Can the Treatment of ADHD Be Cost Effective?

A Presentation from NC-ACCEPT:

The NC Academic Consortium for Cost Effective Psychopharmacologic Treatment

Supported by Community Care of NC and the NC AHEC Program

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NC Academic Consortium for Cost Effective Pharmacologic Treatment

The four academic departments of psychiatry in North Carolina at the University of NC at Chapel Hill, Eastern Carolina, Wake Forest and Duke University and the North Carolina Psychiatric Association with the support of Community Care of North Carolina and the North Carolina Area Health Education Center Program are committed to conserving resources and improving psychiatric medication prescribing. Toward that effort we formed NC ACCEPT: The North Carolina Academic Consortium for Cost Effective Psychopharmacologic Treatment.

The goal of NC ACCEPT is to engage in a dialogue about cost effective use of psychiatric medications with clinicians and trainees in psychiatry and primary care. By promoting discussion about evidence-based approaches to prescribing we will encourage appropriate use of generic medications, reduce unnecessary use of multiple medications, and encourage discontinuing medications when they are no longer needed.

OBJECTIVES

- Discuss an overview of ADHD, including effects on the child and family
- Discuss the current pharmacotherapy of ADHD
- Consider the role of alternative treatments for ADHD
- Discuss the evidence versus the cost for different treatments

DSM-IV Disruptive Behavior Disorders

- Attention Deficit Hyperactivity Disorder
- Oppositional Defiant Disorder
- Conduct Disorder
- Disruptive Behavior Disorder NOS

ADHD: Ending the Controversy Now

- Is it over diagnosed?

  NO

- Scientologists claim we are “drugging” children

  WE AREN’T

- If it is genetic, why does it persist in the gene pool?

  ADAPTIVE TO HUNTER GATHERERS

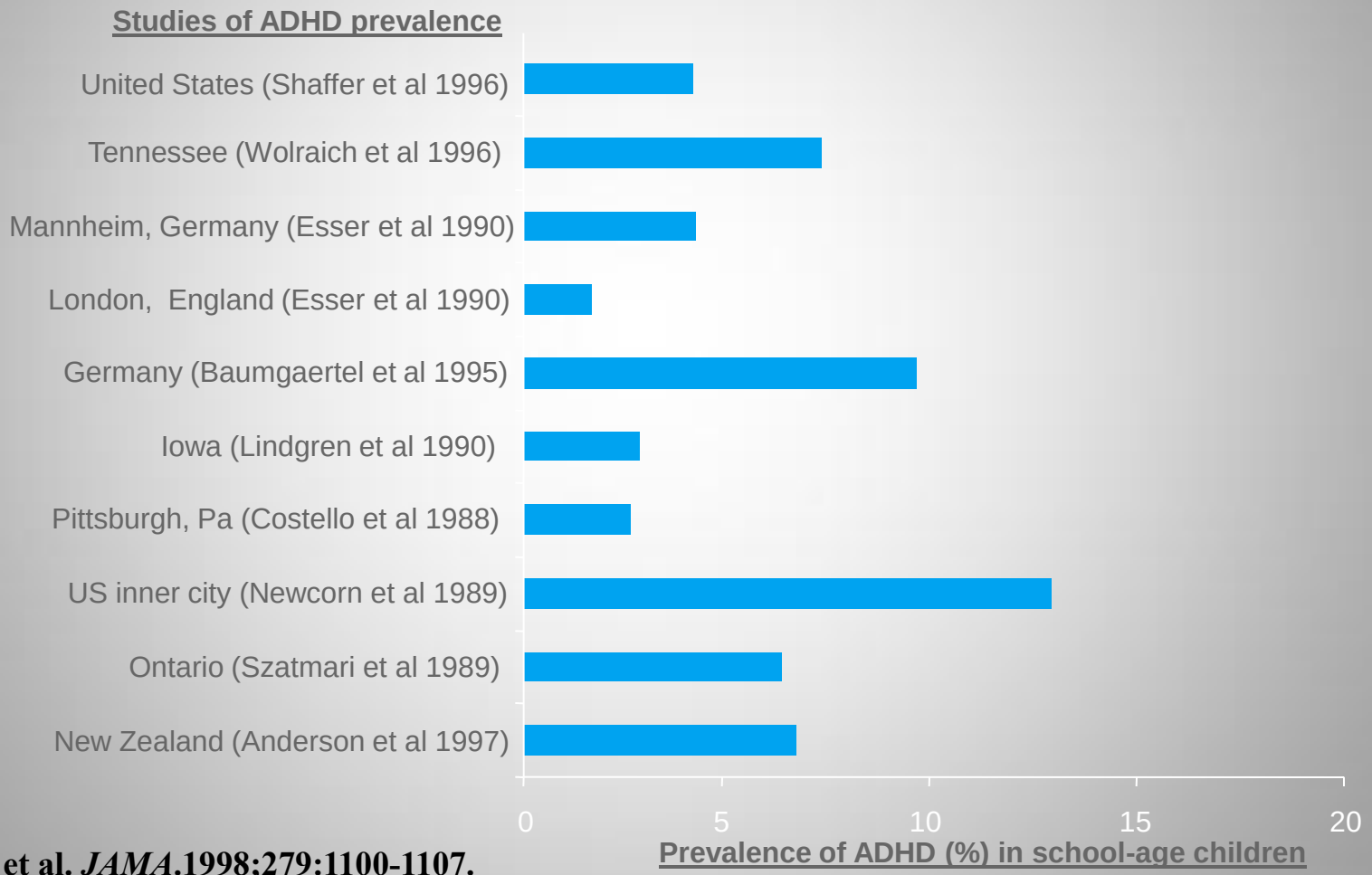
- Do more children have ADHD now, then in earlier times?

  PROBABLY NOT

ADHD Historical Timeline

- Described in 19th century literature
- 1902 ADHD Syndrome first described
- 1918 Possible manifestation of Von Economo's Encephalitis in children
- 1930 Minimal Brain Damage
- 1960 Minimal Brain Dysfunction
- 1968 Hyperkinetic Reaction (DSM-II)
- 1980 ADD ± hyperactivity (DSM-III)
- 1987 ADHD (DSM-IIIR)
- 1994 Attention Deficit/Hyperactivity Disorder (DSM-IV)

Worldwide Prevalence of ADHD Is 3% to 7%



Goldman, et al. *JAMA*.1998;279:1100-1107.

Diagnostic Criteria for ADHD: *DSM-IV-TR*

- Some symptoms present before age 7
- Impairment in 2 or more settings (e.g., school, work, home)
- Evidence of clinically significant impairment in social, academic, or occupational functioning
- Symptoms not a result of other disorders

Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Text Revision. Washington, DC: American Psychiatric Association; 2000.

ADHD: Core Symptom Area

Inattention

Six or more of the following - manifested often*:

- **Inattention to details/ makes careless mistakes**
- **Difficulty sustaining attention**
- **Seems not to listen**
- **Fails to finish tasks**
- **Difficulty organizing**
- **Avoids tasks requiring sustained attention**
- **Loses things**
- **Easily distracted**
- **Forgetful**

*DSM-IV, 1994.

ADHD: Core Symptom Areas

Impulsivity/Hyperactivity

Six or more of the following - manifested often*

Impulsivity
- Blurts out answer before question is finished
- Difficulty awaiting turn
- Interrupts or intrudes on others

Hyperactivity
- Fidgets
- Unable to stay seated
- Inappropriate running/climbing (restlessness)
- Difficulty in engaging in leisure activities quietly
- "On the go"
- Talks excessively

*DSM-IV, 1994.

ADHD: *DSM-IV* Subtypes

- ADHD Predominantly Inattentive Type
  - Criteria met for inattention but not for impulsivity/hyperactivity

Inattention

- ADHD Predominantly Hyperactive-Impulsive Type
  - Criteria met for impulsivity/hyperactivity but not for inattention

Impulsivity/Hyperactivity

- ADHD Combined Type
  - Criteria are met for both inattention and impulsivity/hyperactivity

Inattention

Impulsivity/Hyperactivity

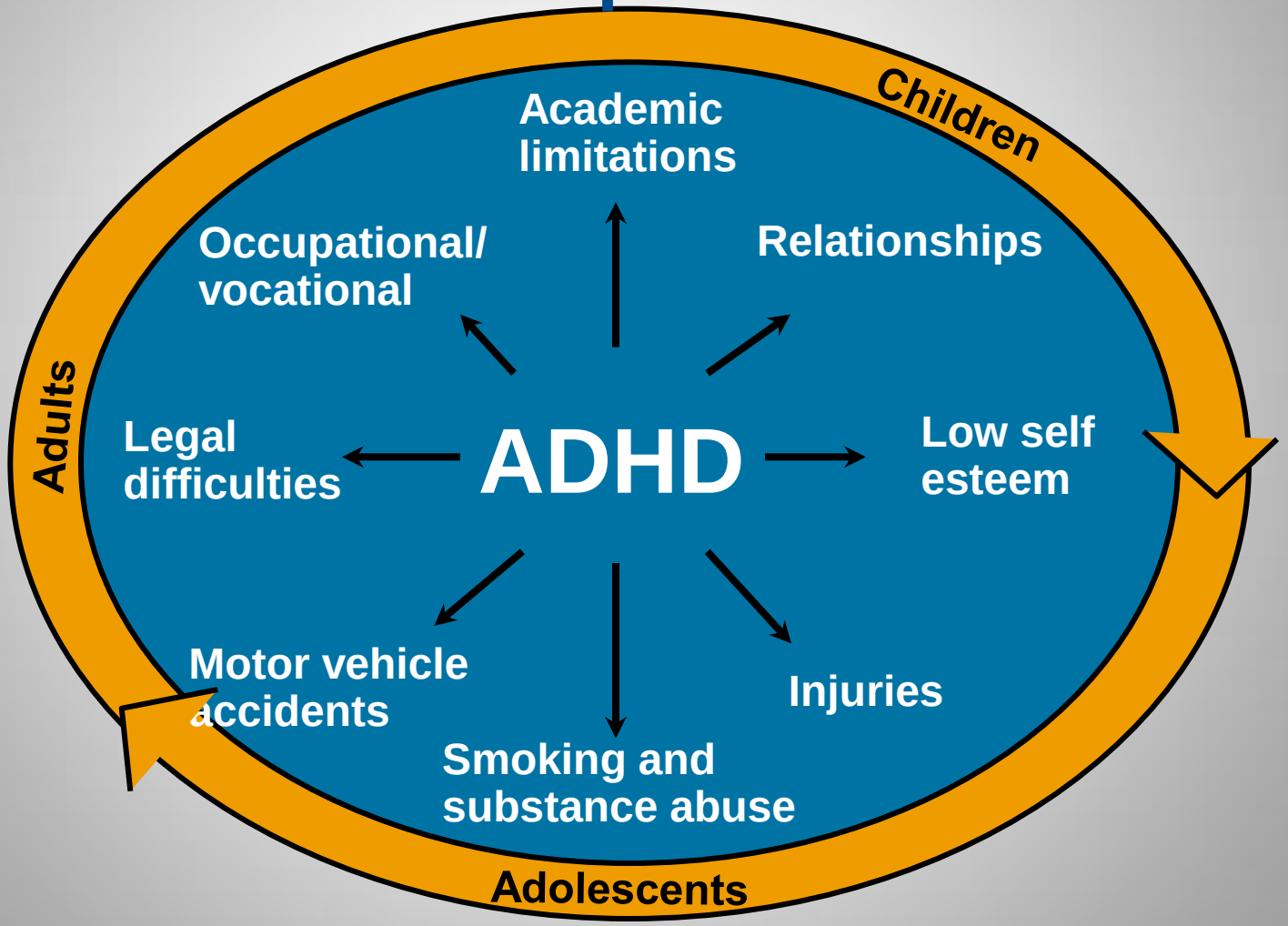
Comorbid Conditions in Children with ADHD

- Conduct Disorder 30-50%
- ODD 35-60%
- Anxiety Disorders 20-30%
- Mood Disorders 20-30%
- Specific LD 20-30%
- No Comorbidity (MTA) 31%

How ADHD Affects Parents

- Increased stress
  - Worry — Anxiety
  - Frustration — Anger
- Lower self-esteem
  - Self-blame — Depression
  - Social isolation
- Increased employment disruption
- Increased marital disruption
- Increased alcohol/substance abuse

Potential Areas of Impairment



Biological Correlates

- Hypoperfusion in frontal lobes and striatum (xenon perfusion studies)
- Low metabolic rates in same area (PET scans)
- MRI: asymmetries of caudate nuclei, differences in the frontal lobes
- QEEG: Possible slow wave activity in the frontal lobes

ADHD is a Clinical Diagnosis

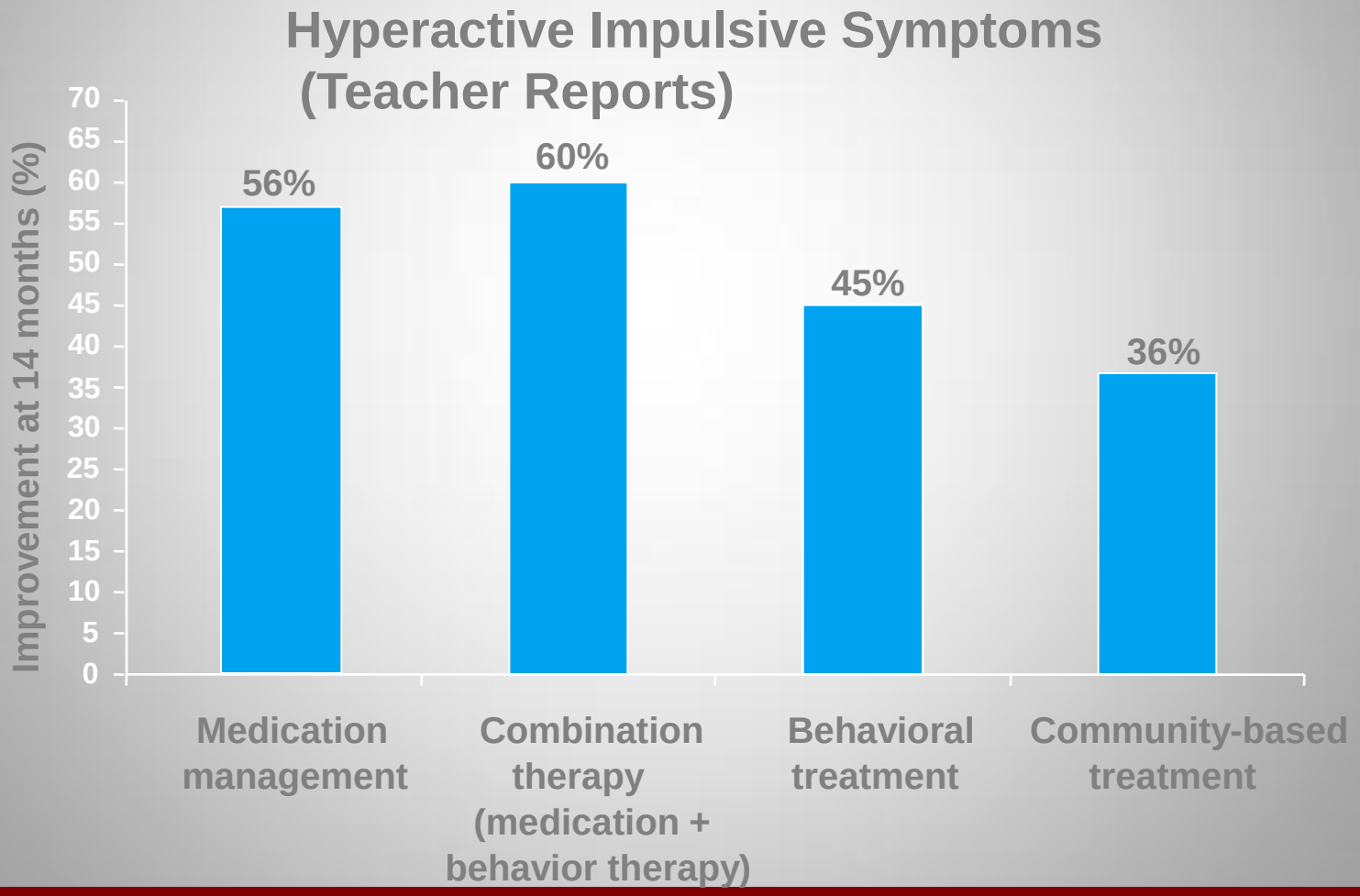
- NO TEST FOR ADHD!!!
- No laboratory measure for ADHD
- Rating Scales are NOT diagnostic instruments alone; probably stronger negative predictive power
- Drug response is NOT diagnostic

The multimodal treatment study of children with ADHD (MTA)

- NIMH funded multisite study in the late 90s
- 14-month clinical trial of treatment strategies
- 579 children with ADHD
- Subjects randomized to 1 of 4 treatment conditions
  - Medication management
  - Behavior management
  - Medication management and behavior management
  - Community-based treatment

MTA Cooperative Group. *Arch Gen Psych.* 1999;56:1073-1086.

Long-term Outcomes of Therapies for ADHD in the MTA Study



MTA Number Needed to Treat

- Medication NNT=3
- Behavioral NNT=11
- Both NNT=2-3

Diagnostic Concerns

- Remember this is a clinical diagnosis, based on DSM criteria
- ADHD is a developmental disorder, it doesn't have an acute or late onset
- Medications have non-specific effects making it more important that a diagnosis precedes treatment

ADHD in Adults

- Diagnosis can be challenging because developmental history may not be available
- Wender Utah rating scale often used to attempt to get childhood information
- Wender has higher sensitivity; some say poor specificity and more false positives
- Beware of comorbidity, or inattention due to other conditions (e.g. adjustments, anxiety)

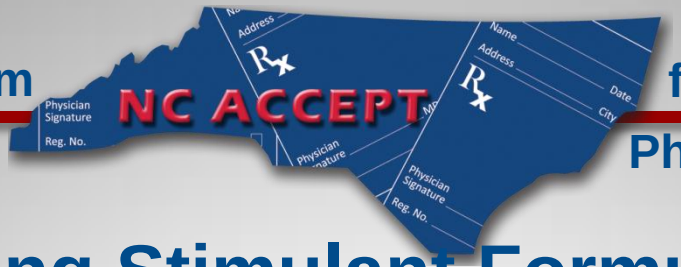
Classes of Medication Used to Treat ADHD

- FDA-approved
  - Stimulants (e.g.. methylphenidate, amphetamine)
  - Norepinephrine reuptake inhibitors (atomoxetine)
  - $\alpha 2$-adrenergic agonists (clonidine, guanfacine)

AACAP. *J Am Acad Child Adolesc Psychiatry*. 1997;36(suppl):85S-121S.

Stimulants

- Methylphenidate (Ritalin)
- Dexmethylphenidate (Focalin)
- Dextroamphetamine (Dexedrine, Dextrostat, Vyvanse)
- Mixed Salts of Amphetamine (Adderall)
- These are the safest, most effective medications to treat ADHD, with decades of use



Long Acting Stimulant Formulations

Focalin XR:	Once daily formulation of Focalin® that mimics b.i.d. dosing and duration and designed to last the school day (8 hours)
Ritalin LA:	once-daily formulation of Ritalin® that mimics b.i.d. dosing
Metadate CD:	methylphenidate formulation designed to mimic b.i.d. duration (8 hours)
Concerta:	methylphenidate formulated to mimic t.i.d. duration (12 hours)
Adderall XR:	extended-release formulation of mixed amphetamines that mimics b.i.d. dosing (8 hours)
Vyvanse:	extended release dextroamphetamine, which may mimic t.i.d. dosing (12 hours)

Alpha Adrenergic Agonists: Clonidine (Catapres, Kapvay) Guanfacine (Tenex, Intuniv)

- Pharmacological opposites of stimulants
- Limited empirical evidence of efficacy, yet widespread use; now FDA approved
- Historical fear of cardiac events combined with stimulants (probably not true)
- Risk of withdrawal hypertension
- Most difficult side effect is sedation, but (usually clonidine) can be a safe, useful adjunct for sleep

Clonidine and Guanfacine

- Clonidine dosing usually up to 0.1 mg q.i.d. (very short half-life)
- Guanfacine dosing based on 1 mg tablets, often given b.i.d. or t.i.d.
- May need EKG monitoring (controversial)
- Blood pressure should be above 90/60
- Heart rate should be above 60
- Long acting Kapvay dosed b.i.d.; long acting Intuniv dosed daily

Atomoxetine (Strattera)

- Selective norepinephrine reuptake inhibitor
- Start at 0.5 mg/kg/day, either qAM or b.i.d.
- Wait three days to increase dose, up to max of 1.4 mg/kg/day
- Watch blood pressure
- Possible greater role in adult ADHD, if concern about substance abuse
- Might be effective for anxiety and depression like a TCA
- May take weeks to see benefit, limited use for severe symptoms

BMJ Clinical Evidence
(August 2009)

- Likely to be beneficial
  - Atomoxetine
  - Clonidine
  - Dextroamphetamine Sulfate
  - Methylphenidate
  - Modafinil

BMJ Clinical Evidence

- Unknown Effectiveness
  - Bupropion
  - Homeopathy
  - Fish Oil

Stimulant costs/month

- Adderall XR $177-$242
- Concerta $154-$194
- Daytrana $158-$181
- Focalin XR $160-$178
- Metadate CD $123-$206 (30, 50 mg)
- Ritalin LA $148-$158
- Vyvanse $140-$147

Sometimes, lowest dose is the most expensive!

Immediate Release Stimulants (generic)

• Mixed Amphetamine Salts	$19-$51
• Dextroamphetamine	$30-$54
• Methylphenidate	$11-$17
• Dexmethylphenidate	$30-$54

Long or short acting stimulant?

- Stimulants have their primary effect when serum levels are rising
- This led to development of OROS or beaded long acting mechanisms
- Short acting meds may lead to inter-dose symptom re-emergence
- Role for a short acting dose in late afternoon

Non-Stimulants

- Clonidine tabs $7-$9
- Catapres Patch $15
- Guanfacine tabs $10-$12
- Intuniv $149-$211
- Strattera $173-$193
- Buproprion SR $76-$106 **(Drugstore.com)**
- Modafinil $700-$1200 (Drugstore.com)

Costs from the MTA Study

- Treatment costs varied by a factor of 4
- Medication management was the lowest cost
- Combined treatment was the most expensive
- Combined treatment may be more cost effective in presence of co-morbidity

Is there a “best” stimulant?

NO!

What makes treatment more expensive?

- Using stimulant alternatives first line
- “Testing” for the diagnosis
- Play therapy
- Atypical antipsychotic medication

  --Aggression associated with ADHD has been shown to respond well to stimulant medication
- Co-morbidity will increase cost

How to start a stimulant

- Get a baseline parent/teacher rating score, such as the Child Attention Profile, Conners Rating Scale, or the Vanderbilt
- Use immediate release for young children
- If long acting meds are preferable in school, discuss with family
- Be certain they can handle 12 hours of an adverse effect if starting with long acting

Starting doses

- 0.3 mg/kg/dose Methylphenidate, but probably not higher than 10 mg in an older child
- Follow response every few weeks (depending on schedule/ability of family to make appointments)
- Up to 1 mg/kg/dose, but probably not higher than 20-30 mg/dose
- Dosing is typically t.i.d. (breakfast, lunch, after school)

Using stimulants

- Dextroamphetamine and Mixed Salts and d-Methylphenidate are twice as potent, so start at 0.15 mg/kg/dose, up to 10 mg/dose
- Example of Long acting conversion: Metadate CD 20 mg is like methylphenidate 10 mg b.i.d.
- Adderall XR 20 is like Adderall 10 mg b.i.d., and probably like Dextroamphetamine 10 mg b.i.d.
- Vyvanse 30=Adderall XR 10; Vyvanse 50=Adderall XR 20; Vyvanse 70=Adderall XR 30

Example of pharmacokinetic considerations: Long acting MPH

- Concerta: slow onset, may cause problems on the bus, yet may last the longest
- Metadate: intermediate onset, typically not as long acting
- Ritalin LA: faster onset, many say the duration of action is shorter

Stimulants in practice

- Assuming no significant side effects, give them 7 days per week, 52 weeks per year
- Increase doses if Vanderbilt, CAP or other scale shows persistent symptoms
- Switch stimulants for intolerable side effects or poor efficacy at higher doses

Conclusions

- Stimulants remain the most effective treatments to date
- Patented meds (all long acting) are very expensive
- Inexpensive short acting stimulants are inconvenient but remain an option
- Avoid atypical antipsychotic meds
- Long term stimulant benefits implied, not yet proven