Effective Use of Medications: What We Know (or at least believe)

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Medication Use Considerations

Dramatic, 4-10 fold Increases in Uses of All Medications in last 10 years

- **Stimulants (80% in primary care)**
- **SSRIs (40% in primary care)**
- **Atypical Antipsychotics (20% in primary care)**
- **Mood stabilizers (15% in primary care)**
- **75% of all meds “off-label” across all of pediatrics**
- **Off-label does not mean inappropriate**
- **FDA mandates to conduct testing in children**
- **Abundant new information**

Medication Knowledge

Scientifically Supported Treatments :

- **ADHD: 7 medications (3 stimulants, 2 TCAs, buproprion, atomoxetine)**
- **Depression: 2 medications (SSRIs)**
- **OCD: 4 medications (SSRIs)**
- **Anxiety Disorders: 2 medications**
- **Conduct disorders: 1 medication**
- **Autism: 2 medications**
- **Tourettes syndrome: 2 medications**
- **Psychosis: 3 medications**
- **Bipolar Disorder: 1 medication**
- **Aggression: 2 medications**

Comparisons & Combinations: What Works?

- **Multi-site Trials for Testing Combined Treatments - generalizability across settings**
  - **MTA Study: Combined (Meds+BT) may be slightly better than Meds only; Meds-only generally better than Behavior therapy only**
- **Studies In Progress**
  - **Depression TADS (SSRI vs CBT vs Combo)**
  - **OCD: CBT vs. SSRI vs. Combo (Foa & March)**
  - **ADHD w/Anxiety: SSRI + methylphenidate (RUPP)**
  - **Bipolar w/Depression: mood stabilizer +/- SSRI**
- **Multisystemic Therapy, Therapeutic Foster Care, Functional Family Therapy**

Medication Side Effects

- Concerta, Adderal, Metadate, Ritalin (stimulants): Appetite, sleep, weight/height effects (temporary)
- Prozac, Luvox, Paxil, Zoloft, Celexa, Remeron (SSRI's): agitation, sleep disturbances, drowsiness, headache, GI sx, disinhibition
- Risperdal, Seroquel, Zyprexa, Geodon, Clozaril (AAMs): excessive weight gain, hyperglycemia, ?diabetes, sedation, TD, extrapyramidal sx
- Clonidine, Guanfacine (alpha 2 agonists): sedation, hypotension
- Lithium, Tegretol, Depakote (mood stabilizers): tremors, nausea/GI sx, polycystic ovaries, liver abnormalities

Medication Problems

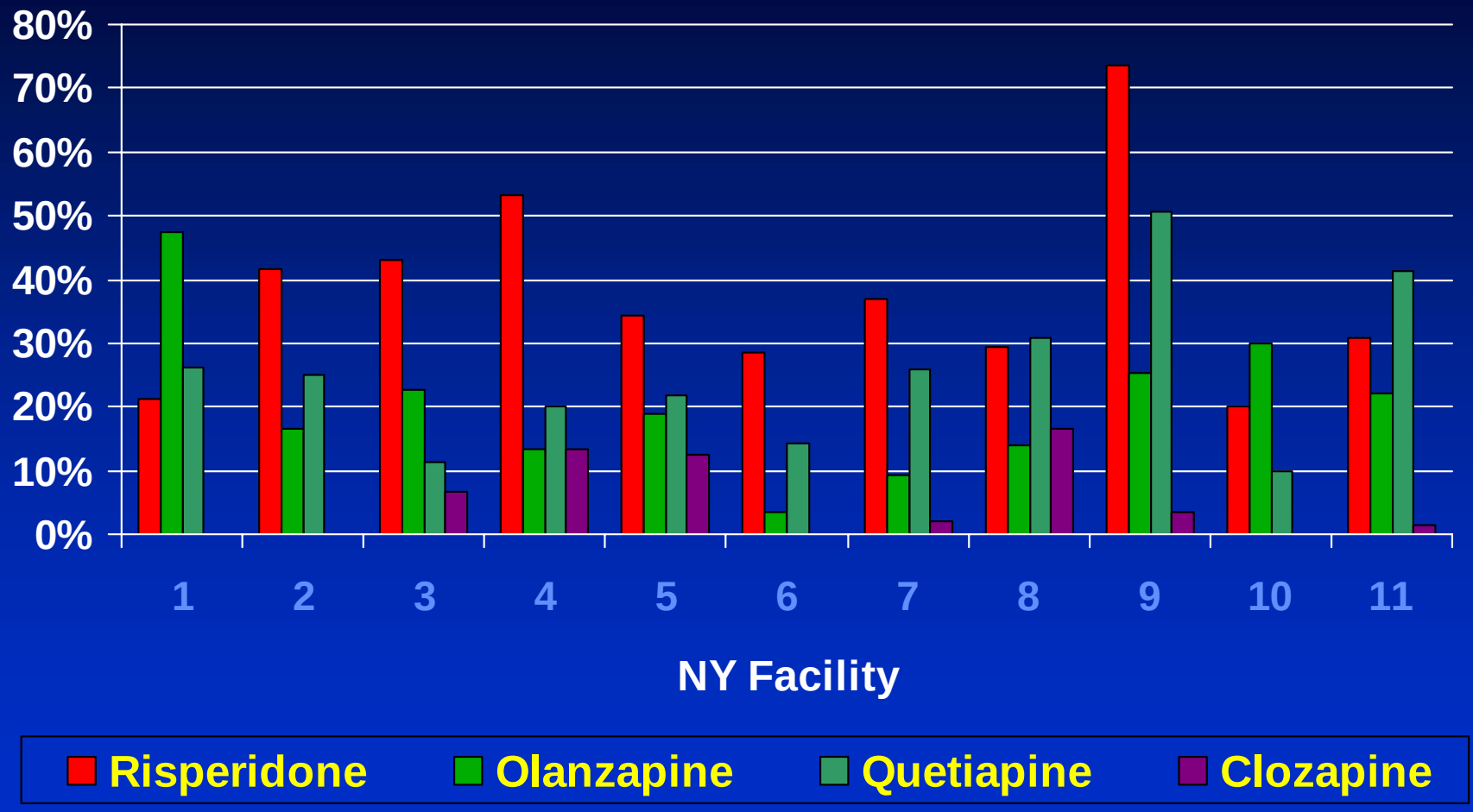
Problem Overview:

- **Too much new information: Physicians may have hard time keeping up**
- **Physicians' practices and clinical treatment needs are often far out in front of the knowledge base**
- **Lack of support for new practices (training,tools, failing to address obstacles, etc.)**
- **Old habits die hard: changing physician behavior is very complex**
- **Lack of public understanding of role of medications**

Critical Issues: Use of Psychotropic Agents in Children & Adolescents in Inpatient Settings

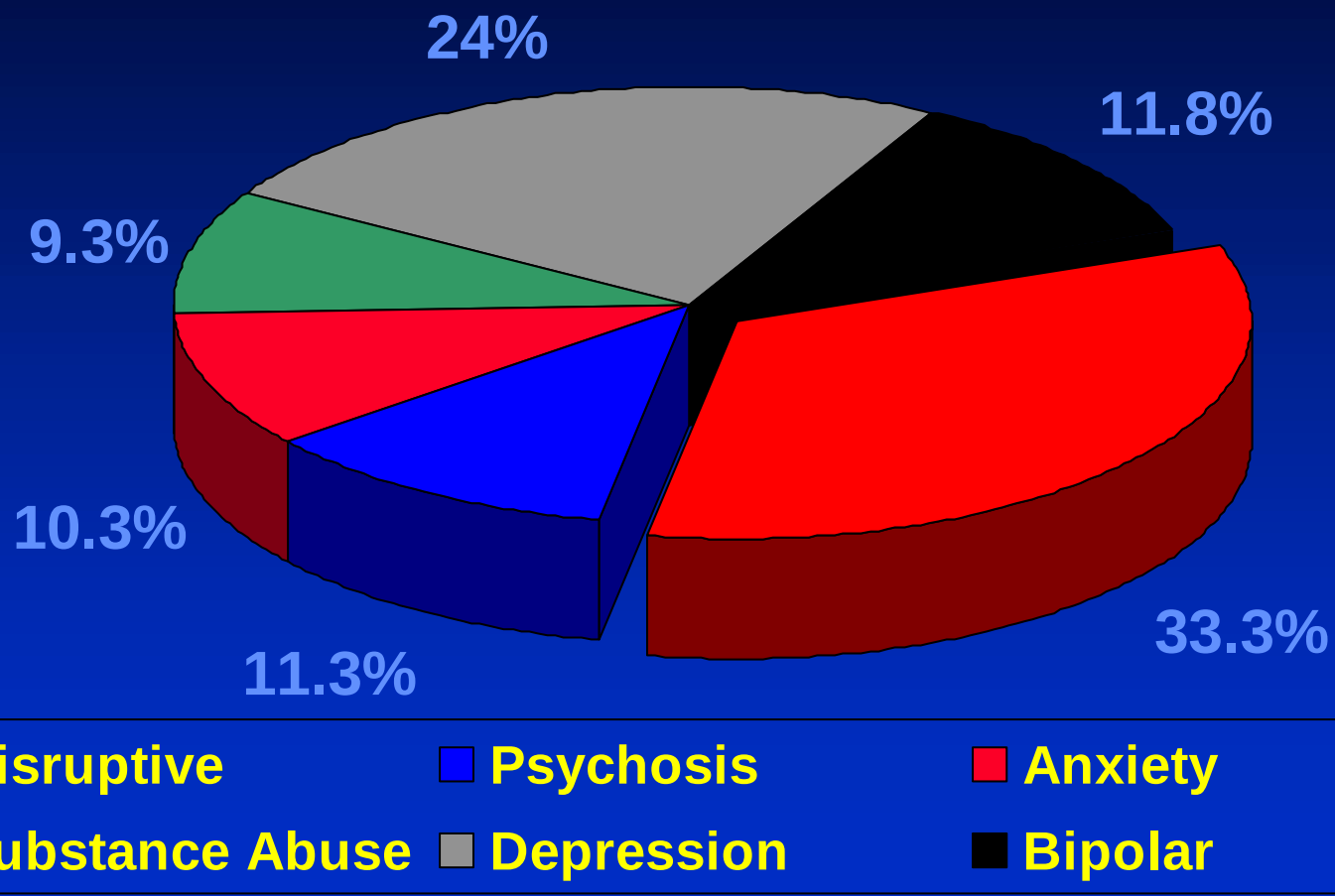
- Frequent use of off-label agents (e.g., atypical antipsychotics) for various conditions
- Frequent use of multiple medications
- Need for evidence-based treatment guidelines for treating aggressive youth with atypicals and other agents

Atypicals Used Varies Across Youth Inpatient Facilities



Sample of NYS-OMH Facilities March 2001 (N=450 Patients)

Diagnoses of Youths Treated with Antipsychotics



204 Diagnoses from a Sample of 100 Inpatient Charts (NYS-OMH)

What Physicians Say: Focus Group Results

- There are significant gaps between what physicians consider to be “best practices” and actual prescribing practices
- Physicians cite obstacles to enacting “best practices”
- Social and financial factors also influence prescribing practices
- Increased use of antipsychotics may correspond to efforts to decrease the use of physical and mechanical restraints on inpatient settings.
- Need for guidelines, tools, and aids for decision-making
- Efforts to disseminate and implement medication “best practices” must also address perceived barriers and methods to overcome them.

Influences on Provider Behavior

Patient & Family Factors:

- Stigma
- Adherence
- Negative attitudes
- Rapport, engagement

Provider Factors:

- Knowledge, training
- Self-efficacy
- Time pressures
- Fear of litigation
- Attitudes & beliefs
- Social conformity
- Lack of information

Systemic & Societal Factors:

- Organizational standards
- Staff support/resistance
- Staff Training
- Funding policy

Economic Influences:

- Compensation
- Reimbursement
- Incentives

Hierarchy of Evidence

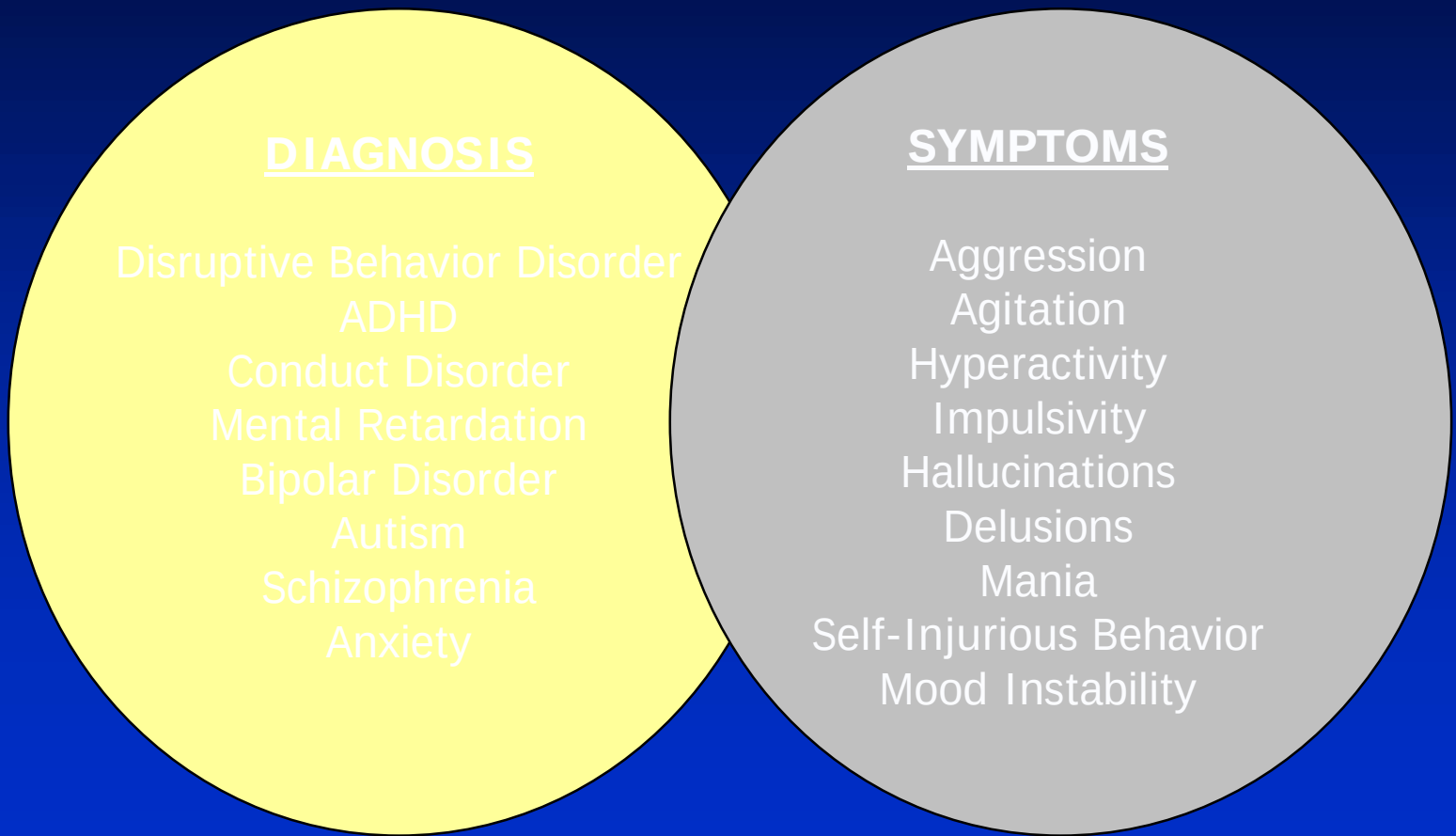
from Gregory Gray, M.D.

- ***Best*** – Systematic review of RCTs
- Individual RCT
- All or none case series
- Systematic review of cohort studies
- Outcomes research
- Systematic review of case-controlled studies
- Individual case-control study
- ***Worst*** – Expert opinion

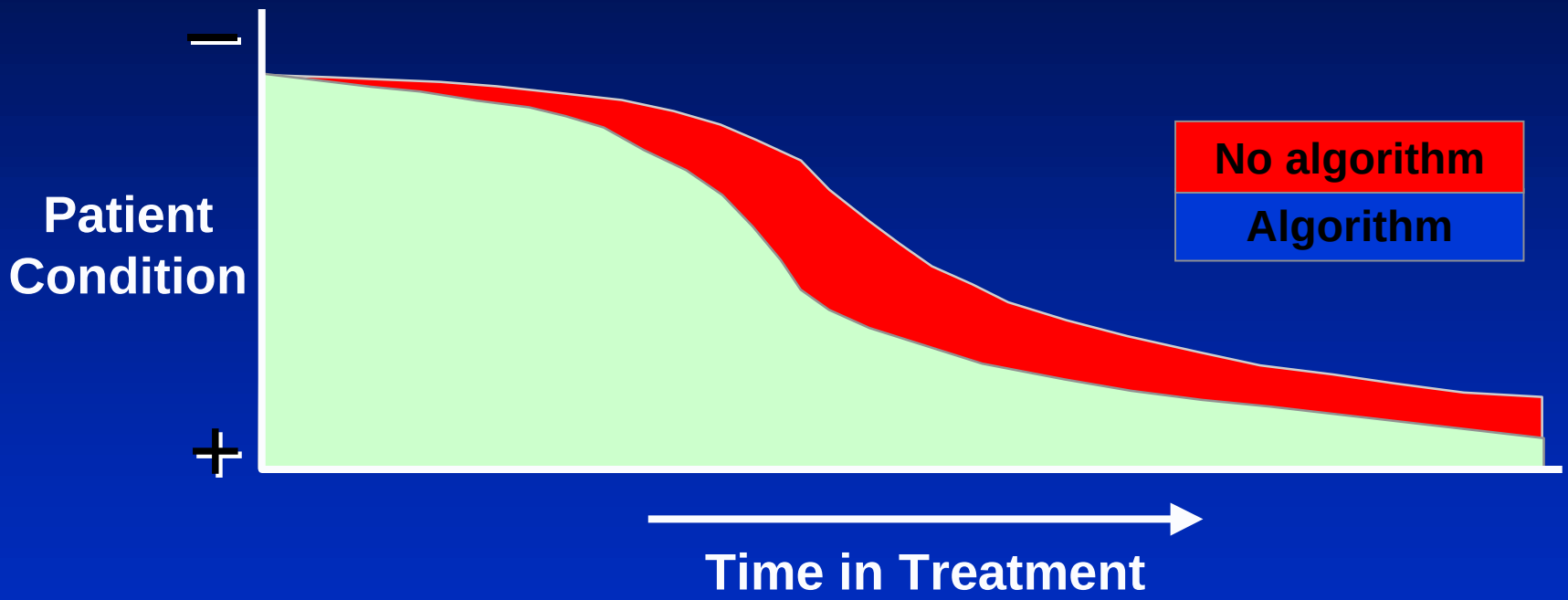
Medication Should Not Be a Substitute For:

- Parent training
- Behavior modification
- Appropriate educational curricula
- Appropriate school placement
- Adequate teaching skills
- Family treatment

Medications used to treat common symptoms observed across different diagnoses



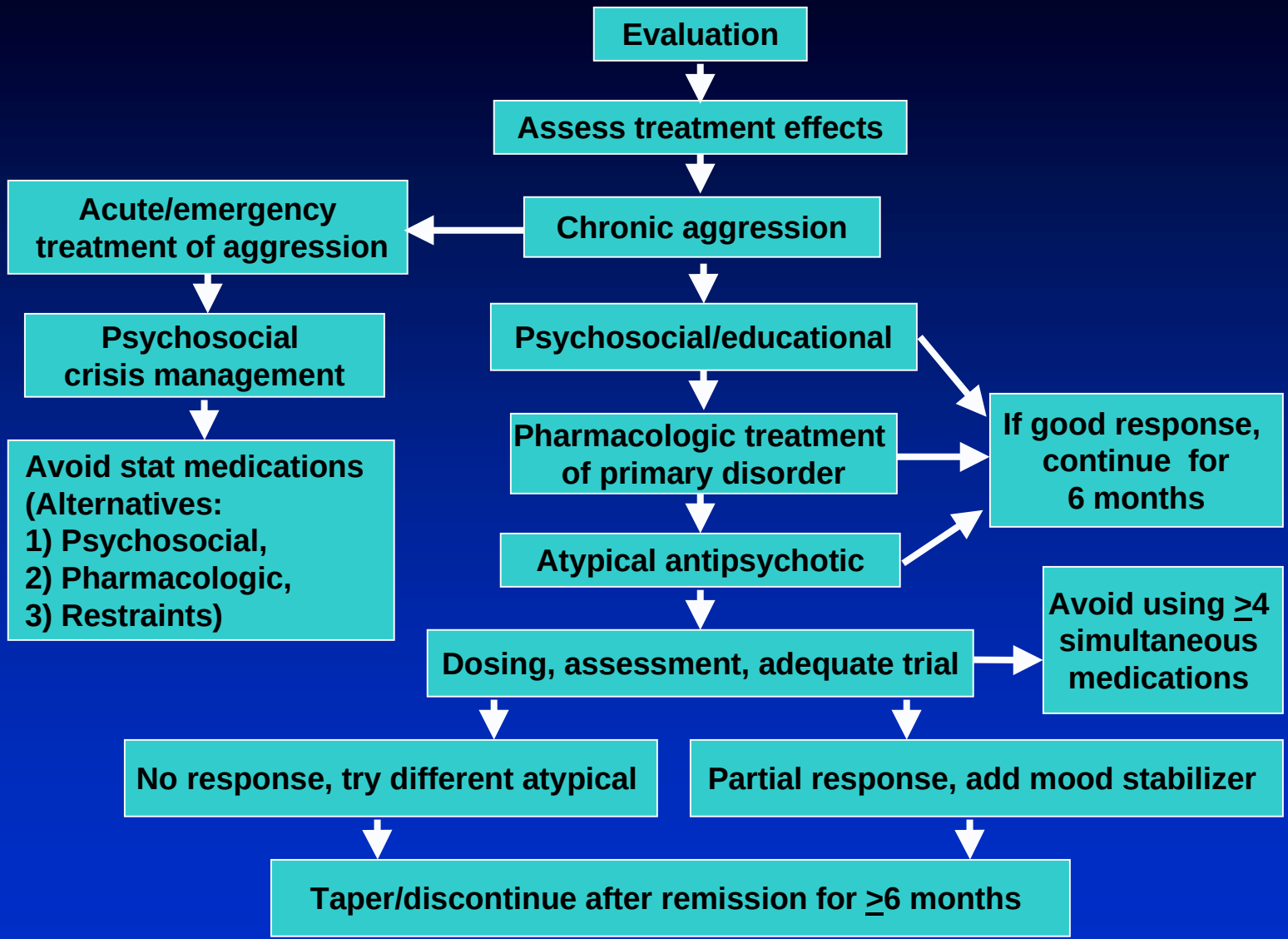
Potential Benefits of Algorithms: More Rapid and Thorough Response



Patient condition refers to combination of symptom severity and psychosocial functioning.
– = patient condition at initiation of treatment; + = improvement during course of treatment.

Rush AJ, et al. *J Clin Psychiatry.* 1998;59(suppl 20):73–84.

Algorithm for Treatment of Aggression in Children/Adolescents



General Considerations

- Every child with a well-diagnosed psychiatric disorder deserves consideration of adequate trials of appropriate medications
  - Stimulants work in up to 90% of children with ADHD
  - Other agents (SSRIs, AAMs) are effective for specific conditions
- Medications must be titrated; this requires close follow-up & clarity re: effects you want to see
- If a child does not respond to a medication, re-examine diagnosis, co-existing conditions, treatment, & adherence
- Medications should not be used as a substitute for necessary environmental modifications and psychotherapeutic approaches
- For maximum effect, medications should usually be used in combination with therapy, and may enhance therapy effects

Initial Evaluation Prior to Pharmacologic Treatment

- Comprehensive diagnostic interview with patient and parent/guardian
  - Contact prior treating physicians
  - Review treatment records
  - Identify other medications being taken
- Physical examination
- Appropriate laboratory studies

Diagnostic Principles

- The assessment of mental disorders requires evidence directly obtained from:
  - parents or caregivers
  - the classroom teacher (or other school professional)
- Evaluation of the child with a suspected disorder should include assessment for coexisting conditions

Assess Treatment Effects and Outcomes

Use standardized symptom/behavior rating scales with proven reliability and validity to measure severity/frequency of target symptoms (e.g., Modified Overt Aggression Scale)

- Prior to treatment
- At regular intervals throughout treatment
- During acute episodes
- When treatments are changed or discontinued

Treatment Principles

- Primary care clinicians should establish a treatment program that recognizes the mental disorder as a chronic condition.
- The treating clinician, parents, and child, in collaboration with school personnel, should specify appropriate target outcomes to guide management.

Nonpharmacologic Treatment of Primary Disorder

- Initiate nonpharmacologic treatment
  - E-B psychotherapy
  - Milieu/social therapy (family, school, friends, etc)
  - Educational Interventions
- Exact therapeutic approach will depend on diagnosis and individual circumstances

Nonpharmacologic Treatment of Primary Disorder

- Assess patient response
- Continue psychosocial and/or educational therapy even if pharmacologic treatment subsequently is initiated to manage disorder

Pharmacologic Treatment of Primary Disorder

- Choose appropriate pharmacologic agent for primary disorder
  - Accurate diagnosis vital
  - Anticipate potential drug interactions
  - Evaluate potential impact of side effects on individual patient
- Use monotherapy whenever possible to simplify
  - Assessment of treatment response
  - Assessment of side effects
  - Medication regimen

Pharmacologic Treatment of Primary Disorder

- Dosage
  - Initial dose should be low – “start low, go slow, stop slow”
  - Titrate dosage carefully
- Assess efficacy
- Monitor side effects regularly and systematically (with standardized ratings)
- If good response, continue for 6-12 months

Evaluating Medication Therapy

When using a medication as a first-line treatment:

- **If no response, try a second agent**
- **If a partial response, consider adding under selected circumstances**

Avoiding Polypharmacy

- Avoid using multiple medications simultaneously whenever possible
- Reevaluate regimen of patient who does not experience improvement while receiving multiple medications
- Consider tapering/discontinuing one or more medications if patient is on $\geq$ 4 medications without clear benefit

Tapering/Discontinuing Medications

- Consider tapering medications in patients showing remission of symptoms for 6-12 months or longer
- If tapering of dose is well tolerated, discontinue the medication

Effective Combined Treatments for Mental Disorders

- **Concurrent Medication**
  - Ideally, m**edication assessment should be begun after parents and school have begun therapy interventions**
  - Medication trial conducted to determine need and required dose to complement the therapy intervention
  - Cycle through medications in order of evidence-base (e.g., for ADHD first methylphenidate and amphetamine-based compounds, then atomoxetine, TCAs, before other drug classes (buproprion, clonidine, guanfacine)
  - Repeated annual trials to adjust dosages and determine continued need

Summary of Medication Management

- "Try it and see" approach unavoidable
- Ensure adequate dose and duration before changing meds or adding another
- Less is more. Avoid (but don't shun) polypharmacy
- Regular follow-up with physician who is expert in use of the meds
- Careful monitoring of side effects and therapeutic response, use of scales, diaries, and checklists, etc.
- If multiple drugs in combination have little effect, consider "wash-out" of all meds, starting over. Some meds may cause SEs that mimic psychiatric symptoms
- Beware over-reliance on previous labels/diagnoses

Child & Family Interventions to Increase Involvement in Medication Treatment

- Shared problem definition and prioritization, and control over process
- “I don’t put your child on medication, that will be your decision.”
- Tailoring to fit specific needs
- Respect of mutual expertise
- Encouragement of ventilation of concerns
- “Non-specific” therapeutic factors
- Engagement strategies

Discussion with Child and Family

- Discuss range of proven therapeutic options
- Explain positives and negatives of medication and other treatments to the family and youth
- Address stigma/misconceptions
- Assist family in arriving at a choice of treatment options. Encourage combined treatment options in severe cases or when one form of treatment has failed
- Determine target behaviors of concern to family and child with input from teachers and others
- Explain to child/youth that meds are not to control behavior, but to help increase self-control
- Encourage self-management, tracking of symptoms, education, and awareness of side effects

Important Clinical Guidelines/Issues-Home

- Before treatment begin by educating parents about disorder
- Give parents the data regarding prognosis and convince them that medication alone may not solve child's problem in the long run
- This information may be critical to “hook” parents into parent training

Adapted from W. Pelham, PhD

Rationale for a Combined Therapy and Pharmacological Intervention

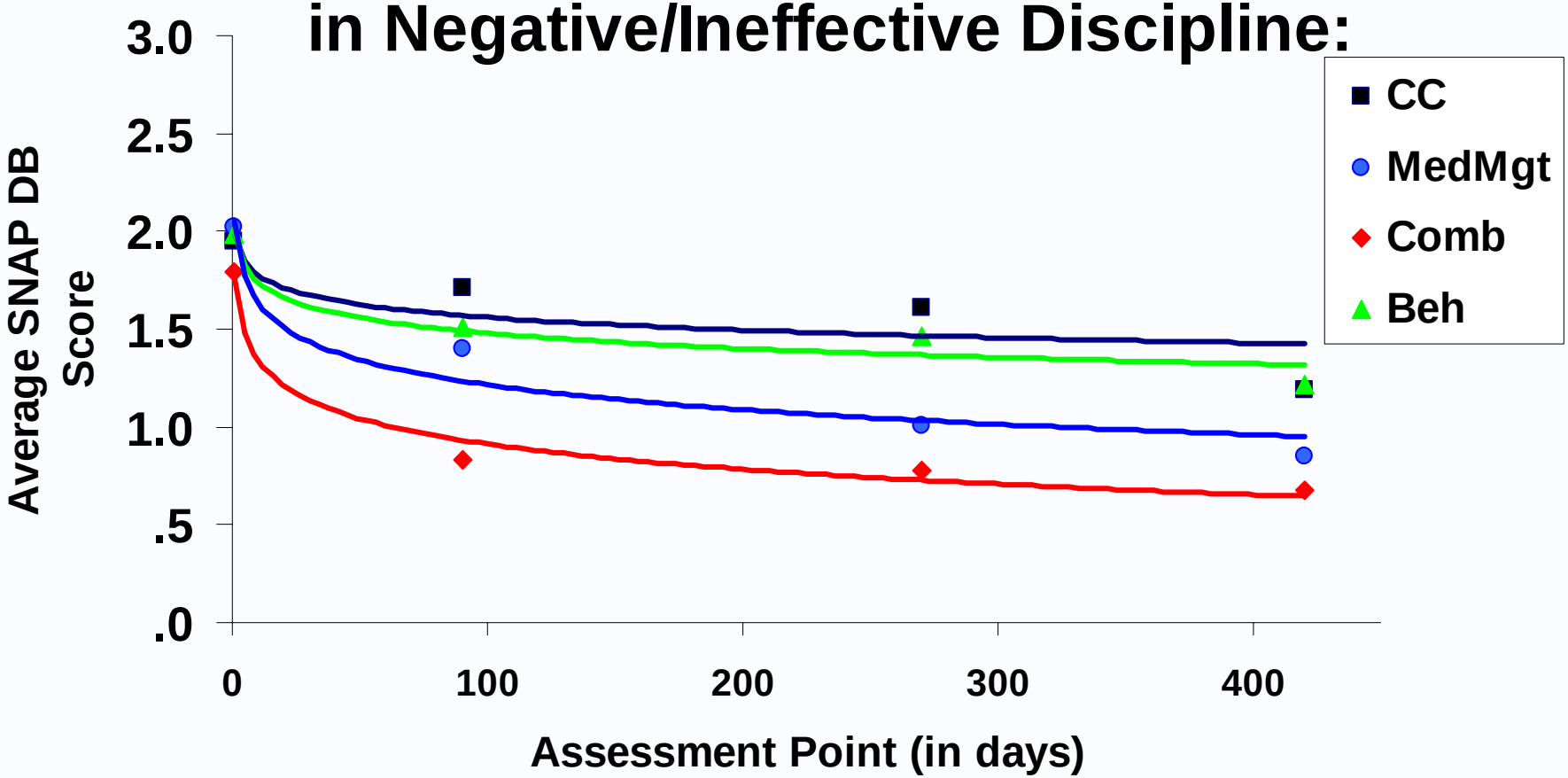
- The two treatments used separately have clear limitations and both fall short of maximizing response
- The combined intervention typically produces additive or interactive effects on many domains, thus bringing children closer to normalized functioning
- Behavior therapy more palatable to parents (and teachers)

Courtesy W. Pelham, PhD

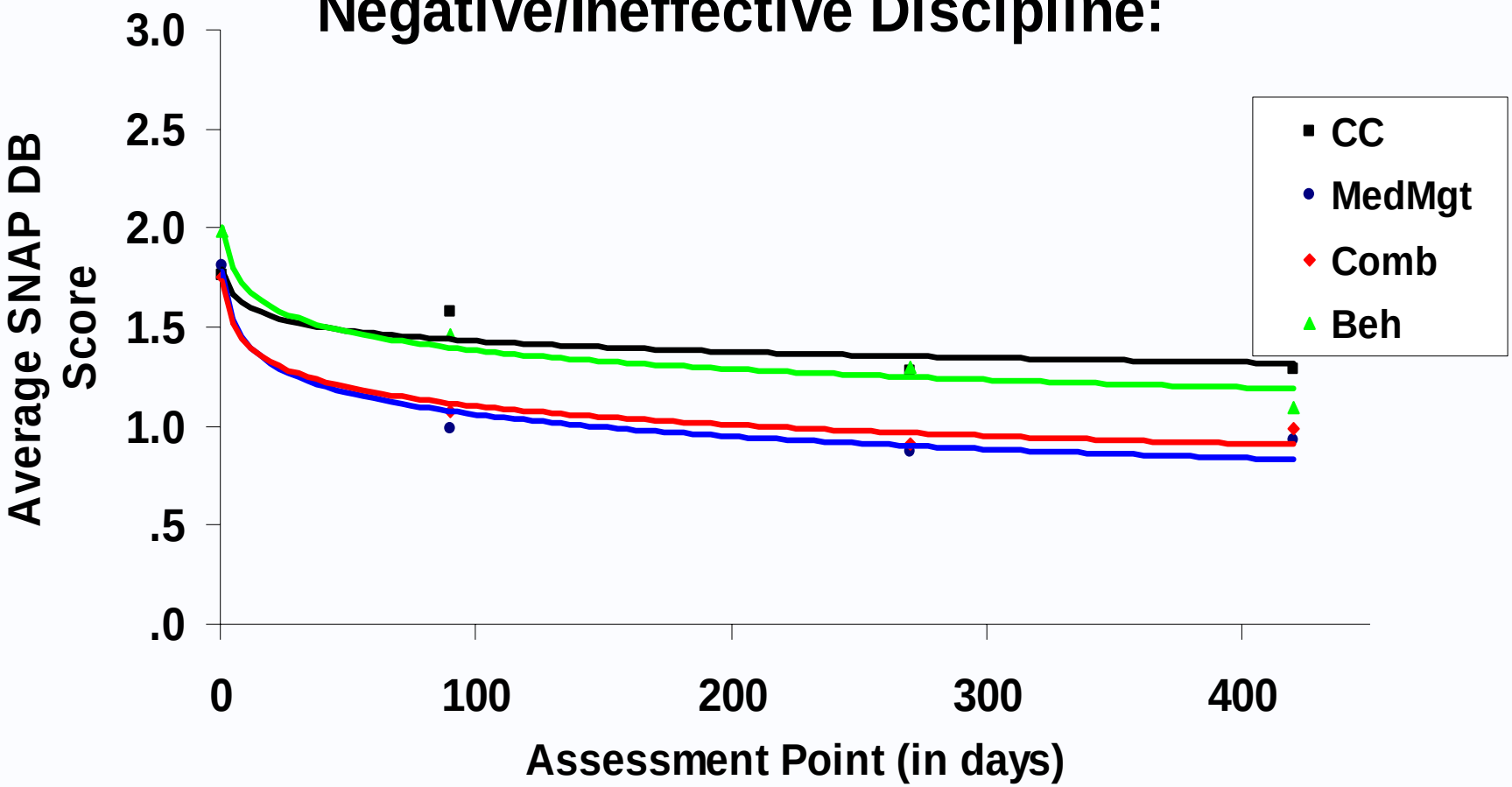
Rationale for a Combined Therapy and Pharmacological Intervention

- Maximal improvement may be reached in school both with a less complex and less restrictive behavioral intervention (e.g. special class placement can often be avoided)
- Maximal improvement may be reached with lower dose of medication

14 month Outcomes, Teacher-rated Disruptive Behavior among Children w/Parents Showing Greatest Decreases in Negative/Ineffective Discipline:



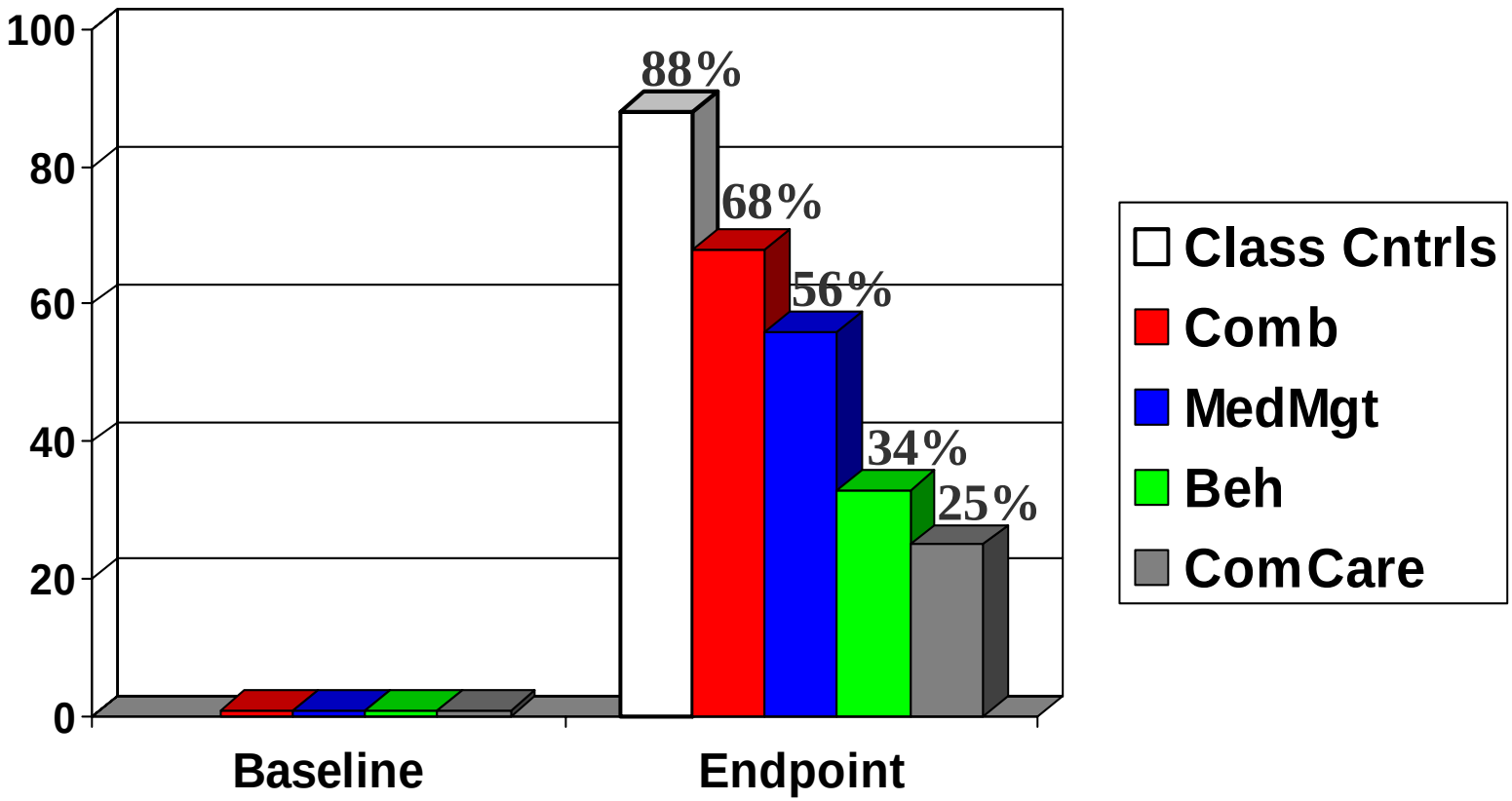
14 month Outcomes, Teacher-rated Disruptive Behavior among Children w/Parents Showing Smallest Decreases in Negative/Ineffective Discipline:



Limitations of Therapy Interventions

- Rarely sufficient to bring a child to normal range of functioning
- Not effective for all children
- Must be broad in scope to affect important familial variables
- Lack of evidence for long-term effects--no studies have yet been conducted
- Can be difficult to get parents and teachers to sustain over a long period of time after therapist contact has ended
- Often insufficient alone

% “Normalized” at 14-month Endpoint MTA Groups vs. Classroom Controls



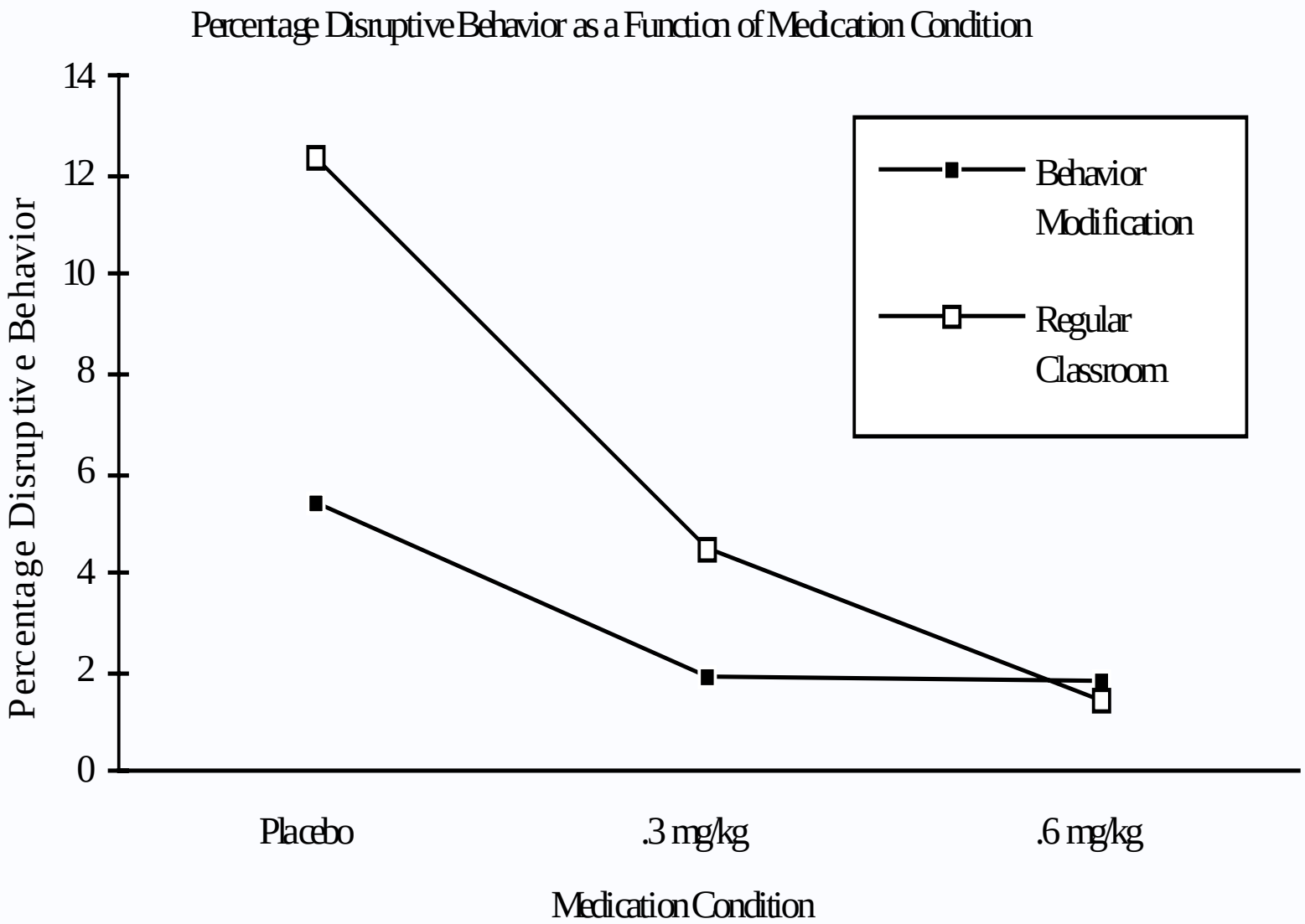
MTA N = 579
Classroom Cntrls N = 288

Do Combined Treatments Enable Lower Dosages of Medication to be Used?

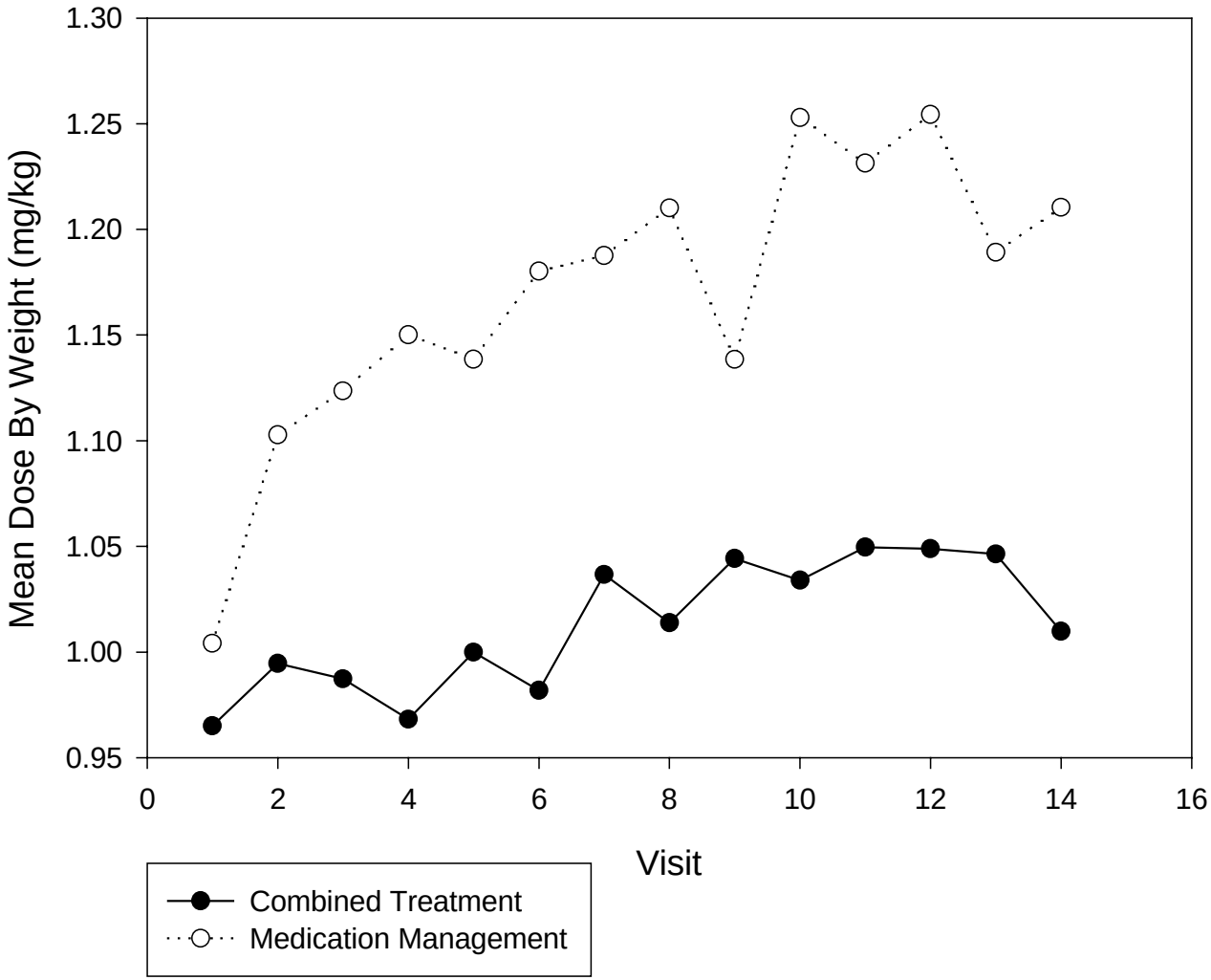
- Pelham et al (1980) found that .25 mg/kg MPH plus clinical behavioral intervention produced the same effects as .75 mg/kg MPH alone

- Carlson et al (1992) reported that .3 mg/kg MPH plus classroom behavioral intervention produced the same effect as .6 mg/kg MPH alone

Carlson et al., 1992



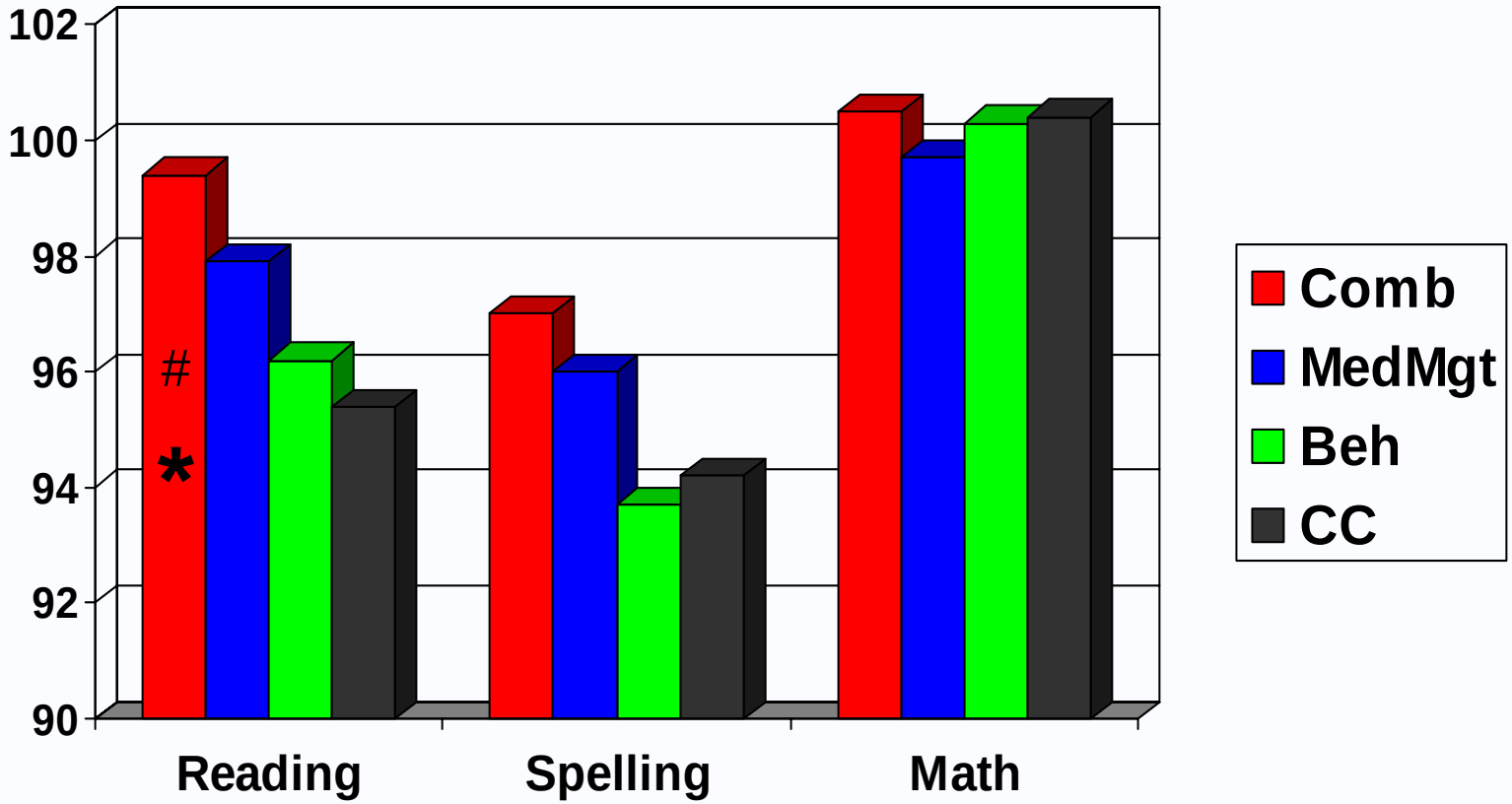
MTA Medication Doses: Comb vs. MedMgt Dose by Weight Over 14 Months



Rationale for a Combined Therapy and Pharmacological Intervention

- Medication appears to facilitate learning, as do behavioral interventions, but the potentially beneficial effects of the two treatments on learning may be dependent on the presence of both
- The two treatments may have complementary effects, with each affecting different symptoms
- Combined treatment may have broader coverage of symptoms than the separate treatments

WIAT Academic Performance at 14 mo. Pairwise Comparisons



* = significantly higher reading scores than CC

= significantly higher reading scores than Beh

Is Combined, MedMgt, or Beh Treatment Better Than the Control (Cc) Over 14 Months?

DOMAIN	Comb >CC?	MedMgt >CC?	Beh >CC?
ADHD Symptoms	Yes	Yes	
Oppos./Aggress.	Yes	Yes	
Anxiety	Yes		
Social Skills	Yes	Yes	
Academics	Yes		
P-C Relations	Yes		Yes

Rationale for a Combined Therapy and Pharmacological Intervention

- Therapy treatment should be initiated prior to medication treatment for practical and theoretical reasons, but solid evidence regarding the sequencing and possible fading of treatments not yet available
- Long-term studies of combined treatment effects, particularly when medication is withdrawn, are needed

Effect Size of Combined Treatment over Medication for Sample Studies

- MTA (Conners)
- Pelham et al (1993)
- Carlson et al (1992)
- Kolko et al (1999)
- All ranging from .27 to .40
- Modest but meaningful incremental benefit, especially with comorbid cases

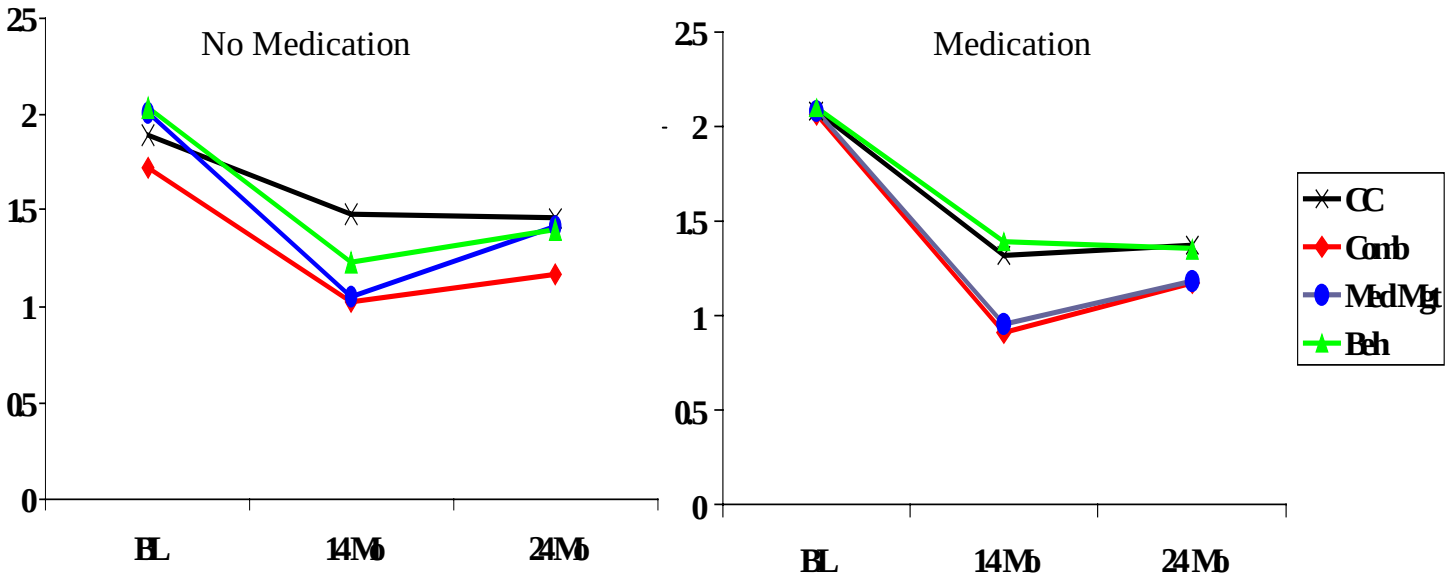
What Happens When Med is Withdrawn in a Combined Treatment Condition ?

(MTA, in review)

24 Month Outcomes: Total ADHD Sx

(Parent/Teacher)

Groups split by med use- Lower scores = better



Barriers to Effective Treatments: Family

- Family financial resources
- Family insurance coverage
- Parental knowledge about disorders and their medication treatment strategies
- Parental beliefs about treatment strategies (e.g., medication)

Barriers to Effective Treatments: School

- Teacher knowledge and beliefs about medication treatments
- Teacher training in classroom management
- School's financial resources (use of spec. ed. monies on school-wide?)
- Oversight
- District 504 and IDEA policies

Barriers to Effective Treatments: Mental Health Settings

- Therapist knowledge and beliefs about medication treatments
- Therapist training in evidence based treatments (formal and continuing)
- Oversight of clinician practices
- Financial resources of the agency/system (e.g., reimbursed contact hours required, acceptable treatments) BUT redirecting resources is the key

Courtesy W. Pelham, PhD

What Is Needed? Tools to Connecting Home, School, and Providers in Children's Care

Tools for Providers

- *-Evidence-based treatments: what works in both meds and therapy*
- *-Easy to use charts/look-up tables to guide use of treatments*

Tools for Parents

- *-Specific information on disorders and treatments*
- *-Info on how to get what you need for your child*

Tools for Teachers

- *-Information on disorders and treatments, classroom methods, etc.*

Connecting Tools

- *-Rating Scales*
- *-Daily Report Card*
- *-Bingo card*
- *-Web-based communication systems*