Interventions for Preschool Children at High Risk for ADHD: A Comparative Effectiveness Review

ALL CAM treatments were excluded

abstract

OBJECTIVES: The US Agency for Healthcare Research and Quality sponsored a comparative effectiveness review of interventions for preschoolers at risk for attention-deficit/hyperactivity disorder (ADHD).

METHODS: Medline, Cochrane CENTRAL, Embase, PsycInfo, and Education Resources Information Center were searched from 1980 to November 24, 2011. Selected studies were comparative, and enrolled children <6 years with clinically significant disruptive behavior, including ADHD. The interventions evaluated were parent behavior training (PBT), combined home and school/day care interventions, and methylphenidate use. Data were extracted by using customized software. Two independent raters evaluated studies as good, fair, or poor by using the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies Risk of Bias. Overall strength of evidence (SOE) was rated for each intervention's effectiveness, accounting for study design, systematic error, consistency of results, directness of evidence, and certainty regarding outcome.

RESULTS: Fifty-five studies were examined. Only studies examining PBT interventions could be pooled statistically using meta-analysis. Eight "good" studies examined PBT, total n = 424; SOE was high for improved child behavior, standardized mean difference = –0.68 (95% confidence interval: –0.88 to –0.47), with minimal heterogeneity among studies. Only 1 good study evaluated methylphenidate, total n = 114; therefore, SOE for methylphenidate was low. Combined home and school/day care interventions showed inconsistent results. The literature reported adverse effects for methylphenidate but not for PBT.

CONCLUSIONS: With more studies consistently documenting effectiveness, PBT interventions have greater evidence of effectiveness than methylphenidate for treatment of preschoolers at risk for ADHD. *Pediatrics* 2013;131:e1584–e1604

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KEY WORDS

attention/deficit hyperactivity disorder, disruptive behavior, preschool children, parent behavior training, methylphenidate

ABBREVIATIONS

AAP—American Academy of Pediatrics
ADHD—attention-deficit/hyperactivity disorder
MAS—mixed amphetamine salts
PATS—Preschool ADHD Treatment Study
PBT—parent behavior training
RCT—randomized controlled trial
SMD—standardized mean difference
SOE—strength of evidence

Dr Charach participated in conceptualization of review and designed the key review question, was responsible for interpretation of data analyses, and was the primary author for the manuscript; Ms Carson was primary investigator for data extraction, evaluation of studies and initial qualitative analyses, preparation of tables and figures, and also reviewed and revised the manuscript; Dr Fox was responsible for initial conceptualization of comparative effectiveness review, participated in interpretation of data, and reviewed and revised the manuscript; Dr Ali was responsible for final meta-analyses, and reviewed and revised the manuscript; Ms Beckett was a primary investigator for search of gray literature and data extraction, and also reviewed and revised the manuscript; Dr Lim participated in initial evaluation of studies and qualitative analyses, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

The findings and conclusions in this article are those of the authors, who are responsible for its content, and do not necessarily represent the views of the Agency for Healthcare Research and Quality. No statement herein should be construed as an official position of the Agency for Healthcare Research and Quality or of the US Department of Health and Human Services.

www.pediatrics.org/cgi/doi/10.1542/peds.2012-0974

doi:10.1542/peds.2012-0974

Accepted for publication Jan 22, 2013

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The American Academy of Pediatrics (AAP) recently updated guidelines regarding best practice for diagnosis, evaluation, and treatment of children and youth with attention-deficit/hyperactivity disorder (ADHD). With growing recognition of the lifelong burden associated with ADHD, and availability of interventions, there has been increasing emphasis on identifying and treating young children before they enter school. Reflecting research available and changes in clinical care over the past decade, the AAP guidelines recommend evaluation of preschool children starting at ages 4 and 5 years for ADHD and other cognitive or developmental conditions when children come for help with academic or behavioral symptoms.[1] Although accurate diagnosis of ADHD in preschool children is possible,[2] making the diagnosis can be challenging. The disorder is frequently obscured by disruptive behavior, including temper tantrums and aggression, and psychosocial difficulties, including parent-child conflict.[3] Unlike older children, academic difficulties because of poor attention and distractibility are rarely a primary concern; disruptive behavior in a preschooler may indicate presence of concurrent problems, such as oppositional defiant disorder, conduct disorder, anxiety disorders, or developmental disabilities, as well as the child's response to stressors in the family or school/day care environment. Studies demonstrating that psychostimulant medications are an effective and safe first-line treatment of core symptoms of ADHD in school-aged children[4] have been used as a precedent to guide treatment of younger children. As a result, the number of off-label prescriptions for psychostimulants and other psychiatric medications for preschoolers has increased substantially.[5] The US Food and Drug Administration does not recommend these medications in children younger than 6 years because of limited investigation of the agents' efficacy and safety in this population. A previous endorsement for mixed amphetamine salts (MAS) no longer appears on the Food and Drug Administration Web site.[6]

Few comprehensive reviews of interventions for preschoolers with ADHD are available, and most have either focused on parent interventions or on psychostimulant use.[7–9] Several were completed by authors involved in the development of the specific interventions reviewed, causing a risk of perceived bias. In contrast, Ghuman et al[10] reviewed a range of interventions for preschool children with ADHD. To address the need for information about medication use, they included studies with a subset of children of preschool age. Based on general clinical consensus, they concluded that parent behavior training (PBT) interventions should be tried before medication among preschoolers with ADHD.[10] Indeed, the Preschool ADHD Treatment Study (PATS), funded by the US National Institute of Mental Health specifically to evaluate efficacy and safety of methylphenidate in this age group, included PBT before randomization as the first phase for all children recruited.[11]

To date, no information is available on the effectiveness of PBT when compared head to head with methylphenidate as treatment of preschoolers with ADHD symptoms. To address this information gap, the current review critically examined and compared effectiveness and adverse events of available interventions in preschool children with clinically significant disruptive behavior, who are therefore at high risk for ADHD.[3] We sought to enlarge generalizability of the results by including studies of preschool children who met criteria for clinically impairing symptoms of disruptive behavior, including ADHD symptoms, for the following reasons: (1) in general practice, aggression and noncompliance are common concerns for parents and frequently reasons for clinical referral; (2) ADHD in preschoolers is commonly identified in the context of comorbid oppositional and aggressive behaviors[12]; (3) accurate diagnosis of ADHD when disruptive behavior is present is especially difficult in preschool-aged children[2]; and (4) most preschoolers with oppositional defiant behavior are at high risk for meeting criteria for ADHD by age 7.[3] The key question that shaped the comparative effectiveness review follows: Among children younger than 6 years with ADHD or disruptive behavior disorder, what are the effectiveness and adverse event outcomes after treatment?

METHOD

Search Strategy

The following databases were searched from 1980 through November 24, 2011: Medline, Cochrane CENTRAL, Embase, PsycInfo, and ERIC (Education Resources Information Center). Strategies used combinations of controlled vocabulary (medical subject headings) and text words (eg, "Attention Deficit and Disruptive Behavior Disorders"/ or attention deficit disorder with hyperactivity/ or Conduct Disorder/ or minimal brain d?sfunction*.tw,sh). For details see Appendix A.

Inclusion Criteria

Included articles were published in English, investigated interventions for children younger than 6 years with clinically significant disruptive behavior identified by referral to treatment; reliable and valid screening measures; or a diagnosis of ADHD, oppositional defiant disorder, or conduct disorder by *Diagnostic and Statistical Manual of Mental Disorders* versions III, IIIR, and IV or *International Classification of*

Diseases version 9 and 10 criteria. Study designs comparing interventions with other conditions were included, grouped with their companion articles. Most included studies were randomized controlled trials (RCTs). Interventions reviewed included pharmacological and nonpharmacological interventions (eg, behavior training for parents, teacher, or child; psychosocial interventions; combinations of these items). Alternative or complementary interventions (eg, diet, massage, biofeedback) were excluded. All effectiveness outcomes or adverse event outcomes were examined.

Data Extraction

For the purposes of this systematic review, trained data extractors used standardized forms developed in DistillerSR (Evidence Partners Inc, Ottawa, Ontario, Canada) and Microsoft Excel for data management. Key study elements extracted were reviewed by a second person to confirm inclusion criteria. Disagreements were resolved by consensus.

Evaluation of Individual Studies

Two independent raters assessed internal validity of reports using the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies Risk of Bias.[13] This tool was chosen because it evaluates the full range of comparative study designs that met inclusion criteria, and has been shown to have excellent interrater reliability on global grades of study quality.[14] Details regarding derivation of global study grade of "good," "fair," or "poor" are provided in Appendix B. Disagreements were resolved by a third rater.

Data Synthesis

For each category of intervention, trials were examined to identify similarly designed studies with independent samples for pooling results. Only the category of PBT interventions provided results that could be synthesized quantitatively, and meta-analytic techniques were performed according to published guidelines.[15] Estimates of overall effect and between-study heterogeneity were obtained by using Review Manager software (RevMan 5.1; Nordic Cochrane Center, Copenhagen, Denmark). Effect estimates were derived for 2 outcome measures: parent-reported child disruptive behavior, including ADHD symptoms, as well as parent-reported parenting skills (competence) outcomes. See Appendix C for details of analyses, including calculation of standardized mean difference (SMD) and evaluation of between-study heterogeneity. Statistical stability was evaluated by comparing the estimate including only those studies rated as good with estimates including both fair and good studies.

To investigate the impact of PBT interventions specifically on core ADHD symptoms, the subset of studies investigating change in hyperactivity, impulsivity, and inattention were identified. In the same manner as in the primary analyses, study outcomes were pooled, effect estimate derived, and between-study heterogeneity and statistical stability evaluated. See Appendix C.

Where reports of intervention outcomes could not be pooled quantitatively, we provide descriptive summaries.

Rating the Body of Evidence

The overall strength of evidence (SOE) for interventions to address disruptive behavior, including symptoms of ADHD, in preschool children was assessed using the Grading of Recommendations Assessment, Development, and Evaluation guidelines.[16,17] The following factors were taken into consideration: internal validity of studies, study design (experimental versus observational), consistency of results across studies, directness of evidence linking intervention and outcome, and precision of effect estimate. For each category of intervention, summary ratings of "high," "moderate," "low," and "insufficient" were assigned based on the Agency for Healthcare Research and Quality Effective Healthcare Program scale for rating evidence.[17] A high rating for SOE represents consistent evidence from good studies in which further research is very unlikely to change the conclusions; a moderate rating indicates that results support the interventions but further research could change the conclusions; a low rating indicates there are few studies available or existing studies are flawed; and an insufficient rating suggests that evidence is not available or that studies offer conflicting results. Summary ratings were reached through consensus among 3 authors (A.C., P.C., S.F.).

RESULTS

Figure 1 provides the flow diagram for search results. The final screening identified 55 reports describing preschool interventions for children <6 years old with disruptive behavior, including ADHD. Of these, 34 described PBT trials, 1 of these combined PBT with a group for children,[18] 15 described psychostimulant trials, primarily immediate-release methylphenidate, and 6 described interventions combining PBT and school- or day care–based components.

PBT Interventions for Preschool Children With Disruptive Behavior, Including ADHD

PBT interventions are designed to help parents manage their child's problem behaviors with more effective discipline strategies by using rewards and nonpunitive consequences. An important aspect of each is to promote a positive relationship between parent and child.

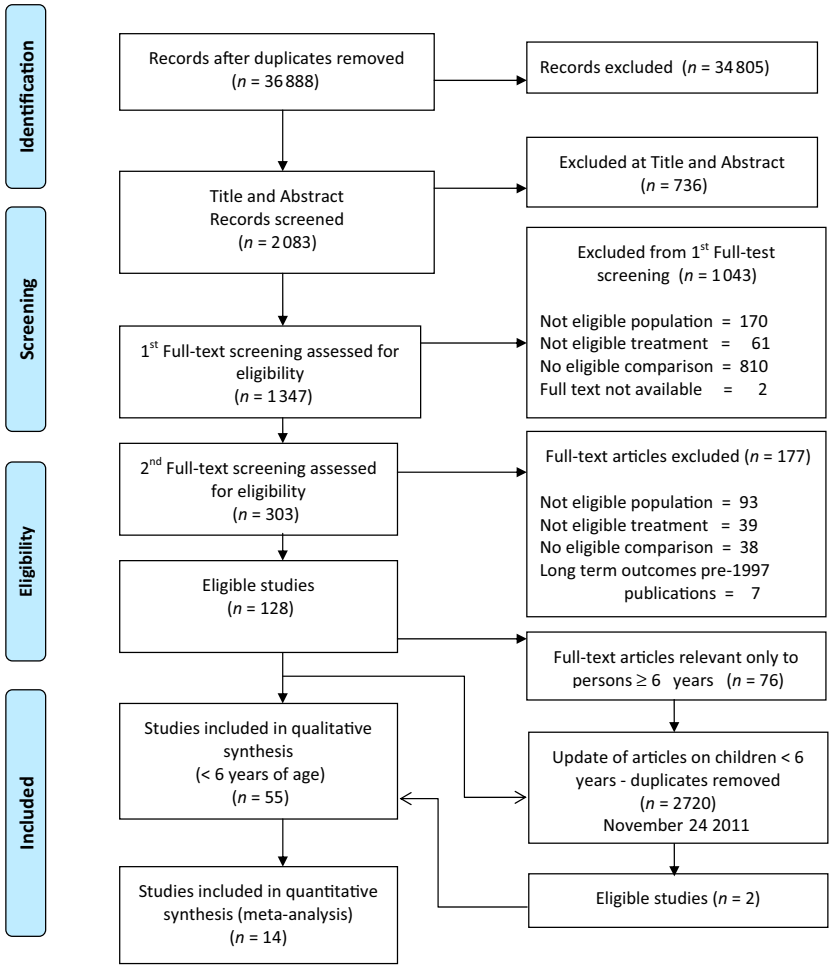

FIGURE 1
Flow diagram for search results.

Each program also includes educational components regarding childhood behavior problems and common developmental issues, and may include coaching or consultation to support parents' efforts. Primary outcomes are improved child behavior and parenting skills.

Several standardized PBT interventions have been developed to address disruptive behavior in preschoolers in the past 25 years, 4 of which figure prominently in the literature. Although each program has its own specific features, the Positive Parenting Program (Triple P),[19–25] Incredible Years Parenting Program (Incredible Years),[18,26–29] Parent-Child Interaction Therapy,[30–37] and the New Forest Parenting Program (New Forest)[38–41] all disseminate instruction manuals to ensure intervention integrity and uniformity across studies. In addition, each of these programs has published more than 1 study evaluating the intervention for preschool children. Over time, some programs have adapted interventions to address symptoms of ADHD.

The literature search identified 34 reports of PBT interventions for disruptive behavior, including ADHD symptoms, in preschoolers.[18–51] Of these, 32 met criteria for good or fair internal validity[18–22,24–49,51] (Tables 1 and 2). Fourteen good or fair RCTs with independent samples were identified.[19–22,28,30,32,33,36,38,41,43,45,49] Of these, 13 reported baseline and post-intervention child behavior outcomes, with total n = 558.[19–22,28,30,32,33,36,38,41,45,49] These were pooled for meta-analysis and resulted in a moderate effect size of SMD = –0.75 (95% confidence interval: –0.93 to –0.58) favoring intervention (Fig 2). Despite use of different outcome measures, heterogeneity among studies was minimal (Q test, P = .65 and I^2 = 0.0%). For the parenting skills outcome, results of 14 good or fair studies were pooled[19–22,28,30,32,34,37,38,41,43,45,49] (Fig 3). With a total n = 707, results showed a moderate effect size favoring the intervention and SMD = 0.55 (0.36–0.73) for parenting skills with low heterogeneity (Q test, P = .18 and I^2 = 25%). To evaluate stability of results, we also examined the pooled results of the 8 good studies, n = 424.[21,22,28,30,33,38,41,49] For child behavior, these 8 studies resulted in a moderate effect size of SMD = –0.68 (–0.88 to –0.47) with minimal heterogeneity (Q test, P = .92 and I^2 = 0%) (Fig 4). For parent skills, SMD = 0.49 (0.30–0.68) with minimal heterogeneity (Q test, P = .90 and I^2 = 0%)[21,22,28,30,34,38,41,49] (Fig 5). Not surprisingly, the SMD from the good studies was somewhat smaller, and showed less between-study heterogeneity than that of the pooled results of the good and fair studies.

Five good and fair trials examined the effect of PBT on 1 or more core symptoms of ADHD, hyperactivity, impulsivity, or inattention.[28,32,33,38,41] Three studies required that the child have ADHD for enrollment,[32,38,41] and 2 described adjusting the intervention to address symptoms of ADHD.[38,41] These 5 studies, total n = 279, were pooled for meta-analysis to examine the effect of PBT on ADHD symptoms and resulted in a moderate effect size of SMD = –0.77 (–1.21 to –0.34) favoring intervention (Fig 6). There was a moderate degree of heterogeneity observed (Q test, P = .04 and I^2= 60%). We examined results from

TABLE 1 Characteristics of Studies of PBT for Preschool-Aged Children With Disruptive Behavior, Including ADHD

Study	Intervention	Length of Intervention Primary/ Follow-up	Characteristics of Intervention								
			Mode of Delivery			Location of Delivery			Adjunctive Components		
			Group	Individual	Self-directed	Home	Community	Clinic	Direct Intervention With Child	Parent Mental Health	Marital Conflict
Bagner, 2007[30]	PCIT	4 mo/0		✓				✓			
Bor, 2002[22]	Triple P	15 wk/1 y		✓			✓			✓	✓
Bywater, 2009[29]	IYPP	12 and18 mo fu									
Connell, 1997[20]	SDBI pre-Triple P	10 wk/4 mo			✓	✓					
Cummings, 2008[42]	SET-PC/IYPP	14 wk/1 y	✓	✓				✓		✓	
Cunningham, 1995[43]	CBPT	8 wk/6 mo	✓	✓			✓	✓			
Dadds, 1992[25]	CMT versus CMT + AST pre-Triple P	8 wk/6 mo	✓					✓			
Eyberg, 1995[36]	PCIT	12 wk/0		✓				✓			
Funderburk, 1998[35]	PCIT	12 mo and 18 mo									
Hood, 2003[31]	PCIT	3-y–6-y fu									
Hutchings, 2007[28]	IYPP	12 wk/6 mo	✓				✓				
Jones, 2007[27]	IYPP	12 wk/6 mo	✓				✓				
Jones 2008[44]	IYPP	1 y and 2 y									
Landy, 2006[45]	HEAR	15 wk/0	✓				✓				
Lavigne, 2008[26]	IYPP	12 wk/1 y	✓	✓			✓				
Markie-Dadds, 2006a[21]	Triple P	17 wk/6 mo			✓	✓					
Markie-Dadds, 2006b[19]	Triple P	12 wk/6 mo			✓	✓					
Matos, 2009[32]	PCIT	12 wk/3.5 mo		✓				✓			
McGrath, 2011[51]	Strongest Families	12 wk/12 mo		✓	✓	✓					
Nixon, 2003[34]	PCIT	12 wk/6 mo		✓	✓	✓		✓			
Nixon, 2001[33]	PCIT	12 wk/6 mo		✓				✓			
Nixon, 2004[46]	PCIT	1 y and 2 y fu									
Pisterman, 1989[47]	PT	12 wk/3 mo	✓					✓			
Pisterman, 1992a[49]	PT	12 wk/3 mo	✓					✓			
Pisterman, 1992b[48]	PT	12 wk/3 mo	✓					✓			
Sanders, 1985[23]	Triple P	7 wk/3 mo		✓		✓		✓			
Sanders, 2007[24]	Triple P	1 y and 3 y fu									
Shuhmann, 1998[37]	PCIT	12 wk/4 mo		✓				✓			
Sonuga-Barke, 2001[38]	NFPP	2 mo/15 wk		✓		✓					
Sonuga-Barke, 2002[40]	NFPP	2 mo/15 wk		✓		✓					
Sonuga-Barke, 2004[39]	NFPP	8 wk/5 wk		✓		✓					
Thompson, 2009[41]	NFPP	8 wk/9 wk		✓		✓				✓	
Webster-Stratton, 2011[18]	IYPP + child group	20 wk/0	✓					✓	✓		
Weeks, 1997[50]	NFPP	8 wk/0		✓		✓					

AST, Ally Support Training; CBPT, Community-Based Parent Training; CMT, Child Management Training; fu, follow-up; HEAR, Helping Encourage Affect Regulation; IYPP, Incredible Years Parenting Program; MPH, Methylphenidate; NFPP, New Forest Parenting Program; PT, parent training; PCIT, Parent Child Interaction Therapy; SDBI, self-directed behavioral intervention; SET-PC, Supportive Expressive Therapy–Parent Child; Triple P, positive parenting program; WLC, wait list control.

the pooled meta-analysis of the 3 good studies,[28,38,41] with n = 213. Results showed SMD = –0.62 (–1.01 to –0.23) favoring intervention, with minimal heterogeneity (Q test, P = .21 and I^2 = 36%) (Fig 7).

Additional support for effectiveness of PBT interventions includes observations of a "dose effect," in which greater benefit is associated with increased number of sessions attended by parents,[26,52] and documentation that benefits are sustained over 6 months compared with wait list control children who show little improvement.[28,38,47] Attrition rates for efficacy trials ranged from <5%[19,20,51] to 28%,[22,24] with no discernible advantage to any specific PBT program. Additional factors influencing outcome were reported for the New Forest program, with maternal ADHD and delivery by nonspecialized health care nurses shown to interfere with effectiveness.[39,40] No studies commented on the complexity of the child's clinical presentation as a moderator of efficacy, and no adverse events for children or parents were described. In summary, PBT interventions reduce disruptive behavior, including ADHD symptoms, in preschool-aged children, and improve parenting skills. Benefits are maintained after completion of the treatment for at least 6 months from baseline. In general, group and individual variants of parenting interventions appear to be similarly effective, as meta-analyses of RCT outcomes show minimal heterogeneity. One primary

TABLE 2 Summary of Good and Fair Studies of PBT for Preschool-Aged Children with Disruptive Behavior, Including ADHD

Study	Quality	*n*, Mean Age, % Male, Attrition	Interventions Compared	Results	
				Child Behavior	Parent Competence
Bagner, 2007[30]	Good	*n* = 30 Age: 54 mo Male: 77% 27% attrition in trial	PCIT versus WLC	Developmentally delayed children showed improved compliance with Tx ECBI-I $P < .002$	Improved parenting skills observed with Tx $P = .006$
Bor, 2002[22]	Good	*n* = 87 Age: 41 mo Male: 68% 28% attrition in trial	Triple P standard versus EBFI versus WLC	Improved behavior with both Tx ECBI-I $P < .01$ Improvements maintained at 1 y	Improved parenting competence with both Tx PSOC $P < .001$ Improvements maintained at 1 y
Bywater, 2009[29] See Hutchings, 2007[28]	Good	*n* = 153 Age: 46 mo Male: 58% 13% attrition at 6 mo	IYPP 12 mo and 18 mo follow-up	Improvements maintained at 12 mo and 18 mo	Improvements maintained at 12 mo and 18 mo
Connell, 1997[20]	Fair	*n* = 24 Age: 49 mo Male: 43% 4% attrition in trial, 40% at 4 mo	Triple P SD versus WLC	Improved behavior with Triple P SD with telephone contact ECBI-I $P < .001$ Improvements maintained at 4 mo	Improved parenting competence PSOC $P < .001$ Improvements maintained at 4 mo
Cummings, 2008[42]	Good	*n* = 54 Age: 50 mo Male: 61% 25% attrition in trial	IYPP versus SET-PC	Improved child behaviors with both Tx over time Improvement maintained at 1 y	Improved parenting skills observed with both Tx over time. Improvement maintained at 1 y
Cunningham, 1995[43]	Good	*n* = 150 Age: 54 mo Male: 51% 24% attrition at 6 mo	CBPT versus clinic/ individual versus WLC	Improved child behavior in home situations with CBPT > clinic and WLC at 6 mo HSQ $P = .05$ Improved child behavior in all 3 conditions from pre to 6 mo on CBCL	Improved parenting competence in clinic/individuals > CBPT and control Pre to post $P < .05$ Improved parenting in all 3 conditions from pre to 6 mo on PSOC
Dadds, 1992[25]	Fair	*n* = 22 Age: 55 mo Male: 68% Attrition NR	CMT versus CMT with support person (ally) (pre-Triple P)	Improved child behavior with both Tx from pre to post Improvement maintained at 6 mo	Improved parenting skills observed with both Tx from pre to post Improvement maintained at 6 mo
Eyberg, 1995[36] Primary study related to Schuhmann, 1998[37] Hood, 2003[31]	Fair	*n* = 50 Age: 64 mo Male: 80% 28% attrition in trial	PCIT versus WLC	Improved behavior with Tx ECBI-I $P < 0.01$	Improved parent locus of control with Tx PLOC $P < .02$
Funderburk, 1998[35]	Good	*n* = 84 Age: 5 4mo Male: 100% 25% attrition at 18 mo	PCIT versus classroom comparison groups at 12 mo and 18 mo	Improved classroom behavior maintained at 12–24 mo versus classroom comparison. Blind observer ratings showed (1) improved compliance and on task behavior maintained at 12 mo, (2) improved compliance maintained at 18 mo	NR
Hood, 2003[31]	Fair	*n* = 28 Age: 60 mo Male: 70% 44% attrition at 3-6 y	PCIT 3–6 y follow-up	Improved behavior maintained at 3 to 6 y	Improved PLOC maintained at 3 to 6 y

TABLE 2 Continued

Study	Quality	*n*, Mean Age, % Male, Attrition	Interventions Compared	Results	
				Child Behavior	Parent Competence
Hutchings, 2007[28] Primary study for Jones, 2007,[27] Bywater, 2009,[29] Jones, 2008[44]	Good	*n* = 153 Age: 46 mo Male: 58% 13% attrition in trial	IYPP versus WLC at 6 mo	Improved behavior with Tx versus WLC at 6 mo ECBI-I $P < .001$ Conners $P < .001$ ITT analysis	Improved parenting skills observed (blind) with Tx versus WLC at 6 mo $P = .002$
Jones, 2007[27]See Hutchings, 2007[28]See also Bywater, 2009[29]; Jones, 2008[44]	Good	*n* = 79 Age: 46 mo Male: 68% 10% attrition in trial	IYPP versus WLC at 6 mo	Controlling for changes in disruptive behavior, ADHD behaviors also improved Connors $P < .013$ ITT analysis	NR
Jones, 2008[44] See Bywater, 2009[29]: See also Hutchings, 2007[28]; Jones, 2007[27]	Good	*n* = 50 Age: 46 mo Male: 64% 12% attrition at 1 y and 2 y	IYPP 1 y and 2 y follow-up	Improvement in ADHD behaviors maintained at 1 y and 2 y	NR
Landy, 2006[45]	Fair	*n* = 35 Age: 54 mo Male: 80% 23% attrition in trial	HEAR versus WLC	Improved behavior with Tx ECBI-I $P < .01$	Improved parent skills and confidence with Tx
Lavigne, 2008[26]	Good	*n* = 117 Age: 54 mo Male: 53% 15% attrition at 1 y	IYPP (RN versus PhD) versus MIT	Improved behavior with all 3 Tx, after 12 wk, and continued improvement at 1 y, including in the MIT (book and pediatric care) Greater improvement when parents attended 7 or more sessions: dose effect versus MIT Improvement maintained or increased at 1 y	NR
Markie-Dadds, 2006a[21]	Fair	*n* = 63 Age: 43 mo Male: 63% 25% attrition in trial 43% attrition at 6 mo	Triple P SD versus WLC	Improved behavior with Triple-P SD, no telephone contact ECBI-I $P < .01$ Improvement maintained at 6 mo	Improved parenting competence with Tx PSOC-Efficacy $P < .05$ Improvement not maintained at 6 mo
Markie-Dadds, 2006b[19]	Good	*n* = 41 Age: 47 mo Male: 76% 3% attrition in trial; 7% at 6 mo	Triple P SD versus ESD versus WLC	Improved behavior with both Tx versus WLC ECBI-I $P < .001$ Disruptive behavior improved in ESD >SD Improvements maintained and additional improvement in SD at 6 mo	Improved parenting competence in ESD versus WLC PSOC-Efficacy $P < .001$ Improvement maintained at 6 mo
Matos, 2009[32]	Fair	*n* = 32 Age: NR Male: NR 9% attrition at 7 mo	PCIT versus WLC	Improved behavior with Tx ECBI-I $P < .0001$ BASC hyperactivity. $P < .0001$ Improvement maintained at 7 mo	Improved parenting skills PPI $P < .0001$ Improvement maintained at 7 mo
McGrath, 2011[51]	Good	*n* = 80 Age: 59 mo Male:78% Attrition: < 5%	Strongest Families versus TAU	Improved behavior with Tx, shown by no longer meeting ODD diagnosis (blind assessor) $P = .01$ Improvement maintained at 6 mo versus TAU Not maintained at 12mo versus TAU ITT analysis	NR

TABLE 2 Continued

Study	Quality	*n*, Mean Age, % Male, Attrition	Interventions Compared	Results	
				Child Behavior	Parent Competence
Nixon, 2001[33]	Fair	*n* = 34 Age: 47 mo Male: 73% Attrition NR	PCIT versus WLC	Improved behavior with Tx; ECBI-I $P < .01$ ADHD symptoms $P < .05$ Improvement maintained at 6 mo	NR
Nixon, 2004[46] Related to Nixon, 2003[34]	Fair	*n* = 37 Age: 47 mo Male: 70% 5% attrition at 2 y	PCIT versus ABB PCIT 1 y and 2 y follow-up	Improved behavior with both interventions maintained at 1-y and 2-y follow-up	Improved parenting skills observed with both TX, maintained at 1-y follow-up
Nixon, 2003[34] Primary study for Nixon, 2001,[33] Nixon, 2004[46]	Good	*n* = 54 Age: 47 mo Male: 70% 13% attrition in trial	PCIT versus ABB PCIT versus WLC	Improved behavior with both Tx versus WLC ECBI-I $P < .001$ Improvements maintained at 6 mo	Improved parenting competence with both Tx versus WLC PSOC $P < .05$ Improved parenting skills observed (blind) with PCIT versus WLC $P < .01$ Improvements maintained at 6 mo
Pisterman, 1989[47]	Good	*n* = 50 Age: 50 mo Male: 80% 8% attrition in trial	PT versus WLC	Improved child compliance with Tx Observed task $P < .01$ Improvements maintained at 6 mo versus WLC	Improved parenting skills with Tx Observed task $P < .01$ Improvements maintained at 6 mo versus WLC
Pisterman, 1992a[49]	Fair	*n* = 57 Age: 50 mo Male: 91% 21% attrition in trial	PT versus WLC	Improved child compliance with Tx Observed task $P < .01$ Improvements maintained at 6 mo versus WLC No improvement on attention task	Improved parenting skills with Tx Observed task $P < .01$ Improvements maintained at 6 mo versus WLC
Pisterman, 1992b[48] See also Pisterman 1989,[47] and 1992a[49]	Good	*n* = 91 Age: 50 mo Male: 86% 15% attrition at 3 mo	PT versus WLC	NR	Improved parenting competence with Tx PSOC $P < .001$ Improvements maintained to 6 mo versus WLC
Sanders, 2007[24] See Markie-Dadds 2006a[21] and 2006b,[19] Bor, 2002[22]	Fair	*n* = 139 Age: 85 mo Male: 68% 18% attrition from trial; 48% attrition at 1 y and 54% at 3 y	Triple P standard versus SD versus EBFI 1-y and 3-y follow-up	Child behavior improved over time for all conditions at 1 y and maintained at 3 y	Improved parenting at 1- and 3-y follow-up
Schuhmann, 1998[37] Related to Eyberg, 1995[36] and Hood, 2003[31]	Fair	*n* = 64 Age: 59 mo Male: 81% 35% attrition at 1 y in trial	PCIT versus WLC	Improved behavior with Tx ECBI-I $P < .01$ ECBI-P $P < .01$ Improvements maintained at 8mo	Improved parenting skills, stress; increased locus of control with Tx PLOC $P < .01$ Improvements maintained at 8 mo
Sonuga-Barke, 2001[38]	Good	*n* = 78 Age: 36 mo Male: 62% 9% attrition in trial	PBT (preNFPP) versus PCS versus WLC	Improved ADHD behavior observed with PBT versus PCS $P = .002$ versus WLC $P = .0001$ Improvements maintained at 23 wk versus WLC ITT analysis	Improved Maternal index with PBT versus PCS $P = .005$ versus WLC $P = .0001$ Improvements maintained at 23 wk versus WLC
Sonuga-Barke, 2002[40] See also Sonuga-Barke, 2001[38]	Good	*n* = 89 Age: 36 mo Male: 63%	PBT (preNFPP) versus WLC	Maternal ADHD interfered with improvements in behavior	

TABLE 2 Continued

Study	Quality	*n*, Mean Age, % Male, Attrition	Interventions Compared	Results	
				Child Behavior	Parent Competence
Sonuga-Barke, 2004[39] See also Sonuga-Barke, 2001[38]	Good	*n* = 89 Age: 36 mo Male: NR 16% attrition in trial	PBT delivered by primary care versus WLC	PBT delivered by nonspecialty care nurses did not improve child ADHD behavior ITT analysis	Maternal well-being diminished in both groups
Thompson, 2009[41]	Good	*n* = 41 Age: 52 mo Male: 100% 5% attrition in trial; 27% attrition at 17 wk	NFPP versus TAU	Improved ADHD behavior with Tx PACS $P < .01$ Improvements maintained to 17 wk versus TAU	Improved parent skills observed with Tx $P = .03$ Improvement not well maintained at 17 wk
Webster-Stratton, 2011[18]	Good	*n* = 99 Age:64 mo Male: 75% 5% attrition in trial	IYPP + Child group versus WLC	Improved behavior with Tx ECBI-I $P < .001$	Improved parent skills observed with Tx $P < .001$

ABB, abbreviated PCIT delivery; BASC, Behavior Assessment Scale for Children; CBCL-At, child behavior checklist-attention; CBCL-E, child behavior checklist-externalizing; CBPT, community-based parenting program; CI, confidence interval; CMT, Child Management Training; EBFI, enhanced behavioral family intervention; ECBI, Eyberg Child Behavior Inventory; ECBI-I, Eyberg Child Behavior Inventory–Intensity; ECBI-P, Eyberg Child Behavior Inventory–Problem; ESD, enhanced self-directed Triple P; ESL, English as a second language; HEAR, Helping Encourage Affect Regulation; HSQ, Home Situations Questionnaire; ITT, intention to treat; IYPP, Incredible Years Parenting Program; MIT, minimal intervention therapy; *n*, sample size; NFPP, New Forest Parenting Program; NR, not reported; NS, not significant; ODD, oppositional defiant disorder; PACS, Parent Account of Child Symptoms; PCIT, Parent-Child Interaction Therapy; PCS, parent counseling and support; PS, parent stress; PS-T, parenting style, total; PSI, parent stress index; PLOC, parental locus of control; PSOC, parenting sense of competence; PPI, Parenting Practices Inventory; PT, parent training; SD, self-directed Triple P; SET-PC, Supportive Expressive Therapy–Parent Child; TAU, treatment as usual; Triple P, positive parenting program; Tx, treatment; WLC, wait list control.

barrier to optimal effectiveness is that some parents do not complete the recommended number of sessions.

Efficacy and Safety of Psychostimulant Interventions for Preschool Children With ADHD

Fifteen articles, representing 10 studies,[53–67] examined the efficacy of psychostimulants, primarily immediate-release methylphenidate, prescribed 2 or 3 times daily in preschool children with documented ADHD. Eleven articles representing 6 studies were rated as good or fair in quality[53,56–59,61–66] (Table 3). The largest randomized clinical trial, the Preschool ADHD Treatment Study,[61–65] with *n* = 165 in the crossover titration phase, and *n* = 114 in the parallel RCT phase, received a good rating for internal validity and is described later in this article. The other 4 studies included samples ranging in size from *n* = 11 to *n* = 44, primarily boys from families with middle socioeconomic status with ADHD combined or hyperactive/impulsive subtypes.[53,56,58,66] Three of these trials were within-subject crossover designs lasting 4 to 5 weeks.[56,58,66] Two studies examined children with ADHD and developmental disabilities or pervasive developmental disorders.[56,58] Almost all studies compared immediate-release methylphenidate with placebo.[53,56,58,66] One study[59] compared the most effective and well-tolerated dose of either methylphenidate or MAS to placebo, although only 6 children received MAS. All studies noted improved ADHD behaviors (ie, inattention, hyperactivity, impulsivity) on active treatment. Those studies examining adverse events noted that behaviors attributed to side effects were also present in subjects on placebo.[56,57,59] Adverse events were more common and of greater intensity at high than low doses.[57] Poor appetite, social withdrawal, lack of alertness, stomach ache, irritability, and rebound were increased on medication relative to placebo.[56,59]

PATS

The multisite National Institute of Mental Health–funded PATS[61–65] offers high-quality evidence about efficacy, safety, and effectiveness of immediate-release methylphenidate, 3 times daily, for preschool children 3 to 5 years of age.

The PATS Study[61–65] addressed a number of important methodological limitations, and documented efficacy of methylphenidate for symptoms of ADHD in preschoolers. Before the trial, parents were offered a series of 10 PBT sessions. Thirteen percent of preschool children with ADHD symptoms benefited sufficiently to no longer meet clinical threshold or parents were satisfied with degree of improvement. Another 12% of parents preferred no further intervention and therefore did not start medication. Documentation about how many families completed the PBT sessions is not provided.

There were 4 consecutive methylphenidate trial phases in total: an open-label safety lead-in phase, RCT within-subject titration phase, best-dose RCT parallel group phase, and a 10-month open-label maintenance phase. Methylphenidate improved core parent-rated and teacher-rated ADHD symptoms during the within-subject crossover titration phase

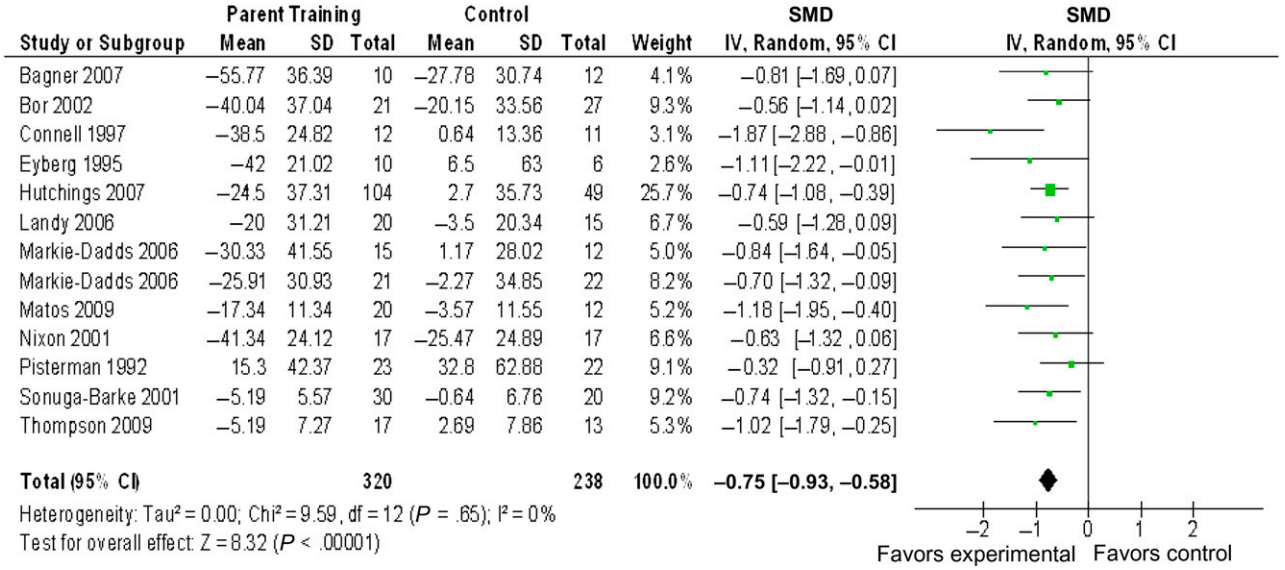

FIGURE 2

Effect of PBT on disruptive behavior in preschool-aged children (good and fair studies). *Includes RCTs rated as good and fair quality (assumes correlation between post- and pre-score of 0.3). Means are post/pre differences; SMD reflects difference of these differences.

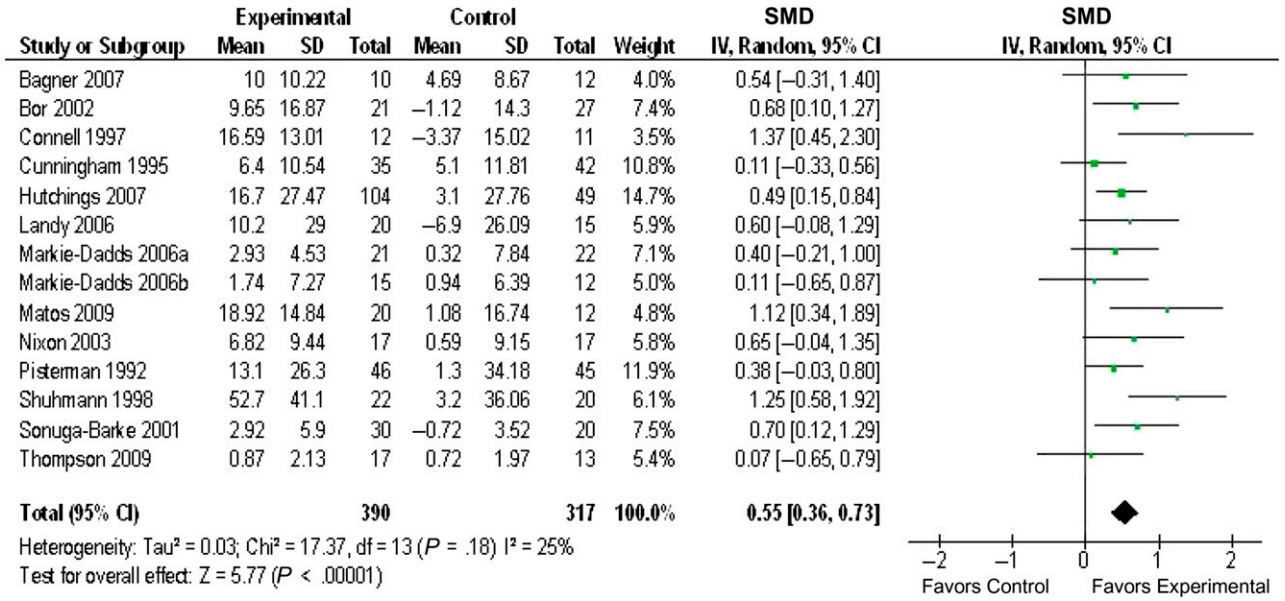

FIGURE 3

Effect of PBT on parenting skills (good and fair studies). *Includes RCTs rated as good and fair quality (assumes correlation between post- and pre-score of 0.3). Means are post/pre differences; SMD reflects difference of these differences.

with a mean optimal single dose of 0.7 ± 0.4 mg/kg, and with a mean optimal total daily dose of 14.2 ± 8.1 mg/kg per day.[65] The RCT parallel group phase documented that best-dose methylphenidate resulted in a small positive effect for teacher- but not parent-rated ADHD symptoms and social competence, no improvement in parental stress, and moderate worsening of parent-rated child mood. In contrast, clinicians rated children as improved with moderate to large effect size.[61,65] Preschool children with 3 or more comorbid conditions at baseline (15% of sample) were least likely to benefit from methylphenidate, with children having only 1 or no comorbid conditions showing greatest benefit.[62] Preschool children experienced dose-related adverse events leading to discontinuation at rates higher than reported for older children,[64] and showed decline

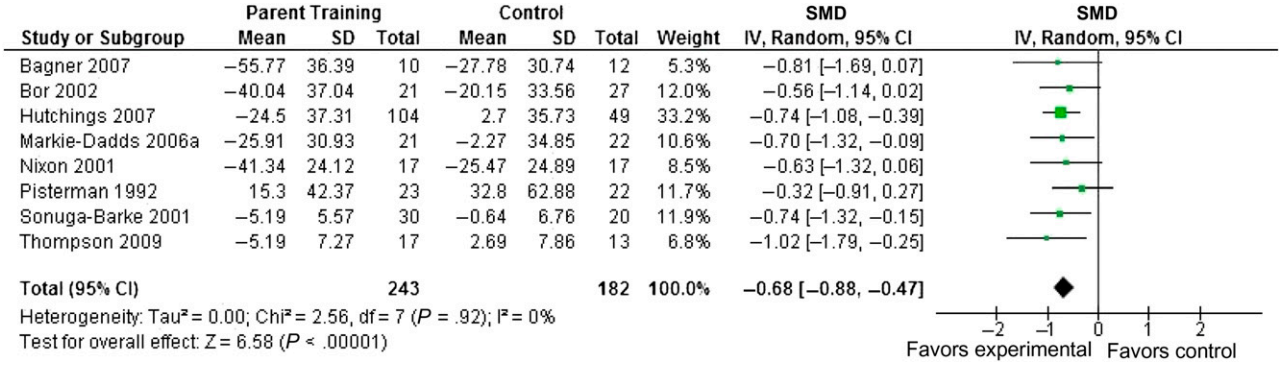

FIGURE 4

Effect of PBT on disruptive behavior in preschool-aged children (good studies). *Includes RCTs rated as good quality (assumes correlation between post- and pre-score of 0.3). Means are post/pre differences; SMD reflects difference of these differences.

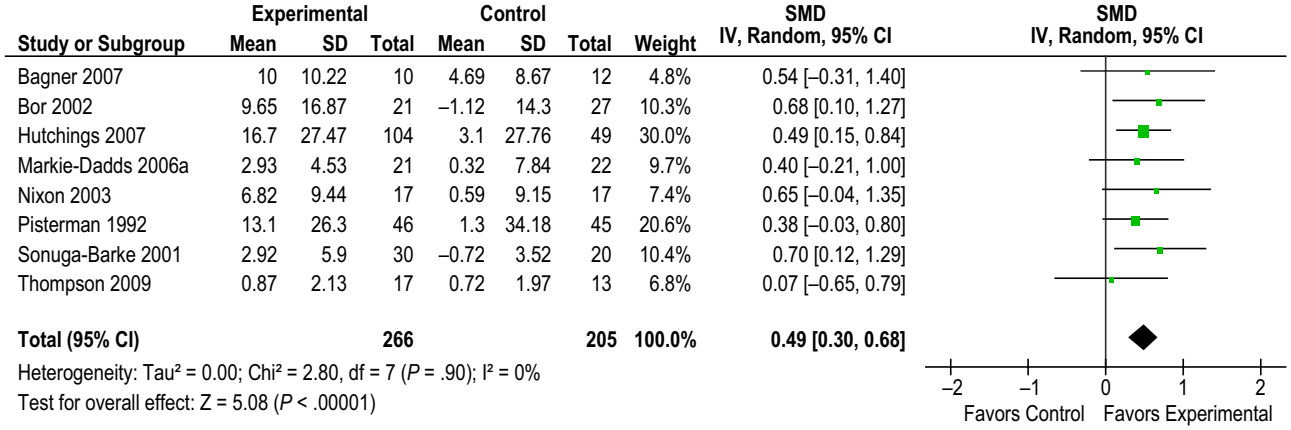

FIGURE 5

Effect of PBT on parenting skills (good studies). *Includes RCTs rated as good quality (assumes correlation between post- and pre-score of 0.3). Means are post/pre differences; SMD reflects difference of these differences.

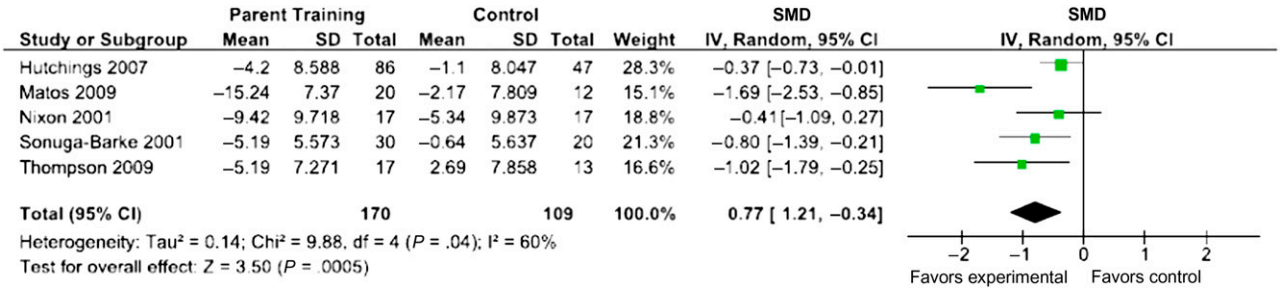

FIGURE 6

Effect of PBT on ADHD symptoms in preschool-aged children (good and fair studies). *Includes RCTs rated as good and fair quality (assumes correlation between post- and pre-score of 0.3). Means are post/pre differences; SMD reflects difference of these differences.

in growth rates over 12 months of the trial and open-label extension.[63] Approximately half of participants who tried medication in the open-label lead-in phase completed the 10-month maintenance phase; 14% discontinued the trial because of adverse effects.[64,65] Parents' concerns about their child's ability to tolerate medication, as well as their treatment preferences, were both likely factors contributing to the low rate of participants entering the long-term extension trial. Acknowledging these concerns should be an important part of providing optimum care for young children with ADHD.

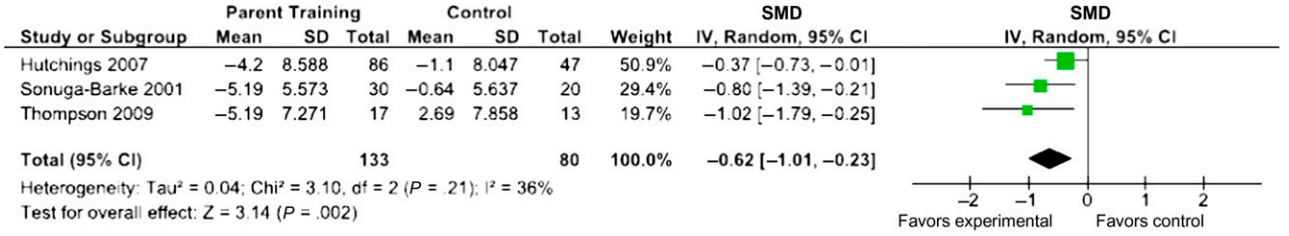

FIGURE 7

Effect of PBT on ADHD symptoms in preschool-aged children (good studies). *Includes RCTs rated as good quality (assumes correlation between post- and pre-score of 0.3). Means are post/pre differences; SMD reflects difference of these differences.

Effectiveness of Combinations of Parent Behavior Training and School- or Day Care–Based Interventions for Preschool Children With Disruptive Behavior, Including ADHD

Six articles representing 5 studies examining multiple-component psychosocial and/or behavioral interventions for disruptive behavior disorder in preschool children met criteria for review.[52,68–72] These studies did not include pharmacology interventions, but examined combinations of PBT and school- or day care–based interventions. Of these, 4 met quality criteria for good,[52,68,69,72] and 2 met criteria for fair internal validity.[70,71] Two studies examined intervention effects on ADHD symptoms and associated difficulties[68,69] (Table 4). The study designs, sample selection, interventions, and outcome measures vary widely, precluding meta-analysis. Two of 5 studies recruited families from low socioeconomic communities.[52,72] Some of these families did not attend group PBT sessions despite convenient times, and babysitting and transportation assistance.[72] Parental attendance at 5 or more sessions was associated with greater improvement in child behavior.[52] Only 1 study demonstrated that children improved more when they received both PBT- and classroom-based interventions.[52] In contrast, 2 trials recruiting children from a more advantaged community did not demonstrate added benefit from an intensive intervention compared with psychoeducation.[68,69] These trials offer conflicting results and therefore provide too little evidence to draw conclusions about combinations of home and school interventions.

SOE

Ratings for SOE were assigned to the body of evidence for each of the 3 identified intervention categories for disruptive behavior, including ADHD, in preschoolers (Table 5). The evidence for PBT was rated high for the consistency of results with 8 good efficacy trials, supported by evidence of dose effect and continued benefit 6 months after baseline. Methylphenidate use was given a low rating for SOE; there is only 1 good trial (PATS study[64,65]) with findings supported by 3 small, within-subject trials of lesser quality.[56,58,66] The evidence for combined home and school behavioral interventions was insufficient, as interventions were diverse and results contradictory.

DISCUSSION

Our systematic literature review revealed 3 primary categories of intervention for disruptive behavior, including ADHD, which have been evaluated in preschool-aged children: (1) PBT; (2) psychostimulant medication, specifically immediate-release methylphenidate; and (3) combinations of PBT and teacher or classroom interventions. The first 2 categories represent the most commonly recommended treatments, frequently simplified as a choice between parent skills training or medication. PBT is evaluated using a between-group design, and methylphenidate is evaluated using a within-subject design, making direct comparisons of effect size difficult to interpret. Therefore, we used the Grading of Recommendation, Assessment, Development, and Evaluation approach to rate SOE for effectiveness, which provides a global comparison of interventions by using clinically relevant evidence from the entire body of literature.[17] Both PBT and methylphenidate were evaluated by experimental studies, and both show dose responsiveness; 8 high-quality studies evaluated PBT but only 1 high-quality study evaluated methylphenidate (Table 5). Overall, we judged PBT to show high SOE for improving child disruptive behavior, including ADHD, in preschoolers; additional reports are very unlikely to change the conclusion that the intervention works. Methylphenidate has low SOE for improving child disruptive behavior, including ADHD, because of the small number of quality studies available. The third category of multiple-component interventions identified diverse home and school interventions, with conflicting results; therefore SOE was insufficient. Considering evidence available, the best first-choice treatment is PBT. In addition, benefits of PBT continue after the intervention is completed, whereas methylphenidate is associated with adverse effects.

TABLE 3 Summary of Good and Fair Studies of Psychostimulant Interventions for Preschool-Aged Children With ADHD

Study	Study Design, Quality Rating	*n*, Mean Age, % Male, Length of Study, Attrition	Interventions Compared				Results		Comments, Duration of Intervention or Follow-up
			MPH	MAS	PT	Placebo	Effectiveness	Safety	
Abikoff 2007[61] (PATS)	RCT Good	*n* = 114 Age: 4.4 y Male: 80% 4 wk 32% attrition	✓			✓	Functional outcomes on MPH varied by informant and measure, ITT LOCF analysis: PR and TR SWAN symptom scores showed no improvement Parent stress no improvement CGI-S improved PR depression worsened TR social competence improved	One subject dropped out for MPH related AE, most attrition due to AEs occurred in titration phase	High attrition from RCT due to behavioral deterioration (see Greenhill 2006)[66]
Ghuman 2007[62] (PATS)	Crossover titration Good	*n* = 165 Age: 4.7 y Male: 74% 5 wk 11% attrition	✓			✓	High (≥3) comorbidity subgroup showed no improvement with MPH compared with significant response in Moderate, Low or No comorbidity subgroups versus placebo	NR	Children in high comorbidity subgroup had more family adversity than other comorbidity subgroups (see also Greenhill 2006)[66]
Greenhill 2006[65] (PATS)	Crossover-titration; & RCT parallel Good	Crossover: *n* = 165 Age: 4.7 y Male: 74% 5 wk 11% attrition RCT: *n* = 114 4 wk 32% attrition	✓			✓	Crossover titration phase; ADHD symptoms decreased on MPH at 2.5 mg, 5.0 mg, and 7.5 mg, with trend at 1.25 mg TID versus placebo RCT parallel phase; ADHD symptoms decreased on best dose versus placebo, ITT LOCF analysis	AE: Emotionality or irritability, appetite loss, sleep, stomach ache, social withdrawal, lethargy; Less common tachycardia, high blood pressure; possible seizure. Decreased wt velocity (see Swanson 2006[64])	Multiphase study Titration trial effect size (0.4–0.8) smaller than for school-aged children Of those who discontinued the RCT due to deterioration in behavior, 74% were on placebo and 15% on methylphenidate
Swanson 2006[63] (PATS)	Extension of RCT Good	*n* = 140 Age: 4.4 y Male: 74% 15 mo	✓			✓		Evaluation of growth rates for those who completed 1 year of MPH use and those who did not ADHD children started out larger and heavier than norms, and while growth slowed on MPH regimen, they still were larger and heavier than norm at end of 1 y	10-mo maintenance phase following screening phase, PBT, open-label lead-in, titration and RCT, approximately 15 mo total
Wigal 2006[64] (PATS)	RCT Good	*n* = 183 Age: 4.8 y Male: 74% 14 mo	✓			✓	Increased ADHD behaviors with MPH withdrawal supports drug efficacy	30% of parents spontaneously report moderate to severe AEs, including emotional outbursts, trouble falling asleep, repetitive behavior/thoughts, decreased appetite, irritability AEs increased with increased dose	1 wk open-label lead-in, 5-wk RCT, 5-wk parallel phase, 10-mo open-label maintenance; attrition occurred with each phase 11% discontinued due to AE

TABLE 3 Continued

Study	Study Design, Quality Rating	*n*, Mean Age, % Male, Length of Study, Attrition	Interventions Compared				Results		Comments, Duration of Intervention or Follow-up
			MPH	MAS	PT	Placebo	Effectiveness	Safety	
Firestone, 1998[66] Same population as Musten, 1997[57]	Crossover Fair	*n* = 44 Age: 4.8 y Male: 87% 1 mo 27% attrition	✓			✓	MPH has positive effect on temperament and negative effect on somatic complaints and sociability at higher dose ($P < .05$ to $P < .001$)	Higher dosage of stimulant medication related to intensified frequency and magnitude of AE	Younger children may display different behaviors than school-aged children while on MPH; behaviors may have been associated with the condition rather than adverse events
Ghuman, 2009[58]	Crossover Fair	*n* = 14 Age: 4.8 y Male: 93% 5 wk 18% attrition	✓			✓	Improved behavior reported by parents and observed in clinic	Buccal-lingual movements significantly increased in Tx group; 50% showed mild to moderate adverse events	Developmentally delayed children with ADHD response to MPH more subtle and variable than among older and/or typically developing children
Handen, 1999[56]	Crossover Fair	*n* = 11 Age: range 4.0 to 5.1 y Male: 82% 5 wk Attrition NR	✓			✓	Significant improvement on TR of hyperactivity and inattention as well as activity levels and compliance	Nearly half the children experienced significant AE: withdrawal, crying, irritability	Developmentally delayed children with ADHD respond to MPH, however may be more susceptible to adverse drug side effects
Heriot, 2007[53]	RCT Fair	*n* = 16 Age: 4.8 y Male: 81% 3 mo 38% attrition	✓		✓	✓	Most clinically significant results in MPH + PT where 4/4 improved in 2 or more domains. In PT only and in MPH only, 3/4 improved in 1 or more domains. In placebo and parent support 1/4 improved in 1 domain	AE not reported	MPH prescribed at 0.3 mg /kg twice daily
Musten, 1997[57] Same population as Firestone, 1998[66]	Crossover Fair	*n* = 31 Age: 4.8 y Male: 83% 1 mo 16% attrition	✓			✓	Dosage effects not uniformly evident; positive effects on cognitive measures	Increased AE and increased severity with higher doses	MPH improves functioning of preschool children similar to school-aged children; no evidence that ODD was contraindication
Short, 2004[59]	Cohort Fair	*n* = 28 Age: 5.3 y Male: 85% 1 mo 18% attrition	✓	✓		✓	Improvement in behavior with either MPH or MAS (*n* = 6)	Titrated to best dose, there were minimal differences between number or severity of AE on active medication or placebo	Comparing best dose and placebo. Best dose of either MPH twice daily or MAS once daily identified by a preliminary trial

PATS studies listed first; ADHD, attention-deficit/hyperactivity disorder; AE, adverse events; CGI-S, Clinical Global Impressions–Severity; H, Hyperactivity; ITT LOCF, intent to treat last observation carried forward; MAS, mixed amphetamine salts; MPH, methylphenidate; NR, not reported; ODD, oppositional defiant disorder; PATS Preschool ADHD Treatment Study; PR, parent rating; PT, parent training; SWAN, Strengths and Weaknesses of ADHD-symptoms and Normal Behaviors; TID, three times daily doses; TR, teacher rating; Tx, treatment.

Until now, there has been little guidance for clinicians and families about which treatment to use first for preschoolers with disruptive behavior, including ADHD. Considerations in addition to efficacy are important and decisions may be based on parent and practitioner preferences and on services available. Parents sometimes prefer to use nonpharmacological options first, often citing concerns about safety and adverse effects.[73] Indeed, preschool-aged children are susceptible to adverse effects of methylphenidate, with high rates of somatic concerns, irritability and moodiness, and decrements in growth,[63–65] whereas adverse effects are not reported for PBT. The PATS study demonstrated that children with more complicated clinical pictures, those with 3 or more comorbid conditions, worsened while on methylphenidate, whereas those with no or a single comorbid condition showed the best response.[62] Other studies support these observations, as preschoolers with developmental delays may respond to methylphenidate with increased adverse effects.[58] Because concurrent developmental issues are

TABLE 4 Summary of Good and Fair Studies of Combined Home and School/Day Care Interventions for Preschool-Aged Children with Disruptive Behavior, Including ADHD

Study	Study Design Quality Rating	Diagnosis	*n*, Mean Age, % Males, SES	Interventions Compared					Intervention Duration, Follow-up Length, Attrition	Results: Effectiveness	Comments, Other Details
				PT Behavioral	Teacher Consult	Classroom	CC/ Parent Edu	None			
Barkley, 2000[71] Follow-up Shelton, 2000[70]	RCT Fair	DBD	*n* = 158 Age: 4.8 y Male: 40% Low to middle SES	✓		✓	✓		Intervention 10 wk Attrition NR	Improvement in DBD with Tx CBCL-At $P = .008$ CBCL-A $P = .002$ No improvement in academic skills	Pragmatic issues interfered with randomization to some degree
Hanisch, 2010[52]	RCT Good	At risk for DBD	*n* = 155 Age: 4.2 y Male: 73% Low SES	✓		✓		✓	Intervention 10 wk 0% attrition	Parent and teacher reports of Improved DB with Tx ITT analysis $P < .001$	Dose response for PBT, with attendance at 5 or more sessions showing greater benefit
Kern, 2007[69]	Prospective cohort Good	ADHD	*n* = 135 Age: 4 y Male: 78.5% Mixed population SES	✓		✓	✓		Intervention 12 mo Follow-up 12 mo 11% attrition	Improved behavior (ADHD & aggression) and social and pre-academic skills in both conditions ITT analysis	Approximately half of intervention participants received/accepted all 3 parts of the multicomponent intervention
McGoey, 2005[68]	RCT Good	ADHD	*n* = 57 Age: 4.0 y Male: 85.9% Primarily middle class	✓		✓	✓		Intervention Mean 17 wk 0% attrition	Effects of early intervention were small to moderate and not consistently in expected direction. Child compliance outcomes similar in both groups	
Shelton, 2000[70] Follow-up to Barkley, 2000[71]	Follow-up to RCT Fair	DBD	*n* = 158 Age: 4.8 y Male: 66.5%		✓		✓		Intervention 10 wk (Barkley) Follow-up 24 mo Attrition NR	Despite ongoing signs of risk in DB children, significant improvement in all groups over time ITT analysis, no significant difference between classroom treated and untreated groups	No differences between classroom treated and untreated DB groups. No difference in percentage of children using available treatments across the follow-up period. Results suggest that early intervention classroom for DB children may not produce enduring effects once treatment is withdrawn.
Williford, 2008[72]	Prospective cohort Good	At risk for ADHD/ ODD	*n* = 96 Age: 4.5 y Male: 70% Predominantly lower SES	✓	✓		✓		Intervention 4 mo (IYPP) Follow-up 12 mo 37% attrition	Intervention decreased child DBD in the classroom	Teachers in consult model and parents in PBT model report improved behavior

ADHD, attention-deficit/hyperactivity disorder; CBCL-A, Child Behavior Checklist–Aggression; CBCL-At, Child Behavior Checklist–Attention; CC/ Parent Edu community care or parent education; DB, disruptive behavior; DBD, disruptive behavior disorder; ITT, intention to treat; IYPP, Incredible Years Parenting Program; MCI, multicomponent intervention; ODD, oppositional defiant disorder; PBT, parent behavior training; SES, socioeconomic status; Tx, treatment.

TABLE 5 Effectiveness of Interventions for Preschool-Aged Children with Disruptive Behavior, Including ADHD

Intervention	SOE	Conclusion
PBT	High SMD = −0.68 95% CI: −0.88 to −0.47	• Eight good RCTs showing efficacy for disruptive behaviors, including ADHD, and for parenting skills • Benefits maintained • Dose effect • No adverse effects reported
Methylphenidate	Low SMD = −0.83 95% CI: −1.21 to −0.44	• One good RCT showing efficacy for ADHD behaviors • Adverse effects are reversible
Combination home and school/day care	Insufficient	• Few reports • Programs highly variable

ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; PBT, Parent behavior training; SMD, standardized mean difference; SOE, strength of evidence.

common among preschoolers with behavior problems, these observations are important to consider when choosing interventions.

Although adverse events are not reported for PBT, important barriers to effective intervention exist, and include lack of access to evidence-based programs. In addition, a significant proportion of parents (up to 28%) fail to complete the intervention, whether offered as group sessions or individually.[22,36] Several studies examined PBT offered in the family home.[19,22,38,41] Although this may overcome parent reluctance to participate in groups and difficulties accessing transportation or child care, it is a time- and resource-intensive method of delivering clinical service. Other less costly and accessible methods of delivery are community-based groups, and self-directed learning programs.[19,21,43] Novel additions to dissemination methods are telephone-based or Web-based PBT for parents.[51]

Methodological limitations in the trials evaluating PBT include small sample sizes, use of wait-list controls, and reliance on parent report for child behavior outcomes, with little information about child behavior in classroom or day care settings; however, 3 studies documented change in parenting skills through blind observations.[25,28,34] One report described child behavior observed in the classroom setting.[35] Although most analyses included only those participants who completed the interventions, studies using intention-to-treat analyses support the conclusion that PBT is effective.[28,38,39,51,52]

Effective interventions exist for preschool-aged children who come to clinical attention for disruptive behavior disorders. As recommended by the recent AAP guidelines, preschool youngsters with disruptive behavior should be referred for a thorough developmental evaluation, including assessment of their adaptive and cognitive functioning, as they are at high risk for >1 developmental disorder, 1 of which may be ADHD.[1] Such an assessment can be the first step toward a comprehensive plan for monitoring and intervention, one that should include PBT as an important component. The evidence-based PBT interventions included in this review improve parenting skills and improve child disruptive behavior, including core symptoms of ADHD. Areas for further research include tailoring PBT interventions to specific subgroups of children and families, and examining barriers to access and acceptance of PBT interventions. Programs under development that show promise include combined PBT with behavior training for kindergarten personnel[52] and combined PBT with a treatment group for children.[18] Where inattention, hyperactivity, and impulsiveness continue to impair functioning after PBT, additional medical intervention may be considered. Use of methylphenidate in conjunction with PBT, as well as once-daily formulations, also requires further evaluation in preschoolers.

Children with more severe impairment may come to clinical attention at an early age in part because of multiple concurrent disorders; unfortunately, those with complex clinical syndromes appear less likely to benefit and more likely to experience adverse effects from methylphenidate. Community physicians are in an excellent position to initiate the assessments required, guide parents to evidence-based programs where available, monitor these conditions over time, and advocate for increased resources in communities where they do not yet exist.

APPENDIXES

APPENDIX A. SEARCH STRATEGIES

The complete search string is detailed below. Gray literature and the reference lists of included articles were also examined. In addition, study authors were contacted via E-mail for missing outcome or design data.

ADHD and Disruptive Behavior Disorder Treatment Search Strategies

Medline-OVID

November 23, 2011

1. "attention deficit and disruptive behavior disorders"/ or attention deficit disorder with hyperactivity/ or conduct disorder/
2. minimal brain d?sfunction*.tw,sh.
3. (attention deficit* or adhd).ti.

4. addh.tw.
5. or/1-4
6. Hyperkinesis/
7. Impulsive Behavior/
8. Child Behavior Disorders/
9. aggression/ or agonistic behavior/
10. inattent*.tw.
11. Impulse Control Disorders/
12. (disruptive adj4 disorder?).tw.
13. or/5-12
14. limit 13 to ("newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)")
15. (preschool* or pre-school*).ti.
16. 13 and 15
17. 14 or 16
18. limit 17 to english language
19. animals/ not humans/
20. 18 not 19
21. limit 20 to (case reports or comment or editorial or in vitro or letter or news or newspaper article or video-audio media or webcasts)
22. 20 not 21
23. limit 22 to ed=20100531-20111123

Embase-OVID

November 23, 2011

1. attention deficit disorder/
2. minimal brain d?sfunction*.tw,sh.
3. (attention deficit* or adhd).ti.
4. addh.tw.
5. or/1-4
6. hyperactivity/
7. disruptive behavior/
8. conduct disorder/
9. oppositional defiant disorder/
10. hyperkinesia/
11. aggression/ or aggressiveness/ or anger/ or bullying/ or hostility/
12. impulsiveness/
13. inattention.tw.
14. (disruptive adj4 disorder?).tw.
15. or/5-14
16. limit 15 to (infant or child or preschool child <1 to 6 years>)
17. limit 16 to (book or book series or conference paper or editorial or letter or note)
18. 16 not 17
19. limit 18 to english language
20. limit 19 to em=201021-201146

PsycINFO-OVID

November 24, 2011

1. attention deficit disorder/ or attention deficit disorder with hyperactivity/
2. minimal brain d?sfunction*.tw,sh.
3. (attention deficit* or adhd).ti.
4. addh.tw.
5. or/1-4
6. conduct disorder/
7. aggressive behavior/
8. impulsiveness/
9. exp impulse control disorders/
10. oppositional defiant disorder/
11. distractability/
12. attention span/
13. hyperkinesis/
14. inattent*.tw.
15. (disruptive adj4 disorder?).tw.
16. or/5-15
17. limit 16 to childhood
18. limit 17 to english language
19. limit 18 to (chapter or "column/opinion" or "comment/reply" or editorial or letter or review-book)
20. 18 not 19
21. limit 20 to up=20100501-20111124

Cochrane Controlled Trial Registry-OVID

November 24, 2011

1. "attention deficit and disruptive behavior disorders"/ or attention deficit disorder with hyperactivity/ or conduct disorder/
2. minimal brain d?sfunction*.tw,sh.
3. (attention deficit* or adhd).ti.
4. addh.tw.
5. or/1-4
6. Hyperkinesis/
7. Impulsive Behavior/
8. Child Behavior Disorders/
9. aggression/ or agonistic behavior/
10. inattent*.tw.
11. Impulse Control Disorders/
12. (disruptive adj4 disorder?).tw.
13. or/5-12
14. limit 13 to yr="2010 -Current"
15. (child* or pediatric* or paediatric* or pre-school or preschool).ti,jn.
16. 14 and 15

APPENDIX B. DETAILS REGARDING EVALUATION OF INDIVIDUAL STUDIES

The Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies Risk of Bias,[13] evaluates a range of study designs: RCTs, observational studies, and before and after studies, with RCTs assigned a better score.[14] Numeric values (1, 2, or 3) representing good, fair, or poor quality are assigned to items evaluating the following domains: selection bias, study design, confounders, data collection methods, withdrawals and dropouts, reliability and validity of outcome measures. Scores in each domain are averaged, and subjective impressions of intervention integrity and analytic methods also contribute to global ratings of study quality, categorized as "good," "fair," or "poor".[14] For this review, blind evaluation of outcomes was not included as a requirement for a good study, as the body of literature routinely depends on parent- and teacher-report outcome measures. Where study reports

described blinded outcomes, intervention integrity, and use of intent-to-treat analyses, these increased ratings of study quality. Any disagreements between 2 raters were resolved by a third rater.

APPENDIX C. DETAILS REGARDING DATA SYNTHESIS

Study results were pooled to estimate overall effect of intervention on both outcomes of interest, parent-reported child disruptive behavior, including symptoms of ADHD, and on parent-reported parenting skills. We used the DerSimonian and Laird random effects model with inverse variance method to generate the summary effect estimates in the form of SMD for each outcome.[74] This model was preferred because of the presence of clinical and methodological diversity across included studies. The SMD was used as a summary statistic because all the studies in the systematic review assessed similar outcomes but used different instruments to measure outcomes. The overall SMD for each outcome was calculated by finding the difference of differences between mean baseline and outcome values for intervention and control groups, standardized against pooled SDs by using Microsoft Excel 2010. See equation below. SMDs were calculated using the assumption that baseline and outcome values were correlated with each other, with a correlation factor = 0.3, chosen following sensitivity analysis of potential correlation factors (0.0, 0.3, 0.5) in which estimates of effect were found to be essentially unchanged. Between-study heterogeneity was quantified with the I^2 statistic and evaluated using the Cochran Q test, where $P < .10$ indicates a high level of between study heterogeneity.[75]

$$SD_{change} = \sqrt{SD^2_{Baseline} + SD^2_{Final} - \{2 \times Corr \times SD_{Baseline} \times SD_{Final}\}}$$

The SDs for the mean differences between baseline and outcome values of intervention and control groups were computed using the following equation:

Where, SD_{change} = SD of mean difference (baseline and outcome values),

$SD_{Baseline}$ = SD of baseline value,

SD_{Final} = SD of outcome value,

Corr = Correlation between baseline and outcome values.

ACKNOWLEDGMENTS

The authors are grateful to the entire research team that assisted with the report: Lynda Booker, BA; Behnoosh Dashti, MD, MPH; Mary Gauld, BA; Emanuela Yeung, BSc(H); Erin Lillie, BSc(H), MSc; Jinhui Ma, MSc; Parminder Raina, BSc, PhD; and Russell Schachar, MD, FRCP(C). We are grateful to our key informants and members of the Technical Expert Panel who were instrumental in the formation of the parameters and goals of this review: Lisa Clements, PhD; Jaswinder Ghuman, MD; George DuPaul, PhD; Lilly Hechtman, MD, FRCP(C); Margaret Weiss, MD, PhD, FRCP(C); Stephen Faraone, MD, PhD; William E Pelham Jr, PhD; L. Eugene Arnold, MD, MEd; Laurence L. Greenhill, PhD, MD; and Julie Zito, PhD. We also thank those who reviewed the draft of the original report: L. Eugene Arnold, MD, MEd; Lisa Clements, PhD; Laurence L. Greenhill, PhD, MD; John Ratey, MD; Maggie Toplak, PhD; and Julie Zito, PhD.

We also thank those who worked so conscientiously retrieving and screening citations, abstracting data, preparing figures, and editing the report: Bryan Cheeseman, Roxanne Cheeseman, Alicia Freeborn, Connie Freeborn, Jeffrey Freeborn, Mary Gauld, Mahbubul Haq, Suzanne Johansen, Sara Kaffashian, Dorothy Kendry, Jinhui Ma, Leah Macdonald, Sandra McIsaac, Rachael Morris, Galatea Papageorgiou, Maureen Rice, Robert Stevens, and Ian White. Our thanks to Drs Michael Boyle and Harry Shannon and Ms Nancy Santesso for providing assistance along the way.

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(Continued from first page)

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

FUNDING: This report is based on research conducted by the McMaster Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality, Rockville, MD (Contract No. MME2202 290-02-0020).

ERRATA

RSV Policy Statement —Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. *Pediatrics* 2014;134(2):415–420

An error occurred in the policy statement from the American Academy of Pediatrics titled "Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection" published in the August 2014 issue of *Pediatrics* (2014;134[2]:415–420). On pages 417–418, the last sentence in the section titled **Use of Palivizumab in the Second Year of Life** should read: "A second season of palivizumab prophylaxis is recommended only for preterm infants born at <32 weeks, 0 days' gestation who required at least 28 days of oxygen after birth and who continue to require supplemental oxygen, chronic systemic corticosteroid therapy, or ***diuretic*** therapy within 6 months of the start of the second RSV season." Bronchodilator therapy has been removed as a consideration for prophylaxis in the second RSV season.

We regret this error.

doi:10.1542/peds.2014-2783

Veres et al. Duodenal Ulceration in a Patient With Celiac Disease and Plasminogen I Deficiency: Coincidence or Cofactors? *Pediatrics.* 2011;128(5): e1302–e1306

An error occurred in the article by Veres et al, titled "Duodenal Ulceration in a Patient With Celiac Disease and Plasminogen I Deficiency: Coincidence or Cofactors?" published in the November 2011 issue of *Pediatrics* (2011;128[5]:e1302–e1306; doi:10.1542/peds.2010-2251). On page e1302, the list of authors reads: "Gabor Veres, MD, PhD,[a] Ilma Korponay-Szabó, MD, PhD,[b] Erika Maka, MD,[c] Tibor Glasz, MD, PhD,[d] Petar Mamula, MD,[e] Maria Papp, MD, PhD,[f] Antal Dezsöfi, MD, PhD,[a] and Andras Arató, MD, Dsc[a]".

The list of authors should have read: "Gabor Veres, MD, PhD,[a] Ilma Korponay-Szabó, MD, PhD,[b] Erika Maka, MD,[c] Tibor Glasz, MD, PhD,[d] Petar Mamula, MD,[e] Maria Papp, MD, PhD,[f] Antal Dezsöfi, MD, PhD,[a] Volker Schuster, MD,[g] Katrin Tefs, PhD,[g] and Andras Arató, MD, Dsc[a]".

The author affiliations should have included: "[g]Children's Hospital, University of Leipzig, Germany".

doi:10.1542/peds.2014-2897

Charach et al. Interventions for Preschool Children at High Risk for ADHD: A Comparative Effectiveness Review. *Pediatrics.* 2013;131(5):e1584–e1604

An error occurred in the article by Charach et al, titled "Interventions for Preschool Children at High Risk for ADHD: A Comparative Effectiveness Review" published in the May 2013 issue of *Pediatrics* (2013;131[5]:e1584–e1604; doi:10.1542/peds.2012-0974). Starting on page e1592, under the PATS heading within the Results section, this reads: "Methylphenidate improved core parent-rated and teacher-rated ADHD symptoms during the within-subject crossover titration phase with a mean optimal single dose of 0.7 +/− 0.4 mg/kg, and with a mean optimal total daily dose of 14.2 +/− 8.1 mg/kg/day."

This should have read: "Methylphenidate improved core parent-rated and teacher-rated ADHD symptoms during the within-subject crossover titration phase with

a mean optimal single dose of 0.7 +/− 0.4 mg/kg, and with a mean optimal total daily dose of 14.2 +/− 8.1 mg/day".

doi:10.1542/peds.2014-3027

Whittingham et al. Interventions to Reduce Behavioral Problems in Children With Cerebral Palsy: An RCT. *Pediatrics.* 2014;133(5):e1249–e1257

A production error occurred in the article by Whittingham et al, titled "Interventions to Reduce Behavioral Problems in Children With Cerebral Palsy: An RCT" published in the May 2014 issue of *Pediatrics* (2014 May;133[5]: e1249–e1257; doi:10.1542/peds.2013-3620). On page e1257, the Financial Disclosure should have read: "As coauthor of the Stepping Stones Triple P program, Dr. Sanders receives royalty payments from Triple P International, in accordance with the University of Queensland Intellectual Property Policy; the other authors have indicated they have no financial relationships relevant to this article to disclose."

doi:10.1542/peds.2014-3029

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Interventions for Preschool Children at High Risk for ADHD: A Comparative Effectiveness Review

Alice Charach, Patricia Carson, Steven Fox, Muhammad Usman Ali, Julianna Beckett and Choon Guan Lim

Pediatrics 2013;131;e1584; originally published online April 1, 2013;
DOI: 10.1542/peds.2012-0974

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Pediatrics 2013;131;e1584; originally published online April 1, 2013;
DOI: 10.1542/peds.2012-0974