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## Multimodal Treatments versus Pharmacotherapy Alone in Children with Psychiatric Disorders:

### Implications of Access, Effectiveness, and Contextual Treatment

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#### Abstract

Practice guidelines for the treatment of youth with mental health problems tend to endorse integrating psychopharmacologic treatment with psychosocial interventions, such as psychotherapy and parent skills training. However, poor access to pediatric mental health specialists and inadequate training of primary care physicians in psychosocial interventions make it difficult for families to receive this standard of care. Large pediatric randomized, multicenter trials, including the Multimodal Treatment Study of ADHD (attention deficit hyperactivity disorder) [MTA] and the Treatment for Adolescents with Depression Study (TADS), have begun to identify specific advantages of multimodal treatment compared with psychopharmacology alone. Advantages of combined treatment include improvement of both symptoms and family functioning. More research is needed to determine effective and appropriate multimodal interventions for complex and severe pediatric mental illness. Advantages of multimodal treatment must be balanced with the treatment burden on the family system.

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Psychosocial interventions are often recommended as a fundamental component of pediatric mental health treatment. These may include psychotherapy, psychoeducation, parenting skills training, or school-based interventions. The executive summary from the 2007 American Psychological Association Working Group on the Use of Psychoactive Medication in Children recommends that psychosocial interventions generally be tried first since they are safer than pharmacotherapy interventions.<sup>[1]</sup>

For youth with moderate-to-severe impairment that may require medication, combining pharmacotherapy and psychosocial interventions has the advantage of targeting issues that may not be adequately addressed by medication alone, including adjustment to life stressors, parent-child conflict, and maladaptive coping behaviors. Multimodal treatment with medication and psychosocial interventions has increasingly been recommended over medication-only treatment for the management of pediatric mental illness. Recent practice parameters developed by the American Academy of Child and Adolescent Psychiatry for the treatment of depression, anxiety, and bipolar disorders stress the benefit of implementing psychosocial interventions as part of comprehensive treatment.<sup>[2–4]</sup> However, recommended standards of care are not always standard practice. Data from two US national ambulatory care surveys, for example, indicate that increases in selective serotonin reuptake inhibitor

(SSRI) antidepressant prescriptions have corresponded with decreases in psychotherapy treatment for pediatric depression.<sup>[5]</sup>

There are several barriers to the widespread adoption of multimodal treatment, including limited access to mental health specialists, few evidence-based psychotherapies for young children, and lack of clear scientific data regarding advantages of multimodal versus medication-only treatment. This article reviews these issues, discusses the 'risk : benefit' ratio of multimodal versus medication-only treatment, and reviews two examples of large multicenter trials that have examined multimodal versus medication-only treatment in the pediatric population. The article focuses on the treatment of pediatric depression and attention deficit hyperactivity disorder (ADHD), as these are two of the more prevalent pediatric mental health disorders and conditions that are currently treated in both primary care and mental health specialist settings.

## 1. Access

A fundamental determinant of whether or not psychosocial interventions are provided in conjunction with medication treatment is whether or not the child and family have access to appropriate mental health providers.

Pediatricians and primary care clinicians, who play a major role in screening and assessment of mental health disorders, often lack the training and time to provide nonmedication mental health interventions. A national survey of US pediatrics residency training directors reported that only 67% of residents receive any training in counseling and even fewer (19%) receive any training in psychotherapy.<sup>[6]</sup> Furthermore, the vast majority of training directors assessed the current training in these areas as inadequate. Improved training of pediatricians and primary care clinicians in psychosocial interventions is crucial, as families may avoid treatment by a mental health specialist because of traveling distance, long waiting lists, inadequate insurance coverage, or stigma. Referrals to mental health specialists are influenced by pediatricians' perception of both the waiting time for an appointment and quality of available therapists.<sup>[7]</sup>

The American Academy of Child and Adolescent Psychiatry Task Force on Workforce Needs estimated that if child psychiatrists provide treatment for only the most severely impaired youth (5% of the general population), each child psychiatrist would have a caseload of 750 youth, underscoring the gap between demand and supply for pediatric mental health services.<sup>[8]</sup>

## 2. Evidence-Based Treatment

For families with access and willingness to see mental health specialists that provide psychosocial interventions, the type of intervention indicated and potential benefit of multimodal treatment may still be unclear. Practice guidelines tend to be developed for the management of specific disorders. Youth with complex psychiatric co-morbidity, or co-occurring language impairment, cognitive delay, or chronic somatic illness, may differ in their ability to participate in and benefit from standard psychosocial interventions. Notably, a recent report showed that the preferred cost-effective treatment for children with ADHD

varied as a function of the co-morbidity of the child and the willingness to pay of the policymaker.<sup>[9]</sup>

The National Institute of Mental Health has recently funded multisite pediatric clinical trials that compare medication-only, psychosocial treatment-only, and multimodal treatment.<sup>[10]</sup> Data are needed to compare the effectiveness, tolerability, and feasibility of these different types of intervention. Psychosocial-only treatment eliminates the risk of medication side effects but may be ineffective in improving functioning for patients with moderate-to-severe illness severity. Also, multimodal treatment may be superior to medication-only treatment in symptom improvement for some disorders, but this type of comprehensive treatment is also likely to involve greater cost, time, and staff training needs.

### **3. Examples of Studies Comparing Pharmacotherapy-Only with Multimodal Treatment**

Two of the studies that included a comparison of medication only with combined medication and psychosocial intervention are the Multimodal Treatment Study of ADHD (MTA) and the Treatment for Adolescents with Depression Study (TADS).<sup>[12]</sup>

#### **3.1 Multimodal Treatment Study of Attention Deficit Hyperactivity Disorder**

In the MTA, 579 youth with ADHD aged 7–9.9 years were randomized to treatment with stimulant medications (MedMgt), behavioral interventions (Beh), combination of stimulant medication and behavioral interventions (Comb), or referral for community care (CC). The 289 participants assigned to the MedMgt and Comb groups were initially exposed to a 28-day double-blind, placebo-controlled titration of methylphenidate followed by monthly medication management.<sup>[13]</sup> By study end, 73.4% of the 289 patients in the MedMgt and Comb groups were being successfully maintained on methylphenidate, 10.4% on dexamfetamine (dextroamphetamine), 1.4% on pemoline, 1.0% on imipramine, 0.3% on bupropion, 0.3% on haloperidol, and 3.1% on no medication. The Beh strategy included group and individual parent training; an intensive, child-focused summer treatment program; a half-time para-professional aide in the classroom; and school-based teacher consultation.<sup>[14]</sup>

At the end of the 14-month MTA,<sup>[11]</sup> analyses of change in ADHD symptom outcomes revealed that MedMgt and Comb did not differ significantly and that both were superior to Beh and CC. In non-ADHD symptom domains, MedMgt and Beh showed better outcomes than CC on only one measure each, whereas Comb was superior to CC on all five areas: aggressive/oppositional behavior, internalizing symptoms, teacher-reported social skills, parent-child relations, and reading scores. Moreover, secondary analyses using a composite variable cutting across symptom and impairment domains<sup>[15]</sup> found that Comb emerged as the most effective intervention, (see table I). Of note, Comb showed significantly greater improvements in objective ratings of constructive parenting (e.g. warmth, positive reinforcement, setting the stage, and behavior management)<sup>[16]</sup> than MedMgt or CC. Such parenting practices are key factors in the development and maintenance of positive outcomes for children with problematic behaviors.<sup>[16–18]</sup>

Once the delivery of randomly assigned treatments stopped at 14 months, the MTA became an observational study in which participants were free to choose their own treatment, subject to the availability of care. Of the youth followed over the 10 months from the end of the MTA, 77% (255 of 331) continued medication use and 73% (139 of 190) continued not to use medication. At the 10-month follow-up assessment, the size of the differences between study arms that included and did not include the MTA medication protocol was reduced by 50%.<sup>[19,20]</sup> At the next follow-up, 12 months later, these differences had disappeared completely; treatment groups did not differ significantly on any of the five clinical and functional outcomes (parent- and teacher-rated ADHD and Oppositional Defiant Disorder symptoms, reading achievement scores, social skills, and functional impairment) or diagnostic status.<sup>[21]</sup> This lack of group differences occurred even though more individuals were taking medication in the MedMgt and Comb groups compared with the Beh and CC groups, and their average dose was larger. Furthermore, the improvements of sustained versus no medication use (regardless of group assignment) on outcomes at 14 months were no longer significant at 36 months. In addition, medication use during the year from 24 to 36 months did not confer any advantage on 36-month outcomes; instead, a tendency toward poorer outcomes was shown, including a greater likelihood of delinquency.<sup>[22]</sup> The latter result did not appear to reflect a self-selection process, that is those with more serious psychopathology would be most likely to have poorer outcomes and longer term treatment.<sup>[23]</sup> Of note, demographic variables had greater effects on 36-month outcomes than the treatment group; boys and children living on public assistance showed less improvement than girls or those not living on public assistance.

It is important to note that, although the differences among treatment groups were not maintained at 36 months, there was clear improvement from baseline for all groups. This pattern of results, along with secondary analyses identifying three latent classes of children with different trajectories of response over the 36 months,<sup>[23]</sup> suggests the need for cautious strategies for the integration of different modes of treatment (e.g. sequencing behavioral and pharmacologic treatments rather than combining them from the outset) based on periodic assessment of progress. Treatments may work, but at different rates, during different time periods for groups of children differing on key risk factors (e.g. co-morbidity, social skills, parental practices).

### 3.2 The Treatment for Adolescents with Depression Study

In the TADS, 327 adolescents 12–17 years of age with a diagnosis of major depressive disorder were randomized to receive short-term treatment with either the antidepressant medication fluoxetine, cognitive behavioral therapy, a combination of fluoxetine and cognitive behavioral therapy, or placebo over a 12-week period.<sup>[24]</sup> Responders and partial responders were continued in a 6-week maintenance/consolidation phase followed by an 18-week maintenance phase. Fluoxetine titration was completed by week 12, and the dosage was maintained for the remaining 24 weeks unless side effects or adverse events warranted a decrease. Placebo treatment was unblinded after the short-term treatment phase, and placebo partial or nonresponders were provided open treatment.<sup>[25]</sup> The remission rate after 12 weeks of treatment was 37% for the combination fluoxetine and cognitive behavioral therapy group, 23% in the fluoxetine group, 16% in the cognitive behavioral therapy group,

and 17% in the placebo-only group. Thus, multimodal treatment with medication and psychotherapy was superior to monotherapy with either medication or psychotherapy.<sup>[26]</sup>

A criticism of the short-term treatment results was that the type of cognitive behavior therapy implemented was overly structured and difficult to individualize.<sup>[27]</sup> Long-term (36-week) follow-up data, however, indicated that response rates were similar in all three active treatment groups.<sup>[28]</sup> An important distinction between medication-only and combination treatment was that the rate of suicidal events was significantly less in the combination treatment arm compared with medication only.<sup>[28]</sup> The investigators concluded that combination treatment was superior because of accelerated recovery time relative to cognitive behavior therapy-only treatment and reduced suicidality relative to medication-only treatment.

#### 4. Contextual Issues in Selecting Treatment

In general, psychosocial interventions ‘prescribed’ for youth and their families should take into account the unique risk : benefit ratio for a specific intervention for that unique child/adolescent. Psychosocial interventions, however, do not always have an ‘additive benefit’ when combined with pharmacotherapy. Proposed interventions need to take into account contextual issues for the unique child/adolescent and family. Appointment time burden (particularly for youth with siblings or parents in active treatment), parental satisfaction, and child functioning with pharmacotherapy alone, as well as cultural issues about psychosocial interventions, may influence the potential feasibility and benefit of multimodal treatment. Another consideration is the timing or sequence of multimodal treatment. Youth with severe symptoms (e.g. extreme aggression or hyperactivity, active psychotic symptoms) may require stabilization with medication for a period of time before being able to benefit from a specific type of psychotherapy. A balancing consideration is that concurrent psychosocial treatment may facilitate a greater treatment alliance between the treatment team and the family. Treatment alliance has been identified as the most important factor in promoting medication adherence.<sup>[29]</sup>

#### 5. Conclusion

There are several potential advantages to multimodal treatment over pharmacotherapy alone for youth with mental health problems. Firstly, psychosocial interventions provide an opportunity for parents to play an active role in the treatment of their child/adolescent, and to enhance parenting skills that can impact other youth in the home. Secondly, pharmacotherapy interventions may address disease-specific target symptoms but often do not address ‘symptom-related’ problems, such as impaired family or peer relationships, adjustment to stressors, or long-standing aggressive behavior. Psychosocial interventions can have a significant impact on child and family functioning, which may reduce the need for further medication dosage increases. Thirdly, the additional time required for psychosocial interventions can allow more support and greater time to monitor for safety issues, such as suicidality or child-abuse concerns.<sup>[29]</sup> Multimodal treatment also allows for more time to address parental concerns about the treatment of their child/adolescent, track adherence to pharmacotherapy, and educate parents about adherence issues.

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**Table 1**

Mean (SD) values of composite outcome<sup>a</sup> by treatment at baseline and 14-month follow-up

Treatment	Baseline	14 months
Behavior therapy	0.108 (1.190)	-1.421 (1.471)
Medication management	0.078 (1.229)	-1.820 (1.611)
Combined <sup>b</sup>	-0.122 (1.137)	-2.234 (1.349)
Community care	-0.062 (1.099)	-1.285 (1.360)

<sup>a</sup>The average of mean z scores of items with loadings of >0.40 on two factors resulting from principal component factor analysis of 19 outcome variables. All scores were computed in a negative direction, with a lower score indicating a reduction in symptoms from baseline (improvement).[15]

<sup>b</sup>Combination of stimulant medication and behavioral interventions.