AD/HD: WE CAN DO THIS!

Pediatric Review

October 24th, 2024

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YES, WE CAN!

DISCLOSURES

01

Review treatments for AD/HD

02

Discuss the role of the primary care provider in the treatment of AD/HD

03

Discuss updates relevant to primary care providers treating patients with AD/HD

OBJECTIVES

CASE 1- LITTLE JOHNNY

- 3-year-old male in the primary care office for concerns of AD/HD and autism, mostly AD/HD
- He has been kicked out of 3 daycares for disruptive behavior
  - Does not sit in circle time and cannot pay attention to lessons or instructions
  - Is constantly moving and often breaks toys
  - Is loud and runs away
  - Hits/bites staff and peers on rare occasions, has never injured anyone
- Hyperactive at home
  - Always running away from mom. She has tried to use a leash, but he can break out of it and runs in front of cars without noticing.

CASE 1

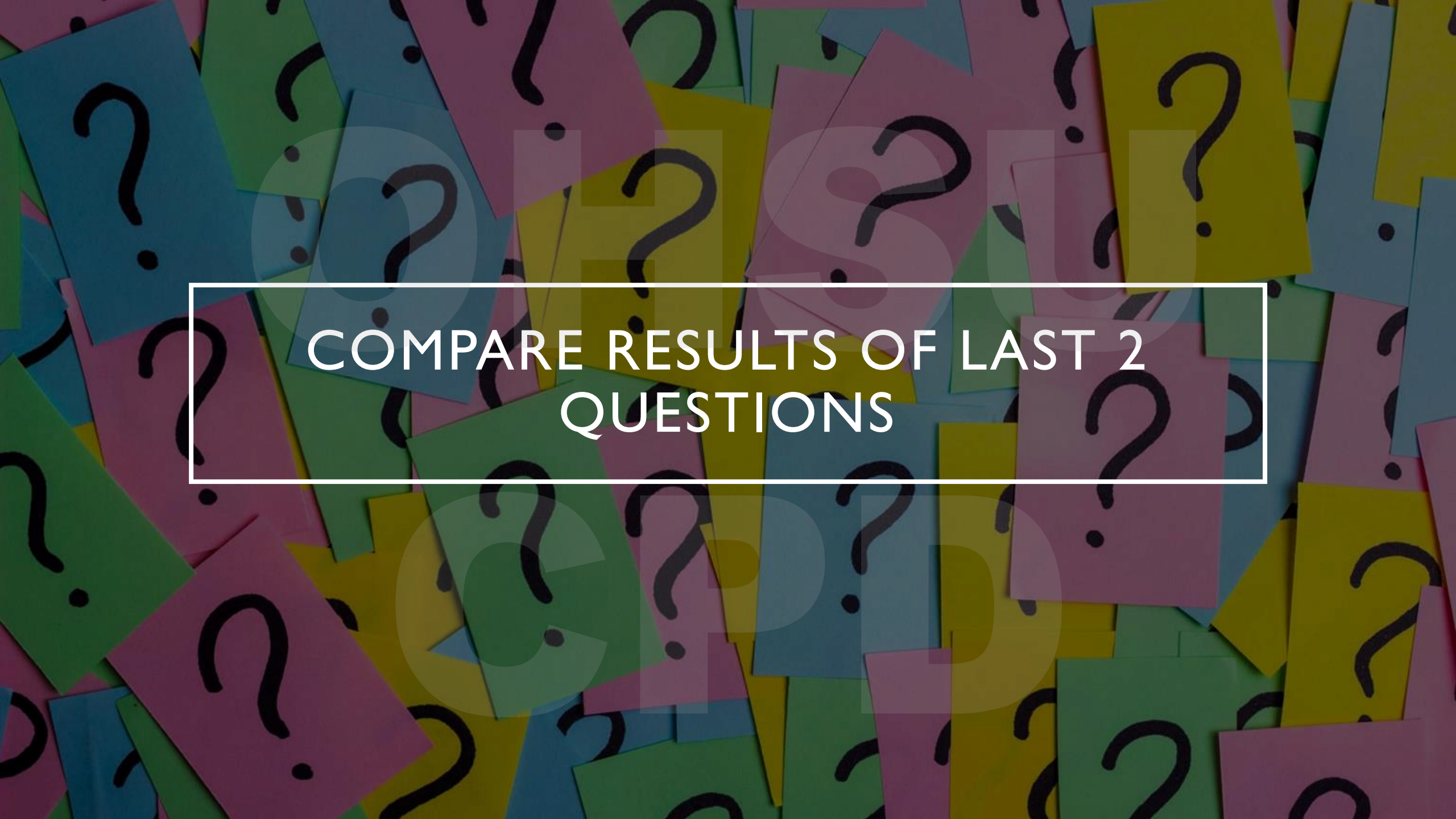
- In your office
  - You can hear him screaming the waiting room
  - During the visit, he is pulling out medical supplies, throws a speculum at his mother, and cannot sit still long enough to make eye contact with you or engage in a conversation
  - The mother appears to be a capable parent and is very worried about him getting kicked out of his current daycare, which specializes on working with kids with challenging behaviors
  - The mother has attended parenting classes and has been working with a social worker for parent management training

CASE 1 – AUDIENCE QUESTION

- What would you do next (select all that apply)?
  A. Refer to child psychiatry, estimated wait is 3-6 months
  B. Refer for an autism evaluation, wait is 2-3 years
  C. Tell mother that he is too young for medications and recommend more parent management training
  D. Refer for occupational therapy
  E. Start dextroamphetamine/amphetamine
  F. Start methylphenidate
  G. Start guanfacine or clonidine

CASE 1 – AUDIENCE QUESTION

- What do think a child psychiatrist would do (select all that apply)?
  A. Refer to child psychiatry, estimated wait is 3-6 months
  B. Refer for an autism evaluation, wait is 2-3 years
  C. Tell mother that he is too young for medications and recommend more parent management training
  D. Refer for occupational therapy
  E. Start dextroamphetamine/amphetamine
  F. Start methylphenidate
  G. Start guanfacine or clonidine


COMPARE RESULTS OF LAST 2 QUESTIONS

REFERRING OUT

- For complex or high acuity cases, apply early and broadly
- Child psychiatry: should be managing medications long term
- Autism evaluation: may or may not be necessary, will need to reassess once AD/HD is under better control
- Occupation therapy would be great for building a sensory profile and making a routine

Medication not first line unless significant concerns

First line:

- Behavioral Parent Training (behavioral modification applied for use in the home)
- Behavioral classroom management (behavioral modification techniques given to teachers)
- Organizational skills training

Consider referral to child psychiatry for complex or severe case in this age group

FOR KIDS < 5 YEARS OLD

MEDICATIONS

- For kids aged 5 and under, there is a higher risk of side effects
- Acuity is high in this case
  - At risk for death and injury (running in front of traffic)
  - Multiple expulsions
  - Stunted development
- Dextroamphetamine/amphetamine FDA approved down to age of 3
- Methylphenidate is recommended as first line for kids under 6 by the American Academy of Pediatrics
- Guanfacine not FDA approved under the age of 6 but sometimes used

Harstad E, Shults J, Barbaresi W, Bax A, Cacia J, Deavenport-Saman A, Friedman S, LaRosa A, Loe IM, Mittal S, Tulio S, Vanderbilt D, Blum NJ. α2-Adrenergic Agonists or Stimulants for Preschool-Age Children With Attention-Deficit/Hyperactivity Disorder. JAMA. 2021 May 25;325(20):2067-2075. doi: 10.1001/jama.2021.6118. Erratum in: JAMA. 2021 Oct 12;326(14):1440. PMID: 33946100; PMCID: PMC8097628.

EFFECT SIZES

- Amphetamine - 0.92
- Methylphenidate - 0.80
- Atomoxetine - 0.73
- Clonidine - 0.58
- Modafinil - 0.49
- Bupropion - 0.32
- Omega Threes: 0.21-0.3

Faraone SV. Using Meta-analysis to Compare the Efficacy of Medications for Attention-Deficit/Hyperactivity Disorder in Youths. P T. 2009 Dec;34(12):678-94. PMID: 20140141; PMCID: PMC2810184.

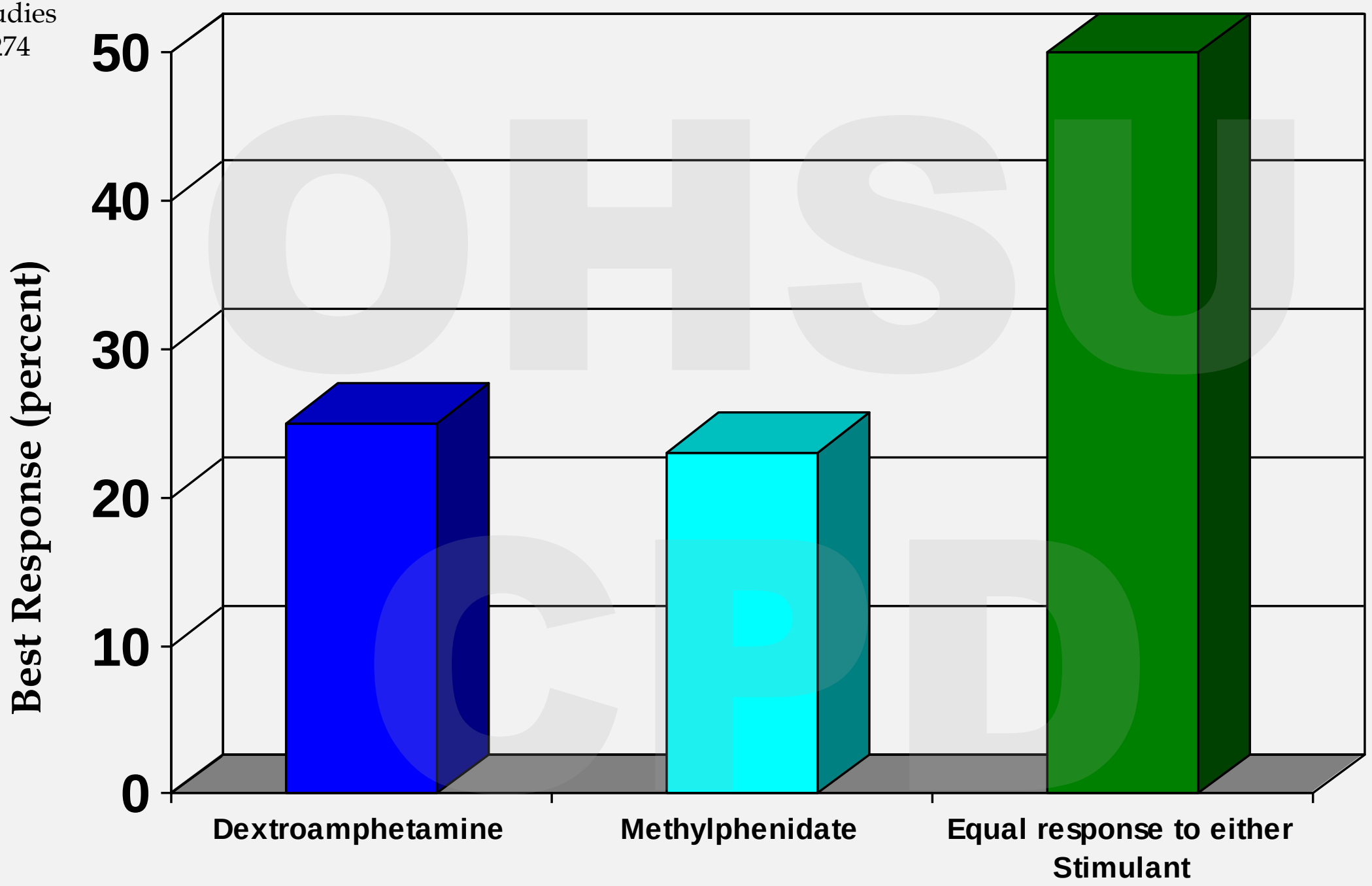
70 + years of study, >250 trials, >6,000 subjects

Effect Sizes:

3-5 yo: 0.5-0.6	6-12 yo: 0.8-1.2	13-17 yo: 0.94	Adults: 0.9

Vaughan BS, Kratochvil CJ. Pharmacotherapy of ADHD in young children. Psychiatry (Edgmont). 2006 Aug;3(8):36-45. PMID: 20963194; PMCID: PMC2957280.

6 studies
N=274



Spencer et al.
Arch of Gen
Psych 2001

MONITOR

WEIGHT, HEIGHT, BMI

PULSE

TICS

BLOOD PRESSURE

VITAMIN D

HEIGHT

- 2008 study showed that treatment with stimulant medication led to statistically significant delays in height and weight.
- Harvard AD/HD team found statistically significant evidence of attenuation of these deficits over time.
- The qualitative review suggested that growth deficits may be dose dependent, deficits may not differ between methylphenidate and amphetamine
- Treatment cessation may lead to normalization of growth, and further research should assess the idea that attention-deficit/hyperactivity disorder itself may be associated with dysregulated growth.

BONE DENSITY

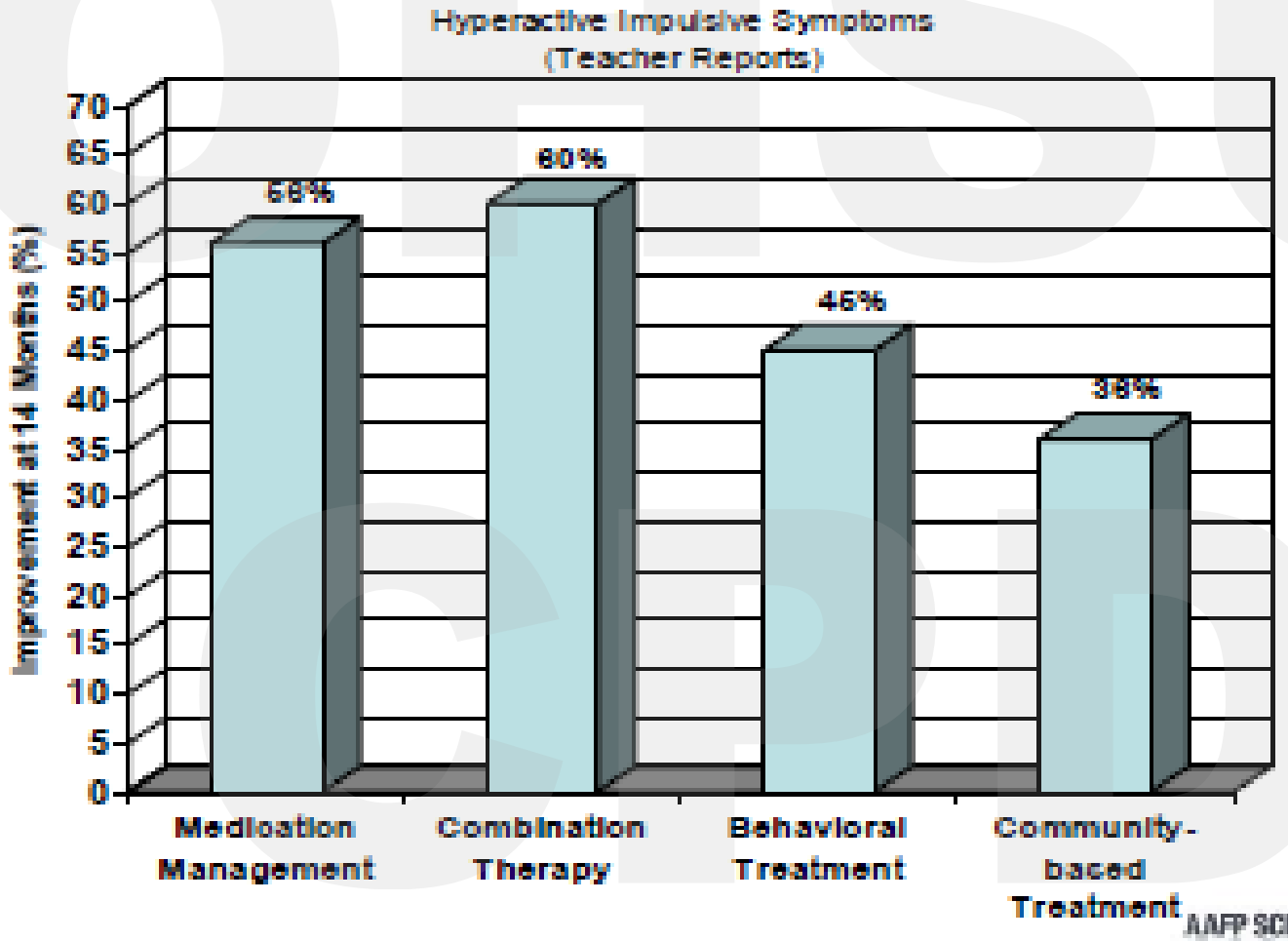
- 6,489 NHANES participants aged 8 to 20 years, of whom 159 were receiving stimulants (primarily amphetamines or amphetamine analogs) for AD/HD. After adjustment for confounders, those using the medications had a total 3.9% lower bone density at the lumbar spine and 3.7% lower bone density at the femoral neck compared with nonusers.
- Recommend:
  - Calcium intake of 800 to 1,300 mg daily
  - 60 minutes of weight-bearing exercise or activity every day
  - Monitor vitamin D levels

RESOURCES FOR PARENTS

- Parent Child Interaction Therapy (PCIT)
- Kazdin Behavior Management Training
- Parent Management Training – Oregon Model (PMTO)
- Collaborative Problem Solving
- Russell Barkley
- Rex Forehand
- Love & Logic

Findings MTA Study

(MTA Cooperative Group, 1999)



ADHD Medication Treatment Algorithm

Based on AACAP Guidelines, 2007 and HEDIS 2010 Performance Measurements

Med & Dosing Reference: *Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention -Deficit/Hyperactivity Disorder,* J. AM. ACAD. Child Adolesc. Psychiatry, 46:7. July 2007

Follow Up Visits Reference: NCQA's *HEDIS 2010 Quality Performance Measurements*

Select Stimulant Agent

Methylphenidate or Amphetamine

Long-Acting
Kids / Adults

or

Methylphenidate or Amphetamine

Short-Acting
Small kids <16kg/35lbs

(low dose is not available in long-acting)

or

Strattera(R)
(Atomoxitene)

- Use for ADHD with co-morbid anxiety or tic disorder
- Use with decreased appetite, and /or decreased sleep from other ADHD meds, or with substance abuse problems

Initial Dose

Select **starting dose** and times of administration

Once daily dosing is helpful for kids in school and prevents the need to send a medication supply to the school nurse.

Twice daily dosing is helpful in kids with late evening behavior episodes

Titrate Dose

Titrate dose upward every one to three weeks until maximum dose is achieved or side effects preclude further dose increase

Achievement Goals
- ADHD Symptoms remit
- No side effects

For students, teacher & parent rating scales are helpful as dose is increased.

Initial Follow Up Visit

Initial follow up should be within 30 days or less of therapy initiation

- **Determine if response is appropriate**
  - 41% will respond to either stimulant medication
  - 44% will respond better to one medication than another
  - Strattera may take up to 6 weeks to see effect
- **Assess for side effects**
  - headache
  - insomnia
  - decreased appetite or weight loss
  - tics
  - emotional lability / irritability
- If side effect is burden to patient:
  - Adjust dose, change medication or wait as many side effects are transient and will resolve

Subsequent Visits

- At least 2 or more visits during the next 9 month period
- If maximum dose of Methylphenidate, amphetamine or atomoxitene has been achieved, continue & monitor for side effects
- If optimal results have not been achieved:
  - Review Diagnosis and assess for any undetected co-morbidities
  - If ADHD diagnosis is reconfirmed, consider behavioral therapy next before adding a non-FDA approved medication

Adding or Stopping Medications

Adding Another Medication

Add-on meds: bupropion, tricyclic antidepressant, clonidine or guanfacine

Often necessary when:
- patient has co-morbid aggression
- necessary to reduce side effects of tics or insomnia

Discontinuing A Medication

If an add on medication is ineffective, titrate dose downward over a 1-2 week period to avoid sudden drops in blood pressure

BEACON HEALTH STRATEGIES

PDIP

CASE 1 – AUDIENCE QUESTION

- What would you do next (select all that apply)?
  A. Refer to child psychiatry, estimated wait is 3-6 months
  B. Refer for an autism evaluation, wait is 2-3 years
  C. Tell mother that he is too young for medications and recommend more parent management training
  D. Refer for occupational therapy
  E. Start dextroamphetamine/amphetamine
  F. Start methylphenidate
  G. Start guanfacine or clonidine

COMPARE TO EARLIER RESPONSES

CASE 2 – BIG CORBY

- 17-year-old male with a history of autism without accompanying intellectual impairment and AD/HD seen in primary care clinic
- Mother expresses concerns of poor hygiene, playing loud music late at night, and messy room
- He recently switched schools and longer has a 1:1 support person at school
- He has been struggling at his new school and mom worries that he may not graduate
- Oh, and by the way, he also screams, threatens to kill his mother, breaks things, and runs away from school and home for a few hours at a time
- The biggest problem time is in the morning as he refuses to take his stimulant for about an hour and then calms down 30 minutes after finally doing so

STIMULANT FORMULATIONS

METHYLPHENIDATE

IMMEDIATE RELEASE

- Methylphenidate oral solution
- Methylphenidate chewable tablet

EXTENDED RELEASE

- Adhansia XR
- Aptensio XR
- Concerta
- Contempla XR ODT
- Quillichew ER
- Quillivant XR
- Jornay PM
- Daytrana (transdermal patch)

AMPHETAMINE

IMMEDIATE RELEASE

- Evekeo
- Procentra
- Zenzedi

EXTENDED RELEASE

- Adzenys XR-ODT / Adzenys ER
- Dyanavel XR
- Mydayis
- Vyvanse (lisdexamfetamine)

CASE 2 – AUDIENCE QUESTION

- What formulation would you suggest (select one)?
  - A. Patch
  - B. Nighttime dosing
  - C. Flavored
  - D. Long-acting

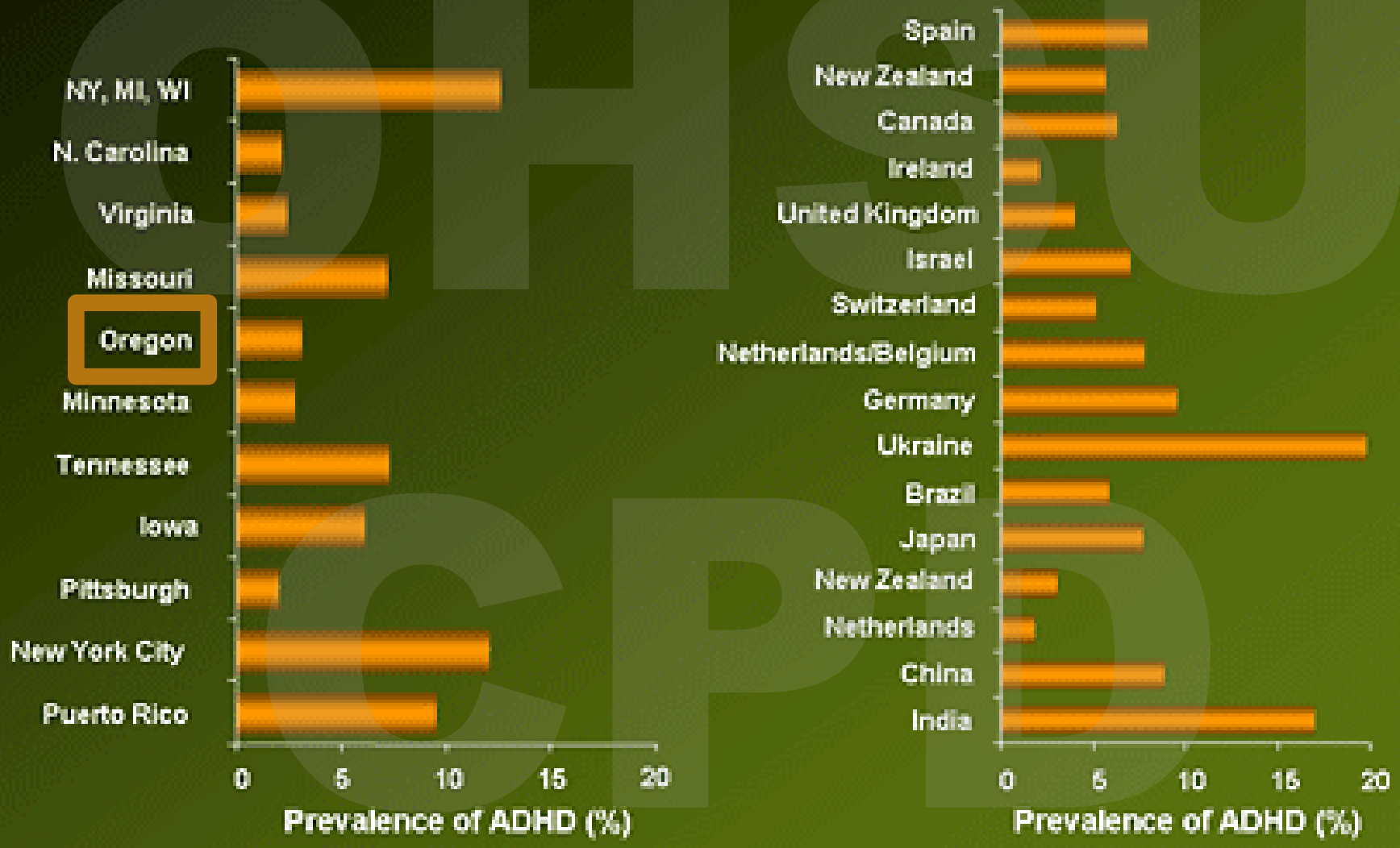
CASE 3 – NORMAL SIZED KELLY

A. 10-year-old female with no psychiatric or medical history
B. Mother brings Kelly to primary care office with concerns of anxiety (shows up 30 minutes late and did not complete any paperwork in advance)
C. Family history of anxiety in mother and older siblings
D. Mother complains that Kelly is not motivated in school, is messy, does not do her chores, and does not have a lot of friends attributing all of this to anxiety
E. Teacher reports that Kelly seems motivated but is often off task, is shy but has a small groups of close friends, and is disorganized
F. Positive for ADHD, inattentive type on Teacher Vanderbilt and for anxiety on SCARED

CASE 3 – AUDIENCE QUESTION

- What do you do next (select one)?
  A. Hold off on medications and refer for psychological testing
  B. Start with an SSRI for the treatment of anxiety
  C. Start with an an alpha-agonist for the treatment of AD/HD and anxiety
  D. Start with a stimulant for the treatment of AD/HD

Worldwide Prevalence of ADHD in Children

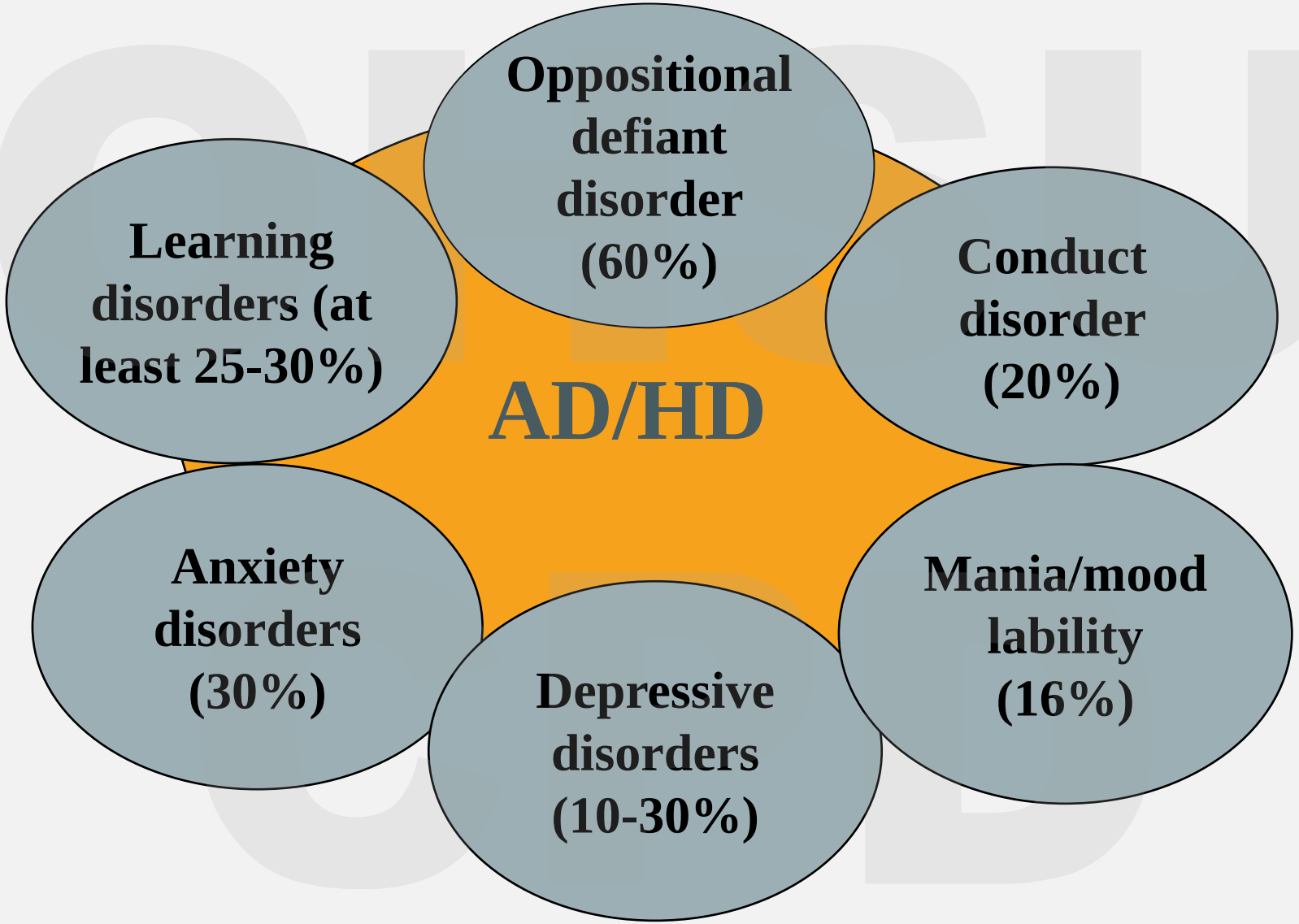


American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, text revision. Washington, DC: American Psychiatric Association; 2000:85-93; Biederman J et al. *J Nerv Ment Dis*. 2004;192:453-454. Faraone SV et al. *World Psychiatry*. 2003;2:104-113.

SLIDE 1

Pre- and Perinatal Risk Factors for ADHD

Sagiv SK, Epstein JN, Bellinger DC, Korrick SA. Pre- and postnatal risk factors for ADHD in a nonclinical pediatric population. J Atten Disord. 2013 Jan;17(1):47-57. doi: 10.1177/1087054711427563. Epub 2012 Jan 31. PMID: 22298092; PMCID: PMC3878902.



Gnanavel S, Sharma P, Kaushal P, Hussain S. Attention deficit hyperactivity disorder and comorbidity: A review of literature. World J Clin Cases. 2019 Sep 6;7(17):2420-2426. doi: 10.12998/wjcc.v7.i17.2420. PMID: 31559278; PMCID: PMC6745333.

WHAT'S THE BIG DEAL IF MY KID DAYDREAMS? I'D RATHER NOT PUT HIM ON MEDICATIONS!

THE AAP SAYS IT'S IMPORTANT

- High prevalence of AD/HD
- Severity of Consequences of AD/HD
- Effective treatments for AD/HD

"Under-achievement can lead to poor self-esteem, which can become the real enemy for those who are struggling to succeed."

Dr. Edward Hallowell
Psychiatrist with AD/HD & Dyslexia
Author of the book "Driven to Distraction"

https://unsplash.com/

TALKING POINTS

Disruptive behavior

- Troublemakers
- Bad sportsmanship
- Excessive talking
- Cannot sit still
- Unfocused, not responsive to others
- Impulsive aggression

Immaturity and impulsiveness

- Center of attention
- Breaks the rules
- Blurting out answers
- Peer rejection

Adolescents continue to demonstrate social problems

- Poor participation in group activities
- Few friends
- Vulnerable to antisocial groups, drug abuse

KEEP IN MIND

- Psychological testing is expensive
- AD/HD more frequently goes unrecognized in girls
- Historians (e.g., teachers and parents):
  - Great at recognizing kids that are loud, hyperactive, or aggressive (boys present this way more often)
  - Do not always notice kids without externalizing symptoms who instead have have more subtle signs such as drifting attention, poor organizational skills, making careless mistakes, losing things, and others
- Ask (and observe) if the parents have AD/HD (do they always show up late?)

CASE 3 – AUDIENCE QUESTION

- What do you do next (select one)?
  A. Hold off on medications and refer for psychological testing
  B. Start with an SSRI for the treatment of anxiety
  C. Start with an an alpha-agonist for the treatment of AD/HD and anxiety
  D. Start with a stimulant for the treatment of AD/HD

COMPARE AUDIENCE QUESTIONS

CASE 4 – BILLY

- 8-year-old male presents for stimulant AD/HD medication check
- The medication is working well
- His weight is down 2 pounds

CASE 4 – AUDIENCE QUESTION

- What do you do next (select one)?
  A. Discontinue stimulant and start atomoxetine
  B. Discontinue stimulant and start alpha-agonist
  C. Discontinue stimulant and refer to child psychiatry
  D. Continue stimulant with close follow up and educate mother of ways to increase nutritional intake

ADVICE FOR BAD EATERS

Get them some nutrition in the afternoon

Big breakfast and big dinner, late night snacking is okay

High calorie foods and nutrition shakes

THE FAMILY HAS A HISTORY OF SUDDEN CARDIAC DEATH!

DO A GOOD PHYSICAL AND TREAT

- April 2008 AHA released policy statement that all youth on stimulants should receive EKG
- May 16, 2008, the AHA and AAP, and AACAP, jointly issued a news release clarifying that obtaining an ECG before starting medication was "reasonable" but not mandatory.
- The risk of cardiac arrest from stimulants is no greater than sudden cardiac arrest in the general pediatric population—Gould et al., 2009

WILL IT GIVE MY KID A TIC?

NO!

STIMULANTS AND TICS

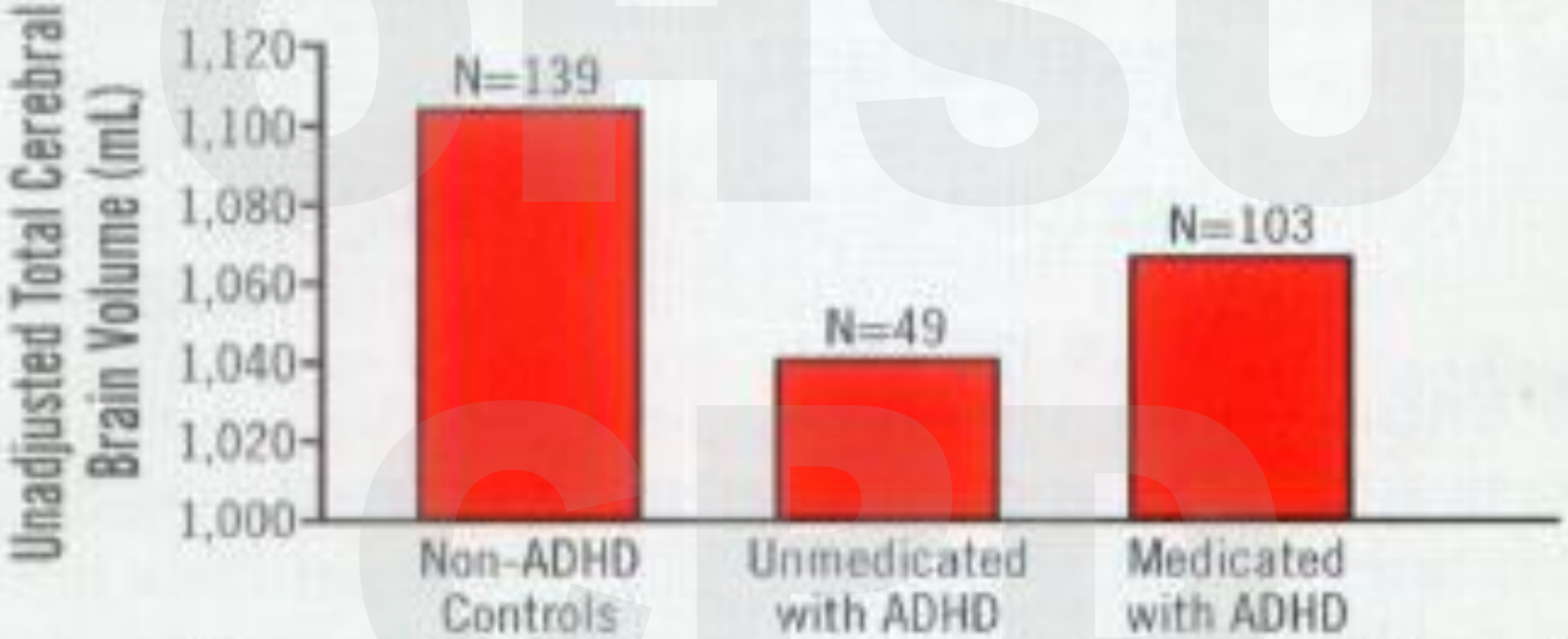
- To date, research has not established a "definitive and causal" relationship of the emergence of tics with stimulant use.
- Though some studies have indicated that transient tics may occur more often in a population of AD/HD patients (with and without a history of tic disorders) treated with stimulants, this data remains controversial…Pidsosny & Virani---2006
- Researchers studied 136 children aged 7 to 14 years with AD/HD and a chronic tic disorder taking MPH.
- Throughout the 4-month study, researchers found improvement in all of the children who received medication.
- "Not only did tics not worsen during treatment, the severity of tics actually decreased in all treatment groups," writes study author Roger Kurlan, MD, of the University of Rochester Medical Center in New York

WILL MY KID BECOME DEPENDENT ON THIS MEDICATION?

NO!

SLIDE 1

Unadjusted Total Cerebral Brain Volume for Unmedicated and Medicated Children and Adolescents with ADHD and Controls[1]



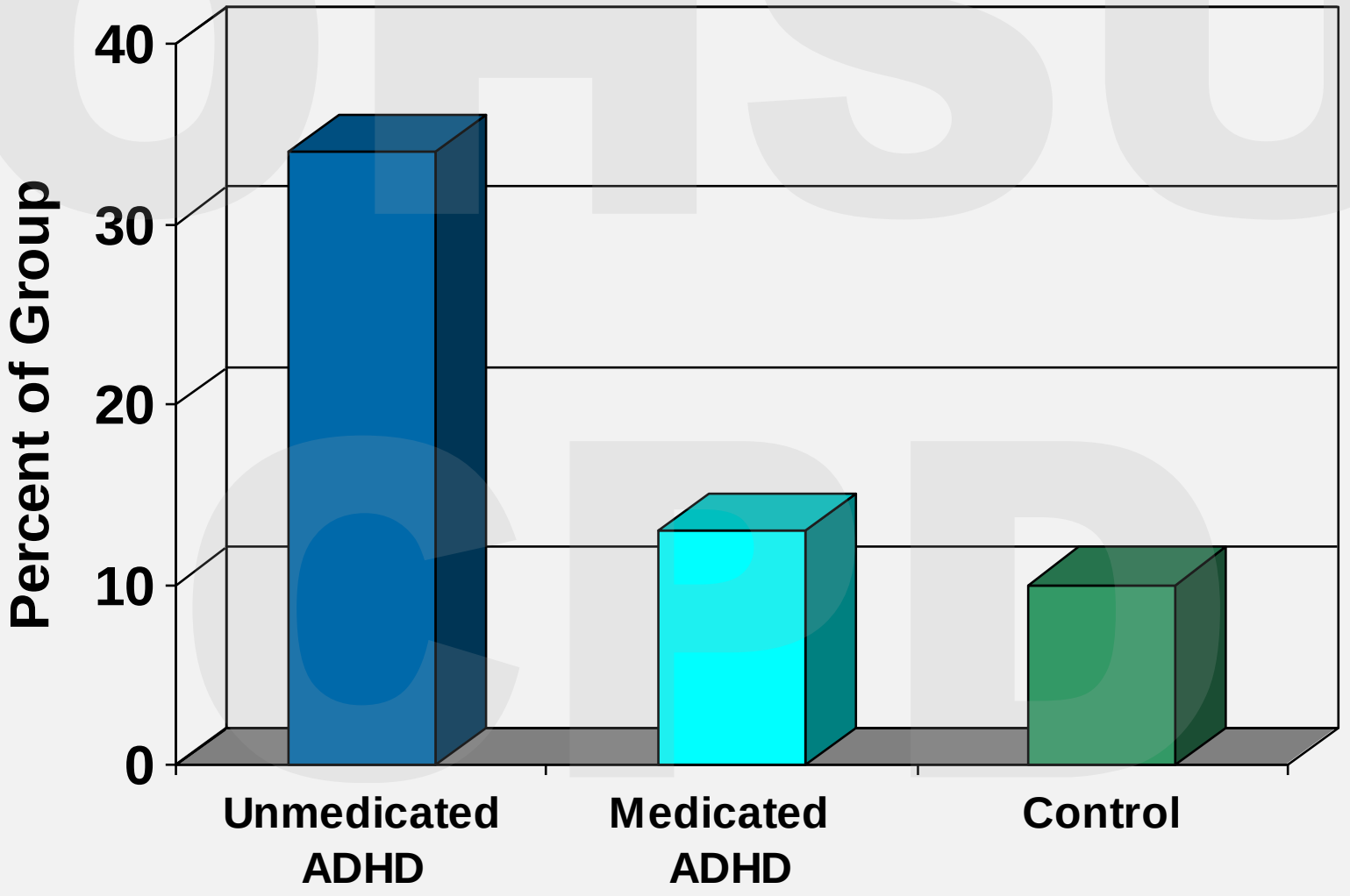
10-year NIMH Study, subjects age 5-18 years at baseline

*P=.001 by 2-way ANOVA (group [medicated vs. unmedicated vs. control] by sex).

DON'T KIDS ABUSE STIMULANTS?

WELL ACTUALLY YES, BUT SO DO ADULTS! WAIT, THAT DOESN'T HELP; SCRATCH THAT AND LOOK AT THIS…

Substance Abuse in AD/HD Youth Growing Up: Effect of Pharmacotherapy



(Biederman, Wilens, Mick et al., Pediatrics 1999)

GOOD NEWS FOR PARENTS WORRIED ABOUT DRUG USE!

- According to a study in the Br J Psychiatry July 11, 2013, stimulant medications appear to lower the risk for substance abuse disorders in adolescents with AD/HD
- In a large, prospective, longitudinal study investigators from the SUNY found that adolescents with AD/HD who were not treated with a stimulant medication for their disorder had a 2-fold increased risk of developing an SUD compared with their counterparts who were treated.
- Untreated adolescents with AD/HD also had a 2.6-fold increased risk of developing an SUD compared with a healthy, age-matched control group.
- Multiple past studies show no connection.

WILL THEY HAVE TO TAKE THIS MEDICATION FOREVER?

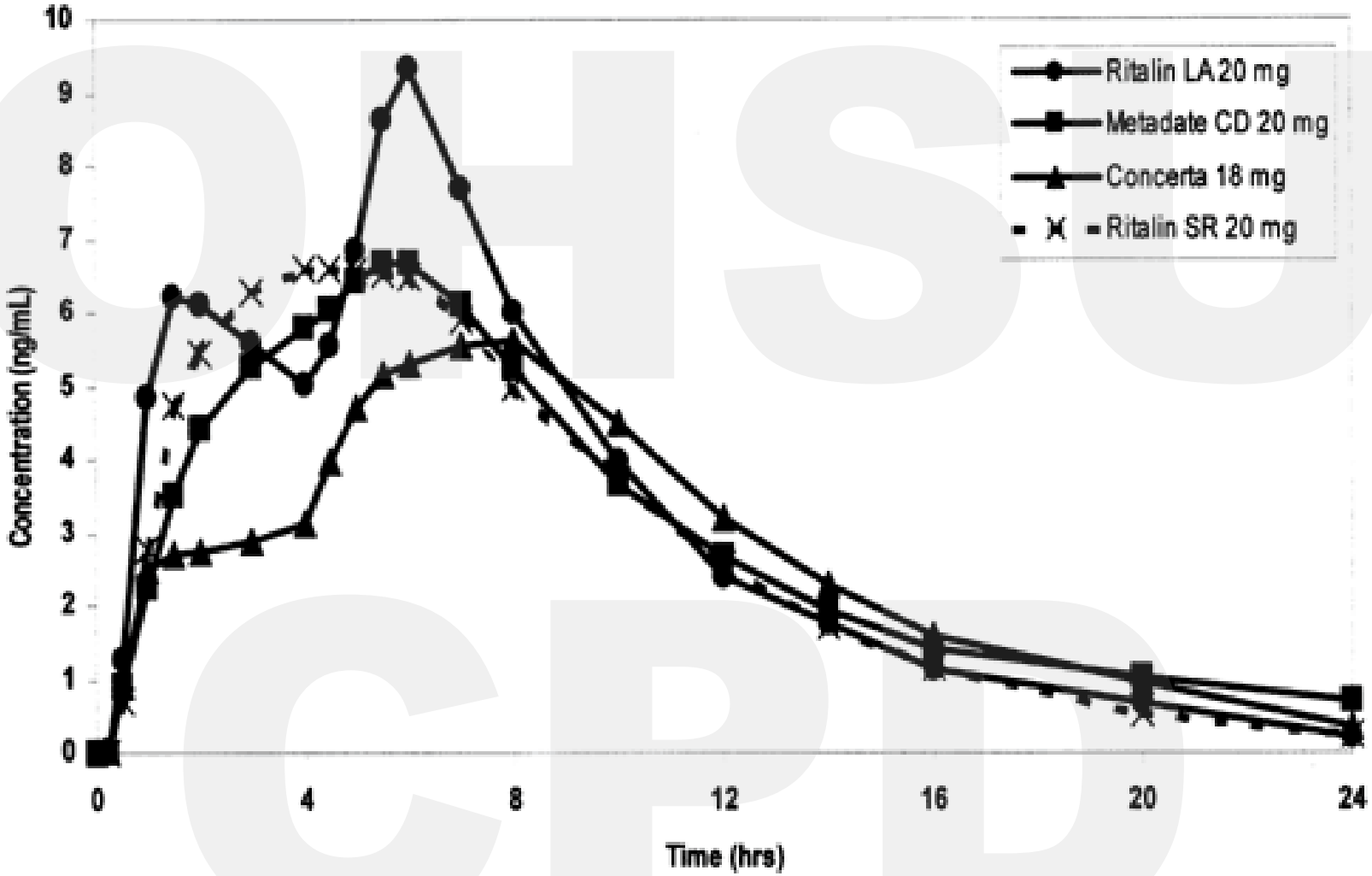
THEY MIGHT CHOOSE TO…

Study	Age of patients and follow-up	Findings at follow-up
Barkley et al, 1990[1]	6 years, follow-up at 14 years	72% with AD/HD
Biederman et al, 1996[2]	6 – 17 years, 4 year follow-up	85% with AD/HD
Gittelman et al, 1995[3]	16 – 23 years	68% with AD/HD in adolescence
Weiss et al, 1985[4]	5 – 12 years, 5, 10 and 15 year follow-up	66% with at least 1 core symptom of AD/HD by adulthood

From ADHD: Focus on Meds, Mary Cook MD

SINCE STARTING THE MEDICATION, MY KID GETS SO MOODY AND HYPER IN THE EVENINGS!

ER Methylphenidate Formulations



*Data presented are intended for illustrative purposes only and are not derived from a single cross-over study. These pharmacokinetic profiles represent the superimposition of data generated in three previously published bioavailability studies of MPH dosage formulations at similar strengths administered to healthy adult volunteers.[102,105,107]

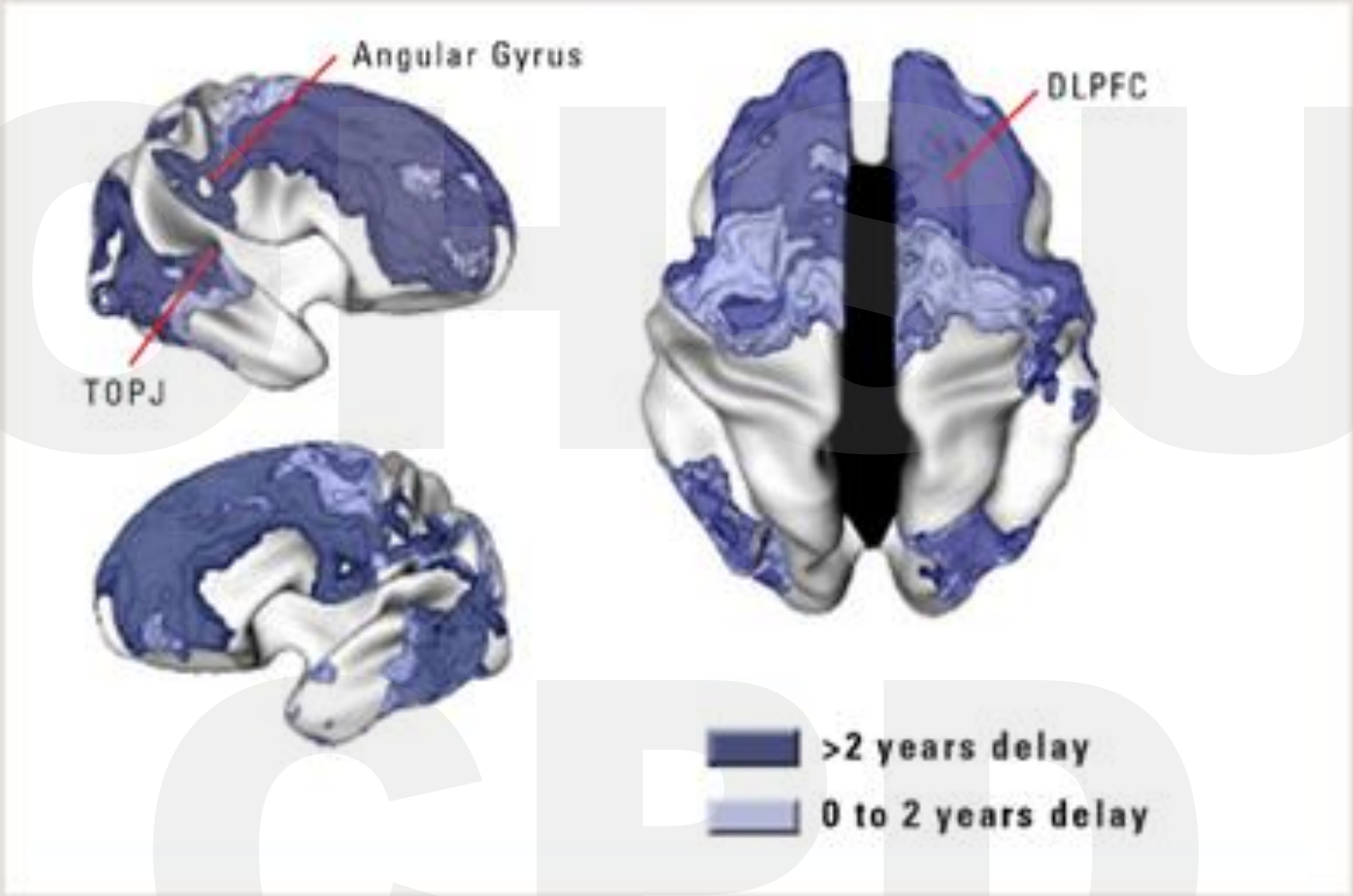
DOES MY KID NEED TO TAKE IT EVERYDAY?

YES, OR NO, IT DEPENDS…

WILL THEY EVER GROW OUT OF THIS?

KIND OF, SOMEWHAT, AND PROBABLY…

ADHD is Characterized By a Delay in Cortical Maturation



DLPFC=dorsolateral prefrontal cortex; TOPJ=temporal-occipital-parietal junction.

Shaw P, Eckstrand K, Sharp W, et al. Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. *Proc Natl Acad Sci U S A.* 2007;104(49):19649-19654. Reprinted with permission from *Proceedings of the National Academy of Sciences*, (Copyright 2007). All rights reserved.

WE PREFER A "NATURAL" APPROACH

IF YOU ARE NEW TO OREGON, BE PREPARED TO ANSWER THIS QUESTION, LIKE A LOT…

THESE DO NOT REPLACE A STIMULANT

- Psychoeducation
- AD/HD diet (INCA study), no artificial colors
- Structure/schedule, exercise, good sleep hygiene, sensory issues (OT eval)
- Restless Legs in AD/HD kids: Ferrous sulfate, magnesium
- AD/HD Supplements: phosphatidylserine, Omega-3
- Sleep supplements: melatonin, magnesium
- Impulsivity/hyperactivity: Zinc, B6
- Cognitive: Vit. D levels (correct low levels)

OPTIMIZE NUTRITION

- Balanced Nutritious Diet
- Raw foods vs processed foods
- High Omega 3 fatty acids
- Iron rich foods
- Minimize/Eliminate Junk Food
- Iron is critical in the synthesis of dopamine
- Iron is essential for the myelination of brain cells
- Some studies show that iron stores are low in up to 84% of AD/HD youth
- Ferritin levels <30 ng/ml need treatment

FISH OIL

- Several studies have shown that AD/HD youth have lower levels of omega 3 fatty acids
- Several studies have shown that AD/HD symptoms are improved with fish oil, flaxseed oil, and primrose oil
- More studies, continuing to learn more

MY KID GETS TOO WOUND UP WHEN STARTING A STIMULANT

ALPHA-2A AGONISTS

Central actions on postsynaptic alpha-2A receptors in the prefrontal cortex leads to mediation of norepinephrine actions

Can be used, alone or in combination with a stimulant, to treat comorbid AD/HD and:

- Hyperactivity
- Anxiety
- Aggression
- Tics

Sometimes, if you start with an alpha agonist, then the stimulant will be better tolerated

ADDITIONAL REFERENCES

- Journal - Silverman WK, Hinshaw SP. The Second Special Issue on Evidence-Based Psychosocial Treatments for Children and Adolescents: A Ten-Year Update. J Clin Child Adolesc Psychol. 2008 Jan-Mar;37(1)
- Book – Evidence-Based Psychotherapies for Children and Adolescents, 2nd Ed by John Weisz and Alan Kazdin, Guilford Press 2010

QUESTIONS