly improve ADHD symptoms. At doses of 300 mg per day, caffeine is no better than placebo for ADHD in children. 1 Coffee= 100mg of caffeine
- Zinc
  - Deficiency may lead to poor response to stimulants, helpful to check and supplement if inadequate response

Other Evaluations to consider in ADHD

- OT- sensory component to behaviors
- Sleep intervention
- Neuropsychology evaluation- underlying learning disability, sensory processing, developmental delay

Approaches for Comorbid ADHD

+ ODD/CONDUCT AGGRESSION

- Stimulants
- Alpha Agonists
- Behavioral therapy/Parent training
- Atypical antipsychotics- low dose risperidone or aripiprazole
- Rule out Autism Spectrum Disorder

+ANXIETY OR DEPRESSION

- Stimulants or Atomoxetine
- Behavioral therapy
- SSRI
- Treat primary disorder first

+ SUBSTANCE ABUSE

- Avoid Stimulant
  - Vyvanse is an option
- Atomoxetine, Guanfacine XR, Clonidine XR, Bupropion
- Treat primary disorder first

Autism Spectrum Disorder

- Core Features of Autism
  - Impaired social interaction and communication
  - Repetitive behavior/restricted interests
- No medications to target core symptoms
- **All medication in ASD target specific behavioral problems**
  - **Aggression/Irritability/Self injury**
  - **Hyperactivity**
  - Anxiety
  - **Sleep**

ADHD and Autism

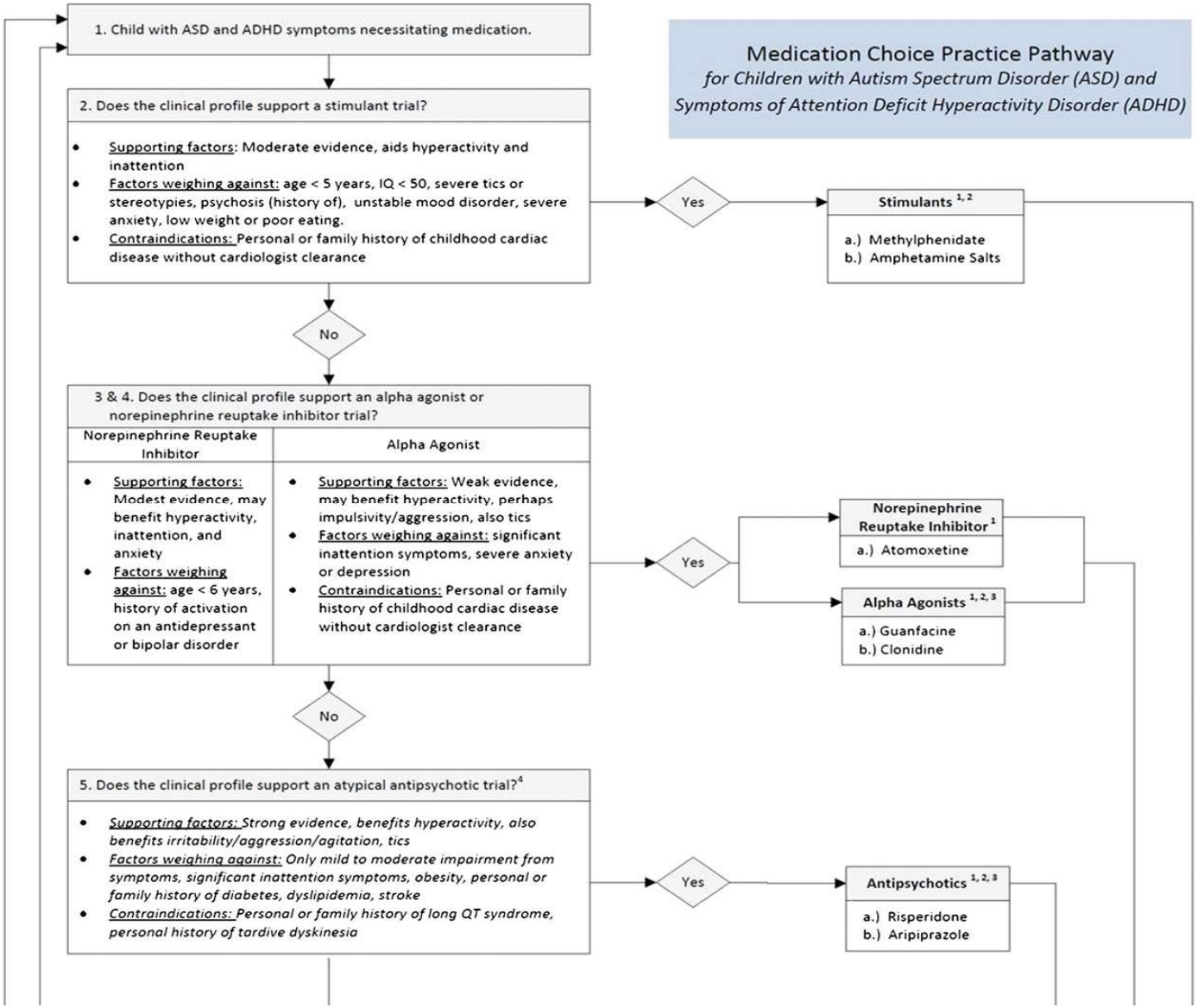
- 70% of youth with Autism have another co-occurring mental health diagnosis
- 37-85% of youth with ASD have ADHD (compared to 2-7% of neurotypical children)

ADHD and Autism: Diagnostic Dilemma

- ADHD/ASD Symptom Overlap
  - Social skills challenges
  - Over reactivity
  - Meltdowns/aggression
  - Sensory differences
- ASD Specific
  - Repetitive motor movements
  - Language regression
  - Difficulties with reciprocal play or conversation
  - Unusual or intense interest in certain topics or items (hyperfocus)
- When to think about ADHD:
  - ASD patients with significant impairments
  - Traditional interventions for ASD are not working
  - Family history of ADHD

ADHD in Autism: Treatment Guidelines

- Behavioral therapy!!!
- School based accomodations
- Pharmacotherapy
  - Stimulants
  - Atomoxetine
  - Alpha 2 agonists


Medication Choice Practice Pathway
for Children with Autism Spectrum Disorder (ASD) and Symptoms of Attention Deficit Hyperactivity Disorder (ADHD)
1. Child with ASD and ADHD symptoms necessitating medication.
2. Does the clinical profile support a stimulant trial?
Supporting factors: Moderate evidence, aids hyperactivity and inattention
Factors weighing against: age < 5 years, IQ < 50, severe tics or stereotypies, psychosis (history of), unstable mood disorder, severe anxiety, low weight or poor eating.
Contraindications: Personal or family history of childhood cardiac disease without cardiologist clearance
Yes
Stimulants 1, 2
a.) Methylphenidate
b.) Amphetamine Salts
No
3 & 4. Does the clinical profile support an alpha agonist or norepinephrine reuptake inhibitor trial?
Norepinephrine Reuptake Inhibitor
Supporting factors: Modest evidence, may benefit hyperactivity, inattention, and anxiety
Factors weighing against: age < 6 years, history of activation on an antidepressant or bipolar disorder
Alpha Agonist
Supporting factors: Weak evidence, may benefit hyperactivity, perhaps impulsivity/aggression, also tics
Factors weighing against: significant inattention symptoms, severe anxiety or depression
Contraindications: Personal or family history of childhood cardiac disease without cardiologist clearance
Yes
Norepinephrine Reuptake Inhibitor 1
a.) Atomoxetine
Alpha Agonists 1, 2, 3
a.) Guanfacine
b.) Clonidine
No
5. Does the clinical profile support an atypical antipsychotic trial? 4
Supporting factors: Strong evidence, benefits hyperactivity, also benefits irritability/aggression/agitation, tics
Factors weighing against: Only mild to moderate impairment from symptoms, significant inattention symptoms, obesity, personal or family history of diabetes, dyslipidemia, stroke
Contraindications: Personal or family history of long QT syndrome, personal history of tardive dyskinesia
Yes
Antipsychotics 1, 2, 3
a.) Risperidone
b.) Aripiprazole

ADHD in Autism- Stimulants

- Largest RCT- looked at methylphenidate
- **Lower effectiveness and higher side effects compared to youth without ASD**
- Irritability and Agitation were more common
- 49% much or very improved
- 23% did best on high dose
- Short acting in multiple doses can be tried if long acting not tolerated
- MPH are better tolerated than AMP

ADHD in Autism: Atomoxetine

- 2 RCTs. CHARTS Study ADHD in Autism
- Takes 3-4 weeks for effect
- Underused
- **45-47% of children with ASD Responded (Handed et al, 2015)**
- Parent improvement > teacher improvement
- Side effects- decreased appetite, and abdominal pain- last 4 weeks of less
- **At 24 weeks, 60% of treatment responders remained responders**
- FDA max dose 1.4mg/kg/day- may need to go as high as 1.8mg/kg (off label). Max dose 100mg/day.

ADHD in Autism: Alpha 2 Agonists

- Guanfacine
  - Small studies indicating likely effective for impulsivity, hyperactivity, anxiety and insomnia
  - Guanfacine ER 1-4mg in ASD+ADHD
  - 50% much improved (mode dose was 3mg)
  - Side effects: sedation, decreased appetite, dry mouth
  - Extended release is more effective for long term management of ADHD and has fewer side effects.

- Clonidine
  - Can be effective, but can be over sedating
  - Guanfacine generally better tolerated
  - Okay to trial one, then the other
  - Sometimes short acting better than the long acting
  - Long acting (Intuniv or Kapvay) can be dosed once or twice a day

How to swallow a pill?

- Bonnie Kaplan at the University of Calgary
- Clear and well organized
- YouTube and her website are great patient resources
- Head posturing
- Simple verbal instructions
- Specialized pill cup
- Flavored throat syrup
- Behavioral training

Take Home Points

- ADHD is common in our pediatric population
- Untreated ADHD has both immediate and long-term implications
- Treatment is focused on behavioral therapy, parent training, school based accomodations and medications
- Stimulants are very effective for school aged children
- Parent training recommended for younger children first
- Side effects are common, yet with anticipatory guidance and monitoring are manageable.
- ADHD rates are high in the Autism population
- Consider non stimulants for refractory ADHD or special populations that cannot tolerated stimulants

Thank you

- Questions?