

Early Intervention for ADHD: Targets, Settings, Methods, and Mechanisms

Intervening Early: Progress and Opportunities in Child Service Settings

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ADHD: Importance to Professionals

Prevalence: 5% of population

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 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 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**

Summary: What to Measure in Intervention Studies

(Pelham, Fabiano & Massetti, JCCAP, 2005)

- **Measure symptoms with parent and teacher rating scales rather than interviews**

- Issue: Extend to laboratory measures of cognition and/or neurobiology?

- **Measure functional impairments in key domains**

- Issue: Cost effective vs. gold standard measures

- **Measure putative mediators and moderators of change (e.g., parenting, peer relations, academic functioning) initially and throughout intervention**

- Issue: Extend to laboratory measures of cognition and/or neurobiology?

- **Overarching issue: incremental costs of measurement for intervention study**

Why Is it Important to Intervene Early with ADHD?

Severity of Problems Across Situations

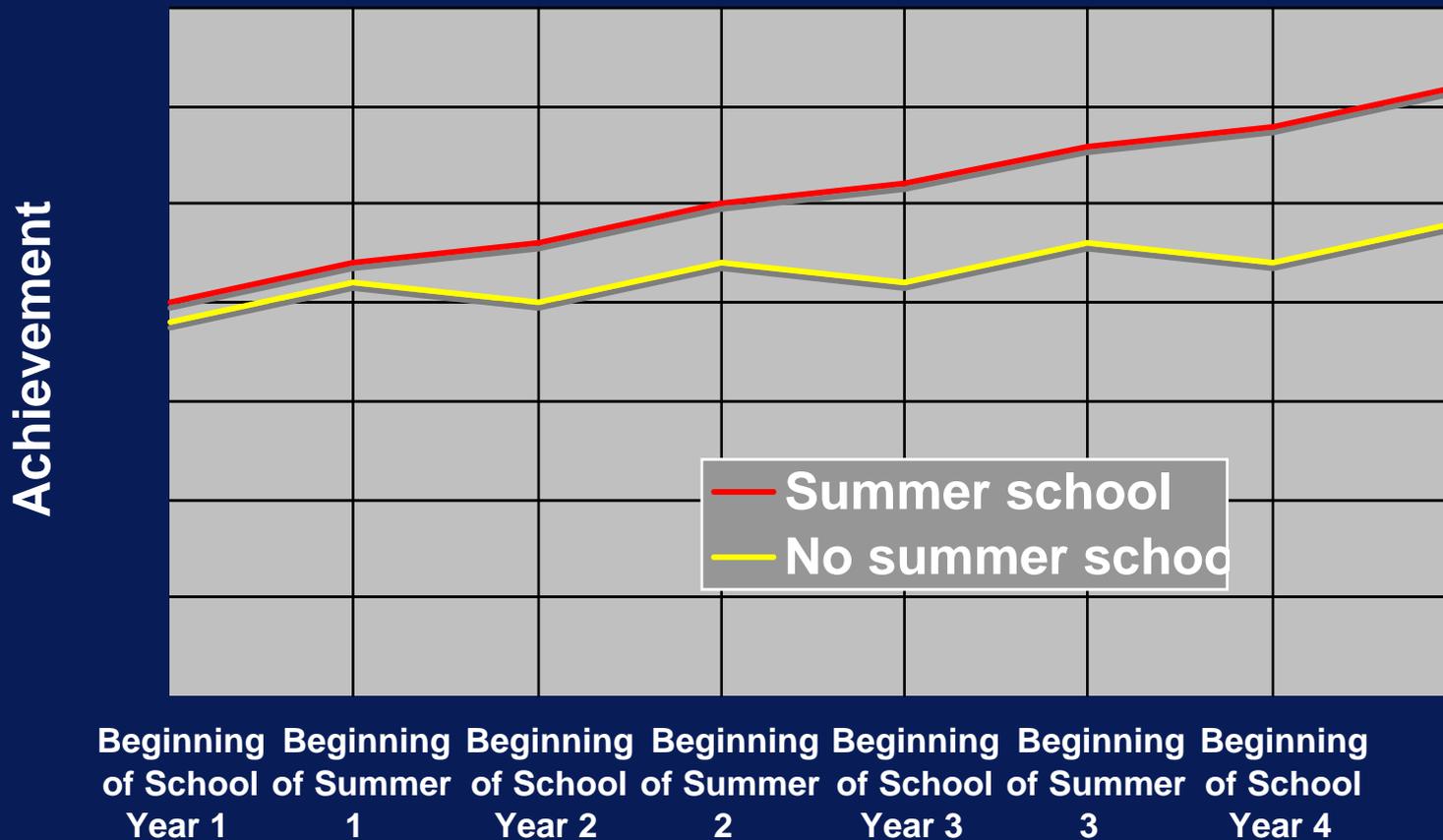
- 2 negative interactions per minute with teachers or peers in school
- 1 negative interaction per minute with parents in the home
- 1 negative interaction per minute in peer settings

Severity of Problems Across Situations

- Estimate how many hours per day children are involved with parents, teachers, and peers and do the math
 - Approaches 500,000 negative interpersonal interactions annually for typical ADHD child
 - Potent learning history to overcome
 - Each year, another 500,000 occur if no intervention
 - Highlights need for early and likely intensive intervention
- Analogous to intervention for reading problems

Hypothetical Changes in Achievement over Time for Low Achieving Children as a Function of Summer School

(Adapted from Cooper et al, SRCD Monograph 2000)



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

Total Annual Incremental Costs Per Child Across Sectors

(Pelham, Foster, & Robb, 2007)

Health and Mental Health \$ 2,636

Education \$ 4,900

Crime and Delinquency \$ 7,040

Total \$14,576

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

Annual Costs of Childhood/Adolescent ADHD

(Pelham, Foster, & Robb, 2007)

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

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?

Evidence-Based Treatments for ADHD

(1) Behavior modification

175 studies in classroom, home, and peer settings

(2) CNS stimulant medication (same settings)

>twice as many studies

(3) The combination of (1) and (2).

>25 studies

Most studies are crossover studies; almost all short-term (few months of treatment); only a handful are early interventions

Median Effect Sizes for Behavioral Treatments with ADHD Children (Fabiano et al, under review)

- Between Group Studies (N=20): **.78**
- Pre-post studies (N=25): **.69**
- Within Group Studies (N=17): **.4.2**
- Single-Subject Designs (N=101): **3.8**
- Large range of effect sizes across studies
- Effect sizes larger when treatment implementation is ensured
- As with medication, most studies are not RCT and represent acute effects, although some assess and demonstrate maintenance of effects, including the MTA

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.

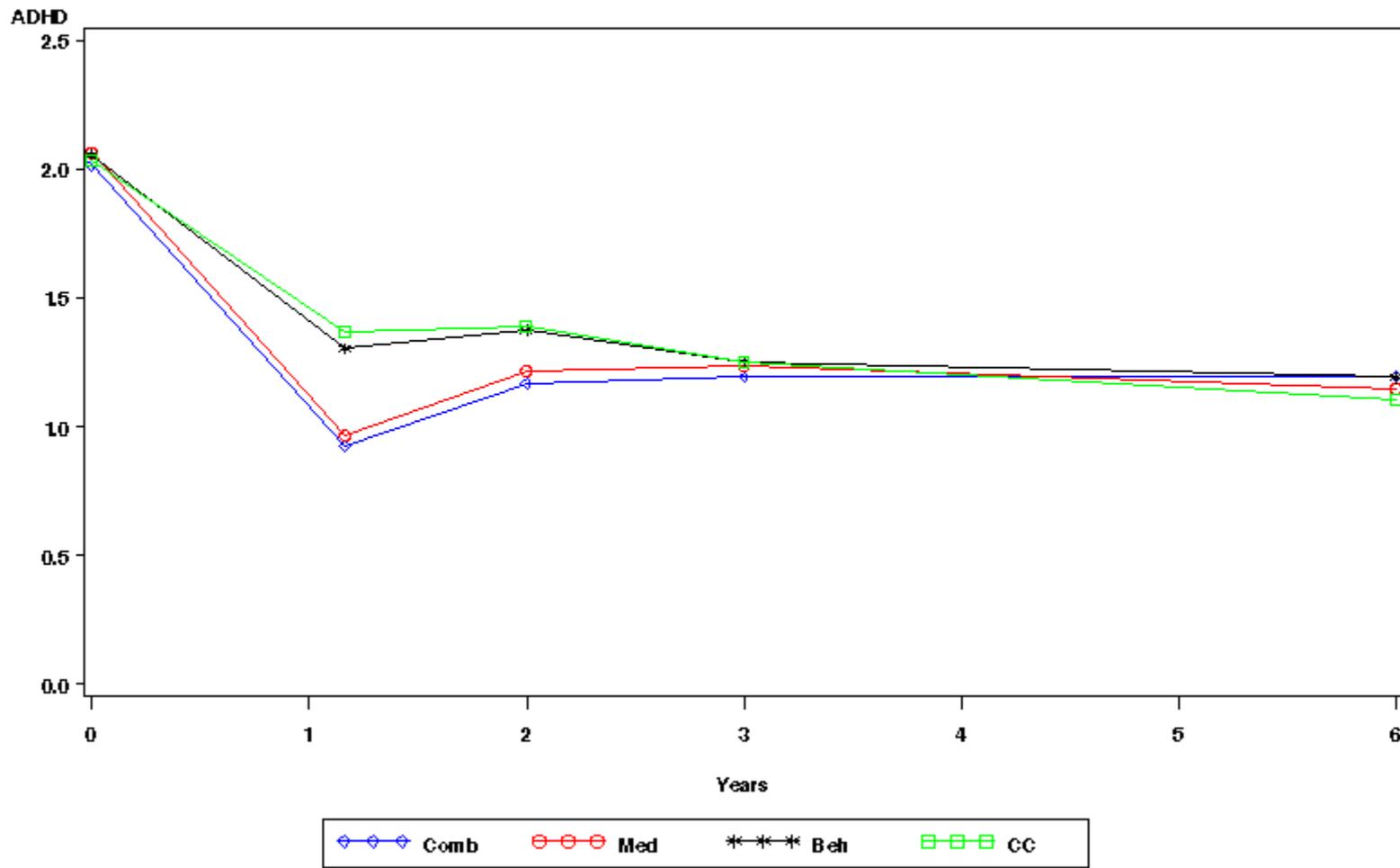
RECOMMENDATION 2: The treating clinician, parents, and the child, in collaboration with school personnel, should specify appropriate **target outcomes** to guide management.

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

Despite the Evidence, There is Controversy about which Treatments Should be Used for ADHD

**The MTA Study has resulted in
widespread agreement amongst
psychiatric professionals, ADHD
experts, pharmaceutical companies,
media outlets, and advocacy groups
that medication is the treatment of
choice for ADHD.**

Average ADHD Over Time for All Subjects by Treatment Group



Our Recent Program of Research: Questions the MTA Did Not Answer

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?

Do these questions have different answers for early intervention, elementary schools, and middle schools?

These are the questions that families, practitioners, and educators face daily, but they have not yet been studied.

Limitations of Pharmacological Interventions When Used Alone

- 1) Rarely sufficient to bring a child 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) Potential serious adverse effects in growth and substance use (data controversial)

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? IS IT SAFE FOR EARLY INTERVENTION?**

Components of Effective, Comprehensive Treatment for ADHD

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

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

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, divorce, and disturbed parent-child relationships
- Parenting styles characteristic of ADHD parents predict long term negative outcomes
- These are transactional processes leading to ever greater dysfunction
- Parenting mediates most negative outcomes and needs to be the main focus of intervention
- No evidence that medicating the child affects these factors

Health States from CSQ

(from PALS mothers)

- Computed health states using the CSQ analogous to those from HRQoL (EQ-5D Group)
- **29%** of mothers of ADHD kids had lifetime health state scores (QALY) = $-.67$
- **31%** had QALY = $-.72$
- Only **8.6%** of control mothers had QALYs this low
- These scores are equivalent to scores for major depression, colitis, diabetes, asthma, migraine, ulcers, and stroke
- Only **2%** said ADHD child did not interfere with daily life activities (vs. **50%** of control mothers)

Caregiver Strain Questionnaire (mother report lifetime-PALS)

	ADHD	Control
Objective caregiver strain	28.1 (10.5)	14.1 (5.6)
Internalized subjective strain	19.7 (5.4)	10.4 (5.5)
Externalized subjective strain	10.3 (2.7)	8.4 (2.3)

Significant group differences ($p < .01$) on all scales

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)

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)

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 during initial assessment based on child's impairment across settings and times (do not assume 24/7 medication)

Use at minimal rather than maximal effective dose

Continue for as long as need exists (typically years--defined by annual trials to adjust dose and evaluate continued need)

Plan for possible emergent iatrogenic effects

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 insufficient response, whether to (a) add the other modality or (b) increase the intensity of initial modality

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

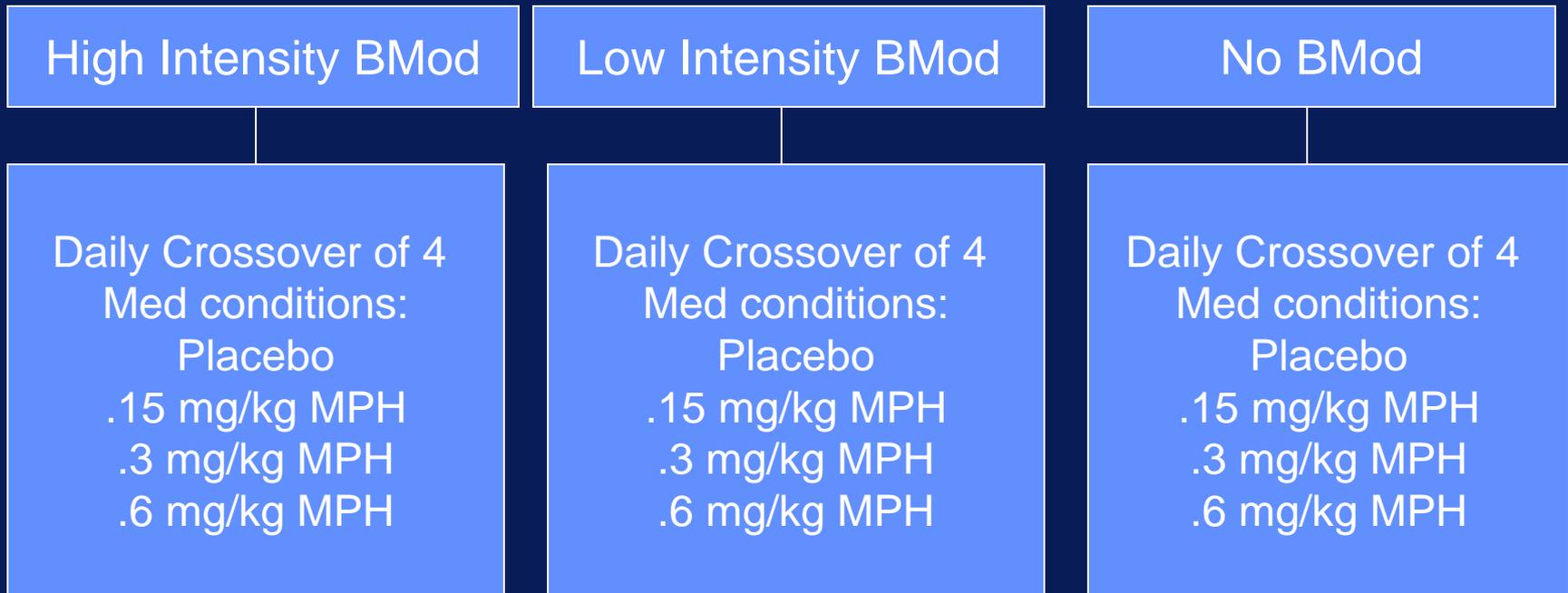
3 Behavioral Modification conditions: No behavioral treatment (NBM), low-intensity (LBM) treatment, and high-intensity (HBM) treatment (BM), varying triweekly in random order by treatment group

3-4 days per medication X Bmod condition.

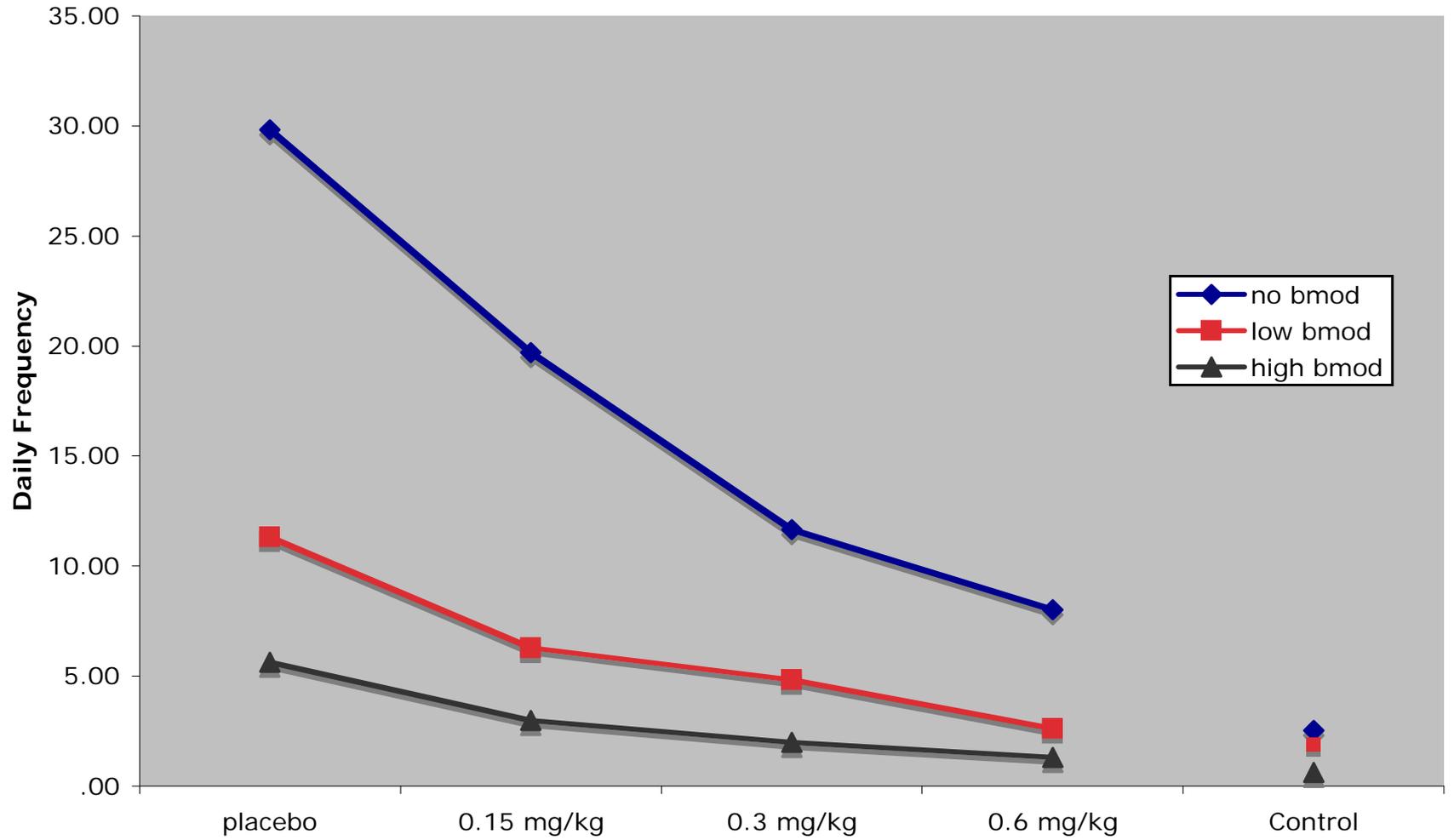
NonADHD comparison group (24/summer).

Comparative and Combined Treatments for ADHD

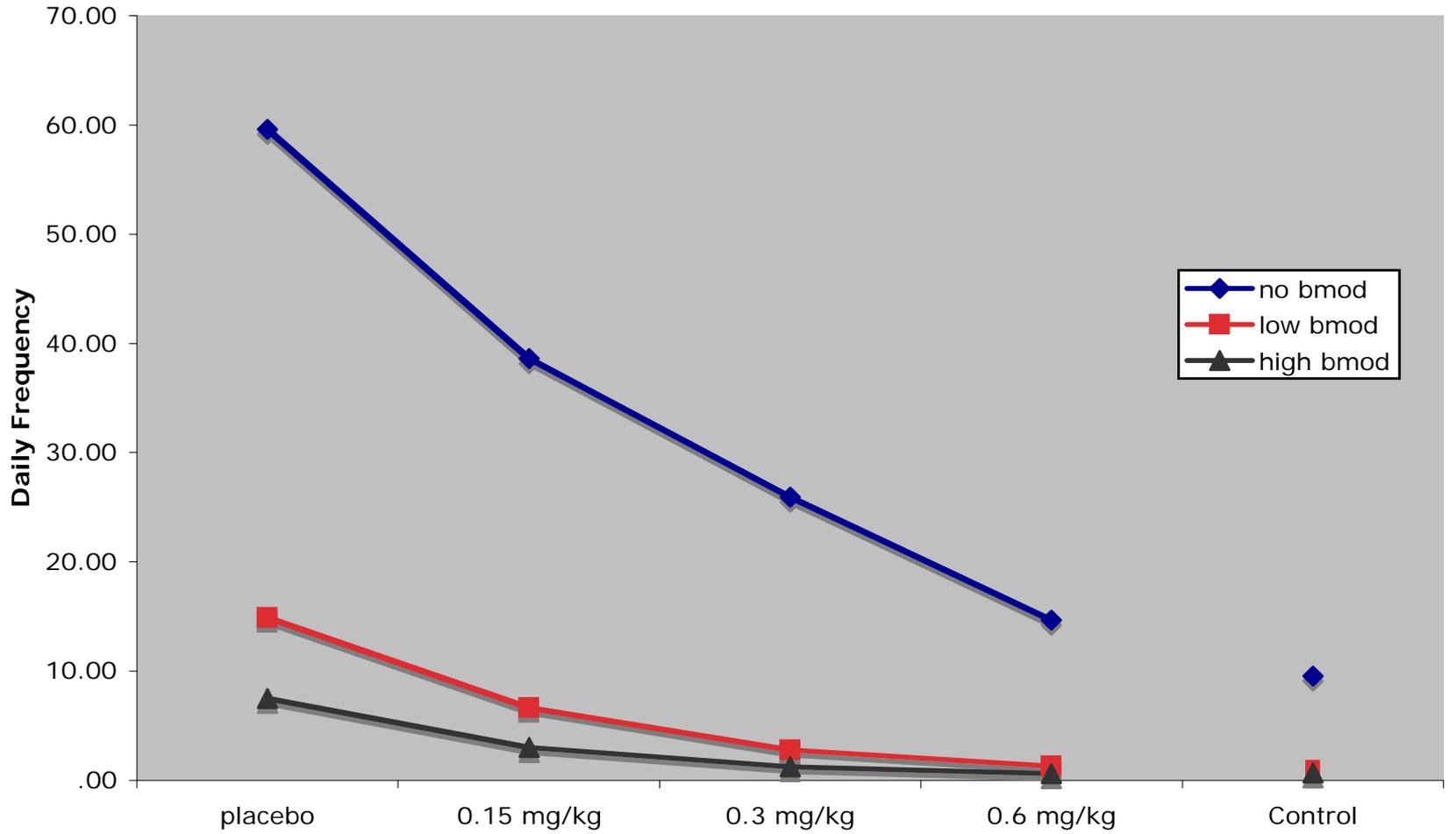
3, 3-week Behavior Modification conditions assigned randomly:



Noncompliance



Classroom Rule Violations



Limitations

- Analogue setting--brief treatments
- All children's parents received parent training across all conditions
- 75% of children previously medicated
- Results did not interact with age but there were relatively few younger elementary aged and older elementary aged children
- What if start with behavioral treatment in the natural setting? Would everyone need medication?

Study 2 Design

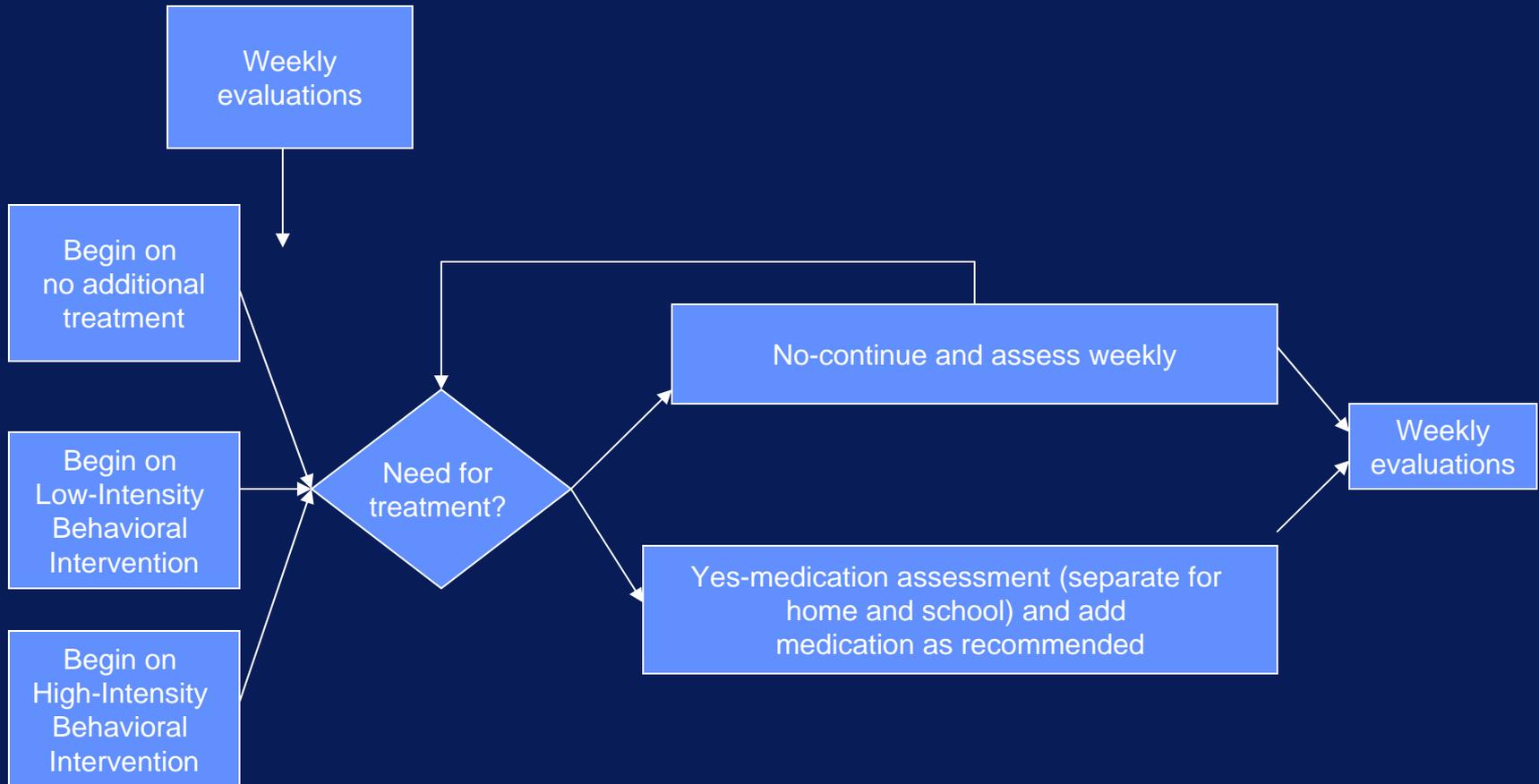
128 participants from the Study 1 were randomly assigned to one of three groups for follow-up treatment:

High behavior modification consultation
(HBC; N=44)

Low behavior modification consultation
(LBC; N=43)

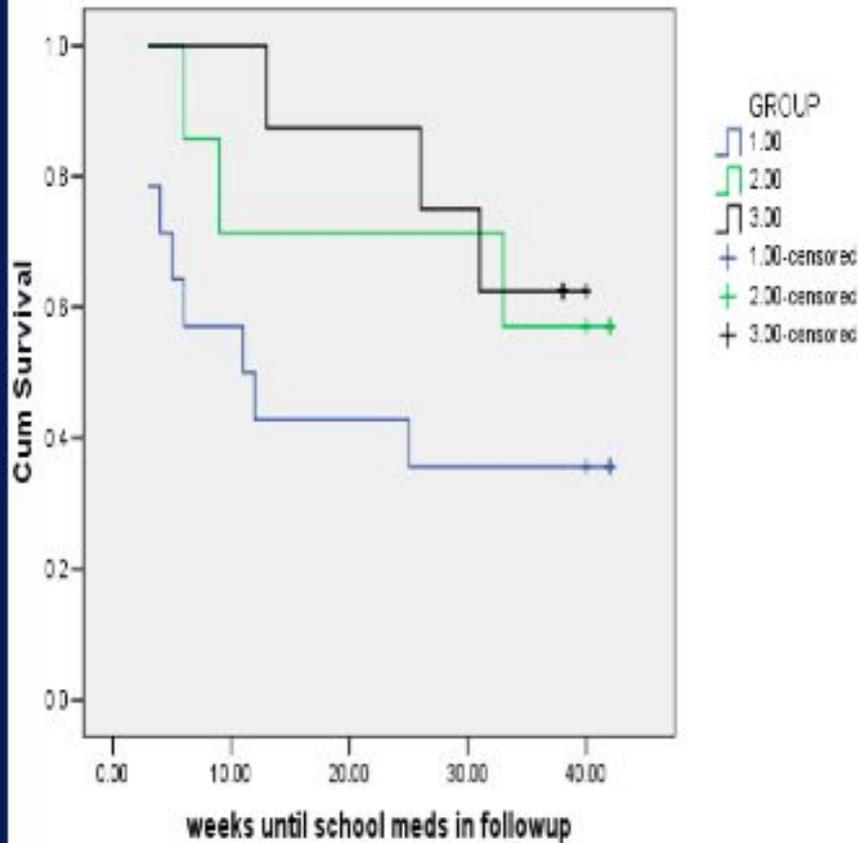
No behavior modification consultation
(NBC; N=41)

School Year Follow-Up

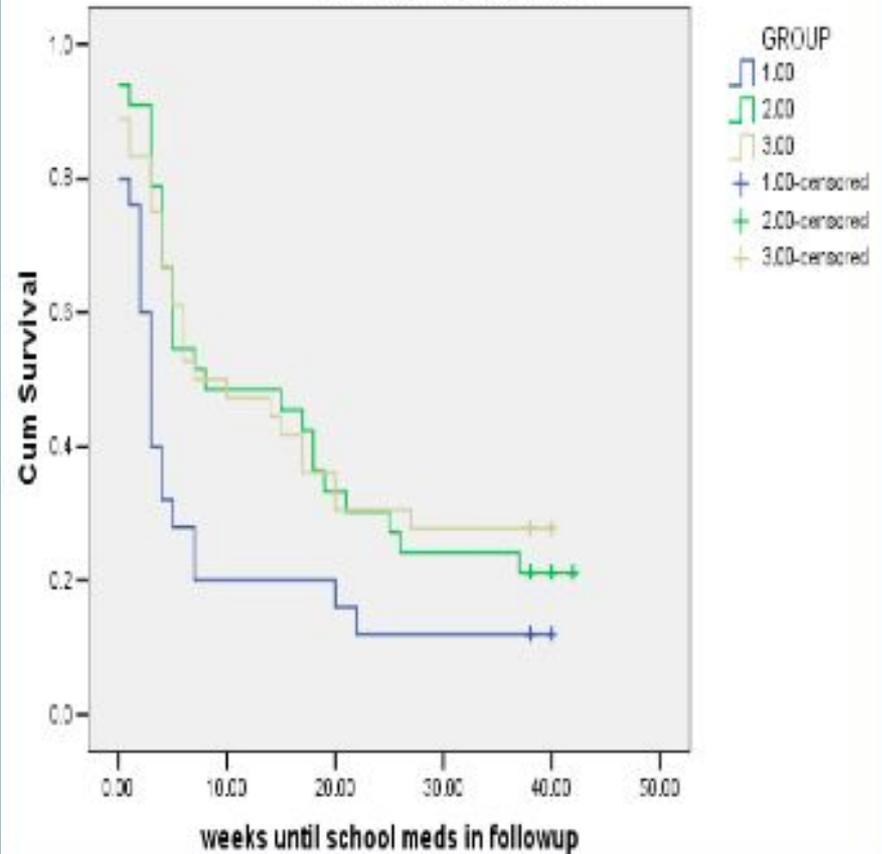


School Survival Curves

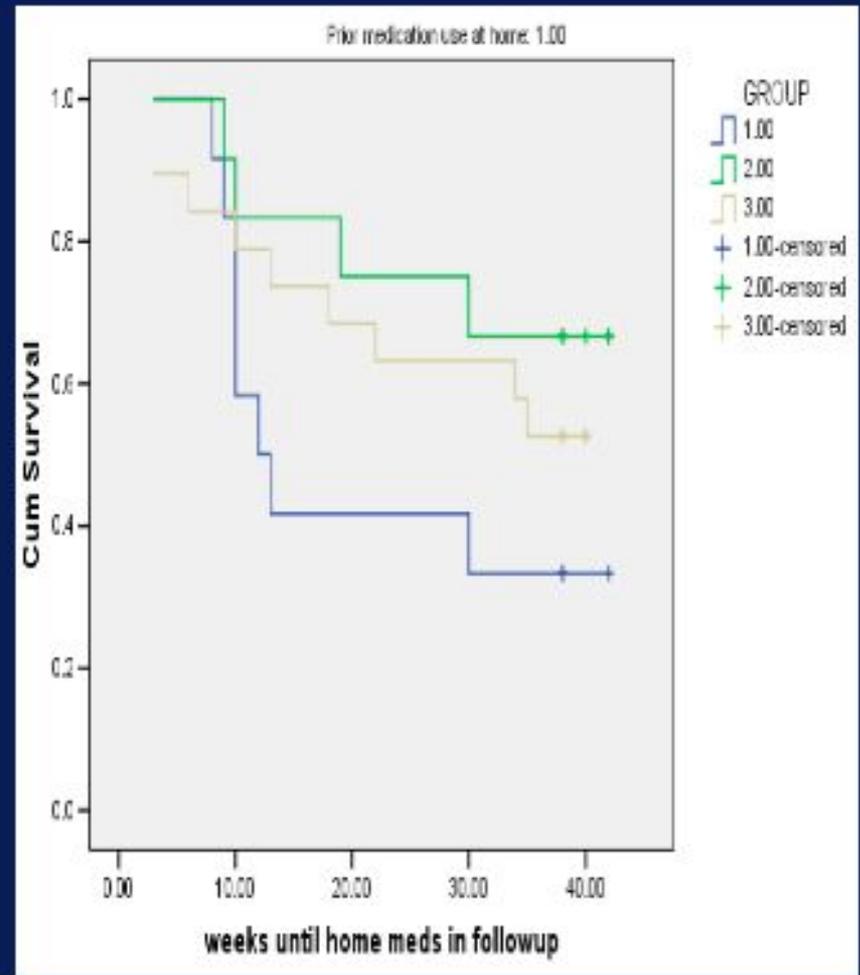
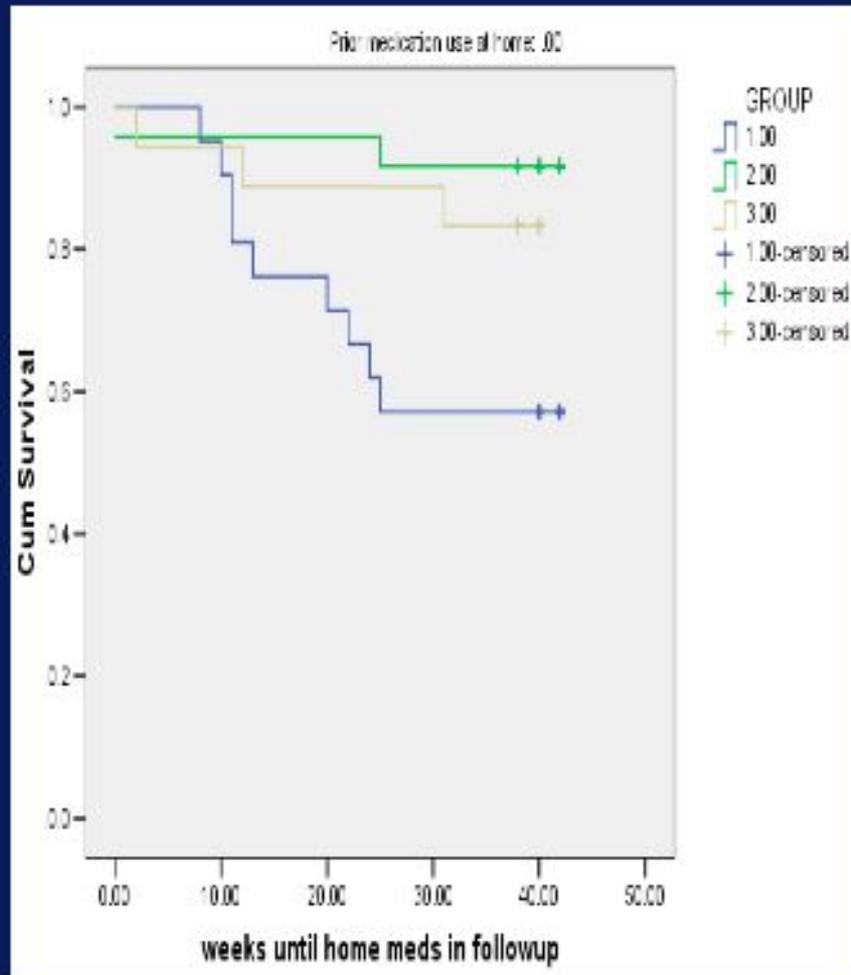
Prior medication use at school: .00



Prior medication use at school: 1.00



Home Survival Curves



Limitations

All children had received both medication and behavior modification in the summer (Study 1); Medication use prior to STP (75% of sample) strongly predicted later medication use at school and home

Both consultation groups ended up receiving the same, low intensity behavioral treatment.

Treatment was not provided adaptively

Results did not interact with age, but there were relatively few young children and therefore low power to detect

Could these strategies prevent need for and use of medication in young, medication naïve ADHD children over a long time period and is more flexibility needed in the behavioral strategies?

**Study 3:
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**
- **As in previous study, 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 Groups

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)

6-week summer treatment program including intensive peer-group social skills and sports skills training, and academic supplement with phonological awareness training component

Saturday program during academic year to extend the summer program interventions

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).

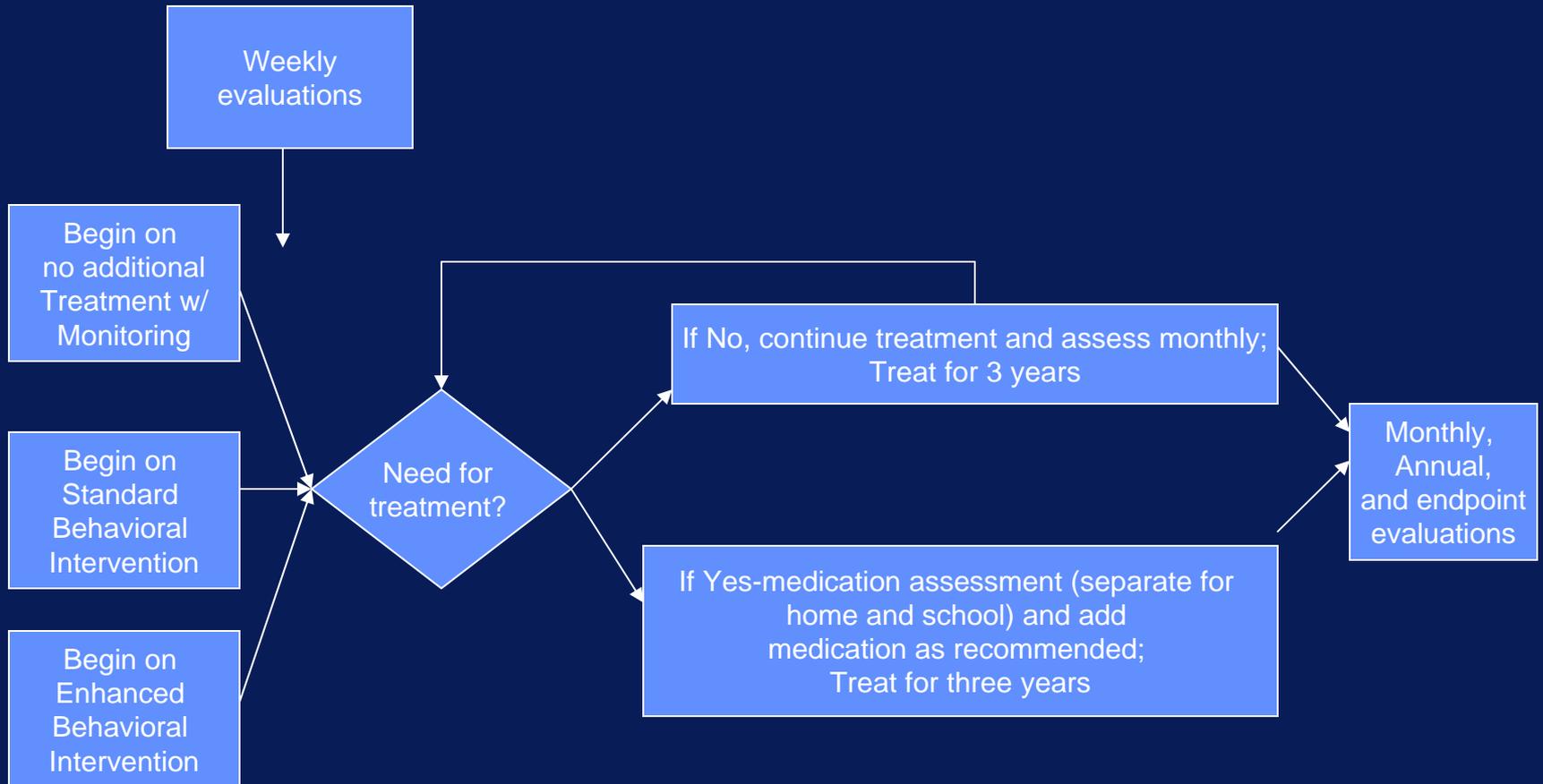
3 initial meetings with teacher to establish program
+ up to 4 individual sessions per year

Weekly group social skills training conducted
along with initial 12 parent training sessions.

Monitoring Group

Treatment as usual plus same monitoring
Medication as needed as in other groups

Design



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

Mediators and Moderators

Family SES and ethnicity

Parenting effectiveness and feelings of self efficacy in the parenting role (PSOC), maternal ADHD (CAARS) and depression (BDI), and treatment acceptability (Kazdin, 1984).

Child severity, comorbidity, and impairment (parent and teacher DBD ODD and CD scores, child IQ and achievement, peer relationships)

Baseline parental attitudes toward medication

Baseline measures of behavioral treatment use

Treatment fidelity and cumulative behavioral treatment

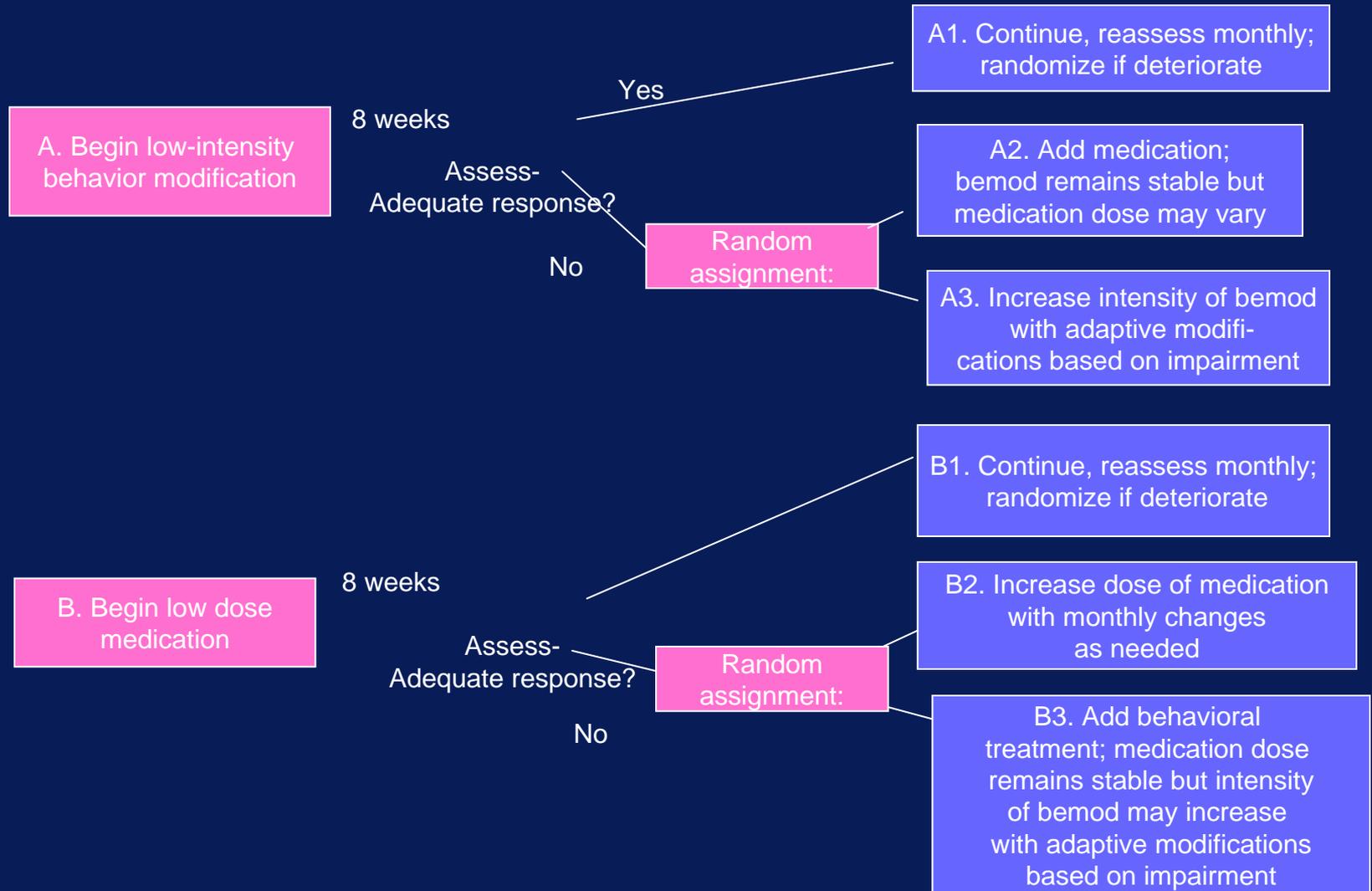
Analysis and Specific Aims

- 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

- Does not address utility of low dose medication as first line
- Does not evaluate escalation of intensity by adding different modalities
- If insufficient response, is it better to increase intensity of initial modality or add the other modality
- How do such strategies influence outcomes and costs

Study 3 Design



Conclusions from Series of Studies

- **Dose** of treatment is important in comparative and combined studies of treatment for ADHD; study results cannot be understood without understanding dose effects
- **Sequencing** of treatments is a critical decision but has not been studied systematically with the exception of our follow up study and ongoing studies; the completed study shows that providing behavioral treatment first reduces need for medication
- **Parents strongly prefer** psychosocial approaches--alone or in combination with medication. Preference is important in part because it affects adherence to long-term regimens.
- 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
- Our ongoing study is the only one addressing these questions in young ADHD children in an early intervention model

What Can Early Intervention Studies Tell us about Underlying Psychopathology?

- **Association between baseline characteristics (moderators) and trajectories over time and ongoing measurement of putative mediators**
 - E.g., environmental, genetic, cognitive
 - Could improve diagnostic precision and understanding of disorder
 - Could explain variability in outcomes
 - Could be used to tailor treatment and improve outcomes
 - Baseline informs about status prior to intervention

Issues to Consider

- **Reliability of measurement limits associations**
- **Lack of knowledge of underlying mechanisms may limit validity and utility (e.g., cognition, biology and ADHD)**
- **N may need to be at least as large as the intervention study**
 - E.g., MRI on 10 index cases and 10 controls won't tell us much about prediction and trajectory
- **Prevention studies need to have sufficient deviance to yield cases and associations**
- **Nature, intensity and chronicity of intervention--both manipulated and as-usual**
- **Long-term studies provide most relevant information**
- **Expense of biological, cognitive, and other measures as add-ons to treatment--funding caps need to be increased for this research**

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