ADHD
Diagnostic and Treatment Challenges

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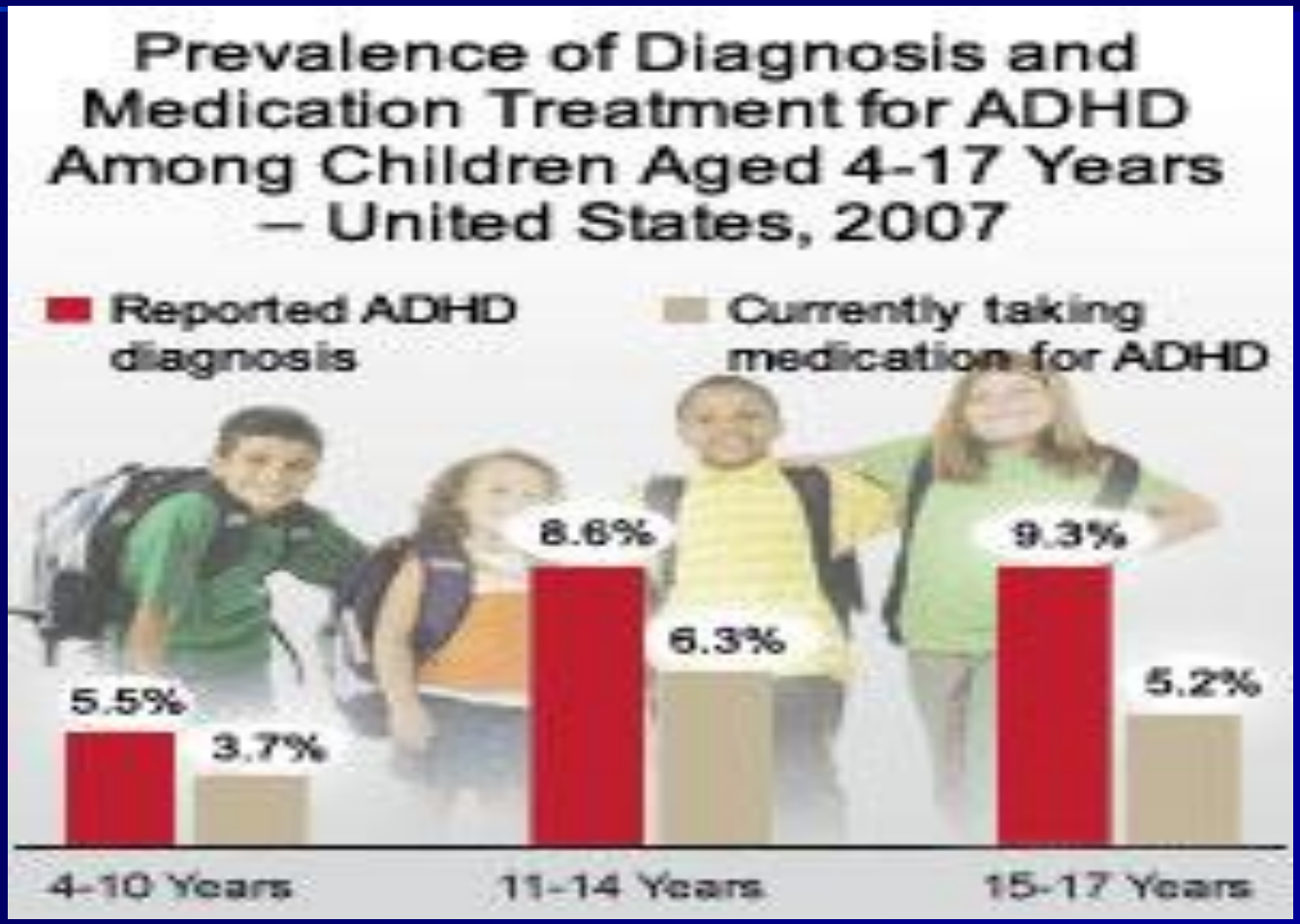
ADHD Prevalence

- ADHD is the most common diagnosed neurobehavioral disorder of childhood
- The American Psychiatric Association states in the Diagnostic and Statistical Manual of Mental Disorders that 3%-7% of school-aged children have ADHD. However, studies have estimated higher rates in community samples.

Data & Statistics
CDC- In the United States

- **National Survey of Children's Health, 2007 -** surveys of parents indicate that:
  - Approximately 9.5% or 5.4 million children 4-17 years of age have ever been diagnosed with ADHD, as of 2007.
  - The percentage of children with a parent-reported ADHD diagnosis increased by 22% between 2003 and 2007.
  - Boys (13.2%) were more likely than girls (5.6%) to have ever been diagnosed with ADHD.
  - Rates of ADHD diagnosis increased at a greater rate among older teens as compared to younger children.

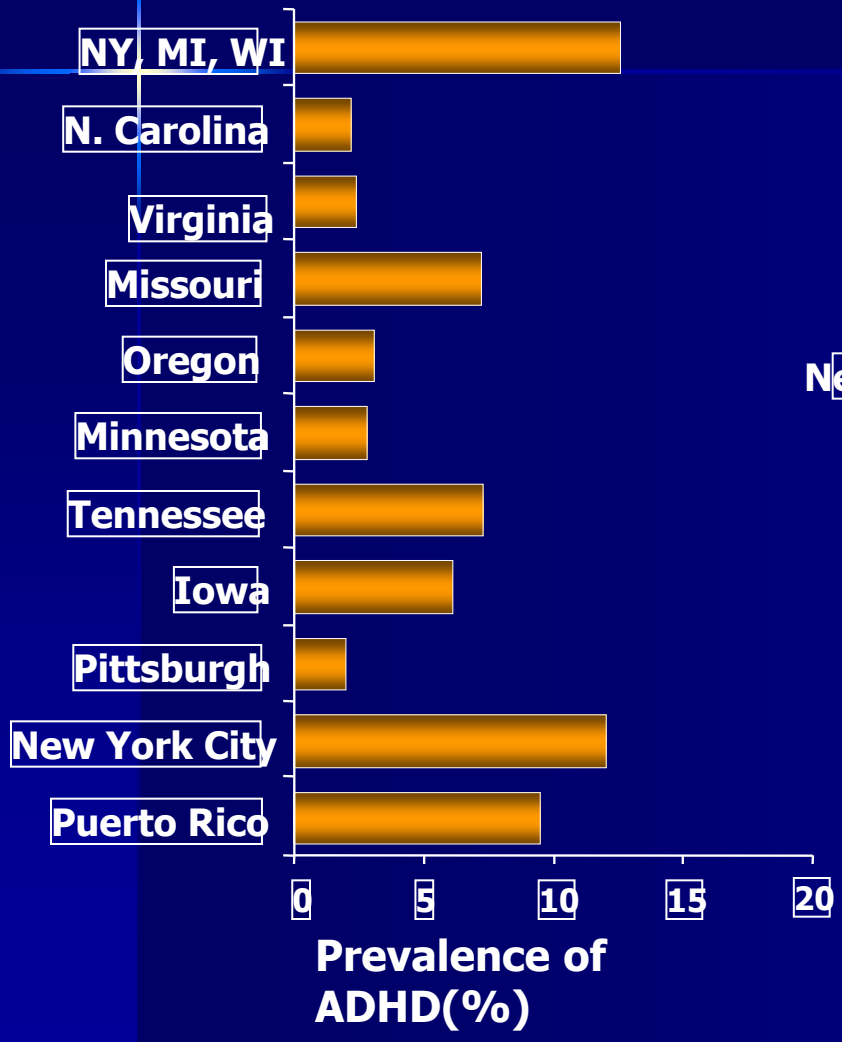
Data & Statistics
Centers for Disease Control and Prevention

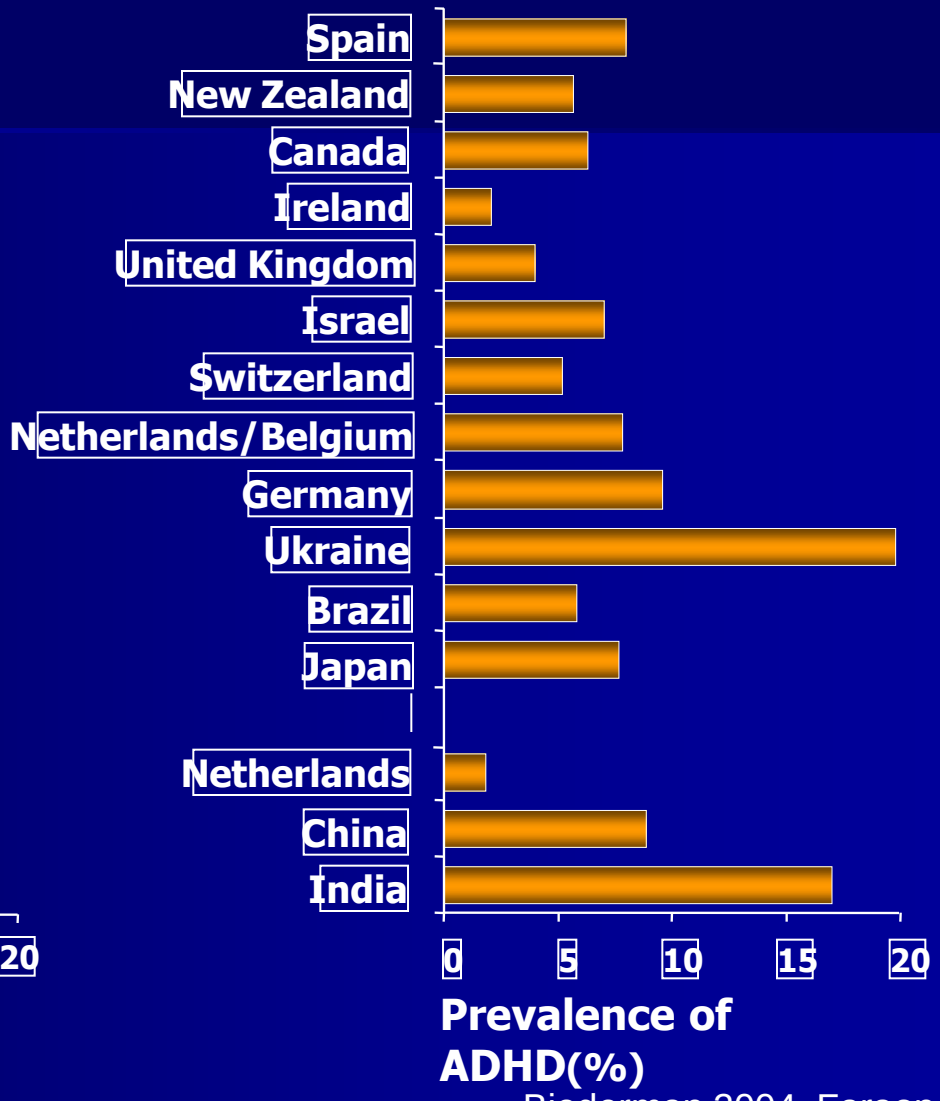


Other Names

- Minimal brain damage
- Minimal Brain dysfunction
- Hyperkinetic reaction of childhood
- ADD
- Preferred term now is ADHD

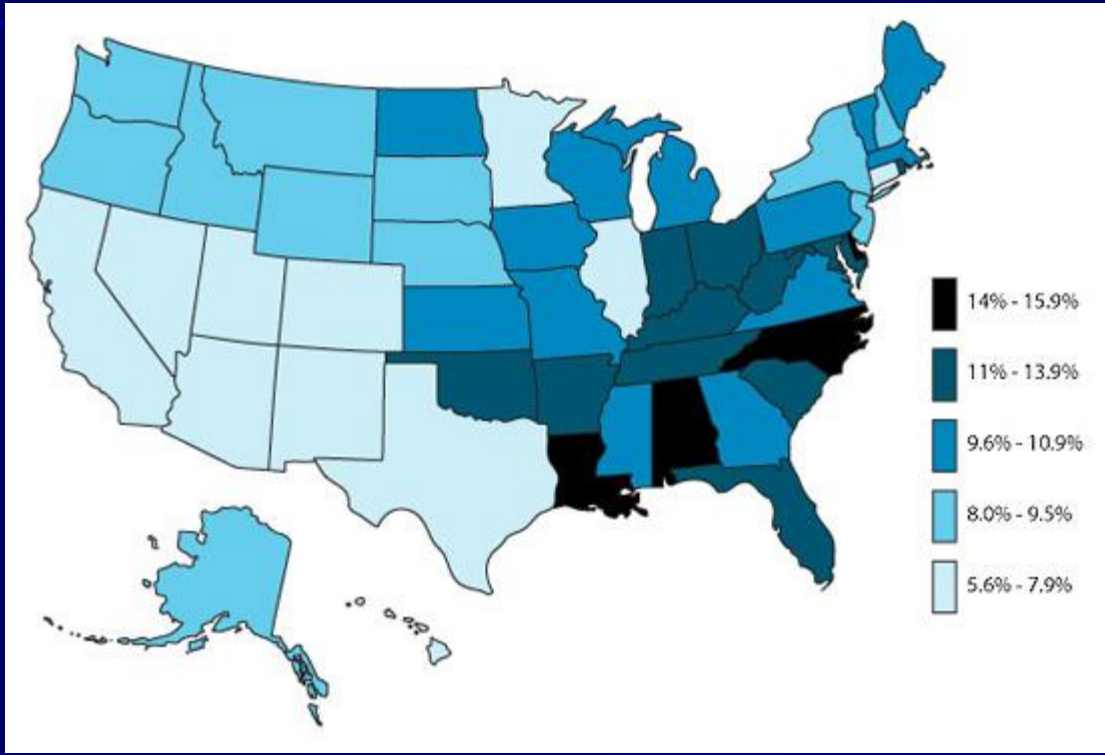
Worldwide Prevalence of ADHD in Children





Biederman 2004. Faraone 2003.

Percent of Youth 4-17 ever Diagnosed with Attention-Deficit/Hyperactivity Disorder by state: National Survey of Children's Health, 2007



Etiology

- Heredity-it is a familial disorder
- Altered brain function in the frontal lobe which regulates attention, planning and impulse control
- TBI
- Prematurity
- Maternal cigarette smoking, alcohol use

Background

- ADHD is a neurobehavioral condition that begins in childhood and usually last into adulthood.
- ADHD is a lifetime disorder
- Hyperactivity decreases
- Inattention remains
- Learn to live with it
- May not function to their best potential at work, home, school and socially

ADHD and DSM-V

- Types
  - Combined Type
  - Predominantly Inattentive Type
  - Predominantly Hyperactive-Impulsive Type
- Symptoms present before age 12
- Persistent Symptoms for at least 6 months
- ***Some Impairment in 2 or more settings***
- Clear evidence for impairment in social, academic, or occupational functioning

ADHD DSM V Criteria

- **A.** Either (1) or (2)

1) Six or more of the following symptoms of **inattention** have persisted for at least six months to a degree that is maladaptive and inconsistent with the developmental level:

Inattention

- Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities
- Often has difficulty sustaining attention in tasks or play activities
- Often does not seem to listen when spoken to directly
- Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure of comprehension)
- Often has difficulty organizing tasks and activities
- Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)
- Often loses things necessary for tasks or activities at school or at home Is often easily distracted by extraneous stimuli
- Is often forgetful in daily activities

ADHD DSM V Criteria

2) **Hyperactivity**

- Often fidgets with hands or feet or squirms in seat
- Often leaves seat in classroom or in other situations in which remaining seated is expected
- Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
- Often has difficulty playing or engaging in leisure activities quietly
- Often talks excessively
- Is often 'on the go' or often acts as if 'driven by a motor

Impulsivity

- Often has difficulty awaiting turn in games or group situations
- Often blurts out answers to questions before they have been completed
- Often interrupts or intrudes on others

ADHD DSM V Criteria

- **B.** Several inattentive or hyperactivity - impulsive symptoms were present prior to age 12.
- **C.** Some impairment from the symptoms is present in more than two or more settings (e.g. at school or work or at home).
- **D.** There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.
- **E.** The symptoms do not occur exclusively during the course of Schizophrenia, or other Psychotic Disorder, and are not better accounted for by another mental disorder (e.g. Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder).
- In addition, the *DSM-V* allows a comorbid diagnosis with autism spectrum disorder.
- Older Adolescents >17 years and adults must present with five out of nine symptoms in areas of inattention /hyperactivity

Based on these criteria, three types of ADHD are identified:

- **ADHD, Combined Type: If both criteria 1 and 2 are met for the past 6 months**
- **ADHD, Predominantly Inattentive Type: If criterion 1 is met but criterion 2 is not met for the past six months**
- **ADHD, Predominantly Hyperactive-Impulsive Type: If Criterion 2 is met but Criterion 1 is not met for the past six months.**

Comparison of ADHD Types*

	Inattentive (IA)	Hyperactive / Impulsive (HI)
Gender (M:F)	▪ 1 : 1	▪ 3-9 : 1
Common Co-existing Conditions	▪ Anxiety ▪ Depression ▪ Shyness/withdrawal	▪ ODD ▪ CD
Special Education	▪ Discrepancy: IQ & achievement (math)	▪ Secondary to behavior
Peer Relations	▪ Neglect	▪ Rejection
Accidents	▪ Less common	▪ Common
Outcomes	▪ Symptoms decline less than HI & CT	▪ ODD-worse outcome ▪ Motor symptoms may decline with time

** The Combined Type (CT) resembles both IA & HI, need 12/18 criteria*

Evaluation for ADHD

- Clinical interview
- Forms/questionnaires for ADHD
- Rule out medical causes- Hyperthyroidism, lead exposure, fetal alcohol
- Rule out Psychiatric causes- Depression, Bipolar, Substance abuse

History

- Developmental history in detail
- When symptoms started
- In which setting – school, home, both
- Severity
- Inattention, hyperactivity, Impulsive behavior

History for Co-morbid Conditions

- Learning disabilities
- Behavior problems- ODD
- Mood disorders
- Anxiety disorder
- Substance abuse
- Tic disorders
- Pervasive development disorder
- Mental retardation

Children With Learning Disabilities

- Learning disabilities affect at least 1 in 10 school children.
- Children with learning disabilities usually have a normal range of intelligence
- Learning disabilities are caused by a difficulty with the nervous system that affects receiving, processing, or communicating information.
- About 20 to 30 percent of children with ADHD also have a learning disability such as a reading disorder called dyslexia, or disabilities that involve writing, spelling, or arithmetic.

Most Frequent Signals of Learning Disabilities

- Has difficulty understanding and following instructions
- Has trouble remembering what someone just told him or her
- Fails to master reading, spelling, writing, and/or math skills, and thus fails
- Has difficulty distinguishing right from left; difficulty identifying words or a tendency to reverse letters, words, or numbers; (for example, confusing 25 with 52, "b" with "d," or "on" with "no")
- Lacks coordination in walking, sports, or small activities such as holding a pencil or tying a shoelace
- Easily loses or misplaces homework, schoolbooks, or other items
- Cannot understand the concept of time; is confused by "yesterday, today, tomorrow"

Medical Conditions

- Vision
- Hearing
- Thyroid
- Seizure disorder
- Heart disease
- Genetic disorders

Family History

- It’s a genetic disorder
- Runs in families

Behavior Rating Scales for ADHD Assessment and Monitoring

- Vanderbilt ADHD Diagnostic Parent and Teacher Scales
- Academic Performance Rating Scale (APRS)
- ADHD Rating Scale-IV
- Brown ADD Rating Scales for Children Adolescents, and Adults
- Child Behavior Checklist (CBCL)
- Conners Parent and Teacher Rating Scales
- Conners Wells Adolescent Self-Report Scale
- Home and School Situations Questionnaire-Revised
- Inattention/Overactivity With Aggression Conners Teacher Rating Scale
- Swanson, Nolan, and Pelham (SNAP-IV) and SKAMP (see internet ADHD.net)

Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. J. Am. Acad. Child Adolesc. Psychiatry. 2007;46(7):894-921.

Case of 6 year old

- 6 year old patient with significant symptoms of inattention and hyperactivity at home and teachers concerned about classroom behavior.
- Vanderbilt Parent Rating Scale
- Vanderbilt Teacher Rating Scale

Vanderbilt Parent and Teacher Rating scales

	Parent Vanderbilt	Teacher Vanderbilt
Inattention score	4/9	7/9
Hyperactivity score	6/9	7/9
Oppositional behavior	1	0
Mood symptoms	0	0
Academic performance	++++	+++
Classroom/home Behavior	0	++++

Vanderbilt Parent and Teacher Rating scales

	Parent Vanderbilt	Teacher Vanderbilt
Inattention score	6/9	6/9
Hyperactivity score	8/9	7/9
Oppositional behavior	5	4
Mood symptoms	0	0
Academic performance	++	+
Classroom/home Behavior	+	++++

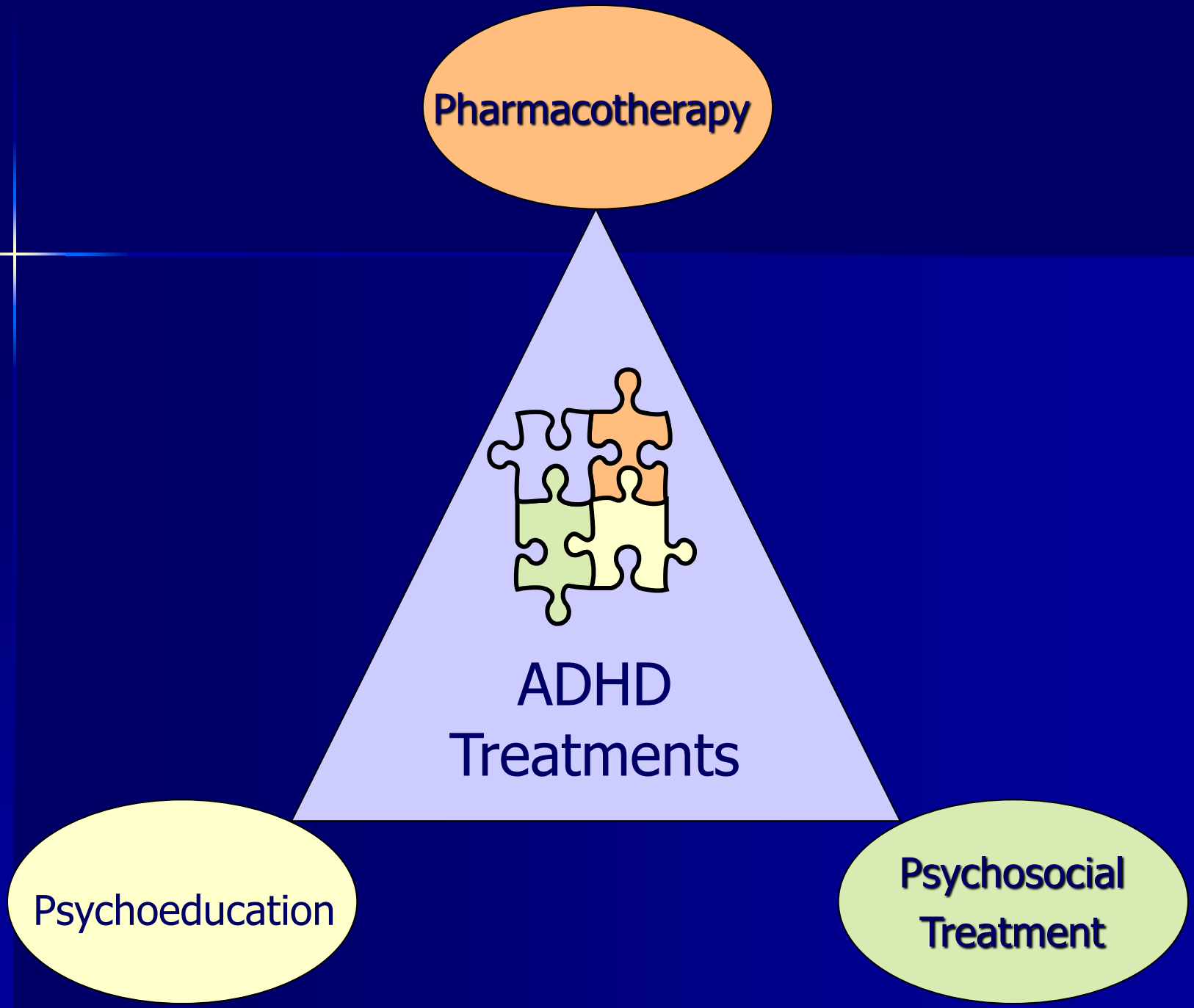
Diagnosis of ADHD

- Sense of relief to many families and patients
- Next step is treatment

Steps to treatment

Step 1 - Diagnostic evaluation

- Clinical interview
- ADHD Rating scales
  Parent & Teacher(s)
- School Observation
- Psychological testing


Pharmacotherapy
ADHD
Treatments
Psychoeducation
Psychosocial
Treatment

Pharmacotherapy

- Very effective for ADHD symptoms, for both inattention and hyperactivity in majority of patients

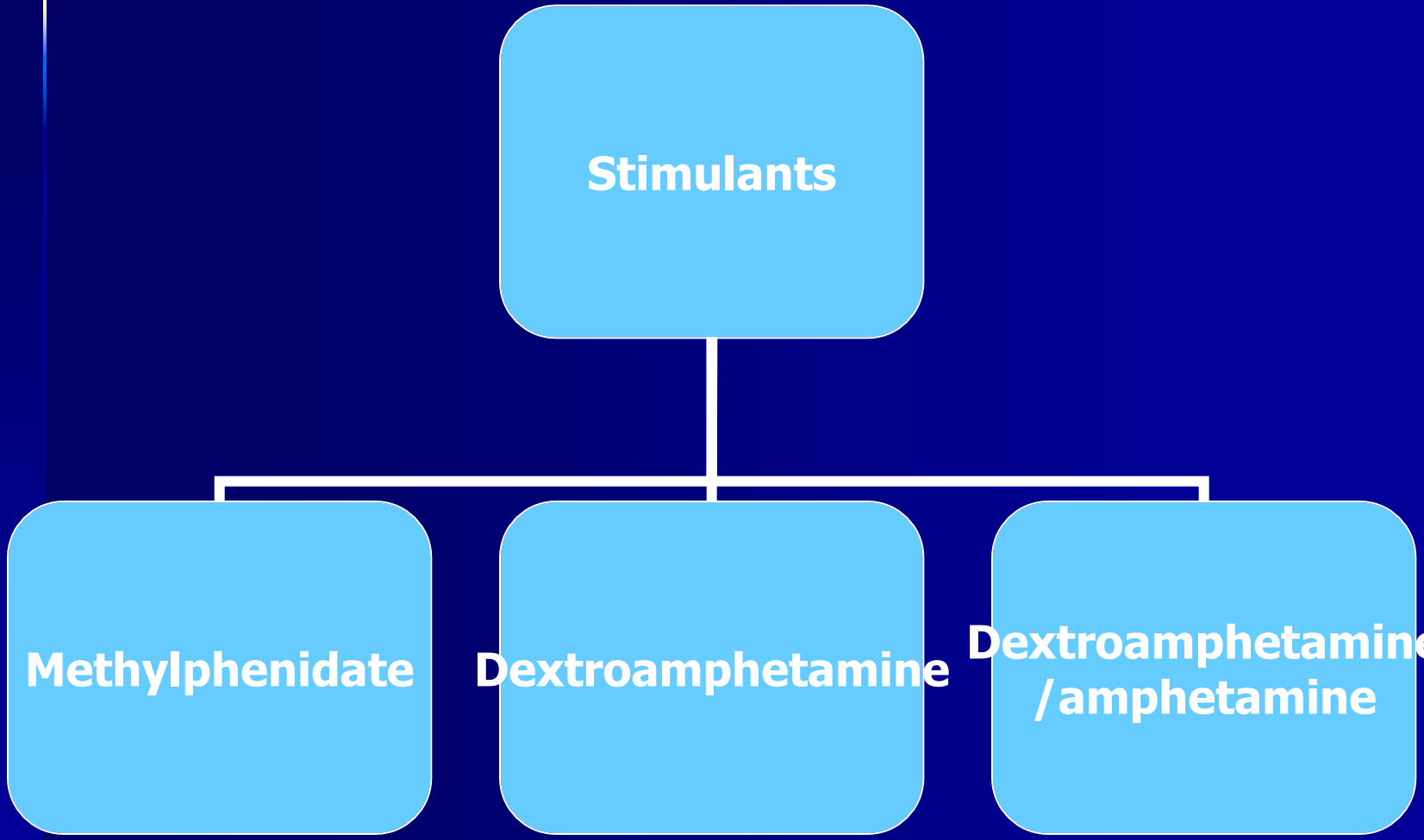
Barriers

- 30% - no benefit from medication
- Side effects prevents taking medications for extended period of time
- Residual symptoms in spite of medications
- Some children/parents have strong objection to taking medications

Medication Classes for ADHD

1. Stimulants
2. Non stimulant
3. Antidepressant

Treatment of ADHD



Methylphenidate products

- Short acting 3-4 hrs
- Intermediate acting 6-8 hrs
- Long acting 12 hrs

FDA Approved Methylphenidate class of medications for ADHD

Drug	Duration of action	Dosing range
Stimulants:		
Methylphenidate products:		
Short-acting		
Methylphenidate (IR) Ritalin®, Methylin®	3-4 hr	5 to 60 mg/day bid or tid,
Dexmethylphenidate (IR) Focalin®	4 hr	2.5 to 10 mg bid at least 4 hr apart without regard to meals
Intermediate-acting		
Methylphenidate (SR, ER, LA) Metadate®, Ritalin®, Methylin®	6-8 hr	10 to 60 mg/day once daily or bid.
Metadate CD	6-8 hr	10 to 60 mg once daily in the morning
Long-acting		
Methylphenidate (long acting) Concerta®	12 hr	18 to 72 mg once daily in the morning.
Methylphenidate (patch) Daytrana®	10-12 hr	10 to 30 mg once daily. Apply 2 hours before effect is needed and remove 9 hours after application.
Dexmethylphenidate (XR) Focalin XR®	8-12hr	5 to 20 mg once daily in the morning.

Dextroamphetamine Products

Dexedrine:

Short acting 3-4 hours

Intermediate acting 6-8 hours

Dextroamphetamine/amphetamine salts

Adderall:

Short acting

Long acting

FDA Approved Amphetamine class of medications for ADHD

Short-acting	Duration	Dosing range
Dextroamphetamine (IR) Dexedrine	4-6 hr	2.5 to 40 mg once daily or bid
Intermediate-acting		
Dextroamphetamine Dexedrine Spansules	6-10 hr	2.5 to 40 mg once daily
Drug	Duration of action	Dosing range
Dextroamphetamine/ amphetamine Products:		
Intermediate-acting		
Dextroamphetamine/ amphetamine (IR) Adderall®	4-6 hr	2.5 to 40 mg/day once daily or bid
Long-acting		
Dextroamphetamine/ amphetamine (XR) Adderall XR®	8-12 hr	Start at 5 mg/day, max 30 mg/day
Lisdexamfetamine (Vyvanse®)	8-12 hr	30 to 70 mg once daily.

Non Stimulant/Antidepressant

- Decreased potential of abuse
- Extended coverage for ADHD symptoms
- Does not exacerbate tics
- No negative effects on growth

FDA Approved Non-Stimulant Class of Medications for ADHD

Non-stimulants:	Duration	Dosing range
Atomoxetine (Strattera ®)	18-24 hr	0.5 mg/kg/day to 1.4 mg/kg/day
Alpha 2- Agonist short acting		
Clonidine hydrochloride	3-6 hr	0.1mg to 0.4 mg/day ,bid- qid
Tenex /Guanfacine	12-24 hr	0.5- 4 mg/ day, bid-tid
Long-acting		
Kapvay/ Clonidine ER	18-24 hr	0.1-0.4 mg/day qd-bid
Intuniv/Guanfacine XR	24 hr	1 mg – 4 mg, q daily am

Methylphenidate and Amphetamine:

- **Advantages**
  - Immediate onset of action
  - Very effective
  - Ability to use drug holidays
  - Well tolerated
  - Multiple options for drug delivery, duration of action
- **Disadvantages**
  - Patients may develop tolerance, psychological dependence
  - May worsen motor and phonic tics

Side effects of stimulant class

- Decreased appetite
- Insomnia
- Stomachache/nausea/vomiting
- Headache
- Tics
- Increased heart rate and blood pressure
- Agitation/irritability/mood swings
- Hallucinations
- Seizures, in patients with history

Monitoring

It is recommended to monitor Height, weight, B.P and Pulse every 3 months

FDA report - Death from ADHD drugs

- 25 people died and 54 had serious cardiovascular problems after taking meds to treat ADHD bet 1999- 2003

- 19 of the deaths and 26 cases of cardiovascular problems were in children.

Warning

- Stimulant class of medication should not be given to children, adolescents or adults with structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease or other cardiac problems

Assess Cardiovascular status

1. Family history of sudden death/ arrhythmia.
2. Symptoms of chest pain
3. History of syncope
4. Physical Exam
5. EKG
6. Echocardiogram

Stimulants

Should not be given to people with-

- Hyperthyroidism
- Glaucoma
- Moderate to severe hypertension
- History of drug use
- Cardiac problems
- Agitated states

Non-stimulants/ Anti-depressants

Drug	Duration of action	Dosing range	Metabolism	FDA approval in adults	Monitoring Recommendations
Atomoxetine (Strattera ®)	Half-life = 5-8 hr	Adults: initiate at 40 mg/day; max dose of 100 mg/day.	Substrate CYP2C19 (minor); CYP2D6 (major)	Yes	Blood pressure; Heart rate
Bupropion (IR, SR, XL) (Wellbutrin ®)	Half-life = 21 hr	150 - 450 mg/day in divided doses depending on formulation	Substrate CYP1A2, 3A4, 2D6 (minor) 2B6 (major);Inhibitor of CYP2D6	No	Signs of suicidal ideation

Strattera (Atomoxetine)

Common side effects

- Dry mouth
- Insomnia
- Nausea
- Appetite suppression
- Decreased libido
- Dizziness

Strattera and liver injury

Ask patients to call –

- Itching
- Right upper belly pain
- Dark urine
- Yellow skin or eyes
- Flu like symptoms

Strattera

- Can cause sudden death in patients with heart defects
- Stroke and heart attack in adults
- Increased blood pressure and heart rate
- Not given to people with glaucoma
- Not given with MAOI's

Wellbutrin

- Available as Regular,SR, XL
- ADHD with Co-morbid depression
- ADHD with Co-morbid Substance abuse
- Contraindicated in Seizure disorder and Eating disorder

Side effects of Wellbutrin

- Headache
- Dry mouth
- Insomnia
- Nausea
- Decreased appetite
- Aches and pains

Non stimulant/Antidepressant

- Decreased potential of abuse
- Extended coverage for ADHD symptoms

How to Choose which medication to start?

- Texas Algorithm for treatment of ADHD
- Age of patient
- Can they swallow pills
- Previous trials/side effects
- Family history of medication response
- Short acting or long acting

Age specific treatments

Adolescents

School age

Preschool age

ADHD in Preschool Children

- Studies reviewed in age < 6 years old
- Associated with significant distress in preschool child and caregivers
- Expulsion from daycare and early education settings

ADHD Treatment in Preschool children

- 12-15 studies of ADHD preschool children , sample 11-59 showed mixed results with Pharmacological treatments
- Another study (Conners 1975, Greenhill 2006) showed 80-83% response
- Side effects vary from minimal to 89%
- Dysphoria, crying, whining, irritability, solitary play were more frequent

PATS Study

- 6 site, 165 children (3-5.5yr), placebo controlled, double blind
- Preschoolers with no or one comorbid disorder had treatment responses at the same level as school age children
- Children with 3 or more coexisting disorders do not respond to stimulant treatment
- 8.3% discontinuation rate due to MPH side effects as compared to 0.5% in MTA study
- Social withdrawal, lethargy higher in preschool children

Pharmacological Treatment: Summary for Preschool ADHD

- In general there is evidence of short and long term efficacy of Psychostimulants in Preschool children
- Response is less robust
- Response rate is lower
- More sensitive to side effects
- Little evidence that medication treatment improves long term interpersonal relationships and behavior

Treatment Challenges Preschool children

- Inability to swallow medications
- Know which medications can be crushed, opened up and available as liquid or patch
- Lower doses to start
- Cost of medications

Psychosocial Interventions in Preschool ADHD

- Limited research has been conducted with Preschool children with ADHD
- There is evidence from studies with school age children
- Stanley 2005, showed Parent training helpful in behavior management in Preschool children
- 15 published reports of Parent training trials, variation in design, method of delivery. Most of them with group treatments, 8-12 sessions.
- In most studies improvements noted in parent skills, interaction and child compliance
- Improvement of behavior vs improvement of ADHD symptoms
- Psychosocial treatments impact is greater in children with high level of problems

PCIT

- Evidence based intensive intervention for preschool children with disruptive behavior disorders
- Parent training in behavior management in play therapy context, parent child dyad and live interactive coaching
- Reduces hyperactive, disruptive behavior and improves compliance
- Gains maintained 6 years later
- No studies specially used to treat ADHD in preschoolers, many children included children who met criteria for ADHD

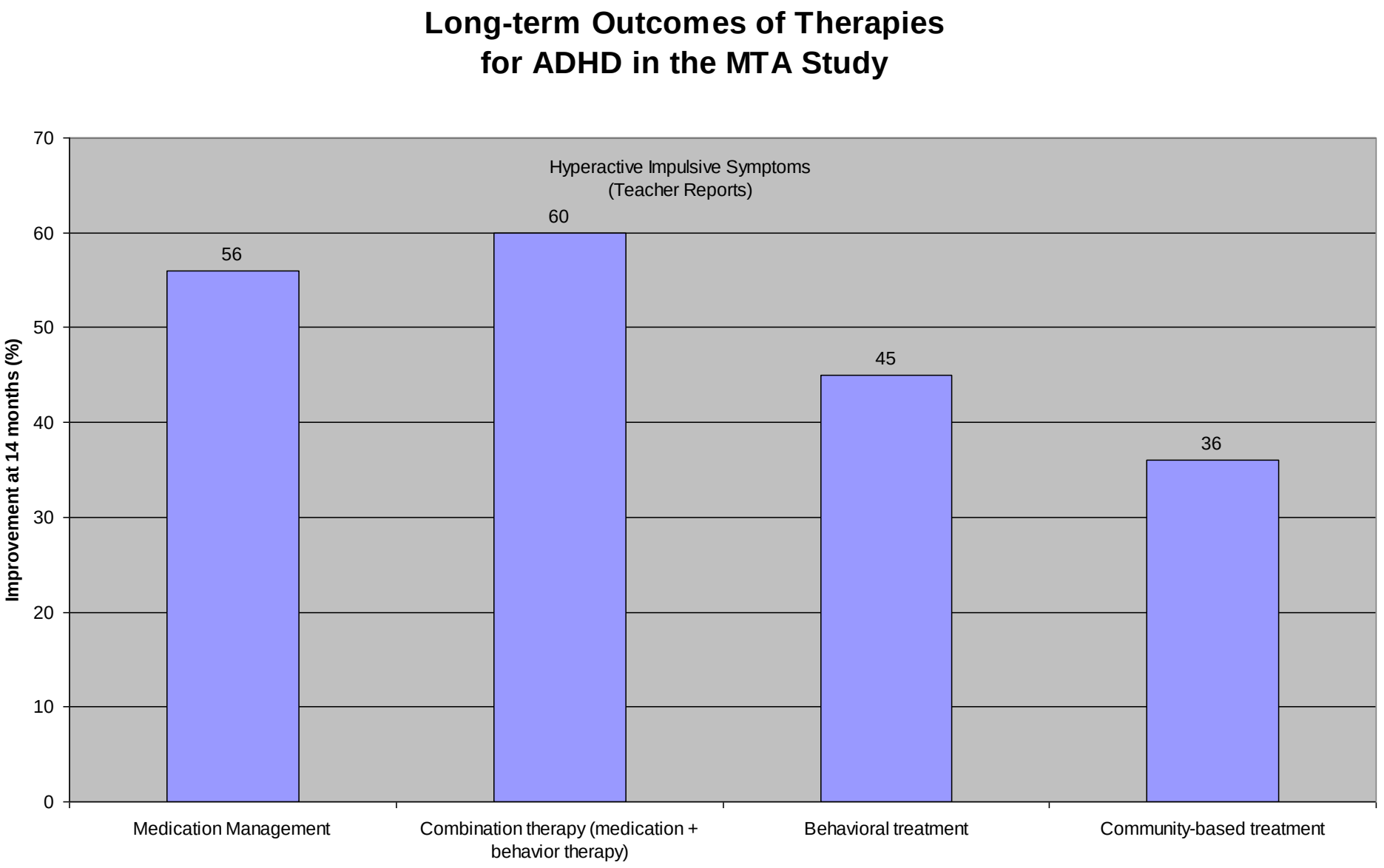
School Age Children: 7-11 yr old

ADHD Symptoms most commonly present in this age group

MTA Study

- 14 month randomized clinical trial
- 579 children
- Age 7- 9.9 years
- Assigned to 4 treatment groups
  - Medication management
  - Intensive behavior treatment
  - Combined
  - Standard community care

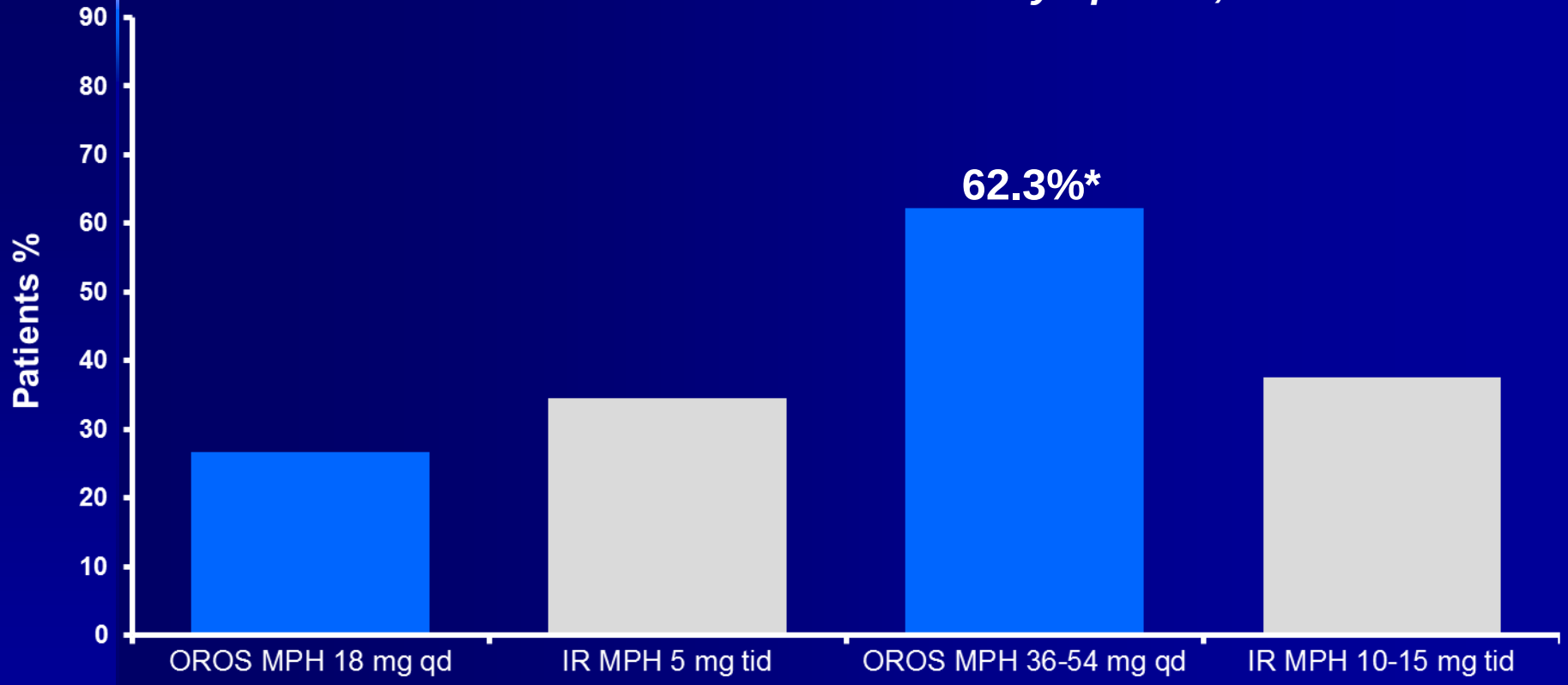
Outcome MTA Study



Remission At Adequate Doses

36-54 mgs Required to Achieve Remission of Symptoms

Remission defined as ≥50% reduction in symptoms, N=282

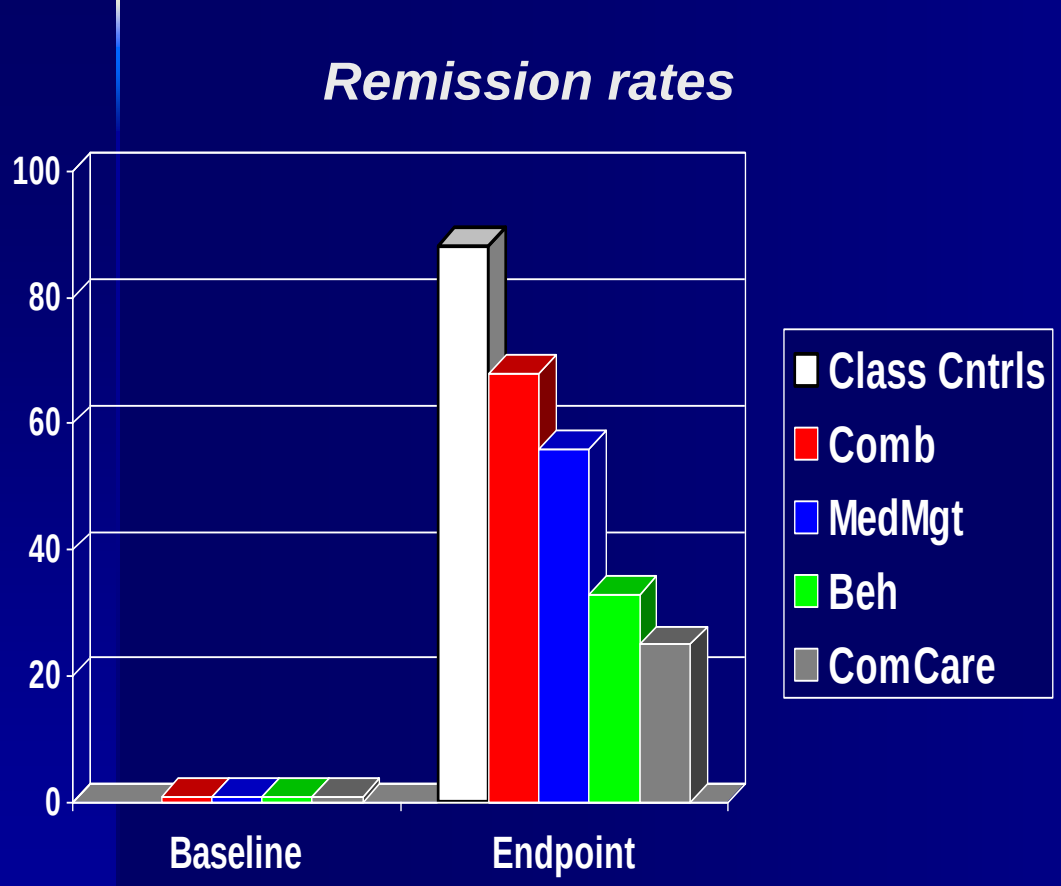


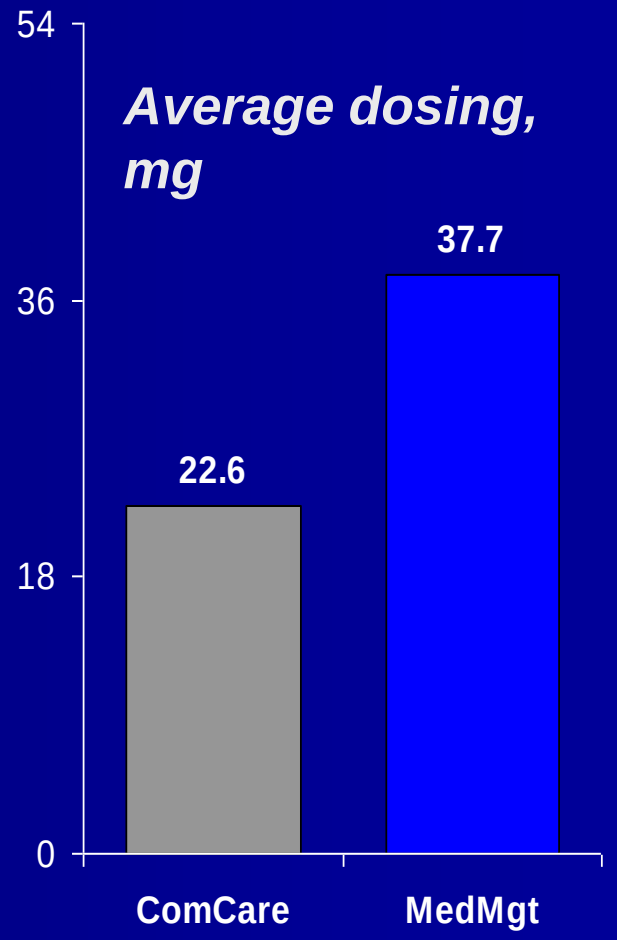
*p<0.05 for OROS MPH 36-54 mg qd group vs all other groups

Greenhill et al. APA. 2004.

Slide - Courtesy of The REACH Institute

MTA Study: Remission Rates Increased with Increasing Dose





Swanson et al. *JAACAP* 2001;40:168-79; Greenhill et al. *JAACAP* 2001;40:180-7

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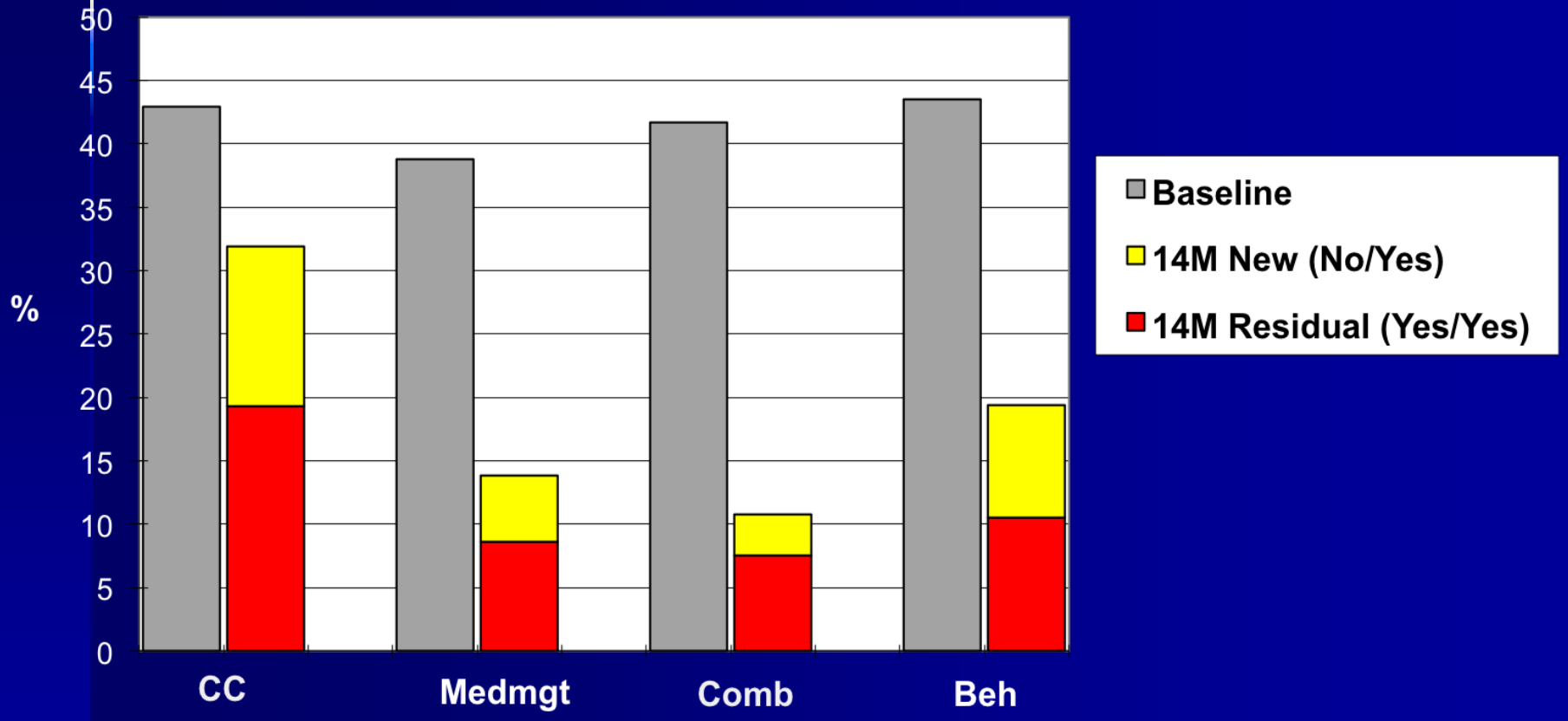
Change in ODD Comorbidity MTA Study, Baseline to 14 Months



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Results of MTA Study

Intensive Behavior Treatment

Combined Treatment

Medication Treatment

Community Care

School age children

Combined treatment had advantages over Behavior treatment in areas of:

- ADHD symptoms
- Oppositional/Aggressive symptoms
- Internalizing symptoms
- Teacher rated social skills
- Parent-Child relations
- Reading achievement
- Lower doses of Medication

Treatment challenges School age ADHD

- Finding the right medication
- Finding the right dose
- Medication taken at school
- Medication after school
- Unwilling to take medicine
- Peer/social concerns- feeling different
- 504 plan/ extra help in school
- Behavior problems at school

Psychosocial treatments

- Social skills training
  - Individual
  - Groups at school
- Parent training
  - Attending & Special Playtime
  - Rewarding and Ignoring
  - Effective commands
  - Time out procedures

Adolescent ADHD

- Affects 2-6%
- Prevalent, distressing, interfering condition
- Even after medication treatment, adolescents experience residual symptoms

Skills Training for Adolescents with ADHD

- Intervention – along with medication

  Behavioral: Skills based Cognitive Behavioral therapy
- Also called as Compensatory executive skills training. 12 weekly sessions
- Includes education about ADHD, instruction in organization skills, reducing distractibility, adaptive thinking
- Adapted from research study in Adults

Adolescents with ADHD

- Although ADHD is not prospectively associated with Substance use disorders, it is a significant risk factor through correlation with CD
- ADHD ➡ CD ➡ SUD
- Factors contributing to CD- family relationship and peers
- Prevention-psychosocial treatment

PsychoEducation

- Study published 2007 (McLeod, Jensen) re: public knowledge about ADHD
- Public is not well informed , only 64% had heard about ADHD. Most could not provide detailed information of the disorder.
- Media and educational efforts to provide accurate information on ADHD
- Special efforts to reach specific populations; men, nonwhite minority groups, elderly

Treatment challenges Adolescents with ADHD

- Non compliance
- Forgetting to take medicine
- Side effects ex. Decreased appetite concerns with height/weight
- Substance use
- Homework challenges later in pm
- Planner/missing assignments

Pharmacotherapy

- Most common reasons for failure:
  - Doses too low
  - Doses too far apart
  - Every child has unique response to treatment; if 1 stimulant doesn't work, try the others
- Titration requires balancing efficacy with side effects:
  - Teacher report for efficacy of medication at school (amount & interval)
  - Parent report for side effects of medications & child-parent relations

Newcorn JH, Stein MA, Cooper K (2010). Dose response characteristics in adolescents with ADHD treated with OROS methylphenidate in a 4-week, open-label, dose-titration study. *J Child Adol Psychopharm.* 20:187-196

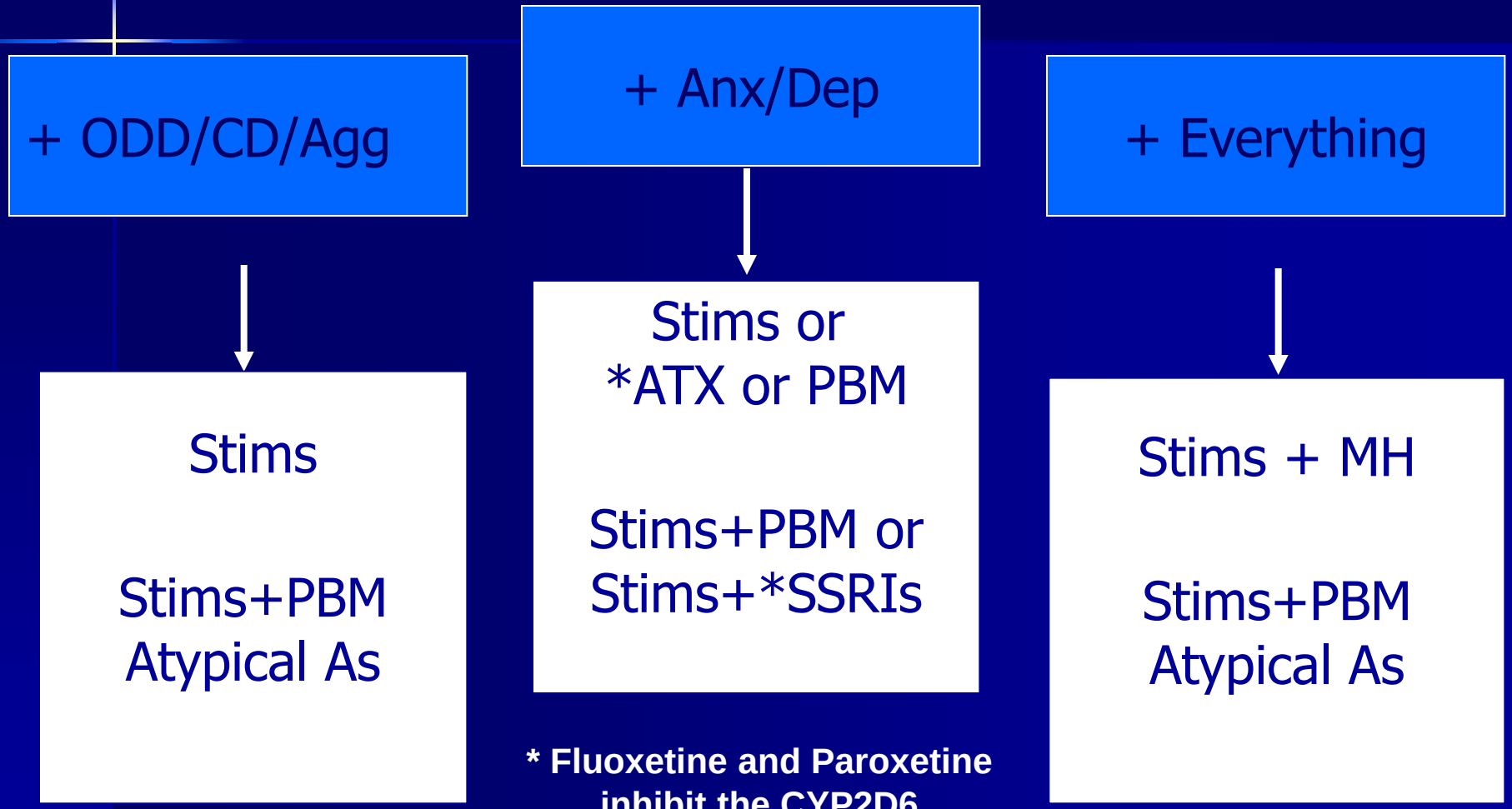
Tips to Manage Side Effects with ADHD medications

- Decreased appetite
- Weight loss
- Decreased sleep
- Irritability
- Tics
- Palpitations
- Slowed down
- Hallucinations

Medications-Principles

- Start low go slow
- Baseline measures need to be established
- Monitor treatment response
- Monitor side effects
- Keep medicine safely- controlled subs.
- Regular follow up

Suggested Approaches for Comorbid ADHD



*** Fluoxetine and Paroxetine inhibit the CYP2D6 enzymes**

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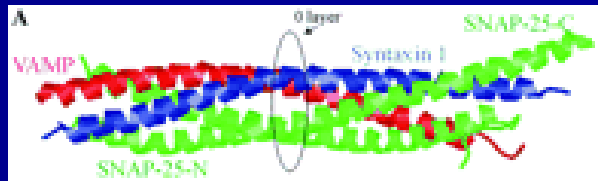
Working with schools

- 504 plan
- IEP
- ADHD is under category of other health disabilities.

Genetics of ADHD

- ADHD is a familial disorder
- 5 fold increased risk for ADHD in first – degree relatives
- Twin studies show mean heritability=7.6
- Gene finding approaches are Genome scans or Candidate gene approach
- Case control studies or Family Association



ADHD Pharmacogenomics

- Preliminary studies suggest genomic role in drug response
- Candidate genes implicated are DRD4, DAT1, DRD5, DBH, 5HTT, SNAP-25
- Sudies showed decreased response to MPH in DAT 10/10,
- DAT 10R and DAT 1*10 is associated with good response to MPH
- DRD4*7R – higher doses are needed

Pharmacogenomics and Side effect Risk

- DRD4-7R was associated with withdrawal
- DRD4-4R associated with picking
- SNAP-25 associated with tics, picking, irritability
- Studies are limited by small sample sizes, conflicting results, different methodologies, lack of genomic controls

Neurofeedback/ EEG Biofeedback

- Considerable need to establish effective treatment alternatives to help children who do not respond to medication or have side effects
- Recent controlled studies have shown positive effects on primary symptoms of ADHD
- Treatment is aimed to decrease the activity theta band and to increase the activity of the beta band, aiming at a more attentive state.
- Second form is training of slow cortical potentials
- Although there is evidence of efficacy there is some skepticism due to methods and specificity

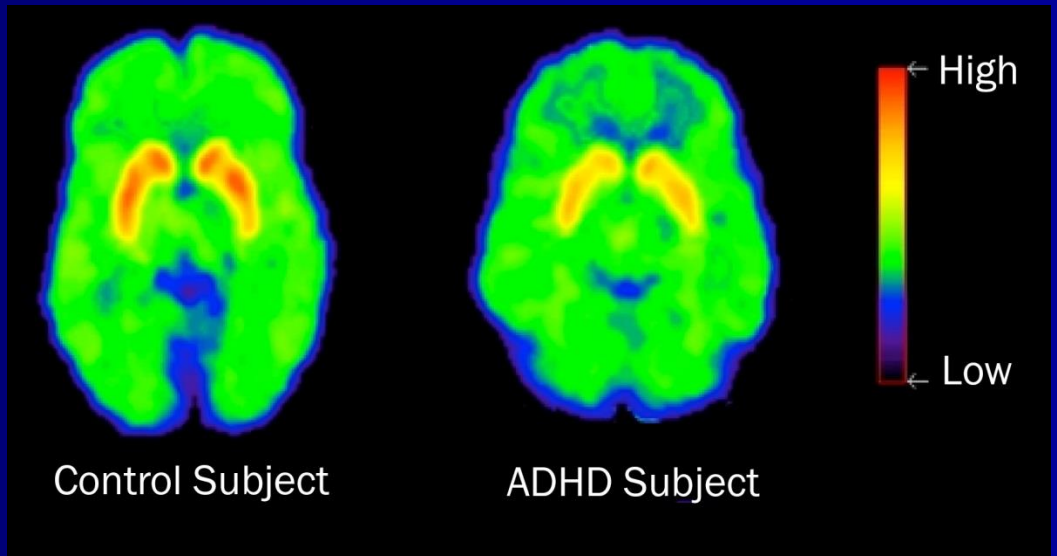
Cogmed Working Memory Training

- Evidence based training to enhance Working Memory, executive function required for learning and attention
- Supported by a strong and growing research base
- This program is now offered at over 180 clinical practices in North America, in addition to many others throughout the world.

Neuroimaging

Complement Clinical Evaluation:

- Accurate diagnosis
- Identify subtypes
- Mode of treatment



Diet

- Dietary elimination – Additive free diet
- RDA (recommended daily allowance) Vitamin /mineral supplementation
- Iron supplementation
- Omega 3 fatty acid

Questions?