ORIGINAL ARTICLE

A 14-Month Randomized Clinical Trial of Treatment Strategies for Attention-Deficit/ Hyperactivity Disorder

The MTA Cooperative Group

Background: Previous studies have demonstrated the short-term efficacy of pharmacotherapy and behavior therapy for attention-deficit/hyperactivity disorder (ADHD), but no longer-term (ie, >4 months) investigations have compared these 2 treatments or their combination.

Methods: A group of 579 children with ADHD Combined Type, aged 7 to 9.9 years, were assigned to 14 months of medication management (titration followed by monthly visits); intensive behavioral treatment (parent, school, and child components, with therapist involvement gradually reduced over time); the two combined; or standard community care (treatments by community providers). Outcomes were assessed in multiple domains before and during treatment and at treatment end point (with the combined treatment and medication management groups continuing medication at all assessment points). Data were analyzed through intent-to-treat random-effects regression procedures.

Results: All 4 groups showed sizable reductions in symptoms over time, with significant differences among them in degrees of change. For most ADHD symptoms, children in the combined treatment and medication management groups showed significantly greater improvement than those given intensive behavioral treatment and community care. Combined and medication management treatments did not differ significantly on any direct comparisons, but in several instances (oppositional/aggressive symptoms, internalizing symptoms, teacher-rated social skills, parent-child relations, and reading achievement) combined treatment proved superior to intensive behavioral treatment and/or community care while medication management did not. Study medication strategies were superior to community care treatments, despite the fact that two thirds of community-treated subjects received medication during the study period.

Conclusions: For ADHD symptoms, our carefully crafted medication management was superior to behavioral treatment and to routine community care that included medication. Our combined treatment did not yield significantly greater benefits than medication management for core ADHD symptoms, but may have provided modest advantages for non-ADHD symptom and positive functioning outcomes.

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ATTENTION-deficit/hyperactivity disorder (ADHD) occurs in 3% to 5% of school-aged children, accounts for as many as 30% to 50% of child referrals to mental health services,[1,2] and results in substantial impairment in peer, family, and academic functioning.[2,3] Although benefits of short-term treatments (principally stimulants, behavior therapy, and both combined) have been well documented,[4-8] few controlled studies have examined effectiveness beyond 3 months. Two exceptions[9,10] suggested that stimulant effects can persist 1 to 2 years when taken faithfully. However, the generalizability and usefulness of these 2 studies are constrained by sample sociodemographic homogeneity, exclusion of stimulant nonresponders, lack of unimodal comparisons (medication management vs behavioral interventions), and inadequate statistical power to examine subject factors that predict treatment response.[9,10]

See also pages 1088 and 1097

Given public concerns regarding stimulant treatment,[11,12] wide variations in treatment practices,[13] and lack of evidence to guide long-term treatments of this chronic disorder, in 1992 the National Institute of Mental Health and Department of Education cosponsored a randomized clinical trial, the Multimodal Treatment Study of Children With ADHD (MTA). Its rationale[14] and methods[15-19] have been detailed previously.

The MTA Cooperative Group posed 3 questions: How do long-term medication and behavioral treatments compare with one another? Are there additional benefits when they are used together? What is the effectiveness of systematic, carefully delivered treatments vs routine community care? This report constitutes

A list of the collaborators and investigators for this study appears on page 1077.

PARTICIPANTS, MATERIALS, AND METHODS

RECRUITMENT PROCEDURES AND SAMPLE CHARACTERISTICS

Recruitment, screening, and selection procedures aimed to collect a carefully diagnosed sample of impaired children with ADHD and a wide range of comorbid conditions and demographic characteristics representative of patients seen in clinical practice. To minimize site-specific referral biases, sites' referral sources necessarily included mental health settings, pediatricians, advertisements, and school notices. For eligibility, children (of either sex) were between ages 7 and 9.9 years, in grades 1 through 4, and in residence with the same primary caretaker(s) for the last 6 months or longer. All met the *DSM-IV* criteria for ADHD Combined Type (the most common subtype in this age group[22]), using the Diagnostic Interview Schedule for Children (DISC), parent report, version 3.0,[23] supplemented with up to 2 symptoms identified by children's teachers for cases falling just below the DISC diagnostic threshold. Exclusion criteria were limited to situations that would prevent families' full participation in assessments or treatment, or that might require additional treatments incompatible with study treatments (**Table 1**).[16-18] The presence of comorbid conditions, such as oppositional-defiant disorder (ODD), conduct disorder (CD), internalizing disorders, or specific learning disabilities, did not lead to exclusions per se; an important aim of the study was to examine their interactions with treatment outcomes.

A 4-phase entry procedure (**Table 2**) screened potential participants, determined ADHD diagnostic status, and assessed each recruit prior to randomization.[17,18] Ninety-five percent of subjects entering the fourth-phase baseline assessment were randomized; they did not differ from initial telephone screen subjects in parental education, ethnicity, or sex. Informed consent (parental permission and child assent) was obtained for all participating families, using forms approved by both local institutional review boards and the National Institutes of Health Office for Protection From Research Risks, Bethesda, Md.

DESIGN

In a 4-group parallel design, children were assigned randomly to medication management, behavioral treatment, combined treatment, or community care for 14 months. (In the method articles for this study, treatment assignments were referred to as *medication*, *psychosocial treatment*, *combined treatment*, and *community-treatment/assessment and referral*. To reflect more accurately the actual treatments, we have changed the terminology for all outcome articles to medication management, behavioral treatment, combined treatment, and community care.)Rather than testing fixed single treatments, we designed each MTA treatment arm as a management *strategy*, such that each was sufficiently robust and flexible to stand on its own and to respond to individual patients' clinical needs throughout the study.

Power analyses indicated 24 subjects per treatment condition per site (96 families at each of 6 sites) for comparisons of core ADHD symptoms between any 2 treatment arms (critical effect size, 0.4; power, 0.81, with a 5% 2-tailed test).[17,24,25] Accordingly, 576 subjects were required; 579 were recruited. Sample demographics, mean scores on standardized Conners teacher and parent scales,[26] comorbidity profile, and impairment ratings (Columbia Impairment Scale) are typical of other ADHD samples this age[26-30] (**Table 3**).

Randomization was done centrally by the National Institute of Mental Health Data Center, Rockville, Md, stratified by site in blocks of 16 (4 to each group). Sealed, ordered envelopes were sent to sites for successive entries. Treatment assignment was concealed until the family confirmed agreement to accept randomization.

ASSESSMENTS

Principal components analyses narrowed the selection of outcome domains from the comprehensive assessment battery,[28] eliminating redundant measures. Six major outcome domains were identified. Within domains, the measures loading highest from each informant were selected: (1) ADHD symptoms were measured with inattention and hyperactivity-impulsivity subscales of parent- and teacher-completed SNAP ratings (an acronym denoting the names of the instrument's developers)[31]; (2) oppositional/aggressive symptoms were measured with a parent and teacher SNAP oppositional-defiant disorder subscale; (3) social skills were measured with a parent- and teacher-completed subscale from the Social Skills Rating System (SSRS)[32]; (4) internalizing symptoms (anxiety and depression) were measured with an internalizing subscale from parent- and teacher-completed SSRS,[32] and children's self-ratings on the Multidimensional Anxiety Scale for Children (MASC)[33]; (5) parent-child relations were measured with 2 composite scales from a parent-child relationship questionnaire; and (6) academic achievement was measured with 3 subscales from the Wechsler Individual Achievement Test[34] (reading, math, and spelling). These measures show acceptable psychometric properties, and are reviewed extensively elsewhere.[31-34] Subjects were assessed at baseline, and at 3, 9, and 14 months (treatment end point). Baseline and end-point values for the outcome domains are presented in **Table 4**.

The open parent, teacher, and child ratings for domains 1 through 5 were augmented by blinded ratings of school-based ADHD and oppositional/aggressive symptoms using the Abikoff Classroom Observational System[35] and social skills and peer relations using peer sociometric procedures. Finally, we videotaped parent-child interactions during standardized laboratory tasks performed by raters blind to treatment condition. Videotaped interactions, parental characteristics, family functioning, cognitive ability, general impairment, and services use, attitudes, and barriers[18] will be reported in later articles.

TREATMENT CONDITIONS AND PROTOCOLS

The 3 MTA-delivered treatment strategies were chosen for well-established efficacy (at least in the short term), portability, sufficient intensity to stand alone, and distinction from each other. For all 3 arms, subjects had up to 8 additional sessions provided when needed to address clinical emergencies or instances of possible study attrition.

Behavioral Treatment

Behavioral treatment included parent training, child-focused treatment, and a school-based intervention organized and integrated with the school year. The parent training, based on work by Barkley[36] and Forehand and MacMahon,[37] involved 27 group (6 families per group) and

8 individual sessions per family. It began weekly on randomization, concurrent with biweekly teacher consultation; both were tapered over time. The same therapist-consultant conducted parent training and teacher consultation, with each therapist-consultant having a caseload of 12 families

The child-focused treatment was a summer treatment program (STP) developed by Pelham[38] as a therapeutic summer camp. The 8-week, 5-days-per-week, 9-hours-per-day STP employed intensive behavioral interventions administered by counselors/aides, supervised by the same teacher-consultants who performed parent training and teacher consultation. Behavioral interventions were delivered in group-based recreational settings, and included a point system tied to specific rewards, time out, social reinforcement, modeling, group problem-solving, sports skills, and social skills training. Summer treatment program classrooms provided individualized academic skills practice and reinforcement of appropriate classroom behavior.

The school-based treatment had 2 components: 10 to 16 sessions of biweekly teacher consultation focused on classroom behavior management strategies[8] and 12 weeks (60 school days) of a part-time, behaviorally trained, paraprofessional aide working directly with the child (methods adapted from Swanson[31]). The aides had been STP counselors, and the program continued in the fall classroom, which helped to generalize STP gains to classrooms. Throughout the school year, a daily report card linked home and school. The daily report card[8,39] was a 1-page teacher-completed checklist of the child's successes on specific preselected behaviors, and was brought home daily by the child to be reinforced by the parent with home-based rewards (eg, television time, snacks).

The treatments outlined above constitute the maximum "dose" of behavioral treatment children/families could receive, given perfect attendance and compliance. In practice, families (given both behavioral and combined treatment) attended an average of 77.8% of parent training sessions and 36.2 of 40 possible STP days. The school component averaged 10.7 teacher consultation visits and 47.6 days (of 60 possible) of work with classroom aides. Sites differed significantly in the extent of attendance for 2 components (parent training and classroom aides), but there were no significant differences between behavioral and combined treatment, either within or across sites, in degree of attendance/implemenation for any behavioral components (tables available from the authors on request). As described in our companion report, a summary measure of attendance/compliance for all behavioral treatment components was unrelated to treatment outcomes; likewise, attendance did not mediate any site×treatment interactions on outcomes.[40]

Consistent with the time-limited involvement of providers in clinical practice, the involvement of our personnel in the delivery of the behavioral treatments was gradually tapered, with the goal that parents would increasingly manage the child's behavioral treatment. In most cases, therapist contact with parents had been reduced to once-monthly sessions or stopped altogether prior to end-point assessment.

Medication Management

Medication management[15] started with a 28-day, double-blind, daily-switch titration of methylphenidate hydrochloride, using 5 randomly ordered repeats each of placebo, 5 mg, 10 mg, and 15 or 20 mg (higher doses for children >25 kg). Each of the doses listed was given at breakfast and lunch, with a half-dose (rounded to the nearest 5 mg) in the afternoon. Cross-site teams of experienced clinicians blindly reviewed graphs portraying parent and teacher ratings of responses to each of the 4 doses and by consensus selected each child's best dose. After agreement on best dose, the blind was broken, and the agreed-on dose (if not placebo) became the subject's initial maintenance dose. For subjects not obtaining an adequate response to methylphenidate during titration, alternate medications were titrated openly in the following order until a satisfactory one was found: dextroamphetamine, pemoline, imipramine, and, if necessary, others approved by a cross-site panel. Of 289 subjects assigned to medication management (n = 144) and combined treatment (n = 145) for initial titration, 18 had no titration: 17 because they refused the entire medication component and 1 who moved away. An additional 15 subjects started but did not complete titration: 4 because of side effects, 7 because of difficulties tolerating the titration procedures, and 4 who supplied inadequate data. Thus, 256 subjects (88.6%) successfully completed titration; of these, 198 (68.5%) of 289 subjects were assigned to an individually titrated best dose of methylphenidate, with average initial doses of 30.5 mg/d. The remaining titration completers were either openly titrated to dextroamphetamine (n = 26) because of unsatisfactory methylphenidate response or initially given no medication (n = 32) because of a robust placebo response (2 of these placebo responders failed to cooperate further after titration).

During half-hour monthly medication maintenance visits, pharmacotherapists provided support, encouragement, and practical advice (but not behavioral treatment). When deemed necessary by the clinician or requested by the parent, readings from an approved list were supplied. After careful review of parent- and teacher-provided information, pharmacotherapists could make algorithm-guided dose adjustments of ±10 mg/d of methylphenidate (or an equipotent amount if the subject was taking another drug). Additional adjustments beyond ±10 mg/d could be authorized by a cross-site panel of experienced pharmacotherapists. In general, dose reductions were allowed only to address dose-related side effects.

By study end, 212 (73.4%) of the 289 subjects given medication management and combined treatment were being successfully maintained on methylphenidate, 30 (10.4%) on dextroamphetamine, 4 (1.4%) on pemoline, 3 (1.0%) on imipramine, 1 (0.3%) on buproprion, 1 (0.3%) on haloperidol, and 18 (3.1%) on no medication (combined treatment [14 subjects] and medication management [4 subjects]) (3.1%), with 20 persistently unmedicated (18 since study outset, 2 during maintenance). There were no differences between the medication management and combined treatment groups in the proportion of subjects maintained on the various medications.

Side effects were monitored monthly—not present, mild, moderate, or severe—using the parent-completed 13-item Pittsburgh Side Effects Rating Scale,[41] reviewed by the pharmacotherapist. At end point, 245 combined treatment/medication management families provided information on side effects, with some reporting more than one: 88 (35.9%) reported no side effects, 122 (49.8%) reported mild side effects only, 28 (11.4%) reported moderate side effects, and 7 (2.9%) reported severe side effects. These figures may overestimate side effects, because 6 of 11 reported severe side effects (depression, worrying, or irritability) could have been due to nonmedication factors.

Continued on next page

Combined Treatment

Combined treatment provided all treatments outlined above for medication management and behavioral treatment; namely, titration followed by monthly medication maintenance, parent group and individual sessions, teacher consultation, STP, and the classroom aide. However, to approximate clinical practice, we integrated the 2 treatment modalities; information was regularly shared between the teacher-consultant and pharmacotherapist and used to guide overall decisions. Manualized guidelines determined if and when an adjustment in one treatment should be made, vs intervening first with the other.[16,17] Consequently, the multimodal combination was not the simple addition of the two unimodal treatments. Consistent with the literature,[42] by treatment end point combined treatment subjects received lower total daily doses of methylphenidate (31.2 mg) than medication management subjects (37.7 mg). Though sites differed significantly in total daily methylphenidate doses (range of mean doses per site, 30.2-41.3 mg), there were no site × treatment interactions in total daily doses (treatment group: $F = 14.6$, $P = .01$; site: $F = 3.2$, $P = .002$; site × treatment group: $F_{11,200} = 1.2$, $P = .24$).

Community Care

Community care participants received none of our treatments, but were provided a report of their initial study assessments, along with a list of community mental health resources. They were subsequently reassessed in parallel with participants in our 3 treatment arms. At each assessment point, the types of treatments they obtained in the community were documented. Most community care subjects (n = 97 [67.4%]) received ADHD medications (principally one of the stimulants) from their own provider during the 14 months: methylphenidate (n = 84), pemoline (n = 7), amphetamine (n = 6), tricyclics (n = 6), clonidine/guanfacine (n = 4), and/or buproprion (n = 1) (10 subjects received more than 1 medication). In addition, 16 of these 97 children were treated by their physician with another antidepressant (not counting tricyclics or buproprion). For those treated with methylphenidate, the mean total daily dose at study completion was 22.6 mg, averaging 2.3 doses per day (vs 3.0 doses per day for MTA-treated subjects). Information concerning community care psychotherapeutic treatments has not yet been coded and will not be presented in this article.

Fidelity and Compliance

The MTA study achieved a high degree of adherence to protocol by cross-arm emphasis on subject rapport, manualization of all treatments, regular supervision of pharmacotherapists and psychotherapists by skilled clinician investigators, cross-site weekly treatment panels, and audiotaping of all sessions. Good compliance (reflected by acceptance and attendance at treatment sessions) by patients with the protocol was facilitated by monthly pill counts, intermittent saliva measurements to monitor taking of methylphenidate, and encouragement of families to make up missed visits. Only 13 (9.0%) of 144 medication management subjects and 5 (3.4%) of 145 combined treatment subjects failed to start medication. More remarkably, none of 144 behavioral treatment subjects and only 1 (0.7%) of 145 combined treatment subjects refused behavioral treatment. There was no difference between medication management or combined treatment in medication session attendance, nor between behavioral treatment and combined treatment in the degree of behavioral treatment acceptance or attendance. These factors did not affect the overall findings.[40]

Subjects/families refusing their respective treatments were encouraged to reconsider their decision throughout the study, as well as to continue to complete all assessments. Thus, including all subjects who continued to participate in assessments (despite refusing part of all of their assigned treatments), the absolute attrition rate over the course of the study was 3.5%, with only 20 complete dropouts by 14 months (6 in the community care group, 3 in behavioral treatment, 8 in medication management, 3 in combined treatment).

STATISTICAL ANALYSES

Given the well-described advantages of random-effects regression (RR) techniques over traditional analyses of variance for clinical trials data,[43-46] we used RR whenever possible for our primary intent-to-treat analyses.[20,21] Rather than define a single outcome, we specified multiple outcome variables, anticipating differential impacts of the treatment modalities on various outcome domains.[5-7,14] Based on our data reduction procedures outlined above, the 6 domains were represented by 19 measures (Table 4). For each outcome variable, tests for site, time, time×treatment (the treatment effect over time), and site×treatment×time were conducted within the intent-to-treat RR analyses. When omnibus RR analyses comparing all 4 groups were significant, 3 sets of pairwise comparisons were performed, each set addressing 1 of the principal study questions: (1) medication management vs behavioral treatment (2 tailed); (2) combined treatment vs medication management and combined treatment vs behavioral treatment (1 tailed, assuming the superiority of combined treatment); and (3) community care vs medication management, community care vs behavioral treatment, and community care vs combined treatment (1 tailed, assuming the superiority of MTA treatments).

Bonferonni corrections were applied to all omnibus tests, based on the number of measures in the respective domain. Thus, for each of 5 measures within the ADHD domain, standard definitions of significance ($P<.05$) were corrected by dividing by 5, requiring $P<.01$ for significance. The 6 pairwise contrasts were likewise adjusted by dividing omnibus-corrected significance levels further by 6 ($P<.01 \div 6 = .0017$ in this example). Given our a priori hypotheses about the superiority of multimodal treatment (combined treatment vs medication management and behavioral treatment), as well as the superiority of all 3 of our treatments over community care (community care vs combined treatment, medication management, behavioral treatment), we used 1-tailed tests for these specific contrasts. This approach was taken as a means of striking a balance between the dangers of committing type II errors vs overinterpreting significant findings that occurred simply by chance (type I errors). Readers are encouraged to exercise caution when interpreting 1-tailed findings and may choose to double 1-tailed P values.

Because initial RR analyses revealed both quadratic and linear effects of time on treatment outcomes, we computed the log of the number of days since randomization for each assessment point and used these log values in all RR analyses.

Despite high compliance, we checked whether compliance with assessments (ie, missing data) could have changed our findings. Random-effects regression analyses were completed 2 ways: once with inclusion of all subjects, and then with only those subjects who provided data over multiple time points during the study. No differences emerged among these 2 sets of analyses, lending confidence to the overall findings.

The Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder Cooperative Group

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Table 1. Subject Exclusion Criteria*

Exclusion Criterion	Reason for Exclusion
Child currently in hospital	Inability to participate in school component
Child currently in another study	Confounding of assessments and procedures
Below 80 on all WISC-III scales and on SIB	Inability to participate in psychosocial treatment
Bipolar disorder, psychosis, or personality disorder	Required treatment, may be incompatible with MTA study
Chronic serious tics or Tourette syndrome	Possible contraindication for stimulants
OCD serious enough to require separate treatment	Treatment may be incompatible with MTA study
Neuroleptic medication in previous 6 months	May need resumption; incompatible with MTA study
Major neurological or medical illness	Inability to participate fully in treatment
History of intolerance to MTA medications	Inability to participate in medication condition
Ongoing or previously unreported abuse	Risk of removal from home
Missed one fourth of school days in previous 2 months	Inability to participate in school component
Same classroom as child already in MTA study	Possible cross-arm contamination by teacher
Parental stimulant abuse in previous 2 years	Risk of parent co-opting child's medications
Non–English-speaking primary caretaker	Inability to participate in parent training groups
Another child in same household in MTA study	Possible cross-arm contamination
No telephone	Inability to participate in ongoing contacts
Suicidal or homicidal	Treatment requirements beyond ability of MTA study

**WISC-III indicates Wechsler Intelligence Scale for Children–Third Edition; SIB, Scales of Independent Behavior; OCD, obsessive-compulsive disorder; and MTA, Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder.*

the first-ever description of the relative effectiveness of these treatments through 14 months, using an intent-to-treat analytic strategy with random-effects regression techniques.[20,21]

RESULTS

For 10 of 19 variables, omnibus tests revealed significant treatment effects over time. For these analyses, we describe the results of the paired comparisons, in order of our original hypotheses.

Do medication and behavioral treatments result in comparable levels of improvement in pertinent outcomes at the end of treatment? Robust differences were found according to 2 different data sources, indicating the superiority of medication management over behavioral treatment for ADHD symptoms (**Table 5**); namely, parents' and teachers' ratings of inattention and teachers' ratings of hyperactivity-

Table 2. Number of Subjects and Reasons for Exclusion

	Assessment Phase			
	Telephone Screen	Mailed Ratings	*DSM-IV* Diagnosis and School Agreement	Baseline Assessment
Reasons for exclusion during each phase, No. (%)				
Wrong age or grade	891 (20)*			
Distance from school and family	600 (14)			
Medical exclusion	78 (2)	15 (1)	17 (2)	8 (1)
Parent refusal	411 (9)	335 (14)	96 (10)	13 (2)
Moving, language, no telephone, school refusal or school ineligible, too late, contamination	224 (5)	113 (5)	111 (12)	6 (1)
Parent or teacher symptom checklist cutpoints not met		522 (22)		
Complete package not returned		423 (18)		
IQ criteria not met			17 (2)	
Diagnostic interview criteria not met			79 (9)	
Parent drug use				3 (1)
Total No. (%) of Subjects Excluded During Each Phase	**2204** (49)	**1408** (60)	**320** (34)	**30** (5)
Total No. of Subjects Entering Each Phase	**4541**	**2337**	**929**	**609**

**Percentages refer to the proportion of subjects excluded for that reason among the total number of subjects who entered that recruitment/assessment phase.*

impulsivity. Medication management and behavioral treatment did not differ significantly on any other outcomes.

Do participants assigned to combined treatment show higher levels of improvement in overall functioning in pertinent outcome domains than those assigned to either medication management or behavioral treatment at the end of treatment (1-tailed hypotheses)? These analyses indicate that combined treatment and medication management did not differ significantly across any domain.

Compared with behavioral treatment, combined treatment was superior in benefitting ADHD symptoms, according to parents' and teachers' ratings of inattention and parent-rated hyperactivity-impulsivity. Combined treatment also significantly outperformed behavioral treatment on parents' SNAP oppositional/aggressive behaviors, parent-rated internalizing symptoms (Table 5), and Weschler Individual Achievement Test reading achievement score (Table 4).

Do participants assigned to each of the 3 MTA treatments (medication management, behavioral treatment, and combined treatment) show greater improvement over 14 months than those assigned to community care (1 tailed)? These analyses reveal that combined treatment and medication management were generally superior to community care for parent- and teacher-reported ADHD symptoms, whereas behavioral treatment was not (Table 5). In non-ADHD domains, medication management and behavioral treatment were superior to community care on 1 domain only (teacher-reported social skills and 1 measure of parent-child relations, respectively). In contrast, combined treatment was significantly superior to community care on all 5 non-ADHD domains of functioning (parent-reported oppositional/aggressive behaviors, internalizing symptoms, teacher-reported social skillls, parent-child relations, and Weschler Individual Achievement Test reading achievement scores).

Because our RR intent-to-treat analyses included all subjects' data points through 14 months, it is possible that some treatment groups (especially behavioral treatment, where 38 crossovers to medication occurred) may have fared better because of the number who had received additional treatments over the course of the study. To address this issue, we conducted additional RR analyses, censoring any observations obtained after crossover subjects had received the additional treatments. These analyses yielded no differences from the findings noted in Table 5 (analyses available from the authors on request).

The **Figure** shows the 4 RR analyses selected to highlight findings from different domains, as well as from raters who were likely to witness the target behaviors: hyperactivity-impulsivity (a core ADHD symptom) (teacher report), internalizing symptoms (parent report), social skills (teacher report), and parent-child arguing (power assertion, parent report). The remaining RR graphs are available from the authors on request.

COMMENT

All 4 groups showed marked reductions in symptoms over time, with significant differences among them in degrees of change. Combined treatment and medication management treatments were clinically and statistically superior to behavioral treatment and community care in reducing children's ADHD symptoms. Combined behavioral intervention and stimulant medication—multimodal treatment, the current criterion standard for ADHD interventions—yielded no significantly greater benefits than medication management for core ADHD symptoms; this parallels findings reported by others.[10,42] Also consistent with previous reports, our combined treatment outcomes were achieved with significantly lower medication doses than used in medication management.[42,47]

For other areas of function (oppositional/aggressive behaviors, internalizing symptoms, social skills, parent-child relations, and academic achievement), few differences among our treatments were noted, and when found, were generally of smaller magnitude. In fact, combined treatment, medication management, and behavioral treatment never differed significantly among

Table 3. Baseline Characteristics of the Sample (N = 579)*†

Variable	Totals Across All Treatment Groups	Combined Treatment (n = 145)	Medication Management (n = 144)	Behavioral Treatment (n = 144)	Community Care (n = 146)	Range of Means Across Sites	Site Differences, *P*
Subject Variables							
Age, y, mean (SD)	8.5 (0.8)	8.4 (0.8)	8.6 (0.8)	8.3 (0.8)	8.5 (0.8)	8.4-8.6	≤.01
Male, No. (%)	465 (80)	114 (79)	118 (82)	114 (79)	119 (82)	71%-87%	≤.05
Ethnicity, No. (%)							
White	351 (61)	87 (60)	91 (63)	83 (58)	90 (62)	22%-81%‡	≤.001
African American	115 (20)	25 (17)	28 (19)	36 (25)	26 (18)	4%-39%‡	
Hispanic	48 (8)	14 (10)	12 (8)	12 (8)	10 (7)	0%-33%‡	
Grade, No. (%)							
1	89 (15)	20 (14)	18 (12)	29 (20)	22 (15)	6%-28%‡	≤.01
2	239 (41)	63 (43)	52 (36)	66 (46)	58 (40)	36%-45%‡	
3	177 (31)	45 (31)	55 (38)	34 (24)	43 (29)	23%-40%‡	
4	73 (13)	17 (12)	18 (13)	15 (10)	23 (16)	7%-20%‡	
5	1 (0.2)		1 (0.7)			0%-1%‡	
WISC-III IQ, mean (SD)							
Verbal	100.8 (14.8)	100.7 (15.4)	98.9 (13.9)	101.1 (14.4)	102.4 (15.3)	97.5-104.4	≤.01
Performance	101.4 (15.6)	101.0 (15.9)	100.1 (14.3)	101.7 (15.7)	102.7 (16.5)	95.8-104.6	≤.001
Total	100.9 (14.8)	100.7 (15.1)	99.3 (13.4)	101.3 (14.7)	102.6 (15.8)	96.1-104.8	≤.001
Conners Teacher Rating Scale, mean (SD)							
Hyperactivity factor	1.82 (0.49)	1.76 (0.50)	1.85 (0.48)	1.87 (0.50)	1.82 (0.49)	1.72-1.98	≤.05
Hyperkinesis index	1.95 (0.53)	1.89 (0.56)	2.00 (0.48)	1.96 (0.53)	1.93 (0.53)	1.87-2.09	. . .
Conduct	1.21 (0.75)	1.13 (0.73)	1.23 (0.76)	1.29 (0.75)	1.20 (0.76)	1.09-1.50	≤.01
Iowa Conners	2.29 (0.54)	2.24 (0.54)	2.34 (0.50)	2.28 (0.57)	2.30 (0.52)	2.20-2.38	. . .
Total	1.32 (0.43)	1.26 (0.42)	1.34 (0.44)	1.37 (0.43)	1.31 (0.42)	1.26-1.47	≤.05
Conners Parent Rating Scale, mean (SD)							
Hyperactive-immature	1.01 (0.37)	1.03 (0.38)	1.00 (0.37)	1.01 (0.36)	1.00 (0.38)	0.92-1.08	≤.05
Hyperkinesis index	1.85 (0.58)	1.82 (0.60)	1.86 (0.57)	1.86 (0.55)	1.87 (0.60)	1.73-1.91	. . .
Conduct	1.26 (0.49)	1.22 (0.50)	1.27 (0.52)	1.23 (0.48)	1.29 (0.47)	1.15-1.36	≤.01
Restless	1.70 (0.60)	1.69 (0.64)	1.70 (0.56)	1.72 (0.59)	1.69 (0.61)	1.58-1.77	. . .
Total	0.83 (0.30)	0.84 (0.31)	0.83 (0.31)	0.83 (0.29)	0.84 (0.30)	0.76-0.89	≤.01
Comorbidity (DISC diagnoses), No. (%)							
Anxiety disorder	194 (33.5)	50 (34.7)	52 (35.9)	50 (34.7)	42 (28.8)	24.5%-37.5%	. . .
Conduct disorder	83 (14.3)	20 (13.9)	23 (15.8)	18 (12.5)	22 (15.1)	7.3%-19.4%	. . .
Oppositional-defiant disorder	231 (39.9)	53 (36.8)	55 (37.9)	60 (41.7)	63 (43.2)	30.2%-46.9%	. . .
Affective disorder	22 (3.8)	5 (3.5)	5 (3.4)	5 (3.5)	7 (4.8)	1.0%-7.4%	. . .
Tic disorder	63 (10.9)	19 (13.2)	11 (7.6)	14 (9.7)	19 (13.0)	7.3%-14.7%	. . .
Mania/hypomania	13 (2.2)	5 (3.5)	2 (1.4)	6 (4.2)	0 (0.0)	0.0%-1.0%	. . .
Other (eg, bulimia, enuresis)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0.0%-5.2%	. . .
Columbia Impairment Scale (parent), mean (SD)	22.0 (8.0)	21.6 (8.8)	21.6 (7.9)	22.7 (7.6)	22.0 (7.8)	20.3-24.6	≤.01
Receiving ADHD medication prior to study, No. (%)	178 (31)	44 (30)	46 (32)	38 (26)	50 (34)	18%-43%	≤.0001
Parent/Family Variables							
High school graduate, No. (%)							
Mother	542 (94)	138 (96)	130 (91)	135 (95)	139 (95)	87%-100%	≤.001
Father	409/453 (90)	110 (93)	99 (87)	99 (92)	101 (89)	75%-99%	≤.001
Employed, No. (%)§							
Mother	406 (71)	97 (67)	95 (66)	109 (77)	105 (72)	59%-78%	≤.01
Father	379/448 (85)	99 (85)	99 (87)	91 (84)	90 (82)	72%-94%	≤.01
Welfare, No. (%)	110 (19)	28 (19)	30 (21)	22 (15)	30 (21)	9%-41%	≤.001
Income, $, No. (%)							
0-20 000	124 (21)	30 (21)	30 (21)	33 (23)	31 (21)	7%-19%‡	≤.001
20 000-50 000	239 (41)	55 (38)	63 (44)	58 (40)	63 (43)	28%-55%‡	
>50 000	213 (36)	59 (41)	49 (34)	53 (47)	52 (36)	28%-43%‡	
Unknown	3 (1)	1 (1)	2 (1)	. . .	. . .		
Married, No. (%)§	374 (65)	98 (68)	94 (66)	85 (59)	97 (66)	52%-73%	≤.05
Family composition, No. (%)	575						
2 Parents	396 (69)	102 (71)	103 (72)	89 (63)	102 (70)	56%-79%	. . .
1 Parent	175 (30)	41 (28)	41 (28)	51 (36)	42 (28)	21%-44%	
Other	4 (1)	1 (1)	0 (0)	1 (1)	3 (2)	0%-3%‡	

**WISC-III indicates Wechsler Intelligence Scale for Children–Third Edition; DISC, Diagnostic Interview Schedule for Children; and ADHD, attention-deficit/hyperactivity disorder. Ellipses indicate that the value was not significant.*

†Treatment groups differed significantly on only 1 variable (age), while sites differed significantly on most variables.

‡Values measured using overall χ^2 test.

§Employed refers to the proportion of the sample whose parents held full-time jobs; married refers to those with intact 2-parent families (married or common law).

Table 4. Baseline and 14-Month Outcome Variables*†

Outcome Domain	Measure and Rater	Combined Treatment		Medication Management	
		Baseline (SD) [No. of Subjects]	14 mo (SD) [No. of Subjects]	Baseline (SD) [No. of Subjects]	14 mo (SD) [No. of Subjects]
ADHD symptoms	Inattention				
	Teacher	2.16 (0.67) [137]	1.12 (0.75) [134]	2.27 (0.61) [135]	1.11 (0.77) [120]
	Parent	2.07 (0.61) [140]	1.02 (0.66) [133]	2.03 (0.64) [140]	1.12 (0.70) [121]
	Hyperactive/impulsive				
	Teacher	1.89 (0.77) [137]	0.75 (0.71) [134]	2.08 (0.71) [135]	0.82 (0.69) [120]
	Parent	1.91 (0.69) [140]	1.85 (0.63) [133]	1.89 (0.62) [140]	0.91 (0.65) [121]
	Classroom observer	0.33 (0.22) [122]	0.21 (0.20) [114]	0.31 (0.21) [119]	0.16 (0.15) [110]
Aggression-ODD	ODD aggression				
	Teacher	1.29 (0.91) [137]	0.61 (0.68) [134]	1.39 (0.92) [0.92]	0.65 (0.68) [120]
	Parent	1.39 (0.71) [140]	0.76 (0.64) [133]	1.45 (0.80) [139]	0.94 (0.74) [121]
	Classroom observer	0.018 (0.038)[122]	0.007 (0.015) [114]	0.014 (0.025) [119]	0.004 (0.011) [108]
Internalizing symptoms	SSRS internalizing symptoms				
	Teacher	0.73 (0.51) [113]	0.68 (0.44) [108]	0.79 (0.47) [117]	0.63 (0.47) [99]
	Parent	0.98 (0.37) [138]	0.67 (0.37) [127]	0.97 (0.37) [137]	0.67 (0.39) [120]
	MASC				
	Child	2.58 (0.47) [144]	2.33 (0.47) [133]	2.48 (0.49) [143]	2.22 (0.47) [125]
Social skills	SSRS‡				
	Teacher	0.84 (0.29) [113]	1.19 (0.30) [108]	0.83 (0.31) [117]	1.15 (0.32) [99]
	Parent	1.04 (0.23) [138]	1.22 (0.27) [127]	1.01 (0.24) [137]	1.17 (0.26) [120]
	Sociometrics§				
	Peers	. . .	2.89 (0.91) [79]	. . .	2.84 (0.91) [68]
Parent-child relations	Power assertion				
	Parent	2.66 (0.54) [141]	2.31 (0.56) [133]	2.75 (0.56) [140]	2.46 (0.57) [122]
	Personal closeness‡				
	Parent	3.56 (0.52) [141]	3.64 (0.52) [133]	3.58 (0.49) [140]	3.55 (0.52) [122]
Academic achievement‖	Child's scores				
	Reading¶	96.5 (14.6) [145]	99.4 (15.2) [136]	96.1 (13.7) [144]	97.9 (14.1) [124]
	Mathematics	97.9 (15.1) [145]	100.5 (16.4) [136]	97.2 (12.6) [144]	99.7 (13.0) [124]
	Spelling	95.1 (14.8) [144]	97.0 (14.4) [136]	95.2 (13.1) [144]	96.0 (14.8) [124]

*ADHD indicates attention-deficit/hyperactivity disorder; ODD, oppositional-defiant disorder; SSRS, Social Skills Rating System; and MASC, Multidimensional Anxiety Scale for Children. Ellipses indicate that the variable was examined only at end point.

†Higher score indicates increased symptoms or impairment unless otherwise indicated.

‡A higher score indicates increased ability.

§Planned contrasts: combined treatment and medication management were more effective than behavioral treatment ($P<.05$, not significant after Bonferroni correction). Analysis of variance compared sociometric scores across group ($N = 281$): treatment group, $F = 2.3$, $P<.08$ (not significant after Bonferroni correction); site × treatment, $F_{23,257} = 1.5$.

‖Analysis of covariance compared reading subtest scores across group ($N = 553$): overall, $F = 33.9$, $P<.001$; treatment group, $F = 3.75$, $P<.001$; and site × treatment, not significant, with an overall df of 23,529. Pairwise comparisons: combined treatment was more effective than behavioral treatment and community care in pairwise contrasts. The analyses of math and spelling yielded no significant main effects for treatment group, so no pairwise comparisons were performed.

¶Measured using Wechsler Individual Achievement Test; a higher score was better.

themselves, with 3 exceptions (combined treatment > behavioral treatment for parent-reported internalizing problems and oppositional/aggressive symptoms, and Weschler Individual Achievement Test reading achievement score).

With respect to comparisons of MTA treatments with community care, combined treatment and medication management fared substantially better than community care on most ADHD outcome measures, while behavioral treatment did not. According to least 1 informant, combined treatment also fared significantly better than community care for all 5 non-ADHD domains: parent-reported oppositional/aggressive symptoms, parent-reported internalizing problems, teacher-reported social skills, parent-child relations, and reading achievement. In contrast, medication management and behavioral treatment each fared better than community care in 1 non-ADHD domain only (teacher-rated social skills and parent-child relations).

Our finding that MTA treatments (most notably combined treatment) offered greater benefits than community care for oppositional/aggressive behaviors, internalizing symptoms, peer interactions, parent-child relations, and reading achievement has not been previously reported in long-term studies.[3,5,14] However, the differential benefits in these non-ADHD domains are consistent with the theoretical aims of multimodal approaches.[14] For example, medication is known to reduce negative peer interactions dramatically, but increases in positive social behavior are far less robust.[48] Such changes might require intensive and long-term application of the behavioral components of combined treatments, such as those found in our STP and school-based interventions.[38] Similarly, parent training, which includes positive parental attention and rewards for the child's appropriate behavior, when combined with medication, might be expected to decrease oppositionality and

Behavioral Treatment		Assessment and Referral	
Baseline (SD) [No. of Subjects]	14 mo (SD) [No. of Subjects]	Baseline (SD) [No. of Subjects]	14 mo (SD) [No. of Subjects]
2.28 (0.64) [136]	1.47 (0.81) [119]	2.19 (0.69) [135]	1.48 (0.82) [128]
1.99 (0.63) [139]	1.40 (0.68) [129]	2.05 (0.65) [142]	1.49 (0.67) [130]
2.05 (0.75) [136]	1.10 (0.77) [119]	1.93 (0.81) [135]	1.25 (0.84) [128]
1.89 (0.64) [140]	1.24 (0.72) [129]	1.95 (0.67) [142]	1.35 (0.72) [130]
0.37 (0.26) [120]	0.29 (0.26) [107]	0.38 (0.27) [118]	0.18 (109) [0.15]
1.43 (0.86) [136]	0.97 (0.80) [119]	1.35 (0.88) [135]	1.00 (0.84) [128]
1.37 (0.70) [140]	1.05 (0.74) [129]	1.49 (0.70) [142]	1.11 (0.67) [130]
0.020 (0.046) [120]	0.010 (0.018) [107]	0.019 (0.026) [118]	0.006 (0.014) [109]
0.82 (0.45) [115]	0.58 (0.40) [102]	0.78 (0.44) [115]	0.69 (0.44) [105]
0.93 (0.43) [133]	0.77 (0.40) [131]	0.97 (0.35) [137]	0.82 (0.43) [125]
2.46 (0.55) [143]	2.27 (0.49) [132]	2.49 (0.58) [145]	2.27 (0.45) [124]
0.80 (0.25) [115]	1.06 (0.32) [102]	0.87 (0.29) [115]	1.05 (0.31) [105]
1.02 (0.22) [133]	1.15 (0.24) [131]	1.03 (0.23) [137]	1.15 (0.24) [125]
. . .	3.23 (1.03) [69]	. . .	3.05 (0.82) [65]
2.75 (0.50) [141]	2.47 (0.47) [131]	2.71 (0.57) [142]	2.52 (0.57) [130]
3.52 (0.49) [141]	3.59 (0.48) [132]	3.58 (0.48) [142]	3.63 (0.44) [130]
95.1 (14.1) [144]	96.2 (14.9) [134]	95.5 (14.3) [146]	95.4 (14.2) [131]
97.7 (13.2) [144]	100.3 (13.7) [134]	98.6 (14.1) [146]	100.4 (15.2) [131]
92.8 (12.5) [144]	93.7 (13.9) [134]	93.7 (13.1) [146]	94.2 (14.1) [131]

enhance parent-child relations more than medication alone. For internalizing symptoms, the relatively greater improvements for subjects given combined treatment are particularly noteworthy, as none of our treatments were designed to address this domain specifically.

The MTA study extends the findings of previous studies that demonstrated short-term, robust efficacy of medication management, showing that these benefits persist during treatment up to 14 months. In contrast to frequently expressed concerns, children given combined treatment and medication management tolerated medication well, including a third dose given in the afternoon. The relative improvements attributed to medication management also parallel findings from other, longer-duration stimulant trials.[9,10,49] Given the MTA's size and scope, however, we saw effects across diverse settings, patient groups, provider characteristics, and outcome domains. These findings were further strengthened by the absence of any site×treatment interactions.

Although combined treatment and medication management were generally superior to community care, community treatments usually included medication; hence, it is unclear which components of the 2 MTA medication treatments may have rendered them more effective than community care. Further analyses of these findings are presented in our companion report,[40] but reviewing the apparent differences is instructive. We used a manualized medication titration procedure and "thrice-daily" dosing, as well as higher, carefully monitored daily doses to maximize positive effects and minimize side effects.[15] We met with parents monthly and obtained systematic feedback, from both them and the children's teachers. Parent guidance and selected readings were provided as needed; this is reported to provide benefits over simple pill dispensing alone.[50] These components, particularly the systematic and regular feedback from teachers, do not seem to be part of routine pediatric ADHD treatment practices,[13] and may have enhanced the effectiveness of our medication management.

The modest benefits for some non-ADHD domains obtained by multimodal treatments have been reported previously[5,51,52] after 3 to 4 months of treatment. In contrast, the study by Hechtman and Abikoff[10] failed to demonstrate these effects after 12 months of active treatment, perhaps because of their smaller sample (103 subjects distributed across 3 groups). In addition to the MTA's sample size advantages, its behavioral component design required that behavioral treatment interventions be delivered across multiple settings and caretakers (home, school, and STP), augmented with further strategies to facilitate the generalization of effects across settings and over time[17,19]—all enhancements not found in previous studies.[8]

Whether there is greater value for multimodal treatments for ADHD depends on which intervention is considered as the comparison. If one assumes that a behavioral intervention should always be used as the first-line ADHD treatment (often the preference for many parents, and the practice in many European countries), and that the possibly greater benefits of combined treatment should be determined, then combined treatment seems to offer a great deal of benefit over behavioral treatment alone. But if one provides carefully monitored medication treatment similar to that used in this study as the first line of treatment, our results suggest that many treated children may not require intensive behavioral interventions.[47]

The significantly lower total daily doses of methylphenidate in the combined treatment arm are noteworthy but not unforeseen.[42,47] The importance of this finding is unclear, and a rigorous test of this question would likely require a different design. Nonetheless, this issue remains an ongoing source of concern of many parents and clinicians and should not be dismissed, particularly since side effects are usually related to dosage. If equivalent, sometimes better results can be obtained by a combined treatment that uses lower doses, such findings may have public health importance.

Concerning the relative benefits of our behavioral treatment alone, results must be understood within the context of the limitations of our study design. Most importantly, our design did not include a no-treatment or placebo group (an ethically unacceptable option for an

Table 5. Random-Effects Regression Analysis*

Outcome Domains†	Measure and Rater	Random Regressions	Results of Pairwise Comparisons‡: Med Mgt vs Behav	*P*	Comb vs Med Mgt and Comb vs Behav
ADHD symptoms	Inattention				
$P \leq .01^a$, $.002^b$	Teacher	Treatment × time: $F_{3,666} = 10.6$; $P < .001$ Treatment × site: F = 0.9; $P = .56$ Site: F = 2.7; $P = .02$	Med Mgt>Behav	.001	Comb/Med Mgt Comb>Behav
	Parent	Treatment × time: $F_{3,669} = 21.5$; $P < .001$ Treatment × site: F = 0.6; $P = .88$ Site: F = 3.0; $P = .02$	Med Mgt>Behav	.001	Comb/Med Mgt Comb>Behav
	Hyperactive-impulsive				
	Teacher	Treatment × time: $F_{3,669} = 10.0$; $P < .001$ Treatment × site: F = 1.3; $P = .49$ Site: F = 3.0; $P = .02$	Med Mgt ≈ Behav	.004§	Comb ≈ Med Mgt Comb ≈ Behav
	Parent	Treatment × time: $F_{3,609} = 21.5$; $P < .001$ Treatment × site: F = 1.3; $P = .23$ Site: F = 4.4; $P = .0006$	Med Mgt>Behav	.001	Comb ≈ Med Mgt Comb>Behav
	Classroom				
	Classroom observer	Treatment × time: $F_{3,417} = 2.6$; $P = .05$ Treatment × site: F = 1.5; $P = .11$ Site: F = 11.5; $P < .001$	Med Mgt ≈ Behav	.02§	Comb ≈ Med Mgt Comb ≈ Behav
Aggression-ODD	ODD = aggression				
$P \leq .02^a$, $.003^b$	Teacher	Treatment × time: $F_{3,663} = 6.5$; $P = .0003$ Treatment × site: F = 1.2; $P = .25$ Site: F = 4.2; $P = .001$	Med Mgt ≈ Behav	.01§	Comb ≈ Med Mgt Comb ≈ Behav
	Parent	Treatment × time: $F_{3,892} = 7.4$; $P < .001$ Treatment × site: F = 1.1; $P = .40$ Site: F = 4.3; $P = .0007$	Med Mgt ≈ Behav	.007§	Comb ≈ Med Mgt Comb>Behav
	Classroom observer	Treatment × time: $\chi^2 = 6.9$; $P = .10$ Treatment × site: $\chi^2 = 18.5$; $P = .30$ Site: $\chi^2 = 85.4$; $P < .001$	. . .	. . .	. . . . . .
Internalizing symptoms	SSRS Internalizing				
$P \leq .02^a$, $.003^b$	Teacher	Treatment × time: $F_{3,679} = 2.1$; $P = .10$ Treatment × site: F = 0.5; $P = .92$ Site: F = 1.6; $P = .17$	. . .	. . .	. . . . . .
	Parent	Treatment × time: $F_{3,883} = 9.2$; $P < .001$ Treatment × site: F = 1.1; $P = .35$ Site: F = 2.2; $P = .05$	Med Mgt ≈ Behav	.03§	Comb ≈ Med Mgt Comb>Behav
	MASC				
	Child	Treatment × time: $F_{3,529} = 0.6$; $P = .65$ Treatment × site: F = 0.07; $P = .78$ Site: F = 2.2; $P = .05$	. . .	. . .	. . . . . .
Social skills	SSRS				
$P \leq .02^a$, $.003^b$	Teacher	Treatment × time: $F_{3,668} = 6.1$; $P = .0004$ Treatment × site: F = .05; $P = .96$ Site: F = 3.9; $P = .002$	Med Mgt ≈ Behav	. . .	Comb ≈ Med Mgt Comb ≈ Behav
	Parent	Treatment × time: $F_{3,887} = 2.2$; $P = .09$ Treatment × site: F = 1.0; $P = .86$ Site: F = 3.8; $P = .02$	Med Mgt ≈ Behav	. . .	Comb ≈ Med Mgt Comb ≈ Behav
Parent-child relations	Power assertion				
$P \leq .03^a$, $.004^b$	Parent	Treatment × time: $F_{3,906} = 5.6$; $P = .0008$ Treatment × site: F = 1.0; $P = .45$ Site: F = 2.8 $P = .02$	Med Mgt ≈ Behav	. . .	Comb ≈ Med Mgt Comb ≈ Behav
	Personal closeness				
	Parent	Treatment × time: $F_{3,908} = 2.0$; $P = .0008$ Treatment × site: F = 1.0; $P = .54$ Site: F = 1.2; $P = .32$	. . .	. . .	. . . . . .

**Med Mgt indicates medication management; Behav, behavioral treatment; Comb, combined treatment; CC, community care; ADHD, attention-deficit/hyperactivity disorder; ODD, oppositional-defiant disorder; SSRS, Social Skills Rating System; and MASC, Multidimensional Anxiety Scale for Children. Ellipses indicate that the omnibus and/or pairwise test result was not significant.*

†Outcome domains were measured by Bonferroni-corrected α levels of significance, with omnibus(a) and pairwise (b) comparisons.

‡Done only when omnibus analysis for treatment × time effect was significant.

§P values not significant after Bonferroni correction.

for 3 Main Study Questions			
P	Comb vs CC, Med Mgt vs CC, and Behav vs CC	*P*	Estimate of Time Trend (SE)
. . .	Comb>CC	.001	−0.188 (0.017)
.005	Med Mgt>CC	.001	−0.196 (0.017)
	Behav ≈ CC	. . .	−0.127 (0.017)
			−0.116 (0.017)
. . .	Comb>CC	.001	−0.181 (0.014)
.001	Med Mgt>CC	.001	−0.161 (0.014)
	Behav ≈ CC	. . .	−0.096 (0.014)
			−0.090 (0.014)
. . .	Comb>CC	.001	−0.197 (0.018)
.04§	Med Mgt>CC	.001	−0.214 (0.018)
	Behav ≈ CC	.05§	−0.159 (0.018)
			−0.121 (0.018)
. . .	Comb>CC	.001	−0.176 (0.013)
.001	Med MgtCC	.001	−0.165 (0.013)
	Behav ≈ CC	. . .	−0.104 (0.013)
			−0.092 (0.013)
. . .	Comb ≈ CC	. . .	−0.057 (0.013)
.04§	Med Mgt ≈ CC	. . .	−0.066 (0.013)
	Behav ≈ CC	.03§	−0.034 (0.013)
			−0.067 (0.013)
. . .	Comb>CC	.004	−0.124 (0.010)
.01§	Med Mgt>CC	.004	−0.124 (0.010)
	Behav ≈ CC	. . .	−0.077 (0.010)
			−0.061 (0.010)
. . .	Comb>CC	.002	−0.105 (0.018)
.001	Med Mgt ≈ CC	.008§	−0.090 (0.018)
	Behav ≈ CC	. . .	−0.057 (0.018)
			−0.056 (0.018)
. . .	. . .	. . .	−0.168 (0.031)
. . .	. . .	. . .	−0.193 (0.030)
	. . .	. . .	−0.108 (0.030)
			−0.169 (0.030)
. . .	. . .	. . .	−0.018 (0.012)
. . .	. . .	. . .	−0.026 (0.012)
	. . .	. . .	−0.034 (0.012)
			−0.005 (0.012)
.04§	Comb>CC	.001	−0.051 (0.007)
.001	Med Mgt ≈ CC	.003§	−0.039 (0.007)
	Behav ≈ CC	. . .	−0.021 (0.007)
			−0.017 (0.007)
. . .	. . .	. . .	−0.038 (0.010)
. . .	. . .	. . .	−0.034 (0.010)
	. . .	. . .	−0.024 (0.010)
			−0.036 (0.010)
. . .	Comb>CC	.001	0.058 (0.007)
.03§	Med Mgt ≈ CC	.009	0.058 (0.007)
	Behav ≈ CC	.03§	0.045 (0.007)
			0.031 (0.007)
. . .	Comb>CC	.02§	0.029 (0.004)
.03§	Med Mgt>CC	. . .	0.024 (0.004)
	Behav ≈ CC	. . .	0.021 (0.004)
			0.019 (0.004)
. . .	Comb>CC	.003	−0.059 (0.008)
. . .	Med Mgt ≈ CC	.006§	−0.050 (0.008)
	Behav ≈ CC	.005	−0.057 (0.008)
			−0.027 (0.008)
. . .	. . .	. . .	0.011 (0.008)
. . .	. . .	. . .	−0.005 (0.008)
	. . .	. . .	0.013 (0.008)
			0.007 (0.005)

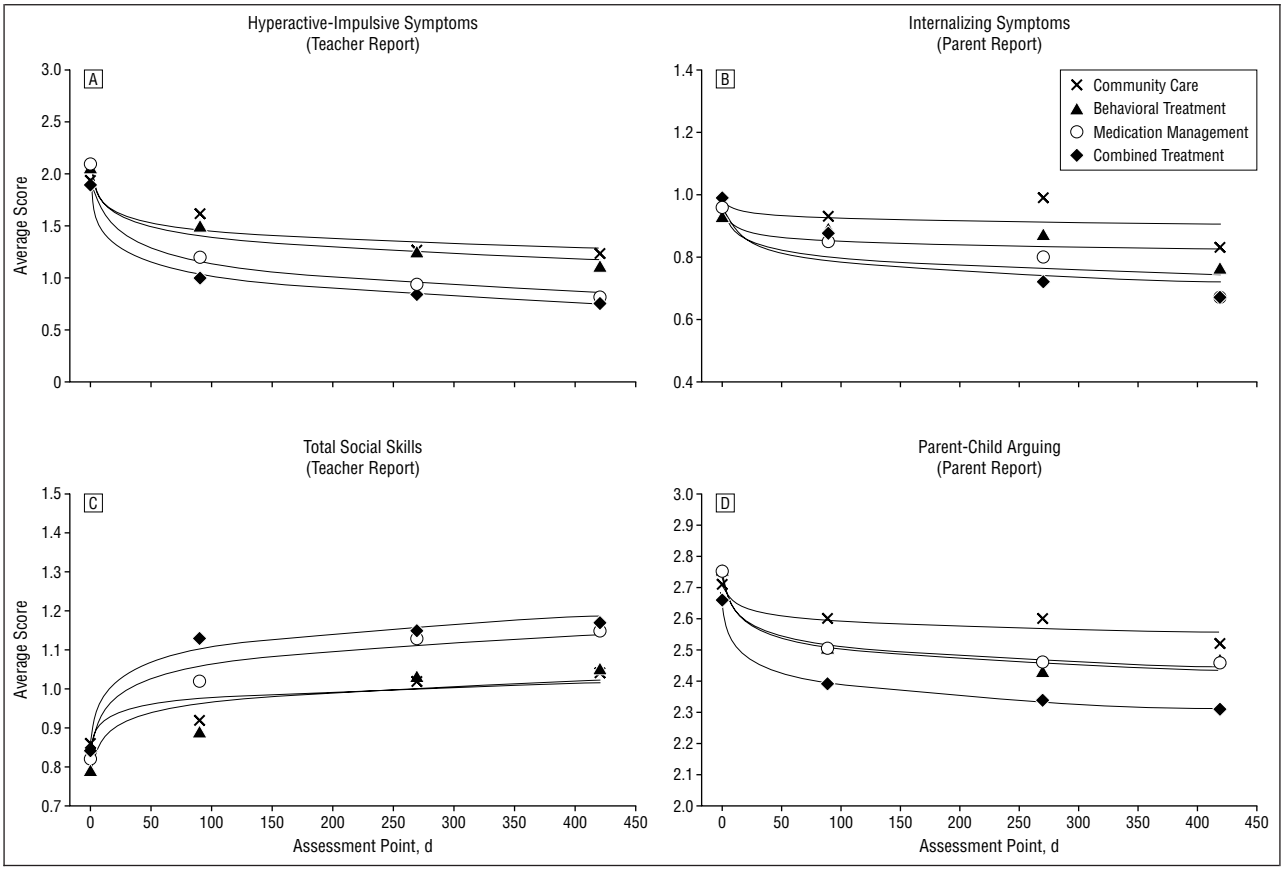
ADHD study of this length), and most subjects given community care received medication for most of the study period—a treatment of known efficacy. Substantial improvement occurred over time across all groups (including community care), regardless of rating source or method. While some of this change could be regression to the mean, this explanation cannot account for the substantial group differences reported here. More than three fourths of subjects given behavioral treatment were successfully maintained without medication throughout the study. Consequently, it should not be concluded that behavioral treatment interventions did not work.

One caveat concerns our choice and number of outcome measures. We felt that the treatment effects in different domains and from different respondents might vary, and that these variations were necessary in interpreting the results of the study. Consequently, despite the loss of power caused by Bonferonni corrections, we chose 19 primary outcome measures rather than a single summary outcome score. Power calculations[17] that underlay the setting of sample size were based on setting as the lower limit of clinical significance an effect size of 0.4 ("small to moderate"[53]) and on the requirement of 80% power (5% level of confidence) to detect effects of that magnitude. Thus, the chance is high of declaring effect sizes lower than 0.4 not statistically significant, even though some clinicians might regard such effects as clinically significant.

Hence, for purposes of assessing clinical significance, the overall pattern of results may be more instructive than any single test statistic or *P* value reported in Tables 4 and 5. The general ordering of treatment groups' benefits is confirmed by simple inspection of the number of times each group placed first compared with all others on the 19 outcome measures: combined treatment, 12; medication management, 4; behavioral treatment, 2; and community care, 1. While combined treatment scored numerically "best" on most outcome measures, we did not have statistical power to detect small effects, such as those that might exist between combined treatment and medication management.[25] Statistical significance, of course, cannot be interpreted as necessarily indicative of clinical or practical significance, and lack of significance is never proof of the equivalency of treatments.

By way of caution, we note that subgroup analyses may yield different treatment effects for specific patient groups than the main intent-to-treat analyses presented herein. In our companion article[40] we report analyses indicating that children with ADHD who have co-occurring disorders, as well as those with fewer family resources, are more likely to benefit specifically from combined and behavioral treatments for some outcome domains. In addition, other unidentified individual factors may yield excellent responses to one of the several treatments.[47] Response patterns and characteristics of such "excellent responders" will likely be obscured by large-group analyses. Future studies will examine these issues in more detail.

Such considerations highlight the need for caution in interpreting our results and argue against a "one size fits all" approach to treatment. Moreover, our results can-



For internalizing symptoms (parent reported), combined treatment and medication management symbols overlapped at the 14-month data point. For parent-child arguing (power assertion, parent reported), medication management and intensive behavioral treatment symbols overlapped at the 3-month and 14-month data points. A, Combined treatment and medication management were more effective than community care. B, Combined treatment was more effective than behavioral treatment and community care. C, Combined treatment and medication management were more effective than community care. D, Combined and behavioral treatment were more effective than community care.

not necessarily be generalized beyond ADHD Combined Type; other ADHD subtypes (eg, inattentive subtype) may warrant somewhat different treatments.

Previous research has shown that the medication benefits persist only so long as treatment is continued.[6,54] Whenever possible, our subjects given combined treatment and medication management received medication throughout the 14 months, including all assessment points. By contrast, and consistent with clinical practice, for subjects given behavioral treatment, the frequency of contact with therapists was gradually reduced to once-monthly contacts 3 to 6 months prior to posttreatment assessment; in general, they were assessed up to 1 month after their last treatment contact. Procedures for maintenance and generalization were incorporated throughout behavioral treatment's implementation; the goal was that benefits would persist as parents and children learned and consolidated their skills. However, our behavioral treatment procedures, increasingly nonintensive during the once-monthly contacts, were insufficient to produce overall effects comparable or additive with 14 months of ongoing medication management for core ADHD symptoms.

Unanswered in our study are important questions concerning behavioral and combined treatments for ADHD. Are there some children for whom medication management is no longer necessary,[9] and if so, why does this occur? Might the behavioral component of combined treatment allow some children to be successfully tapered off medication? Can and should behavioral and pharmacologic treatments be tapered, and how can that be accomplished while maintaining effects? Will findings differ as children age, such that those who have learned increased skills via behavioral interventions eventually function better than those receiving only medication? Follow-up study of our subjects past 14 months (currently under way) will address some of these critical questions.

Since ADHD is now regarded by most experts as a chronic disorder,[14] ongoing treatment often seems necessary. As with other chronic conditions, such as diabetes and asthma, the need for active treatment may wax and wane. Just as exercise, diet, and pollen load may affect these illnesses, persons' learning or work environments and intercurrent stressors may affect the need for, type, and intensity of ADHD treatments over the life course.[55] Under such conditions, behavioral treatments may help families actively cope with their child's disorder and make the necessary life accommodations to optimize family functioning, even when such treatments are not as effective as medication in reducing children's ADHD symptoms. Indeed, 14-month end-point analyses indicated that parent satisfaction ratings differed significantly by treatment group; pairwise contrasts showed that

treatment satisfaction scores for combined treatment and behavioral treatment parents were significantly superior to medication management parents' ratings (though not differing between themselves), suggesting that the behavioral treatment components benefitted this area of family-relevant outcomes.

The absence of any site×treatment×time interactions suggests that both our pharmacological and behavioral treatments could be delivered with fidelity across 6 very different clinical settings. However, the use of these treatments will ultimately be determined by the degree to which they are feasible, transportable, and affordable in real-world settings—topics for future research. In the interim, however, the MTA study, by virtue of its size; scope; length; parallel group design; explicit use of manualized, evidence-based treatments; high degree of compliance across arms and over the course of the study; and comprehensive range of outcome assessments, sets an important benchmark for future trials testing new treatments for childhood ADHD.

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