Nonpharmacologic Treatments for Attention-Deficit/Hyperactivity Disorder: A Systematic Review

Adam P. Goode, DPT, PhD,a,b Remy R. Coeytaux, MD, PhD,c,d Gary R. Maslow, MD, MPH,e,f Naomi Davis, PhD,g Sherika Hill, MHA, PhD,h Behrouz Namdari, MD,i Nancy M. Allen LaPointe, PharmD, MHS,j,k Deanna Befus, PhD,k,l Kathryn R. Lallinger, MSLS,m,n Samantha E. Bowen, PhD,o Andrzej Kosinski, PhD,p Amanda J. McBroom, PhD,p,q, Sherika Hill, MHA, PhD,h and Alex R. Kemper, MD, MPH, MSr

CONTEXT: Nonpharmacologic treatments for attention-deficit/hyperactivity disorder (ADHD) encompass a range of care approaches from structured behavioral interventions to complementary medicines.

OBJECTIVES: To assess the comparative effectiveness of nonpharmacologic treatments for ADHD among individuals 17 years of age and younger.


STUDY SELECTION: We included studies that compared any ADHD nonpharmacologic treatment strategy with placebo, pharmacologic, or another nonpharmacologic treatment.

DATA EXTRACTION: Study design, patient characteristics, intervention approaches, follow-up times, and outcomes were abstracted. For comparisons with at least 3 similar studies, random-effects meta-analysis was used to generate pooled estimates.

RESULTS: We identified 54 studies of nonpharmacologic treatments, including neurofeedback, cognitive training, cognitive behavioral therapy, child or parent training, dietary omega fatty acid supplementation, and herbal and/or dietary approaches. No new guidance was identified regarding the comparative effectiveness of nonpharmacologic treatments. Pooled results for omega fatty acids found no significant effects for parent rating of ADHD total symptoms (n = 411; standardized mean difference −0.32; 95% confidence interval −0.80 to 0.15; I² = 52.4%; P = .10) or teacher-rated total ADHD symptoms (n = 287; standardized mean difference −0.08; 95% confidence interval −0.47 to 0.32; I² = 0.0%; P = .56).

LIMITATIONS: Studies often did not reflect the primary care setting and had short follow-up periods, small sample sizes, variations in outcomes, and inconsistent reporting of comparative statistical analyses.

CONCLUSIONS: Despite wide use, there are significant gaps in knowledge regarding the effectiveness of ADHD nonpharmacologic treatments.
Many options exist for treating attention-deficit/hyperactivity disorder (ADHD) beyond commonly used psychostimulant drugs. Nonpharmacologic approaches either alone or in combination with psychostimulants might improve ADHD symptoms and reduce the risk associated with psychostimulants by decreasing their use. Nonpharmacologic therapies encompass a broad range of approaches, from highly structured behavioral interventions to complementary medicines. Behavioral interventions include neurofeedback, cognitive training, cognitive behavioral therapy (CBT), or child or parent training. Additional approaches have focused on dietary, herbal, or omega fatty acid supplementation.

Our goal was to systematically evaluate the comparative effectiveness and safety of nonpharmacologic approaches to ADHD. This report is a subset of a systematic review sponsored by the Agency for Healthcare Research and Quality (AHRQ) to address broad issues related to the diagnosis and management of ADHD. In this report, we update a previous systematic review published in 2011 that was focused on the effectiveness of ADHD treatment in at-risk preschoolers, the long-term effectiveness of ADHD treatment in all ages, and the variability in ADHD prevalence, diagnosis, and treatment. In the 2011 report, dietary or complementary medicine approaches to the management of ADHD were not considered. In addition, that report only required a comparator group to assess effectiveness of therapy for preschool-aged children. The authors of the 2011 report indicated that, in general, nonpharmacologic (psychosocial and/or behavioral) interventions alone were not as effective as US Food and Drug Administration (FDA)–approved pharmacologic management of ADHD with a slight advantage to combining psychosocial or behavioral interventions with pharmacologic management. Parent behavior training as first-line treatment in preschoolers had high strength of evidence (SOE) in contrast to pharmacologic interventions.

METHODS
We followed the methods for systematic reviews recommended in AHRQ’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist using a published protocol (PROSPERO #CRD42016029134). Complete details are provided in the full AHRQ report.

Data Sources and Search Strategy
We searched Medline, Embase, PsycINFO, and the Cochrane Database of Systematic Reviews, limiting the search to English-language studies published from January 1, 2009 through November 7, 2016. We chose to assess evidence from 2009 forward to (1) ensure that the data represent current therapies and (2) allow this report to build on the previous systematic review published in 2011. Database searches were supplemented with additional searches of clinical study registries and manual search of citations from key articles. Exact search terms are provided in Supplemental Table 16. We required comparison of the intervention to (1) other nonpharmacologic treatments, (2) FDA-approved pharmacologic treatments, or (3) placebo, usual care, or waitlist. Studies had to include a sample size of at least 50 subjects. We set a minimum sample size to exclude pilot studies and potentially low-quality studies. In addition, a sample size of 50 subjects would improve the likelihood of detecting clinically meaningful differences. No restrictions were placed on timing of outcomes or on setting. Complete details of the inclusion and exclusion criteria for the full AHRQ review are in the Supplemental Table 16.

Study Selection and Data Extraction
Pairs of investigators screened titles and abstracts independently. Citations deemed relevant by at least 1 reviewer were promoted to full-text screening, in which 2 investigators independently reviewed each article. Disagreements were resolved through discussion or by a third expert member of the team. Pairs of investigators abstracted data from included studies, with 1 researcher abstracting the data and a second overreading the article and the accompanying abstraction to check for accuracy and completeness. Disagreements were resolved by consensus or by obtaining a third investigator’s opinion.

Quality and Applicability Assessment of Individual Studies
We assessed the methodological quality, or risk of bias, for each individual study using the Cochrane Risk of Bias tool for randomized studies and the Newcastle-Ottawa Scale for observational studies. We rated each study’s quality as good (low risk of bias), fair, or poor (high risk of bias) on the basis of its adherence to well-accepted standard methods (Supplemental Table 17). The assessment was outcome specific such that a given study might receive a “good” quality rating for its analysis...
of 1 outcome but a “poor” quality rating for analysis of a different outcome. We assessed applicability using the method described in AHRQ’s Methods Guide.4,8

Data Synthesis

When meta-analysis was feasible, we computed summary estimates of effect. We aggregated outcomes when there were at least 3 studies with the same outcome using random-effects models with the Knapp-Hartung correction to adjust the SEs for small (≤4) numbers of included studies. All quantitative analyses were performed in R (R Foundation for Statistical Computing, Vienna, Austria).10

If a quantitative synthesis was not feasible, we analyzed the data qualitatively. We placed greater emphasis on the conclusions from evidence from higher quality studies with more precise estimates of effect.

We divided treatment strategies for ADHD by their comparators: FDA-approved pharmacologic versus nonpharmacologic and nonpharmacologic versus nonpharmacologic or placebo. Nonpharmacologic therapies include psychosocial interventions, behavioral interventions, school interventions, cognitive training therapies, learning training, biofeedback or neurofeedback, parent behavior training, dietary supplements (eg, omega fatty acids, vitamins, herbal supplements, probiotics), elimination diets, vision training, and chiropractic treatment. We combined studies of omega-3 and omega-6 fatty acids.

SOE

We assessed the SOE using the approach described in AHRQ’s Methods Guide.4,11 The approach requires assessment of 5 domains: study limitations, consistency, directness, precision, and reporting bias, the last of which includes publication bias, outcome reporting, and analysis reporting bias.

These domains were considered qualitatively, and a summary rating of high, moderate, or low SOE was assigned for each outcome after discussion by 2 reviewers. When no evidence was available or when evidence on the outcome was too weak, sparse, or inconsistent to permit any conclusion to be drawn, a grade of “insufficient” was assigned.

RESULTS

Result of Literature Search

Figure 1 depicts the flow of articles through the literature search and screening process for the full AHRQ systematic review.2 Of 10 764 unique citations screened, 66 articles describing 54 studies provided data relevant to the nonpharmacologic treatment.12–77 For this report, we summarize reported outcomes of changes on standardized symptom scores or progress toward patient-identified goals. Other study outcomes relating to treatment, behavior, and function were abstracted and are presented in the Supplemental Information.

Neurofeedback

Findings for neurofeedback interventions versus nonpharmacologic or pharmacologic...
or placebo, usual care, or waitlist are described in Supplemental Table 18. In 4 randomized controlled trials (RCTs), 19,34,55,68,69 in which a total of 353 participants were enrolled, researchers examined neurofeedback as an intervention versus a nonpharmacologic intervention (n = 3), pharmacologic intervention (n = 1), or placebo, usual care, or waitlist (n = 3).

Nonpharmacologic Versus Pharmacologic

In 3 studies, researchers examined neurofeedback as the primary intervention and evaluated standardized symptoms scores or progress toward patient-identified goals. 34,55,68,69 All 3 studies were RCTs: 2 were of good quality 34,68,69 and 1 was of fair quality. 55 Follow-up times were either not reported or short-term (2 months). In 1 study, researchers found a statistically significant decrease in ADHD symptoms using a standard scale comparing neurofeedback with an attention skills control condition. 34,35,75 In a second study, researchers found significant improvements in ADHD symptoms according to parent and teacher reporting for neurofeedback compared with control. 68,69 Subjects in the control group also had a statistically significant increase in their average dose of stimulant therapy compared with those in the neurofeedback group, who did not have a significant change in stimulant therapy. A third study compared neurofeedback to behavioral treatment and found that the group treated with neurofeedback showed greater improvement in a continuous performance test score. 55

Nonpharmacologic Versus Pharmacologic

In 1 3-arm trial, researchers combined methylphenidate with neurofeedback 35,24 enrolling 91 participants and short follow-up period of 10 weeks. This trial was judged to be of poor quality. The primary outcome measure was the Barkley Rating Scale for Parents. Findings from this study did not support any statistically significant differences between either methylphenidate alone, methylphenidate in addition to neurofeedback when compared with neurofeedback alone (P = .31).

Nonpharmacologic Versus Placebo, Usual Care, or Waitlist

In 3 RCTs, researchers compared neurofeedback to usual care or standard care enrolling a total of 251 participants. Two of the trials were judged to be of good quality 19,68,69 and 1 of fair quality. 55 In 2 of the studies, 55,68,69 researchers found significant differences on the standardized outcome measures when comparing neurofeedback to standard pharmacologic treatment or control.

Other Findings for Neurofeedback

No significant findings for other outcomes were identified. Detailed findings on neurofeedback interventions across the included studies are presented in Supplemental Table 19.

Cognitive Training

Findings for cognitive training interventions are described in Supplemental Table 20. In 5 RCTs 23,24,26,35,41,71,72,75 totaling 405 participants, researchers compared cognitive training to a nonpharmacologic intervention (n = 5) or placebo, usual care, or waitlist control (n = 1). In 1 observational study in which 18, 52 participants were enrolled, researchers compared cognitive training to waitlist control. Cognitive training was not compared to pharmacologic interventions and any studies.

Nonpharmacologic Versus Placebo, Usual Care, or Waitlist

In 1 RCT 28 and 1 observational study, 18 researchers compared cognitive training versus placebo or usual care. The RCT was judged to be of good quality and the observational study was judged to be of fair quality. A total of 127 participants were enrolled and follow-up times varied from 4 to 8 months. In the RCT, researchers compared Cogmed RoboMemo Program to a waitlist control group and at 8 months they report no significant differences on the ADHD rating scale (RS) Teacher or Parent total scores. In the observational study, researchers evaluated standardized symptoms scores or progress toward patient identified goals. Three were good quality 23,72 and the other was fair quality. 71 A total of 330 participants were enrolled across these 3 trials with predominately short follow-up times (≤6 months). In a single, good-quality RCT, researchers found no significant treatment effects in improvement in Wide Range Achievement Test 4 (WRAT-4) Progress Monitoring Version scores compared with a low-level working memory training program that was identical to active intervention with respect to the types of training games used and the number of training trials per session but for which difficulty level was not adjusted according to each user’s performance parameters. 23 No teacher measures revealed any significant changes. In the other study, there was improvement at 2 and 6 months on the parent rated Behavior Rating Inventory of Executive Function (BRIEF) Metacognition Index and at 2 months (but not 6 months) on the BRIEF parent-rated behavioral index. 71

Nonpharmacologic Versus Pharmacologic

No studies were identified in which the comparison of cognitive training to pharmacologic interventions was made.
compared the Cogmed intervention with a waitlist control, and at 4 months the treatment group had significantly better scores on parent report on the ADHD Index; Conners Cognitive Problems/Inattention, Conners Hyperactivity Parent, and BRIEF Metacognition Index.18

Other Findings for Cognitive Training

No significant findings for other outcomes assessed were identified for cognitive training versus nonpharmacologic or placebo, usual care, waitlist. In 1 study, researchers found significant behavioral differences ($P < .001$) on both the parent and teacher SWAN Inattention and Hyperactivity scales at 12 weeks comparing neurofeedback to methylphenidate (Supplemental Table 21).

CBT

Findings for CBT interventions are described in Supplemental Table 22. In 2 RCTs20,21,73 in which 298 participants were enrolled, researchers compared CBT to nonpharmacologic interventions ($n = 1$) or placebo, usual care, or waitlist control ($n = 1$).

Nonpharmacologic Versus Nonpharmacologic

In 1 fair-quality study,20,21 researchers evaluated 159 subjects and compared CBT with and without interventions to improve planning skills. Standard symptom scores or progress toward patient-identified goals were evaluated at 3 and 12 months. In this study, changes in the depression and anxiety scale scores were examined, and it was found that the CBT group had greater improvement in depression and anxiety scores compared with the control group at 3 months; it was found that the depression score improvements were maintained at 12 months. In addition, CBT maintained superiority in ADHD scale scores. In this study, it was also found that there was a greater improvement ($P < .001$) in the Child Behavior Checklist (CBCL) conduct disorder and/or oppositional defiant disorder subscale both immediately after treatment and at 12 months.

Nonpharmacologic Versus Pharmacologic

No studies were identified in which CBT interventions were compared to a pharmacologic intervention.

Nonpharmacologic Versus Placebo, Usual Care, or Waitlist

In 1 good-quality study,73 researchers compared CBT with usual care, finding significant changes ($P < .001$) on the ADHD RS for both adolescent and parents’ inattention and impulsivity at 12 weeks of follow-up.

Other Findings for CBT

In 1 study,20,21 researchers found significant changes in the child depression inventory ($P < .001$) and screen for child anxiety–related emotional disorders at 12 months when comparing CBT to solution-focused CBT. Another set of researchers73 found significant improvements in the Clinical Global Impression-Severity (CGI-S) self-report ($P < .001$) and CGI-S Clinician ($P < .001$) comparing CBT to usual care (Supplemental Table 23).

Child or Parent Training

Findings for child or parent training interventions are described in Supplemental Table 24. In 9 RCTs*, in which 1099 participants were enrolled, researchers compared child or parent training to nonpharmacologic interventions ($n = 4$), pharmacologic ($n = 1$), or placebo or usual care ($n = 5$). In 1 observational study,29 120 participants were enrolled. A range of different types of non-CBT behavioral interventions including organizational skills, social skills, attention skills, positive parenting, psychoeducational, sleep hygiene or behavioral, or parent or teacher behavioral training interventions. The interventions were mixed in terms of their strategies: some were interventions that helped parents learn how to cope with their own emotions, but most strategies were focused on how parents could manage specific behaviors from their children with ADHD.

Nonpharmacologic Versus Pharmacologic

In 3 good quality16,22,62 and 1 fair-quality62 RCTs representing 505 participants, researchers compared child or parent training or behavioral interventions to a nonpharmacologic intervention and evaluated standardized symptoms scores or progress toward patient-identified goals. Findings were mixed. In 1 study,16 researchers found a significant difference in the attention-deficit/hyperactivity disorder rating scale IV (ADHD RS IV) at 3 months comparing psychoeducation and general clinical counseling. Another group of researchers62 found a significant difference when comparing child life and attention skills treatment to parent group component only in the Parent Child Symptom Inventory at both 13 weeks and 7 months and Child Symptom Inventory at 13 weeks. In the third study,42 researchers found a significant difference in the CBCL Change in Attention Problems Subscale at 6 months when comparing behavioral-based social skill training for patient and parent groups to group therapy.

Nonpharmacologic Versus Pharmacologic

In 1 study,55 researchers compared standard pharmacologic treatment with behavioral treatment of children in conjunction with parent and teacher training. In this RCT, 57 participants were enrolled, and the RCT was judged to be of fair quality. At 20 weeks of follow-up, significant changes ($P = .013$) on the Integrated Visual and Auditory Continuous

* Refs 16,22,32,39,42,55,59,60,62.
Performance improvements on the Conners' Psychoeducational Program to a behavioral parent training program finding significant (P < .01) improvement on the CPRS-Parent Scale at 1 year on the Clinical Global Impressions (CGI) parent and clinician ratings. Although adverse effects were reported in 1 trial, the researchers did not find any statistically significant between-group differences.

Other Findings for Omega Fatty Acid Supplements

In 1 study, researchers compared omega fatty acids to methylphenidate and found significant (P = .001) increases in functional impairment at 1 year on the Clinical Global Impression (CGI) parent and clinician scales (Supplemental Table 26).

Herbal or Dietary Approaches

Findings for the herbal intervention and dietary approaches can be found in Supplemental Table 27. In 7 RCTs, researchers examined herbal or dietary approaches against nonpharmacologic treatments.
In 1 study, researchers compared ginkgo biloba to placebo with both groups receiving methylphenidate. At 6 weeks, significant changes were found on the ADHD RS IV for parent and teacher inattention. In another study, researchers compared methylphenidate to ginkgo biloba and found significant changes in appetite ($P = .0002$) and sleep disturbance ($P = .01$) (Supplemental Table 28).

### Other Treatment Approaches

Findings for other treatment approaches to ADHD treatment can be found in Supplemental Table 29. In 3 RCTs in which 207 participants were enrolled, researchers compared other treatment approaches to placebo, usual care, or waitlist control.

#### Nonpharmacologic Versus Placebo, Usual Care, or Waitlist

In 3 fair-quality RCTs representing 207 patients, researchers compared other ADHD treatment approaches to placebo or usual care. Interventions varied between acupuncture, melatonin, and the Incredible Years Program. No significant findings were reported for any of these interventions across standardized symptom scores.

#### Other Findings for Other Treatment Approaches

In 1 study, researchers found significant behavior changes on the PEDIATRICS Volume 141, number 6, June 2018
Vanderbilt teacher and caregiver scale at 25 weeks, comparing telemedicine to usual care plus consulting.57 In another study,58 researchers found significant changes in behavior change on the CPRS revised scale at 12 weeks, comparing homeopathy to placebo. In another study,13 researchers found significant (P = .001) behavior changes on the CPRS at 6.8 months comparing New Forest Parental Package to the waitlist control condition. Hong and Cho40 found significant (P = .012) improvements in functional impairment at 1.5 months comparing acupuncture to waitlist control. In 1 study,58 researchers found significant (P = .001) changes in functional impairment on the CGI-S Scale comparing homeopathy to placebo (Supplemental Table 30).

**Adverse Effects**

Supplemental Table 31 provides the adverse effects and findings from individual studies. Adverse effects were identified in 3 of the included studies examining nonpharmacologic interventions compared with pharmacologic interventions.17,46,65 In 4 studies, researchers measured and reported adverse effects in nonpharmacologic versus nonpharmacologic interventions (omega fatty acids, zinc, and compound of herbal preparation).15,45,47,48 The most commonly occurring adverse effects were gastrointestinal symptoms, sleep disturbances, and changes in appetite. None of researchers of these studies reported significant differences between study groups and the proportion of adverse effects.

**SOE**

Supplemental Table 32 describes the SOE findings for the changes in standardized symptom scores across each intervention. Pharmacologic interventions, neurofeedback, and other treatment approaches all were judged to have insufficient SOE to support conclusions. CBT, cognitive training, and herbal interventions or dietary approaches were all judged to have low SOE. Both omega fatty acid supplementation and child or parent training or behavior interventions were judged to have moderate SOE to support conclusions. No outcomes of interest were judged to have high SOE.

**DISCUSSION**

In this systematic review of studies published from 2009 through 2016, we found little new evidence to guide treatment with nonpharmacologic therapies for ADHD. Overall, there was a low SOE for the impact of nonpharmacologic treatments for ADHD across the outcome measures selected for this review. In 2011, the authors of a systematic evidence review found that parent behavior treatment could improve behavior among preschool-aged children with high risk for ADHD. However, the authors of this updated systematic review were not able to provide further guidance regarding the comparative effectiveness of nonpharmacologic approaches for children and adolescents. The behavioral interventions included in this systematic review were of limited effectiveness alone or in combination with medication therapy.

By limiting our review to studies that included at least 50 subjects, we might have eliminated studies demonstrating effectiveness. Even with setting a sample size threshold, the studies included in this review were too small to determine if there is a subgroup of children and adolescents with ADHD (eg, based on age or other characteristics) for whom these therapies might be more effective. Previous evidence reviews suggest a benefit to behavior therapy, with CBT appearing to be a promising approach.37,8 Generally, a higher proportion of adverse effects was reported with methylphenidate or combination of supplements and methylphenidate compared with supplement. The most common side effects for supplements were dyspepsia with omega fatty acids and increased appetite with ningdong granule.

The studies we included have limited generalizability because they do not reflect patients seen in the primary care setting, where most ADHD treatment occurs, and have short durations of follow-up. To better determine the effectiveness of treatment and address generalizability to primary care, there is a need for pragmatic randomized trials that, ideally, manage subjects for years.

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**ABBREVIATIONS**

ADHD: attention-deficit/hyperactivity disorder
ADHD RS IV: attention-deficit/hyperactivity disorder rating scale IV
AHRQ: Agency for Healthcare Research and Quality
BRIEF: Behavior Rating Inventory of Executive Function
CBCL: Child Behavior Checklist
CBT: cognitive behavioral therapy
CGI: Clinical Global Impression
CGI-S: Clinical Global Impression-Severity
CPRS: Conners’ Parent Rating Scale
FDA: Food and Drug Administration
IVA/CPT: Integrated Visual and Auditory Continuous Performance Test
RCT: randomized controlled trial
RS: rating scale
SOE: strength of evidence
WRAT-4: Wide Range Achievement Test 4
REFERENCES


38. Hariri M, Djazayery A, Djalali M, Saedisomeolia A, Rahimi A, Abdolahian E. Effect of n-3 supplementation on hyperactivity, oxidative stress and inflammatory mediators in


51. Milte CM, Parletta N, Buckley JD, Coates AM, Young RM, Howe PR. Increased erythrocyte eicosapentaenoic acid and docosahexaenoic acid are associated with improved attention and behavior in children with ADHD in a randomized controlled three-way crossover trial. J Atten Disord. 2015;19(11):954–964


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