

Beyond the MTA: Multimodal Treatment of ADHD

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Disclosures

Past Consultant, scientific advisor,
speaker, grant recipient:

McNeil/Alza (Concerta)

Abbott

Shire (Adderall, Adderall XR,
guanfacine)

Noven (Daytrana)

Lilly (Strattera)

Cephalon (Sparlon)

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ADHD: Importance to Professionals

Prevalence: 2-9% of population--higher in boys

Children dealt with by:

- Health Care Professionals
- Mental Health Professionals
- Allied Health Professionals
- Educators

Most common behavioral referral to health care professionals

Most common referral/diagnosis in special education

Most common behavior problem in regular education classrooms

Most common diagnosis in child mental health facilities

Core Symptoms--Same Over Past 50 Years

Inattention

Impulsivity

Hyperactivity

But are symptoms what we should focus on in diagnosis, treatment, and clinical trials?

Domains of Functional Impairment in ADHD Children

- Relationships with **parents**, teachers, and other adults
- Relationships with **peers** and siblings
- **Academic** achievement
- Behavioral functioning at school
- Family functioning at home
- Leisure activities

Central Role of Functional Impairment in Treatment

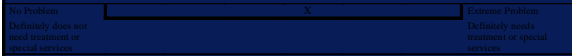
- Impairment—that is, problems in daily life functioning that result from symptoms **and** deficits in adaptive skills—rather than symptoms themselves is
 - (1) why children are referred,
 - (2) **what mediates long-term outcome**, and therefore
 - (3) what should be targeted in treatment.
- **Key domains are peer relationships, parenting/family, and academic achievement**
- **Assessment of impairment in daily life functioning and adaptive skills is the most fundamental aspect of**
 - initial evaluation to determine targets of treatment
 - Ongoing assessment to evaluate treatment response.
- **Normalization or minimization of impairment in daily life functioning **and** maximization of adaptive skills is the goal of treatment—not elimination of symptoms**

Impairment Rating Scale

Fabiano et al, JCCAP, 2005

Raters (parents, teachers) describe what they see as the child's primary problems in narrative format. Raters then rate how the child's symptoms have affected each of the following domains:

- (1) relationship with peers/siblings
- (2) relationship with parents or teachers,
- (3) his or her academic progress,
- (4) your classroom/family in general
- (5) his or her self-esteem , and
- (6) overall problem/need for treatment



Use the Most Efficient Method of Diagnosis/Assessment

(Pelham, Fabiano & Massetti, JCCAP, 2005)

- **Use Parent and Teacher Rating Scales**
 - Either DSM-Based (e.g., SNAP, DBD, Vanderbilt, ADHDRS, Stony Brook)
 - Or Empirically-derived (e.g., IOWA Conners, CAP, BASC)
- **Structured diagnostic interviews unnecessary**
- **Focus on functional impairments (e.g., the IRS; Fabiano et al, 2005) rather than DSM symptoms or comorbid diagnoses (AAP, 2001)**
- **Use behavioral assessment and functional analysis of target behaviors based on clinical interview with caretakers and teachers**
- **Modify treatment based on ongoing functional assessments**

Why Is it Important to Treat ADHD in Childhood?

Economic Impact of ADHD on Society--the Cost of Illness?

Pelham, Robb & Foster
Ambulatory Pediatrics, January 2007

Total Annual Incremental Costs Per Child Across Sectors

Pelham, Foster & Robb, Ambulatory Pediatrics, 2007

Health and Mental Health	\$ 2,636
Education	\$ 4,900
Crime and Delinquency	\$ 7,040
Family Costs (e.g., work loss)	No data
Total	\$14,576

Range (lowest to highest ests.) \$12,500--\$17,458

NOTE: Few studies and many domains not assessed--these are very conservative estimates

Annual Societal Costs of Childhood/Adolescent ADHD in North America

Health and Mental Health	\$7.9 billion
Education	\$13.6 billion
Crime and Delinquency	\$21.1 billion
Parental work loss	?
Total (low estimate based on incomplete data)	\$42.5 billion
Range (lower to upper bounds based on currently available data)	\$36-\$52.4 billion

*Using 5% prevalence estimate and US 2000 Census data

Pelham, Robb & Foster, *Ambulatory Pediatrics*, 2007

Annual Cost of ADHD and Other Disorders in U.S.

Depression (adults):	\$44 billion
Stroke:	\$53.6 billion
ADHD (child, adolescent)	\$50-60 billion
ADHD (adult)	\$30 billion
Alzheimer's	\$100 billion
Alcohol abuse/dep.	\$180

Prognosis for ADHD Children

Chronic disorder extending into adolescence and adulthood

- One-third: **Tolerable outcome**; appear to have mild problems but must constantly work to adapt to their difficulties
- One-third: **Moderately poor outcome**; continue to have a variety of moderate to serious problems, including school difficulties (adolescents) or vocational adjustment difficulties (adults), interpersonal problems, general underachievement, **problems with alcohol, etc.**
- One-third: **Bad outcome**; severe dysfunction and/or psychopathology, including sociopathy, repeated criminal activity and resulting incarceration, **alcoholism, drug use disorders**

What is Effective, Evidence-based Treatment for ADHD in Children?

Treatments That Are Commonly Used but Are Not Evidence-Based (i.e., are Not Effective)

(AAP, 2001; Pelham & Fabiano, 2008)

- (1) Traditional one-to-one therapy or counseling
- (2) Cognitive therapy
- (3) Office based "Play therapy"
- (4) Elimination diets
- (5) Biofeedback/neural therapy/attention (EEG) training
- (6) Allergy treatments
- (7) Chiropractics
- (8) Perceptual or motor training/sensory integration training
- (9) Treatment for balance problems
- (10) Pet therapy
- (11) Dietary supplements (megavitamins, blue-green algae)

Evidence-Based Short-term Treatments for ADHD

- (1) Behavior modification
-175 studies
 - (2) CNS stimulant medication
>300 studies
 - (3) The combination of (1) and (2).
>25 studies
- Moderate to large effect sizes across treatments

(Pelham & Fabiano, 2008; Greenhill & Ford, 2002; Hinshaw et al, 2002; Fabiano et al, under review)

AAP Clinical Practice Guideline: Treatment of the School-Aged Child with Attention-Deficit/Hyperactivity Disorder

Pediatrics, October 2001

RECOMMENDATION 1: Primary care clinicians should establish a management program that recognizes ADHD as a chronic condition.

RECOMMENDATION 2: The treating clinician, parents, and the child, in collaboration with school personnel, should specify appropriate **target outcomes** to guide management.

RECOMMENDATION 3: The clinician should recommend stimulant medication and/or behavior therapy as appropriate, to improve target outcomes in children with ADHD.

Japanese Guidelines for Pediatricians

(Ministry of Welfare and Labor, 2007)

•Start with education and environmental adjustments

•Add behavioral treatment, or medication, or combined treatment (suggested)

New AACAP Guidelines...

...behavioral treatments placed as last line interventions equivalent to nonFDA-approved medications as treatment

APA Task Force on Medication and Psychosocial Treatments in Children and Adolescents

... the decision about which treatment to use first [should] be guided by the balance between anticipated benefits and possible harms of treatment choices ...which should be the most favorable to the child.

By this we mean, the safest treatments with demonstrated efficacy should be considered first before considering other treatments with less favorable profiles.

For most of the disorders reviewed herein, there are psychosocial treatments that are solidly grounded in empirical support as stand alone treatments.

Moreover, the preponderance of available evidence indicates that psychosocial treatments are safer than psychoactive medications.

Thus, it is our recommendation that in most cases psychosocial interventions be considered first.

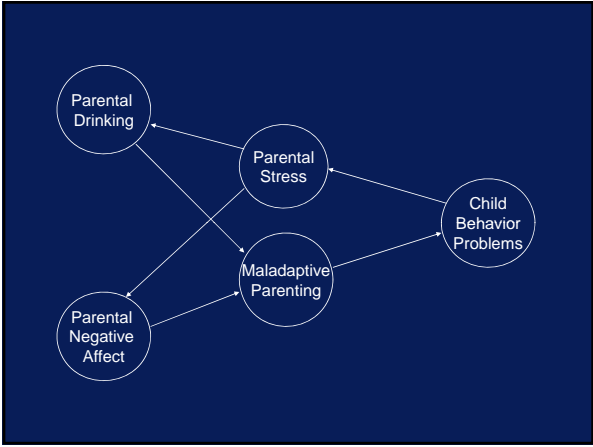
Components of Effective, Comprehensive Treatment for ADHD

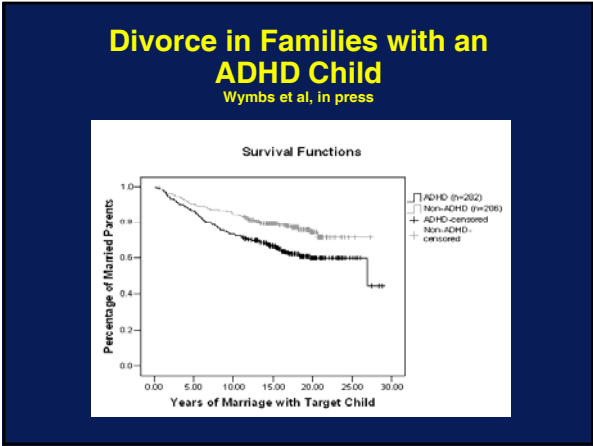
- Behavioral Parent Training--
Use always
- Behavioral School Intervention--
Use always
- Intensive Behavioral Child Intervention--
Use when needed
- Medication--Use when needed

Why is it Important to Include Parent Training in Treatment?

- Parents of ADHD children have significant stress, psychopathology, and poor parenting skills
- ADHD children contribute greatly to parental stress and disturbed parent-child relationships
- Parenting styles characteristic of ADHD parents predict long term negative outcomes
- Parenting mediates most negative outcomes and needs to be the main focus of intervention

Do Your Children Cause You Stress?





Components of Effective, Comprehensive Treatment for ADHD

Parent Training

- Behavioral approach
- Focus on parenting skills, child's behavior, and family relationships
- Parents learn skills and implement treatment with child, modifying interventions as necessary using ongoing functional analysis
- Group-based, weekly sessions with therapist initially (8-16 sessions), then contact faded
- Don't expect instant changes--improvement (learning) often gradual
- Continued support and contact as long as necessary (e.g., 2 or 3 years and/or when deterioration occurs)
- Program for maintenance and relapse prevention (e.g., develop plans for dealing with concurrent cyclic parental problems, such as maternal depression, parental substance abuse, and divorce; make programs palatable and feasible)
- Reestablish contact for major developmental transitions (e.g., adolescence)
- Can be offered in MH, primary care, schools, churches, community centers by individuals with wide variety of training--very cost effective

Behavioral Interventions in the Home

1. Rules for the home
2. Ignore mild inappropriate behaviors and praise appropriate behaviors (choose your battles)
3. Appropriate commands:
 - Obtain the child's attention: say the child's name
 - Use command not question language
 - Be specific
 - Command is brief and appropriate to the child's developmental level
 - State consequences and follow through
4. Daily charts (e.g., School, Home Daily Report Cards)
5. Premack contingencies (e.g., watch TV or phone time contingent upon homework completion)
6. Time out from positive reinforcement/work chores
7. Point/token system with both reward and cost components
8. Level system
9. Homework hour
10. Contracting/negotiating with adolescents

Why is it also important to treat in school settings?

Academic Functioning

(Lifetime-PALS Robb et al, under review)

- 33% of ADHD have academic problems (special ed., academic probation, dropped out, or held back) **every year**, vs. 2% of controls
- 48% of ADHD children have at least one year of **special education** placement vs. 3% of controls (bulk of cost)
- 12% of ADHD vs. 5% of controls have been **held back** a grade
- 9% of ADHD adolescents **drop out** of school vs. 1% of controls
- ADHD adolescents a **full letter grade** lower than controls, with twice the rate of absences

School Discipline Problems

(lifetime-PALS; Robb et al, under review)

Discipline Problems (sent to principal, serious warnings, detention, suspension, expulsion) per Year:

	ADHD	Control
None	20%	41%
< Quarterly	34%	51%
Quarterly	17%	7%
Monthly	19%	1%
Weekly	10%	0%

Components of Effective, Comprehensive Treatment for ADHD

School Intervention

Behavioral approach--teachers are trained and implement treatment with the child, modifying interventions as necessary using ongoing functional analysis

Focus on classroom behavior, academic performance, and peer relationships

Widely available in schools

Teacher training: (1) in service training and follow up or (2) consultant model--initial weekly sessions, then contact faded

Don't expect instant changes--improvement (learning) often gradual

Continued support and contact for as long as necessary--typically multiple years and/or if deterioration

Program for maintenance and relapse prevention (e.g., school-wide programs, train all school staff, including administrators; eventually train parent to implement and monitor)

Reestablish contact for major developmental transitions (e.g., adolescence)

Daily Report Card (Downloadable*)

- An integral part of all of our school interventions with ADHD children
 - Serves as a means of identifying, monitoring, and changing the child's classroom problems
 - Doubles as an avenue of regular communication between the parents and the teacher
 - Costs little, takes little teacher time, and is highly motivating to the children if parents have selected the right rewards for home back-up
 - Effectiveness documented in numerous studies
 - Can be used to titrate medication dose
- *Form can be downloaded in English at <http://ccf.buffalo.edu>

Daily Report Card: Good Example

Child's Name: _____ Date: _____

	Special	LA	Math	Reading	SS/Sci.
Follows class rules with no more than 3 rule violations per period.	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___
Completes assignments within the designated time.	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___
Completes assignments at 80% accuracy.	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___
Complies with teacher requests (< 3 noncompliance per period)	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___
No more than 3 teasings per period.	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___	Y ___ N ___
OTHER					
Follows lunch rules (<3 violations).	Y ___	N ___			
Follows recess rules (<2 violations).	Y ___	N ___			
Total Number of Yeses/Nos:	_____				
Teacher's Initials:	_____				
Comments:	_____				

Why is it Important to Use Psychosocial Treatments for ADHD Peer Relationships?

- We have long known that impaired peer relationships in children are the best predictors of negative adult outcomes
- ADHD children have seriously impaired peer relationships
- ADHD children have the negative adult outcomes that are predicted by disturbances in peer relations
- Peer relationships arguably mediate ADHD children's adult outcomes

Components of Effective, Comprehensive Treatment for ADHD

Child Intervention

Behavioral and developmental approach
Focus on teaching academic, recreational, and social/behavioral competencies, decreasing aggression, increasing compliance, developing close friendships, improving relationships with adults, and building self-efficacy
Paraprofessional implemented (for cost reasons)
Intensive treatments such as summer treatment programs (9 hours daily for 8 weeks), and/or school-year, after-school, and Saturday (6 hours) sessions
Don't expect instant changes--improvement (learning) often gradual
Continued support and contact as long as necessary--multiple years or if deterioration occurs
Program for generalization and relapse prevention (e.g., integrate with school and parent treatments--link all through home/school report card systems)
Reestablish contact for major developmental transitions (e.g., adolescence)

Why Treat ADHD in a Summer Setting?

- Work on peer relationships in an ecologically valid setting (e.g., playing common games in peer group settings)
- Teach sports skills and knowledge and team cooperation
- Build friendships with other ADHD children
- Minimize summer learning loss that characterizes low achieving children
- Teach compliance skills to child and parents
- Teach daily report card concept to child and parents

Comprehensive and Intensive Treatment for ADHD: Summer Treatment Program

Named in 1993 as one of the country's model service delivery program for children and adolescents by the Section on Clinical Child Psychology of the American Psychological Association.

Used successfully in clinical trials at NIMH, CMHS, and NIDA
Innovative Program of the Year, 2003, CHADD

SAMHSA list of Evidence Based Practices (NREP), 2005

Summer Treatment Program Overview

- Eight-week program, 9 hours daily
- Children grouped by age into groups of 12
- Groups stay together throughout the day
- 5 counselors work with each group all day outside of the classroom
- One teacher and an aide staff the classroom for each group
- Treatment implemented in context of recreational and academic activities

Typical STP Schedule

<u>Time</u>	<u>Activity</u>
7:30-8:00	Arrivals
8:00-8:15	Social Skills Training
8:15-9:00	Soccer Skills Training
9:15-10:15	Soccer Game
10:30-11:30	Art Class
11:45-12:00	Lunch
12:00-12:15	Recess
12:15-2:15	Academic/computer class
2:30-3:30	Softball Game
3:30-4:30	Swimming
4:45-5:00	Recess
5:00-5:30	Departures

Summer Treatment Program Overview

Treatment Components:

- Point System
- Social Skills Training, Cooperative Tasks, Team Membership, and Close Friendships
- Group Problem Solving
- Time out
- Daily Report Cards
- Sports Skills Training and Recreation

Summer Treatment Program Overview

Treatment Components:

Positive Reinforcement & Appropriate Commands

Classrooms--Regular, Peer Tutoring, Computer, and Art

Individualized Programs

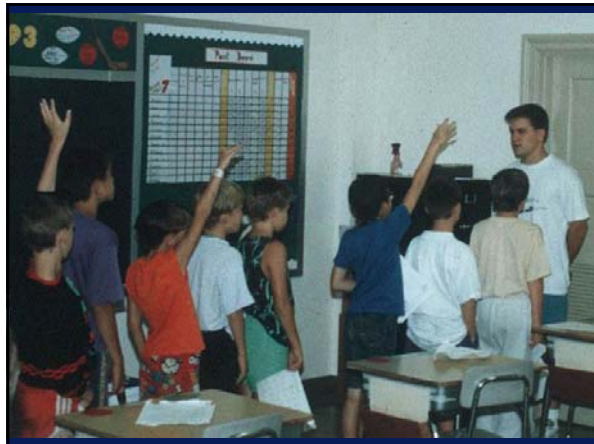
Parent Training

Medication Assessments

Adolescent Program









Major Benefits of the STP
(Pelham et al, 2005; Pelham & Fabiano, 2008)

- 360 hours of treatment (equivalent to seven years worth of weekly social skills training sessions) in an 8-week period
- Produces large improvements in multiple functional domains
- Teaches skills (e.g., sports) not taught in other interventions and provides on-line practice
- Parents have daily contact with treatment staff
- Extremely low dropout rate (3%) compared with up to 50% in other outpatient studies
- High parent attendance at parent training meetings
- Supportive "community" environment for child and family
- Stress-relief for parents and child provided by an 8-week daily treatment program
- Unusually high level of parent and child satisfaction with treatment—critical for long-term palatability and implementation
- Maintains academic gains/prevents summer loss
- Addresses the three key psychosocial predictors—parenting, peer relationships, and academics

Dissemination

- All STP procedures manualized and available on one CD (\$199 US)
- Training available annually in Latrobe PA and Buffalo NY (very low cost)
- Trainers available to come to your site
- After first summer, maintained by your staff
- Adapted for many settings/uses (e.g., after school (UCLA, Cleveland Clinic), summer school (Buffalo), city recreation departments (Chicago), day school and wrap-around (Johnstown, NYC)

STP Sites

- Buffalo (UB, BPS)
- New York City (NYU Medical Center)
- Cleveland, OH (Cleveland Clinic)
- Irvine, CA (UCI)
- Erie, Johnstown, and Indiana PA (3 Community Agencies with 12 different sites)
- SC, WVA, NJ, NYC (Staten Island MH Society) and WA community agencies/professionals
- Birmingham AL (UAB Medical Center)
- Boston (Harvard/JBCC)
- Chicago (UICC/community parks and UICC)
- Kurume, Japan (Kurume University and Kurume schools)
- Smaller, shorter camps in many U.S. cities that use parts of STP

Limitations of Behavioral Interventions

- 1) Not sufficient to bring some children to the normal range of functioning
- 2) Not effective for all children because some parents cannot do it well
- 3) Must be very broad in scope to affect important familial variables (e.g., parental stress)
- 4) Lack of evidence for long-term effects--no studies have yet been conducted other than MTA
- 5) Difficult to get parents and teachers to do over a long period of time (after therapist contact has ended)
- 6) Relatively costly compared to medication initially (but not in long run)

Components of Effective, Comprehensive Treatment for ADHD

Concurrent Psychostimulant Medication

- Rarely should be used as first treatment implemented
- Need determined following initiation of behavioral treatments; timing depends on severity and responsiveness
- Individualized, school-based medication trial conducted to determine need and minimal dose to complement the behavioral intervention
- Cycle through methylphenidate and amphetamine-based compounds before other drug classes
- Need for t.i.d. or long-acting medication also determined based on child's impairment across settings and times
- Use at minimal rather than maximal effective dose
- Continue for as long as need exists (typically years--evaluate need and dose annually)
- Plan for possible emergent iatrogenic effects (e.g., growth suppression)

Main Beneficial Short-term Effects

(Greenhill & Ford, 2002)

1. Decrease in classroom disruption
2. Improvement in teacher ratings of behavior
3. Improvement in compliance with adult requests and commands
4. Increase in on-task behavior and academic productivity and accuracy (but no long-term effect on academic achievement)
5. Improvement in peer interactions
6. Improvement in performance on laboratory measures of attention, impulsivity, and learning

Limitations of Pharmacological Interventions When Used Alone

- 1) Not sufficient to bring some children to the normal range of functioning
- 2) Works only as long as medication taken
- 3) Not effective for all children
- 4) Does not affect several important variables (e.g., academic achievement, concurrent family problems, peer relationships)
- 6) Poor Compliance in long-term use
- 7) Parents are not satisfied with medication alone
- 8) Removes incentive for parents and teachers/schools to work on other treatments
- 9) Uniform lack of evidence for beneficial long-term effects
- 10) Reduction in growth (height and weight)
- 11) Lack of information about long-term safety (Swanson & Volkow, 2008)

Trends in Medication Use

- **Before MTA, Concerta, and Adderall XR**
 - Meds for school hours only-184 days per year
 - Modal total daily dose: 15-20 mg MPH; 10 mg Adderall
 - Weekends and summers medication free
 - Most children medicated 1-3 years
 - **Lifetime dose: 5400 mg to 10,800 mg MPH**
 - **After MTA, Concerta, and Adderall XR**
 - Meds for school and home
 - Equivalent total daily doses: 36 mg Concerta; 20 mg Adderall XR
 - Weekends and summers medicated (so 365 days per year)
 - Current recommendations (e.g., MTA): start early and medicate for all 12 school years
 - **Lifetime dose: 14,600 mg/year X 12 =175,000 mg MPH**
- IS THIS INCREASE SAFE IN THE LONG RUN?

Summary: Components of Effective, Evidence-based, Comprehensive Treatment

- **Parent Training--Use always**
- **School Intervention--Use always**
- **Child Intervention--Use when indicated**
- **Medication--Use when needed**

Comprehensive Psychosocial and Pharmacological Treatment for ADHD: The NIMH/USOE Multimodal Treatment Study (MTACG, Archives of General Psychiatry, 1999)

Randomized Clinical Trial of four treatments:
Community Comparison Control
Psychosocial Alone
Pharmacological Alone
Combined Psychosocial and Pharmacological

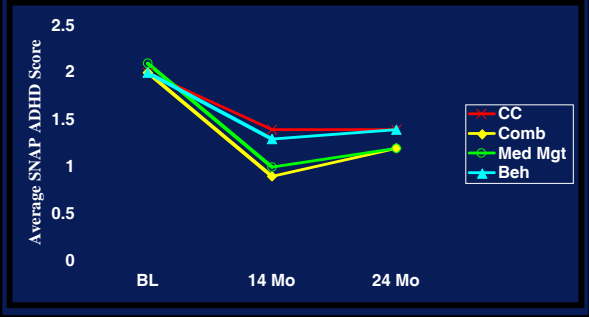
576 subjects, recruited from community, entered between January and May of three consecutive years across six sites

144 subjects per group overall; 24 per group per site

Treatment for 14 months; follow-up for 10 months

Extensive manualization and standardization of treatment:
1000+ pages of treatment manuals
Coordinated staff training across sites
Extensive measures of treatment fidelity for all components
10+ hours of weekly conference calls to standardize protocol

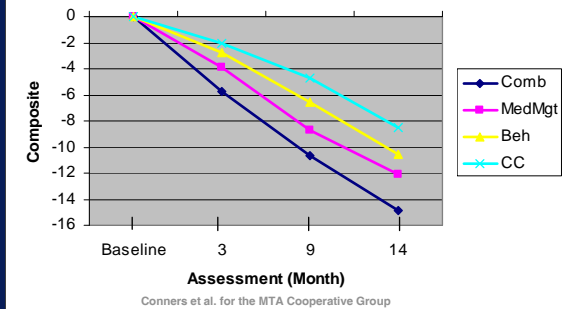
**SNAP-ADHD (Parent/Teacher):
Treatment Group Outcomes across
24 Months (Lower score better)**



Summary of MTA Results at 14 Months

- All four groups improved dramatically with time
- **Active Med** (study: 39 mg MPH/day) was superior to **faded Beh** on ADHD symptom measures and some measures of impairment
- 75% of Beh group were maintained off medication
- Combined (31 mg MPH/day) was superior to Beh on all measures and to Med on most measures of impairment but not significantly on symptoms
- Comb (and sometimes Med) were superior to CC and Beh was equivalent (70% of CC medicated; 24 mg MPH/day)
- Combined produced **more normalization at lower doses** (and lower rates of increase in dose) than Med and was **much preferred** by parents

**Composite Score
Adjusted for Baseline**



Change in Presenting Problems

Pelham & MTA Cooperative Group, under review

	Medmgt	Comb	Beh
Declined/dropped out	12%	4%	0%
Worse/Unchanged	6%	6%	5%
Slightly improved	22%	11%	22%
Improved	38%	37%	43%
Much improved	22%	41%	30%

Would Parent Recommend Treatment?

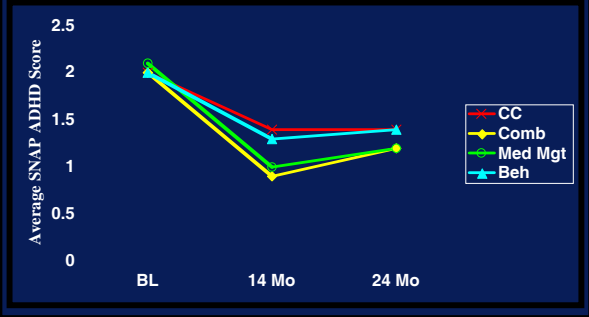
(Pelham & MTA Coop. Group, under review)

	Medmgt	Comb	Beh
Declined/dropped out	12%	4%	0%
Not recommend	8%	3%	5%
Neutral	8%	1%	2%
Slightly Recommend	4%	2%	2%
Recommend	31%	15%	24%
Strongly recommend	38%	76%	67%

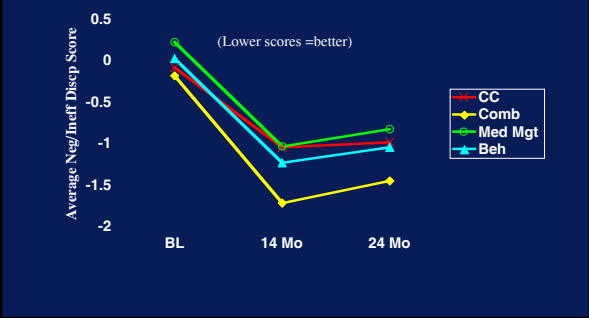
What happened at follow-up?

- Data reported by the MTACG in Pediatrics, 2004, and J. American Academy of Child and Adolescent Psychiatry, 2007
- All groups better than at baseline
- Loss of incremental beneficial medication effects
- No differences among groups on beneficial outcomes
- Adverse effects on growth

**SNAP-ADHD (Parent/Teacher):
Treatment Group Outcomes across
24 Months (Lower score better)**

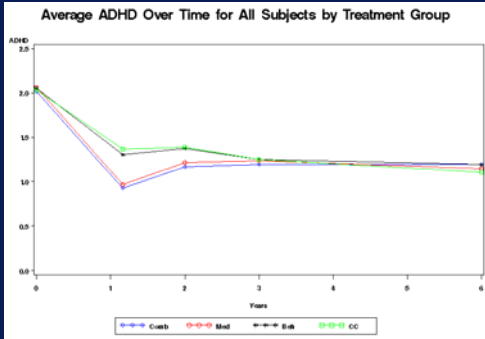


**Negative/Ineffective Discipline:
Treatment Group Outcomes across
24 Months (Lower scores =better)**

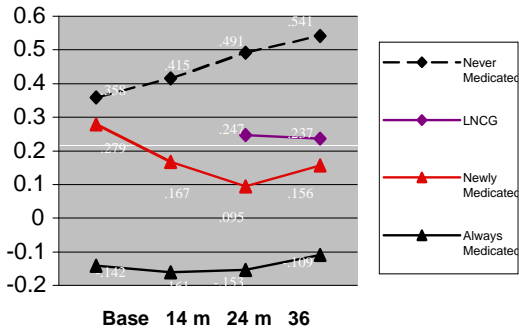


**What happened at 36 months-that
is, one year more of follow-up?**

- Data reported in J. American Academy of Child and Adolescent Psychiatry, August, 2007
- All groups better than at baseline
- No differences among groups on beneficial outcomes
- Adverse effects on growth



MTA Growth Curves for Height for Major Naturalistic Subgroups (MTACG, in press)



Questions the MTA Did Not Answer

How to decide what treatments a child needs?
 Should behavioral treatment begin before medication (parent preference) or vice versa (physician practice) or should they be implemented simultaneously (as in the MTA).
 What are the best "doses" of psychosocial, pharmacological, and combined treatments?
 If one or the other modality is begun first, how long should it be conducted and at what dose before adding in the second modality?
 What are the implications of different doses and sequences for treatment dosing, benefit, and risk of side effects?
 These are the questions that families, practitioners, and educators face daily, but they have not been studied.

Program of Research

Four studies funded by NIMH and IES that examine dose effects and sequencing effects:

- (1) Controlled examination of 3 levels of behavior modification (none, low intensity, high intensity) crossed with 4 doses of medication in a summer program setting and at home
- (2) Follow up to (1); School-year evaluation of effectiveness and need for medication after beginning the year on one of 3 behavior modification levels (none, low intensity, high intensity)
- (3) Evaluation of effectiveness and need for medication in young ADHD children beginning treatment (home, school, peers, academic) with one of the same behavior modification levels as above (with adaptive components) and continuing without fading for 3 years (to pass peak period for medication use)
- (4) SMART (sequential, multiple, adaptive, randomized trial) design to examine whether to begin treatment with medication or behavior therapy and, when nonresponse, whether to add the other modality or increase the intensity of initial modality

Dose-Response Effects of Behavior Modification, Medication, and their Combination in ADHD Children in a Summer Setting

Pelham, Burrows-McLean, Gnagy,
Fabiano, Coles, Hoffman, Massetti,
Waxmonsky, Waschbusch, Chacko,
Walker, Wymbs, Robb, Arnold, Garefino
(NIMH 2001-2006)

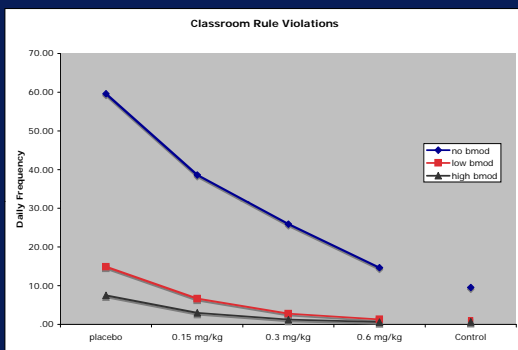
Study 1 Design

48-52 ADHD children per summer for 3 summers
4 Medication conditions: placebo and 3 doses of methylphenidate (.15mg/kg, .3 mg/kg, .6 mg/kg, t.i.d.), with order varying daily within child for 9 weeks
3 Behavioral Modification conditions: No behavioral treatment (NBM), low-intensity (LBM) treatment, and high-intensity (HBM) treatment (BM), varying triweekly in random order by treatment group
3-4 days per medication X Bmod condition.
NonADHD comparison group (24/summer).

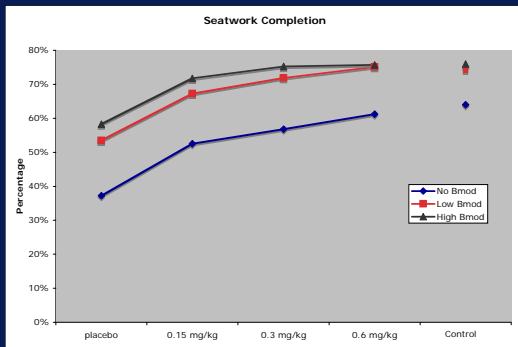
Comparative and Combined Treatments for ADHD

3, 3-week Behavior Modification conditions assigned randomly:

High Intensity BMod	Low Intensity BMod	No BMod
Daily Crossover of 4 Med conditions: Placebo .15 mg/kg MPH .3 mg/kg MPH .6 mg/kg MPH	Daily Crossover of 4 Med conditions: Placebo .15 mg/kg MPH .3 mg/kg MPH .6 mg/kg MPH	Daily Crossover of 4 Med conditions: Placebo .15 mg/kg MPH .3 mg/kg MPH .6 mg/kg MPH

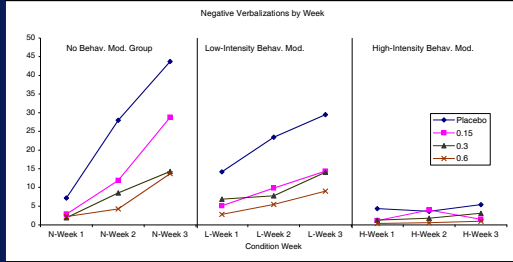


(Fabiano et al. *School Psychology Review*, 2007)



(Fabiano et al. *School Psychology Review*, 2007)

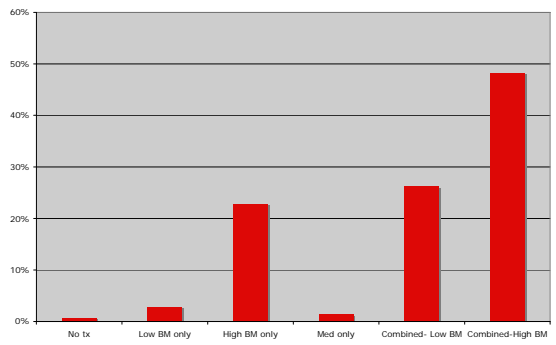
Between-Group Comparison of First Behavioral Condition



Percentages of ADHD Children Within 2 SDs of Control Mean in Each Treatment Condition.

	Rule Viol.	Interruption	Neg. Verbal.	Class Rule Viol.	Work Completion
Placebo					
NBM	37.5%	39.5%	39.5%	34.2%	23.7%
LBM	56.6%	55.3%	53.3%	66.4%	56.6%
HBM	62.5%	66.4%	66.4%	73.0%	64.5%
.15 mg/kg					
NBM	59.2%	54.6%	55.9%	55.3%	55.3%
LBM	74.3%	74.3%	74.3%	83.6%	75.7%
HBM	83.6%	85.5%	82.9%	90.8%	88.2%
.3 mg/kg					
NBM	73.7%	70.4%	65.1%	63.2%	60.5%
LBM	83.6%	84.9%	81.6%	94.7%	86.8%
HBM	88.2%	92.8%	88.2%	97.4%	90.8%
.6 mg/kg					
NBM	82.2%	78.9%	73.0%	80.9%	65.8%
LBM	92.8%	91.4%	87.5%	98.0%	85.5%
HBM	93.4%	95.4%	94.1%	99.3%	90.1%

First Choice for Continued Treatment Over the Next Year



Conclusions

This study is the second largest, between-groups analysis of BMOD for ADHD, following only the MTA Study. In the crossover analysis, it is the largest study of comparative and combined treatment for ADHD.

Both medication and behavioral treatment produced significant and generally comparable effects (moderate to large effect sizes) on nearly all measures of functioning in recreational and classroom settings.

On most measures, the combination of the lowest dose of medication and LBM produced as much and sometimes more change than did the four-times-higher doses of medication in the NBM condition and more change than HBM alone.

Conclusions

We have long argued that a benefit of combining treatment modalities is to produce equivalent improvement using lower doses of medication. The lowest dose used in this study was equivalent to less than 5 mg IR MPH t.i.d.—a very low dose that is only 40% of that utilized in the MTA study. There were no side effects at this dose and many side effects at the higher doses.

The highest dose, which was necessary to optimize effects in the absence of BM, was twice that utilized in the MTA combined treatment group and 50% greater than the Medmgt group, suggesting that optimal doses of medication in the absence of all behavioral treatments requires very high doses.

Notably, at the high dose levels of *either* condition, there were little incremental benefits of adding the *other* intervention. High doses of either treatment make the other unnecessary.

Conclusions

Effect sizes for BMOD were medium to large for most measures when measured after 3 weeks, and as large as the effects of medication. As the figures make clear, this result was obtained because a true NBM condition was employed—analogue to the placebo condition for medication.

This explains why the BMOD effect in the MTA was comparable to and not greater than the CC group, where much behavioral treatment was used by parents and teachers.

Thus, treatment doses, timing of assessments, and control conditions are critical factors in evaluations of combined treatment effects.

Finally, parents strongly preferred psychosocial approaches or combined approaches, never medication alone.

Limitation: Analogue setting and treatments were implemented simultaneously. What would have happened in natural settings and if BM were implemented first?

Three Doses of School-based Behavioral Interventions Following a Summer Treatment Program for Children with ADHD: Impact on Need for Medication

Coles, Fabiano, Pelham, Burrows-McLean, Gnagy, Hoffman, Massetti, Waxmonsky, Waschbusch, Chacko, Walker, Wymbs, Robb, Arnold, Garefino

(NIMH 2003-2007)

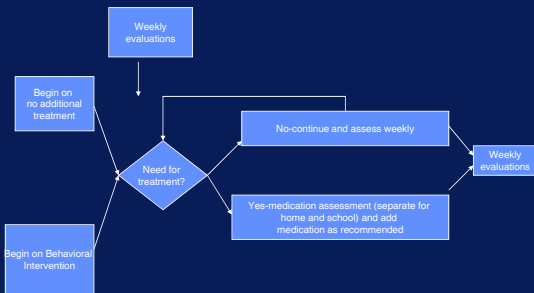
Study 2 Design

128 participants from the Study 1 were randomly assigned to one of two groups for follow-up treatment:

Behavior modification consultation (BM; $N=87$)

No behavior modification consultation (NBC; $N=41$)

School Year Follow-Up



Procedures

BC group: teachers received three initial consultation visits at the beginning of the school year aimed to improve existing classroom behavior modification programs and to institute a daily report card.

Parents also received monthly group booster parent training meetings.

Teachers and parents eligible to receive additional individual meetings if behavior ratings indicated impairment or as otherwise needed.

NBC group: received no consultation from the study staff.

Procedures

Teachers and parents in both groups completed weekly ratings of ADHD symptoms and impairment.

If ratings indicated the need for additional treatment or special services for two weeks in a row, and both parents and teachers agreed that medication was indicated, a medication assessment (Pelham, 1993) was conducted to select the optimal dose and children began a medication regimen.

Medication was introduced in a step-wise manner. Only after a medication regimen was established in school could a medication trial be initiated in the home.

Procedures

Mean numbers of individual consultation sessions actually received ranged from 0.83 to 1.23 across settings and conditions, indicating that very few of the teachers and parents took advantage of the additional possible individual consultations. Mean parent training booster groups attended was 2.5 (out of 9 over 10 months).

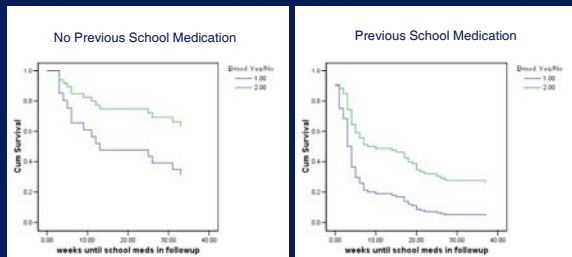
Results

Survival analyses were conducted separately for school and home settings to evaluate whether continued BMOD reduced the need for medication.

Previous medication status was a moderator

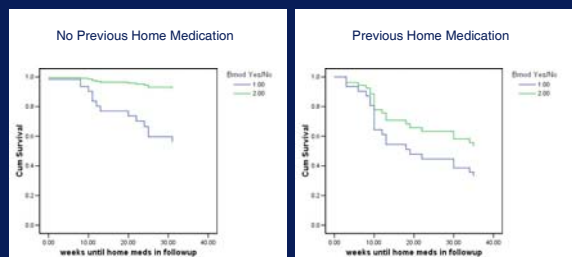
School Survival Curves

Coles et al, NCDEU, 2008



Home Survival Curves

Coles et al, NCDEU, 2008



Medication Doses

- Ending total daily doses were 37 mg/day for the NBC group and 29 mg for the BC group (29 mg and 21 mg for school)
- Doses were much higher for protocol violators than for children who had medication assessments
- Weekly dose totals were 234 mg for NBC and 157 for BC groups (275 for protocol violators)
- BC resulted in 25%-35% decrease in daily/weekly doses

Results

During the Fall, nearly twice as many children--60% vs 30%-- were maintained off medication in the behavioral consultation groups compared to no consultation.

With only one additional teacher consultation being used per group, it is not surprising that more children were medicated as the school year progressed--approximately 60% and 80% of the BM and NBM groups.

Notably, the majority of children who received behavioral consultation (booster group parent sessions)-- approximately 90%-- remained off medication in the home setting, and 60% of those who received summer behavioral parent training without further follow-up remained medication-free at home.

Children who had been medicated prior to the summer study were far less likely to survive medication-free than medication naïve children.

Limitations

All children had received both medication and intensive behavior modification (STP and BPT) in the summer (Study 1); the majority of children had been medicated prior to the STP and during the STP

As discussed above, individual behavioral consultations following the initial few were driven (after the first few sessions) by teacher/parent request, rather than therapist-determined, and most parents and teachers used few additional services.

Could these behavioral strategies prevent need for and use of medication over a long time period, is more flexibility needed to adapt the behavioral strategies to the child's need over time, and is it necessary to have medication naïve children in studies like this?

Dosage of Behavioral Interventions and Long-term Treatment with Young ADHD Children: Can Medication use Be Prevented and at What Cost?

William E. Pelham, Jr., Lisa Burrows-MacLean, James Waxmonsky, Greta Massetti, Daniel Waschbusch, Gregory Fabiano, Martin Hoffman, E. Michael Foster, Elizabeth Gnagy (NIMH 2005-2010)

Study Aims

To expand findings from the STP study to regular classroom settings with young (K and first grade) treatment-naïve ADHD children

To evaluate whether medication need and dose can be minimized by beginning treatment with behavioral intervention and continuing treatment over the long term

To determine the dose of behavioral treatment necessary to minimize medication usage and associated cost:benefit tradeoffs

Design

•Young (k or 1 grade), medication naïve, ADHD children, N=150

•Randomly assigned to

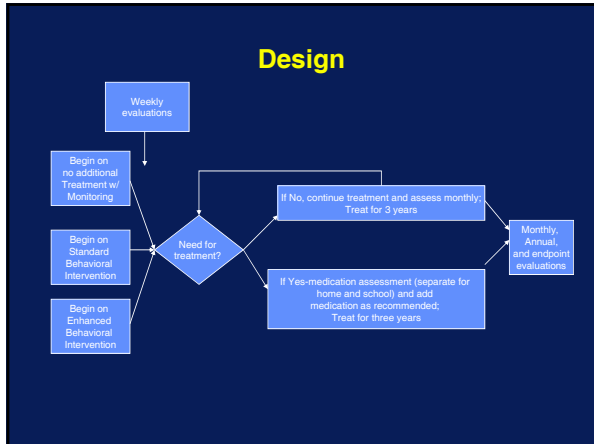
- (1) Treatment as usual (no intervention from study)
- (2) Standard clinical behavioral intervention school and home and peers
- (3) Enhanced behavioral intervention school and home and peers

•Treat for 3 years

•Weekly assessments, as in previous study

•As in previous study, continue treatment if success, add medication if need exists

•Behavioral treatment includes multiple components that differ across dose (e.g., STP, academic intervention) and are tailored to the child.



Behavior Modification

Enhanced:

- 16 sessions of group behavioral parent training (COPE/COPE+) followed by 8 sessions of father-child training and monthly booster sessions and phone calls over 3 years
- Up to 8 individual parent sessions per year, initiated when problems arise
- School intervention including daily report card and classroom management practices analogous to the HBM procedures in the STP (response-cost, Premack contingencies, time out).
- 6 initial meetings with teacher to establish program + up to 8 individual sessions per year
- Paraprofessional aides available temporarily to assist with high-intensity procedure initiation (e.g., RECESS)
- 7-week summer treatment program including intensive peer-group social skills and sports skills training with weekly Saturday program with parent involvement as follow up
- Academic supplement with phonological awareness training component

Behavior Modification

Standard:

- 12 sessions of group parent training (COPE) followed by bimonthly group booster training for 3 years
- Up to 4 individual parent sessions per year, initiated when problems arise
- School intervention including daily report card and lower-intensity procedures (classroom rules, sit-outs, commands).
- 3 initial meetings with teacher to establish program + up to 4 individual sessions per year
- Weekly group social skills training conducted along with initial 12 parent training sessions.

Indicator of Need for Additional Treatment at weekly Assessments:

- (1) Average performance on the ITB is less than 75% AND
- (2) Rating by parents or teachers as impaired (i.e., greater than 3) on the IRS in at least one domain.

Treatment decisions regarding content will be tailored to the specific domains of impairment rated on the IRS

Analysis and Specific Aims

- Survival to medication is main DV
- Functional outcomes secondary measures
- Main questions:
 - Can medication use be prevented in young ADHD children over the entire period of peak medication risk?
 - What dose of behavioral treatment is necessary to do this (a) in school, (b) at home, and (c) with peers?
 - What are individual differences in outcome?
 - Is medication dose lowered if needed in behavioral conditions and does this reduce SE (e.g., growth retardation)
 - What are cost:benefit tradeoffs?
 - Do clinical social skills training and/or STP affect the peer domain
- Limitation: This and previous studies do not address whether it might be more prudent to begin treatment with medication at low dose levels

Adaptive Pharmacological and Behavioral Treatments for Children with ADHD: Sequencing, Combining, and Escalating Doses

William E. Pelham, Jr., Lisa Burrows-MacLean, James Waxmonsky, Greta Massetti, Daniel Waschbusch, Gregory Fabiano, Martin Hoffman, Susan Murphy, E. Michael Foster, Randy Carter, Elizabeth Gnagy
(IES 2006-2010)

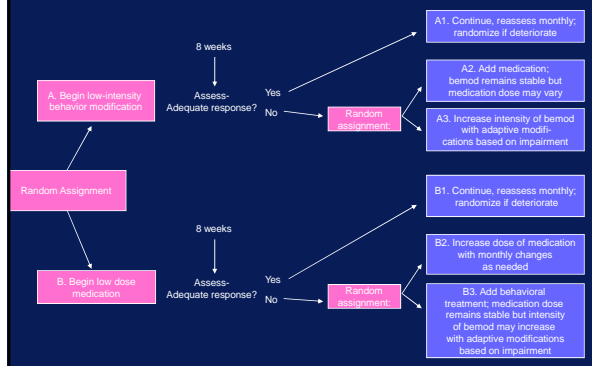
Specific Aims

- 1) How does an initial treatment strategy that includes either medication or behavior modification influence response to treatment and need for additional treatment?
- 2) When additional treatment is needed, what are the relative benefits of increasing the dosage of the initial treatment versus adding the other treatment modality?
- 3) Is dosage in medication usage reduced as a function of treatment strategy?
- 4) Is intensity of behavior modification reduced as a function of treatment strategy?

Specific Aims

- 5) Do these strategies differentially impact parent satisfaction with treatment and future use of treatments?
- 6) In what way do individual difference variables (e.g., severity of impairment, comorbid child psychopathology, prior medication history, parent and teacher treatment acceptability, parental characteristics, SES) influence the answers to questions addressed above?
- 7) What is the relative cost-effectiveness of these treatment strategies?

Study Design



Indicator of Need for Additional Treatment at 8-week and Subsequent Assessments:

- (1) Average performance on the ITB is less than 75% AND
- (2) Rating by parents or teachers as impaired (i.e., greater than 3) on the IRS in at least one domain.

Treatment decisions and content are tailored to the specific domains of impairment rated on the IRS

Preliminary Outcomes

(Pelham, Fabiano et al, 2008)

- Of 51 participants assigned to receive medication first, 12% refused medication.
- Of 50 participants assigned to receive behavioral treatment first, no one refused behavioral treatment; 96% attended at least 75% of 8 assigned parent training sessions; 100% of children had the school intervention implemented.

Preliminary Outcomes

(Pelham, Fabiano et al, 2008)

- 78% of children in the Behavioral Treatment First group were rerandomized at the first 8-week assessment point.
- 77% of children in the Medication First group were rerandomized at the first 8-week assessment point.
- By the end of the school year approximately 90% of each group met criteria for rerandomization.

Preliminary Outcomes

(Pelham, Fabiano et al, 2008)

- Of 24 children rerandomized to receive medication after the initial course of BMOD, 25% refused medication.
- Of 25 children rerandomized to receive BMOD after the initial course of medication, 68% of families attended no more than 25% of 8 assigned group parent training sessions. None refused the school intervention.

Preliminary Conclusions

(Pelham, Fabiano et al, 2008)

- By the end of the school year, 92% of children required intervention beyond a low dose of behavioral treatment (8 group PT sessions and a school-based DRC) or a low dose of medication (.15 mg/kg MPH b.i.d. at school).
- Ending medication doses were comparable to doses in community practice and much lower than the MTA study medicated sample.
- Almost all parents attended parent training when offered first, but more than two-thirds failed to attend parent training when medication was given first.

Preliminary Conclusions

(Pelham, Fabiano et al, 2008)

- Twice as many (25%) of those offered behavioral treatment first refused medication compared to when medication was offered first.
- In other words, the sequence of behavioral treatment THEN medication resulted in better uptake of multimodal treatment when needed.
- Future analyses with the complete study sample will investigate how sequencing and dose moderates treatment effectiveness and adherence. Effects of setting, individual differences, previous medication treatment, and fidelity of classroom behavioral treatments will be evaluated

Conclusions from Series of Studies

- **Dose** of treatment is important in comparative and combined studies of treatment for ADHD; study results (e.g., the MTA) cannot be understood without understanding dose effects
- **Sequencing** of treatments is a critical decision but has not been studied systematically with the exception of these studies, which show that providing behavioral treatment first reduces need for medication and providing medication first reduces parental uptake of behavioral treatment
- **Parents strongly prefer** psychosocial or combined treatment approaches. Parental preference is important because it affects long term adherence.
- Dose and sequencing questions utilizing adaptive designs (e.g., SMART designs) mimic the questions that face practitioners daily and are the next wave of treatment outcome research in ADHD

Summary of Treatment Literature for ADHD

- Behavioral and pharmacological interventions are the only two evidence-based treatments for ADHD
- Behavioral treatments teach skills and maintain after fading; parents and schools must maintain it
- Medication must be continued for long term change
- Parents prefer behavioral treatments to medication alone
- If behavioral treatments are started first and continued, 50-75% of ADHD children do not need medication (fewer at school and more at home) and doses are lower in those who do need medication
- **For children who need them**, multimodal (Beh and Pharm) interventions produce (1) better effects acutely, especially in impairment, with lower doses, (2) lasting behavioral effects if medication is withdrawn, and (3) are strongly preferred by parents and teachers to medication alone and thus more likely to be utilized in the long run
- There are large **individual differences** in response to behavioral and stimulant treatments
- There are few studies of dose effects and sequencing effects
- There are few studies of long-term effects of behavioral and combined treatments

Clinical Recommendations for ADHD

- Focus on impairment in daily life functioning rather than symptoms and monitor impairment to monitor treatment effects
- Depending on severity, **start with behavioral treatment** and add medication when impairment is not minimized and parents prefer medication or resources limit more intensive behavioral treatments
- Dose meds low (**not optimally**) so as not to remove need for behavioral and educational treatments
- Minimize lifetime dose of medication
- Treat for settings and domains of impairment
- Use 12-hr evening and weekend meds only when necessary
- Try all children on both common forms of stimulant
- Stay in regular contact with family to monitor both behavioral treatments and medication--**chronic condition model of treatment**
- Start psychosocial treatments early and continue--reading example
- Interventions need to be feasible for and palatable for families so they will be maintained in the long run
- Effective treatment requires systems cooperation (e.g., collaboration between families, schools, mental health clinics, primary care)
