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Comparative Effectiveness Review
Number 137

Therapies for Children With Autism Spectrum Disorder: Behavioral Interventions Update

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This report is based on research conducted by the Vanderbilt Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2012-00009-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients

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This report may periodically be assessed for the urgency to update. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at: www.effectivehealthcare.ahrq.gov. Search on the title of the report.

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

We welcome comments on this systematic review. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Therapies for Children With Autism Spectrum Disorder: Behavioral Interventions Update

Structured Abstract

Objective. We updated a prior systematic review of interventions for children (0–12 years) with autism spectrum disorder (ASD), focusing on recent studies of behavioral interventions.

Data sources. We searched the MEDLINE® (PubMed®), PsycInfo, and Educational Resources Information Clearinghouse (ERIC) databases as well as the reference lists of included studies and recent systematic reviews. We conducted the search in December 2013.

Methods. We included comparative studies (with treatment and comparison groups) of behavioral interventions with at least 10 participants with ASD in the update, and made our conclusions based on the cumulative comparative evidence across the original report and update. Two investigators independently screened studies against predetermined inclusion criteria and independently rated the quality of included studies.

Results. We included 65 unique studies comprising 48 randomized trials and 17 nonrandomized comparative studies (19 good, 39 fair, and 7 poor quality) published since the prior review. The quality of studies improved compared with that reported in the earlier review; however, our assessment of the strength of evidence (SOE), our confidence in the stability of effects of interventions in the face of future research, remains low for many intervention/outcome pairs. Early intervention based on high-intensity applied behavior analysis over extended timeframes was associated with improvement in cognitive functioning and language skills (moderate SOE for improvements in both outcomes) relative to community controls in some groups of young children. The magnitude of these effects varied across studies, potentially reflecting poorly understood modifying characteristics related to subgroups of children. Early intensive parent training programs modified parenting behaviors during interactions; however, data were more limited about their ability to improve developmental skills beyond language gains for some children (low SOE for positive effects on language). Social skills interventions varied in scope and intensity and showed some positive effects on social behaviors for older children in small studies (low SOE for positive effects on social skills). Studies of play/interaction-based approaches reported that joint attention interventions may demonstrate positive outcomes in preschool-age children with ASD when targeting joint attention skills (moderate SOE); data on the effects of such interventions in other areas were limited (low SOE for positive effects on play skills, language, social skills). Studies examining the effects of cognitive behavioral therapy on anxiety reported positive results in older children with IQs ≥70 (high SOE for improvements in anxiety in this population). Smaller short-term studies of other interventions reported some improvements in areas such as sleep and communication, but data were too sparse to assess their overall effectiveness.

Conclusions. A growing evidence base suggests that behavioral interventions can be associated with positive outcomes for children with ASD. Despite improvements in the quality of the included literature, a need remains for studies of interventions across settings and continued improvements in methodologic rigor. Substantial scientific advances are needed to enhance our

understanding of which interventions are most effective for specific children with ASD and to isolate elements or components of interventions most associated with effects.

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Executive Summary

Background

Autism spectrum disorder (ASD) is a neurodevelopmental disorder marked by impaired social communication and social interaction accompanied by atypical patterns of behavior and interest. ASD is differentiated from other developmental disorders by significant impairments in social interaction and communication, along with restrictive, repetitive, and stereotypical behaviors and activities.[1] Social communication and social interaction features include deficits in social-emotional reciprocity (e.g., deficits in joint attention, atypical social approach and response, conversational challenges, reduced sharing of interest, emotions, and affect); deficits in nonverbal communication (e.g., atypical eye contact, reduced gesture use, limited use of facial expressions in social interactions, challenges understanding nonverbal communication); and deficits in forming and maintaining relationships (e.g., diminished peer interest, challenges joining in play, difficulties adjusting behavior to social context).

ASD features of restricted repetitive patterns of behavior, interests, or activities may include stereotyped motor mannerisms, use of objects, or speech (e.g., simple motor stereotypies, repetitive play, echolalia, and formal or idiosyncratic speech); insistence on sameness, inflexible adherence to routines, or ritualized patterns of behavior (e.g., distress at small changes, rigid patterns of thought and behavior, performance of everyday activities in ritualistic manner); intense preoccupation with specific interests (e.g., strong attachment to objects, circumscribed or perseverative topics of interest); and sensory sensitivities or interests (e.g., hyperreactivity or hyporeactivity to pain and sensory input, sensitivity to noise, visual fascination with objects or movement).[2-4]

ASD symptoms cause impairment across many areas of functioning and are present early in life. However, impairments may not be fully evident until environmental demands exceed children's capacity. They also may be masked by learned compensatory strategies later in life. Many children with ASD may also have intellectual impairment or language impairment, and the disorder may be associated with known medical, genetic, or environmental factors.

Treatments for ASD that families pursue include behavioral, educational, medical, allied health, and complementary approaches. Individual goals for treatment vary for different children and may include combinations of therapies. For many individuals, core symptoms of ASD (impairments in communication and social interaction and restricted/repetitive behaviors and interests) may improve with intervention and over time;[5-8] however, deficits typically remain throughout the lifespan. Lifelong management—often using multiple treatment approaches—may be required to maximize functional independence and quality of life.

Scope and Key Questions

Scope of Review

This systematic review updates the behavioral intervention portion of our comprehensive review of therapies for children with ASD published in 2011.[9] ASD intervention categories overlap substantially, and it can be difficult to cleanly identify the category into which an intervention should be placed. Ultimately, we defined behavioral interventions to include early intensive behavioral and developmental interventions, social skills interventions, play/interaction-focused approaches, interventions targeting symptoms commonly associated with ASD, and other general psychosocial approaches. This behavioral category of intervention explicitly does not include primarily medical interventions, complementary and alternative interventions, allied health interventions, or educationally focused interventions unless a behavioral intervention representative of the operationalization above was included within the study design.

At the time of the 2011 review (available at www.effectivehealthcare.ahrq.gov/ehc/products/106/656/CER26_Autism_Report_04-14-2011.pdf), the strength of the evidence was considered low for the effectiveness of early intensive behavioral and developmental interventions. Positive outcomes from an early and intensive behavioral and developmental intervention were noted in cognitive performance, language skills, and adaptive behavior when the intervention was delivered over substantial intervals of time (i.e., 1–2 years). Variability in response to such approaches was tremendous, with subgroups of children who demonstrated a more modest response. The ability to describe and predict these subgroups was limited.

Some other behavioral interventions that varied widely in terms of scope, target, and intensity had demonstrated effects, but the lack of consistent data limited understanding of whether these interventions were linked to specific clinically meaningful changes in functioning. Information was similarly lacking on modifiers of effectiveness, generalization of effects outside the treatment context, components of multicomponent therapies that drive effectiveness, and predictors of treatment success.

Since the publication of the initial review in 2011, a sizable body of research has been published, particularly addressing behavioral interventions. Additional studies of behavioral interventions have the greatest potential to alter the low and insufficient strength of evidence reported in the original review and may potentially be used to update treatment recommendations due to the number of new studies available. For this reason, the current review update focuses on studies of behavioral interventions.

Key Questions

We focused this review on behavioral treatments for children ages 2–12 with ASD and children younger than age 2 at risk of a diagnosis of ASD. We synthesized evidence in the published literature to address the following Key Questions (KQs).

KQ 1: Among children ages 2–12 with ASD, what are the short- and long-term effects of available behavioral treatment approaches? Specifically—

KQ 1a: What are the effects on core symptoms (e.g., social communication and interaction, restricted and repetitive behaviors) in the short term (≤6 months)?

KQ 1b: What are the effects on commonly associated symptoms (e.g., motor, medical, mood/anxiety, irritability, and hyperactivity) in the short term (≤6 months)?

KQ 1c: What are the longer term effects (>6 months) on core symptoms (e.g., social communication and interaction, restricted and repetitive behaviors)?

KQ 1d: What are the longer term effects (>6 months) on commonly associated symptoms (e.g., motor, medical, mood/anxiety, irritability, and hyperactivity)?

KQ 2: Among children ages 2–12, what are the modifiers of outcome for different behavioral treatments or approaches?

KQ 2a: Is the effectiveness of the therapies reviewed affected by the frequency, duration, and intensity of the intervention?
KQ 2b: Is the effectiveness of the therapies reviewed affected by the training and/or experience of the individual providing the therapy?
KQ 2c: What characteristics, if any, of the child modify the effectiveness of the therapies reviewed?
KQ 2d: What characteristics, if any, of the family modify the effectiveness of the therapies reviewed?

KQ 3: Are there any identifiable changes early in the treatment phase that predict treatment outcomes?

KQ 4: What is the evidence that effects measured at the end of the treatment phase predict long-term functional outcomes?

KQ 5: What is the evidence that specific intervention effects measured in the treatment context generalize to other contexts (e.g., people, places, materials)?

KQ 6: What evidence supports specific components of behavioral treatment as driving outcomes, either within a single treatment or across treatments?

KQ 7: What evidence supports the use of a specific behavioral treatment approach in children under the age of 2 who are at high risk of developing ASD based on behavioral, medical, or genetic risk factors?

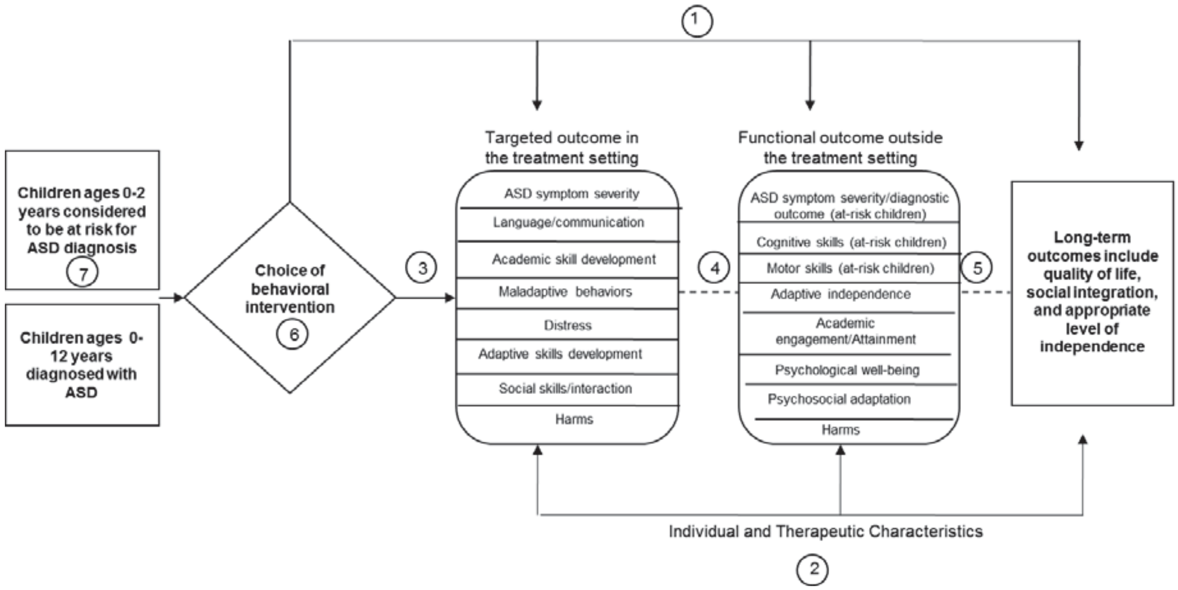
Uses of This Report

We anticipate that the report will be of value to clinicians who treat children with ASD, who can use the report to assess the evidence for different treatment strategies. In addition, this review will be of use to the National Institutes of Health, Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services, and Health Resources and Services Administration–all of which have offices or bureaus devoted to child health issues and may use the report to compare treatments and determine priorities for funding. This report can bring practitioners up to date about the current state of evidence related to behavioral interventions, and it provides an assessment of the quality of studies that aim to determine the outcomes of therapeutic options for the management of ASD. It will be of interest to families affected by ASD because of the recurring need for families and their health care providers to make the best possible decisions among numerous options. We also anticipate it will be of use to private-sector organizations concerned with ASD; the report can inform such organizations' understanding of the effectiveness of treatments and the amount and quality of evidence available. Researchers can obtain a concise analysis of the current state of knowledge related to behavioral interventions for ASD. They will be poised to pursue further investigations that are needed to understand best approaches to behavioral therapies for children with ASD.

Analytic Framework

Figure A illustrates the analytic framework for the current update. The figure illustrates the placement of the review's KQs within the context of treatment choice, potential outcomes, and characteristics that may affect outcomes. A child entering treatment may be between the ages of 0 and 2 and at risk for diagnosis of ASD or ages 0 to 12 with a diagnosis of ASD. Diagnoses may occur before age 2; thus the represented age ranges overlap.

Figure A. Analytic framework for behavioral interventions for children with ASD



ASD = autism spectrum disorder

Note: Numbers in circles represent placement of Key Questions.

Methods

Literature Search Strategy

A librarian employed search strategies provided in Appendix A of the full report to retrieve research on interventions for children with ASD. We searched MEDLINE® via the PubMed® interface, PsycINFO® (psychology and psychiatry literature), and the Educational Resources Information Clearinghouse using a combination of subject heading terms appropriate for each database and key words relevant to ASD (e.g., autism, Asperger). We limited searches to the English language and literature published since the development of the 2011 review. Our last search was conducted in December 2013. We also manually searched the reference lists of included studies and of recent narrative and systematic reviews and meta-analyses addressing ASD.

Inclusion and Exclusion Criteria

We developed criteria for inclusion and exclusion based on the patient populations, interventions, outcome measures, and types of evidence specified in the KQs and in consultation with a Technical Expert Panel. Table A summarizes criteria.

Table A. Inclusion criteria

Category	Criteria
Study population	Children ages 0–12 with ASD or 0–2 considered to be at risk for ASD based on sibling status or early developmental/behavioral vulnerabilities highly suspicious of ASD
Publication language	English only
Admissible evidence (study design and other criteria)	Admissible designs Randomized controlled trials, prospective and retrospective cohort studies, and nonrandomized controlled trials Other criteria Studies must be original research studies providing sufficient detail regarding methods and results to enable use and aggregation of the data and results. Studies must have relevant population and ≥10 participants with ASD. Studies must address 1 or more of the following for ASD: -Behavioral treatment modality -Predictors of treatment outcomes -Generalization of treatment outcomes to other contexts -Drivers of treatment outcomes Relevant outcomes must be able to be abstracted from data in the papers. Data must be presented in the aggregate (vs. individual participant data).

ASD = autism spectrum disorder

Study Selection

Two reviewers independently assessed each abstract identified for potential inclusion using an abstract review form with questions stemming from our selection criteria. If one reviewer concluded that the article could be eligible for the review based on the abstract, we retained it for full-text assessment. Two reviewers independently assessed the full text of each included study using a similar standardized form. Disagreements between reviewers were resolved by a third-party adjudicator. The group of abstract and full-text reviewers included expert clinicians and researchers and health services researchers; abstract and full-text review forms are in Appendix B of the full report.

Data Extraction

We extracted data from included studies into evidence tables that report study design, descriptions of the study populations (for applicability), description of the intervention, and baseline and outcome data on constructs of interest. Data were initially extracted by one team member and reviewed for accuracy by a second. The final evidence tables are presented in their entirety in Appendix C of the full report. For studies that were reported in the 2011 review and have followup data reported here, the evidence table for the original studies can be found in the 2011 report.[9]

Quality Assessment

We used the approach to assessing the quality of individual studies developed for the 2011 review and following methods outlined in the Agency for Healthcare Research and Quality Effective Health Care Program's "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[10] We assessed the quality of studies in domains including study design, participant ascertainment, diagnostic approach, and outcome measurement using specific questions to evaluate a study's conduct. We rated each domain individually and combined them for an overall quality level, as described in the full report. Three levels were possible: good, fair, and poor.

Data Synthesis

We summarized all data qualitatively using evidence tables. We focused on outcomes related to core ASD symptoms (impairments in communication and social interaction and restricted/repetitive behaviors and interests); outcomes including IQ and adaptive behavior; and key symptoms in studies of interventions targeting conditions commonly associated with ASD (e.g., anxiety). For the update, we describe new comparative studies published since the original report, and we make our conclusions and assess the strength of evidence on the cumulative comparative evidence across the original report and update.

Strength of the Body of Evidence

Two senior investigators graded the entire body of evidence (i.e., studies from the 2011 review and studies identified for the current review) based on the "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[10] The team reviewed the final strength-of-evidence designation.

The assessment of the literature was done by considering how confident we were that the true effect was observed and how stable that effect is likely to be in the face of future research. Strength of evidence describes the adequacy of the current research in terms of both quantity and quality, as well as the degree to which the entire body of current research provides a consistent and precise estimate of effect. Strength of the evidence is assessed for a limited set of critical outcomes, typically those related to effectiveness of an intervention. We assessed the strength of the evidence for studies addressing KQs 1 and 7, which deal specifically with the outcomes of intervention.

We established the maximum strength of evidence possible based on criteria for each domain: study limitations, consistency in direction of the effect, directness in measuring intended outcomes, precision of effect, and reporting bias. (See the full report for further description of domains.) Then we assessed the number of studies and range of study designs for a given intervention-outcome pair and downgraded the rating when the cumulative evidence was not sufficient to justify the higher rating. The possible grades were—

- High: High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates.
- Moderate: Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- Low: Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate.
- Insufficient: Evidence is either unavailable or does not permit a conclusion.

Applicability

We assessed applicability by identifying potential population, intervention, comparator, outcome, and setting (PICOS) factors likely to affect the generalizability of results (i.e., applicability to the general population of children with ASD). For this particular review, the most likely factors that could affect applicability are the patient population (e.g., whether or not results are available to assess the utility of given interventions in target populations) and the intervention (e.g., the difficulty of applying the intervention in a nonresearch setting given available resources). We noted where data were available for specific populations and made relative assessments of applicability for intervention components in the context of resource considerations such as availability of services/programs.

Results

Article Selection

We identified 2,639 newly published citations and abstracts. (Figure 2 in the full report shows the disposition of studies.) We excluded 2,012 studies at abstract review and assessed the full text of 627 studies. Of these, 79 publications, comprising 65 unique studies, met our criteria. Eight of these studies report followup data to papers included in the 2011 review of therapies for children with ASD. The 65 new studies described in this update to add to the conclusions of the original report comprise 48 randomized controlled trials (RCTs) and 17 nonrandomized trials or cohort studies. The full report includes detailed references. Appendix E of the full report includes a list of all studies excluded at the abstract and full-text review stages.

KQ 1. Effects of Behavioral Interventions on Core and Commonly Associated Symptoms in Children With ASD

Studies of Early Intensive Behavioral and Developmental Interventions

We located 37 papers comprising 25 unique studies addressing early intensive behavioral and developmental interventions. The studies included five RCTs of good quality, six of fair quality, and one of poor quality. Individual studies using intensive University of California, Los Angeles (UCLA)/Lovaas-based interventions, the Early Start Denver Model (ESDM), the Learning Experiences and Alternate Program for Preschoolers and their Parents (LEAP) program, and eclectic variants reported improvements in outcomes for young children. Improvements were most often seen in cognitive abilities and language acquisition, with less robust and consistent improvements seen in adaptive skills, core ASD symptom severity, and social functioning.

Young children receiving high-intensity applied behavior analysis (ABA)-based interventions over extended timeframes (i.e., 8 months–2 years) displayed improvement in cognitive functioning and language skills relative to community controls (Table B). However, the magnitude of these effects varied across studies. This variation may reflect subgroups showing differential responses to particular interventions. Intervention response is likely moderated by both treatment and child factors, but exactly how these moderators function is not clear. Despite multiple studies of early intensive treatments, intervention approaches still vary substantially, which makes it difficult to tease apart what these unique treatment and child factors may be. Further, the long-term impact of these early skill improvements is not yet clear, and many studies did not follow children beyond late preschool or early school years.

Studies of high-intensity early intervention services also demonstrated improvements in children's early adaptive behavior skills, but these improvements were more variable than those found for early cognitive and language skills. Treatment effects were not consistently maintained over followup assessments across studies. Many studies measured different adaptive behavior domains (creating within-scale variability), and some evidence suggests that adaptive behavior changes may be contingent on baseline child characteristics, such as cognitive/language skills and ASD severity.

Evidence for the impact of early intensive intervention on core ASD symptoms is limited and mixed. Children's symptom severity often decreased during treatment, but these improvements often did not differ from those of children in control groups. Better quality studies reported positive effects of intervention on symptom severity, but multiple lower quality studies did not.

Since our previous review, there have been substantially more studies of well-controlled low-intensity interventions that provide parent training in bolstering social communication skills. Although parent training programs modified parenting behaviors during interactions, data were more limited about their ability to improve broad developmental skills (such as cognition, adaptive behavior, and ASD symptom severity) beyond language gains for some children. Children receiving low-intensity interventions have not demonstrated the same substantial gains in cognitive skills seen in the early intensive intervention paradigms.

Social Skills Studies

We located 13 studies addressing interventions targeting social skills, including 11 RCTs. The overall quality of studies improved in comparison with the previous review, with 2 good-quality and 10 fair-quality studies. Social skills interventions varied widely in terms of scope and intensity. A few studies replicated interventions using the Skillstreaming model, which uses a published treatment manual (i.e., is manualized) to promote a consistent approach. Other studies incorporated peer-mediated and/or group-based approaches, and still others described interventions that focused on emotion identification and Theory of Mind training. The studies also varied in intensity, with most interventions consisting of 1–2 hour sessions/week lasting approximately 4–5 weeks. However, some of the group-based approaches lasted 15–16 weeks.

Most studies reported short-term gains in either parent-rated social skills or directly tested emotion recognition. However, our confidence (strength of evidence) in that effect is low (Table B). Although we now have higher quality studies of social skills interventions that demonstrate positive effects, our ability to determine effectiveness continues to be limited by the diversity of the intervention protocols and measurement tools (i.e., no consistent outcome measures used across studies). Studies also included only participants considered "high functioning" and/or with IQ test scores >70, thus limiting generalization of results to children with more significant impairments. Maintenance and generalization of these skills beyond the intervention setting are also inconsistent, with parent and clinician raters noting variability in performance across environments.

Play-/Interaction-Focused Studies

Since our previous review, more studies of well-controlled joint attention interventions across a range of intervention settings (e.g., clinician, parent, teacher delivered) have been published. This growing evidence base includes 11 RCTs of good and fair quality and suggests that joint attention interventions may be associated with positive outcomes for toddler and preschool children with ASD, particularly when targeting joint attention skills themselves as well as related social communication and language skills (Table B). Although joint attention intervention studies demonstrated changes within this theoretically important domain, data are more limited about their ability to improve broad developmental skills (such as cognition, adaptive behavior, and ASD symptom severity) beyond direct measures of joint attention and related communication and language gains over time.

Specific training that used naturalistic approaches to promote imitation (e.g., Reciprocal Imitation Training) was associated with some improvements, not only in imitation skills, but also potentially in other social communication skills (such as joint attention). Additionally, parent training in a variety of play-based interventions was associated with enhanced early social communication skills (e.g., joint attention, engagement, play interactions), play skills, and early language skills.

Studies of Interventions Targeting Conditions Commonly Associated With ASD

Six RCTs (five good and one fair quality) of interventions addressing conditions commonly associated with ASD identified for the current update measured anxiety symptoms as a primary outcome. Five of these studies reported significantly greater improvements in anxiety symptoms in the intervention group compared with controls. Two found positive effects of cognitive behavioral therapy (CBT) on the core ASD symptom of socialization, and one reported improvements in executive function in the treatment group. The one RCT that did not find a significant benefit of CBT compared it with social recreational therapy rather than with treatment as usual or a wait-listed control group.

The studies examining the effects of CBT on anxiety had largely consistent methodologies. Six studies provided followup data reflecting treatment effects that lasted beyond the period of direct intervention. Two common factors limit the applicability of the results, however. Due to the nature of CBT, which is often language intensive and requires a certain level of reasoning skills to make abstract connections between concepts, most studies included only children with IQs much greater than 70. These studies report positive results regarding the use of CBT to treat anxiety in children with ASD (Table B). They also report some positive results in socialization, executive function, and communication; however, these results were less robust, and it is unclear in some studies if these improvements exceeded improvements related to the impact of ameliorated anxiety itself.

Additional data in the current review relate to parent training to address challenging behavior. Specifically, one fair-quality study combined a parent-training approach with risperidone. This combination significantly reduced irritability, stereotypical behaviors, and hyperactivity, and improved socialization and communication skills. However, these effects were not maintained at 1 year after treatment.

Other Behavioral Studies

Two RCTs (one fair and one poor quality) examined neurofeedback and found some improvements on parent-rated measures of communication and tests of executive function. Three fair-quality RCTs reported on sleep-focused interventions, with little positive effect of a sleep education pamphlet for parents in one, improvements in sleep quality in treatment arms (melatonin alone, melatonin + CBT) in another, and some improvements in time to fall asleep in one short-term RCT of sleep education programs for parents. One poor-quality study of parent education to mitigate feeding problems reported no significant effects.

KQ 2. Modifiers of Treatment Effects

Among the potential modifiers or moderators of early intensive ABA-based interventions, younger age at intake was associated with better outcomes for children in a limited number of studies. Greater baseline cognitive skills and higher adaptive behavior scores were associated with better outcomes across behavioral interventions, but again, these associations were not consistent. In general, children with lower symptom severity or less severe diagnoses improved more than participants with greater impairments. Many studies (e.g., social skills, CBT) restricted the range of participants' impairment at baseline (e.g., recruiting only participants with IQs >70), limiting understanding of intervention impact on broader populations. Studies assessing parental responsiveness to children's communication typically reported better outcomes in children whose parents were more aligned with the child's communication versus those who attempted to redirect or were less synchronized. Regarding intervention-related factors, duration of treatment had an inconsistent effect. Some studies reported improved outcomes with more intervention time and others reported no association. Overall, most studies were not adequately designed or controlled to identify true moderators of treatment response.

KQ 3. Treatment Phase Changes That Predict Outcomes

The reviewed literature offers little information about what specific early changes from baseline measurements of child characteristics might predict long-term outcome and response.

KQ 4. Treatment Effects That Predict Long-Term Outcomes

Few studies assess end-of-treatment effects that may predict outcomes. Several early intensive behavioral and developmental interventions are associated with changes in outcome measures over the course of very lengthy treatments, but such outcomes usually have not been assessed beyond treatment windows. One family of studies attempted to follow young children receiving early joint attention intervention until they were school aged, but this study failed to include adequate followup of control conditions. It also involved children who were receiving many hours of uncontrolled interventions during the course of study.

KQ 5. Generalization of Treatment Effects

The majority of the social skills and behavioral intervention studies targeting associated conditions attempted to collect outcomes based on parent, self, teacher, and peer report of targeted symptoms (e.g., anxiety, externalizing behaviors, social skills, peer relations) at home, at school, and in the community. Although such ratings outside of the clinical setting may be suggestive of generalization in that they improve outcomes in the daily context/life of the child, in most cases, these outcomes are parent reported and not confirmed with direct observation. Behavioral intervention studies rarely measured outcomes beyond the intervention period, and we therefore cannot assume that effects were maintained over time.

KQ 6. Treatment Components That Drive Outcomes

We did not identify any studies meeting our inclusion criteria that addressed this question.

KQ 7. Treatment Approaches for Children Under Age 2 at Risk for Diagnosis of ASD

In the studies addressing interventions for younger children, children who received behavioral interventions seemed to improve regardless of intervention type (including the comparator interventions, which were also behavioral). None of the fair- or good-quality studies compared treatment groups with a no-treatment control group. Potential modifiers of treatment efficacy include baseline levels of object interest. Most outcome measures of adaptive functioning were based on parent report, and the effect of parental perception of treatment efficacy on perception (and report) of child functioning was generally not explored.

Discussion

Key Findings and Strength of Evidence

Since our previous review in 2011, there has been a significant increase in the quantity and quality of studies investigating behavioral interventions. These new studies add to the prior report and strengthen our ability to make conclusions about the effectiveness of behavioral interventions. Of the 45 comparative studies of behavioral interventions (29 RCTs) in the 2011 review, we considered only 2 as good quality. Among the new studies described in this current review, 19 studies are good quality, and 48 of the 65 included studies are RCTs.

Evidence from the original report and this update suggests that early behavioral and developmental intervention based on the principles of ABA delivered in an intensive (≥15 hours per week) and comprehensive (i.e., addressing numerous areas of functioning) approach can positively affect a subset of children with ASD (Table B). Across approaches, children receiving early intensive behavioral and developmental interventions demonstrate improvements in cognitive, language, adaptive, and ASD impairments compared with children receiving low-intensity interventions and eclectic non–ABA-based intervention approaches.

Since our previous review, there have also been substantially more studies of well-controlled low-intensity interventions aimed at parent training for comprehensive impact on social communication skills. Although parent training programs modified parenting behaviors during interactions, data are more limited about their ability to improve broad developmental skills (such as cognition, adaptive behavior, and ASD symptom severity) beyond short-term language gains for some children.

A growing number of studies of improved quality demonstrated positive effects of social skills interventions on at least one outcome measure, but a lack of consistency in the interventions studied and outcome measures used makes it difficult to understand specific effects of different intervention modalities.

A growing evidence base also suggests that children receiving targeted play-based interventions (e.g., joint attention, imitation, play-based interventions) demonstrate improvements in early social communication skills. Children receiving targeted joint attention packages in combination with other interventions show substantial improvements in joint attention and language skills over time. There is also evidence across a variety of play-based interventions that young children may display short-term improvements in early play, imitation, joint attention, and interaction skills. However, evidence that these short-term improvements are linked to broader indexes of change over time is not substantial.

CBT for associated conditions such as anxiety had the largest number of high-quality studies in the current review. A strong evidence base now suggests that school-aged children with average to above average intelligence and comorbid anxiety symptoms receiving manualized CBT therapy show substantial improvements in anxiety compared with wait-list controls. Table B summarizes the strength of the evidence for each category of intervention.

Table B. Strength of the evidence

Intervention	Outcome	SOE	Study Design Quality (N Participants)	Ratings for Domains Used To Assess SOE; Issues	Key Findings
Early intensive behavioral and developmental intervention: ABA based	**IQ/ cognitive**	Moderate for positive effect	RCT: 1 good, 2 fair (360) Prospective cohort: 6 fair, 2 poor (521) nRCT; 1 good, 4 fair (170) Retrospective cohort: 1 fair, 2 poor (182)	Study limitations: Medium Consistency: Consistent Directness: Direct Precision: Precise Reporting bias: Undetected Other concerns: Approaches across studies vary substantially; it is difficult to determine the effects of these unique studies on specific groups of children.	Young children receiving high-intensity interventions display improvements in aspects of cognitive functioning. Most studies found that children in treatment and comparison groups both improved on cognitive skills, with children in early intensive behavioral interventions (target intervention) improving more than children receiving other types of services (eclectic comparators). Not all improvements were maintained at long-term followup Therefore, SOE was moderate for a positive effect relative to eclectic controls.
	Adaptive behavior	Low for positive effect	RCT: 1 good, 1 fair (76) Prospective cohort: 7 fair, 2 poor (616) nRCT: 1 good, 4 fair (170) Retrospective cohort: 1 fair, 2 poor (182)	Study limitations: Medium Consistency: Inconsistent Directness: Direct Precision: Imprecise Reporting bias: Undetected Other concerns: Behavior was always measured by parent report (Vineland Scales of Adaptive Behavior) rather than objective observation.	Most studies found that children in both treatment and control groups improved on adaptive skills. However, children in early intensive behavioral interventions improved more than children receiving other types of services. Not all group differences were maintained over long-term followup Therefore, SOE was low for a positive effect relative to eclectic controls.
	Symptom severity	Low for positive effect	RCT: 1 good, 1 fair (332) nRCT: 1 good, 1 fair (74) Prospective cohort: 4 fair, 2 poor (470) Retrospective cohort: 1 fair (142)	Study limitations: Medium Consistency: Inconsistent Directness: Direct Precision: Imprecise Reporting bias: Undetected Other concerns: Most control groups were also receiving treatments and also showed improvement, making it difficult to tease apart the effect of intervention.	There was mixed impact on symptom severity. SOE is low for a positive effect on symptom severity because 2 good-quality studies showed positive effects but multiple lower quality studies did not. More studies are needed to confirm results.

Table B. Strength of the evidence (SOE) (continued)

Intervention	Outcome	SOE	Study Design Quality (N participants)	Ratings for Domains Used to Assess SOE, and Issues	Key Findings
Early intensive behavioral and developmental intervention: ABA based	**Language/ commun-ication**	Moderate for positive effect	RCT: 1 good, 2 fair (360) nRCT: 1 good, 3 fair (143) Prospective cohort: 6 fair, 2 poor (616)	Study limitations: Medium Consistency: Consistent Directness: Direct Precision: Precise Reporting bias: Undetected Other concerns: Some studies measured language using direct testing, whereas others only used parent-reported measures (Vineland Scales of Adaptive Behavior).	Most studies found a positive effect of treatment on language/communication skills, although the specific domain of improvement (e.g., receptive vs. expressive language) varied across study. Some initial between-group differences disappeared at long-term followup There is moderate SOE of a positive effect on language overall.
	Social skills/social behavior	Low for positive effect	RCT: 1 good, 1 fair (332) nRCT: 1 fair (34) Prospective cohort: 4 fair, 1 poor (406) Retrospective cohort: 1 fair (142)	Study limitations: Medium Consistency: Inconsistent Directness: Direct Precision: Imprecise Reporting bias: Undetected Other concerns: Social skills were assessed almost exclusively using parent-reported standard scores on the Vineland Scales of Adaptive Behavior.	Many studies found that treatment groups improved more than controls on measures of social skills, although a significant minority did not find any treatment effect. SOE is low for a positive effect at this time because, although positive effects were observed, they were not consistent.

Table B. Strength of the evidence (SOE) (continued)

Intervention	Outcome	SOE	Study Design Quality (N participants)	Ratings for Domains Used to Assess SOE, and Issues	Key Findings
Early intensive behavioral and developmental intervention: parent training	**IQ/cognitive**	Low for no effect	RCT: 3 fair (148) Prospective cohort: 1 good, 1 fair, 1 poor (142)	Study limitations: Medium Consistency: Inconsistent Directness: Direct Precision: Imprecise Reporting bias: Undetected Other concerns: None	Most studies of parent-implemented ABA demonstrated no improvements in IQ relative to community-based interventions; in some studies worse outcomes were reported relative to center-based treatment. SOE is low for no effect due to heterogeneity in interventions and outcomes measured.
	Symptom severity	Low for positive effect	RCT: 3 good, 3 fair (361) Prospective cohort: 1 good, 1 fair, 2 poor, (203)	Study limitations: Low Consistency: Inconsistent Directness: Direct Precision: Imprecise Reporting bias: Undetected Other concerns: The measure of symptom severity varied across studies and was inconsistently defined.	Many studies found that treatment groups had improved ASD symptoms relative to controls.
	Language/ commun-ication	Low for positive effect	RCT: 4 good, 6 fair, 1 poor (664) nRCT: 1 poor (22) Prospective cohort: 2 good, 2 poor (176)	Study limitations: Low Consistency: Inconsistent Directness: Direct Precision: Precise Reporting bias: Undetected Other concerns: A mix of outcome measures was used—both parent reported (Vineland Scales of Adaptive Behavior) and more standardized measures such as Reynell or Mullen scales.	Parent training was associated with improvements in language (low SOE for improvements), but interventions and comparators were different across studies, as were the outcome measures. More studies are needed to confirm results. .
Social skills	**Social skills/ social behavior**	Low for positive effect	RCT: 2 good, 11 fair, 6 poor (730) nRCT: 2 fair (45) Retrospective cohort: 1 poor (117)	Study limitations: Medium Consistency: Inconsistent Directness: Direct Precision: Precise Reporting bias: Undetected Other concerns: Interventions varied widely in terms of scope and intensity.	School-aged children diagnosed without concomitant cognitive and language deficits demonstrated short-term gains in social skills and emotion recognition. Maintenance and generalization of these skills beyond the treatment context had variable results.

Table B. Strength of the evidence (SOE) (continued)

Intervention	Outcome	SOE	Study Design Quality (N participants)	Ratings for Domains Used to Assess SOE, and Issues	Key Findings
Play/interaction based interventions	**Joint attention**	Moderate for positive effect	RCT: 3 good, 6 fair (305)	Study limitations: Low Consistency: Consistent Directness: Indirect Precision: Precise Reporting bias: Undetected Other concerns: Children in several studies were also receiving other early intervention; disentangling results is difficult.	Selected joint attention skills consistently increased in treatment arms, but duration of effects is unclear. The SOE is lowered to moderate, as children in most studies were also receiving other early intervention and disentangling effects is difficult.
	Play skills	Low for positive effect	RCT: 3 good, 3 fair, 3 poor (265) Prospective cohort: 1 poor (12)	Study limitations: Medium Consistency: Consistent Directness: Direct Precision: Precise Reporting bias: Undetected Other concerns: Children in several studies were also receiving other early intervention; disentangling results is difficult.	Play skills increased in treatment arms but duration of effects is unclear. Imitation skills improved in treatment arms in 4 small short-term studies and in the treatment and control arms in 1 study.
	Language/ commun-ication	Low for positive effect	RCT: 4 fair (165)	Study limitations: Medium Consistency: Consistent Directness: Direct Precision: Imprecise Reporting bias: Undetected Other concerns: Children in several studies were also receiving other early intervention; disentangling results is difficult.	Expressive, but not receptive, language skills generally increased in the treatment arms in 2 studies; prompted, but not spontaneous, communication improved in 1 study.
	Social skills	Low for positive effect	RCT: 1 good, 3 fair (173)	Study limitations: Medium Consistency: Consistent Directness: Indirect Precision: Precise Reporting bias: Undetected Other concerns: Children in several studies were also receiving other early intervention; disentangling results is difficult.	Joint engagement or positive affect improved in treatment arms in 3 studies.

Table B. Strength of the evidence (SOE) (continued)

Intervention	Outcome	SOE	Study Design Quality (N participants)	Ratings for Domains Used to Assess SOE, and Issues	Key Findings
Interventions addressing commonly associated conditions: CBT	**Anxiety**	High (for positive effect in older children with at least average IQs)	RCT: 6 good, 1 fair, 2 poor (413) nRCT: 1 fair (31)	Study limitations: Low Consistency: Consistent Directness: Direct Precision: Precise Reporting bias: Undetected Other concerns: Studies included older children, typically with IQ >70.	Improvement in anxiety symptoms was greater for CBT vs. control group in 5/6 studies; study that did not show improvement compared CBT with an active treatment instead of a wait-listed control. Improvements were maintained at followup.
	Symptom severity	Low for positive effect	RCT: 2 good (81)	Study limitations: Low Consistency: Consistent Directness: Direct Precision: Imprecise Reporting bias: Undetected Other concerns: None	There was significant improvement in clinician- and parent-rated measures of anxiety severity in both studies, with improvement maintained at followup. SOE is low based on only 2 small studies.

ABA = applied behavior analysis; CBT = cognitive behavioral therapy; nRCT = nonrandomized controlled trial; RCT = randomized controlled trial; SOE = strength of evidence

Applicability

Studies of early intensive behavioral and developmental interventions were conducted primarily in preschool-age and early school-age children (i.e., typically children initially ages 1.5–7 years). The cognitive, language, and adaptive behavior profiles of participants included in these studies were generally in line with those seen in the community (i.e., typically marked by substantial impairment/delay, but with some children with more intact early cognitive/language profiles).

Often studies were conducted in highly controlled environments (e.g., university-supported intervention trials) or the methodology was not well described (i.e., nonmanualized approaches), which substantially limits their applicability to community-based settings. Even available manualized interventions require high degrees of specialization and training that make them difficult to implement in community practices.

Studies of parent training interventions and play-based interventions for preschool children often emphasized principles of ABA, in accordance with current practice recommendations for the target populations typically referred for these services. Training programs included components to improve social communication skills such as joint attention, play-based interactions, and pragmatic language approaches; interventions were conducted for approximately 1–4 hours/week, with parents trained in how to generalize these skills to other natural settings. Several programs offer manualized intervention protocols that can facilitate their use in community settings. Again, however, the number of providers in community settings who are capable of implementing these programs may be limited.

Most studies of social skills interventions targeted elementary school–aged children (6–13 years old) with few studies targeting preschool-age children, although such interventions may be important in this younger age group. Most studies also excluded children with IQs falling outside of the average range. Similarly, CBT for conditions commonly associated with ASD was targeted toward older children with generally average cognitive abilities and comorbid anxiety disorders.

Limitations of the Review Process

We limited this update to comparative studies and included only those with at least 10 individuals. Thus, we did not include data from pre-post studies or those with a very small number of children. These would include a number of single subject design studies that may be helpful for understanding focused questions of short-term efficacy in individual children and that may be useful for explicating mechanisms of action. These studies are less able to contribute to the body of evidence that we sought on population-level and generalizable effects. Users of this review may want to take those studies into account as context when applying our findings. We limited our review to English-language studies, not finding evidence that we were missing relevant research in other languages. We also did not include interventions primarily viewed as medical, educational, complementary/alternative, or allied health in nature.

Limitations of the Evidence Base

Despite improvements, the existing literature still has significant methodological concerns that in many ways continue to limit the strength of these conclusions. Evidence for the impact of intensive ABA-based interventions on cognitive, language, and adaptive skills and ASD symptoms also highlights important limitations of current treatment modalities. First, even children who demonstrate clinically significant improvements in these areas often continue to display substantial impairment in these and other areas over time. Second, not all children receiving intensive ABA-based intervention showed robust improvements in these domains. Thus, it is still challenging to predict long-term functional and adaptive outcomes on an individual level. Further, although children receiving early intensive developmental and behavioral intervention commonly display substantial improvements, the magnitude of these effects varies across studies and may indicate subgroups showing variable responses to particular interventions. Intervention response is likely moderated by both treatment and child factors.

Despite multiple studies of early intensive treatments, intervention approaches still vary substantially, which makes it difficult to tease apart what these unique treatment and child factors may be. Similarly, data on provider type and qualifications are variably reported, and the impact of provider characteristics on treatment outcomes is unclear. Study sample sizes are typically small (total numbers ranging from 11 to 284 for studies in the current review, median = 40), and some studies may be considered pilots for larger studies that may better answer questions about intervention intensity and moderators of effects. At this time, the evidence is insufficient to adequately identify and target the children who are most likely to benefit (or not benefit) from specific interventions.

Many early intervention studies found that children in all groups improved on ASD symptom measures regardless of intervention type, although the degree of improvement was often significantly greater in the treatment group. In many studies, results were confounded by nonrandom assignment of participants, including assignment based on child characteristics (such as having the skills necessary to participate in the intervention setting) or parental preference. The latter is especially problematic when outcomes are measured by parent report, given some evidence that parental stress influences parent perceptions of child outcomes. Additionally, in most studies, both enrolled and control/wait-listed children were receiving concomitant interventions, whose magnitude was inconsistently documented and controlled for in analyses.

A remaining significant challenge to interpreting the early intensive intervention literature relates to how interventions are described and implemented. Although researchers are attempting to manualize approaches as well as operationalize and measure treatment fidelity, most of the body of literature categorized in this report as “early intensive behavioral and developmental intervention” remains an eclectic grouping. This category of intervention presently groups different treatment approaches (i.e., developmental, intensive behavioral, center based, and combinations), intensity (12 hours over 3 months vs. 30 hours over 1 week), and duration (weeks to years); varied inclusion and baseline assessment criteria; children of varying ages (intake age ranging from 18 months to 7 years); and many different outcome measurements over different periods of time (weeks to years). Manualizing intensive interventions to be delivered over the course of months and years for a heterogeneous patient population is intrinsically challenging. However, recent progress toward this end has shown that children may respond differentially to early intensive approaches.

Few studies directly compared the effects of well-controlled treatment approaches, instead comparing interventions with nonspecific “treatment as usual,” which clearly lacks the level of control for expectancy bias in a placebo-controlled medication study. Additionally, little data on the practical effectiveness or feasibility of these treatments beyond research studies exist, and questions remain about whether reported findings would generalize on a larger scale within communities. Furthermore, the studies conducted have used small samples, drastically different treatment approaches and duration, and different outcome measurements. Similarly, no studies reported harms of intervention in terms of child, family, or system impact.

Although there was a fairly robust evidence base on CBT, the literature lacks head-to-head comparisons of treatment or controlled comparisons of combinations of treatments, despite the fact that most children are undergoing multiple concurrent treatments. Although the studies are well designed, the sample sizes are quite modest. Additionally, the CBT approaches were modified for children with ASD and often manualized by the study authors themselves.

Research Gaps and Needs

Given the heterogeneity of the expression of ASD across children, a critical area for further research is understanding which children are likely to benefit from particular interventions. To date, studies have failed to characterize adequately the characteristics of interventions (or the children receiving them) in a manner that helps clarify why certain children show more positive responses than others. It is simpler to identify the characteristics of those children who show at most a minimal benefit from a particular treatment, but most existing studies also fail to adequately describe this population. It is possible that meta-analyses of individual patient data may provide additional information for identifying subgroups of responders.

Further, our understanding of early indicators of treatment response is extremely limited, such that it is not realistic to implement evidence-based changes in intervention based on assessing children's responses. This is quite important to parents, providers, and families, as they often want to know not only when a treatment is working, but also when the lack of a robust response should lead them to pursue other treatment options. Similarly, research is lacking on the durability of treatment gains and approaches needed to maintain gains.

Currently, the evidence suggests that some children will show dramatic improvement overall, others will display robust improvement in some areas with continued areas of vulnerability in others, and still other children will show more modest responses to treatment. It is also unclear how similar groups of children would respond to differing levels of intervention intensity, approaches, and methods. Research suggests that child characteristics such as baseline cognitive, language, and adaptive skills and ASD symptoms correlate with treatment outcome regardless of intervention. However, these correlational data provide limited information to predict what treatments will work best for individual children. Intensive comprehensive intervention strategies are often, by their very nature, multicomponent, but little data exist on whether specific treatment components drive effectiveness. Also, little is known about mediators of change. Finally, intervention research often fails to collect data on pragmatic factors related to family, culture, available resources, and stressors that are likely critical to understanding treatment response in a "real-world" context.

Measuring appropriate outcomes is a primary methodologic concern in the ASD literature. Intervention research has typically measured differing outcomes across studies, which has limited the ability to understand change within and across individual studies.[11] Many studies also used problematic methods to operationalize outcomes, doing so in terms of change on standardized measures that reference normative populations (i.e., IQ measurement, adaptive behavior scores). This may not be an appropriate or adequate method for measuring or predicting early treatment response, changes in quality of life, or long-term functional outcomes. Such measurement, while allowing for comparison with typically developing populations, may miss important information about changes that are relevant within the ASD population specifically. More simply, it is unclear that measures of cognitive ability, language, and ASD diagnostic symptoms are adequately sensitive methods for measuring symptom frequency, intensity, and impairment in children with ASD. Research on appropriate methods for capturing meaningful change will be critical to advancing our understanding of behavioral interventions. In addition, although more studies are reporting primary and secondary outcome measures determined a priori, continued improvements in reporting will benefit the field.

Given that the treatment process for ASD is typically intensive and requires highly specific and well-trained individuals to deliver with fidelity, questions of feasibility and accessibility are pertinent but largely understudied. Our understanding of treatment impact and implementation would be greatly enhanced by research that explicitly evaluates which treatments have the greatest real-world impact. Similarly, evaluations of interventions delivered by community providers are important for comparing effects of such approaches with those of interventions delivered in controlled research environments. Such evaluations are complicated by the complexity of community systems and methodologic challenges, including creating similar treatment and control groups and maintaining fidelity. However, they will be increasingly valuable for scaling intervention for ASD. Also important in addressing this gap is improving our currently limited understanding of the effects of provider training and provider characteristics on outcomes of treatment.

Finally, this literature lacks studies that directly compare interventions or employ combinations of interventions (e.g., comparing medical interventions with behavioral interventions, with educational interventions, or with allied health interventions), despite the fact that most children receive multiple concurrent treatments.

Conclusions

In sum, a growing evidence base suggests that behavioral interventions are associated with positive outcomes for some children with ASD. Despite improvements in the quality of the included literature, a need remains for studies of interventions across settings and continued improvements in methodologic rigor. Substantial scientific advances are needed to enhance our understanding of which interventions are most effective for specific children with ASD and to isolate the elements or components of interventions most associated with effects.

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Introduction

Background

Because no medical or biological marker exists for autism spectrum disorder (ASD), the diagnosis is behaviorally based. Diagnosis is typically established with a combination of history, observation, and/or formal testing, which may include ASD-specific screening and assessment instruments.[1, 2]

ASD is defined in terms of persistent, significant impairments in social interaction and communication as well as restrictive, repetitive behaviors and activities.[3] Social communication and social interaction features include deficits in social-emotional reciprocity (e.g., deficits in joint attention, atypical social approach and response, conversational challenges, reduced sharing of interest, emotions, and affect), deficits in nonverbal communication (e.g., atypical eye contact, reduced gesture use, limited use of facial expressions in social interactions, challenges understanding nonverbal communication), and deficits in forming and maintaining relationships (e.g., diminished peer interest, challenges joining in play, difficulties adjusting behavior to social context). ASD features of restricted, repetitive patterns of behavior, interests, or activities may include stereotyped motor mannerisms, use of objects, or speech (e.g., simple motor stereotypies, repetitive play, echolalia, and formal or idiosyncratic speech); insistence on sameness, inflexible adherence to routines, or ritualized patterns of behavior (e.g., distress at small changes, rigid patterns of thought and behavior, performance of everyday activities in ritualistic manner); intense preoccupation with specific interests (e.g., strong attachment to objects, circumscribed or perseverative topics of interest); and sensory sensitivities or interests (e.g., hyper- or hypo-reactivity to pain and sensory input, sensitivity to noise, visual fascination with objects or movement).[4-6]

ASD symptoms cause impairment across many areas of functioning and are present early in life. However, impairments may not be fully evident until environmental demands exceed children’s capacity. They also may be masked by learned compensatory strategies later in life. Many children with ASD may also have intellectual impairment or language impairment, and the disorder may be associated with known medical, genetic, or environmental factors.

Prevalence and Burden of Disease/Illness

The prevalence of ASD in the United States is 14.7 cases per 1,000 (or 1 in 68) children living in the communities surveyed, with rate estimates varying widely by region of the country, sex, and race/ethnicity.[7] Considerably more males (1 in 42) than females (1 in 189) are affected. For some individuals, the core symptoms of ASD (impairments in communication and social interaction and restricted/repetitive behaviors and interests) may improve with intervention and maturation[8-10]; however, core deficits typically translate into varying developmental presentations that remain throughout the lifespan.[11] Longitudinal studies indicate that adults with ASD struggle to obtain adaptive independence.[12-16] The estimated costs of medical and nonmedical care (e.g., special education and daycare) for individuals with ASD are high. One study estimates that the total yearly societal per-capita cost of caring for and treating a person with ASD in the United States is $3.2 million and about $35 billion for an entire birth cohort of individuals with ASD.[17]

Etiology and Risk Factors

ASD has a strong genetic component, with heritability estimated to be between 40 and 90 percent.[18-20] At least 100 genes are implicated in susceptibility to ASD;[20-22] however, environmental exposures and context also play a role in ASD development and neurogenetic expression.[22, 23] Identification of specific genetic risk variants has been challenging, and many researchers suggest that multiple pathways are involved, including prenatal and postnatal insult.[21] Current research[24, 25]suggests that certain metabolic and other maternal conditions (such as diabetes, hypertension, obesity, and influenza infection) during pregnancy may be associated with increased risk of ASD in offspring. Other studies have investigated the role of advanced maternal and paternal age,[26-28] intrapregnancy interval,[29, 30] pesticide exposure,[31] and exposure to mercury and other heavy metals,[32] among other potential risk factors.

In addition to the potential causative genetic and environmental factors described above, being the sibling of another child diagnosed with ASD increases the risk of receiving an ASD diagnosis from approximately 6.7 to 18.7 percent.[33, 34] This risk varies by gender and increases twofold when two or more older siblings have ASD.

Interventions/Treatment

The manifestation and severity of symptoms of ASD differs widely, and treatments pursued by families include a range of behavioral, psychosocial, educational, medical, and complementary approaches[35-39] that vary by a child's age and developmental status. The goals of treatment for ASD are to improve core deficits in social communication and social interactions and minimize the impact of restricted behaviors, with an overarching goal to help children develop greater functional skills and independence.[5] Treatment frequently is complicated by symptoms or comorbidities that may warrant targeted intervention. There is no cure for ASD and no global consensus on which intervention is most effective.[38, 40] Individual goals for treatment vary for different children and may include combinations of behavioral therapies, educational therapies, medical and related therapies, and allied health therapies; parents may also pursue complementary and alternative medicine (CAM) therapies.

Behavioral approaches are the most common treatment approaches for ASD. In 1987, Ivar Lovaas published findings[41] on a subgroup of children who demonstrated improvements in cognitive abilities and educational placement in response to intensive intervention based on the principles of applied behavior analysis (ABA). As a result, ASD was reconceptualized from a largely untreatable disorder[41] to a condition characterized by plasticity and heterogeneity, where there was hope for higher functioning and better outcomes for children receiving appropriate intervention. Subsequent research focused on social communication and behavioral impairments and used both highly structured approaches and natural/developmental approaches that deliver interventions within natural/everyday contexts (Floortime and the Social Communication Emotional Regulation Transactional Support model), as well as some that integrate these different approaches (Early Start Denver Model [ESDM]). These types of early and intensive treatment programs typically target behaviors and development more broadly, instead of focusing on a specific behavior of interest.[42] Positive effects seen with these approaches in terms of cognition and language have led to the suggestion that beginning intensive therapy at an earlier age may lead to greater improvements.[40, 42, 43] Recent systematic reviews and meta-analyses have highlighted the potential of early intervention to promote behavioral change.[36-39, 43-52]

Other behavioral approaches include interventions focused on joint attention and play, social skills interventions, and cognitive behavioral therapy and other approaches to ameliorate symptoms commonly associated with ASD such as anger or anxiety.

Chronic management throughout different developmental periods is often pursued to maximize functional independence and quality of life by minimizing the core ASD features, facilitating development and learning, promoting socialization, reducing maladaptive behaviors, and educating and supporting families. For many individuals core symptoms of ASD may see improvements with intervention and over time[8-11]; however, deficits typically remain throughout the lifespan, although developmental expression may vary.

Scope and Key Questions

The current systematic review updates our comprehensive review of therapies for children with ASD published in 2011 (available at www.effectivehealthcare.ahrq.gov/ehc/products/106/656/CER26_Autism_Report_04-14-2011.pdf).[39] The 2011 review assessed the literature reporting on any intervention approaches (i.e., behavioral, educational, medical, allied health, and CAM) and included more than 150 unique studies, the majority of which were considered of poor quality. Strength of the evidence for most interventions/outcomes was insufficient, with the exception of moderate and high ratings for the effectiveness and harms of the antipsychotics risperidone and aripiprazole. The strength of the evidence was considered low for the effectiveness of early intensive behavioral and developmental intervention. Positive outcomes from an early and intensive behavioral and developmental intervention were noted in cognitive performance, language skills, and adaptive behavior when the intervention was delivered over substantial intervals of time (i.e., 1–2 years) but at the time, a limited body of comparative evidence led to a low strength of evidence for these effects. Variability in response to such approaches was large, with subgroups of children who demonstrated a more moderated response. The ability to describe and predict these subgroups was limited.

Since the publication of the initial review in 2011, a sizable body of research has been published on behavioral interventions. Additional studies of these interventions have the potential to alter the low and insufficient strength of evidence reported in the original review and potentially affect treatment recommendations.

We recognize that ASD intervention categories overlap substantially, and it is difficult to cleanly identify the category into which an intervention should be placed. We considered multiple approaches for organizing the results with key stakeholders involved in the 2011 review. Ultimately, we defined behavioral interventions to include early intensive behavioral and developmental interventions, social skills interventions, play/interaction-focused approaches, interventions targeting symptoms commonly associated with ASD such as anxiety, and other general psychosocial approaches. This behavioral category does not include interventions that are primarily medical, complementary and alternative interventions, allied health, or educationally focused. We did include some studies that had a primarily behavioral approach combined with another approach (e.g., medical).

We again adopted an approach of assessing effects on core symptoms as well as commonly associated symptoms. Changes in commonly adopted diagnostic criteria related to ASD have changed in the interim since the previous report. These changes include additions to the core symptoms of ASD (e.g., hypo/hyper-sensory reactivity now a core feature).[3] Our approach to the review encompassed both core and associated symptoms, and neither inclusion nor interpretation was affected by whether specific outcomes were considered core or associated.

Key Questions

As noted, this review is focused on behavioral treatments for children ages 0-12 with ASD or very young children at risk of a diagnosis of ASD. We have synthesized evidence in the published literature to address these Key Questions (KQ):

KQ1: Among children ages 2-12 with ASD, what are the short and long-term effects of available behavioral treatment approaches? Specifically,

KQ1a: What are the effects on core symptoms (e.g., social communication and interaction, restricted and repetitive behaviors), in the short term (≤6 months)?
KQ1b: What are the effects on commonly associated symptoms (e.g., motor, medical, mood/anxiety, irritability, and hyperactivity) in the short term (≤6 months)?
KQ1c: What are the longer-term effects (>6 months) on core symptoms (e.g., social communication and interaction, restricted and repetitive behaviors)?
KQ1d: What are the longer-term effects (>6 months) on commonly associated symptoms (e.g., motor, medical, mood/anxiety, irritability, and hyperactivity)?

KQ2: Among children ages 2-12, what are the modifiers of outcome for different behavioral treatments or approaches?

KQ2a: Is the effectiveness of the therapies reviewed affected by the frequency, duration, and intensity of the intervention?
KQ2b: Is the effectiveness of the therapies reviewed affected by the training and/or experience of the individual providing the therapy?
KQ2c: What characteristics, if any, of the child modify the effectiveness of the therapies reviewed?
KQ2d: What characteristics, if any, of the family modify the effectiveness of the therapies reviewed?

KQ3: Are there any identifiable changes early in the treatment phase that predict treatment outcomes?

KQ4: What is the evidence that effects measured at the end of the treatment phase predict long-term functional outcomes?

KQ5: What is the evidence that specific intervention effects measured in the treatment context generalize to other contexts (e.g., people, places, materials)?

KQ6: What evidence supports specific components of behavioral treatment as driving outcomes, either within a single treatment or across treatments?

KQ7**:** What evidence supports the use of a specific behavioral treatment approach in children under the age of 2 who are at high risk of developing ASD based on behavioral, medical, or genetic risk factors?

Organization of This Report

The report describes our review methods including our search strategy, inclusion and exclusion criteria, approach to review of abstracts and full publications, and our method for extraction of data into the evidence table and compiling evidence. We also describe the approach to grading of the quality of the literature and to evaluating the strength of the body of evidence.

The results section synthesizes the findings by category of behavioral intervention (see Categorization of Interventions below). We report the number of comparative studies fully described in the 2011 review, the number and type identified for the current review, and any overlap of studies (i.e., those reporting followup data) between the prior and this current review. We make our conclusions and assess the strength of evidence on the cumulative, comparative evidence across the original report and update.[39]

We differentiate between total numbers of publications and unique studies to bring into focus the number of duplicate publications in this literature in which multiple publications are derived from the same study population. We also integrate discussion of sub-questions within that for each Key Question because there was not adequate distinction in the literature to address them separately. Full details of the results of studies addressed in the prior review can be found in that report.[39]

The report's discussion section expands on methodologic considerations relevant to each Key Question and outlines the strength of the evidence for key outcomes, current state of the literature and challenges for future research on ASD. The report includes a number of appendixes to provide further detail on our methods and the studies assessed. The appendixes are as follows:

- Appendix A: Search Strategies and Results
- Appendix B: Screening and Quality Assessment Forms
- Appendix C: Evidence Tables
- Appendix D: Quality of the Literature
- Appendix E: Excluded Studies
- Appendix F: Characteristics and Outcomes of Studies of Early Intensive Behavioral and Developmental Interventions
- Appendix G: Applicability Summary Tables.

A list of abbreviations and acronyms used in the report follows the References section.

Categorization of Interventions

In line with the 2011 review, we categorized behavioral interventions as follows: early intensive behavioral and developmental interventions, social skills interventions, parent training, play/interaction-focused interventions, interventions targeting symptoms commonly associated with ASD such as anxiety, and other general behavioral approaches. This categorization was largely driven by an end user perspective (i.e., taking into account how parents, clinicians, and systems of care might attempt to access or support intervention decisions). Thus, we categorized studies based on treatment setting/context rather than outcomes examined.

As noted previously,[39] ASD intervention categories overlap substantially, and it is difficult to cleanly identify the category into which an intervention should be placed.[38] We acknowledge that multiple approaches for organizing the results could be used; however, we retained the categorization used in the 2011 review. We note that alternative approaches are unlikely to change our overall findings either in terms of outcomes or strength of evidence for any category of intervention.

Early intensive behavioral and developmental interventions. We adopted a similar approach to the operationalization of the early intensive behavioral and developmental intervention category as Rogers and Vismara in their review of "comprehensive" evidence-based treatments for early ASD.[43] Interventions in this category all have their basis in or draw from principles of ABA, with differences in methods and setting. ABA is an umbrella term describing principles and techniques used to assess, treat, and prevent challenging behaviors and to promote new, desired behaviors. The goal of ABA is to teach new skills, promote generalization of these skills, and reduce challenging behaviors with systematic reinforcement. The principles and techniques of ABA existed for decades before being specifically applied to the study and treatment of ASD.

We include in this category two intensive interventions that have published manuals to facilitate replication: the University of California, Los Angeles (UCLA)/Lovaas model and the Early Start Denver Model (ESDM). These two interventions have several key differences in their theoretical frameworks and in how they are implemented, although they share substantial similarity in the frequent use of high-intensity (many hours per week, one-on-one) instruction using ABA techniques. They are described together here because of these similarities. We note, however, that the UCLA/Lovaas method relies heavily on one-on-one therapy sessions during which a trained therapist uses discrete trial teaching with a child to practice target skills, while ESDM blends ABA principles with developmental and relationship-based approaches for young children.

The other treatment approaches in this category also incorporate ABA principles and may be intensive in nature; often, however, they have not been documented in a manual. We have classified these approaches broadly as UCLA/Lovaas-based given their similarity in approach to the Lovaas model. A third particular set of interventions included in this category are those using principles of ABA to focus on key pivotal or foundational skills and behaviors (such as motivation to communicate or initiation of communication), rather than global improvements. These approaches often emphasize parent training as a modality for treatment delivery (e.g., Pivotal Response Training, Hanen More than Words, social pragmatic intervention, etc.) and may focus on specific behaviors such as initiating or organizing activity or on core social communication skills. Because they emphasize early training of parents of young children, they will be reviewed in this category.

We utilize the term ABA-based interventions to refer to this overarching, broad grouping of early intensive behavioral and developmental interventions throughout the remainder of the work. As such, it is important to recognize this term reflects a broader category of specific interventions that often vary in terms of approach, scope, and intensity.

Social skills interventions. Social skills interventions focus on facilitating social interactions and may include peer training and social stories.

Play/interaction-focused interventions. These approaches use interactions between children and parents or researchers to affect outcomes such as imitation or joint attention skills or the ability of the child to engage in symbolic play.

Interventions focused on behaviors commonly associated with ASD. These approaches attempt to ameliorate symptoms such as anger or anxiety, often present in children with ASD, using techniques such as Cognitive Behavioral Therapy (CBT) and parent training focused on challenging behaviors.

Additional behavioral interventions. We will categorize approaches not cleanly fitting into the behavioral categories above in this group.

Uses of This Report

This evidence report addresses the Key Questions outlined above using methods described in the following section to conduct a systematic review of published literature.

We anticipate that the report will be of value to clinicians who treat children with ASD, who can use the report to assess the evidence for different treatment strategies. In addition, this review will be of use to the National Institutes of Health, U.S. Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services, and the Health Resources and Services Administration–all of which have offices or bureaus devoted to child health issues and who may use the report to compare treatments and determine priorities for funding. This report can bring practitioners up to date about the current state of evidence related to behavioral interventions, and it provides an assessment of the quality of studies that aim to determine the outcomes of therapeutic options for the management of ASD. It will be of interest to families affected by ASD because of the recurring need for families and their health care providers to make the best possible decisions among numerous options. We also anticipate it will be of use to private sector organizations concerned with ASD; the report can inform such organizations' understanding of the effectiveness of treatments and the amount and quality of evidence available. Researchers can obtain a concise analysis of the current state of knowledge related to behavioral interventions for ASD. They will be poised to pursue further investigations that are needed to understand best approaches to behavioral therapies for children with ASD.

Methods

Topic Development and Refinement

The 2011 report was nominated by Autism Speaks in a public process. We drafted the initial Key Questions and analytic framework and refined them with input from key informants and a focus group of family members of children with autism spectrum disorder (ASD). After review from the Agency for Healthcare Research and Quality (AHRQ), the questions and framework were posted to a public Web site. After reviewing the public commentary, we drafted final Key Questions and submitted them to AHRQ for review. The need for an update of that report was documented through an ongoing update assessment project at AHRQ.

For the current update, we identified technical experts on the topic of ASD in children to provide input during the project. Technical Expert Panel (TEP) members represented the clinical and research communities from a range of perspectives. TEP members included both researchers and clinicians with expertise in behavioral, social, and psychological issues. To ensure robust, scientifically relevant work, we called on the TEP to provide reactions to work in progress. TEP members participated in conference calls and discussions through email to:

- Refine the analytic framework and Key Questions to ensure that they continued to represent important decisional dilemmas;
- Discuss the preliminary assessment of the literature, including inclusion/exclusion criteria;
- Ensure that we had captured seminal studies addressing interventions for children with ASD.

After discussions with the TEP and our initial scan of the literature, we retained all of the Key Questions (KQ) from the earlier review in the current report, modifying them slightly to reflect a focus on behavioral interventions. The protocol for the current update is available on the AHRQ Effective Health Care web site.

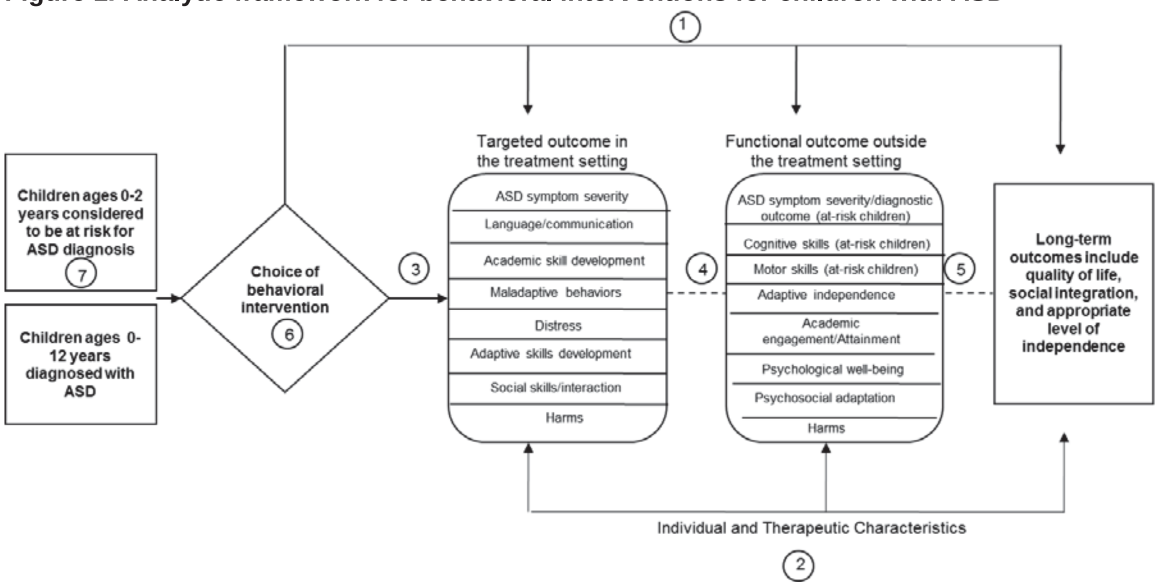
Role of the AHRQ Task Order Officer

The Task Order Officer (TOO) was responsible for overseeing all aspects of this project. The TOO helped to develop a common understanding among all parties involved in the project, resolved questions and ambiguities, and addressed our queries regarding the scope and processes of the project. The TOO reviewed the report for consistency, clarity, and to ensure that it conforms to AHRQ standards.

Analytic Framework

Figure 1 illustrates the placement of the review’s Key Questions within the context of treatment choice, potential outcomes, and characteristics that may affect outcomes. Circled numbers indicate the KQs, and their placement indicates the points in the treatment process where they are likely to arise. This update focuses on behavioral interventions for children with ASD or considered to be at risk for ASD. The population of interest is patients 0–12 years diagnosed with ASD. A child entering treatment may be between the ages of 0 and 2 and at risk for diagnosis of ASD or ages 0 to 12 with a diagnosis of ASD. Diagnoses may occur before age 2; thus the represented age ranges overlap. Individuals engage in behavioral interventions, which may lead to specific outcomes (KQ 1). Outcomes may be modified by characteristics of the child/family or of the intervention (KQ 2). KQ 3 involves identifiable changes early in the treatment process that may affect outcomes. KQ 4 involves the relationship between targeted outcomes in the treatment setting and functional outcomes outside the treatment setting. KQ 5 involves generalization of interventions to other contexts, and KQ 6 addresses components of treatments that may drive outcomes, the "active ingredients" of treatments. KQ 7 addresses treatments for very young children considered to be at risk for ASD. Target outcomes in the treatment setting include ASD symptom severity, language/ communication, academic skill development, maladaptive behaviors, distress, adaptive skills development, and social skills/interaction. Functional outcomes outside the treatment setting include adaptive independence, academic engagement/attainment, psychological well-being, and psychosocial adaptation; for children considered to be at risk, the outcomes include changes in ASD symptom severity or diagnostic outcome, motor skills, and cognitive skills. Long-term outcomes include quality of life, social integration, and appropriate level of independence. Harms of intervention are also considered.

Figure 1. Analytic framework for behavioral interventions for children with ASD



ASD = autism spectrum disorder; KQ = Key Question

Note: Numbers in circles on diagram represent placement of Key Questions.

Literature Search Strategy

Databases

A librarian employed search strategies provided in Appendix A to retrieve research on interventions for children with ASD. Our primary literature search employed three databases: MEDLINE® via the PubMed interface, PsycINFO® (psychology and psychiatry literature), and the Educational Resources Information Clearinghouse. Our search strategies used a combination of subject heading terms appropriate for each database and key words relevant to ASD (e.g., autism, Asperger). We limited searches to the English language and literature published since the development of the 2011 review.

We also manually searched the reference lists of included studies and of recent narrative and systematic reviews and meta-analyses addressing ASD. We also invited TEP members to provide additional citations.

Grey Literature and Hand Searching

As the review focuses on behavioral interventions, we did not search for regulatory information. As noted, we hand searched the reference lists of included studies and recent reviews.

Search Terms

Controlled vocabulary terms served as the foundation of our search in each database (e.g., MEDLINE vocabulary terms including autistic disorder, child development disorders, pervasive), complemented by additional keyword phrases (e.g., Asperger, autism). We also limited searches to items published in English. Our searches were executed in July 2013. Appendix A provides our search terms and the yield from each database. We imported all citations into an electronic database.

Process for Study Selection

Inclusion and Exclusion Criteria

We developed criteria for inclusion and exclusion based on the patient populations, interventions, outcome measures, and types of evidence specified in the Key Questions and in consultation with the TEP. Table 1 summarizes criteria.

Table 1. Inclusion criteria

Category	Criteria
Study population	Children ages 0–12 with ASD or 0–2 considered to be at risk for ASD based on sibling status or early developmental/behavioral vulnerabilities highly suspicious of ASD
Publication languages	English only
Admissible evidence (study design and other criteria)	Admissible designs Randomized controlled trials, prospective and retrospective cohort studies, and nonrandomized controlled trials Other criteria Studies must be original research studies providing sufficient detail regarding methods and results to enable use and aggregation of the data and results Studies must have relevant population and ≥10 participants with ASD Studies must address one or more of the following for ASD: -Behavioral treatment modality -Predictors of treatment outcomes -Generalization of treatment outcomes to other contexts -Drivers of treatment outcomes Relevant outcomes must be able to be abstracted from data in the papers Data must be presented in the aggregate (vs. individual participant data)

ASD = autism spectrum disorder

Study Population

Studies needed to provide adequate information to ensure that participants fell within the target age range. For studies with populations including individuals with ASD in our target range and over age 12, we retained the study if we could infer that at least 80 percent of the study participants were in the 0 to 12 age range or if the mean age of participants did not exceed 12 years and 11 months. Similarly, for studies including individuals with ASD and those with other developmental disabilities, we retained the study if we could isolate data on those participants with ASD.

Sample Size

We included studies with at least 10 individuals with ASD between the ages of 0 to 12 years. Our goal was to identify and review the best evidence for assessing the efficacy and effectiveness of therapies for children with ASD, with an eye toward utility in the treatment setting. Interventions to address ASD are frequently behavioral in nature and highly intensive. They are also frequently adapted to be targeted to specific study participants given the significant heterogeneity of individuals with ASD. In part because this makes behavioral research quite complex and intensive, study sizes tend to be very small. A cutoff sample size of 10 provides a balance, allowing us to review and comment on adequate literature for the review but with studies large enough to suggest effects of the interventions.

With the assistance of our technical experts, we selected a minimum sample size of 10 in order to maximize our ability to describe the state of the current literature, while balancing the need to identify studies that could be used to assess treatment effectiveness.

We recognize that the combination of requiring a comparison group and setting a minimum of 10 participants for studies to be included effectively excluded much of the literature on behavioral interventions using single-subject designs.

Single-subject design studies can be helpful in assessing response to treatment in very short timeframes and under very tightly controlled circumstances, but they typically do not provide information on longer term or functional outcomes, nor are they ideal for external validity without multiple replications.[53] They are useful in serving as demonstration projects, yielding initial evidence that an intervention merits further study, and, in the clinical environment, they can be useful in identifying whether a particular approach to treatment is likely to be helpful for a specific child. Our goal was to identify and review the best evidence for assessing the efficacy and effectiveness of behavioral interventions for children with ASD, with an eye toward utility in the treatment setting.

Study Design

We accepted any comparative study designs; that is, any study that included both a treatment/intervention and a separate control group. Control participants could receive an alternate intervention, no intervention/waitlist, or placebo. While we recognize that case series and single-subject design studies can be useful for testing hypotheses or piloting interventions, we did not include such studies as the potential for bias associated with the lack of a control group limits the utility of their findings.

Outcomes

We assessed outcomes in the broad areas of symptom severity, cognitive skills, motor skills, adaptive behavior, language/communication, maladaptive behavior, distress, social skills, and academic attainment. We considered intermediate outcomes as those that occur directly as a result of the intervention and that may also have longer term implications for the ultimate, functional outcomes that are the long-term goal of therapies. We also assessed the harms of interventions, defined by the AHRQ Effective Health Care program as the totality of adverse consequences of an intervention.[54]

Language

We focused the review on studies published in English. In the opinion of our content experts, most research on ASD is published in English regardless of the native language of the investigators or country of publication.

Screening of Studies

Once we identified articles through the electronic database searches, review articles, and bibliographies, we examined abstracts of articles to determine whether studies met our criteria. Two reviewers separately evaluated each abstract for inclusion or exclusion, using an Abstract Review Form (Appendix B). If one reviewer concluded that the article could be eligible for the review based on the abstract, we retained it for full text assessment.

Two reviewers independently assessed the full text of each included study using a standardized form (Appendix B) that included questions stemming from our inclusion/exclusion criteria. Disagreements between reviewers were resolved by a third-party adjudicator. The group of abstract and full text reviewers included expert clinicians and researchers and health services researchers.

Data Extraction and Data Management

The staff members and clinical experts who conducted this review jointly developed the evidence tables, which were used to extract data from the studies. We used table categories and parameters as outlined in the 2011 review. Tables aim to provide sufficient information to enable readers to understand the studies, including issues of study design, descriptions of the study populations (for applicability), description of the intervention, and baseline and outcome data on constructs of interest.

All team members shared the task of initially entering information into the evidence table. Another member of the team also independently reviewed the articles and edited all initial table entries for accuracy, completeness, and consistency. The full research team met regularly during the article extraction period and discussed issues related to data extraction (e.g., optimal level of detail in the description of the intervention). In addition to outcomes related to treatment effectiveness and modifiers of effects, we extracted all data available on harms. Harms encompass the full range of specific negative effects, including the narrower definition of adverse events.

The final evidence tables are presented in their entirety in Appendix C. Studies are presented in the evidence tables alphabetically by the last name of the first author within each year. When possible to identify, analyses resulting from the same study were grouped into a single evidence table. For those studies reported in the 2011 review and with followup data reported here, the evidence table for the original studies can be found in the 2011 report.[39]

Individual Study Quality Assessment

We used the approach to assessing the quality of individual studies that was developed for the 2011 review and following methods outlined in the AHRQ Effective Health Care program's "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[55] We assessed the quality of studies in the domains below using specific questions to evaluate a study's conduct. We rated each domain individually and combined them for an overall quality level as described below and in Appendix D. Three levels were possible: good, fair, and poor (Table 2).

Study design

1. Did the study employ a group design (have a comparison group)?
2. Were the groups randomly assigned?
3. If no, was there an appropriate comparison group?
4. If yes, was randomization done correctly?

Diagnostic approach

1. Was a valid diagnostic approach for ASD used within the study, or were referred participants diagnosed using a valid approach?
   A. A clinical diagnosis based on the DSM, in addition to the ADI-R and/or ADOS assessments.
   B. A combination of a DSM clinical diagnosis with one other assessment tool; or the ADOS assessment in combination with one other assessment tool.
   C. Either a clinical DSM-based diagnosis alone or the ADOS assessment alone.
   D. Neither a clinical DSM-based diagnosis nor the ADOS assessment

Participant ascertainment

1. Was the sample clearly characterized (e.g., information provided to characterize participants in terms of impairments associated with their ASD, such as cognitive or developmental level)?
2. Were inclusion and exclusion criteria clearly stated?
3. Do the authors report attrition?
4. Were characteristics of the drop-out group evaluated for differences with the participant group as a whole?

Intervention characteristics

1. Was the intervention fully described?
2. Was treatment fidelity monitored in a systematic way? (for non-medical interventions)
3. Did the authors measure and report adherence to the intended treatment process? (for medical interventions)
4. Did the authors report differences in or hold steady all concomitant interventions?

Outcomes measurement

1. Did outcome measures demonstrate adequate reliability and validity (including inter-observer reliability for behavior observation coding)?
2. Were outcomes coded and assessed by individuals blinded to the intervention status of the participants?

Statistical analysis

1. For RCTs, was there an intent-to-treat analysis?
2. For negative studies, was a power calculation provided?
3. For observational studies, were potential confounders and effect measure modifiers captured?

4. For observational studies, were potential confounders and effect measure modifiers handled appropriately?

Table 2. Description of study quality levels

Quality Level	Description
Good	Good studies are considered to have the least bias and results are considered valid. A good study has a clear description of the population, setting, interventions, and comparison groups; uses a valid approach to allocate patients to treatments; has a low dropout rate; and uses appropriate means to prevent bias; measure outcomes; analyze and report results.
Fair	Fair studies are susceptible to some bias, but probably not sufficient to invalidate the results. A study may be missing information, making it difficult to assess limitations and potential problems. As the "fair quality" category is broad, studies with this rating vary in their strengths and weaknesses. The results of some fair-quality studies are possibly valid, while others are probably valid.
Poor	Poor studies are subject to significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; have large amounts of missing information; or have discrepancies in reporting. The results of a poor-quality study are at least as likely to reflect flaws in the study design as to indicate true differences between the compared interventions.

Determining Quality Levels

We assessed each domain described above individually and considered the individual ratings to determine an overall quality assessment of good, fair, or poor. We required that studies receive positive scores questions related to study design and diagnostic approach to be considered good quality. Scores were calculated first by domain and then summed and weighted as described in Table 3 to determine overall study quality. Studies could receive up to two points on the domains of study design, diagnostic approach, participant ascertainment, and intervention, and up to one point on the domains of outcome measurement and statistical analysis.

Table 3. Quality scoring algorithm

Definition and Scoring Algorithm	Rating
Score algorithm for internal validity quality rating	
• ≥8/10 points, including a ++ on study design and ++ on diagnostic approach	Good quality
• ≥6/10 points, including at least a + on intervention	Fair quality
• ≤5/10 points	Poor quality

Data Synthesis

We summarized all data qualitatively using evidence tables. We focused on outcomes related to core ASD symptoms (impairments in communication and social interaction and restricted/repetitive behaviors and interests), outcomes including IQ and adaptive behavior, and key symptoms in studies of interventions targeting conditions commonly associated with ASD (e.g., anxiety). For the update, we describe new comparative studies published since the original report, and we make our conclusions and assess the strength of evidence on the cumulative, comparative evidence across the original report and update.

Grading the Body of Evidence for Each Key Question

The assessment of the literature is done by considering both the observed effectiveness of interventions and the confidence that we have in the stability of those effects in the face of future research. The degree of confidence that the observed effect of an intervention is unlikely to change is presented as strength of evidence, and it can be regarded as insufficient, low, moderate, or high. Strength of evidence describes the adequacy of the current research, both in terms of quantity and quality, as well as the degree to which the entire body of current research provides a consistent and precise estimate of effect. Interventions that have demonstrated benefit in a small number of studies but have not yet been replicated using the most rigorous study designs will therefore have insufficient or low strength of evidence to describe the body of research. Future research may find that the intervention is either effective or ineffective. Strength of the evidence is assessed for a limited set of critical outcomes, typically those related to effectiveness of an intervention. We assessed the strength of the evidence for studies addressing Key Questions 1 and 7, which deal specifically with the outcomes of intervention.

Methods for applying strength of evidence assessments are established in the "Methods Guide for Effectiveness and Comparative Effectiveness Reviews"[55] and are based on consideration of five domains (Table 4): study limitations, consistency in direction of the effect, directness in measuring intended outcomes, precision of effect, and reporting bias. Strength of evidence is assessed separately for major intervention-outcome pairs and incorporates data from the entire body of reviewed evidence on behavioral interventions (i.e., comparative studies—both RCTs and prospective and retrospective cohort studies—reported in the 2011 review[39] and studies reported in the current review). We required at least three fair studies to be available to assign a low strength of evidence rather than considering it to be insufficient. We required at least one good study for moderate strength of evidence and two good studies for high strength of evidence. In addition, to be considered "moderate" or higher, intervention-outcome pairs needed a positive response on two out of the three domains other than study limitations.

Once we had established the maximum strength of evidence possible based upon these criteria, we assessed the number of studies and range of study designs for a given intervention-outcome pair, and downgraded the rating when the cumulative evidence was not sufficient to justify the higher rating. The possible grades were:

- High: High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates
- Moderate: Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate
- Low: Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate
- Insufficient: Evidence is either unavailable or does not permit a conclusion.

Table 4. Domains used to assess strength of evidence[a]

Domain	Explanation
Study Limitations	Degree to which included studies for a given outcome have a high likelihood of adequate protection against bias (i.e., good internal validity), assessed through study design and study conduct.
Consistency	Degree to which included studies find either the same direction or similar magnitude of effect. Assessed through two main elements: • Direction of effect: Effect sizes have the same sign (that is, are on the same side of no effect or a minimally important difference). • Magnitude of effect: The range of effect sizes is similar.

Table 4. Domains used to assess strength of evidence[a] (continued)

Domain	Explanation
Directness	Extent to which evidence links interventions directly to a health outcome of specific importance for the review, and for comparative studies, whether the comparisons are based on head-to-head studies. Evidence may be indirect in several situations such as: • Outcome being graded is considered intermediate in a review that is focused on clinical health outcomes (such as morbidity, mortality). • Data do not come from head-to-head comparisons but rather from two or more bodies of evidence to compare. • Data are available only for proxy respondents instead of directly from patients for situations in which patients are capable of self-reporting and self-report is more reliable.
Precision	Degree of certainty surrounding an effect estimate with respect to a given outcome, based on the sufficiency of sample size and number of events. A body of evidence will generally be imprecise if the optimal information size (OIS) is not met. OIS refers to the minimum number of patients (and events when assessing dichotomous outcomes) needed for an evidence base to be considered adequately powered.
Reporting bias	Degree of selective publishing or reporting of research findings based on the favorability of direction or magnitude of effect.

[a] Excerpted from Berkman et al. 2013[56]

Applicability

Finally, it is important to consider the ability of the outcomes observed to apply both to other populations and to other settings (especially for those therapies that take place within a clinical/treatment setting but are hoped to change behavior overall). Our assessment of applicability included determining the population, intervention, comparator, and setting in each study and developing an overview of these elements for each intervention category.

Peer Review and Public Commentary

Researchers and clinicians with expertise in behavioral, medical, social, psychological and educational issues and individuals representing stakeholder and user communities provided external peer review of this report; AHRQ and an associate editor also provided comments. The draft report was posted on the AHRQ Web site for 4 weeks to elicit public comment. We addressed all reviewer comments, revised the text as appropriate, and documented changes and revisions to the report in a disposition of comments report that will be made available 3 months after AHRQ posts the final review on the AHRQ Web site.

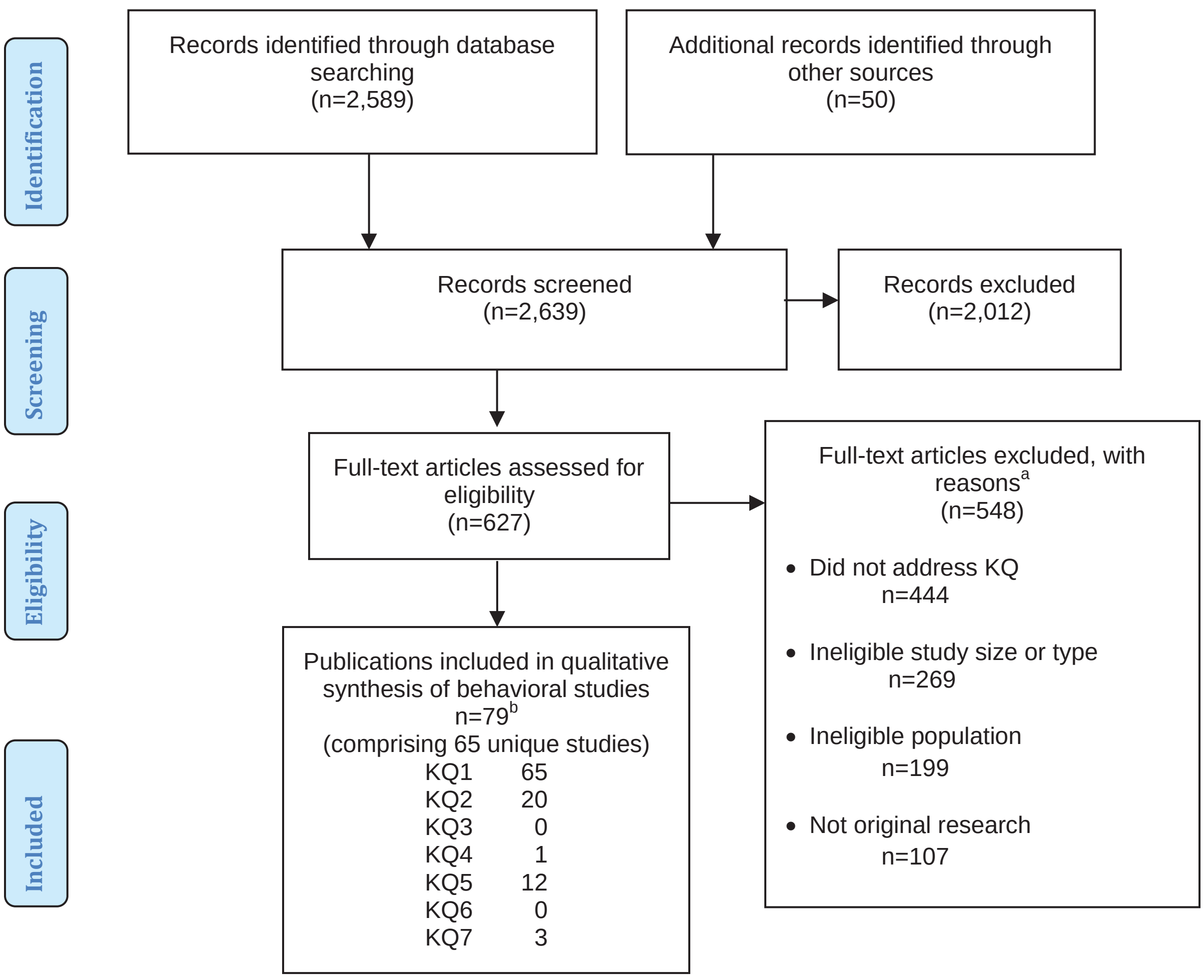
Results

Results of Literature Searches and Description of Included Studies

Article Selection

We identified 2,639 citations and abstracts (Figure 2). We excluded 2,012 studies at abstract review and assessed the full text of 627 studies. Among these, 79 publications, comprising 65 unique studies, met our criteria. Eight of these studies report followup data to papers included in the 2011 review of therapies for children with autism spectrum disorder (ASD). The 65 included studies comprise 48 randomized controlled trials (RCTs) and 17 nonrandomized trials or cohort studies. Table 5 outlines study characteristics. Appendix E includes a list of all studies excluded at the abstract and full-text review stages.

Figure 2. Disposition of studies identified for this review



KQ = Key Question; n = number
[a] Numbers do not tally as studies could be excluded for multiple reasons.
[b] 8 studies among these include followup data from studies reported in the 2011 review.

Table 5. Overview of included studies

Characteristic	RCTs	nRCTs	Prospective Cohort Studies	Retrospective Cohort Studies	Total Literature
	(n=48)	(n=5)	(n=11)	(n=1)	(n=65)
Intervention					
Early intensive behavioral and developmental	12	2	10	1	25
Social skills	11	2	0	0	13
Play-/interaction-based	11	0	1	0	12
Interventions targeting associated behaviors	9	0	0	0	9
Other	5	1	0	0	6
Treatment duration					
<1 month	2	1	0	0	3
≥1 to ≤3 months	24	2	2	0	28
>3 to ≤6 months	12	0	1	0	13
>6 to ≤12 months	8	1	5	1	15
>12 months	2	1	3	0	6
Final followup after end of treatment					
Immediately post-treatment	31	3	9	0	43
≥1 to ≤3 months	8	1	1	0	10
>3 to ≤6 months	4	0	0	0	4
>6 to ≤12 months	1	1	0	0	2
>12 months	4	0	1	0	5
Not reported/unclear	0	0	0	1	1
Study population					
U.S./Canada	33	0	2	1	36
Europe	8	3	7	0	18
Asia	4	0	0	0	4
Other	3	2	2	0	7
Total N participants	2,344	133	660	142	3,279

N = number; nRCT = nonrandomized controlled trial; RCT = randomized controlled trial

Note: Among the 25 early intensive behavioral and developmental intervention studies, four reported followup data from studies addressed in the 2011 review; one social skills study, one play/interaction-based study, and two studies reporting on interventions targeting associated behaviors also reported followup data to studies addressed in the 2011 review.

KQ1. Effects of Behavioral Interventions on Core and Commonly Associated Symptoms in Children With ASD

A wide range of interventions can be classified as behavioral. For the 2011 review and this update, we included studies of early intensive behavioral and developmental interventions, which comprised University of California, Los Angeles (UCLA)/Lovaas-based approaches, the Early Start Denver Model (ESDM), and parent training approaches incorporating principles of Applied Behavior Analysis (ABA) to improve outcomes among young children with ASD; social skills interventions; focal play-based /interaction-based interventions; behavioral interventions focused on commonly associated behaviors; and a small group of other behavioral interventions assessing other interventions in core/associated areas (e.g., sleep workshops).

Early Intensive Behavioral and Developmental Interventions

Key Points

- Of the 25 new studies addressing early intensive behavioral and developmental interventions, eight were good, 13 were fair, and four were poor quality.
- Many studies used parent-report measures of adaptive and ASD symptom-related outcomes, which may be confounded by parental stress, parental involvement in treatment protocols, and nonrandom assignment based upon parental treatment preferences.
- All studies of ABA-based interventions compared a minimum of two treatment groups. No study included a control group that was not receiving some type of intervention (including school enrollment or eclectic community-based therapies, such as medication or occupational therapy), although some limited the number of behaviorally based treatment hours that control participants could receive.
- Studies with parent training components reported improvements in language with inconsistent results for other outcomes.
- No studies reported harms related to children.

Overview of the Literature

In the 2011 review, we identified 17 comparative studies[57-75] (described in 19 papers), of which six were RCTs (two good quality,[73, 75]four fair[57, 69, 71, 72]), five were nonrandomized trials (four fair quality,[64-68, 74] one poor[70]), four were prospective cohort studies (three fair[60, 61, 63] and one poor quality[62]), and two were poor quality retrospective cohort studies.[58, 59] For the current review we identified 25 comparative studies (reported in 37 publications) meeting our inclusion criteria and evaluating either ABA-based early intervention approaches[73, 76-91] or approaches integrating parent training components).[72, 92-109] Four of these studies (published in multiple papers) report followup data for studies reported in the 2011 review.[72, 73, 79, 80, 85-90, 105, 110] Additionally, one study in the current report[95] may include some participants reported in studies in the 2011 review.[111, 112]

ABA-based approaches. Ten studies (reported in 18 publications) assessed ABA-based early intensive behavioral and developmental intervention (Table 6).[73, 76-88, 90, 91, 110, 113] Studies included two RCTs conducted in the United States;[73, 84, 85] two non-randomized controlled trials conducted in Europe;[76],[91] three European,[77-80] one U.S.-based,[83] and one Israeli[81] prospective cohort study; and one Canadian retrospective cohort study that reported on segments of the same population in multiple publications.[86-90, 110] Five studies compared ABA-based approaches to care-as-usual community therapies[73, 78, 79, 81, 85, 86] and five to preschool-based programs.[76, 77, 83, 84, 91] Mean participant age ranged from 15-72 months. Treatment duration ranged from 6 to 24 months. We rated two studies as good, seven studies as fair, and one study as poor quality.

Parent training. We identified 15 studies (reported in 19 publications) of early intervention with parent training components (Table 7).[72, 92-109] Studies included five European[95, 97, 101, 102, 108] and one Australian[100] prospective cohort studies; four RCTs conducted in the United States or Canada,[93, 98, 103, 104, 107, 109] two (including one crossover) in Asia,[92, 99] one in Australia,[96] and two (one with suboptimal randomization) in Europe.[72, 94, 105] Seven studies compared parent training to treatment as usual (community-based intervention).[72, 92-,94, 98, 101, 102, 105- 107] Five compared ABA-based parent training to other parent-training paradigms[97, 100, 103, 104, 108, 109] or multiple other interventions,[95, 96] and the comparison arm in one study received no specific intervention.[99] Mean participant age ranged from 14 to 81 months. Treatment duration ranged from 12 weeks to 2 years. We rated six studies as good, six studies as fair, and three studies as poor quality.

Detailed Analysis

ABA-Based Approaches

One fair quality RCT examined the use of the Learning Experiences and Alternative Program for Preschoolers and Their Parents (LEAP) protocol in preschool classrooms in the United States.[84] The study compared 27 classrooms (n children=177; mean age: 50.1 months±4.6 months) with teachers trained in the full LEAP curriculum (including peer mediated social skills, incidental teaching, pivotal response training, the Picture Exchange Communication System (PECS), and positive behavior support) to 23 classrooms (n children=117; mean age: 50.7 months±4.2 months) where teachers received the LEAP manual but no formal training. Both groups received an average of 17 hours per week of intervention over two years. Relative to the manuals-only group, children in the full LEAP training classrooms showed significant ($p < .05$) improvement on investigator-rated Childhood Autism Rating Scale (CARS) scores, language, cognitive, and social skills measures. The students of teachers rated as having better intervention fidelity showed better outcomes on all measures.

Five additional studies (reported in multiple publications) examined the use of school-based ABA programs (one fair quality nonrandomized controlled trial and four fair quality prospective cohort studies. [76-77, 78, 81-83] All five compared standard special education preschool curriculums to special education preschools with some sort of enhanced intervention modality, including general ABA,[81, 82] individual UCLA/Lovaas-based behavioral intervention,[76, 78] Treatment and Education of Autistic and Communication related handicapped Children (TEACCH)- or LEAP-programs,[83] and a mix of behaviorally-based operant conditioning techniques.[77] Mean treatment intensity ranged from 13.8-28.38 hours per week, with length of enrollment varying from 8-24 months. Mean child ages ranged from 25.1-53.5 months.

The effects of enhanced school-based interventions relative to standard special education preschool curricula were mixed. Some studies[76-78] found that the enhanced intervention groups showed greater gains in cognitive outcomes and parent-reported adaptive skills. Other studies found that children in all groups improved on cognitive, adaptive, and ASD symptom measures[76, 81-83] regardless of intervention type, although in some cases treatment groups showed greater improvements.[76] Others found declines in both groups on standardized scores of motor skills.[81, 82] Intervention efficacy was associated with baseline cognitive scores in one study of TEACCH classrooms,[83] with lower baseline cognitive scores associated with more improvement.

Lower baseline ASD severity was associated with parent-reported cognitive and adaptive growth for children who received eclectic vs. ABA intervention, but not with standardized test scores.[81, 82] Additional UCLA/Lovaas-style intervention over-and-above classroom involvement was associated with reduced ASD symptoms as rated by clinicians on the CARS[78] but not as rated by parents using the Scale of Pervasive Developmental Disorder in Mentally Retarded Persons.[76] Where examined, total hours of intervention per week were not associated with cognitive or adaptive outcomes, although hours were similar across intervention groups within each study (e.g., comparing half-day programs to other half-day programs).

Four studies (reported in multiple publications) compared ABA-based early intervention to eclectic treatment as usual.[73, 79, 80, 85-91, 110] One good quality RCT compared ESDM to community-based interventions.[73, 85] It randomized children into two groups based on gender and IQ. For two years, 24 children in the ESDM arm (mean age: 23.9±4.0 months at study entry, mean IQ: 61.0±9.2) received 1:1 therapist-delivered manualized intervention (mean of 15.2±1.4 hours/week) as well as parent-delivered treatment (mean 16.3±6.2 hours/week). The comparison group of 21 children (mean age: 23.1±3.9 months, mean IQ: 59.4±8.6) received individual (mean 9.1 hours/week) and group (mean 9.3 hours/week) therapies, including speech-language therapy, occupational therapy, and developmental preschool enrollment. The ESDM intervention targets social communication and engagement as well as general child development. After one year of treatment, The ESDM group showed significantly greater improvement in IQ but not adaptive behavior. After two years of treatment, the ESDM group continued to show significantly more IQ improvement as well as receptive and expressive language. Both groups improved in all domains of adaptive behavior but socialization, with greater improvements in the ESDM group. Neither group showed significant differences in Autism Diagnostic Observation Schedule (ADOS) severity scores or repetitive behavior, although the ESDM group demonstrated a diagnostic shift toward a milder diagnosis (PDD-NOS) at followup. Electroencephalography (EEG) measures of engagement and cognitive processing for children in the ESDM group with usable data were comparable to typically developing children.

A good quality non-randomized trial from Europe[91] compared children (mean age=62.52±16.96 months) with ASD and co-occurring intellectual disability receiving school-based ABA therapy (n=20) to a matched control group of children receiving care-as-usual (e.g., enrollment in TEACCH classrooms, PECS; n=20). The intervention group received one-to-one treatment (mean=4.98 hours, SD=1.45; range: 1.32-7.11) from master's level interventionists. Eleven participants received 2 years of treatment and 9 participants received only one year due to funding loss and school noncompliance. Independent ratings indicated high treatment fidelity (90.3%). Monthly meetings between therapists and parents and teachers provided them with strategies on skill instruction and maintenance.

Cognitive, adaptive, and language skills, and ASD symptoms, were assessed at 12- and 24-months after starting treatment. Both the treatment and control groups showed significant improvement from baseline to 12-month and from 12-month to 24-month followups in developmental age, adaptive skills, and receptive language, with the treatment group showing significantly more improvement than the control (p values<.04, effect sizes ranging from 1.09-2.61). The treatment group showed significant improvements in IQ (p<.001, effect size=.40) between baseline and the 12-month assessment but not the 24-month assessment, whereas the control group did not show significant IQ gains at either time point. Fifty-five percent of treatment group participants showed reduced levels of intellectual disability post-treatment versus 5 percent in the control group. The treatment group (but not the control group) also had reduced ASD symptoms as measured by the CARS and ADOS (p values<.01, effect sizes 1.50-1.51). Neither group significantly improved in expressive language. Multiple baseline child factors were significantly correlated with progress over time, including developmental age, hours of treatment per week, IQ, adaptive and play skills, and receptive language.

A fair quality Canadian retrospective cohort study[86-90, 110] matched children receiving a large-scale, publicly funded, community-based early intensive intervention program that incorporated ABA, discrete trial training, and naturalistic approaches (n=61, mean age=42.93±11.53 months) to waitlisted children receiving care-as-usual (n=61, mean age=42.79±10.51 months). The intervention group received treatment (mean 25.81±3.44 hours/week) conducted by trained instructor therapists in specialized centers, preschools, and the home environment. The control group received a mean of 17.9±12.3 hours/week of school-based services and <10 hours/week of behavioral intervention conducted by community-based interventionists in community settings. The approaches included low-intensity ABA, speech and occupational therapy, and behavioral consultation. Children in the treatment arm were enrolled in treatment longer (mean=27.84±8.11 months) than children in the waitlist group (mean=17.01±2.81months), and analyses controlled for this difference.

ASD severity improved for the treatment group compared with control, as did Vineland composite standard and ratio scores and IQ estimates (p values≤.033, effect sizes ranging from 0.53 to 0.83). Although treatment group participants had cognitive scores an average of 19 points higher than controls at followup, this should be interpreted with caution due to a lack of baseline cognitive data. Outcomes were related to age at enrollment, treatment duration, and higher baseline adaptive scores, with duration becoming nonsignificant after accounting for group membership (correlation of duration, group=.57, p<.01). A significant interaction emerged between age at enrollment and group membership, with younger starting age influencing outcomes for the treatment group but not control. Analyses including participants in the cohort study and additional participants found that younger age at intake, higher initial developmental levels[90] and treatment intensity[88, 90] were related to treatment outcomes.

Additional analyses of some children in these earlier Canadian studies (overlap not clear) assessed the effects of baseline age and IQ on cognitive and adaptive outcomes in 207 children, and, in a separate analysis of matched older and younger children, effects of baseline age on the same outcomes.[110] In the initial retrospective analysis of 207 children, participant ages at intake ranged from 2 to 14.5 years, IQ from 10 to 104, and mental age from 3 months to roughly 7.5 years. Higher baseline IQ and younger age were significantly associated with greater cognitive rate of change (pre-post change in mental age/time in intervention) and with higher IQ at followup (all p<.001), but change in IQ was not significantly associated with higher initial IQ. Higher baseline IQ was also associated with higher adaptive behavior scores at followup (p<.001), but age was not a significant predictor. Longer duration of intervention was associated with slower rate of IQ and adaptive behavior development (p values ≤.01); however, as this analysis was not prospective, the children who received more intervention could have been making slower progress. In the analysis of older (n=60, age 6-13.58 years at baseline) and younger (n=60, age 2.08-5.92 at baseline) children matched on developmental trajectory (i.e., number of intervention hours, baseline IQ and adaptive behavior), younger children had significantly better followup IQ outcomes compared with the older group. Younger children gained an average of roughly 17 IQ points (effect size=0.80) while older children gained an average of 2 points. Cognitive rate improved significantly for younger (effect size=3.19) but not older children. Both groups improved over time in adaptive behavior, but differences between groups were not significant (improvement of 4 points in younger children and 5 in older).

Finally, a poor quality UK study[79, 80] compared the long-term effects (2 years post-treatment) of 1:1 home-based early intervention (both university-provided and privately-provided) to community-based treatment-as-usual, including PECS, TEACCH, and medication. The early intervention group included 23 children (mean age=35.7±4 months; mean IQ=61.43±16.43 months), and the community-based group included 18 (mean age=38.4±4.4 months; mean IQ=62.33±16.64) at the two-year followup, with children in the community-based group significantly older at the start of treatment ($p< .05$). For 24 months, children in the early intervention group received an average of 25.6 hours/week of ABA-based intervention using discrete trial training in the home environment, whereas children in the community-based arm received an unspecified amount of eclectic treatment. After 24 months of intervention, IQ, mental age, and language comprehension/expression improved significantly for the ABA group versus community-based ($p \leq .05$; effect size for IQ change=0.77). At the two year followup, IQ gains were only maintained for children who received privately-provided ABA-based intervention. IQ remained stable for children in the community-based group and significantly declined for children who received university-provided intervention (effect size=.49). This result is confounded by nonrandom assignment and the fact that at baseline, the university-based group had higher levels of ASD symptoms, lower levels of adaptive behavior, and fewer total intervention hours.

Table 6. Key outcomes of ABA-based early intervention studies

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Peters-Scheffer et al. 2013[91] Netherlands **G1:** Low intensity Lovaas-based intervention+specialized preschool, 20/20 **G2:** Specialized preschool, 20/20 Quality: Good	**G1+G2:** 62.52±16.96 (median) **G1:** 40.66±20.1 **G2:** 40.14±18.3	• 9/20 participants in G1 received 1 year of treatment vs. 2 years • Developmental age in both groups improved over time, but increase was greater in G1 vs. G2 (p=.001); effect size for change=1.09 • IQ improved significantly from baseline to 12 months (mean 40.66 to 48.17, P<.001) in G1 and remained stable from 12-24 months; no significant change over time in G2 (baseline mean=40.14, 24-month mean=39.42); effect size for change=0.40 • Total Vineland and subscale scores improved in both groups with greater improvements in G1 vs. G2 (p values<.001); effect size for change in total score=1.74 • Receptive language improved at 24 months in G1 vs. G2 (p=.04); expressive language improve over time in both groups but between group differences at 24 months were not significant (effect size for change=0.40) • Both groups generally improved over time on Early Social Communication Scales domains but between group differences were not significant at 24 months • Severity ratings (CARS, ADOS) decreased significantly over time for G1 but not G2; effect size for change in ADOS=1.51, CARS=1.50) • Differences between groups in measures of emotional and behavioral problems and behavioral flexibility were not significant • More G1 participants achieved clinical and reliable significant on developmental age, adaptive behavior, interpersonal relationships, play and leisure time, receptive and expressive language, ASD severity, and responding to social interaction vs. G2 • More G2 vs. G1 participants obtained clinical and reliable significance on measures of problem behavior and maternal stress; equal numbers of G1 and G2 participants obtained clinical and reliable significance on IQ, behavioral flexibility, joint attention, behavioral requests, and initiating social interaction • Diagnoses changes from autism to PDD-NOS in 45% of G1 and 20% of G2; 10% in G1 classified as non-autistic at 24 months (0 in G2); level of intellectual disability declined in 55% of G1 and 5% of G2 • Baseline hours of treatment, developmental age, IQ, level of adaptive behavior, play skills , receptive language significant predictors of progress

Table 6. Key outcomes of ABA-based early intervention studies (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Dawson et al. 2012[73, 85] US **G1:** ESDM, 24/24 **G2:** Community-based interventions, 24/21 Quality: Good	**G1:** 23.9±4.0 **G2:** 23.1±3.9 **G1:** 61.0±9.2 **G2:** 59.4±8.6	1 year outcomes: • Significantly greater improvement in IQ for G1 (54 vs. 22 points) compared with G2 • No adaptive behavior differences 2 year outcomes: • Significantly more improvement in G1 vs. G2 on IQ; receptive language, and expressive language • Adaptive behavior improvements in both groups (all domains except socialization); significantly greater improvements in G1; no change in ADOS severity scores or repetitive behavior • Diagnostic shift toward milder diagnosis (PDD-NOS) greater for ESDM group • No differences between groups in EEG measurements of perceptual face processing • EEG measures of engagement/cognitive processing comparable to those of typically developing children for G1 children with usable EEG data; 11/15 G1 participants and 4/14 G2 showed faster neural response to faces vs. objects
Boyd et al. 2013[83] US **G1:** TEACCH preschools, 85/81 **G2:** LEAP preschools, 54/48 **G3:** Non-model specific preschools, 59/56 Quality: Fair	G1: 48±6.84 G2: 47.52±8.4 G3: 48.84±7.68 NR	• Groups differed at baseline on ASD characteristics and severity (p=.0013), communication (p<.001), parent-rated reciprocal social interaction (p=.0241) and fine motor (p=.0066) composite scores • All groups showed significant change over time on ASD characteristics and severity, fine motor, and communication composites (p values ≤.05); G1 and G2 improved on teacher-rated reciprocal social interaction (p≤.05). G1 improved on parent-rated reciprocal social interaction (p<.05) • No significant differences among groups on any measure at followup • Children with higher Mullen scores made fewer gains in G1; children with high Preschool Language Scale scores at baseline had higher communication and ASD characteristics and severity composite scores in G1 • Females in G2 had smaller communication gains, although few females in study overall (n=33)

Table 6. Key outcomes of ABA-based early intervention studies (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	**Age, Mean Months±SD IQ, Mean±SD**	• **Key Outcomes**
Eldevik et al. 2012[77] Norway **G1:** Preschool-based early intensive intervention, 31/31 **G2:** Usual care preschool, 12/12 Quality: Fair	**G1:** 42.2±9.0 **G2:** 46.2±12.4 **G1:** 51.6±16.9 **G2:** 51.7±18.1	• Greater gains in cognitive outcomes (p=.004) and overall adaptive behavior (p=.036), Vineland communication (p=.034) and socialization (p=.008) for G1 vs. G2; no significant differences in Vineland daily living skills between groups • Effect size for change in IQ=1.03 (95% CI: .34 to 1.72) and for change in overall adaptive behavior=.73 (95% CI: .05 to 1.36) • Baseline age and PDD-NOS or Asperger diagnosis correlated with larger gains in overall adaptive behavior, communication, and daily living skills; baseline IQ positively correlated with Vineland socialization gains
Eikeseth et al. 2012[78] Norway/Sweden **G1:** Early intensive intervention, 35 / 13-15 depending on outcome **G2:** Standard care , 24 / NR Quality: Fair	**G1:** 3.9±0.9 years **G2:** 4.4±1.2 years Vineland age equivalent: **G1:** 1.9±0.9 **G2:** 2.1±0.8	• G1 scored significantly higher on all Vineland scales as compared withG2 (p<0.05) with an effect size of Total (composite)=0.92, Communication=1.08, ADL=0.71, Socialization=0.75,Motor=0.70, and Learning rate=0.97 • G1: CARS scores continued to decrease significantly during the second year of treatment (from 31.8 (SD=8.5) to 27.2 (SD=6.2), p<.05), effect size of 0.59 • Children receiving G1 scored significantly higher on standard scores of adaptive behavior. • Significant improvements were found in maladaptive behaviors and excess and deficit behaviors as compared with G2 • Largest gains were observed during the first year. Effect size on all measures at year one were moderate to large
Flanagan et al. 2012[86-88, 90, 110] Canada **G1:** Intensive behavioral intervention, 61/61 **G2:** Wait list control (matched by age), 61/61 Quality: Fair	**G1:** 42.93±11.53 **G2:** 42.79±10.51 NR	• In 2008 retrospective case series (Perry 2008) reporting on ~30% of G1 participants ASD severity (CARS), cognitive level, adaptive behavior, and rate of development improved significantly (all p <.001); outcomes varied across children: approximately 25% showed substantial improvements, 30% showed clinically significant improvement, 19% showed some/modest improvement, 25% showed no improvement or worsening of outcome. Analyses of a subset of the total participants (n=89) showed similar improvements (Freeman 2010) • Age (younger at baseline), IQ, adaptive behavior, and ASD severity were correlated with outcome; IQ was strongest predictor, accounting for 5-12% of the variance in outcomes (Perry 2011); in sub-set analysis (Shine 2010), duration of intervention also associated with better outcomes • ASD severity improved for G1 vs. G2 as did Vineland composite

Table 6. Key outcomes of ABA-based early intervention studies (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	• Key Outcomes
		standard and ratio scores and IQ estimates (p values≤.033, effect sizes ranging from 0.53 to 0.83); 19 point difference in IQ at end of intervention in favor of G1 • Younger age at intervention and higher adaptive skills associated with better outcomes; adaptive skills also associated with better outcomes for G2. Duration of intervention became nonsignificant after intervention type was entered into statistical models (Flanagan 2012) • In retrospective analyses (Perry 2013), higher baseline IQ predicted gains in IQ, and children starting early intervention at younger ages (2-5 years) gained significantly more IQ points (mean 17 points vs. mean 2 points) than children entering intervention at older ages (6-13 years); differences in adaptive behavior gains were not significant
Strain et al. 2011[84] US **G1**: LEAP program with coaching and training, 28 classrooms (27 analyzed)/177 children **G2**: LEAP intervention manuals only, 28 classrooms (23 analyzed)/117 children Quality: Fair	**G1:** 50.1±4.6 **G2:** 50.7±4.2 **G1:** 59.6±6.9 **G2:** 63.2±6.6	• Significant gains on CARS, language, cognitive, and social skills measures for G1 vs. G2 (P<.05) • G1 improved by 18.5 points compared with 9.4 for G2 on the Preschool Language Scale (effect size difference=0.92, p<.01) • G1 improved by 28.6 points compared with 12 for G2 on socials skills rating (effect size difference=1.22, p<.01) • Greater intervention fidelity associated with better outcomes on all measures
Itzchak et al. 2011[81, 82] Israel **G1:** ABA-based approach, 45/45 **G2:** Eclectic approach, 33/33 Quality: Fair	**G1:** 25.1±3.9 **G2:** 26.0±4.6 **G1:** 72.2±19.2 **G2:** 73.3±22.2	• Cognitive abilities (Mullen Scales) and overall Vineland raw and standard scores improved in both groups (p<.05) over time; no significant differences between groups at followup • Vineland motor skills domain decreased over time for both groups (p<.001),with greater decline for those with higher severity; children in G1+G2 with lower severity (ADOS) improved significantly more than those with higher severity on cognitive and adaptive measures; G2 participants with lower severity improved significantly on Vineland communication and socialization measures compared with G1 (p<.001) • In analyses combining G1 and G2, higher cognitive abilities at baseline,

Table 6. Key outcomes of ABA-based early intervention studies (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	• Key Outcomes
		particularly verbal abilities, and older maternal age were associated with greater adaptive skills at followup ($p<.05$); among those with greater severity, greater verbal ability was associated with better adaptive skills at followup ($r=.672$, $p<.001$); cognitive gains greater for those with lower severity ($p<.01$) and older, more educated mothers (p values <.001, .05); younger children had a better chance of cognitive improvement with intervention (p=NS)
Peters-Scheffer et al.2010[76] Netherlands **G1:** Specialized preschool +UCLA/ Lovaas-based intervention, 12/12 **G2:** Specialized preschool, 22/22 Quality: Fair	**G1:** 53.5±5.52 **G2:** 52.95±11.14 **G1:** 47.00±10.33 **G2:** 45.73±15.99	• Both groups improved over time on cognitive and adaptive measures; G1 improved significantly compared with G2 on IQ/developmental age and Vineland composite, communication, daily living, and socialization domains (all $p\leq.02$) • G2 had greater emotional and behavioral problem scores at baseline vs. G1 ($p<.05$), changes in scores not significant for either group over time • Decreases in symptom severity not significant between groups

Table 6. Key outcomes of ABA-based early intervention studies (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Kovshoff et al. 2011[79, 80] UK **G1:** Early intensive intervention (publicly-funded or privately purchased), 23/23 **G2:** Usual care, 21/18 Quality: Poor	**G1:** 35.7±4.0 **G2:** 38.4±4.4 **G1:** 61.43±16.43 **G2:** 62.33±16.64	• Groups differed significantly on age at baseline ($p<.05$); IQ, mental age, and language comprehension improved significantly for G1 vs. G2 after 24 months of intervention ($p\leq.05$); effect size for IQ change=0.77 • Vineland daily living and motor skills scores improved for G1 vs. G2 ($p<.05$) but composite, communication, severity, and socialization scores did not differ significantly between groups at the 24 month followup • Parents noted more positive social behavior for G1 vs. G2 at the 24 month followup; responders had higher IQ, higher mental age, higher Vineland composite, communication, and socialization scores, lower motor skills, more behavior problems, and more autistic symptoms and fewer hours of intervention in Year 2; at 2-year followup no significant group differences in IQ, adaptive behavior, communication, socialization, or behavior; more G1 participants achieved standard score on receptive language measure vs. G2 ($p=.048$) • In analyses of G1 participants in privately purchased vs. publicly funded early intensive intervention programs, IQ declined for publicly funded group compared with control or privately purchased participants ($p<.0001$); privately purchased participants maintained IQ and adaptive behavior gains from end of intervention to the 2 year followup. Publicly funded group had more severe ASD symptoms, lower adaptive behavior, and received less intensive intervention than the privately purchased group

ABA = applied behavior analysis; ADOS = Autism Diagnostic Observation Schedule; ASD = autism spectrum disorder; CARS = Childhood Autism Rating Scale; G-group; IQ = intelligence quotient; LEAP = Learning Experiences and Alternate Program for Preschoolers and their Parents; N = number; PDD-NOS = Pervasive Developmental Disorder-Not Otherwise Specified; SD = standard deviation; TEACCH = Treatment and Education of Autistic and Related Communication-Handicapped Children

Parent Training Approaches

One good quality RCT examining parent training[96] was conducted in Australia and compared two variations of the Building Blocks® program—home or center-based-- to waitlisted controls. The program targeted social and communication skill development. Mean child ages at enrollment ranged from 41.5 to 43.7 months. Mean IQs ranged from 57-66. Treatment duration was 40 weeks. Not all enrolled children had autism spectrum diagnoses; the breakdown was 100 percent of the home-based group, 82.8 percent of the center-based group, and 78.6 percent of the control group. To be enrolled in the center-based group, children had to have a baseline level of "social maturity," a lack of "high levels" of problem behavior, and parents willing to attend sessions. The home-based group (n at followup=27) received individualized 2-hour visits every 2 weeks in the home environment. Center-based children (n=29) received weekly manualized, 2-hour, center-based sessions in small groups of 4 to 6 children, as well as parent training and a parent support group. The control group (n=28) comprised a non-randomized treatment comparison waitlist. All groups received concomitant additional interventions classified as educational (home-based: 2.37 interventions±1.28; center-based: 2.41±1.50; control: 3.11±1.64) or ASD-specific (home-based: .22±.42; center-based: .14±.35; control: .54±.79). Providers were multidisciplinary teams of teachers, speech-language pathologists, occupational therapists and psychologists.

Children in all three groups showed significant improvements in Vineland Communication scores. Compared with the home-based group, children receiving center-based intervention had significantly greater improvement in language comprehension and expression as measured by the Reynell Developmental Language Scales. Waitlisted children had significantly greater improvements in followup Vineland Socialization scores than children in either treatment group. No other significant differences emerged among the three groups on other child outcomes. When analyses were limited only to children with autism spectrum diagnoses, the magnitude of the effects increased, but the presence of statistical significance did not change.[96]

Another good quality RCT from the United States [109] compared the language development of two groups of children with ASD diagnoses, one whose parents received training in a component of ABA, Pivotal Response Training (n=20, mean age=29.5 months, SD=6.9), and another whose parents received training in PECS (n=19, mean age=28.9, SD=4.2). Exclusion criteria included having more than nine intelligible words and having primary diagnoses of intellectual disability, neurological pathology or major sensory impairment. Participants were matched on word use, age, and cognitive functioning. Over the course of 23 weeks, parents completed weekly or biweekly 2-hour parent training sessions from doctoral students. Participants received one-on-one treatment in the home (mean=247 hours, range=181-263) from undergraduate student therapists. Therapist and parent-educator fidelity was maintained at 80 percent. Participants continued to receive outside interventions (e.g., speech therapy) and this was monitored via weekly parent report, with no significant between-group differences emerging.

Outcome variables were assessed at intake, immediately post-treatment, and three months post-treatment. Not all post-treatment coders were blind to participant condition, but no differences were found across blinded vs. not blinded sites. Data were not available on all participants at followup (n=38 for Mullen Scales of Early Learning, 35 for MacArthur Communicative Development Inventories, 35 for Vineland). No differences emerged between Pivotal Response Training and PECS groups. Both improved similarly on all variables over time, with effect sizes across collapsed groups of .216 for expressive communication (Mullen Scales of Early Learning; p<.001), .486 for words produced (MacArthur Communicative Development

Inventories; p<.001), and .110 for adaptive communication skills (Vineland; p=.037). The authors reported significant variability in participants' responses to treatment. Parent satisfaction post-treatment was similar across groups, with the only significant difference being the parent-reported difficulty of PECS (p=.005).

Two prospective cohort studies also received good quality ratings. The first was conducted in Australia[100] and compared professional-led parent training (n=17; mean child age, 36.38 months±7.54; 88.2% male) to a self-directed video-based parent intervention (n=22; mean=35.71 months±6.92; 72.7% male). Nearly 80 percent (77%) of participants were diagnosed with autism and the rest with an ASD. Mean IQ was 53.06±9.06 for the professionally led group and 52.86±6.53 for the video-based group. Exclusion criteria included being enrolled in early intervention, passing the Modified Checklist for Autism in Toddlers (M-CHAT), or receiving more than 20 hours/week of services. No information was provided about manualization.

In the professionally led group, parents attended a two-day group workshop and completed a series of 10 hour-long home visits, which occurred two times a week for 5 to 6 weeks. These visits focused on parental stress and child communication. In the video group, parents received an interactive instructional DVD called "Being Responsive: You and Your Child with Autism." They independently completed video lessons and accompanying worksheets. Followup assessments were conducted 3 months after treatment finished. All outcomes were based on parent report. Children in the professionally led arm showed significantly greater improvement in social communication than children in the video-based arm, regardless of baseline scores. Parents in the professionally led group also reported reduced child-related stress relative to parents in the video group, with fathers reporting more stress than mothers in both groups. Parents in the professionally led group with low baseline self-efficacy reported higher followup self-efficacy levels than parents in the video arm.[100]

The second good quality prospective cohort study was conducted in Italy and reported in two papers.[101, 102] It compared staff- and parent-led ABA-based intervention (n=24, 92% male; mean age=55.67±17.63 months) to eclectic community-based therapy (n=20, 95% male; mean age=41.94±13.07 months). Group assignments were not random and were based upon parental preference. Children were excluded based on the presence of major medical issues. In the parent training group, children alternated between one week (average of 25 hours) of therapist-led center-based intervention (discrete trial training, incidental teaching, natural environment teaching) and 3 weeks (average of 14 hours/week) of parent-led home intervention. Treatment focused on individual skills, problem behaviors, and facilitated play and social interactions. In the eclectic group, children received in-home developmental and cognitive behavioral treatments (approximately 12 hours/week) with minimal parent involvement. Treatment goals were based upon staff expertise and preferences.

Compared with the eclectic group, children in the parent training arm showed a significant decrease in ASD symptom severity and increases in language production and mental development. The parents of children in the eclectic group reported that their children showed improved socialization and motor skills, but this was not confirmed by behavioral observation. In the parent training group, older children achieved better adaptive behavior outcomes; younger children made more gains in early language comprehension and production. Children who gained more language comprehension had higher adaptive behavior scores pre-treatment. Pre-treatment language comprehension predicted post-treatment language production. In the eclectic group, higher pre-treatment mental development state and early language skills predicted better outcome on parent-reported adaptive behaviors. Initial higher adaptive behaviors predicted better post-treatment early language comprehension. In both groups, child outcomes on early language skills, mental developmental state, and adaptive behaviors were significantly influenced by self-reported parental stress, children's ability to respond correctly to prompts, the number and difficulty of treatment targets, and children's problem behaviors in sessions. Children who were perceived by their parents as more difficult had less improvement in ASD severity.[101, 102]

Two studies compared interventions focused on increasing parental responsivity. A good quality RCT from Europe (reported in two papers)[72, 105] compared treatment-as-usual + a manualized, communication-focused parent training (n=14, median age 48 months) to treatment-as-usual alone (n=14, median age=51 months) over 12 months. The intervention focused exclusively on parents and targeted increased parental response to child communication. The additional targeted treatment consisted of a recommended 30 minutes/day of parent-led intervention. Parents received monthly training for 6 months followed by training every 2 months for another 6 months. The intensity of treatment as usual alone was not reported but approaches consisted of speech pathology and ABA-based community treatments. The additional treatment group showed improvements in ASD symptoms, expressive language, and number of communicative acts during interactions with parents. Parents in the additional treatment group showed increased responsiveness to their children during videotaped interactions, which was correlated with reduced ASD symptom severity. No between-group differences were found in adaptive behavior or parenting stress. Greater language gains were seen in children who were younger with lower functioning levels at baseline.

A second fair quality RCT conducted in the United States also focused on enhancing parental responsivity and child communication.[93] It compared Hanen's More Than Words intervention to treatment-as-usual. The More Than Words group (n=29, mean age=21.11±2.71 months) received eight manualized group sessions with parents only and three in-home individualized parent-child sessions over a span of 3.5 months, whereas the control group (n=26, mean age=21.61±2.82 months) received no treatment or treatment as usual. There was no treatment effect on parental responsivity. The More Than Words group showed differential effects on child communication depending on children's baseline object interest; children with lower levels of baseline object interest had greater growth in communication skills, whereas children with higher levels of object interest showed attenuated growth.

A good quality RCT conducted in the United States compared the manualized Assessment Evaluation and Programming System for Infants (AEPS) with and without additional joint attention and social interaction opportunities.[103, 104] Both the AEPS group (n=24, mean age=28.6±2.6 months; mean intervention hours=205.66±18.63) and the control (n=24; mean age=28.8±2.8 months; mean intervention hours=196±21) received identical amounts of classroom-based treatment (10 hours/week), home-based parent training (1.5 hours/month), parent education (38 hours), and intervention methods. However, AEPS children received extra training in "interpersonal synchrony," targeting the three outcome variables of socially engaged imitation, initiation of joint attention, and shared positive affect. No significant ($p<.05$) differences emerged post-treatment on variables of interest. At the 6-month followup, the AEPS treatment group engaged in significantly more socially engaged interaction than controls ($p<.05$), with most of the growth in this skill occurring during the treatment period ($p<.05$) but not during followup ($p=.24$). No between-group differences were found for initiations of joint attention, shared positive affect, expressive language, or nonverbal problem solving. The AEPS group showed significant growth over time for all variables (p values<.01), but the control group only showed significant growth for expressive language ($p=.01$). Combined group analyses including

34 children from both the AEPS and control groups examined long-term outcomes an average of 37.6 months after the end of treatment (mean participant age=72.6±months). In this sample, cognitive skills and Vineland-II communication standard scores increased significantly from baseline (mean change 21.4±22.9, effect size=1.02, p<.001 and 12.7±19.4, effect size=0.81, p<.001, respectively), but there was no significant change in ASD symptom severity based on the ADOS.

A fair quality prospective cohort study[95] compared outcomes for four different types of intervention after 9 months of treatment: 1:1 home-based, manualized ABA (n=14, mean age=39±6.9 months); special education classroom enrollment (n=21, mean age=41.5±4.0 months); comparatively low-intensity, home-based, manualized behavioral intervention ("portage;" n=18, mean age 39.5±6.3 months), and 1:1 behavioral intervention ("local authority") that included an intensive introductory 5-day parent training component (n=13, mean age=40.2±6.3 months). The home-based ABA group received an average of 30.4 hours/week of intervention, 28.3 of which were 1:1. The special education group received an average of 12.7 hours/week (3.1 hours 1:1). The portage group received an average of 8.5 hours/week (6.5 1:1), and the local authority group received an average of 12.6 hours/week (12.2 1:1). Participants were not receiving any other teaching interventions during the study.

Post-treatment, mean cognitive and adaptive scores were not significantly different across groups. Children in the home-based ABA group showed significant improvements in educational outcomes as measured by the British Abilities Scale relative to other groups (p<.05). The authors created composite scores based on cognitive, adaptive, and educational functioning, but between-group comparisons only approached significance (p<.06). Baseline ASD severity and total intervention hours did modify effects of treatment significantly. First, baseline ASD severity was inversely related to composite change scores for all but the home-based ABA group and was positively related that group. That is, children with more severe ASD symptoms made more progress in ABA and less in the other intervention groups. Second, more intervention time was negatively related to composite change scores for children in ABA but not in the other groups. More hours of ABA were associated with less progress relative to school enrollment or other home-based interventions.[95]

One fair quality U.S. RCT (reported in two papers) compared parent-delivered ESDM to community-based treatment-as-usual.[98, 106] The ESDM group included 49 children (mean age 21.02±3.51 months, mean developmental quotient [DQ]=64.88±17.22); their parents completed 12 1-hour sessions that included manualized parent-training and coaching. Both the ESDM group and the community group (N=49; mean age=20.94±3.42 months, mean DQ=63.08±15.93) continued receiving community-based treatment-as-usual services as well, including the Developmental, Individual Difference, Relationship-based (DIR) model, TEACCH, ABA, and occupational and speech therapies (range of hours: 0-15.9), with the community group receiving significantly more intervention hours at the second time point (mean 3.68 vs. 1.48; p<.05). Compared with the ESDM group, children in the community-based arm had more severe social affect deficits, poorer imitation skills, and higher nonsocial orienting scores at baseline (p<.05). After treatment, both groups showed improvement in DQ and ADOS Social Affect scores with no main effects of group assignment. Both groups of parents showed significant increases in parent-child interaction behaviors, with greater increases in the ESDM group (effect size=.57) than the community-based group (.37).). Parents in the ESDM group reported significantly less parenting stress at followup (p=.04) but did not report more parenting competence. When examining combined groups, two key effects emerged. First, total intervention hours were associated with reduced restrictive and repetitive behavior and nonsocial orienting and improved DQ and vocabulary comprehension. Second, children younger than 24 months showed greater increases in DQ scores (effect size=-1.20, p=.002).

A fair quality RCT from Canada compared a DIR-based model, MEHRIT (Milton and Ethel Harris Research Initiative Treatment Program), (n=25; mean age=42.52 months, SD=8.76) to community care-as-usual (n=26; mean age=46.38 months, SD=8.29).[107] Data were collected 12 months into an ongoing 24-month treatment course. MEHRIT was administered by trained occupational therapists and speech-language pathologists who worked with participants' parents for two hours per week. Community intervention included no more than 15 hours per week of ABA, speech and occupational therapy, social skills groups, and alternative treatments (mean intervention hours: 3.9 per week). Post-treatment, the MEHRIT group showed significantly more initiation of joint attention (p<.001), involvement in activities (p<.01), and attention to activities (p<.05). They also showed more enjoyment in interaction, but this group difference was also present at baseline (p<.05). Both groups showed significantly improved language skills adjusted for developmental quotients, with no significant between-groups effects (effect sizes of .451 for MEHRIT and .915 for community treatment).

Another fair quality RCT from Asia examined DIR/Floortime (n=15) compared with center-based ABA (n=16).[92] Groups were stratified based on age (24-47 months, 28-72 months) and ASD severity, based upon CARS scores. Both groups continued to receive treatment-as-usual, including enrollment in preschool programs and community-based services (such as speech or behavioral therapies.) Relative to the center-based group, the DIR/Floortime group showed significant improvement on the Functional Emotional Assessment Scale (p<.05) and ASD symptoms as rated by the CARS (2.9 vs. .08, p<.01). Parents in the DIR/Floortime group also rated their children as showing significant improvements in emotional development (p<.01). A fourth fair quality RCT comparing parent training plus special education preschool to special education preschool alone reported no between-group differences on language development after 12 months of intervention, though language skills within both groups improved over time.[94]

Three poor quality studies, two European prospective cohort studies [97, 108] and a crossover RCT from China,[99] compared parent training to lower intensity supportive interventions. Mean ages ranged from 25.33-33.6 months. Both involved home visits and working with children and parents. A lower intensity treatment model, Autism-1-2-3, compared two groups that received the same series of 10 half-hour child- and parent-training sessions, with one group having a lagged start date and serving as a control. It did not yield group differences on ASD symptoms, language skills, or parent stress scores.[99] Another lower intensity model, the Barnet Early Autism Model (BEAM), incorporated aspects of ABA, TEACCH, PECS, and other occupational and speech-language interventions. It provided an average of 6.4 hours of home-based intervention per week over ten months. Participants were compared with a care-as-usual group and were not randomly assigned. Relative to the control group, BEAM recipients improved significantly more in adaptive behavior (p<.001) and receptive language (p<.05) but not IQ, with baseline levels of parenting stress negatively related to language and adaptive outcomes. [108] The Keyhole model incorporated elements of Hanen's More Than Words and the TEACCH programs. It compared 15 to 18 home visits over a 9 month period (n=35) targeting adaptive skills, ASD symptoms, and parent stress to a lower-intensity intervention model (n=26; 5 home visits, no additional services or supports). Compared with the lower-intensity group, children in the Keyhole intervention showed improved adaptive, imitation, and communication skills, based upon parent report. Mothers in in the Keyhole group also reported improved health but not stress.[97]

Table 7. Key outcomes of early intervention studies with parent training components

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Schreibman et al. 2013[109] US **G1:** Pivotal Response Training, 20/20 **G2:** PECS, 19/19 Quality: Good	**G1:** 29.5±6.9 **G2:** 28.9±4.2 NR	• Children in both G1 and G2 showed gains in language from baseline to followup 3 months after the end of treatment but no between group differences reported; effect sizes for change ranged from .001 to .486 • In the PECS group 12/19 children mastered requesting and were learning to comment using pictures • Mean number of spoken words gained across groups=80; individual progress varied widely , with 78% of children using at least 10 spoken words at final followup
Landa et al. 2012[103, 104] US **G1:** Assessment Evaluation and Programming System for Infants and Children (AEPS) curriculum+ additional joint attention and social interaction opportunities, 25/24 **G2:** AEPS curriculum, 25/24 Quality: Good	**G1:** 28.6±2.6 **G2:** 28.8±2.8 G1+G2: **60.1±11.9**	• Greater socially engaged imitation in G1 compared with G2 at end of intervention and at 6-month followup (effect size=0.86, p.01); growth occurred during intervention period vs. followup period • Initiations of joint attention did not differ significantly between groups at the 6-month followup, though each group improved over time • Measures of expressive language and nonverbal cognition did not differ between groups at the 6-month followup • At long-term followup of G1+G2 (n=34) at mean 37.6 months after end of intervention (mean age=72.6±17.5 months), IQ and Vineland communication scores increased from baseline (mean change 21.4±22.9, effect size=1.02, p<.001 and 12.7±19.4, effect size=0.81, p<.001, respectively) • No change in symptom severity (ADOS) at the long-term followup

Table 7. Key outcomes of early intervention studies with parent training components (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Strauss et al, 2012[101, 102] Italy **G1**: Staff & parent mediated early intervention, 24/24 **G2**: Eclectic, 20/20 Quality: Good	**G1**: 55.67±17.63 **G2**: 41.94±13.07 **G1**: 55.65±20.06 **G2**: 74.29±29.37	• Compared with G2, children in G1 showed significant decrease in ASD symptom severity, increases in language production and mental development • Compared with G1, children in G2 had improved parent-reported socialization and motor skills • In G1, older children achieved better adaptive behavior outcomes; younger children made more gains in early language comprehension and production. Children who gained more language comprehension had higher adaptive behavior scores pre-treatment. Pre-treatment language comprehension predicted post-treatment language production • In G2, higher pre-treatment mental development state and early language skills predicted better outcome on adaptive behaviors. Initial higher adaptive behaviors predicted better post-treatment early language comprehension • In both groups, child outcomes on early language skills, mental developmental state and adaptive behaviors were significantly influenced by parental stress, child ability to respond correctly to prompts, number and difficulty of treatment targets, and child problem behaviors in sessions. The predictive power of parental stress on outcome ASD severity was modified by perception of difficult child, with higher perceptions of difficulty associated with lower decreases in ASD severity
Aldred et al. 2011[72, 105] UK **G1:** Parent training in social communication intervention plus community intervention, 14/14 **G2:** Community intervention, 14/14 Quality: Good	**G1:** 51.4±11.8 **G2:** 50.9±16.3 NR	• G1 showed improvements in ADOS scores, social interaction, expressive language, child communication acts during interaction; no adaptive behavior differences or differences in parenting stress between groups • Language gains particularly prominent in younger, lower functioning children. • Increased parental synchrony (communication which maintained vs. redirected or controlled child responses) in G1 associated with reduction in child ADOS score (decreased impairment, p=.014); reduction in synchrony for G2 and small increase in mean ADOS scores. In tests of mediation, change in parental synchrony accounted for 34% of total treatment effect on ADOS outcome
Roberts et al. 2011[96] Australia **G1**: Individualized home-based program, 34/27 **G2**: Small group center-based program combined with parent training and support group, 33/29 G3: Waitlist, 28/28 Quality: Good	**G1**: 41.5 **G2**: 43.1 **G3:** 43.7 **G1**: 57±11.7 **G2**: 66±17.7 **G3:** 63.3±15.5	• Significant greater improvement in Reynell comprehension standard score for G2 compared with G1 (-7.3; 95% CI (-13.9, - 0.7), p=0.02); greater improvement for expression standard score of the Reynell for the G2 compared with G1 (-3.0; 95% CI (-9.0, 2.9), P=0.31) • Reynell standard comprehension and expression scores G3 performed better than G1, but not significantly • For the Reynell standard comprehension and expression scores G2 performed better than G3 but not significantly. • G3 improved significantly more than the G1 for the social scale of the Vineland • No statistically significant differences among the three groups for other child outcomes. When analyses were limited only to children with autism spectrum diagnoses, the magnitude of the effects increased but the presence or absence of statistical significance did not. • Parent outcomes: Parenting: statistically significant differences favoring G2 vs. G1 • No significant difference between groups for stress

Table 7. Key outcomes of early intervention studies with parent training components (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Keen et al. 2010[100] Australia **G1:** Professional parent intervention, 17 families/NR **G2:** Self-directed video based parent intervention, 22 families/NR Quality: Good	**G1:** 36.38±7.54 **G2:** 35.71±6.92 **G1:** 53.06±9.06 **G2:** 52.86±6.53	• G1 showed significantly greater improvement on social communication at followup than G2 regardless of values at baseline • Parents low in self-efficacy at baseline demonstrated relatively higher levels of self-efficacy if they received G1 vs. G2 • G1 reduced child-related stress relative to G2 for both mothers and fathers • Fathers reported higher levels of stress than mothers in both groups. • Behavior sample scores at followup not affected by group condition • All outcomes are based on parent report.
Casenhiser et al. 2013[107] Canada **G1:** MEHRIT (developmental individualized relationship-based intervention), 25/25 **G2:** Community-based treatment, 26/26 Quality: Fair	**G1:** 42.5±8.8 **G2:** 46.4±8.3 NR	• At pretreatment, G2 had higher scores on investigator-rated "enjoyment in interaction" domain of the modified Child Behavior Rating Scale; at followup, G1 improved significantly more compared with G2 on the domains of attention to activity, involvement, initiation of joint attention, and enjoyment in interaction (p values <.05, effect sizes 0.63-1.02); no significant difference in compliance domain • Both groups improved from baseline to followup on language developmental quotient measure but no significant between group difference • Greater baseline language skills, initiation of joint attention, and involvement were significant predictors of language change

Table 7. Key outcomes of early intervention studies with parent training components (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Rogers et al. 2012[98, 106] US **G1**: Parent-delivered Early Start Denver model (ESDM), 49/49 **G2**: Community treatment as usual, 49/49 Quality: Fair	**G1:** 21.02±3.51 **G2:** 20.94±3.42 **G1:** 64.88±17.22 **G2:** 63.08±15.93	• At followup, G1 received mean 1.48 hours treatment/week G2 received 3.68 (p<.05) • G2 had more severe social affect symptoms at baseline, poorer imitation and nonsocial orienting scores compared with G1 (p<.05) • No significant group differences on ADOS scores or measures of development at followup • Parent stress significantly lower in G1 vs. G2 (p=.04); numbers of intervention hours did not affect parent stress or sense of competence • Measures of parent acquisition of parent-child interaction skills did not differ between groups at followup • Social orienting and imitation skills were not found to be moderators of outcomes; increased hours of intervention and younger child age were significantly associated with improved developmental and vocabulary scores in a pooled analysis (p≤.05). In analyses by group, age and hours of intervention associated with improvements in vocabulary for G1 (p≤.05)
Reed et al. 2012[95] UK **G1:** ABA, 14 **G2:** Special nursery, 21 **G3:** Portage, 18 **G4:** Local authority-developed parent training, 13 Quality: Fair	**G1:** 39.0±6.9 **G2:** 41.5±4.0 **G3:** 39.5±6.3 **G4:** 40.2±6.3 **G1:** 55.1±17.3 **G2:** 52.2±17.1 **G3:** 54.0±15.4 **G4:** 51.7±14.5	• Scores on cognitive and adaptive measures were not significantly different among groups • Scores on British Abilities Scale improved for G1 vs. G2-G4 (p<.05) • Composite change scores (mean of change scores on cognitive, adaptive, and educational measures) were not statistically significantly different across groups, although G1 vs. G2-4 and G2 vs. G3-4 approached significance (p<.06) • Composite change scores were inversely related to initial ASD severity for G2-G4 but positively related for G1; the strength of that relationship only differed significantly between G1 and G3 (p<.05) • As time in intervention increased, composite scores improved for G2-G4 but worsened for G1 (p<.05). No differences were found in the amount of improvement between G2-4
Pajareya et al. 2011[92] Thailand **G1:** DIR/Floortime,16/15 **G2:** Usual care, 16/16 Quality: Fair	**G1:** 56.6±10.1 **G2:** 51.5±13.9 NR	• G1 improved significantly on the Functional Emotional Assessment Scale compared with G2 (p=.045) • CARS scores decreased (improved) for G1 vs. G2 (mean change 2.9 vs. 0.8, p=.004) • G1 scores on parent-rated measure of emotional development significantly improved compared with G2 (mean change 7.7 vs. 0.8, p=.007)
Carter et al. 2011[93] US **G1**: More than Words, 32/29 **G2**: Control, 30/26 Quality: Fair	**G1:** 21.11±2.71 **G2**: 21.51±2.82 NR	• No treatment effect on parental responsivity • G1 showed differential effects on child communication depending on a baseline child factor • Children with lower levels of baseline object interest exhibited facilitated growth in communication • Children with higher levels of object interest exhibited growth attenuation

Table 7. Key outcomes of early intervention studies with parent training components (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Oosterling et al. 2010[94] **G1:** Nonintensive parent training+specialized preschool, 40/36 **G2:** Specialized preschool, 35/31 Quality: Fair	**G1:** 35.2±5.5 **G2:** 33.3±6.4 **G1:** 58.4±16.8 **G2:** 58.0±16.9	• No between group differences on language development after 12 months of intervention, though language skills within groups improved over time • No differences in CGI-Improvement scores (G1: 57% much improved, G2: 52% much improved) • No significant effects on parenting skills in either group; engagement, early social communication precursors, parental skills not found to be mediators of effects. DQ not a significant moderator
Reed et al. 2011[108] UK **G1:** Barnet Early Autism Model (BEAM), 16/16 **G2:** Portage Treatment, 16/16 Quality: Poor	**G1:** 43.6±5.8 **G2:** 40.1±8.3 **G1:** 83.3±23.7 **G2:** 72.3±12.5	• Significant gains from baseline to followup for G1 vs. G2 in investigator-and parent-rated measures of adaptive behavior and language (p values<.05) • Greater reduction in parental stress and increase in satisfaction in G1 vs. G2 (p values <.01) • Lower parent stress at baseline correlated with gains in adaptive behavior and language (p values <.05)
Wong et al., 2010[99] China **G1**: Early intervention, 9/9 **G2**: Control, 8/8 Quality: Poor	**G1**: 25.33±6 **G2**: 27.88±5.57 **G1**: 17.85±4.16 **G2**: 17.91±4.49	• No significant group difference on communication, reciprocal social interaction or symbolic play • No between group differences on parent observation on language and relationship to people • No group difference on total parent stress scores
McConkey et al., 2010[97] UK **G1**: Keyhole early intervention program m, 36/35 **G2**: Control, 26/26 Quality: Poor	**G1**: 2.8 years **G2**: 3.4 years NR	• G1 showed significant improvements on different indices of communication than G2 • Mothers improved on measures of health G1 more than G2 but not of stress • Higher percentage of parents in G2 reported the children were improving on language and imitation at Time 1 compared with G1 percentages comparable at Time 2 • Only parents in G1 reported significant improvements from Time 1 to Time 2 on language, imitation and relating to others

ADOS = Autism Diagnostic Interview Schedule; CI = confidence interval; CGI = Clinical Global Impression; DQ = developmental quotient; EEG = electroencephalography; ESDM = Early Start Denver Model; G = group; IQ = intelligence quotient; N = number; NR = not reported; PDD-NOS = Pervasive Developmental Disorder-Not Otherwise Specified; PECS = Picture Exchange Communication System; SD = standard deviation

Social Skills Interventions

Key Points

- Thirteen behavioral studies examined different social skill interventions and included children and adolescents with ASD. Overall, the quality of the studies improved in comparison to the 2011 review. Two studies were rated as good quality, while 10 studies were fair quality, and one was poor.
- Most studies included school-aged children, without concomitant intellectual disability or language deficits. Most children had average cognitive skills (IQ>70).
- Most studies reported short-term gains in social skills and emotion recognition as reported by parents or within study measures. Maintenance and generalization of skills beyond the treatment context was addressed within the majority of the studies, but with variable results.
- The diversity of the intervention protocols and assessments utilized to measure outcomes continues to be a limiting factor for determining effectiveness of social skills interventions.

Overview of the Literature

In addition to the nine comparative studies assessing social skills included in the 2011 review, eight RCTs of fair[114-116] and poor[117-121] quality and one poor quality retrospective cohort[122]), 13 studies of good,[123, 124] fair,[117, 125-134]and poor[135] quality addressed interventions targeting social skills. Followup data for one study reported in the original review is included in this update.[117, 134] Studies addressed in the current review included a total of roughly 462 participants (mean/study=36). Seven RCTs were conducted in the United States,[117, 124-127, 129, 134, 136] one in Europe,[137] one in Japan,[135] and two in Australia.[123, 132] Two nonrandomized studies were also conducted in Australia.[131, 133] Participant ages across studies ranged from 4 to 13 years, and participants typically had high functioning ASD (IQ>70). Studies assessed group-based approaches including replications of studies evaluating the Skillstreaming model;[126, 127, 129, 136] the Children's Friendship Training model; [117, 134] a Japanese pilot RCT of the Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) model;[135] incorporated peer-mediated components;[124, 125, 138] and targeted emotion recognition in children with ASD.[123, 128, 132, 133]

Detailed Analysis

Four fair quality RCTs conducted in the United States addressed group-based social skills approaches.[126, 127, 129, 136] Among these, three studies evaluated the manualized Skillstreaming model (Table 8).[127, 129, 136] The studies included between 13 and 52 total participants, all of whom were considered to be high-functioning, and most of whom were male. One RCT compared a manualized performance-based approach, Sociodramatic Affective Relational Intervention, versus the knowledge-based Skillstreaming social skills intervention, which emphasizes social skills, face-emotion recognition, interest expansion, and interpretation of non-literal language. The study included 13 boys with ASD between the ages of 9 and 12. Weekly 90-minute sessions treatment sessions were held over 4 weeks after school. Treatment sessions, regardless of the intervention, included content covering considering others, emotions, consolidating, and generalization of skills. Participants in both groups increased in reciprocal friendship nominations (p=.027) and staff-reported social skills (effect size=0.59, p=.002). Participants in the sociodramatic group interacted more with each and rated one another more favorably after one session, which slightly decreased over time (effect size=0.70, p=.001). Skillstreaming participants also demonstrated gains in interactions and more favorable ratings over the course of the intervention, but at a slower rate as compared with the sociodramatic group (effect size=0.37, p=.001). No significant differences in parent report of social functioning were demonstrated for either group.[129]

A second RCT[127] examined the short-term outcome of a 5-week trial of the Skillstreaming approach and replicates the intervention reported in a study[115] described in our 2011 review. The study included 36 children (mean age=9.47), primarily male (94% of the total sample) with high functioning ASD (mean IQ=103) randomized either to Skillstreaming or a wait-list control group. Participants in the treatment group showed significant improvements in most parent-rated measures of social skills compared with the control group (Social Responsiveness Scale: effect size=0.625, p=.003; Adapted Skillstreaming Checklist: effect size=0.584, p=.006; Behavioral Assessment System for Children (BASC)-Withdrawal scale: effect size=1.055, p<.001); however, group differences on the BASC-Social Skills scale were not significant. Staff-report measures found similar outcomes, with significant improvements in ASD symptomology and program-targeted social skills, as well as a decrease in withdrawn behaviors in the treatment group compared with the control arm (effect sizes ranging from 0.69 to 1.4, p values ≤.007). Child-rated measures similarly improved in the Skillstreaming group compared with control (Skillstreaming Knowledge Assessment: effect size=1.272, p<.001; understanding of idioms: effect size=0.390, p<.001).[127]

Another RCT replicating the Skillstreaming model reported by Lopata et al.[127] included 35 children with high functioning ASD between the ages of 7 and 12.[136] Skillstreaming involved five 70-minute sessions treatment sessions per weekday over 5 weeks. Treatment sessions involved skill instruction (nonliteral language and face-emotion recognition) and practice as well as a behavioral system to encourage participation and decrease problem behaviors. Weekly 90-minute parent trainings were also conducted, which involved education on ASD as well as training on the treatment program. Scores on the parent-rated Skillstreaming Checklist, Social Responsiveness Scale, and Behavior Assessment System for Children-2 Withdrawal scales improved for the Skillstreaming group compared with the control (effect sizes 0.85, 0.67, 0.70 respectively, all p<.01). Child-rated measures also improved for the treatment group compared with control (Skillstreaming Knowledge Assessment effect size 1.15; language assessment=0.34, p<.001). No group differences were found in face-emotion recognition. Maintenance of effects on the Skillstreaming Knowledge Assessment and BASC Social Skills scale for the treatment group was demonstrated 2 to 3 months post-treatment (effect sizes 0.47 to 0.68).[136]

Another RCT examined the short-term outcome of a trial of a manualized outpatient 15-week social skills program, the Social Skills Group Intervention – High Functioning Autism (SS GRIN-HFA).[126] The study included 55 children, primarily male (98% of the total sample) with IQ>85 randomized either to SS GRIN-HFA group (mean age 10.2 years) or to a traditional SS GRIN group (mean age 9.9). Participants in the SS GRIN-HFA group showed significant improvement in social skills, with significantly better scores than the control arm on all Social Responsiveness Scale domains except social cognition (effects sizes ranging from -0.67 to -0.94). In addition, parents of children in the treatment group reported significant improvement in the areas of their child's social awareness, motivation for social interaction, social communication skills, and unusual mannerisms associated with ASD. No significant difference was found between the treatment group and control group regarding child self-report of self-efficacy or loneliness.

A final RCT examined followup of the Children's Friendship Training (CFT) manualized program.[117, 134] In the initial report included in the 2011 review, [117] 76 children with ASD enrolled in second to fifth grades were randomly assigned to the treatment group (n= 40) or the delayed treatment group (n=36). Weekly 60-minute treatment sessions were held over 12-weeks, with parent and child training occurring concurrently in separate locations. Skills targeted as part of the treatment included conversational skills, peer entry skills, developing friendship networks, good sportsmanship, host behavior during play dates, and handling teasing.
Participants in the treatment group demonstrated modest gains in the number of hosted play dates ($p<.001$) as well as a decrease in electronics-use during play dates ($p<.001$). Participants in the treatment group also demonstrated less disengaged behavior ($p < .001$), internalizing behavior ($p<.001$), and less conflict during play dates ($p =.069$). In a followup analysis,[134] 24 participants from the initial study were followed to examine maintenance of skills. At long-term follow-up 1 to 5 years post-participation in the training, participants continued to demonstrate increased social opportunities through invited play dates, maintenance of friendships, and decreases in loneliness from baseline ($p<.05$). Participants also demonstrated maintenance of gains in overall social skills along with reduction of problem behaviors ($p<.05$).

One Japanese pilot RCT[135] examined the Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH)-based manualized group social skills training. The study included 11 children (mean age=64 months) with High Functioning Autism (HFA) (IQ >75) and their mothers, who were randomly assigned to the TEACCH program (n=5) or a wait-list control group (n=6). The treatment group consisted of weekly 2-hour sessions, with 20 sessions over 6 months. The control group consisted of group meetings with the mothers on a bi-monthly basis, consisting of 30-60 minute meetings with two social workers. Participants in the treatment group showed moderate improvement in adaptive behaviors and social reciprocity of the children, parenting stress, and parent–child interactions compared with the control group.

Two RCTs[124, 125] and one nonrandomized controlled trial[138] assessed interventions targeting social skills and incorporating typically developing peers or siblings. Studies included 21 to 60 participants, generally with high functioning ASD. One RCT examined short-term outcomes of a trial of an outpatient peer tutor social skills training program.[124] The study included 44 children (mean age=9 years, IQ>70) who met criteria for a pervasive developmental disorder. Sixteen out of 23 participants in the treatment group were considered treatment responders as rated by their parents, compared with 0/18 in the control arm ($p\leq.001$). Children with Asperger syndrome were more likely to be responders compared with children with PDD-NOS ($p=.03$); IQ was not associated with response status. No significant differences were found between the treatment group and wait list group on social competence measures.

A second fair quality RCT evaluated child-directed social skills training (CHILD) compared with peer-mediated social skills training (PEER) applied to children with high-functioning autism attending regular education classrooms.[125] The study included 60 children (mean age=8.14, mean IQ=90.7) randomized to one of four treatment groups (n=15/group): 1) CHILD group 2) PEER group 3) CHILD+PEER and 4) a control group. Treatment occurred over 6 weeks. In the CHILD condition, it included 1:1 training and practice in social skills targeting deficits identified for each child. In the PEER arm, it included peer interaction focused on positive social modeling. Participants who received PEER interventions (PEER alone or PEER+CHILD) showed significant improvements in social network salience (prominence of a child within the classroom social network) compared with the other groups ($p\leq.006$). At the final followup 12 weeks after the end of the intervention, salience remained higher for the

CHILD+PEER arm compared with CHILD alone and the control group but not compared with PEER alone. Teacher ratings of social skills also improved from baseline to final followup for the peer-mediated group as did measures of solitary engagement and joint attention.

One fair quality, non-randomized trial examined the effectiveness of including siblings in social skills training groups for boys with Asperger's Syndrome.[131] The study included 21 children with Asperger syndrome between the ages of 8 and 12. Investigators partially randomized participants to one of three treatment groups (first 15 randomly assigned to one of three groups; later recruits assigned based on whether they had an older sibling; if no sibling, participants were randomly assigned to "no sibling" training or wait-list control group). Eight weekly 2-hour sessions treatment sessions were held in a clinical setting. Treatment sessions included content covering nonverbal social cues, such as eye contact, body language, tone of voice, and facial expression. Techniques included extended time, repeated practice, conceptual explanations, role play, and use of social dilemmas. Participants were also assigned a different partner each week to encourage social interaction and cooperation. Sibling participants were not given any specific training or instruction other than what was provided as part of the treatment sessions. Homework tasks were given to facilitate generalization. Participants in the active treatment groups demonstrated significant improvement in identification of nonverbal cues to identify emotions compared with the waitlist control group (effect size=0.47, $p<.001$). While the ability to identify social cues was maintained by the participants in the active treatment groups, no increase in skills was demonstrated at 3-months post-intervention. Parents in all groups rated socials skills for both children with ASD and siblings as improved over time (effect size=0.55, $p<.001$). No difference in teacher report of social skills for target participants or siblings was demonstrated.

Three RCTs, one of good and two of fair quality, addressed interventions targeting emotion recognition in children with ASD.[123, 128, 132] Two studies used specialized DVDs to demonstrate emotions and one used a manualized, group-based intervention focused on Theory of Mind training, which includes recognizing emotions, understanding differences between fantasy and reality, perspective taking, and reasoning about other people's mental states. Two RCTs conducted in Australia (one good quality[123] and one fair[132]) assessed the outcome of The Transporters DVD series as an intervention for emotion recognition. The first RCT examined changes in emotion recognition and generalization of newly acquired skills to improvements in social perception skills over a 3-month period. The study included 55 children with ASD between the ages of 4 and 7 randomly assigned to view either the Transporters DVD series or the control DVD series (Thomas the Tank Engine) for four weeks (15 minutes per day in their home setting). Parents were also provided with a diary to record the number of hours watched per day. Compared with control participants, participants in the treatment group improved in emotion identification and matching of emotions (anger only) immediately following the intervention, with improvements maintained 3-months post-intervention. Gains were also seen in the treatment group 3-months post-intervention for identification of happiness and emotion recognition within situations. In both groups, no difference was found in affect recognition, theory of mind, or social skills immediately following the intervention or at the maintenance phase. Long-term improvements in identification of happiness expressions were associated with greater ADOS severity, as was matching of emotions overall and of sadness specifically. Age was correlated with identification of fear expressions, affect recognition, and the mind reading desire-based task. Verbal IQ was also associated with some short term improvements.[123]

A second, 3-week RCT comparing The Transporters DVD with the control series included 25 children with PDD between the ages of 4 and 8. Parents were also provided with a user guide to facilitate their child's participation in watching the episodes as well as logbook to record the number of sessions watched per day. Participants in the treatment group improved on standardized measures of emotion and facial recognition (effect sizes range 0.48-0.92, $p<.001$), while both groups improved on social peer interest (effect size=0.24, $p=.01$) and eye contact (effect size=0.44, $p<.001$). In both groups, no difference was found in gaze aversion or stereotyped behavior. This study provided little information on the demographics of the participants. This study also did not provide information on the user guide, which may be a confounding variable to the obtained findings. The authors also refer to Nonverbal IQ in one of their tables, but only administered the Block Design subtest, which does not fully measure all aspects of nonverbal IQ.[132]

A fair-quality study examined the short-term outcome of a trial of a manualized Theory of Mind training program.[128] The study included 40 children (mean age=10 years) with a diagnosis of high functioning ASD and cognitive abilities within the average range (mean IQ=100.1 in the treatment group and 103.3 in the control group). The participants were randomized either to a 16-week Theory of Mind training group or a wait list control group. Participants in the treatment group improved on their conceptual theory of mind skills compared with the control group (awareness of multiple emotions, effect size=0.84, $p<.05$; complex emotions, effect size=1.19, $p<.01$), but no significant differences were found between groups on elementary theory of mind understanding, self-reported emphatic skills, or parent-reported social behavior.

An additional study examined the short-term outcome of a trial of a pictorial system called thought bubble training on Theory of Mind tasks, including difficulty with false belief tests.[133] The study included 24 children (mean age=7 years) with a diagnosis of ASD. The participants were not randomized into the thought bubble intervention group (n=17) or control group (n=7) based on standardized means, but rather on preference by school staff. The two groups were comparable in terms of chronological age, verbal intelligence, semantic language skill, syntactic language ability, and nonverbal intelligence. In addition, a within-group rather than between-group statistical analysis was utilized. Within-group analyses indicated that the children in the thought bubble intervention group showed significantly higher post-training test scores on all Theory of Mind variables. These post-test gains were also maintained at three-week followup. In contrast, the children in the control group did not show any significant improvements in their pre- and post-test scores on Theory of Mind variables, nor did they show any improvements at followup. Seven children in the thought bubble intervention group and one child in the control group were not available at followup.

Table 8. Summary of outcomes of social skills studies

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
Group-based Social Skills Approaches		
Lerner et al. 2012[129] US **G1:** Sociodramatic Affective Relational Intervention (SDARI), 7/7 **G2:** Skillstreaming, 6/6 Quality: Fair	**G1:** 10.86±1.68 **G2:** 11.33±1.63 NR	• Study included only boys with high functioning ASD, 69% diagnosed with Asperger syndrome • Compared with G2, G1 participants decreased in both positive and negative interactions over time (effect size=-1.17) • G2 participants increased in social preference (effect size=0.37); both groups increased in number of reciprocated friendship nominations (effect size=0.31, p=.048) and in interventionist-rated social skills (effect size=0.59, p=.002) • No significant effects on parent-rated measures
Thomeer et al. 2012[136] US **G1:** Skillstreaming, 17/17 **G2:** Wait list control, 18/18 Quality: Fair	**G1:** 9.24±1.64 **G2:** 9.39±1.91 **G1:** 104.26±14.13 **G2:** 103.42±13.26	• Study replicates Lopata 2010[127] and included children with high functioning ASD (71% Asperger syndrome, mean IQ G1+G2=103.83±13.49) • G1 scores on parent-rated Skillstreaming Checklist, Social Responsiveness Scale, and Behavior Assessment System for Children-2 Withdrawal scales improved compared with G2 (effect sizes 0.85, 0.67, 0.70 respectively, all p<.01) • G1 scores on child-rated Skillstreaming Knowledge Assessment and language measure improved compared with G2 (effect sizes 1.15, 0.34 respectively, p<.001) • G1 improved from baseline to followup 2-3 months post-intervention on the Skillstreaming Checklist (effect size=0.47, p=.006) and Behavior Assessment System for Children Social Skills scale (effect size=0.68, p=.004)
Lopata et al. 2010[127] US **G1:** Skillstreaming, 18/18 **G2:** Wait list control, 18/18 Quality: Fair	**G1:** 9.39±1.72 **G2:** 9.56±1.54 **G1:** 101.63±13.75 **G2:** 104.45±15.46	• Study replicates intervention reported in earlier studies (Lopata 2006, 2008[115]) and included children with high functioning ASD, 78% with Asperger syndrome, 94% male • Most scores on parent-rated measures were improved for G1 vs. G2 (Social Responsiveness Scale effect size=0.625, p=.003; Adapted Skillstreaming Checklist effect size=0.584, p=.006; Behavioral Assessment System for Children (BASC)-Withdrawal effect size=1.055, p<.001). Differences on the BASC-Social Skills measure were not significant • Staff-rated measures were significantly improved for G1 vs. G2 (Social Responsiveness Scale effect size=0.711; BASC Withdrawal and Social Skills effect sizes ranging from 0.69 to 0.78, p≤.007; Adapted Skillstreaming Checklist effect size=1.421, p<.001 • Most child measures improved significantly for G1 vs. G2 (Skillstreaming Knowledge Assessment effect size=1.272, p<.001; understanding of idioms effect size=0.390, p<.001). Child Faces scores were not significantly different
DeRosier et al. 2010[126] US **G1:** Social Skills Group Intervention-High Functioning Autism (S.S.GRIN-HFA), 27/24 **G2:** Traditional S.S.GRIN, 28/28 Quality: Fair	**G1:** 10.2±1.3 **G2:** 9.9±1.1 NR	• Study included participants with high functioning ASD, 98% male • G1 improved significantly compared with G2 on all Social Responsiveness Scale domains except cognition (p≤.05, effect sizes ranged from -0.67 to -0.94) and on the Achieved Learning Questionnaire (effect size=0.75, p<.05) • Child reported measures of self-efficacy and loneliness did not differ by group

Table 8. Summary of outcomes of social skills studies (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
Group-based Social Skills Approaches		
Mandelberg et al., 2013 [117, 134] US **G1:** Children's Friendship Training, 35/24 (at mean 43 month followup) G2: Control, 33/31 (at 12 week followup) Quality: Fair	At 43 month Followup **G1:** 12.6 **G1:** 104.1±17.8	• After 12 weeks treatment, parents of G1 reported that their children hosted significantly more play dates after treatment relative to G2 (p<0.0001), but were not invited to significantly more play dates • Parents reported that G1 spent less time engaged in minimally socially interactive activities during play dates compared with G2 (p<0.001), but did not spend significantly more time in socially interactive activities (such as talking) • Parents of G1 reported increased self-control in children (p<0.05) when provoked by others. No changes reported by teachers • G1 showed significant decreases in loneliness (p<0.025) and increases in popularity (p<0.025) following treatment relative to G2 • At long-term followup of G1, children with ASD demonstrated increased social opportunities for invited play dates and maintained at least one close friendship • Child report of loneliness also decreased in the long-term followup • Overall ratings of social skills continue to demonstrate gains along with reduction of problems behaviors over time
Ichikawa et al. 2013 [135] Japan **G1:** TEACCH, 5/5 **G2:** Wait list control, 6/6 Quality: Poor	**G1:** 64 months **G2:** 62 months DQ (Kyoto Scale of Psychological Development): **G1:** 87 **G2:** 88	• Pilot study of Japanese participants with high functioning ASD and their mothers • G1 showed moderate improvement with regard to the children's adaptive behaviors, social reciprocity, parenting stress, and parent–child interactions
Peer Approaches		
Koenig et al. 2010[124] US **G1:** Peer tutor social skills training, 25/23 **G2:** Wait list control, 19/18 Quality: Good	**G1:** 9.2±1.2 **G2:** 9.3±1.2 **G1:** 96.4±20.5 **G2:** 95.9±17.3	• Study included high functioning children with ASD (IQ≥70) • 16/23 G1 participants and 0/18 G2 were considered treatment responders (much improved or very much improved on CGI-I), p=.001 • Children with Asperger syndrome more likely to be responders vs. children with PDD-NOS, p=.03; no differences between those with autism and Asperger syndrome or PDD-NOS • IQ not associated with response status • No significant differences at followup within groups or between groups on social competence measures

Table 8. Summary of outcomes of social skills studies (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
Peer Approaches		
Kasari et al. 2012[125] US **G1:** Individualized child-directed social skills training (CHILD), 15/14 **G2:** Peer-mediated social skills training (PEER), 15/15 **G3:** CHILD+PEER, 15/15 **G4:** Control, 15/15 Quality: Fair	**G1:** 8.23±1.48 **G2:** 7.60±1.35 **G3:** 8.67±1.68 **G4:** 8.07±1.69 **G1:** 93.93±19.60 **G2:** 84.80±10.12 **G3:** 90.33±14.17 **G4:** 95.07±19.44	• Study included high functioning children with ASD attending regular education classrooms for ≥80% of day, overall mean IQ=90.97±16.33; significantly more females in G2 compared with other groups, p=.004 • Social network salience increased for G2 and G3 compared with other groups, effect sizes for G2 ranged from 1.12 to 1.18 vs. G1 and G4 (p≤.006) at end of intervention; at followup 12 weeks post-intervention, salience significantly higher for G3 compared with G1 and G4 but not G2 • Solitary engagement on playground and joint attention improved at final followup for G2 • Teacher ratings of social skills improved from baseline for G2 (p=.01) but not G1, G3, or G4. No significant differences for any group at final followup
Castorina et al. 2011[131] Australia **G1:** Social skills training with sibling, 7/7 **G2:** Social skills training without sibling, 8/8 **G3:** Wait list control, 6/6 Quality: Fair	**G1+G2+G3:** 10.30±1.15 NR	• Study included only boys with Asperger syndrome • In post-hoc comparisons, both G1and G2 had significantly higher Child and Adolescent Social Perception measure scores than G3 at followup (p≤.003); differences between G1 and G2 were not significant • Ability to read social cues improved in G1 and G2 from baseline to end of intervention • No significant difference between groups on parent or teacher rated social skills measures (Social Skills Rating System)
Emotion Recognition Approaches		
Williams et al. 2012[123] Australia **G1:** Emotion recognition training (Transporters DVD), 29/21 **G2:** Control (Thomas the Tank Engine DVD), 31/25 Quality: Good	**G1:** 62.83 months±11.17 **G2:** 61.93 months±9.91 **G1:** 77.93±13.96 **G2:** 74.56±13.58	• G1 improved in identification of expressions of anger (p=.01), overall emotion identification (p=.00) and identification of anger (p=.03) compared with G2 from baseline to end of intervention; Vineland socialization, theory of mind task scores, and affect recognition scores did not differ significantly between groups • Compared with G2, G1 improved on identification of happy facial expressions (p=.02) and mindreading situational task scores 3-months post-intervention; scores on identifying expressions of anger and on the theory of mind contextual task decreased for G1 vs. G2 (p≤ .02) • Long term improvements in identification of happiness expressions associated with greater ADOS severity. Age was correlated with identification of fear expressions, affect recognition. Verbal IQ was associated with some short term improvements
Young et al. 2011[132] Australia **G1:** Emotion recognition training (Transporters DVD), 13/13 **G2:** Control (Thomas the Tank Engine DVD), 12/12 Quality: Fair	**G1+G2 (range):** 4-8 years **G1:** 11.31 (4.17) **G2:** 8.67 (4.05)	• Videos provided to groups differed in level of emphasis on emotion recognition • Affect recognition improved significantly in G1 vs. G2 (effect size=0.53, p<.001) as did Faces task scores (effect size=0.31, p=.005) • Both groups improved significantly on measures of social peer interest and eye contact; between group differences were not significant • Improvements in G1 were associated with extent of attention to faces in the DVD in G1 (r=0.59, p=.036) but not in G2; IQ was not correlated with improvements in either group

Table 8. Summary of outcomes of social skills studies (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
Emotion Recognition Approaches		
Begeer et al. 2010[128] Amsterdam **G1:** Theory of Mind training, 20/19 **G2:** Wait list control, 20/17 Quality: Fair	**G1:** 10.3±1.3 **G2:** 10.3±1.1 **G1:** 100.1 (15.3) **G2:** 103.3 (12.9)	• Study included children with high functioning ASD: 28% diagnosed with Asperger syndrome,67% with PDD-NOS • G1 improved on overall Theory of Mind test vs. G2 (effect size=0.75, p<.03) and on elementary theory of mind tasks (effect size=1.00, p<.01) but not on theory of mind precursors (e.g., perception, emotion recognition) • Significant improvements for G1 vs. G2 on some emotional awareness measures (multiple emotions, effect size=0.84, p<.05); complex emotions, effect size=1.19, p<.01) • No effects on self-reported empathy or parent-reported social skills
Paynter et al. 2013[133] Australia **G1:** Thought bubble intervention 17/9 **G2:** Control 9/6 Quality: Fair	**G1:** 79.41±20.20 months **G2:** 94.86±28.69 months NR	• Within-subjects rather than between-subjects statistical design • G1 showed within-group significant improvements on trained false-belief concept, generalization false belief test, and developmental Theory of Mind Scale following thought bubble training. G2 did not show any significant improvement pre- and post- test on Theory of Mind variables • Improvements were maintained at 3-week followup in G1; no significant improvements in G2 • Seven children in the thought bubble intervention group and 1 child in the control group were not available at followup

ADOS = Autism Diagnostic Observation Schedule; ASD = autism spectrum disorder; G = group; N = number; PDD-NOS = Pervasive Developmental Disorder-Not Otherwise Specified; SD = standard deviation

Play/Interaction-Based Interventions

Key Points

- Twelve studies addressed interaction-based approaches: three good and eight fair quality RCTs and one poor quality prospective cohort.
- Studies of interventions targeting joint attention and delivered by teachers, parents, and interventionists reported gains in joint attention skills in treatment groups compared with controls typically over a short duration (8 to 16 weeks). Children in both treatment and comparison groups, typically received early intervention in addition to the targeted intervention.
- One small, poor quality study of an intervention targeting pretend play showed an increase in play dialog in both groups, with a greater increase in the intervention group.
- Studies targeting parental responsiveness to child communication reported increases in responsive parent behaviors in the treatment arms and limited increases in child communication.

Overview of the Literature

In addition to seven (reported in nine publications) comparative studies (two RCTs of fair[139-141] and five of poor[142-147] quality) addressing play- or interaction-based approaches described fully in the 2011 review, we identified 12 studies (reported in 16 papers) evaluating such interventions for the current review (Table 9). Among these 12 studies, one includes a population addressed in the 2011 review.[140, 141, 148, 149] We considered three studies in the current review to be of good quality,[150-153] eight of fair quality,[140, 141, 148, 149, 154-160] and one of poor quality.[161] Studies were conducted in the United States[140, 141, 148-154, 156-158, 160, 161] and Europe[155, 159] and included a total of 383 participants between the ages of 21 and 82 months. Intervention duration ranged from 6 to 16 weeks; three studies reported long term (≥12 months post-intervention) followup of participants.[140, 141, 148-150, 156] While all studies used approaches incorporating focused interactions directed by teachers or interventionists[140, 141, 148, 149, 151-153, 155, 157-159, 161] or parents/caregivers,[150, 154, 160, 162] studies typically addressed outcomes related to joint attention, pretend play, imitation, or child/parent communication.

Detailed Analysis

Studies Addressing Joint Attention Outcomes

A fair quality pilot RCT evaluating a teacher-implemented joint attention intervention randomized child-teacher dyads in public preschools to either intervention (n=9 children, mean child age=46 ±5 months, mean mental age=30.3 ±5.01 months) or wait list control (n=7, mean age=43.01±6 months, mean mental age=33.8±8.74 months).[157] The manualized JASP/ER (Joint Attention and Symbolic Play/Engagement and Regulation) intervention trained teachers in eleven key strategies including setting up the environment, following the child's lead, imitating the child's play action, contingent language, and modeling joint attention. Teachers received a 1-hour training workshop and 1-hour of individual training with the child from a JASP/ER interventionist per week. Interventionists also instructed teachers to use JASP/ER strategies daily. At the 5-week followup, children in the intervention group improved in total initiations of joint attention and in pointing compared with the control arm ($p<.005$) and in showing ($p<.01$) in classroom observations (large effect sizes for each measure, 1.85 to 2.02). Groups did not differ on measures of looking or giving. Most scores on the Early Social Communication Scales joint attention measures and frequency of joint attention initiations in videotaped interactions did not differ significantly between groups. Object engagement declined and supported engagement improved in the treatment group compared with control (large effect sizes, d=1.24 to 1.41, $p\leq.05$). Observations of teachers also demonstrated increased use of JASP/ER strategies in the treatment arm.

In another good quality pilot RCT of JASP/ER, investigators randomized minimally verbal (<10 spontaneous functional communicative words) preschoolers enrolled in intensive ABA-based interventions for at least 12 months to either JASP/ER or control (standard intensive preschool, n=8, mean age=54.68±10.25, mean mental age=13.91±3.85).[151] Treatment group participants (n=7, mean age=48.73±11.68 months, mean mental age=17.21±3.91 months) received 1-hour of JASP/ER training per week in addition to the intensive preschool. At the 3-month followup, the JASP/ER group increased in play types and decreased time unengaged significantly from baseline ($p=.04$). Changes were not significant for the control group. The JASP/ER group also spent less time disengaged during class observations compared with the control group (effect size=1.63, $p=.05$), initiated more requesting gestures (effect size=1.51, $p=.01$) and evidenced more diversity of spontaneous play (effect size=0.81, $p=.04$). Groups did not differ on Early Social Communication Scales variables related to joint attention.

Another fair quality RCT[155] conducted in 59 Norwegian preschools over 8 weeks evaluated a manualized adaptation of a joint attention intervention reported below.[140, 141, 148, 149] Children in the intervention group (n=34, mean age=47.6±8.30 months, DQ=53.3±19.2) attended regular or specialized ASD preschools and also received up to 80 sessions (20 minutes twice daily, 5 days/week) of intervention focused on promoting joint attention and engagement within play activities. Children in the control group (n=27, age=50.3±8.3 months, DQ=59.9±19.7) also attended regular or specialized preschools. Groups did not differ in number of preschool hours or 1:1 training or support. The control group had greater expressive language age at baseline compared with the treatment group (mean 24.9±12.8 vs. 18.8±10.5, p=.047). At the 8-week followup, frequency of joint attention skills during teacher-child play were significantly better in the treatment group compared with control (effect size=0.44) but the duration of joint engagement did not differ between groups. Duration of joint engagement was greater in mother-child play in the treatment group vs. control (mean 12.2% longer duration of joint engagement, effect size=0.67). Although initiation of joint attention skills increased in the treatment group, group differences were not significant, thus effects on joint attention seen with teachers did not generalize. Frequency of joint attention initiation as measured on the Early Social Communication Scales did not differ between groups. Adjusting analyses to account for expressive language differences did not change results. Further, investigators found no putative moderators (age, DQ, language age, program philosophy) to be significant, suggesting that the intervention may be applicable across developmental levels.[155]

Another fair quality RCT comparing joint attention and symbolic play interventions delivered via an interventionist included 58 children with ASD between 3 and 4 years of age. Investigators assessed language development, joint attention and play skills, and mother-child interactions at pre- and post-intervention and 6 and 12 months after the end of the 5 to 6 week intervention.[140, 141, 148, 149] Children in both groups showed significantly greater growth in expressive language, initiation of joint attention, and duration of child-initiated joint attention over time than did participants in the control group (p<.01 to <.05, moderate to large effect sizes). Growth in receptive language was not significantly affected by the intervention from pre-intervention to 12 months post-intervention. Children in the symbolic play group also showed significantly more growth in play level than did children in either the joint attention (p<.01) or control (p<.001) groups.

In a subsequent report on 52 of the 58 RCT participants assessing joint attention quality, both the joint attention and symbolic play groups improved in shared positive affect during joint attention and in shared positive affect with utterances during joint attention at 6 and 12 months post-intervention (p<.05) but not at intervention exit.[149] Differences between groups at the 6 and 12 month time points were not significant. The control group generally declined in instances of shared affect over the followup time points. Forty of the 58 participants in the RCT also participated in followup 5 years post-intervention.[148] Fifteen of 20 children in the joint attention group, 14 of 21 in the symbolic play group, and 11 of 17 in the control returned at 5 years; mean age across groups was 8 years and 8 months. Of the 40 participants, five were enrolled in regular education, 17 in regular education with some special education support, and 18 were in special education classrooms; placement did not differ among groups. At followup, 5/15 participants in the joint attention group, 1/14 in the symbolic play group, and 2/11 in the control arm were considered non-spectrum. Thirty-two of the 40 participants achieved valid scores on language assessments at followup. Ability to use spoken language at followup ("passing" the language assessments) was predicted by children's average play level at baseline (p<.01). Number of functional play types at baseline predicted greater cognitive skills. Age at baseline, initiation of joint attention, play level and treatment group assignment predicted subsequent vocabulary ability (all p<.03); these factors together explained 64 percent of spoken language variability.

In a fair quality RCT of a joint attention intervention adapted from this study[140, 141, 148, 149]investigators randomized 38 caregiver/child dyads to either immediate, parent-mediated treatment (n=19) or a wait list control group (n=19).[150] The 8-week treatment included individualized, developmentally appropriate play routines to promote parents' following of their children's interests and activities. Children in both groups ranged in age from 21 to 36 months (mean=30.82 months, mean mental age=19.2 months). At the end of intervention, children in the treatment group demonstrated less object-focused play, more responsiveness to joint attention, more functional play acts, and more joint engagement than children in the control group ($p<.05$). Groups did not differ in initiations of joint attention, diversity of symbolic play, or unengaged actions. At followup of the treatment group 12 months after the end of intervention, results suggested maintenance of gains in joint engagement, response to joint attention, and reduction of object engagement, but changes in scores were not significant. Types of functional play acts improved in the treatment group at the 12-month followup ($p<.01$). In analyses of potential predictors of outcome, greater caregiver quality of involvement (rated by investigators) predicted increased joint engagement ($p<.05$) but not other play skills or engagement outcomes. Parent-rated adherence or competence did not predict changes in any outcome. Number of hours of other intervention similarly did not predict any outcomes.

A fair quality RCT of a classroom-based joint attention or symbolic play intervention based on the manualized approaches in other studies reported above[140, 141] randomized 14 special education teachers to either a symbolic play followed by a joint attention intervention (n=10 children, mean age=54.50±5.06 months, mean mental age=25.29±15.77 months), the joint attention intervention followed by symbolic play (n children=14, mean age=56.21±10.42, mean mental age=36.25±11 months), or a waitlist control (n children=9, mean age=59.67±10.61, mean mental age=30.38±13.19).[158] Treatment occurred in eight weekly sessions over 8 weeks (4 weeks on either joint attention or symbolic play followed by 4 weeks on the other approach), groups did not differ on play or joint attention behaviors in classroom observations at followup. Children randomized to either treatment arm spent more time in a joint engagement state compared with the control arm (effect size=0.63). In analyses combining the treatment groups, joint engagement time, joint attention responses/minute, joint attention initiations/minute, symbolic play acts/minute, all assessed via classroom observations, increased significantly from baseline to post-intervention (effect sizes of 0.41, 0.43, 0.21, and 0.51 respectively). In investigator-mediated rating of early social communication, the number of joint attention responses increased from baseline (effect size=0.23); children were able to generalize increases in responding to joint attention to a novel individual. Initiation of joint attention did not increase significantly nor did functional play or level of structured play. No potential modifiers (age, ASD severity, mental age) were significantly associated with treatment outcomes.

Another fair quality RCT conducted in Belgium included 36 children (18 in each arm) receiving either standard care in low-intensity rehabilitation centers for children with ASD (focus on communication, social skills, play, and motor skills for 3 to 5 hours/week) or standard care + a joint attention- and imitation-focused intervention delivered for 1 hour/week (two 30-minute sessions for a total of 24 sessions).[159] The joint attention/imitation intervention included games and activities to promote following and initiating requests; gaze following; pointing; initiating joint attention; and gestural, vocal, symbolic, or social imitation. Children ranged in age from 4.07 to 6.92 years, with IQs in the average to mild intellectual disability range (50-105 full scale IQ). After 12 weeks of intervention, the joint attention/imitation group had higher total joint attention scores, improved gaze following, and greater request initiations than the treatment as usual group (effect sizes 0.11 to 0.22, all p values $\leq$.05). The number of elicited joint attention acts increased from 6.53 to 8.41 and the number of spontaneous declarative joint attention acts increased from .89 to 1.72 for the treatment group from baseline to followup; correct imitations increased from 34.11 to 41.12. Initiating declarative joint attention decreased significantly for both groups from baseline to followup (p<.05). Scores on measures of imitation did not differ between groups, though both groups improved over time. Higher baseline verbal IQ was associated with gains in imitation in the treatment group (p<.05), but no other variables tested (age, mental age, full scale IQ, performance IQ, baseline imitation and joint attention skills) were statistically significant. Children in the treatment group improved equally regardless of age or IQ level.

Finally, a fair quality RCT of a joint attention intervention assessed the effects of a roughly 7-month home-based parent training approach targeting focusing on faces, reciprocal communication/turn-taking, and joint attention compared with community-based treatment as usual.[160] The 11 participants in the experimental arm had a mean age of 24.6±4 months and mean Mullen expressive language score of 24.6±6.7 (control group: mean age=27.5±3.4, mean expressive language=24.8±6.9). Reported weekly hours, including the joint intervention sessions for experimental group participants ranged from 2.98±1.25 to 17.88±9.06. Hours/week ranged from 6.25±6.49 to 21.35±11.51 in the control arm. At followup 4 weeks post-intervention focusing on faces and responding to joint attention were significantly improved in the treatment group compared with control (p<.001); scores for the treatment arm remained significantly improved vs. the control group from the 4 week to the 8 week followup and from baseline to the 8 week followup. The effect size for between group differences at the 8 week followup on the focusing on faces outcome was 0.84 and 1.18 for responding to joint attention. Effect sizes for initiations of joint attention were not significant. Language outcomes were significantly improved for the treatment group compared with control. While both groups improved over time, Mullen receptive language and Vineland communication scores were significantly better in the treatment vs. control arm (p values <.05). Effect sizes for differences at the 4-week followup were 0.59 (Vineland) and 0.34 (Mullen); scores for the 8-week followup were not reported.

Studies Addressing Pretend Play

One poor quality nonrandomized, crossover study conducted in a private preschool included 12 high functioning children with ASD (age range 55-75 months).[161] Intervention group participants received the Picture Me Playing intervention, which included scripted stories built around specific toys to model and encourage pretend play. Instances of play dialogue increased significantly following intervention for the treatment group compared with control (3.6 times more utterances over baseline vs. 1.79 times, p<.05), though frequency of play utterances in both groups improved from baseline. Gains in pretend play for both groups also generalized to a toy not used in the intervention and without scripted utterances.

Studies Addressing Imitation

A good quality pilot RCT of Reciprocal Imitation Training, which uses naturalistic approaches to promote imitation and social interaction, allocated 27 children to either Reciprocal Imitation Training (n=14, mean age=39.3±7.3 months, mental age=20.8±6.6) for 3 hours/week for 10 weeks or control/treatment as usual (n=13, mean age=36.5±8.00, mental age=17.9±7.5).[152, 153] The interventionist-led imitation training included modeling of play and gestures and contingent imitation of children's responses and actions with toys. Children in both arms continued to receive between .25 and 25.5 hours of additional intervention per week. Data for 21 of the children was also reported in an earlier pilot,[153] which reported gains in imitation for the treatment group compared with control ($p<.05$). Gains in imitation were associated with the number of spontaneous play acts at baseline. In the followup RCT,[152] the intervention group made more joint attention initiations compared with control ($p<.05$). Intervention participants also improved on the Social-Emotional Scale compared with the control arm ($p=.02$). Changes in imitation were not shown to be associated with gains in social functioning.

Studies Addressing Parent/Child Communication

In a fair quality randomized trial of a focused play intervention, investigators allocated children to either the play intervention (n=36, mean age=58.3±12.7 months) or a control group (n=34, mean age=55.9±11.9 months).[156] Parents of children in the treatment and the control groups could participate in a parent education program focused on advocacy for their children. Parents in the treatment group also participated in a manualized play time intervention, which used home-based sessions (90 minutes/week for 12 weeks) to promote parental engagement and encouragement of child communication. Children in both groups continued to receive a mean of 14 hours (± 5-8 hours) of school programming and individual services such as ABA-based approaches for a mean of 12±10 to 12 hours/week during the treatment phase. Children also received a mean of >12 hours of school or individual services during the 12-month followup period.

In analyses at the end of intervention, maternal synchronization (maternal direction of child attention or utterances in line with toys/actions in which child was already engaged vs. redirecting or not synchronized with child's actions) was significantly greater in the treatment group compared with control (effect size=0.08, $p<.05$). Maternal synchronization was moderated by baseline maternal insightfulness ($p<.05$) and synchronization was greater in those mothers rated as insightful compared with non-insightful (effect size=0.31, $p<.05$). Expressive language scores did not differ between groups at the end of intervention or at followup 12 months post-intervention (effect size for baseline to followup change=0.03, p=ns). Children with baseline expressive language abilities below 11.3 months showed greater gains in language in the intervention group vs. control (effect size=0.25 for 24 children with low language skills). The link between short-term gain in maternal synchronization and long-term language (12 months post-treatment) gains was not moderated by maternal insightfulness, nor did initial language skills moderate the link between gains in maternal synchronization after 12 weeks and long term gains in expressive language.[156]

Another fair quality RCT included 14 participants (age range 28 to 68 months, mean 41.14) randomized to either an adapted More Than Words curriculum focused on teaching parents to understand child communication and promote verbal responsiveness or to a waiting list.[154] Treatment group parents received approximately 12 hours of training and 14 small-group parent-child coaching sessions. Overall, children had mean auditory language age of 14.79 months and expressive age of 20.21 months with greater baseline language abilities in the waitlist group compared with the treatment group. At followup, treatment group parents improved significantly compared with the control group in measures of verbal engagement with their children (p values $\leq.03$). Children in the treatment group increased in prompted communication acts compared with control ($p<.03$), but spontaneous verbal and nonverbal communication acts did not differ between groups.

Table 9. Summary of outcomes of studies of play/interaction-based interventions

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Joint attention studies		
Goods et al. 2013[151] US **G1:** Joint attention intervention, 8/6 **G2:** Control, 7/5 Quality: Good	**G1:** 48.73±11.68 **G2:** 54.68±10.25 **G1:** 37.70±15.21 **G2:** 26.67±10.12	• Joint attention intervention delivered by preschool teachers; G1 demonstrated more spontaneous play types, spent less time unengaged in classroom, and initiated more requesting gestures than G2 (effect sizes 0.81, 1.63, 1.51 respectively, p values≤.05) • No significant group differences on the Early Social Communication Scales measures of joint attention
Kasari et al. 2010[150] US **G1:** Immediate joint attention intervention, 19/19 **G2:** Waitlist control, 19/19 Quality: Good	**G1:** 30.35±0.93 **G2:** 31.31±0.90 **G1:** 64.80±5.35 **G2:** 59.81±3.14	• Joint attention intervention implemented by caregivers. Children in G1 exhibited significantly less object-focused play, responsiveness to joint attention, functional play types, and greater joint engagement than G2 at initial followup (p<.05); gains in joint engagement, responsiveness to joint attention, and types of functional play were maintained at 1-year followup of G1 • Groups did not differ on other/unengaged play time at followup. G1 did not show greater joint attention initiations or diversity of symbolic play compared with G2 • Greater caregiver quality of involvement predicted increased joint engagement
Lawton et al. 2012[157] US **G1:** Immediate joint attention intervention, 9/9 **G2:** Delayed treatment, 7/7 Quality: Fair	**G1:** 46.0±5.00 **G2:** 43.01±6.00 **G1:** 30.3±5.01 **G2:** 33.8±8.74	• Joint attention intervention delivered by preschool teachers. In classroom observations, G1 demonstrated greater initiations of joint attention vs. G2 (effect size=1.85, p<.005) and used more pointing and showing gestures (effect sizes 2.02, 1.85 respectively); no differences in looking or giving • Total joint attention scores on the Early Social Communication Scales did not differ between groups • On intervention exit play observations, no group differences in any joint attention skills • G1 demonstrated less object engagement (effect size=1.41) and more supported engagement (effect size=1.24) compared with G2
Kaale et al. 2012[155] Norway **G1:** Joint attention intervention, 34/34 **G2:** Control, 27/27 Quality: Fair	**G1:** 47.6±8.30 **G2:** 50.3±8.3 **G1:** 53.3±19.2 **G2:** 59.9±19.7	• Joint attention intervention delivered by preschool teachers • G1 demonstrated more frequent joint attention skills in play with teachers vs. G2, with G1 nearly 5 times more likely to demonstrate initiation of joint attention vs. G2 (effect size=0.44); duration of joint engagement with teachers did not differ between groups • G1 spent longer time in jointly engaged play with mothers vs. G2 post-intervention (effect size=0.67); frequency of joint attention skills with mothers did not differ between groups • Frequency of joint attention measured on the Early Social Communication Scales did not differ between groups • Child age, language age, DQ, or preschool treatment approach did not moderate effects

Table 9. Summary of outcomes of studies of play/interaction-based interventions (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Joint attention studies		
Wong 2013[158] US **G1:** Joint attention-symbolic play interventions, 14/14 **G2:** Symbolic play-joint attention intervention, 10/10 **G3:** Waitlist, 9/9 Quality: Fair	**G1:** 56.2±10.4 **G2:** 54.5±5.1 **G3:** 59.7±10.6 **NR**	• No group differences on measures of play or joint attention in classroom observations • Increased time in joint engaged state for G1 and G2 vs. G3 (effect size=0.63) • For G1+G2, joint engagement time, joint attention responses/minute, joint attention initiations/minute, symbolic play acts/minute increased significantly from baseline to post-intervention (effect sizes of 0.41, 0.43, 0.21, and 0.51 respectively) • Increases in joint attention responses from baseline for G1+G2 as measured on the Early Social Communication Scales; no significant increases in functional play level or structured play • No significant modifiers identified
Warreyn et al. 2013[159] Belgium **G1:** Joint attention/imitation intervention, 18/18 **G2:** Treatment as usual, 18/18 Quality: Fair	**G1:** 5.7±0.6 years **G2:** 5.7±0.7 years **G1:** 78.9±15.5 **G2:** 76.9±16.8	• Total joint attention scores more improved for G1 vs. G2 (p<.01); gaze following, initiating requests also significantly improved for G1 vs. G2 (p values <.05) • G1 increased number of elicited joint attention acts by 1.88, number spontaneous declarative joint attention actions by .83, and number correct imitations by 7.01 from baseline • Both groups combined improved in imitation but no between group differences • Initiating declarative joint attention significantly decreased in both groups from baseline to followup (p<.05) • Verbal IQ significantly correlated with growth in imitation for G1 (p<.05); age, mental age, full scale IQ baseline imitation and joint attention skills, performance IQ were not significant modifiers of outcomes
Schertz et al. 2013[160] US **G1:** Joint attention-focused parent training, 11/11 **G2:** Treatment as usual, 12/12 Quality: Fair	**G1:** 24.6±4.0 **G2:** 27.5±3.4 **NR**	• Scores on responding to joint attention significantly improved for G1 vs. G2 at 4-week post-intervention followup (effect size for differences=1.39), as were scores on focusing on faces (effect size=1.24); effects sizes at 8-week followup were 1.18 (responding to joint attention) and .84 (faces) • Mullen receptive language and Vineland communication significantly improved for G1 but not G2; effect sizes for 4 week differences=.59 (Vineland) and .34 (Mullen) • Mullen expressive language improved in both groups from baseline to followup (p<.027)

Table 9. Summary of outcomes of studies of play/interaction-based interventions (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Joint attention studies		
Kasari et al. 2012[140, 141, 148, 149] US **G1:** Joint attention intervention, 20/20 **G2:** Symbolic play intervention, 16/16 **G3:** Control, 16/16 Quality: Fair	**G1:** 43.05±6.863 **G2:** 41.41±6.491 **G3:** 41.31±4.542 NR	• Joint attention interventions delivered by interventionists; children in the intervention groups showed greater growth in expressive language, initiation of joint attention, and duration of child-initiated joint attention than did control group children (p=<.01, <.05); receptive language growth not significantly affected by intervention • Amount of intervention services received post-intervention was not related to growth in skills at followup 12 months after the ~6 week intervention, except for child-initiated joint attention: children receiving fewer hours of additional services showed greater growth in child-initiated joint attention • Quality of joint attention (shared positive affect, shared positive affect with utterances) improved in G1 and G2 at 6 an 12 month followups • At followup of 40/58 participants 5-years post-intervention, 32/40 had passing scores on the Expressive Vocabulary Test of spoken language; only baseline play level predicted ability to use spoken language. • Younger age at baseline, initiation of joint attention, and play level were predictors of spoken language ability at 5-year followup • Greater functional play types at baseline predicted better overall cognitive ability at 5-year followup
Pretend play studies		
Murdock et al. 2011[161] US **G1:** Pretend play intervention, 6/6 **G2:** Comparison, 6/6 Quality: Poor	**G1:** 69.33±5.9889 **G2:** 62.17±6.2102 NR	• Intervention included typically developing peers as play models • Both groups gained play dialog skills from baseline to followup (p=.003), with greater gains in G1 vs. G2 (260% vs. 136%, p=.041) • Participants were able to generalize play dialog skills to a toy not used in the intervention (p=.012) with an increase in play dialog utterances
Imitation studies		
Ingersoll. 2010[152, 153] US **G1:** Reciprocal imitation training, 15/14 **G2:** Control, 14/13 Quality: Good	**G1:** 41.36±4.30 **G2:** 37.20±7.36 NR	• Pilot evaluation of a reciprocal imitation training program • G1 made greater gains in spontaneous and prompted imitation, object imitation, gesture imitation, initiation of joint attention, and on the Social-Emotional Scale than G2 (p values ≤.05) • Number of spontaneous play actions associated with gains in spontaneous imitation and gesture imitation (p<.05) • Changes in imitation skills not associated with social functioning changes in mediation analysis

Table 9. Summary of outcomes of studies of play/interaction-based interventions (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months±SD IQ, Mean±SD	Key Outcomes
Parent-child communication studies		
Siller et al. 2013[156] US **G1:** Parental responsiveness intervention, 36/31 **G2:** Control, 34/31 Quality: Fair	**G1:** 58.3±12.7 **G2:** 55.9±11.9 NR	• Intervention focused on increasing parents' responsiveness to child communication • Mothers of children in G1 demonstrated greater synchronization with child communication vs. G2 (p<.05, effect size=0.08) • No significant effects of intervention on expressive language • Mothers rated as more insightful at baseline had greater gains in synchronization
Venker et al. 2011[154] US **G1:** Parental responsiveness intervention, 7/7 **G2:** Delayed treatment, 7/7 Quality: Fair	**G1+G2:** 41.14±10.40 NR	• Intervention targeting parents' verbal responsive and engagement with child play • Both groups increased prompted communication acts from baseline to followup; in between group comparisons, G1 had greater increases vs. G2 (p<.03) • Number of children increasing spontaneous communication acts did not differ between groups

DQ = developmental quotient; G = group; IQ = intelligence quotient; N = number; NR = not reported; SD = standard deviation

Behavioral Interventions Focused on Associated Behaviors

Key Points

- Five good quality and two fair quality studies evaluated the effects of cognitive behavioral therapy (CBT) on behaviors associated with ASD.
- CBT improved anxiety symptoms and effects were maintained over time in six of the seven studies. The one study that did not show significant benefit compared with control group demonstrated an improvement in anxiety symptoms in the CBT group; however, it was not greater than that seen in the control group. This study was also the only study to use an active control (social recreational therapy) rather than a waitlist or treatment as usual control.
- Two RCTs with treatment as usual control groups demonstrated significant positive effects of CBT on socialization. One study did not demonstrate significant positive effects of CBT on socialization; however, the comparison group engaged in social skills training.
- One small RCT rated as fair demonstrated improvement in emotion regulation after treatment with CBT.
- One good quality RCT demonstrated improvements in executive function in the CBT treatment group compared with control group receiving social skills intervention.
- In a large fair quality RCT, augmentation of risperidone with parent training produced more significant improvement in adaptive behavior, socialization and communication than risperidone alone, but effects were not maintained after one year. This study also evaluated changes in observed appropriate behavior and did not find any between group changes.

Overview of the Literature

We identified nine comparative studies addressing interventions targeting conditions/behaviors commonly associated with ASD in the 2011 review. These studies included four RCTs[163-167] and one nonrandomized trial[168] of fair quality and three RCTs[169-171] and one prospective cohort[172] of poor quality. Studies addressed CBT for anger or anxiety or parent training approaches. In addition to these studies, we identified nine new studies (reported in 15 publications);[165-167, 173-184]two of these nine studies, one evaluating CBT[165, 166, 178] and one assessing parent training plus risperidone,[167, 179-181, 184]report on populations addressed in studies in the 2011 review. As in the 2011 review, studies address either CBT or parent training modalities (Table 10).

Among the studies identified for the current review, eight RCTs evaluated CBT: seven conducted in the United States,[173, 175-178, 182, 183] and one in Singapore.[185] Three studies examined CBT compared with control groups receiving treatment as usual.[173, 177, 182] Three studies examined CBT compared with wait listed controls,[165, 166, 175, 176, 178] one study compared CBT with social recreational therapy,[174] and another with a social skills intervention.[183] Studies included two populations: five studies (reported in multiple publications) included subjects with both ASD and primary anxiety disorder diagnoses,[165, 166, 173, 176-178, 182]and three studies included subjects with ASD only (subjects may or may not have had a formal diagnosis of primary anxiety disorder or studies did not target anxiety).[174, 175, 183] Outcomes measured included improvements in anxiety alone in five studies,[173, 174, 176, 177, 182] improvements in anxiety and daily living skills in one study;[165, 166, 178] improvements in executive function in one study,[183] and improvements in emotion regulation in one study.[175]
Subjects ranged in age from 4 to 16 years. Five study interventions were conducted over 16 weeks,[165, 166, 173, 174, 176-178] one study intervention was conducted over 28 weeks ,[183] one over 32 weeks,[182] and one over 9 weeks.[175] We rated six studies as good quality[165, 166, 173, 174, 176-178, 183] and two as fair.[175, 182]

We identified one fair quality RCT reported in multiple publications and addressing parent training approaches (also reported in the 2011 review).[167, 179-181, 184]The study examined the utility of augmenting risperidone with parent training vs. risperidone alone for treatment of serious behavior problems and irritability. Children had diagnoses of ASD in addition to serious behavior problems as defined by reaching specific cutoff scores on measures of irritability and problem behavior, and ages ranged from 4 to 13 years. Outcomes measured included measures of adaptive behavior in addition to measures of problem behavior and irritability and one observed measure of appropriate behavior.

Detailed Analysis

Most studies investigating CBT as the primary intervention identified anxiety as the target symptom. One good quality RCT measured changes in anxiety symptoms in addition to core ASD symptoms.[177] The study included 36 children ages 7 to 11 with both ASD and primary anxiety disorder diagnoses. Subjects were randomized to an intervention group receiving 16 weekly CBT sessions or a control group receiving treatment as usual. There were no significant group differences with the exception of slightly higher proportion of subjects with Autistic Disorder compared with PDD or Asperger's in the intervention group. Primary outcome measures included the following measures of anxiety; Pediatric Anxiety Rating Scales (PARS), Anxiety Disorders Interview Schedule-IV-Child/Parent Version and Clinical Global Impressions-Severity (CGI-S). Secondary outcome measures included other measures of anxiety such as the Multidimensional Anxiety Scale for Children-Parent Version and Child Behavior Checklist, a measure of social responsiveness, the Social Responsiveness Scale, and the Columbia Impairment Scale-Parent Version, which assesses interpersonal, social and academic skill. All measures were collected at baseline, the end of the intervention and 3 months following termination of the intervention. At the end of the intervention, large treatment effects were observed in all primary outcome measures. Pediatric Anxiety Scale ratings were reduced by 21 percent in the CBT group vs. 9 percent in the control group. CGI-S scores were more improved in the CBT group than the control group (effect size 1.06, $p<0.01$). On the blinded, clinician-rated Anxiety Disorders Interview Schedule, 38 percent of CBT participants vs. 5 percent of control participants showed clinical remission of anxiety symptoms (effect size 1.37, $p=0.01$). Scores on all measures did not change significantly between the end of intervention and the 3-month followup evaluation. Among secondary outcome measures, group differences were observed with greater improvements on the Columbia Impairment Scale, internalizing symptoms on the Child Behavior Checklist, Revised Children's Manifest Anxiety Scale anxious arousal subscale, total score and social communication and social mannerisms subscales on Social Responsiveness Scale. No group differences were observed on externalizing symptoms of the Child Behavior Checklist, dysphoric mood, oversensitivity and worry subscales of the Revised Children's Manifest Anxiety Scale, or social awareness, social cognition and social motivation subscales of the Social Responsiveness Scale.

Another good quality RCT assessed a CBT-based intervention specifically developed for children with ASD ("Facing Your Fears").[173] The study included 48 children ages 7 to14 with ADOS-confirmed diagnosis of ASD randomized to either the CBT group or treatment as usual. Participants were required to be able to speak in full complex sentences and have clinically significant symptoms of anxiety measured on the Screen for Child Anxiety and Related Emotional Disorders-parent version (SCARED). No group differences were identified relative to age, IQ, sex, parents' marital status, mother's education, ethnicity, specific ASD diagnosis, or use of psychiatric medications. The intervention consisted of 12 multifamily group sessions over 4 weeks following the manualized CBT treatment. The Anxiety Disorders Interview Schedule for Children was performed at baseline and again at the end of the intervention. The CGI-S scale was obtained at the end of intervention. Independent Clinical Evaluators (ICEs) blinded to the participant's condition assigned DSM-IV diagnoses and provided summary codes of clinical severity and interferences called Clinician Severity Ratings. Group differences in severity ratings were noted for all anxiety diagnoses with medium to large effect sizes. The overall number of anxiety disorders at followup was significantly reduced in the intervention group, and there was a large effect size noted in the reduction of generalized anxiety disorder diagnoses. There were no group differences noted in diagnostic status for other anxiety diagnoses. Significant improvement was noted on the CGI-S in the intervention group as compared with the control group (effect size 1.03 and $p=0.003$). The SCARED was repeated at 3 and 6 months for the intervention group and indicated that reduction in anxiety symptoms had been maintained.

A third good quality RCT investigated the effects of the Coping Cat CBT program on anxiety symptoms in 22 children ages 7 to 14 with diagnosis of ASD and at least one primary anxiety disorder.[176] Twelve children were assigned to the intervention group and the remaining 10 children were enrolled as waitlisted controls. There were no baseline group differences with the exception of more children in the control group receiving stimulant medications. The intervention consisted of 16 weekly 60 to 90 minute CBT sessions following the Coping Cat treatment manual. Anxiety measures were repeated just after completion of the intervention and again at 2 months after completion of treatment. At the completion of the intervention, 58 percent of the intervention group compared with 0 percent of the control group no longer met criteria for a primary anxiety disorder (p=0.003). Spence Children's Anxiety Scale ratings improved significantly in the intervention group (34.92 to 20.08) but not in the control group (32.3 to 31.7) (p=0.02). Co-morbid diagnoses decreased in the intervention group compared with control group from baseline to end of intervention (p<0.001). After 2 months, four of 11 intervention group participants continued to not meet requirements for anxiety disorder diagnosis. The authors reported a number needed to treat for the intervention of 1.72.

A good quality RCT conducted in Singapore compared the effects of CBT to an established social recreational intervention on anxiety symptoms.[174] Seventy children with ASD diagnoses, verbal IQ>80, and perceptual reasoning IQ>90 were randomly assigned to the CBT group (n=36) or social recreational group (n=34). The CBT group had slightly higher verbal IQ (100.25 in CBT group compared with 93.06 in social recreational group), otherwise there were no significant differences between groups. The CBT group underwent 16 weekly 90 minute small group CBT sessions. The social recreation group underwent 16 weekly 90 minute small group sessions following a manualized treatment protocol that included activities aimed at independent living, self-engagement, motor coordination, intellectual stimulation and socialization. The Spence anxiety scale and CGI-S were repeated at the end of treatment, 3 months and 6 months after the end of treatment. Both groups demonstrated reduction in anxiety on the Spence scale between baseline and at 6-month followup; however, only the social recreational group demonstrated reduction in anxiety immediately following intervention. CGI-S scores improved over time for both groups, but group differences at final followup were not significant.

Another fair quality RCT was conducted in the United States[182] evaluating the Building Confidence CBT program modified for use in children with ASD. The study included 12 children ages 7 to 11 years meeting criteria for both ASD and at least one anxiety disorder who had verbal IQs greater than 70 and no other primary psychiatric diagnosis. The intervention group underwent 32 weekly 90 minute sessions and was compared with a treatment as usual control group. There were no significant differences between groups. The outcome measured in this study was diagnosis of anxiety disorder and severity of symptoms at the end of the intervention. At the end of intervention, fewer children in the treatment group had an anxiety diagnosis (p=0.013); severity of anxiety was also more significantly reduced in the treatment group compared with the treatment as usual arm (p=.017)

One good quality RCT reported in multiple publications[165, 166, 178] examined the effects of the Building Confidence CBT program adapted for children with ASD on anxiety symptoms, daily living skills, and, in a subgroup of children, socialization. Forty children ages 7 to 11 with ASD and separation anxiety, social phobia, or obsessive-compulsive disorder and IQ >70 were randomized to the CBT group or to waitlist control group. No group differences were noted with the exception of more children in the CBT vs. control group having comorbid diagnosis of major depressive disorder or dysthymia (18% vs. 0%, respectively). The intervention consisted of 16 weekly 60-90 minute CBT sessions. Assessments of anxiety included the Anxiety Diagnostic Interview Schedule, the Multidimensional Anxiety Scale for Children parent and child reports, and the Clinical Global Impressions-Improvement (CGI-I) scale. Measures of daily living skills included the Vineland and the Parent Child Interaction Questionnaire, which assesses the level of parent involvement in daily living skills. Socialization was measured with the Social Responsiveness Scale in a group of 19 children from the early stages of recruitment. Most measures were repeated at baseline, at the end of the intervention and, for 10 intervention participants who were still available, at 3 months after the end of intervention. The CGI-I was only collected at the end of intervention and at the 3-month followup. At the end of intervention, 92.2 percent of the intervention group met criteria for positive treatment response based on CGI-I and 64.3 percent no longer met criteria for any anxiety disorder on the Anxiety Disorders Interview Schedule, compared with only 9.1 percent demonstrating positive treatment response on the CGI-I and ($p<0.0001$) and 9.1 percent no longer meeting criteria for anxiety disorder in the control group ($p<0.0001$). Overall this data did not change significantly at the three-month followup period. The MASC scores were significantly lower in the intervention group vs. the control group at followup ($p<0.0001$) for the parental report however the child report did not demonstrate significant differences. This data also did not change significantly at the 3-month followup period. Vineland total daily living and personal daily living raw scores significantly improved for the intervention vs. the control group ($p<0.05$) with effect sizes of 0.45 for total daily living skills and 0.50 for personal daily living skills. Unnecessary parental involvement and parental involvement in child self-care were significantly reduced in the intervention vs. control groups ($p<0.05$ and $p<0.01$, respectively). Treatment effects on the Vineland and parental intrusiveness scales were maintained at 3 months post intervention in the 10 children for whom followup data were available. Among those participants receiving the Social Responsiveness Scale, differences favoring the intervention group were found on three of the five subscales including social communication, social motivation and social awareness ($p<0.05$).

A small, fair quality pilot RCT examined the utility of CBT to improve emotion regulation in a young group of 11 verbal children ages 5 to7 years.[175] Children randomized to the intervention group (n=5) underwent 9 weekly 60 minute sessions of CBT focusing on skill-building, stress management and understanding expression of emotions. The remaining 6 children were randomized to a waitlist control group. This study reported demographic data for all participants but did not present data regarding potential differences between groups. Measures of the child's capacity for emotion regulation was assessed through his report of number emotion regulation strategies that might be used during the reading of a vignette, parental report on an emotion regulation scale, parent observation and notation of frequency and duration of anger/anxiety episodes, and parent report of their own self-confidence and confidence in their children's abilities to handle emotions. Measures were collected at baseline and at the end of intervention. At the end of intervention children in the CBT group reported a greater number of emotion regulation strategies in response to the vignettes (4 vs. 1.29 in control group $p<0.05$, effect size 0.65) and parents had greater confidence in their ability to manage child's anger and greater confidence in the child's ability to manage their own anger ($p<0.05$, effect sizes 0.84 to 0.89).

A good quality RCT investigated the effects of a CBT program, Unstuck and On Target compared with a social skills intervention on 57 children ages 7 to 11 with ASD.[183] Children received either intervention weekly for 28 30-40 minute sessions. All children were required to meet ADOS criteria for ASD, have a full scale IQ greater than 70 and mental age greater than 8 years old. Baseline measures were obtained but not reported. The study does not report at what point post intervention measures were obtained. Both groups improved on most measures from baseline to followup. The CBT group improved significantly more on interventionist-rated measures of problem solving, flexibility, and parent and teacher-rated executive function measures when compared with the social skills group ($p<0.05$ with medium to large effect sizes). In classroom observations, the CBT group demonstrated greater improvement in ability to follow directions, transition smoothly and avoid "getting stuck" (p values <0.05). Higher baseline scores predicted greater improvements in flexible thinking, social tasks, parent- and teacher-rated executive function shift and planning/organization measure, parent-rated Social Responsiveness Scale total score (p values <0.05). Higher IQ predicted greater improvements in flexible thinking and the challenge task plan measure. Younger age predicted greater improvement on the challenge task and parent-rated executive function measures of shift and planning/organization (p<0.05). Female sex predicted greater improvement on the parent –rated Social Responsiveness Scale total score (p values <0.05).

One fair quality RCT (reported in multiple publications) assessed a parent training approach (treatment with risperidone alone vs. risperidone augmented with a parent-training program) to improving adaptive behavior and communication and socialization skills.[167, 179-181, 184] The parent training program included 11 core sessions, one home visit and up to three optional sessions during the first 16 weeks, followed by four booster sessions over the next 8 weeks. The training focused first on antecedents, purpose, and reinforcements of problem behaviors and then on teaching parents management strategies for these behaviors. Investigators recruited 124 children ages 4 to 14 years with ASD, severe problem behaviors evidenced by positive scales on the Aberrant Behavior Checklist-Irritability subscale and CGI-S subscales, and IQ>35. Forty-nine participants were randomized to risperidone plus parent training intervention group and 75 to the risperidone alone control group. No group differences were observed with the exception of slightly higher ABC-irritability subscale scores in the intervention group.

The Aberrant Behavior Checklist, Vineland, the Home Situations Questionnaire, and the Standardized Observation Analogue Procedure were completed at baseline, at 24 weeks after completion of intervention and, for the Aberrant Behavior Checklist and Home Situations Questionnaire, one year after intervention. At 24 weeks, scores on the Home Situations Questionnaire demonstrated decreased severity in more children in the intervention group vs. control (p<0.006), and greater improvements were noted in the intervention group on the Aberrant Behavior Checklist Irritability (p=0.01), Stereotypic behavior, (p=0.04) and Hyperactivity (p=0.04) subscales compared with the control group. Also at 24 weeks post intervention, greater improvements in the intervention group were noted on Vineland socialization (p=0.01) and adaptive composite (p=0.05) standard scores and on Vineland noncompliance (p=0.03), socialization (p=0.03) and communication (p=0.05) age equivalent scores. These treatment gains were not associated with IQ or adaptive or maladaptive behaviors. Analysis indicated higher baseline Home Situations Questionnaire scores predicted greater improvement regardless of treatment (p=0.007). Authors also analyzed 21 potential moderator variables and none significantly moderated Home Situations Questionnaire or Aberrant Behavior Checklist-Hyperactivity scores, suggesting that parent training may be effective for a range of children. Scores on the standardized observation measure indicated no between group differences in child inappropriate behavior in direct observations under various conditions (free play, restrictive, etc.). In analyses combining both groups, child inappropriate behavior decreased from baseline in the demand and tangible restrictive conditions (p values<.01). Additionally, this measure reported an increase in compliance in the demand condition (p=.0004) when groups were combined.

At 1-year followup, data were available for 87 participants. Group differences at one year on the Home Situations and Aberrant Behavior Checklists were no longer significant. Data were not available for Vineland at one-year followup.[167, 179-181]

Table 10. Summary of outcomes of studies of interventions targeting conditions commonly associated with ASD

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
CBT Studies		
Storch et al. 2013[177] US **G1:** CBT, 24/22 **G2:** Usual care, 21/21 Quality: Good	**G1:** 8.83±1.31 **G2:** 8.95±1.40 NR	• Significantly greater improvements in all primary outcomes for G1 compared with G2; effect sizes ranged from 0.84 to 1.06 • Pediatric Anxiety Rating Scale ratings were reduced by 29% for G1 vs. 9% for G2 (effect size=1.03, p<.01) • CGI-S improved from a mean 3.50 for G1 at baseline to 2.67 at followup compared with baseline mean of 4.00 and followup of 3.57 for usual care (effect size=1.06, p<.01) • On the blinded, clinician-rated Anxiety Disorders Interview Schedule, 38% (9/24) G1 participants vs. 5% (1/21) G2 participants achieved clinical remission of anxiety symptoms (effect size=1.37, p=.01) • At followup of G1 three months post-treatment, 11/15 maintained treatment response and 6/9 maintained remission (p=NS); scores on the CGI-S, Anxiety Disorders Interview Schedule, and Pediatric Anxiety Rating Scale did not change significantly from end of treatment
Keehn et al. 2013[176] US **G1:** CBT, 12/12 **G2:** Wait list control, 10/10 Quality: Good	**G1:** 11.65±1.41 **G2:** 11.02±1.69 **G1:** 108.42±17.70 **G2:** 110.40±17.39	• On blinded, clinician-rated Anxiety Disorders Interview Schedule, 58% of G1 no longer met criteria for primary anxiety diagnosis at followup; 100% of G2 still met criteria (p=.003) • Parent-reported Spence Children's Anxiety Scale ratings improved over time for G1 compared with G2 (baseline means: G1=34.92, G2=32.20; at followup G1=20.08, 31.70, p=.02) • Co-morbid diagnoses decreased in G1 compared with G2 from baseline to followup (p<.001) • 4/11 treatment group participants with 2-month post-treatment followup data continued not to meet criteria for anxiety diagnosis • NNT=1.72
Reaven et al. 2012[173] US **G1:**CBT**,** 24/21 **G2:** Usual care, 26/26 Quality: Good	**G1:** 125.75 months±21.47 **G2:** 125.00 months±20.45 **G1:** 107.08±16.85 **G2:** 102.23±17.33	• Blinded clinician severity ratings significantly reduced from baseline for all anxiety diagnoses in G1 compared with G2; effect sizes ranged from medium to large • Significant reduction in overall number of anxiety disorders in G1 compared with G2 at followup; large effect size for reduction in generalized anxiety disorder diagnoses (effect size=0.85) but no significant between group differences in diagnostic status for other anxiety diagnoses • 50% of G1 and 8.7% of G2 had clinically meaningful improvement in anxiety symptoms on the CGI-S (effect size=1.03, p=.003) • At 6 month post-intervention followup for G1, parent and child SCARED scores suggested maintenance of reduction of anxiety symptoms

Table 10. Summary of outcomes of studies of interventions targeting conditions commonly associated with ASD (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
CBT Studies		
Sung et al. 2011[174] Singapore **G1:** CBT, 36/36 **G2:** Social recreational program, 34/34 Quality: Good	**G1:** 11.33±2.03 **G2:** 11.09±1.53 **G1:** 100.25±13.97 **G2:** 93.06±12.81	• Both groups reported reductions in anxiety from baseline to end of treatment; reports of panic attacks were significantly reduced from baseline in G2 (p<.01); differences between groups at final followup (6 months post-treatment) were not significant • CGI-S scores improved over time in both groups, but between group differences at final followup were not significant
Drahota et al. 2011[165, 166, 178] US **G1:** CBT, 17/14 **G2:** Wait list control, 23/22 Quality: Good	**G1:** 9.18 ±1.42 **G2**: 9.22 ±1.57 NR	• 92.9% of G1 met criteria for positive treatment response; 64.3% of G1 no longer met criteria for any anxiety disorder on the Anxiety Disorders Interview Schedule • Multidimensional Anxiety Scale for Children scores were significantly lower (i.e., reduction in anxiety) in G1 vs. G2 at followup (p<0.0001) with maintenance of response for G1 at followup 3-months post-intervention • Vineland total daily living and personal daily living raw scores significantly improved for G1 vs. G2 at followup (p≤.05); effect sizes were 0.45 (total daily living skills) and 0.50 (personal daily living skills) • Mean age equivalency for total daily living skills increased from 5.2 years at baseline to 6.0 for G1 and from 5.4 years at baseline to 5.7 for G2; for personal daily living skills, mean age equivalency increased from 4.1 to 5.0 years in G1 and 4.5 to 4.6 years in G2 • Unnecessary parental involvement and parental involvement in child self-care were significantly reduced in G1 vs. G2 (p<.05, p<.01 respectively) • Treatment effects on the Vineland and parental intrusiveness scales were maintained at followup 3-months post-intervention for 10 children with followup data
Fujii et al. 2013[182] US **G1:** CBT, 7/7 **G2:** Treatment as usual, 5/5 Quality: Fair	**G1:** 8.7±1.8 **G2:** 9.0±1.6 **G1+G2:** >70	• At followup after 32 weeks of intervention, 5/7 G1 participants no longer met diagnostic criteria for primary anxiety diagnosis; 1 participant retained diagnosis of social phobia disorder and 1 retained generalized anxiety disorder diagnosis • All control group participants retained anxiety diagnoses at followup: 2 with separation anxiety, 3 social phobia disorder

Table 10. Summary of outcomes of studies of interventions targeting conditions commonly associated with ASD (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
CBT Studies		
Kenworthy et al. 2013[183] US **G1:** School-based CBT executive function intervention, 47/43 **G2:** Social skills intervention, 20/19 Quality: Good	**G1:** 9.49±1.0 **G2:** 9.58±1.1 **G1:** 108.8±18.5 **G2:** 107.63±17.2	• Both groups improved on most measures from baseline to followup; G1 improved significantly more on interventionist-rated measures of problem solving, flexibility, and parent and teacher-rated executive function measures (shift, planning/organization) compared with G2 (p values <.05, medium to large effect sizes) • In classroom observations, greater improvement in G1 vs. G2 ability to follow directions, transition smoothly, and avoiding “getting stuck” (p values<.05) • Higher baseline scores predicted greater improvements in flexible thinking, social tasks, parent- and teacher-rated executive function shift and planning/organization measure, parent-rated Social Responsiveness Scale total score (p values <.05) • Higher IQ predicted greater improvements in flexible thinking, challenge task plan measure; younger age at baseline predicted greater improvement on challenge task plan measure and parent-rated executive function measures of shift and planning/organization (p values <.05) • Female sex predicted greater improvement on parent-rated Social Responsiveness Scale total score (p values <.05)
Scarpa et al. 2011[175] US **G1:** CBT, 5/5 **G2:** Delayed treatment control, 6/6 Quality: Fair	**G1+G2 (range):** 5-7 years **IQ:** NR	• Pilot study to assess utility of CBT approach to improve emotion regulation (Sofronoff, 2005, 2007) in younger children • G1 articulated significantly greater number strategies in response to vignettes than G2 (mean 4 vs. 1.29, p<.05, effect size=0.65) • Greater parental confidence in own ability to manage child’s anger and greater confidence in child’s ability to manage anger and anxiety in G1 vs. G2 (p<.05, effect sizes=0.84 tob0.89)

Table 10. Summary of outcomes of studies of interventions targeting conditions commonly associated with ASD (continued)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
Parent Training Studies		
RUPP 2012[167, 179-181, 184] **G1:** Risperidone, 49/36 (1-yr followup) **G2:** Risperidone+parent training, 75/51 (1-yr followup) Quality: Fair	**G1:** 7.5±2.80 **G2:** 7.38±2.21 IQ>70, n (%) **G1:** 23 (46.9) **G2:** 46 (63) IQ<70, n(%) **G1**: 26 (53.1) **G2:** 27 (37)	• After 24 weeks of treatment, significant group by time interaction on the Home Situations Questionnaire (HSQ) (p<0.006); HSQ scores declined (i.e., decreased severity) in more children in G2; Aberrant Behavior Checklist (ABC) irritability, stereotypic behaviors, hyperactivity subscales all showed significant group differences over time with less severe symptoms in each of the domains in G2 • After 24 weeks, Vineland socialization and adaptive composite standard scores and socialization, noncompliance, and communication age equivalent scores were significantly better in G2 vs. G1 (p≤.05, effect sizes ranging from 0.14 to 0.35); treatment gains were not associated with IQ or adaptive or maladaptive behaviors • Higher baseline HSQ scores predicted greater improvement regardless of treatment (p=.007); effect size of 0.81 (p<.01) for those with greater severity • Of 21 potential moderator variables (e.g., child age, maternal education) none significantly moderated HSQ or ABC-Hyperactivity scores, suggesting that parent training may be effective for a range of children • At followup of 87 participants 12-months post-intervention, between group differences on the HSQ or ABC were no longer significant • No between group differences in child inappropriate behavior in direct observations under various conditions (free play, restrictive, etc.); in analyses combining G1 and G2, child inappropriate behavior decreased from baseline in the demand and tangible restrictive conditions (p values<.01); increase in compliance in the demand condition (p=.0004)

ABC = Aberrant Behavior Checklist; ASD = autism spectrum disorder; CBT = cognitive behavioral therapy; CGI = Clinical Global Impression; G = group; HSQ = Home Situations Questionnaire; IQ = intelligence quotient; N = number; NR = not reported; RUPP = Research Units on Pediatric Psychopharmacology; SCARED = Screen for Child Anxiety Related Disorders; SD = standard deviation

Other Behavioral Interventions

Key Points

- In one study comparing CBT plus melatonin to either melatonin or CBT alone, all participants improved on measures of sleep quality, with the combination group generally improving more than the others.
- One small, short-term study of a sleep education pamphlet for parents demonstrated little positive effect of the pamphlet; similarly, a short-term study of parent training in sleep routines reported some within-group improvements in time to fall asleep.
- Small, short-term studies of neurofeedback reported some improvements on parent-rated measures of communication and tests of executive function

Overview of the Literature

We classified studies not cleanly fitting in any of the other categories as "other." In addition to two poor quality RCTs targeting neurofeedback[186, 187]and described fully in the 2011 review, we identified six new studies (seven publications) evaluating interventions targeting sleep behaviors,[188-190] feeding difficulties in ASD,:[191] and neurofeedback [192-194] (Table 11).We considered one RCT comparing the effects of CBT with or without melatonin with placebo on sleep habits as fair quality,[189] two RCTs evaluating the effects of sleep education as fair quality,[188, 190] and two studies (reported in three publications)[192-194]of neurofeedback as fair[192] and poor[193, 194] quality, and one study targeting mealtime behaviors as poor quality.[191] Studies were conducted in Europe[189, 192-194] and the United States[188, 190, 191] and included 303 total participants with ages ranging from 2 to 12 years. Duration of intervention ranged from 3 to 12 weeks.

Detailed Analysis

One fair quality RCT compared CBT alone, melatonin alone, CBT plus melatonin, and placebo in 160 children with ASD between the ages of 4 and 10 years.[189] CBT consisted of four 50-minute sessions focused on recognizing dysfunctional attitudes about sleep, parent-management of children's sleep, and replacing poor sleep habits with appropriate behavior. Participants received 3 mg controlled release melatonin administered at the same time each day. Investigators allocated 40 participants to each group; mean age across groups ranged from 6.3 to 7.1 years, and each group lost 5 to 8 participants over the 12-week intervention due to withdrawals or missing actigraphy data. All active treatment groups improved in most measures of sleep quality compared with the control group ($p<.01$). In general, the combination group improved more than the others, followed by the melatonin alone and CBT alone groups. Scores for children who received melatonin alone improved on bedtime resistance, sleep onset delay, sleep duration, and night waking compared with the CBT group ($p<.001$). Effect sizes (exact data not reported) ranged from medium to high. Sleep onset latency (time to fall asleep) and sleep efficiency (ratio of total sleep time to total time in bed) were reduced by 50 percent (sleep latency) or 85 percent (efficiency) in 85 and 63 percent of children in the combination group and 39 and 46 percent of children in the melatonin group, respectively. In the CBT arm, 10 percent of children met each criterion, and no children in the control arm achieved these percentages of reduced latency or improved efficiency. The study reported no significant harms.

One fair quality RCT evaluated the effects of a sleep education pamphlet compared with no intervention in 36 children with ASD between the ages of 2 and 10 years.[188] Parents of children in the intervention group received a four-page pamphlet with information about sleep environment, promoting bedtime routines and schedules, teaching children to fall asleep alone, avoiding naps where possible, and promoting a sleep/wake schedule; parents did not receive additional instruction. At the 2-week followup, groups did not differ significantly on sleep latency, waking after sleep onset, total sleep time, or sleep fragmentation. Sleep efficiency (total sleep time/time in bed) improved slightly in the intervention group (baseline mean 75.5%±6.1, followup 77.8%±7.0 vs. baseline mean of 76.8%±6.0, followup 75.1%±6.7 for the control group, p=.04).

A final fair quality RCT assessed short-term group or individual format sleep education for parents.[190] Participants (n=80) received 1 to 4 hours of education focused on bedtime routines, sleep environment, and sleep resistance in ASD. Followup measures did not differ for any outcome at followup; however, in analyses combining data for the group and individual-education arms, sleep latency (time to fall asleep) was significantly reduced from baseline (p<.001) as was sleep efficiency (p<.001), though the improvement in efficiency (% sleep time out of total time in bed) was not clinically meaningful. Insomnia-related parameters on the parent-rated Children's Sleep Habits Questionnaire (sleep onset delay, night wakings, sleep duration, bedtime resistance, sleep anxiety) were also significantly improved from baseline to followup (all p<.001) in combined analyses.

In a nonrandomized trial including 14 high functioning children with PDD-NOS (IQ≥70) investigators assigned children to 40 sessions of neurofeedback (n participants=7, mean age=9.63±1.53 years) sessions designed to treat individuals with ADHD or to a wait-list control group (n=7, mean age=10.64±1.41 years).[194, 195] Electroencephalogram data did not differ significantly between groups at followup; however, the treatment group improved on some executive function measures (auditory selective attention, inhibition of verbal responses and impulsive tendencies, all p<.05) and in nonverbal communication compared with the control group. Cognitive flexibility and goal setting improved for the treatment group vs. control but ability to recognize words did not. Parents of children in the treatment arm also rated their children's communication skills as improved following neurofeedback training. In analyses 12-months post-treatment combining data for the treatment and control group participants who went on to complete neurofeedback training (n=NR), gains in auditory selective attention, non-verbal communication, and parent measures of social behavior continued.

In an RCT evaluating neurofeedback, 10 children (mean age=9.43±1.44 years) received 40 neurofeedback sessions aimed at decreasing theta power in the frontal and central brain areas. Ten children served as controls (mean age=9.14±1.34 years); the study did not specify if control children received any type if intervention.[192] In contrast to the prior neurofeedback study, children had diagnoses across the ASD spectrum, treatment occurred in school and at home, and both parents and teachers completed outcome questionnaires. Immediately after treatment, theta activity was reduced in 60 percent of the intervention group. Social behavior, especially reciprocal social interaction, as measured on the parent-rated Social Communication Questionnaire, improved for the treatment group compared with control (p<.05) as did scores on the Children's Communication Checklist and on the set-shifting domain of executive function (p<.05). Scores on other domains of executive function did not differ between group nor did scores on teacher-rated measures. At followup 6-months post-treatment, the intervention group showed continued improvement on parent-rated measures of social behavior, communication, and repetitive behavior as well as set-shifting compared with the control arm (p<.05) Parents were not blinded to treatment condition.

Finally, one poor quality RCT assessed the effectiveness of an 8-week manualized parent training program on mealtime behaviors.[191] Baseline BMI among the 19 participants (age range 68-91 months) was in the normal range. Between group differences at followup were not significantly different on any mealtime behavior measures. Parenting stress was significantly reduced in the treatment group compared with the waitlist control (p=.01).

Table 11. Summary of outcomes of behavioral-other studies

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Years±SD IQ, Mean±SD	Key Outcomes
Cortesi et al. 2012[189] Italy **G1:** Melatonin+CBT, 40/35 **G2:** Melatonin alone, 40/34 **G3:** CBT alone, 40/33 **G4:** Placebo, 40/32 Quality: Fair	**G1:** 6.4±1.1 **G2:** 6.8±0.9 **G3:** 7.1±0.7 **G4:** 6.3±1.2 NR	• G1, G2, and G3 improved in measures of sleep compared with G4 (p<.01), with G1 improving more than the others, though not significantly • On actigraphy measures, G1 improved more than G2 and G3 • Primary effects of CBT alone were on sleep latency and sleep anxiety
Malow et al. 2014[190] US **G1:** Individual sleep education for parents, 41/41 **G2:** Group-based sleep education for parents, 39/39 Quality: Fair	**G1:** 5.6±2.6 **G2:** 5.9±2.8 **% IQ>70** **G1:** 64 **G2:** 45	• No between group differences on any measure • Sleep latency (# minutes to fall asleep) improved from baseline to followup when data from both arms combined (mean 58.2±29.1 minutes to 39.6±21.4 minutes, p<.001) as did sleep efficiency (76.3 ±6.9% to 79.2±5.5%, p<.001),insomnia-related subscales of the Children's Sleep Habits Questionnaire and measures related to sleep habits
Adkins et al. 2012[188] US **G1:** Sleep education pamphlet, 18/18 **G2:** No intervention, 18/18 Quality: Fair	**G1+G2:** 6.4±2.6 **G1:** 75.1±25.5 **G2:** 85.6±27.1	• No between group differences in sleep latency, waking after sleep onset, total sleep time, or sleep fragmentation at the 2 week post-intervention followup • Sleep efficiency improved somewhat in G1 vs. G2 (p<.04)
Kouijzer et al. 2009[194, 195] US **G1:** Neurofeedback, 7/7 **G2:** Control, 6/6 Quality: Poor	**G1:** 9.63±1.53 **G2:** 10.64±1.41 **G1:** 92.5±16.05 **G2:** 93.83±13.67	• Improvements in some measures of executive function in G1 vs. G2 (p<.05); improvements in nonverbal communication and parent-rated communication and behavior measures in G1 vs. G2 • Analyses combining groups (G1 and some G2) suggested maintenance of improvement in social behavior
Kouijzer et al. 2009[192] US **G1:** Neurofeedback, 10/10 **G2:** Control, 10/10 Quality: Fair	**G1:** 9.43±1.44 **G2:** 9.14±1.34 **IQ:** NR	• Parent-rated scores in reciprocal social interaction and communication improved for G1 vs. G2 (p<.05) • Set-shifting skills improved for G1 vs. G2 (p=.045); parent-rated measures at 6 months post-treatment suggested maintenance of improvements in communication and set-shifting for G1
Sharp et al. 2013[191] US **G1:** Parent training in mealtime behaviors, 15/10 **G2:** Waitlist, 15/9 Quality: Poor	**G1:** 70.8±20.5 **G2:** 64.8±16.9 NR	• Participants had BMI in normal range at baseline and no specific feeding issues set a inclusion criteria • No significant group differences at followup in terms of feeding behavior, food refusal, food selectivity, "autism features" as rated on mealtime behavior inventory

CBT = cognitive behavioral therapy; G = group; IQ = intelligence quotient; NR = not reported; SD = standard deviation

KQ2. Modifiers of Treatment Effects

Key Points

- Not all studies were adequately designed or powered to assess modifiers of effects.
- Associations of outcome and baseline measures of cognition, adaptive behavior, language, and ASD severity were mixed across studies.
- In early intervention studies, younger age was associated with greater improvements, though effects were not always consistent.

Overview of the Literature

Understanding the degree to which child characteristics (i.e., specific ASD-related difficulties and skills), treatment factors (e.g., type, duration, intensity), and systems (e.g., family, community) influence response to treatments could improve targeting of treatments to the appropriate children and circumstances. Twenty papers (described in multiple publications) reported predictor, moderator, or mediator data;[72, 76, 77, 79, 81-84, 86, 87, 90, 93, 95, 100, 101, 105, 123, 124, 132, 152, 153, 156, 159, 167, 179-181, 183] however, not all studies were adequately designed or powered to assess modifiers of effects.

Detailed Analysis

Child-Related Factors

Age

As in the 2011 review, several studies reported associations between age at intake and improved outcomes. In one RCT of an approach incorporating parent training, younger age was associated with greater improvements: greater language gains were seen in children who were younger with lower functioning levels at baseline.[72, 105]

Age effects were not consistent, however, and may reflect characteristics of subgroups and treatment characteristics that need further elucidation. For example, one study comparing preschool-delivered intensive early intervention and treatment as usual reported larger adaptive behavior gains for older children in the early intervention group.[77] Another RCT compared early intensive treatment delivered by parents and by specialized center staff with eclectic treatment and identified predictors of progress: in the parent training group, older children achieved better adaptive behavior outcomes; younger children made more gains in early language comprehension and production.

In a retrospective cohort study of a community-based early intervention program, outcomes were related to age at enrollment, treatment duration, and higher baseline adaptive scores. A significant interaction emerged between age at enrollment and group membership, with younger starting age influencing outcomes for the treatment group but not the waitlist control.[86] In contrast to the early intervention studies, in an RCT assessing emotion recognition, older age was correlated with improved identification of fear expressions, affect recognition, and the mind reading desire based task.[123] Another RCT of a preschool-based joint attention intervention compared an 8-week treatment program focused on increasing initiating, giving, and sharing joint attention skills plus preschool to preschool alone in 61 children with ASD.[155] In exploratory analyses, investigators found no putative moderators (age, developmental quotient, language age, program philosophy) to be significant, suggesting that the intervention may be applicable across developmental levels.

IQ/Cognition

Associations of outcome and IQ or measures of cognition were mixed across studies. Intervention efficacy was associated with baseline cognitive scores in one early intervention study comparing preschool models classrooms,[83] with higher baseline cognitive scores associated with less improvement in children in TEACCH model classrooms. In an early intervention prospective cohort study, baseline IQ was positively correlated with socialization, communication, daily living, and composite score gains on the Vineland in the treatment group; however, baseline IQ did not correlate with IQ at followup.[77] In another early intervention study, higher pre-treatment mental development state and early language skills predicted better outcome on parent-reported adaptive behaviors in the eclectic treatment group.[101, 102] In a study assessing emotion recognition, higher verbal IQ was associated with some short term improvements in fear recognition and mind reading tasks,[123] while in another emotion recognition RCT, IQ was not correlated with improved outcomes in either the treatment or control groups.[132] In another RCT of a group-based social skills approach, IQ was not associated with response status;[124] similarly, treatment gains were not associated with IQ in an RCT comparing parent training plus risperidone to risperidone alone.[167, 179-181] In one study of CBT focused on executive function outcomes, higher baseline scores predicted greater improvements in flexible thinking, social tasks, parent- and teacher-rated executive function shift and planning/organization measure, parent-rated Social Responsiveness Scale total score (p values <0.05). Higher IQ predicted greater improvements in flexible thinking and the challenge task plan measure. Younger age predicted greater improvement on the challenge task and parent-rated executive function measures of shift and planning/organization ($p<0.05$). Female sex predicted greater improvement on the parent –rated Social Responsiveness Scale total score (p values <0.05). [183] In a play-interaction study targeting imitation and joint attention, higher baseline verbal IQ was associated with gains in imitation in the treatment group ($p<.05$), but no other variables tested (age, mental age, full scale IQ, performance IQ, baseline imitation and joint attention skills) were statistically significant. Children in the treatment group improved equally regardless of age or IQ level.[159]

ASD Severity/Symptom Severity and Diagnoses

In some studies, children with lower symptom severity or less severe diagnoses improved more than participants with greater impairments. In an RCT assessing ABA-based early intervention, lower baseline ASD severity was associated with parent-reported cognitive and adaptive growth for children who received eclectic vs. ABA intervention, but not with improvements in standardized cognitive test scores.[81, 82] A prospective cohort study of preschool-based early intensive intervention reported that children in the early intervention group with PDD-NOS or Asperger diagnoses (but not autism) had greater gains in overall adaptive behavior, communication, and daily living skills.[77] A prospective cohort study comparing four early intervention approaches (home-based 1:1 ABA intervention, low intensity home-based programming for children with special needs [portage], home-based, local health authority-developed intervention incorporating parent training, and special education nursery/preschool) evaluated relationships between ASD severity, time in intervention, and effectiveness of intervention.[95] Hours of intervention ranged from 2 to 40 across groups, with the home-based

ABA group receiving the most (mean 30.4/week) and the Portage group the least (mean 8.5/week). Baseline ASD severity and total intervention hours modified effects of treatment significantly. First, baseline ASD severity was inversely related to composite change scores for all but the home-based ABA group and was positively related in that group. That is, children with more severe ASD symptoms made more progress in ABA and less in the other intervention groups. Second, more intervention time was negatively related to composite change scores for children in ABA but not in the other groups. More hours of ABA were associated with less progress relative to more hours of school enrollment or other home-based interventions.

Two reports[88, 90] including participants in a retrospective cohort study evaluating an early intervention approach[86] assessed potential outcome predictors including baseline age, Vineland scores, IQ, and ASD severity (CARS). Younger age at intake, higher initial developmental levels[90] and treatment intensity[88, 90] were related to better treatment outcomes. Vineland standard scores and IQ and mental age were higher for the 32 children whose followup standard scores on cognitive and/or adaptive behavior were in the low average range or better (>85) and whose CARS scores were in or very close to the non-ASD range (<30), Similarly, these "average outcome" children had significantly lower intake CARS severity scores, began intervention earlier (mean 42 months vs. 55 for rest of sample), and received intervention for a longer duration. More of these children also had diagnoses of PDD-NOS. Children who had poor outcomes at followup (n=75) had statistically significantly lower baseline IQ , mental age, rate of development, and Vineland scores (except for the socialization domain), with p values ranging from .01 to <.001. Differences likely were not clinically significant, however, and diagnostic category, severity, age at entry, and duration of therapy were not significantly different in the poor outcome group compared with the rest of the sample.

In an RCT evaluating an emotion recognition intervention, long term improvements in identification of happiness expressions were associated with greater ADOS severity, as was matching of emotions overall and of sadness specifically.[123] In an RCT of a theory of mind training program, children with PDD-NOS improved on most measures of emotion recognition while children with Asperger syndrome improved only in understanding of complex emotions.[128] In another RCT of a group-based social skills approach, children with Asperger syndrome were more likely to be responders compared with children with PDD-NOS (p=.03).[124]

Finally, an RCT assessing a parent training approach targeting challenging behaviors examined 21 candidate predictors and moderators of outcome scores on the Home Situations Questionnaire (HSQ) and the Aberrant Behavior Checklist, Hyperactivity/Noncompliance (ABC-H) scale.[167, 179-181] Children received either parent training plus risperidone (n=75, mean age=7.4) or risperidone alone (n=49, mean age=7.5); thus, potential moderation of effect reflects the combination of parent training and risperidone while predictors of effects reflect the impact of risperidone with or without parent training. Investigators examined variables including parent training adherence, age, IQ, family income, maternal education level, parent stress, and child baseline ratings on measures including the Vineland and ABC. Only higher baseline scores on the HSQ (greater noncompliance) predicted greater improvement in either treatment condition (p=.007), with the lower HSQ group demonstrating less mean improvement than those with higher baseline HSQ scores. Though not significant, older children had slightly more improvement than younger children. No variables predicted ABC-H outcomes, though children with higher baseline Vineland composite and communication subscale scores had greater improvement on the ABC-H. While not a significant predictor of outcomes, greater parent adherence to the training program was correlated with better HSQ outcomes (p=.006), but adherence did not correlate with ABC-H scores. No candidate variables were found to moderate the relationship between parent training and HSQ or ABC-H outcomes, which may suggest that parent training is appropriate for the broader range of children with ASD.

Adaptive Behavior

Studies reported mixed findings related to outcomes associated with baseline adaptive behavior. In one retrospective cohort, positive outcomes in both the early intervention and the waitlist control groups were related to higher baseline adaptive scores.[86] In one early intervention study, initial higher adaptive behaviors predicted better post-treatment early language comprehension.[101, 102] In an RCT comparing risperidone alone and risperidone plus parent training, treatment gains were not associated with adaptive or maladaptive behaviors.[167, 179-181]

Language/Communication

The impact of language skills and attention to objects (vs. people) were assessed in three studies. In one RCT of the More Than Words program, the treatment group showed differential effects on child communication depending on children's baseline object interest; children with lower levels of baseline object interest had greater growth in communication skills, whereas children with higher levels of object interest showed attenuated growth.[93] In another study of play-focused intervention, children with baseline expressive language abilities below 11.3 months showed greater gains in language in the intervention group vs. control (effect size=0.25 for 24 children with low language skills).[156] In another early intervention study, children who gained more language comprehension had higher adaptive behavior scores pre-treatment. Pre-treatment language comprehension also predicted post-treatment language production.[101, 102]

An RCT evaluating an imitation-based approach to affect social functioning[152, 153]assessed whether changes in social functioning were tied to changes in participants' imitation skills. Gains in imitation were associated with the number of spontaneous play acts at baseline; however, changes in imitation were not shown to be associated with gains in social functioning. This finding could be because the study had too few participants (n=27) to detect such an effect.

Other Factors

One RCT compared the effects of a 6-week joint attention or symbolic play intervention with a control arm in participants receiving 30 hours of early intervention; at the 5 year followup, investigators assessed diagnoses and language skills for 40 of the 58 original participants.[140, 141, 148, 149]Investigators also identified potential predictors of vocabulary and cognitive changes via regression analyses. Potential predictors included child age, sex, maternal education, play levels and types, and joint attention responses. Ability to use spoken language at followup ("passing" the language assessments) was predicted by children's average play level at baseline ($p<.01$). Number of functional play types at baseline predicted greater cognitive skills. Younger age at baseline, initiation of joint attention, play level and treatment group assignment (either joint attention or symbolic play) predicted subsequent vocabulary ability (all $p<.03$); these factors together explained 64 percent of spoken language variability. Importantly, this study is limited in that children were often receiving intensive levels of intervention outside of the intervention setting, making impact of prescribed intervention hard to determine.

Parent-Related Factors

Four early intervention studies assessed variables related to parents/caregivers. In one RCT incorporating parent training,[72, 105] parents in the additional treatment group showed increased responsiveness to their children during videotaped interactions, which was correlated with reduced ASD symptom severity (p=.049). No between-group differences were found in adaptive behavior or parenting stress. In another parent training RCT, parents in the professionally led group with low baseline self-efficacy reported higher followup self-efficacy levels than parents in the video arm.[100] In a report[87] also including a population reported in a retrospective cohort[86], parental stress was not associated with any outcomes. In both the early intensive intervention and eclectic treatment control group in one study, child outcomes on early language skills, mental developmental state, and adaptive behaviors were significantly influenced by self-reported parental stress, children's ability to respond correctly to prompts, the number and difficulty of treatment targets, and children's problem behaviors in sessions. Children who were perceived by their parents as more difficult demonstrated less improvementin ASD severity.[101, 102]

Two play/interaction-focused RCTs assessed parent responsiveness and adherence to the treatment approach on treatment effects. One study comparing an 8-week caregiver-delivered joint attention approach with a waitlist control assessed intensity of total hours of intervention (external to the study), investigator-rated quality of caregiver participation, and parent-rated adherence as predictors of outcomes at the 12-month followup.[150] Greater caregiver quality of involvement predicted increased joint engagement (p<.05) but not other play skills or engagement outcomes. Parent-rated adherence or competence did not predict changes in any outcome. Number of hours of other intervention similarly did not predict any outcomes.[150]

Another RCT compared a 12-week intervention targeting parental responsiveness to children's playtime communication compared with a control group that received some parental education about developmental and educational needs.[156] Investigators also explored relationships among maternal synchronization (responsiveness to child communications) and long-term (12 months post-intervention) child language outcomes. Maternal synchronization was moderated by baseline maternal insightfulness (p<.05) and synchronization was greater in those mothers rated as insightful compared with non-insightful (effect size=0.31, p<.05). The link between short-term gain in maternal synchronization and long-term language (12 months post-treatment) gains was not moderated by maternal insightfulness, nor did initial language skills moderate the link between gains in maternal synchronization after 12 weeks and long term gains in expressive language.[156]

Intervention-Related Factors

Several studies of early intensive behavioral and developmental approaches evaluated potential effects associated with characteristics of the interventions themselves. In an RCT evaluating the LEAP program (full training compared with training manuals only), the students of teachers rated as having better intervention fidelity showed better outcomes on all measures.[84] In other studies assessing ABA-based early intervention, where examined, total hours of intervention per week were not associated with cognitive or adaptive outcomes, although hours were similar across intervention groups within each study (e.g., comparing half-day programs to other half-day programs).[76-78, 81-83] In a retrospective cohort study,[86] outcomes were related to age at enrollment, treatment duration, and higher baseline adaptive scores, with duration becoming nonsignificant after accounting for group membership (correlation of duration, group=.57, p<.01). A significant interaction emerged between age at enrollment and group membership, with younger starting age influencing outcomes for the treatment group but not control.[86]

In a study comparing 1:1 home-based ABA early intervention (both university-provided and privately-provided) to community-based treatment-as-usual, IQ remained stable for children in the community-based group and significantly declined for children who received university-provided ABA intervention (effect size=.49). This result is confounded by nonrandom assignment and the fact that at baseline, the university-based group had higher levels of ASD symptoms, lower levels of adaptive behavior, and fewer total intervention hours.[79, 80] Finally, in a prospective cohort study, hours of intervention did not correlate with outcomes.[77]

KQ3. Treatment Phase Changes That Predict Outcomes

No studies were identified that provided data on changes early in treatment that predicted outcomes.

KQ4. Treatment Effects That Predict Long-Term Outcomes

Few studies assess end-of-treatment effects that may predict long-term outcomes. Several early intensive behavioral and developmental interventions change measures over the course of very lengthy treatments, but such outcomes usually have not been assessed beyond treatment windows. One family of studies[140, 141, 148, 149] attempted to follow young children receiving early joint attention intervention until they were school-aged, but it failed to include adequate followup of the control group. It also involved children who were receiving many hours of uncontrolled interventions during the course of study.

KQ5. Generalization of Treatment Effects

Key Points

- Some studies of imitation and joint attention reported generalization of skills, setting, and individual/provider from the treatment context to a novel context.

Overview of the Literature

Twelve studies (reported in multiple publications) reporting on different interventions measured generalization of effects seen in treatment. However, several studies incorporated parent- or teacher-delivered components, which may promote generalization of skills to the home and classroom.[93, 101-104, 126, 129, 151-153, 155, 157, 158, 161, 166, 178, 196]

Detailed Analysis

Few studies measured generalization of effects seen in treatment; however, several studies incorporated parent- or teacher-delivered components, which may promote generalization of skills to the home and classroom. Among play/interaction-focused studies, one study of imitation training reported that gains in elicited imitation skills in the treatment group were also reflected in improvements in motor imitation skills, suggesting transfer of skills learned in the intervention.[152, 153] In a prospective cohort study assessing an intervention targeting pretend play, treatment group participants maintained their level of play dialog with novel toys when scripted dialog (a component of the initial intervention) was not provided.[161] Four interventions targeting joint attention skills based in preschools reported generalization: in one, increases in joint attention initiations with preschool teachers generalized to longer duration of joint engagement with mothers (10% increase from baseline compared with 2% decrease for control group).[155] Time jointly engaged with preschool teachers, however, did not increase. Two other studies[151, 157] suggested that joint attention skills training transferred to the classroom with treatment group participants spending less unengaged time and/or initiating more gestures. In a final study, children receiving either a joint attention or symbolic play interventions were able to generalize increases in responding to joint attention to a novel individual.[158]

Studies of early intervention approaches reported greater socially engaged imitation that generalized across settings and context in the treatment group,[103, 104] increased frequency of joint attention acts with an unfamiliar examiner,[93] and maintenance of skills over time and in the home and center-based setting.[101, 102] One study of a social skills intervention reported increases in participant social skills on intervention staff-rated but not parent-rated measures for either a Skillstreaming group or comparison group receiving a sociodramatic relational intervention.[129] In another social skills study, parents of children in a program enhanced for children with high functioning ASD reported improvements in their children's skills in various settings while parents of children in a traditional social skills group did not.[126] Finally, an analysis of Vineland and parental intrusiveness scores across income categories revealed no significant differences in one study of CBT, suggesting that the intervention is applicable across income levels.[166, 178, 196]

KQ6. Treatment Components That Drive Outcomes

We did not identify any studies meeting our inclusion criteria that addressed this question.

KQ7. Treatment Approaches for Children Under Age 2 at Risk for Diagnosis of ASD

Key Points

- Mean ages in studies identified were all under three years, and all studies address interventions that can be used with children under age 2
- Studies reported improvements in young children regardless of type of behavioral intervention

Overview of the Literature

This section presents the results of our literature search and findings regarding the use of treatment approaches in younger children who are at high risk of developing ASD based upon behavioral, medical, or genetic risk factors. In our 2011 review we identified two comparative studies (one good quality RCT[73] and one fair quality nonrandomized clinical trial[74]) addressing interventions for very young children. For the current review, we identified three studies[93, 97, 99] addressing treatment approaches for very young children. One crossover RCT was conducted in China (poor quality),[99] one prospective cohort study in Europe (poor quality),[97] and one RCT in the United States (fair quality).[93]

The mean age in most studies exceeded 24 months, although one[93] included children under age two. Mean ages were all under three years, and all studies address interventions that can be used with children under age 2. The average age for diagnosis of ASD in the United States is not until at least age 3, but a reliable diagnosis can be made as early as age 2.

One fair quality RCT was completed in the clinic and home settings.[93] Two poor quality studies, one crossover RCT and one prospective cohort study,[97, 99] included groups receiving in-home parent training.

Detailed Analysis

A fair quality RCT focused on enhancing parental responsivity and child communication.[93] It compared Hanen's More Than Words intervention to treatment-as-usual. The treatment group (n=29, mean age=21.11±2.71 months) received eight manualized group sessions with parents only and three in-home individualized parent-child sessions over a span of 3.5 months, whereas the control group (n=26, mean age=21.61±2.82 months) received no treatment or treatment as usual. There was no treatment effect on parental responsivity. The treatment group showed differential improvement on child communication depending on children's baseline object interest; children with lower levels of baseline object interest had greater growth in communication skills, whereas children with higher levels of object interest showed attenuated growth. Two poor quality studies compared parent training to lower intensity supportive interventions. Mean ages ranged from 25.33 to33.6 months. Both involved home visits and working with children and parents. The lower intensity treatment model, Autism-1-2-3, compared two groups that received the same series of ten thirty-minute child- and parent-training sessions, with one group having a lagged start date and serving as a control. It did not yield group differences on ASD symptoms, language skills, or parent stress scores.[99] The higher intensity model, Keyhole, incorporated elements of Hanen's More than Words and the TEACCH programs.[97] It compared 15-18 home visits over a 9 month period (n=35) targeting adaptive skills, ASD symptoms, and parent stress to a lower-intensity intervention model (n=26; 5 home visits, no additional services of supports). Compared with the control group, children in the treatment group showed improved adaptive, imitation, and communication skills, based only upon parent report. Mothers in the treatment group also reported improved health but did not report decreases in parenting stress.

In summary, young children who received behavioral interventions seemed to improve regardless of intervention type. It is important to note that none of the fair or better quality studies of young children compared children getting treatment to a no treatment control group. One poor quality study reported positive effects of treatment,[97] but the level of intervention intensity varied significantly between groups, and it is unclear whether the effects were due to intensity versus the treatment type. Potential modifiers of treatment efficacy include baseline levels of object interest.[93] Most outcome measures of adaptive functioning were based upon parent report, and the effect of parental perception of treatment efficacy on perception of child functioning was generally not explored.

Discussion

In this chapter, we summarize our findings about behavioral interventions for children with autism spectrum disorder (ASD). We provide an overview of the state of the literature by intervention type, detail the strength of evidence for the impact of each major intervention on relevant outcomes, and describe major issues and gaps in the current body of evidence.

Assessing the literature requires consideration of two main components, namely the observed effectiveness of interventions and our confidence that those effects will remain stable in the face of future research. Our confidence that the observed effect is the true effect and that perceived effectiveness is unlikely to change with future research is presented as strength of evidence, and can be insufficient, low, moderate or high. Strength of evidence describes the adequacy of the current research, both quantity and quality, and whether the entire body of current research provides a consistent and precise estimate of effect.

Methods for applying strength of evidence assessments are established in the Evidence-based Practice Centers' "Methods Guide for Effectiveness and Comparative Effectiveness Reviews"[55] and are based on consideration of five domains: study limitations, consistency in direction of the effect, directness in measuring intended outcomes, precision of effect, and reporting bias. We considered comparative studies—both RCTs and prospective and retrospective cohort studies—from the prior 2011 review plus the studies identified for the current review in determining strength of the evidence for major outcomes.

We required at least three fair studies to be available to assign a low strength of evidence rather than considering it to be insufficient. We required at least one good study for moderate strength of evidence and two good studies for high strength of evidence. In addition, to be considered "moderate" or higher, intervention-outcome pairs needed a positive response on two out of the three domains other than study limitations.

Once we established the maximum strength of evidence possible based upon these criteria, we assessed the number of studies and range of study designs for a given intervention-outcome pair, and downgraded the strength of evidence rating when the cumulative evidence was not sufficient to justify the higher rating.

Key Findings and Strength of Evidence

KQ1. Effects of Behavioral Interventions on Core and Commonly Associated Symptoms in Children With ASD

Early Intensive Behavioral and Developmental Interventions

Within this category, we included intensive behavioral and developmental interventions derived from applied behavior analysis (ABA) principles that targeted a broad range of skills and vulnerabilities. As such, this category includes defined manualized approaches that vary substantially in terms of their structure, approach and setting (e.g., University of California, Los Angeles [UCLA]/Lovaas, Early Start Denver Model [ESDM], Learning Experiences and Alternate Program for Preschoolers and their Parents [LEAP]) as well as more eclectically defined and delivered approaches. ABA is an umbrella term describing principles and techniques used in the assessment, treatment and prevention of challenging behaviors and the promotion of new desired behaviors. The goal of ABA is to teach new skills, promote generalization of these skills, and reduce challenging behaviors with systematic reinforcement. The principles and techniques of ABA existed for decades prior to specific application and study within ASD.

An additional set of interventions included here uses the principles of ABA to focus on key pivotal behaviors rather than global improvements. These approaches emphasize parent training (e.g., Pivotal Response Training, Hanen More than Words, social pragmatic intervention, etc.) and may focus on core social-communication skills or specific behaviors, such as initiating activities.

In the 2011 review, we identified 17 comparative studies of early intensive behavioral and developmental intervention[57-75] (described in 19 papers), of which six were RCTs (two good quality,[73, 75]four fair[57, 69, 71, 72]), five were nonrandomized trials (four fair quality,[64-68, 74]one poor[70]), four were prospective cohort studies (three fair[60, 61, 63] and one poor quality[62]), and two were poor quality retrospective cohort studies.[58, 59] We located 37 papers comprising 25 unique studies addressing early intensive behavioral and developmental interventions for this review update. Individual studies using intensive UCLA/Lovaas-based interventions, ESDM, the LEAP program, and eclectic variants reported improvements in outcomes for young children. Our strength of the evidence assessment considers studies from both the 2011 and current reviews.

Improvements were most often seen in cognitive abilities and language acquisition with less robust and consistent improvements seen in adaptive skills, core ASD symptom severity, and social functioning. Young children receiving high intensity ABA-based interventions over the course of extended time frames (i.e., 8 months--2 years) commonly display substantial improvement in cognitive functioning and language skills relative to community controls. However, the magnitude of these effects varies across studies and this variation may describe subgroups showing different responses to particular interventions. Intervention response is likely moderated by both treatment and child factors, but exactly how these moderators function is not entirely clear. Despite multiple studies of early intensive treatments, intervention approaches still vary substantially, which makes it difficult to tease apart what these unique treatment and child factors may be. Sample sizes of studies in the current review are typically small (total Ns ranging from 11-284, median=40), and some studies may be considered pilots for larger studies that may better elucidate questions about interventions intensity and moderators of effects. Further, the long-term impact of these early skill improvements is not yet clear, and many studies did not follow children beyond late preschool or early school years.

Studies of high intensity early intervention services also demonstrated improvements in children’s early adaptive behavior skills, but these improvements are more variable than those found for early cognitive and language skills. Treatment effects are not consistently maintained across studies. Many studies measure different adaptive behavior domains (which creates within scale variability) and some evidence suggests that adaptive behavior changes may be contingent upon baseline child characteristics, such as cognitive/language and ASD severity.

Evidence for the impact of early intensive intervention on core ASD symptoms is more limited and mixed than its impact on cognitive and adaptive behavior skills. Children’s symptom severity often decreased during treatment, but these improvements did not often differ from those of children in control groups. In fact, almost equal numbers of studies report treatment impact versus null treatment effects.

Since our previous review, there have been substantially more studies of well-controlled low intensity interventions that provide parent training in bolstering social communication skills. This growing literature base provides increasing data about the utility of such interventions for younger children with ASD, particularly when targeting social communication and language use.

However, although parent training programs reported that parenting behaviors were modified during interactions, data are more limited about improvement in broad developmental skills (such as cognition, adaptive behavior, and ASD symptom severity) beyond language gains for some children. Children receiving low-intensity interventions have not demonstrated the same substantial gains as seen in the early intensive intervention paradigms regarding cognitive and adaptive skills.

Strength of the Evidence

A growing evidence base suggests that some children receiving early intensive behavioral and developmental interventions (e.g., many hours of intervention a week over the course of 1–2 years) show substantial improvements in cognitive and language skills over time compared with children receiving low-intensity interventions, community controls, and eclectic non-ABA based intervention approaches. With this growing literature, our confidence (strength of evidence) in the effects of ABA-based early intensive approaches on cognitive and language outcomes is moderate, based on the need for additional research that identifies which groups of children benefit the most from specific high intensity approaches. Our strength of evidence in these high intensity interventions to affect adaptive behavior skills, social skills, and core ASD symptom severity is low. At present it is challenging to understand which approaches to high intensity intervention have the greatest effects for specific children (Table 12).

The strength of the evidence for parent training interventions is low for a positive effect of their impact on early language and communication skills and low for a positive impact on ASD symptom severity. The strength of the evidence is low for no effect on early cognition. Data are not yet sufficient in this literature base to understand impact on adaptive behavior skills. Available studies indicate variable responses, with modest improvement for some children in some approaches, but limited improvement in other parent training paradigms (Table 13).

Table 12. Strength of evidence for ABA-based early intensive behavioral and developmental studies

Outcome **Strength of Evidence Grade**	**Study Design** **Quality and Number of Studies (N Total Participants)**	**Study Limitations**	**Consistency**	**Directness**	**Precision**	**Reporting Bias**	**Finding**
IQ/cognitive **Moderate for positive effect**	RCT: 1 good, 2 fair (360) Prospective cohort: 6 fair, 2 poor (521) nRCT; 1 good, 4 fair (170) Retrospective cohort: 1 fair, 2 poor (182)	Medium	Consistent	Direct	Precise	Undetected	Young children receiving high intensity interventions display improvements in aspects of cognitive functioning. Most studies found that children in treatment and comparison groups both improved on cognitive skills, with children in high intensity early intensive intervention improving more than children receiving other types of services. Not all of these improvements were maintained at long-term followups. Many children display a positive response to this intervention, but the effect is somewhat variable across studies and may be indicative of subgroups with variable response. Across studies where positive effects were seen, the actual treatment impact on skills may vary based on child and intervention factors. A key limitation is that approaches across studies vary substantially, and it is hard to determine the effects of these unique studies on specific groups of children.

Table 12. Strength of evidence for ABA-based early intensive behavioral and developmental studies (continued)

Outcome Strength of Evidence Grade	Study Design Quality and Number of Studies (N Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding
Adaptive behavior **Low for positive effect**	RCT: 1 good, 1 fair (76) Prospective cohort: 7 fair, 2 poor (616) nRCT: 1 good, 4 fair (170) Retrospective cohort: 1 fair, 2 poor (182)	Medium	Inconsistent	Direct	Imprecise	Undetected	Most studies found that children in both treatment and control groups improved on adaptive skills. However, children in high intensity early intensive intervention improved more than children receiving other types of services. Not all group differences were maintained over long-term followup. There was variability within domains, such that some studies found improvement whereas others found declines in domain standard scores. For example, one study found a decrease in the motor skills domain for both treatment and control groups. An important limitation is that adaptive behavior was always measured by parent report (Vineland) rather than objective observation. Some studies suggested that adaptive behavior outcomes were dependent on baseline child characteristics, such as cognitive and verbal abilities and ASD severity.

Table 12. Strength of evidence for ABA-based early intensive behavioral and developmental studies (continued)

Outcome Strength of Evidence Grade	Study Design Quality and Number of Studies (N Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding
Symptom severity **Low for positive effect**	RCT: 1 good, 1 fair (332) nRCT: 1 good, 1 fair (74) Prospective cohort: 4 fair, 2 poor (470) Retrospective cohort: 1 fair (142)	Medium	Inconsistent	Direct	Imprecise	Undetected	Mixed impact on symptom severity; SOE is low for a positive effect on symptom severity because 2 good studies showed positive effects but multiple lower quality studies did not. More studies are needed to confirm results. Most control groups were also receiving treatment and also showed improvement, making it difficult to tease apart the effect of early intensive intervention specifically vs. any kind of intervention. Evidence emerged that baseline symptom severity predicts response to treatment, although the direction is inconsistent.
Language/ commun-ication **Moderate for positive effect**	RCT: 1 good, 2 fair (360) nRCT: 1 good, 3 fair (143) Prospective cohort: 6 fair, 2 poor (616)	Medium	Consistent	Direct	Precise	Undetected	Most studies found a positive effect of treatment on language/communication skills, although the specific domain of improvement (e.g., receptive vs. expressive language) varied across study. Some initial between-group differences disappeared at long-term followup. Some evidence that baseline child factors such as gender and cognitive skills influenced effects of treatment on language outcomes. A limitation is that some studies measured language using direct testing, whereas others only used the Vineland Communication domain.

Table 12. Strength of evidence for ABA-based early intensive behavioral and developmental studies (continued)

Outcome Strength of Evidence Grade	Study Design Quality and Number of Studies (N Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding
Social skills/social behavior **Low for positive effect**	RCT: 1 good, 1 fair (332) nRCT: 1 fair (34) Prospective cohort: 4 fair, 1 poor (406) Retrospective cohort: 1 fair (142)	Medium	Inconsistent	Direct	Imprecise	Undetected	Many studies found that treatment groups improved more than controls on measures of social skills, although a significant minority did not find any treatment effect. A significant limitation is that social skills were assessed almost exclusively using parent-reported standard scores on the Vineland.

ABA-applied behavior analysis; nRCT-nonrandomized controlled trial; RCT-randomized controlled trial

Table 13. Strength of the evidence for early intervention-parent training studies

Outcome Strength of Evidence Grade	Study Design Quality and Number of Studies (N Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding
IQ/cognitive **Low for no effect**	RCT: 3 fair (148) Prospective cohort: 1 good, 1 fair, 1 poor (142)	Medium	Inconsistent	Direct	Imprecise	Undetected	Most studies of parent-implemented ABA demonstrated no improvements in IQ relative to community-based interventions; in some studies worse outcomes were reported relative to center-based treatment. SOE is low for no effect due to heterogeneity in interventions and outcomes measured.

Table 13. Strength of the evidence for early intervention-parent training studies (continued)

Outcome Strength of Evidence Grade	Study Design Quality and Number of Studies (N Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding
Symptom severity **Low for positive effect**	RCT: 3 good, 3 fair (361) Prospective cohort: 1 good, 1 fair, 2 poor, (203)	Low	Inconsistent	Direct	Imprecise	Undetected	Many studies found that treatment groups had improved ASD symptoms relative to controls. However, a significant limitation is that the measure of symptom severity varied across studies and was inconsistently defined, from videotaped behavioral observations to standardized parent report forms like the GARS to interactive assessments like the ADOS. This makes it difficult to meaningfully compare outcomes across studies.
Language/ commun-ication **Low for positive effect**	RCT: 4 good, 6 fair, 1 poor (664) nRCT: 1 poor (22) Prospective cohort: 2 good, 2 poor (176)	Low	Inconsistent	Direct	Precise	Undetected	Parent training was associated with improvements in language (low SOE for improvements), but interventions and comparators were different across studies, as were the outcome measures. More studies are needed to confirm results. Of studies that assessed language outcomes, two possible child variables influencing treatment efficacy emerged. The first is that younger child age was associated with greater language improvements at followup in two studies. Second, another study found that higher baseline levels of object interest in children were associated with attenuated growth in communication skills.

ADOS = Autism Diagnostic Observation Schedule; GARS = Gilliam Autism Rating Scale; nRCT = nonrandomized controlled trial; RCT = randomized controlled trial

Social Skills Studies

In addition to the nine comparative studies assessing social skills included in the 2011 review (eight RCTs of fair[114-116] and poor[117-121] quality and one poor quality retrospective cohort[122]),we located 13 studies addressing interventions targeting social skills for this review update. The overall quality of studies improved compared with the previous review with two good quality and 10 fair quality studies, and one of poor quality. Social skills interventions varied widely in terms of scope and intensity. A few studies replicated interventions using the manualized Skillstreaming model; one reported longer term results from research on the Children's Friendship Training model. Other studies incorporated peer-mediated and/or group-based approaches, and still others described interventions that focused on emotion identification and theory of mind training. The studies also varied in intensity, with most interventions consisting of 1-2 hour sessions/week lasting for approximately 4-5 weeks. However, some of the group-based approaches lasted for 15-16 weeks.

Most studies reported some short term gains in either parent-rated social skills or directly tested emotion recognition. However, our confidence (strength of evidence) in that effect is low. While we now have higher quality investigations of social skills interventions demonstrating positive effects, our ability to determine the effectiveness of these interventions continues to be limited by the diversity of the intervention protocols and measurement tools (i.e., no consistent outcome measures used across studies). Maintenance and generalization of these skills beyond the intervention setting is also inconsistent, with parent- and clinician-raters noting variability in performance across settings. No studies reported harms of intervention.

Strength of the Evidence

The strength of evidence for the effect of social skills interventions on social outcomes for school aged children with ASD is low. All studies demonstrated benefit on at least one outcome measure, but a lack of consistency in the interventions or measures used makes it difficult to assess consistency or precision. Most studies relied on parent or teacher report of intermediate outcomes, although some studies have attempted to included ratings and outcomes (peer/teacher nominations, social networks/maps) with potential for assessment of generalization (Table 14).

Table 14. Strength of the evidence for social skills studies

Outcome Strength of Evidence Grade	Study Design Quality and Number of Studies (N Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding
Social skills/social behavior **Low for positive effect**	RCT: 2 good, 11 fair, 6 poor (730) nRCT: 2 fair (45) Retrospective cohort: 1 poor (117)	Medium	Inconsistent	Direct	Precise	Undetected	School-aged children diagnosed without concomitant cognitive and language deficits demonstrated short-term gains in social skills and emotion recognition. Maintenance and generalization of these skills beyond the treatment context had variable results. Social skills interventions varied widely in terms of scope and intensity.

nRCT = nonrandomized controlled trial; RCT = randomized controlled trial

Play- /Interaction-Focused Studies

Studies incorporating play or interaction-based elements have targeted either joint attention skills, early imitation skills, or focused play in younger children. No studies reported harms of intervention. Since our previous review, which included seven (reported in nine publications) comparative studies (two RCTs of fair[139-141] and five of poor[142-147] quality) addressing play- or interaction-based approaches, there have been substantially more studies of well-controlled joint attention interventions across a range of intervention settings (e.g., clinician, parent, teacher delivered). Regarding joint attention skills, interventions were delivered by parents, teachers, and interventionists over typically short durations (≤ 12 weeks). Three studies reported longer-term followup (≥12 months).[140, 141, 148-150, 156]As with other studies reported in this review, participants in play/interaction studies often received other early intervention services in addition to the targeted intervention, making disentangling effects of the intervention difficult.

This growing evidence base supports positive effects for young and preschool children with ASD, particularly when targeting joint attention skills themselves as well as related social communication and language skills. Although joint attention intervention studies certainly demonstrated changes within this theoretically important domain, data are more limited about their ability to improve broad developmental skills (such as cognition, adaptive behavior, and ASD symptom severity) beyond communication and language gains over time.

Specific and focal training regarding imitation skills utilizing naturalistic approaches to promote imitation (i.e., Reciprocal Imitation Training) has shown positive results in improving not only imitation skills, but potentially other social communication skills such as joint attention as well.[152, 153] Additionally, parent training in a variety of play-based interventions is associated with positive outcomes for encouraging early social communication skills (e.g., joint attention, engagement, play interactions), play skills, and early language skills.[154, 156, 160]

Strength of the Evidence

A growing evidence base reports on effects in children receiving early joint attention-related intervention in combination with other interventions show substantial improvements in joint attention and language skills over time. Within this growing literature, our confidence (strength of evidence) in this effect is moderate, based on the need for additional research that identifies which groups of children benefit the most from this approach and how this intervention relates to other ongoing concurrent offered interventions. Results from a variety of play-based interventions also suggest that young children often display short-term improvements in early play, imitation, language, and social interaction skills. However, our confidence in these estimates is low, and substantial evidence that these short-term improvements are linked to broader indices of change over time is lacking (Table 15).

Table 15. Strength of the evidence for play/interaction-based studies

Outcome Strength of Evidence Grade	Study Design Quality and Number of Studies (N Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding
Joint attention **Moderate for positive effect**	RCT: 3 good, 6 fair (305)	Low	Consistent	Indirect	Precise	Undetected	Selected joint attention skills consistently increased in treatment arms, but duration of effects is unclear. The SOE is lowered to moderate as children in most studies were also receiving other early intervention and disentangling effects is difficult.
Play skills **Low for positive effect**	RCT: 3 good, 3 fair, 3 poor (265) Prospective cohort: 1 poor (12)	Medium	Consistent	Direct	Precise	Undetected	Play skills increased in treatment arms but duration of effects is unclear. Imitation skills improved in treatment arms in 4 small, short-term studies and in the treatment and control arms in 1 study.
Language/ Commun-ication **Low for positive effect**	RCT: 4 fair (165)	Medium	Consistent	Direct	Imprecise	Undetected	Expressive but not receptive language skills generally increased in the treatment arms in 2 studies; expressive and receptive language improved in 1 study; prompted but not spontaneous communication improved in 1 study.
Social skills **Low for positive effect**	RCT: 1 good, 3 fair (173)	Medium	Consistent	Indirect	Precise	Undetected	Joint engagement or positive affect improved in treatment arms in 3 studies.

RCT = randomized controlled trial

Interventions Targeting Conditions Commonly Associated With ASD

Most studies in this category evaluated the impact of cognitive behavioral therapy (CBT) on co-occurring conditions, such as problem behaviors or anxiety, rather than core ASD symptoms or broader developmental domains (e.g., cognition, language, adaptive behavior). We identified nine comparative studies addressing interventions targeting conditions/behaviors commonly associated with ASD in the 2011 review. These studies included four RCTs[163-167] and one nonrandomized trial[168] of fair quality and three RCTs[169-171] and one prospective cohort[172] of poor quality.

Seven of nine RCTs identified for the current and 2011 review measured anxiety symptoms as a primary outcome.[164-166, 169, 171, 173, 174, 176-178, 182] Six of these studies reported significantly greater improvements in anxiety symptoms in the intervention group compared with controls. Two of these studies found positive effects of CBT on the core ASD symptom of socialization. The one RCT that did not find a significant benefit of CBT compared it to social recreational therapy rather than treatment as usual or a waitlisted control group. Although the CBT group had improved anxiety symptoms, this improvement did not significantly differ from participants receiving social recreational therapy.[174]

The studies examining the effects of CBT on anxiety had largely consistent methodologies and primarily conducted weekly 60-90 minute treatment sessions over a period of 4 months. All studies provided followup data reflecting treatment effects that lasted beyond the period of direct intervention. Two common factors limit the applicability of the results, however. Due to the nature of CBT, which is often language-intensive and requires a certain level of reasoning skills to make abstract connections between concepts, most studies included only children with IQs much greater than 70. This likely restricts the applicability of findings to the general population of people with ASD. Additionally, the CBT interventions described in these studies included both children and parents, suggesting that both components may be necessary for effective treatment.

These studies are encouraging regarding the use of CBT to treat anxiety in children with ASD. They also suggest that CBT could potentially be associated with improvements in socialization and communication, although these results were less robust and it is unclear if these improvements were beyond improvements related to the impact of ameliorated anxiety itself.

Additional data in the current review relate to parent training to address challenging behavior. Specifically, one fair quality study combined a parent training approach with risperidone. This combination significantly reduced irritability, stereotypic behaviors, and hyperactivity, and improved socialization and communication skills. However, these effects were not maintained at one-year post-treatment. The followup sample size also decreased from 124 to 87.[167, 179-181, 184]

Strength of the Evidence

A growing evidence base suggests that school-aged children with average to above average intelligence and comorbid anxiety symptoms receiving manualized CBT therapy show substantial improvements in anxiety compared with wait-list controls. Within this population our confidence (strength of evidence) in this effect is high. Our strength of evidence of the impact of this intervention for this same group on ASD symptoms (social communication functioning and repetitive behaviors) is low with future research likely affecting our understanding of the unique impact of this intervention (Table 16). With regard to parent training paradigms to address challenging behavior, results of parent training studies and parent training in addition to treatment with risperidone have demonstrated short-term improvements in terms of the frequency and intensity of challenging behavior. With few higher quality studies in this area, we considered the strength of the evidence to be insufficient (Table 17).

Table 16. Strength of the evidence for studies addressing interventions targeting commonly associated conditions

Intervention/ Outcome Strength of Evidence Grade	Study Design Quality and Number of Studies (N Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding
CBT							
Anxiety **High for positive effect in older children with IQ ≥70**	RCT: 6 good, 1 fair, 2 poor (413) nRCT: 1 fair (31)	Low	Consistent	Direct	Precise	Undetected	Most studies included older children with average IQs. Improvement in anxiety symptoms for greater for CBT vs. control group in 5/6 studies. The study that did not show improvement compared CBT to an active treatment instead of a waitlisted control. Improvement was maintained at followup. Some evidence emerged that CBT may be more effective for some types of anxiety disorders than others.
Symptom severity **Low for positive effect**	RCT: 2 good (81)	Low	Consistent	Direct	Imprecise	Undetected	Significant improvement in clinician- and parent-rated measures of anxiety severity in both studies with improvement maintained at followup. SOE is low based on only 2 small studies.

CBT = cognitive behavioral therapy; nRCT = nonrandomized controlled trial; RCT = randomized controlled trial

Other Behavioral Studies

In addition to two poor quality RCTs targeting neurofeedback[186, 187] and described fully in the 2011 review, we identified we identified six new studies (seven publications) evaluating interventions targeting sleep behaviors,[188-190] feeding difficulties in ASD,[191] and neurofeedback.[192-194] The neurofeedback RCTs reported some improvements on parent-rated measures of communication and tests of executive function. The clinical implications of changes in brainwave patterns reported in the studies are unclear, and the studies were small and short-term.[192, 194, 195] Three studies reported on sleep-focused interventions, with little positive effect of a sleep education pamphlet for parents in one,[188] improvements in sleep quality in treatment arms (melatonin alone, melatonin+CBT) in another,[189] and some improvements in time to fall asleep in one short terms RCT of sleep education programs for parents.[190] One poor quality study of parent education to mitigate feeding problems reported no significant effects.[191]

Strength of the Evidence

With few studies of additional behavioral interventions, all of limited quality, evidence was insufficient to evaluate the relative effect of other behavioral interventions on targeted outcomes including ASD symptom severity, problem behaviors, and sleep concerns as well as outcomes for Key Question 7 (interventions for very young children at risk for ASD diagnosis). Table 17 outlines interventions/outcomes for which we considered the strength of the evidence to be insufficient.

Table 17. Behavioral interventions/outcomes with insufficient strength of evidence

Intervention	Anger	Adaptive Behavior	Challenging Behavior	Executive Function	Feeding Behaviors	Language/ Communication	Outcomes for children age 0-2 yrs at risk for ASD diagnosis	Repetitive Behavior	Symptom Severity	Sleep Parameters	Social Skills
ABA-based early intensive behavioral and developmental interventions							✓				
CBT (commonly associated conditions)	✓	✓		✓							
CBT(other behavioral interventions)										✓	
Neurofeedback (other behavioral interventions)				✓		✓					✓
Parent training (commonly associated conditions)		✓	✓						✓		
Parent training targeting feeding behaviors (other behavioral interventions)					✓						
Play/interaction-based interventions			✓								
Sleep education pamphlet (other behavioral interventions)										✓	
Social skills						✓		✓	✓		

ABA = applied behavior analysis; ASD = autism spectrum disorder; CBT = cognitive behavioral therapy; yrs = years

Note: Checked outcome/intervention pairs=insufficient strength of evidence.

KQ2. Modifiers of Treatment Effects

Understanding the degree to which child characteristics (i.e., specific ASD-related difficulties and skills), treatment factors (e.g., type, duration, intensity), and systems (e.g., family, community) influence response to intervention could help professionals target treatments to the appropriate children and circumstances. However, as was reported in the 2011 review, few studies were clearly designed or powered to allow for analysis of heterogeneous effects. Primarily studies in this section are those in which potential correlates were identified that may be moderators, but have not been studied as such. These potential moderators should be assessed in properly designed and powered studies for this purpose.

Among early intensive ABA-based interventions potential modifiers or moderators, younger age at intake was generally associated with better outcomes for children; however, this finding was not present in some other studies.[123, 167, 179-181] Higher cognitive skills and higher adaptive behavior scores at baseline also were often associated with better outcomes across behavioral interventions, but the associations were not consistent. In general, children with lower symptom severity or less severe diagnoses improved more than participants with greater impairments. However, many studies (e.g., those of social skills, CBT) often restricted the range of participants' impairment at baseline, limiting understanding of intervention impact on broader populations. Studies assessing parental responsiveness to children's communication typically reported better outcomes in children whose parents were more aligned with the child's communication versus those who attempted to re-direct or were less synchronized with it.

Regarding intervention-related factors, duration of treatment had an inconsistent effect, with some studies reporting improved outcomes with greater intervention time and others reporting no association. Studies have often not been adequately designed or controlled in order to help identify true moderators of treatment. More often post-hoc evaluation of differences across groups has been examined.

KQ3. Treatment Phase Changes That Predict Outcomes

The reviewed literature offers little information about what specific early changes from baseline measurements of child characteristics might predict long-term outcome and response. Some evidence suggests that the best predictor of long-term outcome is not baseline characteristics at all, but rather the magnitude of change seen over the course of treatment (e.g., cognitive shifts in first years of early intensive treatments).[73, 85]

KQ4. Treatment Effects That Predict Long-Term Outcomes

Few studies assess end-of-treatment effects that may predict outcomes. Several early intensive behavioral and developmental intervention paradigms change measures over the course of very lengthy treatments, but such outcomes usually have not been assessed beyond treatment windows. One family of studies[140, 141, 148, 149] attempted to follow young children receiving early joint attention intervention until they were school aged, but this study failed to include adequate followup of control conditions. It also involved children were receiving many hours of uncontrolled interventions during the course of study.

KQ5. Generalization of Treatment Effects

Few studies included in this review explicitly measured generalization of treatment effects to different conditions or locations. Often, early intensive behavioral and developmental interventions attempted to index change by examining standardized cognitive skills, adaptive behavior, and language measures in addition to metrics of ASD symptoms. Presumably, changes measured on these instruments document important skills with potential impact in other areas. However, some caution is warranted: In some instances, the interventions themselves may actually target component skills of these assessments, particularly in the case of cognitive and language assessments.

The majority of the social skills and behavioral intervention studies targeting associated conditions attempted to index outcomes based on parent, self, teacher, and peer report of targeted symptoms (e.g., anxiety, externalizing behaviors, social skills, peer relations) at home, at school, and in the community. While such ratings outside of the clinical setting may be suggestive of generalization in that they improve outcomes in the daily context/life of the child, in most cases, these outcomes are parent reported and not confirmed with direct observation. Behavioral intervention studies rarely measured outcomes beyond the intervention period, and therefore we cannot assume that effects are maintained over time.

KQ6. Treatment Components That Drive Outcomes

We again did not identify any studies meeting our inclusion criteria that addressed this question.

KQ7. Treatment Approaches for Children Under Age 2 at Risk for Diagnosis of ASD

In the studies addressing interventions for younger children,[93, 97, 99] children who received behavioral interventions seemed to improve regardless of intervention type. None of the fair or good quality studies compared treatment groups to a no treatment control group. One poor quality study found positive differential effects of treatment,[97] but the level of intervention intensity varied significantly between groups, making it difficult to differentiate the effects of treatment intensity vs. type. Potential modifiers of treatment efficacy include baseline levels of object interest.[93] Most outcome measures of adaptive functioning were based upon parent report, and the effect of parental perception of treatment efficacy on perception (and report) of child functioning was generally not explored.

Findings in Relation to What Is Already Known

Other reviewers have also synthesized the impact of early intensive behavioral interventions. We rated three meta-analyses evaluating early intervention for children with ASD that were published since the 2011 review as good quality.[45, 52, 197] We also summarize two overview meta-analyses (not quality rated) addressing early intervention.[198, 199] Findings of other reviews assessing effects of early intensive ABA-based intervention largely align with our evaluation of the strength of evidence. Specifically, other reviews have demonstrated consistent impact on cognitive and language skills with fairly large effect sizes across these somewhat overlapping syntheses. These same investigations have also noted much less consistent changes in adaptive behavior skills. Further, these reviews have highlighted similar methodological concerns as noted in our current review: relatively small sample sizes, inclusion of nonrandomized studies, lack of standardized control groups, errors in interpretation of studies, and wide variations in the early intervention approaches assessed.

One Cochrane review compared early intervention to treatment as usual and included RCTs or controlled trials with participants under 6 years of age at intake.[45] The review included 5 studies (one RCT) with a total of 203 participants (mean age range: 30.2 to 42.5 months). The investigators rated all studies as having high risk of bias (low overall quality) and found positive effects for early intervention on all outcomes. Mean difference effect sizes were 0.76 for IQ (95% CI=0.40 to 1.11, p<.0001), 0.69 for adaptive behavior (95% CI=0.38 to 1.01, p<.0001) and ranged from 0.42 to 0.74 for measures of communication, socialization, and daily living skills (p values .0005 to .03). Tests of heterogeneity and small sample sizes precluded assessment of moderators of effects.

One meta-analysis of ABA-based interventions included studies with at least five children with ASD receiving at least 10 hours of intervention per week for 45 weeks. Twenty-two studies met criteria and assessed outcomes including IQ, receptive and expressive language, and adaptive behavior (Vineland composite and subscales). Studies included 323 patients (mean age 22.6 to 66.3 months, 55.6 to 97% male). Study quality was low to moderate, ranging from 1.2 to 3.6 on a five point scale (mean 2.5). Thirteen studies had control groups (six with random/quasi-random assignment). Positive effects were associated with ABA-based intervention in 18 studies assessing the outcome with a pooled effect size of 1.19 (95% CI: 0.91 to 1.47, p<.001). Similarly, ABA was associated with positive effects on language (general, expressive, and receptive, effect sizes from 1.07 to 1.48) and adaptive behavior (communication, socialization, motor skills, daily living skills domains as well as composite scores; pooled effect sizes ranging from 0.61 to 1.45). The effect size for the composite score was 1.09 (95% CI: 0.70 to 1.47, p<.001), and total treatment duration was associated with better adaptive behavior and language outcomes but not IQ. Results restricted to studies with control groups were consistent with results for all studies across outcomes. Across outcomes, effect sizes were generally slightly better for clinic-based approaches vs. parent-delivered. Similarly, the investigators note the potential for publication bias for the outcomes of IQ and language and the adaptive behavior domains of communication and socialization.[52]

Another meta-analysis of ABA-based early intervention included 11 small comparative studies (one RCT) with 344 children with ASD (mean age 33.56 to 65.68 months, 65.7% male).[197] The mean quality of studies as rated on the Downs and Black scale was 24.65 out of 32 (range 23-27). The early intervention group had greater gains on all variables assessed compared with control group participants, with full scale IQ improving by 11.98 points over improvements in the control group. Receptive and expressive language scores for the early intervention group compared with control each improved by more than 13 points, while improvements on Vineland subscales scores ranged from 4.96 to 10.44 points. Total effect sizes for daily living skills improvements were moderate (0.68) and were large for improvements in IQ, language, and adaptive behavior (effect sizes ranging from 0.91 to 2.00). The authors noted some evidence of publication bias. Table 18 outlines key characteristics of these early intervention meta-analyses.

A sequential or cumulative meta-analysis compiled data from 15 studies rated as adequate or high quality in five previously published meta-analyses (Eldevik 2009, Makrygianni 2010, Peters-Scheffer 2011, Reichow 2009, Spreckley 2009).[198] The 15 studies included 263 children with ASD. The sequential meta-analysis found a medium treatment benefit for early intervention vs. comparison interventions for the outcomes of intellectual functioning, language, and adaptive behavior. The magnitude of treatment benefit varied for outcomes when assessing pre- to post-differences in the early intervention group. For IQ, the standardized mean difference effect size for group differences was 0.61 ($p<.001$) and the pre to post differences in the early intervention group was 0.71 ($p<.01$). Between group effect sizes for adaptive behavior and language were also considered medium (0.60 and 0.72, respectively, p values <.001). Pre to post effect sizes for adaptive behavior (0.35, p=ns) and language (0.69, $p<.05$) did not reach sufficiency and could not be considered as providing evidence of medium pre to post treatment benefit. The authors note that meta-analyses for pre to post differences in adaptive behavior and language were underpowered.

An overview of four of the same meta-analyses noted above plus one additional (Virues-Ortega 2010) described methodologic limitations across the meta-analyses.[199] Limitations included small sample sizes in included studies, inclusion of nonrandomized studies, lack of standardized control groups, errors in interpretation of studies, and variations in the early intervention approaches assessed. Four of the five meta-analyses concluded that early intervention was an effective approach. For IQ, the weighted mean effect size across meta-analyses ranged from 0.38 to 1.19 and from 0.30 to 1.09 for adaptive behavior. Despite the need for additional research, particularly in understanding effective treatment component and child characteristics associated with optimal outcomes, the authors conclude that early intervention can produce significant effects on IQ and adaptive behavior for many young children with ASD.

Table 18. Summary of meta-analyses of early intervention approaches

Author, Year	Study Type As Defined In Review (N) Total Participants/Group (N)	Mean Participant Age (Months)	Treatment Intensity, Hours/Week Treatment Duration, Mean Months (Range)	Effect Sizes (95% CI)
Reichow 2012[45]	RCT: 1 Controlled trial: 4 Early intervention: 116 Comparison: 87	30.2-42.5	>24 hours/week 26.3 months (14-36)	IQ: 0.76 (0.40 to 1.11) Expressive language: 0.50 (0.05 to 0.95) Receptive language: 0.57 (0.20 to 0.94) Vineland adaptive behavior: 0.69 (0.38 to 1.01) Vineland communication: 0.74 (0.30 to 1.18) Vineland socialization: 0.42 (0.11 to 0.73) Vineland daily living: 0.55 (0.24 to 0.87)
Virues-Ortega 2010[52]	Total studies (type not defined): 22 Early intervention: 323 Comparison: 180	22.6-66.3	12-45 hours/week 4-34 months	IQ: 1.19 (0.91 to 1.47) Expressive language: 1.47 (0.85 to 2.08) Receptive language: 1.48 (0.96 to 1.97) General language: 1.07 (0.34 to 1.79) Vineland adaptive behavior: 1.09 (0.70 to 1.47) Vineland socialization: 0.95 (0.53 to 1.37) Vineland communication: 1.45 (1.02 to 1.88) Vineland daily living: 0.62 (0.30 to 0.93) Vineland motor skills: 0.71 (0.19 to 1.22)
Peters-Scheffer 2011[197]	RCT: 1 Pre-test/post-test with control: 10 Early intervention: 168 Comparison: 144	33.65-65.68	12.5-38.6 hours/week 10-24+ months	IQ: 2.00 Non-verbal IQ: 0.98 Expressive language: 1.10 Receptive language: 2.91 Vineland adaptive behavior: 0.91 Vineland communication: 1.32 Vineland daily living: 0.68 Vineland socialization: 1.49

CI = confidence interval; IQ = intelligence quotient; n = number; RCT = randomized controlled trial

Applicability

ASD is characterized by significant heterogeneity within the population. Variation in both core and associated symptoms across and within children over time is substantial. Individual therapies are developed and tested to ameliorate specific symptoms or groups of symptoms, often in a fairly circumscribed subset of children. Ideally, research on therapies for ASD should target specific children most likely to benefit from a particular focus; thus details on the population, intervention, comparator, outcomes, and setting (PICOS) for each intervention category are provided in Appendix G. These data may help to support translation of our findings and assessment of the applicability of each for differing circumstances and children.

Furthermore, although interim, clinically based improvement is important, longer term functional outcomes are the goal for ASD interventions. In terms of followup for assessing durability of effects, most studies report on outcomes collected immediately post-treatment or within 3 months of treatment (roughly 75% of studies in the behavioral literature), although more studies than in our previous report attempt to assess impact over the course of much longer timespans. Additional research is needed on the degree to which changes observed during treatment translate to functional outcomes over time should treatment be discontinued. Importantly, ASD is often construed as a lifespan disorder and there has not yet been research assessing the long-term functional impact of treatment in childhood on lifespan development and functioning.

Studies of early intensive behavioral and developmental interventions were conducted primarily in preschool age and early school age children (i.e., typically children initially ages 1.5–7 years) and as such questions remain about how these approaches apply to and benefit younger children diagnosed with or at-risk for ASD. The cognitive, language, and adaptive behavior profiles of participants included in these studies were generally in line with those seen in the community (i.e., typically marked by substantial impairment/delay, but with some children with more intact early cognitive/language profiles). However, the availability and accessibility of the approaches studied are substantially limited in many community based settings. That is, the studies were often either conducted in highly controlled environments (e.g., university supported intervention trials) or the methodology was not well-described (i.e., non-manualized approaches). Thus, the generalizability (i.e., applicability) of these methods to common practice should be assessed carefully. Even available manualized interventions require high degrees of specialization and training that will likely continue to make translation into common practice difficult.

Studies of parent training interventions and play-based interventions for preschool children, often emphasizing principles of ABA aligned with current practice and the target populations that are typically referred for these services. Training programs often included components to improve social communication skills such as joint attention, play-based interactions, and pragmatic language approaches; interventions were conducted for approximately 1–4 hours/week with parents asked to introduce learned techniques within natural settings. Several programs offered manualized versions of training that can be adopted in other settings with appropriate training. Again the availability of providers capable of translating these programs may be limited in some community settings.

Most studies of social skills interventions targeted elementary school aged children (between 6 and 13 years old) with few studies targeting preschool age children, although such interventions may be important in this younger age group. Most studies also excluded children with IQ falling outside of the average range and certainly those below 70. Therefore, evidence on social skills interventions is likely applicable to older, higher functioning children only. Similarly, CBT for commonly associated conditions was targeted toward older children with gross average cognitive abilities and comorbid anxiety disorders. The effectiveness of both of these types of interventions in other groups of children with ASD is currently unknown.

Implications for Clinical and Policy Decisionmaking

This review may be useful to groups producing guidelines for practice, including professional organizations, state-level Medicaid medical directors, Federal entities and insurers. It provides an overview of available behavioral interventions and benefits observed to date that clinicians may find useful in making individual clinical recommendations to their patients and patient families. The larger body of literature of higher quality than in the previous review provides continued support for earlier conclusions that behavioral interventions can be beneficial for some children. Guidelines developed on the basis of the prior review warrant updating based on the level of new information and the degree to which strength of evidence shifted in the current review.

The evidence in favor of the efficacy of several types of behavioral interventions has increased, but there remains clinical uncertainty about whether and how individual children will benefit from specific programs of intervention, which creates a challenge for implementation. Further, some interventions are limited in terms of the subset of the ASD population they are designed to treat (e.g., CBT and social skills interventions for older children with relatively intact cognitive abilities). In addition, pragmatic issues such as the availability of skilled providers and interventions themselves, resources to pay for interventions, as well as family considerations and preferences, may influence and guide treatment decisions.

Although there is increasing evidence that children with ASD who receive appropriate behavioral intervention can have substantial improvements in functioning, we have limited knowledge of the actual numbers of families able to access such services on a community level. Young children with ASD (below 36 months) are often eligible for services through Early Intervention (Part C) programs, with all states and eligible territories currently providing such programs. These systems presumably allow children to receive services based on risk prior to diagnosis as well as post-diagnosis, but services may range in intensity and focus. Children who are over age 3 often have access to additional services through their school district, but the nature of appropriate services provided within these systems varies. A majority of U.S. states (estimated at over 35[200]) have enacted ASD insurance reform legislation that provides for specific access to evidence-based intervention services through private insurance. Again the availability and accessibility of resources for referral varies dramatically across communities

Limitations of the Review Process

We limited this update to comparative studies of behavioral interventions and included only those with at least 10 individuals. Thus, we did not include data from pre-post studies or those with a very small number of children. These would include single-subject design studies that are helpful for understanding focused questions of short-term efficacy in individual children, and that may be useful for explicating mechanisms of action. These studies are less able to contribute to the body of evidence that we sought on population level and generalizable effects. Users of this review may want to take those studies into account as context when applying our findings.

We limited our review to English language studies, not finding evidence that we were missing relevant research in other languages. We did not do a quantitative synthesis given the substantial heterogeneity of the literature base, but we recognize that this lack of synthesis may mitigate the ease with which the findings are applied. Therefore we have tried to provide substantial description that will help end users apply the findings.

Limitations of the Evidence Base

Despite improvements, the existing literature still has significant methodological concerns that in many ways continue to limit the strength of these conclusions. Evidence for the impact of intensive ABA-based interventions on cognitive, language, adaptive skills, and ASD symptoms also highlights important limitations of current treatment modalities. First, even children who demonstrate clinically significant improvements in these areas often continue to display substantial impairment in these same and other areas. Second, not all children receiving intensive ABA-based intervention showed robust improvements in these domains. Thus, although this updated review makes it clearer that early intensive ABA-based intervention improves early impairment related to ASD, it is still challenging to describe the ultimate effect of these improvements in terms of long-term functional and adaptive outcomes on an individual level. Further, although children receiving early intensive developmental and behavioral intervention commonly display substantial improvements, the magnitude of these effects varies across studies and may indicate subgroups showing variable responses to particular interventions. Intervention response is likely moderated by both treatment and child factors. Despite multiple studies of early intensive treatments, intervention approaches still vary substantially, which makes it difficult to tease apart what these unique treatment and child factors may be. Similarly, data on provider type and qualifications are variably reported, and the impact of provider characteristics on treatment outcomes is unclear. Further, researchers have not commonly utilized explicit methodologies or analyses to help elucidate moderation of treatment response across studies. As such, the current evidence is insufficient to adequately identify and target children most likely to benefit from specific interventions.

When examining treatment outcomes, many early intervention studies found that children in all groups improved on cognitive, adaptive, and ASD symptom measures regardless of intervention type, although the degree of improvement was often greater in the treatment group. Results were often confounded by nonrandom assignment of participants, including assignment based on child characteristics (such as having the skills necessary to participate in intervention setting) or parental preference. The latter is especially problematic when outcomes are measured by parent report, given some evidence that parental stress influenced parent perceptions of child outcomes. Additionally, in most studies, both enrolled and control/waitlisted children were receiving concomitant interventions, the magnitude of which was inconsistently documented and controlled for in analyses.

A remaining significant challenge to interpreting the early intensive intervention literature relates to how interventions are described and implemented (see Appendix F for further characterization of the early intervention studies in this review). Although researchers are increasingly attempting to manualize approaches as well as operationalize and measure treatment fidelity, most of the body of literature categorized in this report as "early intensive behavioral and developmental intervention" remains an eclectic grouping. This category of intervention presently groups different treatment approaches (i.e., developmental, intensive behavioral, center based, and combinations), intensity (12 hours over 3 months vs. 30 hours over 1 week), and duration (weeks to years); varied inclusion and baseline assessment criteria; children of varying ages (intake age ranging from 18 months to 7 years); and many different outcome measurements over different periods of time (weeks to years). Manualizing intensive interventions to be delivered over the months and years for a very heterogeneous patient population is intrinsically challenging. However, recent progress toward this end has shown that children will often respond differentially to early intensive approaches. Unfortunately, we do not yet understand how these specific intervention approaches differentially affect specific subgroups of children with ASD.

Few studies directly compared the effects of well-controlled treatment approaches, instead comparing interventions to non-specific "treatment as usual." Additionally, little data on the practical effectiveness or feasibility of these treatments beyond research studies exist, and questions remain about whether reported findings would generalize on a larger scale within communities. Furthermore, the studies conducted have used small samples, drastically different treatment approaches and duration, and different outcome measurements. Similarly, no studies in this category reported harms of intervention in terms of child, family, or system impact.

Although there was a fairly robust evidence base on CBT, the literature lacks head to head comparisons of treatment or controlled comparisons of combinations of treatments despite the fact that most children are undergoing multiple concurrent treatments. Although well designed, the sample sizes are quite modest. Additionally, the CBT approaches were modified for children with ASD and oftentimes manualized by the authors themselves, which highlights the need for replication by outside investigators. Lastly, the only study that did not show significant benefit in the CBT intervention group compared with it to an active treatment control as opposed to a waitlist or treatment as usual control.[174] This suggests that more studies including active control groups are needed to examine if CBT reduces anxiety more than other treatment modalities.

Research Gaps and Needs

Several behavioral treatment approaches report positive outcomes in children with ASD, increasingly using rigorous designs. Despite this recent and improved rigor, treatments remain understudied. In addition, few studies have attempted to systematically replicate findings of previous work.

Given the heterogeneity of the expression of ASD within and across children, a critical area for further research is understanding which children are likely to benefit from particular interventions. To date, studies have failed adequately to characterize interventions or children receiving intervention such that we can better understand which children are most likely to experience positive outcomes and why. Further, our understanding of early indicators of treatment response is extremely limited, such that evidence-based changes in treatment planning based on an observed response or lack thereof are not possible. This is important to parents, providers, and families as they often want to know not only when a treatment is working, but when limited benefit of treatments may suggest pursuing other treatment options. Similarly, research is lacking on the durability of treatment gains and approaches needed to maintain gains.

Again the accumulated evidence base suggests that although children receiving early intensive intervention demonstrate substantial gains in several areas of functioning (e.g., cognitive ability, language, adaptive, ASD symptoms) on a group level, not all children receiving early intensive intervention demonstrate robust gains. Currently, the evidence suggests some children will show dramatic improvement, others will display robust improvement in some areas with continued areas of vulnerability in others, and other children will show more moderated response to treatment overall. It is also unclear how similar groups of children will perform at differing levels of intensity of interventions or different treatment approaches and methods.

Child characteristics like baseline cognitive, language, adaptive skill, and ASD symptoms may correlate with treatment outcome; however, such correlational data provides limited information in making predictions of what treatments will work best for individual children. It is possible that meta-analyses of individual patient data may provide additional information for identifying subgroups of responders.

Further, intensive, comprehensive intervention strategies are by their very nature often multi-component. Data on whether specific functional components of the interventions drive effectiveness are currently unavailable as are data on mediators of change. Finally, the intervention research often fails to describe whether treatment effect is modified by family, culture, available resources, and stress. Early intensive behavioral and developmental approaches therefore warrant further research to understand individual response and benefit in the short and long-term across heterogeneous populations. Similarly, evaluations of intervention delivered by community providers are important for comparing effects of such approaches with those of interventions delivered in controlled research environments. Such evaluations are complicated by the complexity of community systems and methodologic challenges including creating similar treatment and control groups and maintaining fidelity; however, they will be increasingly valuable for scaling intervention for ASD. Also important in addressing this gap is improving our currently limited understanding of the effects of provider training and provider characteristics on outcomes of treatment.

A primary methodological concern relates to outcome measurement. Intervention research in the field of ASD has often relied on various and differing ways of marking change, which has limited our ability to understand change within and across individual studies. [201] The manner in which outcomes are operationalized in many studies is often problematic as well. Quite often outcome is operationalized and studied in terms of change on standardized measures of ability referencing normative populations (i.e., IQ measurement, adaptive behavior scores), which may not necessarily be an appropriate or adequate method for measuring or predicting early treatment response, changes in quality of life, or long-term functional outcomes. Such measurement, while providing data that can be compared with that in typically developing populations, may unfortunately miss important information about changes that are relevant within the ASD population. More simply, it is unclear that measures of cognitive ability, language, and ASD diagnostic symptoms are actually ideal or adequately sensitive methods for measuring frequency, intensity, and impairment in children with ASD. Research on appropriate methods to capture meaningful change will be critical to advance our understanding of behavioral interventions. In addition, while studies have improved in reporting a priori determined primary and secondary outcome measures, continued improvements in reporting will benefit the field.

In some aspects of the literature treatments with some replicated studies have emerged. Specifically both social skills interventions and cognitive behavioral interventions for anxiety have demonstrated short-term benefit for some children with ASD. However, this literature focuses almost entirely on older children with ASD and intact cognitive skills. Understanding the impact or lack thereof of such interventions for others with ASD is important. Further, this work has often relied on parent or teacher reports of functioning to gauge change. Such reporting may be useful as a preliminary index or potentially as a component of a broader measurement strategy attempting to index change, but reliance these ratings provides only an intermediate and often biased assessment of change, with potentially very limited value to understanding how interventions translate in to meaningful long-term functional outcomes.

Because the treatment process for ASD is typically intensive and often requires highly specific and well-trained individuals to deliver to fidelity, questions of feasibility and accessibility are pertinent but largely understudied. Explicit evaluation of treatments of highest impact in community settings as well as studies explicitly evaluating settings and providers would benefit our ability to understand impact and implementation.

Finally, this literature lacks comparisons of interventions and combinations of interventions (e.g., medical interventions, with behavioral interventions, with educational interventions, with allied health interventions), despite the fact that most children are undergoing multiple concurrent treatments. The current review also focused solely on behavioral interventions. Systematic reviews of studies of interventions in other categories (e.g., medical, allied health) would provide useful information for clinicians, researchers, policy makers, and families.

Conclusions

Since our previous review in 2011, we have seen a significant increase in the quality of studies investigating behavioral interventions. Of the 45 comparative studies of behavioral interventions (29 RCTs) in the 2011 review, we considered only two as good quality. Among the new studies of behavioral interventions described in this current review, 19 studies are good quality, and 48 of the 65 included studies are RCTs.

These improvements allow us to make some stronger conclusions about certain elements of the behavioral intervention literature. Considerable and consistent evidence suggests that early behavioral and developmental intervention based on the principles of ABA delivered in intensive (≥15 hours per week) and comprehensive (i.e., addressing numerous areas of functioning) form can significantly affect the development of some children with ASD. The current review includes RCTs of the UCLA/Lovaas-focused approach, a developmentally focused ESDM approach, a school delivered training (LEAP), as well as prospective comparisons of eclectic variants of ABA approaches. Across approaches, children receiving early intensive behavioral and developmental interventions have demonstrated improvements in cognitive, language, adaptive, and ASD impairments compared with children receiving low-intensity interventions and eclectic non-ABA based intervention approaches.

Since our previous review, there have also been substantially more studies of well-controlled low intensity interventions including parent training aimed at social communication skills. This growing evidence base suggests that such interventions may have positive results in very young children's social communication and language use. However, although parent training programs certainly modified parenting behaviors during interactions, data are more limited about their ability to improve broad developmental skills (such as cognition, adaptive behavior, and ASD symptom severity) beyond short-term language gains for some children.

A growing number of studies of improved quality have demonstrated benefit of social skills interventions on at least one outcome measure, but a lack of consistency in the interventions studied and outcome measures utilized makes it difficult to understand the consistency or precision of impact across intervention modes. Further, social skills interventions have also been limited to a restricted range of children to date.

A growing evidence base suggests that children receiving targeted play-based interventions (e.g., joint attention, imitation, play-based interventions) demonstrate improvements in early social communication skills. Children receiving targeted joint attention packages in combination with other interventions show substantial improvements in joint attention and language skills over time. Young children in play-based interventions may display short-term improvements in early play, imitation, joint attention, and interaction skills. However, there is not substantial evidence that these short-term improvements are linked to broader indices of change over time.

CBT for associated conditions such as anxiety has the largest number of high quality studies in the current review. A strong evidence base suggests that school-aged children with average to above average intelligence and comorbid anxiety symptoms receiving manualized CBT therapy show substantial improvements in anxiety compared with wait-list controls. Importantly, CBT therapy is often targeted, delimited, and has numerous manualized approaches available for study. Further, CBT intervention for anxiety has been studied within a restricted population to date (e.g., average to above average cognitive skills with comorbid anxiety).

In sum, a growing evidence base suggests that behavioral interventions are associated with positive outcomes for children with ASD. Despite improvements in the quality of the included literature, a need remains for studies of interventions across settings and continued improvements in methodologic rigor. Substantial scientific advances are needed to enhance our understanding of which interventions are most effective for specific children with ASD and to isolate elements or components of interventions most associated with effects.

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Abbreviations

ABA	Applied Behavior Analysis
ABC-H	Aberrant Behavior Checklist – Hyperactivity/Noncompliance
ADI-R	Autism Diagnostic Interview - Revised
ADOS	Autism Diagnostic Observation Schedule
AEPS	Assessment Evaluation and Programming System for Infants
AHRQ	Agency for Healthcare Research and Quality
ASD	Autism Spectrum Disorder
BASC	Behavioral Assessment System for Children
CAM	Complementary and Alternative Medicine
CARS	Childhood Autism Rating Scale
CBT	Cognitive Behavioral Therapy
CER	Comparative Effectiveness Review
CGI-I	Clinical Global Impression-Improvement
CGI-S	Clinical Global Impression-Severity
DIR	Developmental, Individual Differences, Relationship-based model
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4^{th} Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5^{th} Edition
DQ	Developmental Quotient
EEG	Electroencephalogram
EPC	Evidence-based Practice Center
ERIC	Educational Resources Information Clearinghouse
ESDM	Early Start Denver Model
GARS	Gilliam Autism Rating Scale
HSQ	Home Situations Questionnaire
IQ	Intelligence Quotient
KQ	Key Question
JASP/ER	Joint Attention and Symbolic Play/Engagement and Regulation Intervention
LEAP	Learning Experiences and Alternative Program for Preschoolers
M-CHAT	Modified Checklist for Autism in Toddlers
MEHRIT	Milton and Ethel Harris Research Initiative Treatment Program
NR	Not Reported
nRCT	Non-Randomized Controlled Trial
NS	Not Statistically Significant
PARS	Pediatric Anxiety Rating Scale
PDD-NOS	Pervasive Developmental Disorder- Not Otherwise Specified
PECS	Picture Exchange Communication System
PEER	Peer-Mediated Social Skills Training
PICOTS	Population, Intervention, Comparator, Outcomes, Timing, and Setting
RCT	Randomized Controlled Trial
SCARED	Screen for Childhood Anxiety Related Emotional Disorders
SDARI	Sociodramatic Affective Relational Intervention
SOE	Strength of the evidence
SS GRIN-HFA	Social Skills Group Intervention – High Functioning Autism
TEP	Technical Expert Panel
TOO	Task Order Officer
TEACCH	Treatment and Education of Autistic and Related Communication Handicapped Children
UCLA	University of California, Los Angeles

Appendix A. Search Strategies

Table A-1. PubMed search strategies

Search terms		Search results
#1	Autistic[tiab] OR autism[tiab] OR autistic disorder[mh] OR asperger syndrome[mh] OR child development disorders, pervasive[mh:noexp] OR asperger[tiab] OR asperger's[tiab] OR aspergers[tiab] OR pervasive development[tiab] OR pervasive developmental[tiab] OR pdd[tiab]	26442
#2	therapy[sh] OR therapeutics[mh] OR teaching[mh] OR psychotherapy[mh] OR treatment outcome[mh]	6660534
#3	#1 AND #2 AND eng[la] AND humans[mh]	6377
#4	newspaper article[pt] OR letter[pt] OR comment[pt] OR case reports[pt] OR review[pt] OR practice guideline[pt] OR news[pt] OR editorial[pt] OR historical article[pt] OR meta-analysis[pt] OR legal cases[pt] OR published erratum[pt] OR congresses[pt]	4864950
#17	#3 NOT #4 AND 2000:2013[dp]	2505

Key: [mh] Medical Subject Heading; [tiab] title/abstract word; [pt] publication type; [sh] subheading; [dp] publication date; [la] language; [pt] publication type

Table A-2. PsycINFO search strategies (ProQuest interface)

Search terms		Search results
#1	SU.EXACT.EXPLODE("pervasive developmental disorders" or "aspergers syndrome" or "autism")	24282
#2	SU.EXACT.EXPLODE("Treatment") OR SU.EXACT.EXPLODE("Medicinal Herbs and Plants") OR SU.EXACT.EXPLODE("Dietary Supplements") OR SU.EXACT.EXPLODE("Nutrition") OR SU.EXACT.EXPLODE("Vitamins")	562313
#3	#1 and #2 and DTYPE(journal article) and (ME(empirical study) or ME(field study) or ME(followup study) or ME(longitudinal study) or ME(prospective study) or ME(qualitative study) or ME(quantitative study) or ME(retrospective study) or ME(treatment outcome/clinical trial)) and LA(English), limited to peer-reviewed journals and human population, limited to publication date 2000 to present	1089**

Key: DE subject descriptor; PT publication type; ME methodology; AE age group

Table A-3. ERIC search strategies (ProQuest interface)

Search terms		Search results
#1	SU.EXACT.EXPLODE("Autism") OR SU.EXACT("Pervasive Developmental Disorders") OR SU.EXACT.EXPLODE("Asperger Syndrome")	9380
#2	SU.EXACT.EXPLODE("Therapy") OR SU.EXACT.EXPLODE("Intervention") OR SU.EXACT.EXPLODE("Outcomes of Treatment") OR SU.EXACT.EXPLODE("Special Education") OR SU.EXACT.EXPLODE("Dietetics") OR SU.EXACT.EXPLODE("Nutrition") OR SU.EXACT.EXPLODE("Adapted Physical Education") OR SU.EXACT.EXPLODE("Therapeutic Environment") OR SU.EXACT.EXPLODE("Food")	80298
#3	#1 and #2 and LA(English), limited to peer reviewed journals, 2000 to present	1782**

Key: DE subject descriptor, KW keyword

Appendix B. Screening and Quality Assessment Forms

Abstract Review Form

REF ID: **Reviewer Initials:**			
1. Addresses **intervention approach and outcomes** for young children (0-12 years) with ASD or at risk for ASD.	Yes	No	Cannot Determine
2. Original research (includes primary research studies and systematic reviews and meta-analyses)	Yes	No	Cannot Determine
3. Includes individuals with ASD in target age range (0-12 years).	Yes	No	Cannot Determine
4. Addresses one of the following: • treatment modality for ASD intended to modify core symptoms of ASD in individual diagnosed/at risk • short or long term outcomes of treatment intended to modify core symptoms/co-morbidities of ASD in individual diagnosed/at risk; outcomes include parent or child QOL • modifiers of treatment outcomes in young children with ASD • generalization of treatment outcomes to another person/context • drivers of treatment outcomes • harms/adverse effects associated with treatment intended to modify core symptoms of ASD in individual diagnosed/at risk	Yes	No	Cannot Determine
5. Eligible study size (at least 10 total participants in target population)	Yes	No	Cannot Determine
6. If excluded, retain for review of references or background/contextual questions (screening or treatment resources, stability of diagnosis)?	Yes	No	Cannot Determine
Comments:			

Full Text Review Form

REFID: **Reviewer Initials:**		
1. Does the study include participants ages 2-12 (mean age+SD less than or equal to 12 yrs 11 mo) diagnosed with ASD or 0-2 at risk for ASD diagnosis?	Yes	No
2. Is the study original research (includes systematic review or meta-analysis)?	Yes	No
3. Does the study include at least 10 individuals with ASD in the target age range?	Yes	No
4. Does the study provide data related to at least one of the following? • Effects of intervention on core ASD symptoms OR commonly associated symptoms (e.g., motor, sensory, medical, mood/anxiety, irritability, IQ/cognition, and hyperactivity) • Modifers of treatment outcomes • Generalizability of intervention effects to other contexts (e.g., people, places, materials) • Intervention components that drive outcomes • Harms of intervention • Child or caregiver quality of life	Yes	No
5. If excluded, retain this paper for background or review of references?	Yes	No
Comments:		

Quality/Risk of Bias Rating Form

REFID:____________ REVIEWER:_____________

Question				
Study Design				
Did the study employ a group design?	Yes	No		
Were the groups randomly assigned?	Yes	No		
Was there an appropriate comparison group?	Yes	No or NR		
If an RCT, was randomization done correctly?	Yes	No	NR	NA (non-RCT)
Participant Ascertainment/Inclusion				
Was a valid diagnostic approach for ASD used within the study, or were referred participants diagnosed using a valid approach?	A. clinical DSM-IV-based diagnosis + ADI-R and/or ADOS B. [clinical DSM-IV-based diagnosis + other] OR [ADOS + other, such as SRS, CARS, SCQ, CAST, ASSQ, OR STAT, MCHAT for under 30 months] C. Only clinical DSM-IV-based diagnosis OR Only ADOS D. Neither clinical DSM-IV-based diagnosis NOR ADOS			
Was the sample clearly characterized (e.g., information provided to characterize participants in terms of impairments associated with their ASD, such as cognitive or developmental level)?	Yes	No or NR		
Were inclusion and exclusion criteria clearly stated?	Yes	No or NR		
Do the authors report attrition?	Yes	No		
Were characteristics of drop-out group evaluated for differences with the participant group as a whole?	Yes	No or NR	NA or minimal attrition	
Intervention				
Was the intervention fully described?	Yes	No or NR		
For behavioral studies, was treatment fidelity monitored in a systematic way?	Yes	No or NR	NA	
Did the authors measure and report adherence to the intended treatment process?	Yes	No or NR		
Did the authors report differences in or hold steady all concomitant interventions?	Yes	No or NR		
Outcome Measurement				
Did outcome measures demonstrate adequate reliability and validity	Yes	No or NR		

(including interobserver reliability for behavior observation coding)?			
Were the primary & secondary outcomes clearly specified a priori?	Yes	No or NR	
Were outcome data collected from sources appropriate to the target outcome (e.g. parent report, teacher report, direct behavior observation)?	Yes	No or NR	
Were outcomes coded by individuals blinded to the intervention status of the participants?	Yes	No or NR	
Analysis			
Was an appropriate statistical analysis used?	Yes	No	
a. For RCT's, was there an intent-to treat analysis?	Yes	No	NA
b. For negative studies, was a power calculation provided?	Yes	No	NA
c. Did the study correct for multiple testing?	Yes	No	NA
d. For observational studies, were potential confounders and effect measure modifiers captured?	Yes	No	NA
e. For observational studies, were potential confounders and effect measure modifiers handled appropriately?	Yes	No	NA
External Validity			
Were outcomes measured in at least one context outside of the treatment setting?	Yes	No or NR	
Were outcomes measured in natural environments to assess generalization?	Yes	No or NR	
Were follow-up measures of outcome conducted to assess maintenance of skills at least 3 months after the end of treatment?	Yes	No or NR	NA
Other			
Record duration of intervention:			
Timing of last follow-up after completion of intervention (e.g., immediately, 3 months after end of intervention):			

Note: See more information on quality approach in Appendix D

Appendix C. Evidence Table

Table C-1. Evidence table

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Boyd et al., 2013[1] **Country:** US **Intervention setting:** Public school classrooms **Enrollment period:** NR **Funding:** Institute of Education Sciences, US Department of Education **Design:** Quasi-experimental study	**Intervention:** LEAP and TEACCH, 6-week time window at the beginning and end of school year (at least 6 months apart) **Assessments:** parent; teacher; researchers **Groups:** **G1:** TEACCH **G2:** LEAP **G3**: non-model specific practices **Provider:** teachers **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:**	**Inclusion criteria:** Teachers**:** • public school classrooms • teachers had to be certified to teach • TEACCH and LEAP teachers needed to attend formal training Children**:** • 3-5 years of age at time of enrollment • previous clinical diagnosis or educational label consistent with Autism spectrum disorder (ASD) or developmental delay • met diagnostic criteria on Autism Diagnostic Observation Schedule (ADOS) and/or Social Communication Questionnaire (SCQ) **Exclusion criteria:** Teachers**:** • teaching < 2 years in their respective	**Overall ratings:** Autism characteristics and severity **G1:** -0.11 ± 0.76 **G2:** 0.066 ± 0.765 **G3:** 0.381 ± 0.859 **Social skills, mean ± SD:** Reciprocal social interaction, teacher-rated **G1:** 0.014 ± 0.999 **G2:** 0.24 ± 0.877 **G3:** 0.18 ± 0.874 Reciprocal social interaction, parent-rated **G1:** 0.005 ± 0.834 **G2:** -0.056 ± 1.015 **G3:** 0.325 ± 0.785 **Communication/ language, mean ± SD:** Communication: **G1:** 0.214 ± 0.858 **G2:** 0.081 ± 1.045 **G3:** -0.403 ± 0.784 **Repetitive behavior, mean ± SD:** Sensory and repetitive behaviors, teacher-rated (SRB-T): **G1:** -0.069 ± 0.809 **G2:** -0.176 ± 0.768 **G3:** 0.179 ± 0.92	**Overall ratings:** Autism characteristics and severity **G1:** -0.299 ± 0.928 **G2:** -0.144 ± 0.837 **G3:** 0.124 ± 0.866 p=NS **Social skills, mean ± SD:** Reciprocal social interaction, teacher-rated **G1:** -0.28 ± 1.149 **G2:** -0.152 ± 1.039 **G3:** -0.077 ± 0.926 p=NS Reciprocal social interaction, parent-rated **G1:** -0.257 ± 0.969 **G2:** -0.117 ± 1.012 **G3:** 0.17 ± 0.845 p=NS **Communication/ language, mean ± SD:** Communication: **G1:** 0.441 ± 0.937 **G2:** 0.238 ± 1.102 **G3:** -0.317 ± 0.878 p=NS **Repetitive behavior:** Sensory and repetitive behaviors, teacher-rated:

	Classrooms: **G1:** 25 **G2:** 22 **G3:** 27 Participants: **G1:** 85 **G2:** 54 **G3:** 59 **N at follow-up:** **G1**: 81 **G2**: 48 **G3**: 56	classroom types prior to enrollment • failing to meet prior determined classroom fidelity and/or quality rating scales Children**:** • previous exposure to the comparison comprehensive treatment model (CTM) • < 6 months of exposure to the treatment or control intervention • significant uncorrected vision or hearing impairment, uncontrolled seizure disorder or traumatic brain injury • family not proficient in English **Age, mean/yrs ± SD:** **G1:** 4.00 ± 0.57 **G2:** 3.96 ± 0.70 **G3:** 4.07 ± 0.64 **Mental age, mean/yrs (range):** NR **Sex, n (%):** Male: **G1**: 71 (83.5) **G2**: 42 (77.8) **G3**: 52 (88.1)	Sensory and repetitive behaviors, parent-rated: **G1:** 0.025 ± 0.879 **G2:** -0.017 ± 1.03 **G3:** 0.169 ± 1.06 **Motor skills:** Fine motor (FM): **G1:** 0.01 ± 0.632 **G2:** -0.165 ± 0.812 **G3:** -0.364 ± 0.648	**G1:** -0.069 ± 0.809 **G2:** -0.176 ± 0.768 **G3:** 0.179 ± 0.92 p=NS Sensory and repetitive behaviors, parent-rated: **G1:** 0.025 ± 0.879 **G2:** -0.017 ± 1.03 **G3:** 0.169 ± 1.06 p=NS **Motor skills:** Fine motor : **G1:** 0.44 ± 0.763 **G2:** 0.072 ± 0.821 **G3:** -0.183 ± 0.682 p=NS **Harms:** NR **Modifiers:** NR

Female:
G1: 14 (16.5)
G2: 12 (22.2)
G3: 7 (11.9)

Missing:
G1: 1 (1.2)
G2: 0 (0)
G3: 0 (0)

Race/ethnicity, n (%):
White:
G1: 32 (37.6)
G2: 25 (46.3)
G3: 35 (59.3)

Black:
G1: 14 (16.5)
G2: 3 (5.6)
G3: 6 (10.2)

Hispanic:
G1: 31 (36.5)
G2: 23 (42.6)
G3: 15 (25.4)

Asian:
G1: 5 (5.9)
G2: 2 (3.7)
G3: 3 (5.1)

Missing:
G1: 3 (3.5)
G2: 1 (1.9)
G3: 0 (0)

SES:
Caregiver education, n (%):
Less than college:
G1: 44 (51.8)

G2: 25 (46.3)
G3: 25 (42.4)

College or higher:
G1: 39 (45.9)
G2: 28 (51.9)
G3: 32 (54.2)

Missing:
G1: 2 (2.4)
G2: 1 (1.9)
G3: 2 (3.4)

Household income, n (%):
< $20K-$39,000:
G1: 30 (35.3)
G2: 14 (25.9)
G3: 16 (27.1)

$40 k-$79,999:
G1: 22 (25.9)
G2: 18 (33.3)
G3: 13 (22.0)

>$80K:
G1: 29 (34.1)
G2: 18 (33.3)
G3: 25 (42.4)

Missing:
G1: 4 (4.7)
G2: 4 (7.4)
G3: 5 (8.5)

Diagnostic approach:
Referral

Diagnostic tool/method:
Autism Diagnostic Observation Schedule

	(ADOS) and/or Social Communication Questionnaire (SCQ) **Diagnostic category, n (%):** NR **Other characteristics, n (%):** School setting: **G1**: Urban: 13 (52) Suburban: 12 (48) Rural: 0 (0.00) **G2**: Urban: 10 (45.45) Suburban: 11 (50.0) Rural: 1 (4.55) **G3**: Urban: 18 (64.29) Suburban: 10 (35.71) Rural: 0 (0.00)	

Comments: All data reflect composite variables

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Casenhiser et al., 2013 [2] **Country:** USA and Canada **Intervention setting:** Treatment center, home **Enrollment period:** NR **Funding:** Harris Steel Foundation and the Harris Family, Unicorn Foundation, Cure Autism Now, the Public Health Agency of Canada, the Templeton Foundation, and York University **Design:** RCT	**Intervention:** Milton & Ethel Harris Research Initiative Treatment program (MEHRIT), 2hrs/week Community treatment, 3.9hrs/week **Assessments:** Modified Child Behavior Rating Scale (mCBRS), Pre School Language Scale IV (PLS) and Comprehensive Assessment of Spoken Language (CASL) conducted by licensed speech language pathologists at 0 and 12 months post intervention Parent behavior scores from MEHRIT fidelity scale conducted by MEHRIT therapists at 0 and 12 months post intervention **Groups:** **G1:** MEHRIT **G2:** Community treatment **Provider:** Speech language pathologists Occupational therapists **Treatment manual**	**Inclusion criteria:** All children who had completed 12 months of MEHRIT (or 12 months in the CT group) and for whom a semi-structured parent-child interaction was videotaped both prior to intervention and following 12 months of intervention. Previously diagnosed with Autism Spectrum disorders(ASDs) Diagnoses confirmed using ADOS and Autism Diagnostic Interview (ADI) **Exclusion criteria:** Neurological or developmental diagnoses other than ASD Families not able to meet the time requirements of the study **Age, mean/months ± SD:** **G1:** 42.52 ± 8.76 **G2:** 46.38 ± 8.29 **Mental age, mean/yrs (range):** NR **Sex:** NR	**Mean ± SD:** **mCBRS:** Attention to Activity **G1**: 2.96 ± 0.735 **G2**: 3.08 ± 0.796 Involvement **G1**: 2.56 ± 0.583 **G2**: 2.62 ± 0.697 Compliance **G1**: 2.68 ± 0.748 **G2**: 2.85 ± 0.784 Initiation of Joint Attention **G1**: 1.28 ±0.542 **G2**: 1.31 ±0.987 Enjoyment in Interaction **G1**: 3.08 ±0.277 **G2**: 3.35 ±0.485 PLS and CASL: Mean ± SD Developmental quotient (DQ): **G1:** 0.64 ±0.32 **G2:** 0.54 ±0 .26 **Parent behavior scores (from MRHRIT Fidelity scale), Mean ± SD:**	**Mean ± SD:** **mCBRS:** Attention to Activity **G1**: 3.72 ±0.614 **G2**: 3.38 ±0.752 p<0.05, d=0.69 Involvement **G1**: 3.20 ±0.866 **G2**: 2.69 ±0.788 p<0.01,d=0.87 Compliance **G1**: 3.48 ±0.963 **G2**: 3.35 ±0.797 p=ns, d=0.51 Initiation of Joint Attention **G1**: 1.84 ±0.549 **G2**: 1.23 ±0.430 p<0.001, d=1.02 Enjoyment in Interaction **G1**: 3.28 ±0.458 **G2**: 3.23 ±0.430 p<0.05, d=0.63 PLS and CASL: Mean ± SD DQ: **G1:** 0.72 ± 0.39 p = 0.038 d =0.451 **G2:** 0.64 ± 0.32 p < 0.001 d = 0.915

	followed: NR **Defined protocol followed:** NR **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies:** **G1:** NR **G2:** Yes **N at enrollment:** **G1:** 25 **G2:** 26 **N at follow-up:** **G1:** 16 **G2:** 13	**Race/ethnicity, n (%):** NR **SES:** Maternal education, n (%): Advance degree **G1:** 2 (8) **G2:** 6 (23.07) Bachelor's degree **G1:** 15 (60) **G2:** 11 (42.30) Associates degree **G1:** 1 (4) **G2:** 3 (11.53) Some University/college **G1:** 7 (28) **G2:** 4 (15.38) High school **G1:** 0 (0) **G2:** 2 (7.69) Household income, n >100,000 (in Canadian $) **G1:** 12 **G2:** 11 50,000-100,000 **G1:** 6 **G2:** 4 <50,000 **G1:** 4 **G2:** 8 NR **G1:** 3 **G2:** 3	Co-regulation **G1:** 1.32 ±1.0 **G2:** 1.23 ±.86 Expression of enjoyment **G1:** 1.80 ±1.23 **G2:** 1.69 ±1.10 Sensory-motor **G1:** 1.60 ±0.87 **G2:** 1.31 ±0.83 Joining **G1:** 1.76 ±0.60 **G2:** 1.58 ±0.50 Reciprocity **G1:** 1.12 ±0.78 **G2:** 0.85 ±0.73 Independent thinking **G1:** 0.60 ±0.65 **G2:** 0.42 ±0.76 Use of Affect **G1:** 1.92 ±0.15 **G2:** 1.65 ±0.80	**G1 vs G2** p = 0.214 **Parent behavior scores (from MEHRIT Fidelity scale), Mean ± SD** N=51 Co-regulation **G1:** 1.92 ±1.22 **G2:** 1.00 ±.69 p<0.001 d=0.996 Expression of enjoyment **G1:** 2.60 ±1.23 **G2:** 1.53 ±1.03 p<0.01 d=0.79 Sensory-motor **G1:**1.88 ±1.1 **G2:**1.19 ±.75 p=ns d=0.393 Joining **G1:** 2.16 (.80) **G2:** 1.19 (.63) p<0.01 d=0.92 Reciprocity **G1:** 1.76 ±1.13 **G2:** .65 ±.80 p<0.01 d=0.863 Independent Thinking **G1:** 1.0 ±.87 **G2:** .50 ±.76 p=ns d=0.389

	Diagnostic approach: In Study Diagnostic tool/method: **For ASD diagnosis:** ADOS (Autism Diagnostic Observation Schedule); ADI (Autism Diagnostic Interview) **Diagnostic category, n (%):** ASD: **G1:** 25 **G2:** 26 **Other characteristics**, n (%)**:** Parental marital status: Married/partnered **G1:** 24 (96) **G2:** 22 (84.61) Single/divorced/separated **G1:** 1 (4) **G2:** 4 (15.38) Mother's native language: English **G1:** 15 (60) **G2:** 12 (46.15) Other **G1:** 10 (40) **G2:** 14 (53.84) Language most often spoken at home English	Use of Affect **G1:** 2.48 ±.82 **G2:** 1.46 ±.71 $p<0.001$ $d=0.962$ **Harms:** NR **Modifiers:** NR

G1: 23 (92)
G2: 23 (88.46)

Other
G1: 2 (8)
G2: 3 (11.53)

Table C-1. Evidence table, continued Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Fujii et al. 2013 **Country:** US **Intervention setting:** university clinic or associated autism community clinic **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** CBT provided to individual families for 90 minutes (30 minutes separately with child and parents, 30 minutes conjointly with child and parent(s)) using Building Confidence CBT program modified for use with children with ASD; 32 weekly sessions **Assessments:** child and parent report **Groups:** **G1:** intervention **G2:** treatment as usual **Provider:** • 5 graduate students in clinical or educational psychology and 4 postdoctoral students in psychology or psychiatry **Treatment manual followed:** No **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** No **Co-interventions held**	**Inclusion criteria:** Children age 7-11 years old meeting ADOS and ADI-R criteria for ASD $\geq$ 1 anxiety disorder **Exclusion criteria:** Verbal IQ < 70 Primary comorbid diagnosis other than anxiety (e.g. dysthymic disorder) **Age, mean/yrs ± SD:** **G1:** 8.7 ± 1.8 **G2:** 9.0 ± 1.6 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 5 (71) **G2:** 4 (80) F, n (%): **G1:** 2 (29) **G2:** 1 (20) **Race/ethnicity, n (%):** White **G1:** 6 (86) **G2:** 3 (60) Asian/Pacific Islander: **G1:** 1 (14) **G2:** 0 (0)	**Overall ratings:** Global Rating of Severity, mean ± SD: NR Social skills: NR Communication/ language: NR Repetitive behavior: NR Problem behavior: NR Adaptive behavior: NR **Commonly occurring co-morbidities:** Anxiety diagnoses, n (%): Separation anxiety disorder: **G1:** 3 (43) **G2:** 2 (40) Social phobia disorder: **G1:** 2 (29) **G2:** 3 (60) Obsessive compulsive disorder:	**Overall ratings:** Global Rating of Severity, mean ± SD: NR Social skills: NR Communication/ language: NR Repetitive behavior: NR Problem behavior: NR Adaptive behavior: NR **Commonly occurring co-morbidities:** Anxiety diagnoses, n (%): p=0.013 for any anxiety diagnosis at follow-up between groups vs. baseline Separation anxiety disorder: **G1:** 0 (0) **G2:** 2 (40) Social phobia disorder:

	stable during treatment: yes **Concomitant therapies, n (%):** Medication: **G1:** 2 (29) **G2:** 4 (80) Therapy from psychologist, social worker, or behaviorist: **G1:** NR **G2:** 4 (80) School services (aides, speech therapy, or social skills group) **G1:** NR **G2:** 5 (100) Speech therapy: **G1:** 4 (57) **G2:** NR Social skills group in year before enrollment: **G1:** 6 (86) **G2:** NR N at enrollment: **G1:** 10 **G2:** 6 N at follow-up: **G1:** 7 **G2:** 5	African American: **G1:** 0 (0) **G2:** 1 (20) Multiracial: **G1:** 0 (0) **G2:** 1 (20) **SES:** Parent graduated from college, n (%): **G1:** 5 (71) **G2:** 3 (60) **Diagnostic approach:** In Study Diagnostic tool/method: ADOS and ADI-R; anxiety disorders diagnosed suing Anxiety Disorders Interview Schedule: Child and Parent versions **Diagnostic category, n (%):** Autism **G1:** 7 (100) **G2:** 4 (80) PDD-NOS **G1:** 0 (0) **G2:** 1 (20) **Other characteristics, n (%):** NR	**G1:** 1 (14) **G2:** 0 (0) Generalized anxiety disorder: **G1:** 1 (14) **G2:** 0 (0)	**G1:** 1 (14) **G2:** 3 (60) Obsessive compulsive disorder: **G1:** 0 (0) **G2:** 0 (0) Generalized anxiety disorder: **G1:** 1 (14) **G2:** 0 (0) **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Goods et al. 2013[3] **Country:** US **Intervention setting:** non-public preschool **Enrollment period:** 2008-2010 **Funding:** Organization for Autism Research grant 20072725; Autism Speaks grant 5666, NIH/NICHD, and Department of Health and Human Services **Design:** RCT	**Intervention:** Joint Attention and Symbolic Play/Engagement and Regulation Intervention (JASPER) for 12 weeks, 30 minutes twice weekly **Assessments:** observation and researcher assessments **Groups:** **G1:** JASPER intervention **G2:** Standard practice **Provider:** Study personnel (graduate students in educational psychology) **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** Yes **Concomitant therapies, n (%):** NR	**Inclusion criteria:** • diagnosed with autism • between 3-5 years of age • attended non-public school • used less than 10 spontaneous, functional, and communicative words by parent and teacher report and during baseline or entry assessments **Exclusion criteria:** • see inclusion criteria **Age, mean/months ± SD:** **G1:** 48.73 ± 11.68 **G2:** 54.68 ± 10.25 **Mental age, mean/months ± SD:** **G1:** 17.21 ± 3.91 **G2:** 13.91 ± 3.85 **Sex:** NR **Race/ethnicity, n (%):** NR **SES:** Maternal education, n (%): NR	**Social skills:** SPA (baseline, month 0) Play types, mean ± SD: **G1**: 21.14 ± 7.58 **G2**: 17.13 ± 6.83 Entry (3 months later) **G1**: 11.00 ± 8.74 **G2**: 11.50 ± 5.10 **Communication/ language:** RDLS verbal comprehension, mean ± SD: **G1**: 12.14 ± 0.41 **G2**: 12.00 ± 0.34 RDLS expressive language, mean ± SD: **G1**: 13.63 ± 4.57 **G2**: 11.93 ± 0.09 ESCS, initiating joint attention, mean ± SD: **G1**: 2.57 ± 4.39 **G2**: 0.75 ± 2.12 ESCS, initiating requesting, mean ± SD: **G1**: 5.00 ± 3.70 **G2**: 1.88 ± 1.55 Class observation (entry, month 3) Initiating joint attention, mean ± SD:	**Social skills:** SPA Play types, mean ± SD: **G1**: 22.00 ± 10.17 **G2**: 14.33 ± 9.69 p = 0.04 **Communication/ language:** RDLS verbal comprehension, mean ± SD: **G1**: 14.59 ± 5.36 **G2**: 12.05 ± 0.38 p=NS RDLS, expressive language, mean ± SD: **G1**: 14.52 ± 5.38 **G2**: 11.95 ± 0.16 p=NS ESCS, initiating joint attention (IJAs), mean ± SD: **G1**: 0.40 ± 0.89 **G2**: 1.00 ± 1.73 p=NS ESCS, initiating requesting , mean ± SD: **G1**: 4.00 ± 1.87 **G2**: 3.20 ± 2.39 p=NS Class observation initiating joint attention,

	N at enrollment: **G1:** 7 **G2:** 8 **N at follow-up:** **G1:** 5 **G2:** 6	Household income, mean (range): NR **Diagnostic approach:** In Study Diagnostic tool/method: ADOS **Diagnostic category, %)** Autism: 100% PDD-NOS: 0 Aspergers: 0 **Other characteristics**, n (%)**:** MSEL baseline development quotient, mean ± SD: **G1:** 37.70 ± 15.21 **G2:** 26.67 ± 10.12 MSEL baseline, visual reception, mean ± SD: **G1:** 22.42 ± 3.26 **G2:** 21.50 ± 4.44 MSEL baseline fine motor, mean ± SD: **G1:** 21.71 ± 3.04 **G2:** 19.13 ± 4.29 MSEL baseline receptive language, mean ± SD: **G1:** 13.86 ± 7.36 **G2:** 8.63 ± 4.66 MSEL baseline expressive language, mean ± SD: **G1:** 10.86 ± 7.76 **G2:** 6.38 ± 3.74	**G1**: 1.50 ± 3.21 **G2**: 0.20 ± 0.45 Class observation, initiating requesting, mean ± SD: **G1**: 1.50 ± 1.76 **G2**: 0.20 ± 0.45 Class observation, (entry, month 3) unengaged, mean % ± SD: **G1:** 44.50 ± 14.86 **G2:** 57.40 ± 34.11	mean ± SD: **G1**: 0.60 ± 1.34 **G2**: 0.25 ± 0.50 p=NS Class observation, initiating requesting, mean ± SD: **G1**: 4.80 ± 4.49 **G2**: 0.00 ± 0.00 p=0.01 Class observation, unengaged, mean ± SD: **G1:** 12.60 ± 10.85 **G2:** 35.00 ± 16.08 p = 0.05 **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Ichikawa et al. 2013[4] **Country:** Japan **Intervention setting:** Psychiatric medical center **Enrollment period:** NR **Funding:** Grant from Meiji Yasuda Mental Health Foundation **Design:** RCT	**Intervention:** TEACCH-based social skills training: group intervention with weekly 2-hour sessions, with 20 sessions over 6 months. Wait list control group: group meetings every 2 months for 6 months with 2 social workers for 30-60 minutes **Assessments:** observed, parent report, teacher report **Groups:** **G1:** TEACCH **G2:** wait list control **Provider:** • 2 psychologists, 2 nursery teachers, 2 social workers, and 2 graduate students, with supervision by an additional psychologist **Treatment manual followed:** yes **Defined protocol followed:** yes **Measure of treatment fidelity reported:** no	**Inclusion criteria:** Age 5-6 years Diagnosis of autism spectrum disorder confirmed by child psychiatrists IQ $\geq$ 75 CARS-TV $\geq$ 25 **Exclusion criteria:** Severe psychiatric comorbidities (e.g. obsessive compulsive disorder, conduct disorder, oppositional defiant disorder) Mother with mental illness with a major obstacle in daily life (e.g. schizophrenia, severe depression, drug or alcohol dependency) **Age, median months (range):** **G1:** 64 (60 – 66) **G2:** 62 (60 – 70) **Mental age, median (range):** DQ (Kyoto Scale of Psychological Development): **G1:** 87 (84-117) **G2:** 88 (78 – 145) **Sex:** M, n (%): **G1:** 4 (80) **G2:** 5 (83.3)	**Social skills:** Interaction Rating Scale, mean ± SD: **G1:** 38.9 ± 4.8 **G2:** 41.5 ± 3.0 **Adaptive behavior:** Strengths and Difficulties Questionnaire, mean ± SD: **G1:** 19.0 ± 3.5 **G2:** 13.2 ± 3.3	**Social skills:** Interaction Rating Scale, mean ± SD: **G1:** 40.2 ± 5.1 **G2:** 39.7 ± 6.0 Difference (95% CI): 2.72 (-5.83, 11.27) Effect size (d): 0.69 **Adaptive behavior:** Strengths and Difficulties Questionnaire, mean ± SD: **G1:** 14.4 ± 4.7 **G2:** 12.5 ± 3.2 Difference (95% CI): -3.12 (-8.42, 2.18) Effect size (d): 0.71 **Harms** None **Modifiers** NR

	Co-interventions held stable during treatment: NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 5 **G2:** 6 **N at follow-up:** **G1:** 5 **G2:** 6	F, n (%): **G1:** 1 (20) **G2:** 1 (16.7) **Race/ethnicity, n (%):** NR **SES:** Maternal education, n (%): High school: **G1:** 2 (40) **G2:** 1 (16.7) Junior college: **G1:** 3 (60) **G2:** 2 (33.3) University: **G1:** 0 **G2:** 3 (50) Household income, mean (range): NR **Diagnostic approach:** In Study Diagnostic tool/method: ICD-10 **Diagnostic category, n (%):** Autism, high functioning: **G1:** 0 (0) **G2:** 3 (50) PDD-NOS **G1:** 4 (80) **G2:** 2 (33.3) Aspergers **G1:** 1 (20)	

G2: 1 (16.7)

Other characteristics, n (%):
Autism severity, CARS, median (range):
G1: 32.5 (27.5 – 33.5)
G2: 31.0 (26.5 – 33.0)

SQ (Japanese version of Social Maturity Scale), median (range):
G1: 90 (81 - 101)
G2: 96 (71 – 105)

Comments: Does not report p-values for between group differences; between group differences account for baseline as a covariate

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Kenworthy et al. 2013[5] **Country:** US **Practice setting:** Children's National Medical Center, Center for Autism Spectrum Disorders, Rockville, MD, USA **Intervention setting:** School **Enrollment period:** NR **Funding:** National Institute of Mental Health Organization for Autism Research Isadore and Bertha Gudelsky Family Foundation NIH **Design:** RCT	**Intervention:** Unstuck and On Target (UOT) CBT intervention or Social skills intervention (SS); both interventions for one school-year in 28, 30-40min lessons **Assessments:** Direct Child measures, Parent-rated report, Teacher-rated report IQ and Verbal mental age measured by WASI (Wechsler Abbreviated Scale of Intelligence) Verbal, Performance and Full Scale IQ scores **Groups:** **G1:** CBT **G2:** Social skills **Provider:** Interventionists School staff Parents **Treatment manual followed:** Yes **Defined protocol followed:** NR **Measure of treatment fidelity reported:** Yes	**Inclusion criteria:** Full Scale IQ score >70, a verbal mental age ≥8 years old Met criteria for ASD (ADOS diagnostic algorithm ≥'ASD' threshold Met DSM-IV-TR (American Psychiatric Association, 1994) criteria for a Pervasive Developmental Disorder **Age, mean/yrs ± SD (range):** **G1:** 9.49 ± 1.00 (7.83–11.08) **G2:** 9.58 ± 1.10 (7.92–11.08) **Mental age, mean/yrs (range):** NR **Sex, %** M: **G1:** 87 **G2:** 90 F: **G1:** 13 **G2:** 10 **Race/ethnicity, %:** White **G1:** 70 **G2:** 55 **SES:** **Education, mean ± SD**	NR	**Overall ratings:** Global Rating of Severity, mean ± SD: NR **Direct child measures change scores (post intervention minus preintervention), n, mean ± SEM:** WASI block design **G1:** (n=41), 3.00 ± 1.03 **G2**: (n=17), -0.94 ±1.11 **G1 vs G2** $p<0.05$ CI 0.65(0.18-1.17) Challenge task flexibility: **G1:** (n=43), -0.53 ± 0.07 **G2:** (n=19), -0.15 ± 0.14 **G1 vs G2** $p<0.05$ CI -0.72(-1.38 to 0.14) Challenge task plan:

	Co-interventions held stable during treatment: NR **Concomitant therapies, % :** Psychometric medication: **G1:** 54.5 **G2:** 60 **N at enrollment:** **G1:** 47 **G2:** 20 **N at follow-up:** **G1:** 43 **G2:** 19	Maternal education **G1:** 1.91 ± 0.88 **G2:** 1.95 ± 0.76 Father's education **G1:** 2.04 ±1.12 **G2:** 1.95 ± 0.91 **Diagnostic approach:** In Study/Referral Diagnostic tool/method: Diagnosis of ASD by ADOS (Autism Diagnostic Observation Schedule, Module 3) Pervasive developmental disorder diagnosis met by DSM-IV-TR **Diagnostic category, n :** ASD **G1:** 47 **G2:** 20 **Other characteristics**, %: Public school: **G1:** 96 **G2: 75** **WASI FSIQ, mean ± SD [range]:** **G1:** 108.80 ± 18.52 [75-151] **G2:** 107.63 ± 17.20 [82-150] **ADOS social + communication, Mean ± SD (range):** **G1:** 11.77 ± 3.64		**G1:** (n= 43), -0.33 ± 0.07 **G2:** (n=19), -0.22 ± 0.06 -0.27(-0.77 to 0.18) Challenge task social: **G1:** (n=43), 0.47 ± 0.16 **G2:** (n=19), 0.26 ± 0.30 CI 0.17(-0.42 to 0.77) **Teacher-rated measures change scores (post intervention minus pre intervention), n, mean ± SEM:** BRIEF shift T score **G1:** (n=27), -24.44 ± 3.30 **G2:** (n=18), -9.78 ± 3.59 **G1 vs G2** p<0.01 CI -0.89(-1.62 to 0.33) BRIEF plan/org T score **G1:** (n=28), -19.14 ± 2.39 **G2:** (n=18),

	(7-21) **G2:** 12.40 ± 4.17 (7-20) **ADOS stereotyped behavior, mean ± SD (range):** **G1:** 1.98 ± 1.71 (0-6) **G2:** 1.90 ± 1.33(0-5)	-11.72 ± 3.16 **G1 vs G2** p<0.05 CI -0.57(-1.26 to 0.01) SRS total score **G1:** (n=25), -5.40 ±1.34 **G2:** (n=19), -4.79 ± 2.05 CI -0.08(-0.78 to 0.51) **Parent-rated measures change scores (post intervention minus preintervention), n, mean ± SEM:** BRIEF shift T score **G1:** (n=41), -9.56 ± 2.31 **G2:** (n=19), -0.16 ± 2.99 **G1 vs G2** p<0.01 CI -0.66(-1.24 to 0.15) BRIEF plan/org T score **G1:** (n=42), -5.17 ± 2.00 **G2:** (n=18) 0.61 ± 2.90 **G1 vs G2**

p<0.05
CI -0.45(-0.97 t 0.07)

SRS total score
G1: (n=42)
-7.31 ± 1.65
G2: (n=18)
-4.11 ± 2.97
CI 0.28(-0.84 to 0.33)

Classroom Observations:
Ability to follow directions
G1 vs G2
p<0.001

Transition smoothly
G1 vs G2
p<0.001

Avoid getting stuck
G1 vs G2
p<0.05

Reduced negativity
G1 vs G2
p=0.053

Social reciprocity
G1 vs G2
p=ns

Classroom participation
G1 vs G2
p=ns

Harms: NR

Modifiers: NR

Comments: Baseline measures not provided. Only post-pre treatment change scores reported.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Malow et al. 2014[6] **Country:** US **Intervention setting:** Home **Enrollment period:** NR **Funding:** UDSHHS, HRSA, Maternal and Child Health Research Program; research was conducted as part of Autism Speaks Autism Treatment Network. **Design:** RCT	**Intervention:** Sleep education curriculum for parents. Parents in the group program received two 2-hour sessions conducted 1 week apart and parents in the individual received one 1-hour session with two follow-up phone calls. **Assessments:** observed, parent report (Actigraphy and parent questionnaires) collected at baseline and 1 month after treatment **Groups:** **G1:** individual sleep education **G2:** group sleep education **Provider:** • Trained educators **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held**	**Inclusion criteria:** age 2-10 years diagnosis of ASD based on interview conducted by psychologist or developmental pediatrician with expertise in ASD that incorporated DSM-IV-TR criteria and confirmation by ADOS Sleep onset latency of at least 30 minutes on three out of 7 nights/week based on parent report and confirmed by 14 scorable days of actigraphy. Children with other sleep difficulties identified as problems by parents Medication free or on stable dose of medication (no change within 30 days of enrolling) with parents agreeing to avoid medication changes during time of study participation Ability to tolerate actigraphy and parental willingness to complete sleep diary Family primary language English	Actigraphy results, mean ± SD Sleep latency, minutes, **G1:** 59.8 ± 31.6 **G2:** 56.0 ± 25.2 Sleep efficiency, % **G1:** 76.2 ± 6.2 **G2:** 76.4 ± 8.0 WASO, min **G1:** 63.8 ± 28.4 **G2:** 60.4 ± 22.1 Total sleep time, min **G1:** 486.9 ± 48 **G2:** 482.4 ± 56.7	Sleep latency, minutes, mean ± SD **G1:** 39.5 ± 21.6 **G2:** 39.7 ± 21.5 **G1 vs G2:** p=0.63 Sleep efficiency, % **G1:** 78.7 ± 5.1 **G2:** 79.8 ± 6.0 **G1 vs G2:** p=0.56 WASO, min **G1:** 59.3 ± 27.3 **G2:** 58.3 ± 23.7 **G1 vs G2:** p=0.37 Total sleep time, min **G1:** 481.1 ± 49.5 **G2:** 488.3 ± 50.3 **G1 vs G2:** p=0.37 **Harms** NR **Modifiers** NR

	stable during treatment: Yes **Concomitant therapies, n (%):** Medication type Psychotropic **G1:** 7 (15) **G2:** 6 (18) Melatonin **G1:** 7 (15) **G2:** 5 (15) Stimulants **G1:** 8 (17) **G2:** 6 (18) **N at enrollment:** **G1+ G2:** 114 **N at follow-up:** **G1:** 47 **G2: 33**	Screening by developmental pediatrician to identify medical and behavioral comorbidities that affect sleep (see below) **Exclusion criteria:** children with untreated comorbidities that affect sleep including sleep apnea, epilepsy, gastrointestinal reflux disease, and depression were not enrolled in study until after co-occurring conditions were addressed. Age, mean years ± SD: **G1:** 5.6 ± 2.6 **G2:** 5.9 ± 2.8 **Mental age:** IQ >70, n (%): **G1:** 27 (64%) **G2:** 15 (45%) **Sex:** M, n (%) **G1:** 39 (83) **G2:** 25 (76) F, n (%) **G1:** 8 (17) **G2:** (8 (24) **Race/ethnicity, n (%):** White **G1:** 37 (80) **G2:** 26 (84) **SES:**	

Hollingshead Four-Factor Index, mean ± SD:
G1: 44.3 ± 13.5
G2: 44.7 ± 10.6

Diagnostic approach:
In Study

Diagnostic tool/method:
DSM_IV-TR, ADOS

Diagnostic category, n (%):
Autism
G1: 32 (68)
G2: 26 (79)

PDD-NOS
G1: 4 (8.5)
G2: 2 (6)

Asperger syndrome
G1: 11 (23.4)
G2: 5 (15)

Other characteristics, n (%): NR

Comments: The Children's Sleep Habits Questionnaire and Behavior and Family Questionnaire results are presented for both groups combined.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Mandelberg et al. 2013[7] **Country:** US **Intervention setting:** Home & school **Enrollment period:** average of 43.2 months after initial intervention (2004-2008) **Funding:** National Institute of Mental Health, NICHD, NIDCD and NINDS **Design:** RCT Note: See study reporting on this population[8] in 2011 AHRQ review[9]	**Intervention:** UCLA Children's Friendship Training (CFT) Program mode, with 12 weekly hour-long sessions involving separate groups for children and parents; children with other diagnoses were included as peer models **Assessments:** parent and child report **Groups:** **G1:** CFT **Provider:** Psychologist L.C.S.W. Undergraduate psychology students **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR	**Inclusion criteria:** Attending 2nd through 5th grade regular classroom for most of the day without a closely supervising adult Wechsler Intelligence Scale for Children-III (WISC-III) Verbal IQ > 60 Able to switch topics in a conversation when the other person was interested in talking about something else Adequate knowledge of rules in playing $\geq$ 2 common age-appropriate board games Knowledge of rules to play common school yard games **Exclusion criteria:** Currently prescribed any psychotropic medicine Thought disorders Clinical seizure disorder, gross neurologic disease, or other medical disorder History of taking either CFT or teen adaptation of CFT (PEERS) during follow-up	**Social skills:** Guest play dates, median: **G1:** 1.0 Hosted play dates, median: **G1:** 1.0 Conflict play dates, mean ± SD: **G1:** 5.2 ± 5.0 Social Skills Rating System (SSRS), Social Skills, mean ± SD: **G1:** 72.3 ±12.2 Loneliness, mean ±SD: **G1:** 39.2 ± 12.5 **Problem behavior:** SSRS, Problem Behaviors, mean ± SD: **G1:** 118.7 ± 11.9	**Social skills:** Guest play dates, median: **G1:** 1.8 p<0.05 vs. baseline Hosted play dates, median: **G1:** 1.7 p=NS vs. baseline Conflict play dates, mean ± SD: **G1:** 2.3 ±3.1 p<0.05 vs. baseline Social Skills Rating System (SSRS), Social Skills, mean ± SD: **G1:** 91.5 ± 14.7 p<0.001 vs. baseline Loneliness, mean ±SD: **G1:** 35.5 ± 14.0 P=0.05 vs. baseline Parent report of $\geq$ 1 friend that child was pretty close with:

	Concomitant therapies, n (%): Report of other treatment(s) during follow-up: **G1:** 16 (66) Individual therapy at follow-up: **G1:** 7 (29) Psychotropic medication use at follow-up: **G1:** 5 (21) Complementary therapies used at follow-up: **G1:** 7 (29) **N at enrollment:** **G1:** 66 **N at follow-up (1-5 years post-treatment):** **G1:** 24	**Age, mean/yrs ±SD:** **G1:** 8.7 ± 1.4 (original) G1: 12.6 (current) **Mental age:** WISC-III verbal IQ, mean ± SD: **G1:** 104.1 ± 17.8 **Sex:** M, n (%): **G1:** 20 (83) F, n (%): **G1:** 4 (17) **Race/ethnicity, n (%):** White **G1:** 16 (67) **SES:** Hollingshead scale, mean ± SD: **G1:** 46.2 ±12.9 **Diagnostic approach:** In Study Diagnostic tool/method: ADOS and ADI-R **Diagnostic category, n (%):** Autism: **G1:** 24 (100) **Other characteristics, n (%):** Wing score, mean ± SD: **G1:** 24.3 ± 8.0		**G1:** 20 (83) Child report of $\geq$ 1 pretty close friend: **G1:** 21 (88) **Problem behavior:** SSRS, Problem Behaviors, mean ± SD: **G1:** 109.3 ± 13.1 $p<0.001$ vs. baseline **Harms:** NR **Modifiers:** NR

Comments: Original RCT included a wait list control; this paper combines the intervention group with the wait listers who later received the CFT intervention.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: McNally et al., 2013 [10] **Country:** US **Intervention setting:** Academic (Alliant International University) **Enrollment period:** June 2009 – September 2009 **Funding:** National Foundation for Autism Research; Autism Society of America – San Diego Chapter **Design:** RCT	**Intervention:** Modification of Coping Cat program (cognitive-behavioral therapy, CBT); one 60-90min session per week for 16 weeks **Assessments:** structured interview, parent self-report, child self-report **Groups:** **G1:** cognitive-behavioral therapy **G2:** waitlist **Provider:** Study staff **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** No **Concomitant therapies, n (%):** SSRI: **G1:** 2 (17)	**Inclusion criteria:** • diagnosis of ASD • at least one primary anxiety disorder, e.g., separation anxiety (SAD), generalized anxiety (GAD), or social phobia (SP) • IQ ≥70 • ages 7 – 14 years • English as primary language **Exclusion criteria:** • see inclusion criteria **Age, mean/yrs ± SD:** **G1:** 11.65 ± 1.41 **G2:** 11.02 ± 1.69 **Mental age, mean/yrs (range):** NR **Sex, n (%):** M: **G1:** 12 (100) **G2:** 9 (90) F: **G1:** 0 (0) **G2:** 1 (10) **Race/ethnicity, n (%):** Caucasian: **G1:** 8 (66)	**Commonly occurring co-morbidities:** ADIS-P Interference Ratings: **G1:** 7.00 ± 1.21 **G2:** 7.10 ± 1.10 SCAS total score: **G1:** 27.08 ± 19.75 **G2:** 28.89 ± 17.15 SCAS-P total score: **G1:** 34.92 ± 13.71 **G2:** 32.20 ± 16.54 ADIS-P comorbid diagnoses, mean ± SD: **G1:** 4.00 ± 1.04 **G2:** 3.70 ± 1.06 Baseline anxiety diagnoses, n (%) Separation Anxiety: **G1:** 5 (42) **G2:** SAD: 3 (30) Generalized Anxiety: **G1:** 11 (92) **G2:** 7 (70) Specific phobia: **G1:** 8 (67) **G2:** 7 (70) OCD:	**Commonly occurring co-morbidities, n (%) or mean ± SD:** Anxiety (n, % children no longer meeting criteria for primary anxiety diagnosis) Post-treatment **G1:** 7 (58) **G2:** 0 (0) p=0.003 2-month follow-up **G1:** 4 (36) **G2:** NR ADIS-P Interference Ratings: Post-treatment **G1:** 3.67 ± 2.50 **G2:** 6.50 ± 1.18 Group x time: p<0.01 2-month follow-up **G1:** 4.45 ± 2.54 **G2:** NR SCAS total score, Post-treatment **G1:** 26.75 ± 20.79 **G2:** 36.11 ± 16.46 p=NS 2-month follow-up **G1:** 29.00 ± 22.43

	G2: 1 (10) Anti-psychotic: **G1:** 3 (25) **G2:** 0 (0) Stimulant: **G1:** 0 (0) **G2:** 4 (40) Psychological/behavioral: **G1:** 3 (25) **G2:** 2 (20) School-based: **G1:** 5 (42) **G2:** 5 (50) **N at enrollment:** **G1:** 12 **G2:** 10 **N at follow-up:** Post-treatment: **G1:** 12 **G2:** 10 2 month follow-up: **G1:** 11 **G2:** NR	4 (40)Hispanic/Latino: **G1:** 2 (17) **G2:** 1 (10) Other/mixed ethnicity: **G1:** 2 (17) **G2:** 1 (10) Not reported: **G1:** 0 (0) **G2:** 4 (40) **SES:** Parent highest education, n (%): High school graduate: **G1:** 4 (33) **G2:** 1 (10) College graduate: **G1:** 7 (59) **G2:** 6 (60) Graduate degree: **G1:** 1 (8) **G2:** 3 (30) Household income, mean (range): NR Diagnostic approach: In Study and Referral Diagnostic tool/method: For ASD diagnosis: Referral: diagnosis of ASD by ADOS (Autism Diagnostic Observation Schedule); ADI-R (Autism Diagnostic Interview-Revised), and expert clinical judgment based on DSM-IV criteria In Study: ADOS, ADI-R to confirm referral diagnosis	**G1:** 2 (17) **G2:** 0 (0) Baseline comorbid diagnoses, n (%) ADHD: **G1:** 8 (67) **G2:** 8 (80) Oppositional defiant disorder: **G1:** 4 (33) **G2:** 5 (50) Major depressive disorder: **G1:** 1 (8) **G2:** 0 (0) **Educational/ cognitive/ academic attainment, mean ± SD:** IQ (WASI): **G1:** 108.42 ± 17.70 **G2:** 110.40 ± 17.39 Verbal IQ: **G1:** 105.83 ± 17.89 **G2:** 107.00 ± 15.71 Performance IQ: **G1:** 108.58 ± 16.96 **G2:** 111.90 ± 18.62	**G2:** NR SCAS-P total score: Post-treatment **G1:** 20.08 ± 11.34 **G2:** 31.70 ± 13.36 Group x time: p=0.02 2-month follow-up **G1:** 21.64 ± 9.15 **G2:** NR ADIS-P comorbid diagnoses: Post-treatment **G1:** 2.42 ± 1.38 **G2:** 4.00 ± 1.25 Group x time: p<0.001 2-month follow-up **G1:** 3.00 ± 1.67 **G2:** NR **Harms:** NR **Modifiers:** NR

	For anxiety diagnosis: Referral: ADIS-P (Anxiety Disorders Interview Schedule-Parent Version) In Study: ADIS-P to confirm referral diagnosis **Diagnostic category, n (%):** **G1:** Autism: **G1:** 3 (25) **G2:** 3 (30) Asperger syndrome: **G1:** 9 (75) **G2:** 6 (60) PDD-NOS: **G1:** 0 (0) **G2:** 1 (10) **Other characteristics**, Parent marital status, n (%)**:** Single: **G1:** 1 (8) **G2:** 2 (20) Married/remarried: **G1:** 11 (92) **G2:** 7 (70) Cohabitating: **G1:** 0 (0) **G2:** 1 (10)	

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Paynter et al. 2013[11] **Country:** Australia **Intervention setting:** NR **Enrollment period:** NR **Funding:** NR **Design:** Controlled trial	**Intervention:** Thought bubble training including individual training on how to represent beliefs via cartoon bubbles and two dimensional cardboard stimuli; training targeted 5 key Theory of Mind concepts about thinking over the course of 1-3 sessions based on when the participant mastered each key task **Assessments:** observed theory of mind measures **Groups:** **G1:** thought bubble intervention **G2:** control **Provider:** NR **Treatment manual followed:** No **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** No **Co-interventions held stable during treatment:** NR	**Inclusion criteria:** diagnosis of an ASD by qualified clinicians **Exclusion criteria:** NR **Age, mean, months (range):** **G1:** 79.41 ±20.20 **G2:** 94.86 ±28.69 **Mental age, mean ± SD:** Non-verbal mental age (raw Raven's score): **G1:** 5.41 ±2.81 **G2:** 6.14 ±5.46 Verbal mental age, months (Peabody Picture Vocabulary Test): **G1:** 70.06 ±21.31 **G2:** 81.14 ±33.99 **Sex, n (%):** M: 21 (87.5) F: 3 (12.5) **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** Referral Diagnostic tool/method: DSM-IV	**Social skills, mean ± SD:** Sally-Ann false belief (out of 2): **G1:** 0.29 ±0.47 **G2:** 0.71 ±0.76 Total false belief (out of 4): **G1:** 1.18 ±0.73 **G2:** 1.86 ±1.22 Total Theory of Mind scale (out of 5): **G1:** 2.00 ±0.94 **G2:** 2.71 ±1.11	**Social skills:** Sally-Ann false belief (out of 2): Immediate post-assessment: **G1:** 1.53 ±0.80 p<0.01 vs. baseline **G2:** 0.57 ±0.79 p=NS vs. baseline 3 week follow-up: **G1:** 1.56 ±0.73 p=0.02 vs. baseline **G2:** 1.67 ±0.82 p=NS vs. baseline Total false belief: Immediate post-assessment: **G1:** 2.94 ±1.25 p<0.01 vs. baseline **G2:** 1.43 ±1.40 p=NS vs. baseline 3 week follow-up: **G1:** 3.44 ±0.88 p<0.01 vs. baseline **G2:** 3.00 ±1.55 p=NS vs. baseline Total Theory of Mind scale: Immediate post-assessment: **G1:** 3.06 ±1.00 p<0.01 vs. baseline **G2:** 2.86 ±1.68

	Concomitant therapies, n (%): NR **N at enrollment:** **G1:** 17 **G2:** 7 **N at final follow-up (mean 23 days after immediate post assessment):** **G1:** 9 **G2:** 6	**Diagnostic category, n (%):** NR **Other characteristics, n (%):** Syntactic language skill, raw TROG-2, mean ± SD: **G1:** 5.41 ± 2.81 **G2:** 6.14 ± 5.46	p=NS vs. baseline 3 week follow-up: **G1:** 4.11 ± 0.60 p<0.01 vs. baseline **G2:** 3.33 ±1.51 p=NS vs. baseline **Harms:** NR **Modifiers:** NR

Comments: G1 at final follow-up is calculated to be 10 in the text, and 9 in the table note. Study only includes within-group statistical comparisons; no between-group analysis reported

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Perry et al. 2013[12] **Country:** Canada **Intervention setting:** **Treatment centers in the community, and children's homes** **Enrollment period:** NR **Funding:** York University **Design:** Retrospective chart review Note: See study reporting on this population[13] in 2011 AHRQ review; table includes data from comparative study only—related studies include Shine 2010,[14] Freeman 2010,[15] Perry 2011,[16] Flanagan 2012[17]	**Intervention:** Intensive behavioral Intervention (IBI) 20 hours/week **Assessments:** Cognitive and adaptive outcomes **Groups:** **G1a:** Younger age group (2-5 years) **G1b:** Older age group (6-14 years) **Provider:** • Psychologists and psychometrists **Treatment manual followed:** Yes **Defined protocol followed:** NR **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR N at enrollment: **G1a:** 60 **G1b:** 60	**Inclusion criteria:** Children (from the community effectiveness program conducted in Canada who had IBI) matched on their initial IQ prior to the intervention. **Exclusion criteria:** see inclusion **Age, mean/yrs (range):** **G1a:** 4.26 ± 1.09 (2.08–5.92) **G1b:** 7.45 ± 1.87 (6.00–13.58) **Mental age, mean/yrs (range):** **G1a:** 1.67 ±.93 (.25–5.64) **G1b:** 3.02 ± 1.57 (.71–7.45) **Sex:** NR **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** NR Diagnostic tool/method: NR **Diagnostic category, n (%):** Autism: 100 **Other characteristics**: **Duration IBI (months)** mean ± SD (range)	**IQ, mean ± SD:** **G1a:** 43.47 ± 21.26 **G1b:** 42.68 ± 21.38 **Cognitive rate:** G1a: .42 ± .21 G1b: .43 ± .21 **Adaptive behavior** VABS composite standard score: **G1a**: 55.89 ± 9.11 **G1b:** 53.63 ± 12.63 Adaptive rate **G1a:** .34 ±.14 **G1b:** .34 ± .14	**IQ, mean ± SD:** **G1a:** 60.11 ± 31.39 **G1b:** 44.44 ± 21.18 p <.001 **Cognitive rate:** G1a:1.09 ± .92 G1b:.47 ± .65 p<.001 **Adaptive behavior** VABS composite standard score: **G1a:** 59.52 ± 17.40 **G1b:** 58.88 ± 13.81 p=.47 **Adaptive rate** **G1a:**.86 ±.81 **G1b**: .62 ±.76 p=.09 **Harms:** NR **Modifiers:** NR

	N at follow-up: **G1a:** 60 **G1b:** 60	**G1a**: 20.53 ± 8.99 (10–42) **G1b**: 20.20 ± 8.23 (10–41)

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Peters-Scheffer et al. 2013 [18] **Country:** Netherlands **Intervention setting:** School **Enrollment period:** 2007-2011 **Funding:** Stichting De Driestroom at Elst, The Netherlands **Design:** nRCT	**Intervention:** School-based treatment based on ABA principles provided one-on-one for 4–10 hours/week over 2 years (1 year for 9 of the participants) Children in the control group received standard care **Assessments**: Parent, teacher & staff report **Groups:** **G1:** Low intensity behavioral treatment (LIBT) **G2:** Treatment as usual **Provider:** **G1**: university-student therapists, pre-school staff and teachers, and MScS in psychology or special education **G2**: Clinical psychologist or special educator (MSc) **Treatment manual followed:** Yes **Defined protocol followed:** Yes	**Inclusion criteria:** • Previous DSM-IV or ICD-10 diagnosis of intellectual disability (ID) and autism or Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) by a clinician who was independent of the study **Exclusion criteria:** See inclusion **Age, mean (SD) /months / range:** **G1**+**G2**: 62.52 months ± 16.96 **Mental age, mean/yrs (range):** NR **Sex, n (%):** M **G1**: 18 (90) **G2**: 18 (90) F **G1**: 2 (10) **G2**: 2 (10) **Race/ethnicity, n (%):** NR	**Mean (SD)** Cognitive functioning Developmental age, in months **G1**:23.34 (7.32) **G2**:23.43 (6.34) Ratio IQ **G1**:40.66 (20.07) **G2**:40.14 (18.27) Visual reception **G1**:26.30 (8.47) **G2**:26.95 (5.46) Fine motor **G1**:27.50 (6.20) **G2**:27.65 (6.43) Receptive language **G1**:19.75 (9.26) **G2**:20.15 (8.57) Expressive language **G1**:19.80 (8.32) **G2**:18.95 (9.12) Adaptive behavior Composite **G1**:18.35 (3.41) **G2**:19.82 (4.71) Communication **G1**:23.94 (7.64) **G2**:24.35 (9.80) Daily living skills	**Mean (SD):** **At 24 months**: Cognitive functioning Developmental age **G1**:39.70 (11.99) **G2**:32.44 (11.55) d=1.09, p=0.001 Ratio IQ **G1**:48.12 (19.71) **G2**:39.42 (19.89), d=0.40, p<0.001 Visual reception **G1**:44.50 (14.39) **G2**:36.10 (11.99) Fine motor **G1**:44.45 (14.66) **G2**:34.65 (10.37) Receptive language **G1**:36.55 (11.63) **G2**:30.80 (13.27), d=1.22 Expressive language **G1**:33.30 (12.02) **G2**:28.20 (14.03), d=0.40 Adaptive behavior Composite **G1**:37.35 (13.05) **G2**:26.71 (9.84), d=1.74, p<0.001

	Measure of treatment fidelity reported: yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1**: 23 **G2**: 20 **N at follow-up:** **G1**: 20 **G2**: 20	**SES:** NR **Diagnostic approach:** Referral & in study Diagnostic tool/method: ADOS, CARS **Diagnostic category, n (%):** **G1**: Autism:18, PDD-NOS:2 **G2**:Autism:19, PDD-NOS:1 **Other characteristics**, Mean (SD)/range: No major medical diagnoses reported **G1**: Received on average 4.98 h / week of treatment (SD = 1.45; range: 1.32–7.11). **G1:** 9 children received only 1 year of behavioral intervention	**G1**:20.82 (6.12) **G2**:23.00 (9.26) Socialization **G1**:19.76 (3.36) **G2**:22.88 (5.79) Social emotional development Interpersonal relationships **G1**:14.44 (5.19) **G2**:16.94 (6.50) Play and leisure time **G1**:15.38 (5.82) **G2**:18.75 (5.87) Early social communication Initiating joint attention **G1**:7.43 (6.02) **G2**:7.64 (9.52) Responding to joint attention **G1**:96.60 (62.68) **G2**:118.80 (58.92) Initiating requests **G1**:24.64 (4.77) **G2**:25.71 (4.50) Responding to requests **G1**:69.16 (35.05) **G2**:70.07 (22.53) Initiating social interaction **G1**:3.21 (1.48)	Communication **G1**:43.71 (17.68) **G2**:32.35 (14.56), d=1.41 Daily living skills **G1**:39.29 (11.13) **G2**:29.71 (12.15), d=1.62 Socialization **G1**:39.35 (10.58) **G2**:29.71 (9.99), d=2.61 Social emotional development Interpersonal relationships **G1**:29.25 (9.60) **G2**:22.31 (6.59), d=1.57, p=0.001 Play and leisure time **G1**:36.19 (12.97) **G2**:25.31 (7.58), d=2.42 Early social communication Initiating joint attention **G1**:11.50 (7.62) **G2**:11.21 (7.75) Responding to joint attention **G1**:84.70 (73.19) **G2**:95.31 (83.88) Initiating requests **G1**:26.36 (5.21

G2:2.07 (1.49) Responding to social interaction **G1**:7.50 (2.74) **G2**:7.00 (2.91) Receptive language **G1**:25.00 (4.48) **G2**:24.70 (3.21) Expressive language **G1**:18.35 (6.72) **G2**:17.65 (6.64) Autism; total score ADOS **G1**:17.00 (3.28) **G2**:15.45 (2.72) Autism; total score CARS **G1**:43.84 (4.30) **G2**:40.79 (6.20) Emotional/behavioral problems **G1**:67.00 (26.38) **G2**:68.29 (33.47) Behavioral flexibility **G1**:10.00 (6.96) **G2**:11.29 (6.64) Maternal stress **G1**:78.38 (28.75) **G2**:95.08 (30.31)	**G2**:26.86 (4.75), P=ns Responding to requests **G1**:88.21 (17.60) **G2**:89.33 (15.90), P=ns Initiating social interaction **G1**:3.79 (2.36) **G2**:3.29 (2.02), p=ns Responding to social interaction **G1**:9.79 (3.98) **G2**:9.07 (3.45), p=ns Receptive language **G1**:34.30 (10.54) **G2**:29.30 (7.42) Expressive language **G1**:34.15 (14.54) **G2**:30.80 (15.12), d=0.40 Autism; total score ADOS **G1**:12.05 (5.41) **G2**:15.15 (4.26), d=1.51 Autism; total score CARS **G1**:34.89 (3.62) **G2**:39.95 (4.62), d=1.50 Emotional/behavioral problems **G1**:52.86 (23.52) **G2**:65.21 (32.62)

p = .16
Behavioral flexibility
G1:9.14 (4.59)
G2:11.14 (6.49)
G1 vs. **G2**, p=ns

Maternal stress
G1:71.38 (30.76)
G2:87.08 (31.43),
d=0.33, p=0.29

Harms: NR

Modifiers: NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Reed et al. 2013[19] **Country:** UK **Intervention setting:** Home **Enrollment period:** NR **Funding:** NR **Design:** Prospective Cohort	**Intervention:** Barnet Early Autism Model (BEAM)- home based program delivered by trained facilitators under direction of an advisory teacher; individualized program for each participant and daily visits by facilitator Portage- a home-based teaching program; supervised by trained Portage worker who visits parents once a week; training sessions last about 40-60 min/day **Assessments:** observed, parent report **Groups:** **G1:** BEAM **G2:** Portage **Provider:** • Trained facilitators **Treatment manual followed:** Yes **Defined protocol followed:** No **Measure of treatment fidelity reported:** No	**Inclusion criteria:** diagnosis of autism or PDD-NOS made by pediatrician independent of the study participants had to be at start of their intervention and not receiving any other major intervention for duration of study < 5 years old **Exclusion criteria:** See above Age, mean months ± SD: **G1:** 43.6 ± 5.8 **G2:** 40.1 ± 8.3 **Mental age, mean/yrs:** NR **Sex:** NR **Race/ethnicity, n (%):** NR **SES:** Maternal education: NR Household income, mean (range): NR **Diagnostic approach:** Referral Diagnostic tool/method: DSM-IV **Diagnostic category, n (%):** NR	**Global Rating of Severity** Autism Behavior Checklist, mean ± SD: **G1:** 59.8 ± 16.1 **G2:** 58.8 ± 23.8 Intellectual functioning (Leiter overall): **G1:** 83.3 ± 23.7 **G2:** 72.6 ± 12.5 Adaptive behavior (Vineland composite) **G1:** 70.2 ± 4.1 **G2:** 68.6 ± 6.0 Language (Peabody overall) **G1:** 59.9 ± 19.5 **G2:** 55.3 ± 14.7 Behavior Problems (DBC total) **G1:** 41.1 ± 11.6 **G2:** 35.8 ± 12.8	**Global Rating of Severity** Autism Behavior Checklist, mean ± SD No change between groups at follow-up **Communication/ language:** Mean group change scores were significantly different for G1 vs G2; F(1,30)=5.83, p<0.05 **Adaptive behavior:** Mean group change scores were significantly different for G1 vs G2; F(1,30)=90.27, p<0.001 **Educational/ cognitive/ academic attainment:** No change between groups at follow-up **Harms:** NR **Modifiers:** No significant relationship between baseline parenting stress and follow-up child intellectual functioning, r(30) = - 0.217, p > 0.10 Statistically significant negative relationships between parenting stress at baseline and

	Co-interventions held stable during treatment: Participants could not receive any other "major intervention" during the study **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 16 **G2:** 16 **N at follow-up:** **G1:** 16 **G2:** 16	**Hours per week of intervention** **G1:** 6.4 ± 2.1 **G2:** 8.5 ± 6.8		followup linguistic functioning, $r(30) = -0.355$, $p < 0.05$

Comments: Outcome measures were reported in figure format only (results reported as change from baseline to follow-up).

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Schertz et al. 2013[20] **Country:** US **Intervention setting:** home **Enrollment period:** NR **Funding:** Autism Speaks **Design:** RCT	**Intervention:** Joint attention mediated learning (JAML), with weekly home visits to parents and child conducted by intervention coordinators Participants spent a mean of 7 months (range 4-12 months) in either intervention or control **Assessments:** observed, parent report **Groups:** **G1:** JAML **G2:** Treatment as usual **Provider:** • 2 interventionists with master's degrees in early childhood education and 1 with an Ed.S. degree in counseling **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes	**Inclusion criteria:** scores above designated cut-off levels on ADOS (4 on the Communication of Section 1 and 4 on the Social section) absence of joint attention during interaction with parents based on direct observation chronological age < 30 months at onset of intervention **Exclusion criteria:** confounding diagnosis (e.g. failure to thrive, premature birth > 6 weeks, other developmental disabilities such as Down syndrome) **Age, mean months ± SD:** **G1:** 24.6 ± 4.0 **G2:** 27.5 ± 3.4 **Mental age, mean months ± SD:** NR **Sex:** NR **Race/ethnicity, n (%):** NR **SES:** Participating parent education, mean years ±	**Communication/ language:** Focusing on faces, mean ± SD: **G1:** 6.75 ± 5.18 **G2:** 6.28 ± 5.14 Turn-Taking, mean ± SD: **G1:** 1.67 ± 1.66 **G2:** 1.94 ± 2.74 Responding to Joint Attention, mean ± SD: **G1:** 0.06 ± 0.13 **G2:** 0.25 ± 0.32 Initiating Joint Attention, mean ± SD: **G1:** 0.14 ± 0.26 **G2:** 0.19 ± 0.33 VABS, communication, mean ± SD: **G1:** 63.73 ± 9.42 **G2:** 69.55 ± 10.73 MSEL, receptive language, mean ± SD: **G1:** 21.0 ± 2.0 **G2:** 25.9 ± 9.1 MSEL, expressive language**,** mean ± SD: **G1:** 24.6 ± 6.7 **G2:** 24.8 ± 6.9	**Communication/ language:** Focusing on faces, mean ± SD: **G1:** 14.85 ± 8.99 **G2:** 7.33 ± 6.81 Time x group interaction: p=NS Turn-Taking, mean ± SD: **G1:** 2.47 ± 2.17 **G2:** 2.85 ± 3.06 Time x group interaction: p=NS Responding to Joint Attention, mean ± SD: **G1:** 5.61 ± 4.77 **G2:** 0.75 ± 1.18 Time x group interaction: p=NS Initiating Joint Attention, mean ± SD: **G1:** 4.40 ± 4.48 **G2:** 2.40 ± 3.72 Time x group interaction: p=NS VABS, communication, mean ± SD: **G1:** 75.90 ± 13.51 **G2:** 68.08 ± 19.77 Time x group interaction: p<0.05 MSEL, receptive language, mean ± SD:

	Co-interventions held stable during treatment: No **Concomitant therapies, n (%):** Weekly hours of intervention, mean ± SD (G1 includes JAML hours): Indiana: **G1:** 7.41 ± 4.67 **G2:** 12.82 ± 14.06 Kansas **G1:** 17.88 ± 9.06 **G2:** 21.35 ± 11.51 North Carolina: **G1:** 2.89 ± 1.25 **G2:** 6.25 ± 6.49 **N at enrollment:** **G1:** 11 **G2:** 12 **N at follow-up:** **G1:** 11 **G2:** 12	SD: **G1:** 14.4 ± 2.3 **G2:** 15.8 ± 2.3 Household income, mean (range): NR **Diagnostic approach:** In Study Diagnostic tool/method: initial screening with M-CHAT, followed by ADOS **Diagnostic category, n (%):** NR **Other characteristics, mean ± SD:** ADOS, Communication: **G1:** 6.4 ± 1.1 **G2:** 6.0 ± 1.8 ADOS, Social: **G1:** 11.0 ± 2.6 **G2:** 10.8 ± 1.8 ADOS, Play: **G1:** 3.7 ± 0.8 **G2:** 2.8 ± 1.5 ADOS, Stereotypy: **G1:** 1.0 ± 1.1 **G2:** 1.7 ± 1.8		**G1:** 28.27 ± 11.35 **G2:** 25.33 ± 8.52 Time x group interaction: p<0.05 MSEL, expressive language, mean ± SD: **G1:** 33.27 ± 15.79 **G2:** 27.17 ± 11.21 Time x group interaction: p=NS **Harms:** NR **Modifiers:** NR

Comments: outcome data is reported as a composite (mean) of 2 follow-up scoring sessions (4 and 8 weeks after intervention ceased)

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Schreibman et al., 2013 [21] **Country:** US **Intervention setting:** Laboratory and home **Enrollment period:** NR **Funding:** USPHS grants from NIMH **Design:** RCT	**Intervention:** Picture Exchange Communication System (PECS) Pivotal Response Training (PRT) For the first 15 weeks parent and children participated in 2 weekly, 2 hour parent education sessions in the laboratory and children received additional five 2-hour sessions at home. Following 8 weeks of one 2-hour parent education session per week and two 2-hour/week home sessions. Children received average of 247 hours of treatment during the study (range 181-263) **Assessments:** observed, parent report **Groups:** **G1:** PECS **G2:** PRT **Provider:** • Undergraduate student therapists trained in PECS and PRT.	**Inclusion criteria:** diagnosis of autistic disorder confirmed by ADI-R and ADOS-G < 48 months old No more than 9 intelligible words Absence of evidence for diagnosis of primary mental retardation, neurological pathology or major sensory impairment Absence of prior treatment involving PECS or PRT Parental willingness to participate in training and to refrain from non-assigned treatment for duration of the study **Exclusion criteria:** See above **Age, mean months ± SD**: **G1:** 28.9 ± 4.2 **G2:** 29.5 ± 6.9 **Mental age, mean/yrs:** NR **Sex:** M, n (%) **G1:** 16 (84.2) **G2:** 18 (90) F, n (%) **G1:** 3 (15.8) **G2:** 2 (10)	**Communication/ language:** Mullen Scales of Early Learning, mean ± SD (n=38): Expressive communication (n=38) **G1:** 20.3 ± 3.2 **G2:** 18.5 ± 2.8 MacArthur CDI, mean ± SD (n=35): Words produced **G1:** 5.3 ± 9.4 **G2:** 11.9 ± 20.5 VABS, mean ± SD (n=35): Communication **G1:** 62.2 ± 4.7 **G2:** 60.2 ± 7.5	**Communication/ language:** Mullen Scales of Early Learning, mean ± SD (n=38): Expressive communication **G1:** 28.7 ± 16.5 **G2:** 23.7 ±11.2 Group x time interaction: p=NS MacArthur CDI, mean ± SD (n=35): Words produced **G1:** 129.8 ± 117.9 **G2:** 113.3 ± 108.3 Group x time interaction: p=NS VABS, mean ± SD: Communication **G1:** 68.4 ± 14.5 **G2:** 62.6 ± 12.7 Group x time interaction: p=NS **Harms:** NR **Modifiers:** NR

	Parent educators were doctoral students **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, hours/week:** Speech therapy and occupational therapy: **G1:** .94 **G2**: .94 Preschool/daycare: **G1**:.3 **G2:** 1.5 In-home early intervention **G1:** 2.4 **G2:** 3.4 (No significant differences in the amount of other treatments received) **N at enrollment:** **G1:** 19 **G2:** 20 **N at follow-up:** **G1:** 19 **G2:** 20	**Race/ethnicity, n (%):** NR **SES:** Maternal education: NR Household income, mean (range): NR **Diagnostic approach:** In Study/Referral Diagnostic tool/method: ADI-R, ADOS-G **Diagnostic category, n (%):** Autism: 100 **Other characteristics, n (%):** Word use, n (%) No words **G1:** 11 (57.9) **G2:** 10 (50) 1-10 words **G1:** 8 (42.1) **G2:** 10 (50) Cognitive functioning, n (%) Low **G1:** 8 (42.1) **G2:** 12 (60) High **G1:** 11 (57.9) **G2:** 8 (40) Parent satisfaction with intervention results

	*some loss to followup but group not clearly reported	(overall): Mean rating: **G1**: 6.0 **G2**: 5.7 Difficulty of the strategy: **G1**: 4.6 **G2:** 5.6 **G1 vs G2**: p=0.005

Table C-1. Evidence table, continued Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Sharp et al. 2013 [22] **Country:** US **Intervention setting:** Home **Enrollment period:** NR **Funding:** 2008 Applied Research Grant sponsored by the Organization for Autism Research **Design:** RCT	**Intervention:** Autism Meal Plan involving eight, 1-h-long parent-training group sessions covering topics as general behavior management strategies applied during meals, specific interventions for feeding problems associated with ASD and strategies for promoting self-feeding Waitlist control group received email correspondence involving handouts on nonfeeding-related topics with limited behavioral content subsequently offered the educational curriculum **Assessments:** Social Responsiveness Scale (SRS)–parent report form. Brief Autism Mealtime Behavior Inventory (BAMBI) Parenting Stress Index–short form (PSI-SF) Food Preference Inventory (FPI) Social validity and parent perception of improvement	**Inclusion criteria:** ASD diagnosis among children aged between 3 and 8 years a total SRS score in the mild, moderate, or severe range (total standard score (T-score) > 60) **Exclusion criteria:** See inclusion **Age, mean ± SD /months /range:** **G1:** 70.8 ± 20.5/36–104 **G2:** 64.8 ± 6.9/45–94 **Mental age, mean/yrs (range):** NR **Sex , n(%):** G1+G2: M: 8 (80) F: 7 (78) **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** In Study Diagnostic tool/method: Social Responsiveness Scale (SRS) parent report form **Diagnostic category, (%):** ASD : 100	**Mean ± SD** BAMBI total score **G1:**51. ± 1 7.1 **G2:**52. ± 1 7.8 BAMBI limited variety **G1:**28.2 ± 5.1 **G2:**28.2 ± 5.1 BAMBI food refusal **G1:**12.9 ± 3.5 **G2:**11.9 ± 3.3 BAMBI autism features **G1:**10.0 ± 2.1 **G2:**12.0 ± 3.54 FPI selectivity score **G1:**32.6 ± 22.3 **G2:**37.2 ± 17.8	**Mean ± SD** BAMBI total score **G1:**47.2 ± 9.6 **G2:**47.2 ± 12.6 p=.79 (F=.07) BAMBI limited variety **G1:**26.0 ± 5.2 **G2:**26.8 ± 6.6 p=.55 (F=.36) BAMBI food refusal **G1:**12.6 ± 4.1 **G2:**11.0 ± 3.0 p=.51 (F=.46) BAMBI autism features **G1:**8.6 ± 2.0 **G2:**9.5 ± 3.6 p=.57 (F=.34) FPI selectivity score **G1:**38.8 ± 27.5 **G2:**37.2 ± 25.9 p=.21 (F=1.7) **Harms:** NR **Modifiers:** NR

Groups: **G1:** Autism Meal Plan **G2:** Wait-list control **Provider:** • Behavioral psychologist and a post-doc psychology fellow **Treatment manual followed:** yes **Defined protocol followed:** yes **Measure of treatment fidelity reported:** yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 15 **G2:** 15 **N at follow-up:** **G1:** 10 **G2:** 9	**Other characteristics**, Mean ± SD/range: SRS total score **G1:**82.4 ± 8.4/70–91 **G2:**80.6 ± 7.9/68–91	

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Siller et al. 2013[23] **Country:** US **Intervention setting:** home **Enrollment period:** 2004- to 2007 **Funding:** National Institute of Child Health and Development, M.I.N.D. Institute Research Program, and PSC-CUNY grants **Design:** RCT	**Intervention:** Focused Playtime Intervention (FPI)- a parent education program involving 12 in-home training sessions (once/week for 12 weeks, 90 min each) follows standardized treatment manual uses capacity building approach to promote coordinated toy play between parent and child. Parents in both groups received monthly sessions to enhance parent advocacy in multiple formats including workbook, teaching, video and demonstrations. **Assessments:** Mullen Scales of Early Learning (MSEL); Early Social Communication Scale, Insightfulness Assessment (IA); observations of mother-child interaction; medical history questionnaire; survey of non-project services; ADI-R and ADOS Baseline assessment (T1) conducted in three	**Inclusion criteria:** • < 6 years old • previously diagnosed with ASD • limited or no use of spoken language (generally < 25 words and no phrases) • mother fluent in English and willing/available to participate in all assessment and treatment sessions • families lived reasonable distance from research lab (generally < 90 min) **Exclusion criteria:** known genetic diagnosis including Fragile X, tuberous sclerosis or Rett syndrome. **Age, mean/mos ± SD (range):** **G1:** 58.3 ± 12.7 (33-82) **G2:** 55.9 ± 11.9 (32-76) **Mental age, mean/yrs (range):** NR **Sex:** M, 64 (91.4%):	**Language/communication:** Mullen scales of early learning, mean ± SD (range): Fine motor **G1:** 28.6 ± 10.4 (12-55) **G2:** 28.3 ± 11.8 (10-59) Visual reception **G1:** 26.6 ± 9.4 (11-50) **G2:** 24.6 ± 11.2 (1-11) Receptive language **G1:** 17.5 ± 8.0 (5-36) **G2:** 16.5 ± 8.-0 (1-33) Expressive language **G1:** 16.5 ± 9.8 (4-36) **G2:** 15.1 ± 8.2 (4-37) ADOS Social affect total **G1:** 14.7 ± 3.3 (6-20) **G2:** 14.8 ± 3.4 (4-20) Restricted and repetitive behavior **G1:** 4.9 ± 2.0 (0-8) **G2:** 5.2 ± 2.2 (0-8) Total **G1:** 19.6 ± 4.1 (9-26) **G2:** 20.0 ± 4.2 (7-26) ESCS Response to joint attention	**Language/communication:** Maternal synchronization, mean ± SE Time 2 **G1:** 0.72 ± 0.04 **G2:** 0.61 ± 0.04 T1 to T2 **G1:** 0.06 ± 0.04 **G2:** -0.06 ± 0.04 Expressive language, mean ± SE T2 **G1:** 4.02 ± 0.16 **G2:** 3.90 ± 0.17 T3 **G1:** 4.38 ± 0.17 **G2:** 4.17 ± 0.17 T1 to T3 **G1:** 0.08 ± 0.09 **G2:** -0.09 ± 0.10 **Harms:** NR **Modifiers** Children with baseline expressive language abilities < 11.3 months showed larger gains in expressive language when randomized to G1

	sessions (two at research lab and one at home), at exit (T2), Follow up approximately 12 mos after exit (T3). **Groups:** **G1:** intervention **G2:** control **Provider:** Trained graduate and postdoctoral students in developmental psychology and counseling **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** Yes **Concomitant therapies, n (%):** Medication to control seizures (n=3) **N at enrollment:** **G1:** 36 **G2:** 34 **N at follow-up:** **G1:** 31 **G2:** 31	F, 6 (8.6%): **Race/ethnicity, n (%):** Hispanic/Latino **G1:** 17 (47.2) **G2:** 14 (41.2) White **G1:** 8 (22.2) **G2:** 6 (17.6) Asian **G1:** 4 (11.1) **G2:** 9 (26.5) Black **G1:** 3 (8.3) **G2:** 2 (5.9) Mixed **G1:** 4 (11.1) **G2:** 3 (8.8) **SES:** Maternal education, n (%): 10^{th}-11th grade **G1:** 1 (2.8) **G2:** 0 High school graduate **G1:** 7 (19.4) **G2:** 2 (5.9) Partial college **G1:** 13 (36.1) **G2:** 13 (38.2) Standard college graduate **G1:** 8 (22.2) **G2:** 10 (29.4)	**G1:** 47.0 ± 24.1 (8-100) **G2:** 39.6 ± 24.1 (5-88) Non-project services Twelve months prior to intake **G1:** 8.8 ± 10.4 (0-44) n=36 **G2:** 8.8 ± 10.9 (0-46) n=32 Between intake and exit **G1:** 12.4 ± 11.0 (0-40) n=34 **G2:** 12.1 ± 10.2 (0-44) n=30 Between exit and follow up **G1:** 12.5 ± 11.7 (0-36) n=27 **G2:** 13.7 ± 9.5 (0-37) n=27 School programs Twelve months prior to intake **G1:** 11.5 ± 6.6 (0-29) n=36 **G2:** 12.6 ± 7.1 (0-25) n=32 Between intake and exit **G1:** 14.6 ± 8.8 (0-30) n=34 **G2:** 14.8 ± 5.5 (1-28) n=30 Between exit and follow up **G1:** 17.1 ± 9.0 (0-29) n=27 **G2:** 16.2 ± 6.9 (0-25) n=27 Maternal synchronization, mean ± SE **G1:** 0.57 ± 0.03 **G2:** 0.63 ± 0.03 Expressive language, mean ± SE	

	Graduate degree **G1:** 7 (19.4) **G2:** 9 (26.5) Household income, mean (range): Below $19,999 **G1:** 6 (16.7) **G2:** 2 (5.9) $20,000-$39,999 **G1:** 9 (25.0) **G2:** 4 (11.8) $40,000-$74,999 **G1:** 7 (19.4) **G2:** 10 (29.4) Above $74,999 **G1:** 14 (38.9) **G2:** 18 (52.9) **Diagnostic approach:** Referral Diagnostic tool/method: ADI-R and ADOS **Diagnostic category,n (%):** NR **Other characteristics, n (%):** NR	**G1:** 3.70 ± 0.16 **G2:** 3.75 ± 0.16

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Storch et al. 2013[24] **Country:** USA **Intervention setting:** University-based mental health clinic **Enrollment period:** NR **Funding:** National Institutes of Health (NIH) Centers for Disease Control (CDC) Agency for Healthcare Research and Quality National Alliance for Research on Schizophrenia and Affective Disorders (NARSAD) International Obsessive-Compulsive Disorder Foundation (IOCDF)	**Intervention:** Cognitive-behavioral therapy (CBT),16 weekly sessions with 3 month follow-up **Assessments:** Clinician-rated measurements PARS ADIS-C/P Clinical Global Impression (CGI)-Severity and Improvement Parent-rated measures Child Behavior Checklist (CBCL) Columbia Impairment Scale-Parent Version (CIS-P) Multidimensional Anxiety Scale for Children-Parent Version (MASC-P) Social Responsiveness Scale (SRS) SACA Child-Rated Measures Revised Children's Manifest Anxiety Scale (RCMAS) **Groups:** **G1:** CBT **G2:** standard care	**Inclusion criteria:** • diagnosis of autism, Asperger's syndrome, or PDD-NOS diagnosed by ADI-R and ADOS • primary diagnosis of separation anxiety disorder (SAD), social phobia, generalized anxiety disorder (GAD), or obsessive compulsive disorder (OCD) • age 7-11 years old **Exclusion criteria:** • full scale or verbal comprehension IQ < 70 on a standardized test • concurrent participation in psychosocial interventions • suicidality or suicidal behavior in the last six months • diagnosis of BPAD or psychotic disorder **Age, mean/yrs ± SD:** **G1:** 8.83 ± 1.31 **G2:** 8.95 ± 1.40	**Overall ratings:** **Global Rating of Severity, mean ± SD:** CGI-Severity**:** **G1:** 3.50 ± 0.72 **G2:** 4.00 ± 0.63 **Social skills:** SRS total, mean ± SD: **G1:** 100.83 ± 25.10 **G2:** 110.14 ± 22.41 SRS, awareness, mean ± SD: **G1:** 12.67 ± 3.94 **G2:** 12.67 ± 3.14 SRS, motivation, mean ± SD: **G1:** 14.33 ± 4.86 **G2:** 19.10 ± 5.37 SRS, mannerisms, mean ± SD: **G1:** 19.63 ± 5.86 **G2:** 20.62 ± 6.75 **Communication/ language:** SRS, communication, mean ± SD: **G1:** 33.83 ± 9.31 **G2:** 36.67 ± 7.83 **Problem behavior:** CIS-P, mean ± SD: **G1:** 21.13 ± 9.51	**Overall ratings:** **Global Rating of Severity, mean ± SD:** CGI-Severity**:** **G1:** 2.67 ± 0.48 **G2:** 3.57 ± 0.87 p < 0.01 3-month follow-up **G1:** 2.73 ± 0.96 p < 0.01 vs. baseline **Social skills:** SRS total, mean ± SD: **G1:** 88.88 ± 19.85 **G2:** 106.19 ± 26.00 p < 0.05 3-month follow-up **G1:** 93.33 ± 27.64 p=NS SRS, awareness, mean ± SD: **G1:** 12.04 ± 2.63 **G2:** 12.57 ± 3.67 p=NS 3-month follow-up **G1:** 12.00 ± 3.32 p < 0.05 vs. baseline SRS, motivation, mean ± SD: **G1:** 12.46 ± 3.91 **G2:** 17.57 ± 5.64 p=NS 3-month follow-up **G1:** 14.00 ± 6.65 p=NS vs. baseline

Tourette Syndrome Association Janssen Pharmaceuticals **Design:** RCT	**Provider:** Therapists Parents Self-therapy **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** SSRI: **G1:** 6 (25) **G2:** 4 (19) Atypical antipsychotic: **G1:** 2 (8.3) **G2:** 5 (23.8) Stimulant, atomoxetine, or guanfacine: **G1:** 7 (29.2) **G2:** 7 (33.3) Benzodiazepine: **G1:** 0 **G2:** 1 (4.8) **N at enrollment:** **G1:** 24 **G2:** 21	**Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1**: 19 (79.2) **G2**: 17 (81) F, n (%): **G1**: 5 (20.8) **G2**: 4 (19) **Race/ethnicity, n (%):** **G1**: White: **G1**: 22 (91.7) **G2**: 16 (76.2) Asian/Pacific: **G1**: 1 (4.2) **G2:** 1 (4.8) Latino/Latina: **G1**: 1 (4.2) **G2**: 4 (19) **SES:** **Household income, n (%)**: < $40,000: **G1**: 1 (4.2) **G2**: 3 (14.3) Between $40,001 and $90,000: **G1:** 6 (25) **G2:** 6 (28.6) >$90,000: **G1:** 17 (70.8) **G2**: 11 (52.4)	**G2:** 24.71 ± 10.35 CBCL, internalizing, mean ± SD: **G1:** 18.08 ± 9.09 **G2:** 23.71 ± 7.99 CBCL, externalizing, mean ± SD: **G1:** 13.67 ± 9.58 **G2:** 20.10 ± 14.25 **Anxiety:** PARS, mean ± SD: **G1:** 16.33 ± 1.93 **G2:** 17.62 ± 2.04 ADIS Highest CSR, mean ± SD: **G1:** 5.42 ± 0.72 **G2:** 5.62 ± 0.92 MASC-P, mean ± SD: **G1:** 58.58 ± 13.15 **G2:** 63.19 ± 10.51 RCMAS, dysphoric mood, mean ± SD: **G1:** 2.88 ± 2.01 **G2:** 3.33 ± 1.85 RCMAS, oversensitivity, mean ± SD: **G1:** 2.21 ± 2.13 **G2:** 3.38 ± 2.01 RCMAS, worry, mean ± SD: **G1:** 3.67 ± 2.35 **G2:** 4.05 ± 2.27 RCMAS, anxious arousal,	SRS, mannerisms, mean ± SD: **G1:** 17.46 ± 5.93 **G2:** 21.00 ± 5.91 p < 0.05 3-month follow-up **G1:** 17.00 ± 7.05 p < 0.05 **Communication/ language:** SRS, communication, mean ± SD: **G1:** 29.71 ± 7.83 **G2:** 36.33 ± 9.83 p < 0.05 3-month follow-up **G1:** 31.07 ± 8.73 p=NS **Problem behavior:** CIS-P, mean ± SD: **G1:** 15.54 ± 6.88 **G2:** 23.90 ± 10.25 p < 0.01 3-month follow-up **G1:** 14.13 ± 7.96 p < 0.05 vs. baseline CBCL, internalizing, mean ± SD: **G1:** 11.79 ± 5.36 **G2:**19.57 ± 9.85 p < 0.05 3-month follow-up **G1:** 11.47 ± 6.21 p < 0.01 vs. baseline CBCL, externalizing, mean ± SD:

	N at post-treatment: **G1:** 22 **G2:** 21 **N at 3 month follow-up:** **G1:** 15 **G2:** NA	**Diagnostic approach:** NR **Diagnostic category, n (%):** Autism: **G1**: 10 (41.7) **G2**: 3 (14.3) PDD-NOS: **G1**: 9 (37.5) **G2**: 9 (42.9) Asperger's syndrome: **G1**: 5 (20.8) **G2**: 9 (42.9) **Other characteristics, n (%):** Primary anxiety disorder n (%): Social Phobia: **G1:** 10 (41.7) **G2:** 8 (38.1) SAD: **G1:** 3 (12.5) **G2:** 6 (28.6) OCD: **G1:**2 (8.3) **G2:** 2 (9.5) GAD: **G1:** 9 (37.5) **G2:** 5 (23.8) **Other comorbid diagnoses n (%):** SAD: **G1**: 6 (25.0)	mean ± SD: **G1:** 2.50 ± 1.69 **G2:** 3.24 ± 1.87 **Educational/ cognitive/ academic attainment:** SRS, cognition, mean ± SD: **G1:** 19.00 ± 4.62 **G2:** 21.10 ± 5.02	**G1:** 11.08 ± 8.35 **G2:** 17.24 ± 12.81 p=NS 3-month follow-up **G1:** 9.33 ± 8.77 p < 0.05 vs. baseline **Anxiety:** PARS, mean ± SD: **G1:** 11.58 ± 3.15 **G2:** 16.05 ± 3.22 p < 0.01 3-month follow-up **G1:** 11.20 ± 4.28 p < 0.01 vs. baseline ADIS Highest CSR, mean ± SD: **G1:** 3.38 ± 1.81 **G2:** 4.90 ± 1.51 p < 0.01 3-month follow-up **G1:** 3.47 ± 2.45 p < 0.01 vs. baseline MASC-P, mean ± SD: **G1:** 51.96 ± 13.44 **G2:** 58.43 ± 12.81 p=NS 3-month follow-up **G1:** 47.80 ± 9.78 p < 0.01 vs. baseline RCMAS, dysphoric mood, mean ± SD: **G1:** 3.21 ± 1.93 **G2:** 3.10 ± 1.76 p=NS 3-month follow-up **G1:** 1.93 ± 1.91 p≤0.05 vs. baseline

	G2: 5 (23.8) Social phobia: **G1**: 7 (29.2) **G2**: 11 (52.4) GAD: **G1**: 11 (45.8) **G2**: 11 (52.4) ADHD: **G1**: 17 (70.8) **G2**: 16 (76.2) Dysthymia/MDD: **G1**: 1 (4.2) **G2**: 2 (9.5) ODD/CD: **G1**: 9 (37.5) **G2**: 11 (52.4) Specific phobia: **G1**: 16 (66.7) **G2**: 13 (61.9) **OCD:** **G1:** 3 (12.5) **G2:** 6 (28.6)	RCMAS, oversensitivity, mean ± SD: **G1:** 2.54 ± 1.98 **G2:** 3.29 ± 1.90 p=NS 3-month follow-up **G1:** 1.40 ± 2.03 p=NS vs. baseline RCMAS, worry, mean ± SD: **G1:** 3.58 ± 2.41 **G2:** 3.86 ± 2.41 p=NS 3-month follow-up **G1:** 2.73 ± 2.49 p=NS vs. baseline RCMAS, anxious arousal, mean ± SD: **G1:** 2.29 ± 1.43 **G2:**3.48 ± 1.63 p < 0.05 3-month follow-up **G1:** 1.93 ± 1.67 p=NS vs. baseline **Educational/ cognitive/ academic attainment:** SRS, cognition, mean ± SD: **G1:** 17.38 ± 5.33 **G2:** 18.86 ± 5.72 p=NS 3-month follow-up: **G1:** 19.27 ± 6.13 p=NS vs. baseline **Harms:** NR **Modifiers:** NR

Comments: Only CBT responders were analyzed in the 3-month follow-up phase.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Warreyn et al. 2013[25] **Country:** Belgium **Intervention setting:** 10 rehabilitation centers **Enrollment period:** NR **Funding:** Grants from Marguerite-Marie Delacroix Foundation; VVA, the Flemish Parent Association **Design:** Quasi-RCT (patients matched in pairs before randomization)	**Intervention:** Intervention promoting joint attention and imitation; training package delivered to usual therapist for execution; 30-minute sessions administered twice/week, 24 total sessions over mean 4.5-5 months **Assessments:** observation **Groups:** **G1:** Joint attention and imitation intervention **G2:** Usual care **Provider:** • Patient's usual therapist (psychologist, speech-language therapist, or special educationalist) **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** No **Co-interventions held stable during treatment:**	**Inclusion criteria:** age 3-7 years mental age < 7 years basic language understanding (simple instructions and requests) diagnosis of PDD-NOS or ASD **Exclusion criteria:** see inclusion criteria **Age, mean/yrs ± SD (range):** **G1:** 5.72 ± 0.59 (4.70 – 6.80) **G2:** 5.74 ± 0.72 (4.07 – 6.92) **Mental age, mean ± SD (range):** Full-scale IQ: **G1:** 78.94 ± 15.49 (50.00 – 103.00) **G2:** 76.86 ± 16.79 (50.00 – 105.00) Verbal IQ: **G1:** 71.86 ± 13.55 (53.00 – 91.00) **G2:** 79.33 ± 14.55 (53.00 – 101.00) Performance IQ: **G1:** 79.38 ± 16.19 (52.00 – 97.00) **G2:** 77.66 ± 16.36 (56.00 –	**Communication/ language, mean ± SD:** Total joint attention: **G1:** 1.46 ± 0.60 **G2:** 1.65 ± 0.60 Ambiguous behavior: **G1:** 0.21 ± 0.21 **G2:** 0.17 ± 0.18 Gaze following: **G1:** 0.61 ± 0.19 **G2:** 0.69 ± 0.16 Initiating requests: **G1:** 0.33 ± 0.36 **G2:** 0.31 ± 0.31 Initiating declarative JA: **G1:** 0.31 ± 0.39 **G2:** 0.47 ± 0.44 Spontaneous declarative JA: **G1:** 0.89 ± 0.96 **G2:** 0.67 ± 1.33 Total imitation: **G1:** 3.12 ± 0.70 **G2:** 3.16 ± 0.65 Gestural imitation: **G1:** 0.67 ± 0.19 **G2:** 0.67 ± 0.25	**Communication/ language, mean ± SD:** Total joint attention: **G1:** 1.81 ± 0.73 **G2:** 1.24 ± 0.56 Group x time: p<0.01 Ambiguous behavior: **G1:** 0.24 ± 0.23 **G2:** 0.08 ± 0.15 Group x time: p=NS Gaze following: **G1:** 0.82 ± 0.22 **G2:** 0.67 ± 0.29 Group x time: p<0.05 Initiating requests: **G1:** 0.57 ± 0.38 **G2:** 0.30 ± 0.25 Group x time: p<0.05 Initiating declarative JA: **G1:** 0.17 ± 0.30 **G2:** 0.19 ± 0.30 Group x time: p=NS Spontaneous

	No **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 24 **G2:** 24 **N at follow-up:** **G1:** 18 **G2:** 18	110.00) **Sex:** M, n (%): **G1:** 14 (77.8) **G2:** 13 (72.2) F, n (%): **G1:** 4 (22.2) **G2:** 5 (27.8) **Race/ethnicity, n (%):** NR **SES:** Maternal education, n (%): NR Household income, mean (range): NR **Diagnostic approach:** Referral Diagnostic tool/method: DSM-IV TR **Diagnostic category, n (%):** NR **Other characteristics**, n (%)**:** **Language age, mean years ± SD (range):** **G1:** 4.27 ± 1.12 (2.00 – 6.00) **G2:** 4.48 ± 0.70 (2.90 – 5.80)	Verbal imitation: **G1:** 0.85 ± 0.27 **G2:** 0.90 ± 0.16 Object imitation: **G1:** 0.54 ± 0.19 **G2:** 0.55 ± 0.15 Symbolic imitation actions: **G1:** 0.69 ± 0.25 **G2:** 0.70 ± 0.31 Symbolic imitation vocalizations: **G1:** 0.37 ± 0.30 **G2:** 0.35 ± 0.30	declarative JA: **G1:** 1.72 ± 2.19 **G2:** 0.78 ± 1.00 Group x time: p=NS Total imitation: **G1:** 3.64 ± 0.61 **G2:** 3.42 ± 0.54 Group x time: p=NS Gestural imitation: **G1:** 0.69 ± 0.13 **G2:** 0.67 ± 0.29 Group x time: p=NS Verbal imitation: **G1:** 0.95 ± 0.10 **G2:** 0.88 ± 0.25 Group x time: p=NS Object imitation: **G1:** 0.62 ± 0.24 **G2:** 0.67 ± 0.15 Group x time: p=NS Symbolic imitation actions: **G1:** 0.88 ± 0.13 **G2:** 0.86 ± 0.11 Group x time: p=NS Symbolic imitation vocalizations: **G1:** 0.51 ± 0.29 **G2:** 0.35 ± 0.34

Group x time: p=NS

Harms: NR

Modifiers
No significant effect modification by age or FSIQ

Significant positive correlation between VIQ and progress on imitation ($p<0.05$) for G1

Comments: Baseline and population characteristics only reported for the subpopulation that completed the study (36 of 48 initial participants)

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Wong 2013[26] **Country:** US **Intervention setting:** classroom **Enrollment period:** NR **Funding:** Autism Speaks; Institute of Education Sciences **Design:** RCT	**Intervention:** Special education teachers trained during 8 1-hour sessions delivered weekly, with 4 sessions each on symbolic play (SP) and joint attention (JA) Groups received the SP and JA training in random order (JA/SP or SP/JA), with the wait-list control group receiving no intervention for 1st 4 weeks, followed by randomization to either JA/SP or SP/JA **Assessments:** observed **Groups:** **G1:** JA/SP **G2:** SP/JA **G3:** wait list control **G3a:** JA/SP **G3b:** SP/JA **Provider:** • Classroom teacher **Treatment manual followed:** Yes **Defined protocol followed:** Yes	**Inclusion criteria:** Children aged 3-6 years diagnosed with autism and in special education classroom **Exclusion criteria:** See inclusion criteria **Age, mean months ±SD:** **G1:** 56.21 ± 10.42 **G2:** 54.50 ± 5.06 **G3:** 59.67 ± 10.61 **Mental age, mean months ± SD:** Mullen Scales of Early Learning (MSEL): **G1:** 36.25 ± 11.00 **G2:** 27.39 ± 14.47 **G3:** 30.38 ± 13.19 MSEL, receptive language age, mean months ± SD: **G1:** 38.55 ± 16.51 **G2:** 25.29 ± 15.77 **G3:** 29.50 ±13.58 MSEL, receptive language age, mean months ± SD: **G1:** 29.73 ± 10.05 **G2:** 24.00 ±16.41 **G3:** 24.00 ± 11.22 MSEL, early learning composite, mean ± SD: **G1:** 59.91 ± 16.42	**Social skills:** Functional play, mean acts/min ±SD: **G1+G3a:** 0.42 ± 0.45 **G2+G3b:** 0.94 ± 0.81 Symbolic play, mean acts/min ± SD: **G1+G3a:** 0.06 ± 0.14 **G2+G3b:** 0.03 ± 0.08 Structured play level, mean ± SD: **G1+G3a:** 8.41 ± 4.21 **G2+G3b:** 8.14 ± 3.82 **Communication/ language:** Joint attention: G1 vs. G2 vs. G3 at 4 weeks: p=NS Joint engagement, mean % time of observation ±SD: **G1+G3a:** 22.42 ± 14.07 **G2+G3b:** 15.85 ± 11.61	**Social skills:** Play measures: G1 vs. G2 vs. G3 at 4 weeks: p=NS Functional play, mean acts/min ±SD: **G1+G3a:** 0.62 ± 0.69 **G2+G3b:** 0.94 ±0.77 p=NS Symbolic play, mean acts/min ± SD: **G1+G3a:** 0.10 ±0.17 **G2+G3b:** 0.15 ± 0.26 p<0.05 Structured play level, mean ± SD: **G1+G3a:** 8.30 ± 3.87 **G2+G3b:** 8.07 ± 4.53 p=NS **Communication/ language:** Joint attention measures: G1 vs. G2 vs. G3 at 4 weeks: p=NS

	Measure of treatment fidelity reported: Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 14 **G2:** 10 **G3:** 10 **N at follow-up:** **G1:** 14 **G2:** 10 **G3:** 9 **G3a:** 5 **G3b:** 4	**G2:** 56.14 ± 15.15 **G3:** 57.50 ± 10.61 **Sex:** M, n (%): **G1:** 12 (86) **G2:** 9 (90) **G3:** 8 (89) F, n (%): **G1:** 2 (14) **G2:** 1 (10) **G3:** 1 (11) **Race/ethnicity, n (%):** African American: **G1:** 6 (43) **G2:** 5 (50) **G3:** 5 (56) Hispanic: **G1:** 7 (50) **G2:** 5 (50) **G3:** 1 (11) White: **G1:** 1 (7) **G2:** 0 (0) **G3:** 3 (33) **SES:** Maternal education, n (%): High school or less: **G1:** 4 (29) **G2:** 4 (40) **G3:** 6 (67) Some college/vocational training: **G1:** 5 (36) **G2:** 3 (30) **G3:** 2 (22)	Joint attention responses, mean acts/min ±SD: **G1+G3a:** 0.28 ± 0.24 **G2+G3b:** 0.51 ± 0.37 Joint attention initiations, mean acts/min ±SD: **G1+G3a:** 0.11 ± 0.17 **G2+G3b:** 0.06 ± 0.12 Early Social Communication Scales (ESCS), mean joint attention responses ± SD: **G1+G3a:** 6.61 ± 3.01 **G2+G3b:** 4,40 ± 3.22 ESCS, mean joint attention initiations ± SD: **G1+G3a:** 10.94 ± 9.57 **G2+G3b:** 5.73 ± 8.70	Joint attention: G1 vs. G2 vs. G3 at 4 weeks: p=NS Joint engagement, mean % time of observation ±SD: **G1+G3a:** 54.08 ± 21.86 **G2+G3b:** 28.88 ± 15.38 p<0.001 Joint attention responses, mean acts/min ±SD: **G1+G3a:** 0.81 ± 0.61 **G2+G3b:** 0.53 ± 0.29 p<0.05 Joint attention initiations, mean acts/min ±SD: **G1+G3a:** 0.27 ± 0.21 **G2+G3b:** 0.07 ± 0.11 p<0.05 Early Social Communication Scales (ESCS), mean joint attention responses ± SD: **G1+G3a:** 8.11 ± 3.85

	College/professional/ graduate: **G1:** 5 (36) **G2:** 3 (30) **G3:** 1 (11) Household income, mean (range): NR **Diagnostic approach:** In Study Diagnostic tool/method: CARS **Diagnostic category, n (%):** Autism **G1:** 14 (100) **G2:** 10 (100) **G3:** 9 (100) **Other characteristics**, mean ±SD**:** CARS **G1:** 35.93 ± 7.49 **G2:** 39.60 ± 7.74 **G3:** 38.89 ± 6.95	**G2+G3b:** 4.93 ± 3.49 p<0.05 ESCS, mean joint attention initiations ± SD: **G1+G3a:** 6.72 ± 6.29 **G2+G3b:** 2.47 ± 4.00 p=NS **Harms** NR **Modifiers** Chronological age, autism severity as rated by CARS, and mental age by MSEL had no statistically significant effect on treatment response

Comments: teachers were the unit of randomization, not the individual children
G1: 5 teachers; **G2:** 4 teachers; **G3:** 5 teachers; **G3a:** 2 teachers; **G3b:** 2 teachers

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Adkins et al. 2012[27] **Country:** US **Intervention setting:** home **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** Sleep education pamphlet for parents **Assessments:** actigraphy to measure sleep parameters;parents trained in use; and daily diary forms; CSHQ parental questionnaire describing sleep behaviors in children; Stanford Binet 5 or Mullen Scales of Early Learning. Data collected two weeks after randomization **Groups:** **G1:** pamphlet **G2:** no pamphlet **Provider:** • Parents **Treatment manual followed:** No **Defined protocol followed:** NR **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** Yes	**Inclusion criteria:** aged 2-10 years diagnosis ASD based on DSM-IV confirmed by ADOS sleep onset latency of at least 30 minutes on 3 of 7 nights /week based on parent report and confirmed by 14 scorable days of actigraphy showing mean sleep latency of 30 minutes or more medication free or on stable dose of medications (no changes within 30 days of enrollment) parents agreeing to avoid changes in current meds during study time ability of child to tolerate actigraphy and willingness of parents to complete corresponding sleep diary English family primary language **Exclusion criteria:** medical and behavioral comorbidities that affect sleep, including sleep apnea, epilepsy, gastrointestinal reflux disease, depression,	Sleep latency, min mean ± SD: **G1:** 56.7 ± 27.1 **G2:** 52.1 ± 25.1 Sleep efficiency, % mean ± SD: **G1:** 75.5 ± 6.1 **G2:** 76.8 ± 6.0 Wake after sleep onset, min mean ± SD: **G1:** 61.9 ± 27.4 **G2:** 53.2 ± 20.2 Total sleep time, min mean ± SD: **G1:** 465.7 ± 66.3 **G2:** 461.4 ± 42.4 Fragmentation, min mean ± SD: **G1:** 36.8 ± 9.0 **G2:** 32.2 ± 7.2	Sleep latency, min mean ± SD: **G1:** 49.5 ± 26.7 **G2:** 61.3 ± 47.0 p=0.16 Sleep efficiency, % mean ± SD: **G1:** 77.8 ± 7.0 **G2:** 75.1 ± 6.7 p=0.04 Wake after sleep onset, min mean ± SD: **G1:** 60.4 ± 32.1 **G2:** 59.9 ± 24.2 p=0.22 Total sleep time, min mean ± SD: **G1:** 483.0 ± 67.8 **G2:** 470.8 ± 35.3 p=0.55 Fragmentation, min mean ± SD: **G1:** 36.3 ± 10.9 **G2:** 33.3 ± 7.5 p=0.52 **Harms:** NR **Modifiers:** NR

Concomitant therapies, n (%): Psychotropic **G1:** 5 (27.8) **G2:** 9 (50) Melatonin **G1:** 3 (16.7) **G2:** 3 (16.7) Stimulants **G1:** 2 (11.1) **G2:** 2 (11.1) **N at enrollment:** **G1:** 18 **G2:** 18 **N at follow-up:** **G1:** 19 **G2:** 17	anxiety, and attention deficit/hyperactivity disorder untreated co-morbid conditions **Age, mean/yrs (range):** 6.4 ± 2.6 **Mental age, mean/yrs (range):** **Sex:** M, n (%): **G1:** 10 (55.6) **G2:** 14 (77.8) F, n (%): **G1:** 8 (44.4) **G2:** 4 (22.2) **Race/ethnicity, n (%):** White **G1:** 15 (83.3) **G2:** 14 (77.8) African American **G1:** 3 (16.7) **G2:** 3 (22.2) **SES:** Mean ± SD **G1:** 34.0 ± 16.7 **G2:** 41.1 ± 11.9 **Diagnostic approach:** In Study/Referral Diagnostic tool/method: DSM-IV and ADOS **Diagnostic category, n (%):** Autism **G1:** 16 (88.9) **G2:** 13 (72.2)

	PDD-NOS **G1:** 0 **G2:** 1 (5.6) Aspergers **G1:** 2 (11.1) **G2:** 4 (22.2) **Other characteristics**, n (%)**:** IQ, mean ± SD **G1:** 75.1 ± 25.5 **G2:** 85.6 ± 27.1	

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Aldred et al. 2012[28] **Country:** UK **Intervention setting:** Clinic **Enrollment period:** NR **Funding:** Grant from Shirley Foundation **Design:** RCT Note: See initial publication in 2011 AHRQ review [29] for efficacy results	**Intervention:** Communication-focused parent mediated intervention over 12 months (6 months of monthly clinic sessions and 6 months of bi-monthly maintenance sessions) **Assessments:** Parent-Child Interaction (PCI), Autism Diagnostic Observation Schedule, MacArthur Communicative Development Inventory **Groups:** **G1:** Parent mediated communication-focused intervention **G2:** Treatment as usual **Provider:** Speech and language therapists in clinic, with additional home program **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** NR	**Inclusion criteria:** • clinical diagnosis of core autistic disorder confirmed by ADOS and ADI-R by assessing professional team **Exclusion criteria:** NR **Age, mean months ± SD:** **G1:** 51.4 ± 11.8 **G2:** 50.9 ± 16.3 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 13 (93) **G2:** 12 (86) F, n (%): **G1:** 1 (7) **G2:** 2 (14) **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** In Study/Referral Diagnostic tool/method: ADOS and ADI-R **Diagnostic category, n (%):** Autism (100)	Parent synchrony, mean ± SD: **G1:** 57.8 ± 15.0 **G2:** 56.4 ± 16.5 ADOS social communication algorithm total, mean ± SD: **G1:** 16.1 ± 4.5 **G2:** 15.6 ± 4.9	Parent synchrony, mean ± SD: **G1:** 65.1 ± 14.3 **G2:** 48.9 ± 19.5 ADOS social communication algorithm total, mean ± SD: **G1:** 11.8 ± 6.4 **G2:** 16.1 ± 4.4 **Harms:** NR **Modifiers** Increase in parental synchronous response within parent-child interaction partly mediated positive intervention effect on ADOS social communication algorithm scores, accounting for 34% of effect

	Co-interventions held stable during treatment: NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 14 **G2:** 14 **N at follow-up:** **G1:** **G2:**	**Other characteristics**, n (%)**:** Vineland adaptive behavior composite, mean ± SD **G1:** 25.6 ± 9.2 **G2:** 22.0 ± 5.6 Vineland communication sub-domain **G1:** 22.6 ± 13.3 **G2:** 20.0 ± 10.8 Vineland social sub-domain **G1:** 18.2 ± 5.8 **G2:** 16.3 ± 3.6 MacArthur Communicative Developmental Inventory words produced, median (range): **G1:** 69.5 (467) **G2:** 78.5 (683) MacArthur Communicative Developmental Inventory vocabulary comprehension, median (range): **G1:** 95.0 (381) **G2:** 144.0 (426) PCI- Child Communication Acts, mean ± SD: **G1:** 30.8 ± 10.2 **G2:** 30.1 ± 11.1

Comments: Secondary analysis of communication intervention trial (Aldred et al. 2004)

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Cortesi et al. 2012[30] **Country:** Italy **Intervention setting:** Clinic and home **Enrollment period:** 2007 to 2010 **Funding:** NR **Design:** RCT	**Intervention:** Melatonin- 3 mg controlled release administered daily at 21:00 h. Cognitive behavioral therapy (CBT)- four weekly 50 min individual treatment sessions outpatient clinic. A sleep-focused multifactorial intervention involved cognitive, behavioral and educational components. **Assessments:** Children's Sleep Habits Questionnaire (CSHQ); actigraphy monitoring, sleep monitoring. Completed at baseline and after 12 weeks. **Groups:** **G1:** Combination therapy **(**Melatonin and CBT) **G2:** Melatonin only **G3:** CBT only **G4:** Placebo **Provider:** CBT- clinical psychologists **Treatment manual followed:** NR	**Inclusion criteria:** • age 4-10 years • DSM-IV-TR diagnosis of autistic disorder confirmed by ADI-R • Mixed sleep onset and maintenance insomnia defined as sleep onset latency and wake after sleep onset > 30 min on 3 or more nights/week • Absence of other serious neurological, psychiatric or medical conditions **Exclusion criteria:** • see above Age, mean/yrs ± SD: **G1:** 6.4 ± 1.1 **G2:** 6.8 ± 0.9 **G3:** 7.1 ± 0.7 **G4:** 6.3 ± 1.2 **Mental age, mean/yrs (range):** NR **Sex:** M, %: **G1:** 80 **G2:** 82 **G3:** 83 **G4:** 84 **Race/ethnicity, %:** White	Total sleep time (TST), mean ± SD: **G1:** 414.03 ± 45.34 **G2:** 410.28 ± 45.07 **G3:** 408.08 ± 49.03 **G4:** 413.00 ± 45.13 Sleep onset latency (SOL), mean ± SD: **G1:** 85.84 ± 20.02 **G2:** 81.21 ± 32.35 **G3:** 76.34 ± 31.70 **G4:** 78.20 ± 33.83 Wake after sleep onset (WASO), mean ± SD: **G1:** 69.50 ± 23.35 **G2:** 73.71 ± 45.00 **G3:** 68.72 ± 31.77 **G4:** 69.75 ± 45.21 Naptime, mean ± SD: **G1:** 28.26 ± 49.13 **G2:** 33.57 ± 56.63 **G3:** 35.31 ± 60.17 **G4:** 37.33 ± 56.19 Sleep efficiency (SE), mean ± SD: **G1:** 70.26 ± 4.83 **G2:** 71.10 ± 4.91 **G3:** 71.37 ± 4.77 **G4:** 71.13± 4.99 Bedtime, mean ± SD: **G1:** 23.33 ± 1.35 **G2:** 23.45 ± 1.15	Total sleep time (TST), mean ± SD: **G1:** 505.01 ± 31.18 **G2:** 481.10 ± 33.15 **G3:** 445.13 ± 48.37 **G4:** 416.23 ± 43.60 P< 0.001 Sleep onset latency (SOL), mean ± SD: **G1:** 33.69 ± 14.40 **G2:** 45.21 ± 23.21 **G3:** 59.13 ± 27.60 **G4:** 79.60 ± 31.85 P<0.001 Wake after sleep onset (WASO), mean ± SD: **G1:** 29.69 ± 12.97 **G2:** 42.21 ± 22.35 **G3:** 61.17 ± 28.93 **G4:** 70.15 ± 42.76 P<0.001 Naptime, mean ± SD: **G1:** 9.20 ± 22.48 **G2:** 17.00 ± 33.11 **G3:** 12.29 ± 24.24 **G4:** 36.10 ± 33.28 P=0.23 Sleep efficiency (SE), mean ± SD: **G1:** 84.46 ± 4.23 **G2:** 82.71 ± 4.00 **G3:** 79.58 ± 2.82 **G4:** 71.93± 4.62

	Defined protocol followed: Yes **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** NA **Concomitant therapies, n (%):** All subjects drug free for at least 6 months prior to beginning of study and throughout the study **N at enrollment:** **G1:** 40 **G2:** 40 **G3:** 40 **G4:** 40 **N at follow-up:** **G1:** 35 **G2:** 34 **G3:** 33 **G4:** 32	**G1:** 100 **G2:** 100 **G3:** 100 **G4:** 96 **SES:** Low SES (index of 3 or less on Hollingshead Two-Factor Index of Social Position), %: **G1:** 24 **G2:** 25 **G3:** 23 **G4:** 26 Maternal education, mean years ± SD: **G1:** 13 ± 4 **G2:** 14 ± 7 **G3:** 13 ± 6 **G4:** 13 ± 5 **Diagnostic approach:** Referral Diagnostic tool/method: DSM-IV-TR confirmed by ADI-R **Diagnostic category, n (%):** ASD: 100% **Other characteristics**, n (%)**:** NR	**G3:** 23.39 ± 1.03 **G4:** 23.41 ± 1.19 CSHQ, total score, mean ± SD: **G1:** 66.11 ± 5.47 **G2:** 66.67 ± 8.55 **G3:** 64.48 ± 5.48 **G4:** 64.20 ± 4.85 CSHQ, bed resistance, mean ± SD: **G1:** 14.53 ± 1.82 **G2:** 13.85 ± 2.23 **G3:** 13.44 ± 2.08 **G4:** 13.63 ± 1.82 CSHQ, sleep onset delay, mean ± SD: **G1:** 2.88 ± 0.32 **G2:** 2.85 ± 0.35 **G3:** 2.89 ± 0.30 **G4:** 2.90 ± 0.31 CSHQ, sleep anxiety, mean ± SD: **G1:** 7.95 ± 1.83 **G2:** 8.35 ± 2.19 **G3:** 8.62 ± 1.98 **G4:** 7.66 ± 1.73 CSHQ, night-wakings, mean ± SD: **G1:** 7.61 ± 0.89 **G2:** 7.67 ± 0.94 **G3:** 7.62 ± 0.94 **G4:** 7.76 ± 0.93 CSHQ, sleep duration, mean ± SD: **G1:** 7.34 ± 1.35	P<0.001 Bedtime, mean ± SD: **G1:** 22.06 ± 1.05 **G2:** 22.30 ± 1.10 **G3:** 22.55 ± 1.01 **G4:** 23.51 ± 1.12 P<0.001 CSHQ, total score, mean ± SD: **G1:** 47.84 ± 2.94 **G2:** 54.78 ± 6.22 **G3:** 60.06 ± 4.71 **G4:** 64.80 ± 4.52 p <0.001 CSHQ, bed resistance, mean ± SD: **G1:** 8.46 ± 1.39 **G2:** 10.50 ± 2.20 **G3:** 11.62 ± 2.22 **G4:** 14.10 ± 1.93 p <0.001 CSHQ, sleep onset delay, mean ± SD: **G1:** 1.69 ± 0.73 **G2:** 2.10 ± 0.68 **G3:** 2.51 ± 0.57 **G4:** 2.93 ± 0.25 p <0.001 CSHQ, sleep anxiety, mean ± SD: **G1:** 5.23 ± 0.95 **G2:** 7.21 ± 1.87 **G3:** 7.17 ± 1.48 **G4:** 7.93 ± 1.99 p <0.001

G2: 7.17 ± 1.51 **G3:** 7.01 ± 1.48 **G4:** 6.46 ± 1.25 CSHQ, parasomnias, mean ± SD: **G1:** 9.15 ± 1.68 **G2:** 9.10 ± 2.42 **G3:** 9.75 ± 2.11 **G4:** 8.96 ± 1.80 CSHQ, daytime sleepiness, mean ± SD: **G1:** 13.92 ± 2.86 **G2:** 13.35 ± 3.84 **G3:** 13.31 ± 2.67 **G4:** 13.13 ± 3.11	CSHQ, night-wakings, mean ± SD: **G1:** 4.42 ± 0.90 **G2:** 5.03 ± 1.10 **G3:** 7.06 ± 1.06 **G4:** 7.86 ± 0.81 p <0.001 CSHQ, sleep duration, mean ± SD: **G1:** 4.38 ± 1.02 **G2:** 4.82 ± 0.94 **G3:** 6.68 ± 1.16 **G4:** 6.40 ± 1.29 p <0.001 CSHQ, parasomnias, mean ± SD: **G1:** 8.92 ± 1.38 **G2:** 9.35 ± 1.78 **G3:** 9.82 ± 2.25 **G4:** 9.16 ± 1.53 p =0.82 CSHQ, daytime sleepiness, mean ± SD: **G1:** 10.84 ± 1.68 **G2:** 11.39 ± 2.34 **G3:** 11.96 ± 1.97 **G4:** 12.96 ± 1.97 p <0.001 **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Dawson et al. 2012[31] **Country:** USA **Intervention setting:** NR **Enrollment period:** NR **Funding:** NR **Author industry relationship disclosures:** NR **Design:** RCT Note: See earlier study reporting on this population[32] in 2011 AHRQ review[9]	**Intervention:** ESDM intervention for 2hours,twice a day, 5 days a week, for 2 years. Community intervention: Families were given resource manuals And reading materials at baseline and twice yearly **Assessments:** ADI-R, ADOS, MSEL, Vineland Scales of Adaptive Behavior, PDD Behavioral Inventory, EEG **Groups:** **G1:** ESDM **G2:** Community intervention **Provider:** Trained therapists **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR	**Inclusion criteria:** • age <30 months at entry, • meeting criteria for an autistic disorder on the Toddler Autism Diagnostic Interview (ADI) and for autism or ASD on the Autism Diagnostic Observation Schedule(ADOS) and a clinical diagnosis based on DSM-IV criteria • residing within 30 minutes of the University of Washington. **Exclusion criteria:** • neurologic disorder of known genetic etiology, • significant sensory or motor impairment, major physical problems, seizures at the time of entry, • use of psychoactive medications, • a history of a serious head injury and/ or neurologic disease, alcohol or drug exposure during the	MSEL Verbal IQ **G1:** 45.3, ± 17.5; **G2:** 48.1, ± 21.2 MSEL Nonverbal IQ **G1:** 83.6, ± 13.3 **G2:** 79.2, ± 11.3	Verbal IQ **G1:** 95.1, ± 15.7 **G2:** 75.1, ± 18.4 (p=0.004) Nonverbal IQ: **G1:** 93.1, ± 16.5 **G2:** 80.0, ± 15.8 (p=0.04) Vineland Communication **G1:** 95.3 ± 15 **G2:**mean76.1, ± 14.7 (p=0.02) Social **G1:** 74.7,± 10.0 **G2:** 66.5 ± 8.3 (p=0.02) Daily Living Skills **G1:** 72 ± 11.9 **G2:** 58.9 ± 7.9 (p=0.006), Aberrant Behaviors **G1:** 76.9, ± 13.6 **G2:** 61.2, ± 7.9 (p=0.001) PDD-BI Expressive Social Communication composite scores: **G1:** 65.4, ± SD 6.5; **G2:**54.5, ± SD10.2; (p=0.004)

	Concomitant therapies, n (%): NR **N at enrollment:** **G1:** 17 **G2:** 14 **N at follow-up:** **G1:** 17 **G2:** 14	prenatal period • -nonverbal IQ below 35 **Age, mean/yrs (range):** **G1:** 54.1 months ± 4.9 months; **G2:** 54.1 months, ± 7.8 months **Mental age, mean/yrs (range):** NR **Sex:** Male to female ratio: **G1+G2:** 3.5:1 **Race/ethnicity, n (%):** **G1+G2**: Asian 12.5%, white (72.9%), Latino (12.5%), and multiracial 14.6%) **SES:** NR **Diagnostic approach:** In Study Diagnostic tool/method: ADI, ADOS, DSM-IV **Diagnostic category, n (%):** Autism : 100% **Other characteristics, n (%):** ADOS Social scores: **G1:** 10.3, SD 2.3 **G2:** 11.1, SD 2.7) ADOS Restricted and Repetitive Behaviors:		PDD-BI Receptive/Expression Social Communication composite scores: **G1:** 65.5, ± 5.6 **G2:**55.3, ± 10.3 (p=0.006) **Harms:** NR **Modifiers:** NR

G1: 2.6, SD 1.3
G2: 3.6, SD 2.0)

Comments: 11/15 children (73%) in G1 and 4/14 in G2 showed a faster Nc response to faces than to objects. ERP and cortical activation data not included here. Greater cortical activation while viewing faces associated with improved social behavior.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Eikeseth et al. 2012[33] **Country:** Sweden/Norway **Intervention setting:** Mainstream public preschools or kindergartens, and children's homes **Enrollment period:** March 2008 – May 2010 (experimental group); 2005 – 2010 (control group) **Funding:** NR **Design:** Retrospective cohort	**Intervention:** Early and Intensive Behavioral Intervention (EIBI) for 1 year (15-37 hours per week; mean = 23, sd = 5.3) in preschool/kindergarten classrooms and homes **Assessments:** Conducted by child's supervisor: • VABS (Vineland Adaptive Behavior Scales), adaptive and maladaptive behavior subscales • CARS (Childhood Autism Rating Scale) **Groups:** **G1:** EIBI **G2:** standard care **Provider:** EIBI education team: Therapist: school staff, no academic degree, no training/experience with EIBI prior to study Parents Supervisor from Banyan Center (Sweden) with	**Inclusion criteria:** • diagnosis of autism • no EIBI prior to enrollment (G1) **Exclusion criteria:** • prior EIBI treatment (G1) **Age, mean/yrs ± SD:** **G1:** 3.9 ± 0.9 **G2:** 4.4 ± 1.2 **Mental age, mean/yrs (SD):** NR **Sex, n (%):** **G1:** M: 29 (83) F: 6 (17) **G2:** M: 20 (83) F: 4 (17) **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** G1; NR G2: all children diagnosed at Akershus University Hospital based on ICD-10 criteria	**Overall ratings:** Global Rating of Severity, mean ± SD: CARS **G1:** 37.2 ± 7.7 **G2:** NR **Social skills, mean ± SD:** VABS, socialization **G1:** 65.4 ± 9.8 **G2:** 63.3 ± 7.0 **Communication/ language, mean ± SD:** VABS, communication **G1:** 67.1 ± 14.0 **G2:** 65.5 ± 14.2 **Repetitive behavior:** NR **Problem behavior, mean ± SD:** VABS maladaptive **G1:** 19.5 ± 2.4 **G2:** NR **Adaptive behavior, mean ± SD:** VABS, total **G1:** 67.0 ± 10.3 **G2:** 63.6 ± 8.1 VABS age equivalent: **G1:** 1.9 ± 0.9 **G2:** 2.1 ± 0.8	**Overall ratings:** Global Rating of Severity, mean ± SD: CARS, 1-year follow-up: **G1:** 30.6 ± 7.1 **G2:** NR p < .001 2-year follow-up: **G1:** 27.2 ± 6.2 **G2:** NR p < .05 **Social skills, mean ± SD:** 1-year follow-up: VABS, socialization **G1:** 72.5 ± 12.3 **G2:** 64.3 ± 9.4 p<0.01 **Communication/ language:** 1-year follow-up: VABS, communication **G1:** 81.3 ± 16.9 **G2:** 63.6 ± 16.0 p<0.001 **Problem behavior, mean ± SD:** 1-year follow-up: VABS, maladaptive **G1:** 16.9 ± 2.5 **G2:** NR **Adaptive behavior,**

	bachelor's or master's degrees Other significant adults Standard care education team: • Special education teacher with minimum of bachelor's degree Teacher assistant, typically no academic degree **Treatment manual followed:** No – Based on UCLA model **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 35 **G2:** 24 **N at follow-up:** VABS Adaptive: 1-year follow-up: **G1:** 35	**Diagnostic category, n (%):** Autism **G1:** 35 (100) **G2:** 24 (100) **Other characteristics**, n (%)**:** NR	VABS, ADL **G1:** 71.8 ± 12.8 **G2:** 67.5 ± 10.9 **Motor skills, mean ± SD:** VABS, motor **G1:** 75.9 ± 12.8 **G2:** 72.5 ± 10.6	**mean ± SD:** 1-year follow-up: VABS, total **G1:** 75.3 ± 12.0 **G2:** 64.0 ± 12.5 p<0.01 VABS, ADL 1-year follow-up: **G1:** 78.3 ± 14.4 **G2:** 68.0 ± 14.8 P<0.01 **Motor skills, mean ± SD:** 1-year follow-up: VABS, motor **G1:** 80.6 ± 10.6 **G2:** 71.8 ± 14.4 p<0.05 **Educational/ cognitive/ academic attainment:** VABS, learning rate: mean ± SD 1-year follow-up: **G1:** 1.13 ± 0.66 **G2:** 0.59 ± 0.43 2-year follow-up: **G1:** 0.81 ± 0.72 **G2:** NR p<0.001 **Harms:** NR **Modifiers:** NR

G2: NR

2-year follow-up:
G1: 15
G2: NR

VABS Maladaptive:
1-year follow-up:
G1: 24
G2: NR

2-year follow-up:
G1: 14
G2: NR

CARS:
1-year follow-up:
G1: 27
G2: NR

2-year follow-up:
G1: 13
G2: NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Eldevik et al. 2012[34] **Country:** Norway **Intervention setting:** school **Enrollment period:** January 2000 to February 2011 **Funding:** NR **Design:** cohort	**Intervention:** EIBI pre-school model **Assessments:** Bayley Scales of Infant Development (BSID), Stanford-Binet Intelligence Scale: Fourth or Fifth Edition, Norwegian version of the Wechsler Preschool and Primary Scale Intelligence-Revised (WPPSI); Vineland Adaptive Behavior Scales I or II (VABS). Assessment done after two years. **Groups:** **G1:** EIBI intervention **G2:** Treatment as usual **Provider:** Psychologist was consultant for the supervisors at the preschools- Supervisors had bachelor's degrees and between 2-10 years of experience with EIBI programs; school staff also administered EIBI **Treatment manual followed:** "The intervention was	**Inclusion criteria:** • independent diagnosis of autism or PDD-NOS based on ADI-R • between 2 and 6 years of age at intake • full-scale intelligence test and measure of adaptive behavior at intake and after two years of intervention • at least 5 hours/week of intervention **Exclusion criteria:** -See above Age, mean/months ± SD (range): **G1:** 42.2 ± 9.0 (26-70) **G2:** 46.2 ± 12.4 (24-67) **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 25 (80.6) **G2:** 8 (66.7) F, n (%): **G1:** 6 (19.4) **G2:** 4 (33.3) **Race/ethnicity, n (%):** 16 of 31 children in EIBI group from ethnic minority groups in Norway (51.6%)	Intellectual functioning, mean ± SD (range) **G1:** 51.6 ± 16.9 (24-94) **G2:** 51.7 ± 18.1 (30-89) **Adaptive behavior**: VABS Adaptive behavior composite **G1:** 62.5 ± 8.2 (46-77) **G2:** 58.9 ± 7.8 (50-73) Communication **G1:** 61.9 ± 10.2 (48-89) **G2:** 60.0 ± 9.6 (49-81) Daily living **G1:** 69.9 ± 10.8 (48-89) **G2:** 64.8 ± 10.6 (54-91) Socialization **G1:** 63.3 ± 9.8 (49-97) **G2:** 63.1 ± 8.9 (53-82)	Intellectual functioning, mean ± SD (range) **G1:** 66.6 ± 24.8 (23-110) **G2:** 52.2 ± 22.0 (23-86) **Adaptive behavior:** VABS Adaptive behavior composite **G1:** 68.4 ± 12.6 (46-97) **G2:** 59.6 ± 11.8 (47-83) Communication **G1:** 70.5 ± 16.9 (42-114) **G2:** 60.0 ± 14.5 (42-84) Daily living **G1:** 72.0 ± 12.9 (47-93) **G2:** 63.2 ± 14.2 (48-95) Socialization **G1:** 69.1 ± 12.0 (49-90) **G2:** 60.8 ± 8.6 (41-80) **Harms:** NR **Modifiers** Three variables associated with outcome in G1: Age at intake correlated positively with gains in ABC scores. Other diagnosis (PDD-NOS or Asperger, rather than autism) was associated with larger gains in ABC scores and

	based on several widely used EIBI manuals." **Defined protocol followed:** NR **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 31 **G2:** 12 **N at follow-up:** **G1:** 31 **G2:** 12	**SES:** NR **Diagnostic approach:** EIBI group: Referral from pedagogical-psychological services through local educational authorities to specialist evaluation Diagnostic tool/method: ADI-R **Diagnostic category, n (%):** Autism **G1:** 25 (80.6) **G2:** 9 (75) PDD-NOS **G1:** 5 (16.1) **G2:** 3 (25)) Aspergers **G1:** 1 (3.2) **G2:** 0 (0) **Other characteristics, n (%):** Level of intellectual disability No ID **G1:** 4 (12.9) **G2:** 2 (16.7) Mild ID **G1:** 10 (32.3) **G2:** 4 (33.3) Moderate ID **G1:** 12 (38.7) **G2:** 5 (41.7)		larger gains in communication and daily living skills sub domain. IQ at intake correlated positively with change in socialization sub domain of the VABS.

Severe ID
G1: 5 (16.1)
G2: 1 (8.3)

Profound
G1: 0 (0)
G2: 0 (0)

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures*	Outcomes
Author: Scahill et al. 2012[35-38] **Country:** USA **Intervention setting:** (e.g., clinic, home, etc.) **Enrollment period:** NR **Funding:** Federal grant **Author industry relationship disclosures:** 6/24 **Design:** RCT	**Intervention:** Risperidone (0.5 to 3.5 mg/day) or aripiprazole if risperidone was ineffective ((aripiprazole started at 2 mg and adjusted up to 15 mg) or a combination of medication plus parent training (Combined group) . Parents of children in combined group received an average of 11.4 PT sessions. **Assessments:** Home Situations Questionnaire (HSQ), Aberrant Behavior Checklist-Irritability (ABC-I), Vineland Adaptive Behavior Scales (VABS), Noncompliance index. Assessed weekly for 8 weeks then every 4 weeks until week 24. Follow-up study at 1 year **Groups:** **G1:** risperidone **G2:** risperidone + parent training **Co-interventions held stable during treatment:** Yes **Frequency of contact**	**Inclusion criteria:** Age between 4 and 14 years DSM-IV-TR diagnosis of autistic disorder, Asperger's disorder, or PDD-NOS based on clinical assessment and corroborated by the ADI-R Serious behavioral problems (e.g tantrums, aggression and self-injury) evidenced by score ≥ 18 on ABC-Irritability subscale and CGI-severity score ≥ 4 IQ ≥ 35 or mental age of 18 months from Stanford-Binet 5, Leiter International Performance Scale or Mullen Scales of Early Learning Anticonvulsant treatment permissible if medication was stable (≥ 4 wks) and subject was seizure free (≥ 18 mos) criterion 2 **Exclusion criteria:** significant medical condition by history, exam or lab test lifetime diagnosis of psychosis, bipolar	**HSQ, mean ± SD:** Average severity score **G1:** 4.16 ± 1.47 **G2:** 4.31 ± 1.67 "Yes" count **G1:** 18.9 ± 3.46 **G2:** 18.6 ± 4.65 **ABC, mean ± SD:** Irritability **G1:** 29.7 ± 6.10 **G2:** 29.3 ± 6.97 Social withdrawal **G1:** 17.1 ± 8.37 **G2:** 15.2 ± 9.01 Stereotypic behavior **G1:** 10.6 ± 5.46 **G2:** 7.59 ± 5.20 Hyperactivity/non compliance **G1:** 36.1 ± 6.86 **G2:** 35.3 ± 9.30 Inappropriate speech **G1:** 6.37 ± 4.03 **G2:** 5.75 ± 3.43 **VABS, mean ± SD: Standard Score** Daily living skills **G1:** 41.14 ± 19.81 **G2:** 50.79 ± 18.49 Socialization	**24 Week Follow-Up** **VABS, mean ± SD: Standard Score** Daily living skills **G1:** 45.34 ± 20.48 **G2:** 55.65 ± 21.86 Socialization **G1:** 56.59 ± 17.38 **G2:** 67.42 ± 18.48 Communication **G1:** 53.57 ± 20.23 **G2:** 63.90 ± 22.65 Adaptive Composite **G1:** 47.84 ± 15.81 **G2:** 57.87 ± 19.03 **Age Equivalent Score** Daily living skills **G1:** 3.49 ± 1.72 **G2:** 4.36 ± 2.25 Socialization **G1:** 2.71 ± 1.51 **G2:** 3.99 ± 2.56 Communication **G1:** 3.42 ± 2.18 **G2:** 4.58 ± 2.85 Adaptive Composite **G1:** 12.88 ± 10.83 **G2:** 8.41 ± 8.69 **One Year Follow-up**** **(**G1, n=36, G2, n=51) **HSQ-mean** **G1:** 2.12 ± 1.87

	during study: ~weekly across groups **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 49 **G2:** 75 **N at follow-up (1 year):** **G1:** 36 **G2:** 51	disorder or current diagnosis of major depression, obsessive-compulsive disorder, substance abuse, or girls with positive Beta HCG pregnancy test criterion 2 **Age, mean/yrs ± SD:** **G1:** 7.5 ± 2.80 **G2:** 7.38 ± 2.21 **Mental age, mean/yrs (range):** NR **Sex, n (%):** G1+G2: M: 105 (85) F: 19 (15) **Race/ethnicity, n (%):** White/non Hispanic **G1:** 34 (69.4) **G2:** 59 (78.7) Hispanic **G1:** 7 (14.3) **G2:** 4 (5.3) African American **G1:** 7 (14.3) **G2:** 9 (12.1) Asian American **G1:** 0 **G2:** 3 (4.0) Native American **G1:** 1 (2.0) **G2:** 0 **SES, mean ± SD:**	**G1:** 53.48 ± 14.41 **G2:** 59.55 ± 15.01 Communication **G1:** 53.18 ± 19.94 **G2:** 61.15 ± 20.95 Adaptive Composite **G1:** 45.84 ± 15.5 **G2:** 53.15 ± 15.66 **Age Equivalent Score** Daily living skills **G1:** 2.85 ± 1.52 **G2:** 3.63 ± 1.94 Socialization **G1:** 2.09 ± 1.08 **G2:** 2.80 ± 1.84 Communication **G1:** 3.12 ± 2.15 **G2:** 3.99 ± 2.65 Adaptive Composite **G1:** 18.91 ± 14.18 **G2:** 16.59 ± 11.44 **Standard Observation Analog Procedure** Free Play Condition Child inappropriate mean % intervals, mean ± SD: 20 ± 23 Parent restrictive mean raw score, mean ± SD: 0.88 ± 1.72 Parent positive mean raw score, mean ± SD: 1.34 ± 2.01	**G2:** 1.84 ± 1.46 **HSQ "yes"** **G1:** 13.67± 7.04 **G2:** 12.69 ± 5.91 **ABC, mean ± SD** Irritability **G1:**15.25 ± 3.36 **G2:** 14.10 ± 3.60 Lethargy **G1:** 7.39 ±6.83 **G2:** 4.65 ± 5.21 Stereotypy **G1:** 5.61 ± 5.31 **G2:** 4.06 ± 3.67 Hyperactivity **G1:** 18.94 ± 11.42 **G2:** 17.37 ± 11.78 Inappropriate speech **G1:** 3.22 ± 3.36 **G2:** 3.27 ± 2.77 **Predictors, F** **HSQ Total Score** Income: 0.02 Maternal education: 0.40 Child age: 4.96 IQ: 3.18 ABC-Irritability: 1.13 ABC-Hyperactivity: 0.36 CGI-S: 0.08 CASI-ADHD/Combined: 0.02 CASI-ODD: 0.06 CASI-GAD: 0.77 CASI-Mood disorder: 0.84 CASI-PDD: 0.11 CYBOCS: 0.42

	Income (US $) <20,000 **G1:** 12 ± 25.0 **G2:** 14 ± 18.7 20,001-40,000 **G1:** 14 ± 29.2 **G2:** 21 ± 28.0 40,001-60,000 **G1:** 10 ± 20.8 **G2:** 11 ± 14.7 60,001-90,000 **G1:** 7 ± 14.6 **G2:** 16 ± 21.3 >90,000 **G1:** 5 ± 10.4 **G2:** 13 ± 17.3 Maternal education <8th grade **G1:** 1 ± 2.0 **G2:** 4 ± 5.3 Some high school **G1:** 4 ± 8.2 **G2:** 3 ± 4.0 High school graduate/GED **G1:** 15 ± 30.6 **G2:** 18 ± 24.0 Some collage **G1:** 17 ± 34.7 **G2:** 28 ± 37.3 College graduate **G1:** 10 ± 20.4 **G2:** 12 ± 16.0	Child+parent social attention, mean ± SD: Child inappropriate mean % intervals, mean ± SD: 32 ± 29 Parent restrictive mean raw score, mean ± SD: 1.45 ±3.27 Parent positive raw score, mean ± SD: 0.30 ± 0.83 Demand Condition Child inappropriate mean % intervals, mean ± SD: 40 ± 27 Child mean compliance, Child inappropriate mean % intervals, mean ± SD: 75 ± 25 Parent restrictive mean raw score, mean ± SD: 1.49 ± 2.05 Parent positive raw score, mean ± SD: 1.48 ± 1.99 Parent repeated mean raw score, mean ± SD: 10.25 ± 7.15 Parent mean contingent reinforcement, mean ± SD: 39 ± 29	HSQ: 7.23 (p=0.007) PSI-Parental distress: 0.20 PSI-Total stress: 0.78 VABS-daily living: 0.18 VABS-socialization: 0.34 VABS-communication: 0.58 VABS-composite: 0.60 **ABC-Hyperactivity/Non-compliance** Income: 1.02 Maternal education:0.02 Child age: 3.23 IQ: 3.43 ABC-Irritability: 0,02 ABC-Hyperactivity: 0.31 CGI-S: 0.21 CASI-ADHD/Combined: 0.30 CASI-ODD: 0.00 CASI-GAD: 0.17 CASI-Mood disorder: 0.04 CASI-PDD: 2.47 CYBOCS: 0.38 HSQ: 0.29 PSI-Parental distress: 0.54 PSI-Total stress: 0.84 VABS-daily living: 3.62 VABS-socialization: 1.45 VABS-communication: 5.04 VABS-composite: 4.56 **Moderators, F** **HSQ Total Score** Income: 0.58 Maternal education:0.08 Child age: 0.43 IQ: 0.04 ABC-Irritability: 0.08 ABC-Hyperactivity: 0.15 CGI-S: 0.32 CASI-ADHD/Combined: 0.01

	Advanced degree **G1:** 2 ± 4.1 **G2:** 10 ± 13.3 **Diagnostic approach:** In Study Diagnostic tool/method: DSM-IV-TR diagnosis based on clinical assessment and corroborated by the ADI-R **Diagnostic category, n (%):** Autism **G1:** 32 (65.3) **G2:** 49 (65.3) PDD-NOS **G1:** 13 (26.5) **G2:** 22 (29.3) Aspergers **G1:** 4 (8.2) **G2:** 4 (5.3) **Other characteristics:** **Educational placement, n (%):** F/T, regular education **G1:** 10 (20.4) **G2:** 18 (24.0) F/T, regular education with aide **G1:** 0 **G2:** 3 (4.0) Regular education, some	Tangible Restriction Condition Child inappropriate mean % intervals, mean ± SD: 42 ± 27 Parent restrictive mean raw score, mean ± SD: 2.32 ± 3.30 Parent positive raw score, mean ± SD: 1.13 ± 1.97	CASI-ODD: 3.38 CASI-GAD: 0.43 CASI-Mood disorder: 1.14 CASI-PDD: 0.39 CYBOCS: 1.96 HSQ: 2.27 PSI-Parental distress: 0.05 PSI-Total stress: 0.11 VABS-daily living: 0.12 VABS-socialization: 0.00 VABS-communication: 0.00 VABS-composite: 0.12 **ABC-Hyperactivity/Non-compliance** Income: 0.07 Maternal education: 0.67 Child age: 0.65 IQ: 0.96 ABC-Irritability: 0.04 ABC-Hyperactivity: 0.46 CGI-S: 2.13 CASI-ADHD/Combined: 0.73 CASI-ODD: 5.70 CASI-GAD: 0.84 CASI-Mood disorder: 1.92 CASI-PDD: 0.08 CYBOCS: 1.60 HSQ: 1.02 PSI-Parental distress: 0.01 PSI-Total stress: 0.00 VABS-daily living: 0.09 VABS-socialization: 0.09 VABS-communication: 0.22 VABS-composite: 0.04 **Standard Observation Analog Procedure** Free Play Condition Child inappropriate mean % intervals, mean ± SD: 17 ±21

	special **G1:** 5 (10.2) **G2:** 4 (5.3) Special education classroom **G1:** 8 (10.3) **G2:** 14 (18.7) Special elementary school **G1:** 3 (6.1) **G2:** 2 (2.7) Home school **G1:** 4 (8.2) **G2:** 5 (6.7) Special preschool **G1:** 11 (22.4) **G2:** 11 (14.7) Regular preschool **G1:** 6 (12.2) **G2:** 8 (10.7) No school **G1:** 2 (24.1) **G2:** 12 (16.0)	G1 vs. G2: p=0.17 Parent restrictive mean raw score, mean ± SD: 1.10 ± 1.79 G1 vs. G2: p=0.27 Parent positive mean raw score, mean ± SD: 2.23 ± 3.19 G1 vs. G2: p=0.004 Child inappropriate mean % intervals, mean ± SD: 29 ± 27 G1 vs. G2: p=0.41 Parent restrictive mean raw score, mean ± SD: 0.65 (1.51) G1 vs. G2: p=0.03 Parent positive raw score, mean ± SD: 0.53 ± 1.24 G1 vs. G2: 0.13 Demand Condition Child inappropriate mean % intervals, mean ± SD: 29 ± 21 G1 vs. G2: p=0.0002 Child mean complains, Child inappropriate mean % intervals, mean ± SD: 84 ± 19 G1 vs. G2: p=0.004 Parent restrictive mean raw score, mean ± SD: 1.21 ± 2.06 G1 vs. G2: p=0.39

Parent positive raw score, mean ± SD: 2.42 ± 2.62
G1 vs. G2: p=0.001

Parent repeated mean raw score, mean ± SD: 7.33 ± 6.61
G1 vs. G2: p=<.0001

Parent mean contingent reinforcement, mean ± SD: 41 ± 25
G1 vs. G2: p=0.77

Tangible Restriction Condition
Child inappropriate mean % intervals, mean ± SD: 33 ± 24
G1 vs. G2: p=0.012

Parent restrictive mean raw score, mean ± SD: 1.62 ± 2.18
G1 vs. G2: p=0.10

Parent positive raw score, mean ± SD: 1.58 ± 2.33
G1 vs. G2: p=0.09

Modifiers
No predictors / moderators tested were significant at p<0.01

*Baseline values for HSQ and ABC extracted from Scahill 2012, which reports on entire sample.
**Mean differences in change from baseline to one-year followup for all measures was not significant

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Flanagan et al. 2012[17] **Country:** Canada **Intervention setting:** Treatment centers in the community, and children's homes **Enrollment period:** NR **Funding:** Regional Autism Programs of Ontario Network, CIHR STIHR Program **Design:** Retrospective cohort Note: See study reporting on this population[13] in 2011 AHRQ review; table includes data from comparative study only—related studies include	**Intervention:** Intensive Behavioral Intervention (IBI) for 20 and 40 h per week, except when transitioning to or from treatment with a mean duration of 27.84 months, SD = 8.11 Wait-list control group had low intensity behavioral intervention <10 h/week with a mean duration of 17.01, SD = 2.81 **Assessments:** Autism severity, adaptive and cognitive skills assessed with Childhood Autism Rating Scale (CARS), Vineland Adaptive Behavior Scale (VABS), Mullen Scales of Early Learning, Weschler Preschool Primary Scale of Intelligence or Stanford-Binet Intelligence Scale **Groups:** **G1:** IBI **G2:** Wait-List control **Provider:** Master's level psychometrists or graduate-level psychology	**Inclusion criteria:** • children who had completed IBI or left the waitlist within the previous 4 years • in IBI or on the waitlist for at least 12 months • complete information available about adaptive functioning, autism severity and cognitive skills, with all measures at the same time point completed within 3 months of one another • if on the waitlist: received fewer than 10 hours/week of IBI from private agencies • -if received IBI: received IBI for at least 80% of the interval between Time 1 and Time 2 testing **Exclusion criteria:** • received initial testing long before IBI program began • See inclusion **Age, mean ± SD/months:** **G1:** 42.93 ± 11.53 **G2:** 42.79 ± 10.51	Mean ± SD CARS **G1:** 32.83 ± 3.99 **G2:** 32.62 ± 3.74 VABS standard scores composite **G1:** 55.38 ± 7.00 **G2:** 55.49 ± 7.11 VABS Ratio scores Composite **G1:** 30.78 ± 10.78 **G2:** 30.79 ± 10.67 Communication **G1:** 25.47 ± 15.81 **G2:** 25.50 ± 11.97 Daily Living Skills **G1:** 42.79 ± 11.97 **G2:** 42.87 ± 12.11 Socialization **G1:** 24.08 ± 9.36 **G2:** 23.99 ± 11.22	Mean ± SD CARS **G1:** 30.20 ± 4.97 **G2:** 32.57 ± 5.55 Estimated marginal scores (adjusted for duration of treatment and age at time 2 and initial scores): **G1:** 30.00 **G2:** 32.77 (p= 0.033) VABS standard scores composite **G1:** 56.34 ± 14.40 **G2:** 52.19 ± 8.77 Estimated marginal score: **G1:** 56.96 **G2:** 50.66 (p=0.008) Ratio scores composite **G1:** 41.77 ± 20.26 **G2:** 31.15 ± 11.82 Estimated marginal score **G1:** 40.75 **G2:** 30.32 (p=0.002) Communication: **G1:** 46.60 ± 29.91 **G2:** 30.33 ± 16.98 Estimated marginal score: **G1:** 43.45 **G2:** 29.80 (p=0.006)

Shine 2010,[14] Freeman 2010,[15] Perry 2011,[16] Perry 2013[12]	students working under the supervision of registered psychologists **Treatment manual followed:** NR **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** NR **Concomitant therapies,%:** Specialized diets or special supplements: **G1:** NR **G2:** 14 Speech therapy **G1:** NR **G2:** 68 Occupational therapy **G1:** NR **G2:** 53 Behavioral consultation **G1:** NR **G2:** 34 Took medication for autism: **G1:** NR **G2:** 7	**Mental age, mean/yrs (range):** NR **Sex:** Male (%) **G1:** (87) **G2:** (84) **Race/ethnicity, n (%):** NR **SES:** **G1+G2:** Education: neither parent attending college or university: 29% , at least one parent attending college or university : 51%, at least one parent completing a professional or graduate degree: 20% Household income, mean (range): NR **Diagnostic approach:** In Study Diagnostic tool/method: CARS, in combination with clinical observation and a diagnostic and adaptive interview **Diagnostic category,%:** Autism: 50 PDD-NOS: 50 **Other characteristics**, n (%)**:** NR		Daily Living Skills: **G1:** 44.83 ± 14.01 **G2:** 40.03 ± 11.06 Estimated marginal score: **G1:** 45.04 **G2:** 38.80 (p=0.023) Socialization: **G1:** 33.90 ± 19.04 **G2:** 23.11 ± 10.85 Estimated marginal score: **G1:** 33.49 **G2:** 21.88 (p=0.001) Cognitive skills: IQ estimate **G1:** 55.80 ± 26.97 **G2:** 39.50 ± 18.93 Estimated marginal score: **G1:** 55.71 **G2:** 36.46 (p=0.002) **Harms :** NR **Modifiers :** Younger initial age predicted better cognitive outcomes in G1 but not in G2

	Low intensity (< 10 hours/week) behavioral intervention **G1:** NR **G2:** 14 **N at enrollment:** **G1:** 79 **G2:** 61 **N at follow-up:** **G1:** 61 **G2:** 61	

Comments: Interval between test periods (duration) was longer for G1 so participants were older at time of second assessment. Differences in duration and age were statistically controlled for in analysis

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Ingersoll et al. 2012 [39, 40] **Country:** US **Intervention setting:** Psychology clinic **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** Reciprocal Imitation Training (RIT), 10 weeks, 1 hr/day, 3 days/week **Assessments:** parent; observation in clinic **Groups:** **G1:** Reciprocal Imitation Training (RIT) **G2:** Standard treatment **Provider:** Therapists **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** Yes **Concomitant therapies, n (%):** Outside intervention per week, mean hours ± SD: **G1:** 11.0 ± 8.1	**Inclusion criteria:** • diagnosed with autism • age between 27 and 47 months **Exclusion criteria:** • see inclusion criteria **Age, mean/months ± SD:** **G1:** 39.3 ± 7.3 **G2:** 36.5 ± 8.0 **Nonverbal mental age, mean/months ± SD:** **G1:** 20.8 ± 6.6 **G2:** 17.9 ± 7.5 **Expressive language age, mean/months ± SD:** **G1:** 17.3 ± 5.5 **G2:** 16.2 ± 5.9 **Sex:** M, n (%): **G1:** 13 (93) **G2:** 11 (85) F, n (%): **G1:** 1 (7) **G2:** 2 (15) **Race/ethnicity, n (%):** % minority status: **G1:** 36 **G2:** 39 **SES:**	**Number of spontaneous play acts (SPA):** **G1:** 30.27 ± 19.43 **G2:** 20.10 ± 13.35 **Response to joint attention (ESCS):** **G1:** 51.72 ± 22.90 **G2:** 49.50 ± 24.37 **Initiation of joint attention (ESCS):** **G1:** 2.73 ± 2.72 **G2:** 2.10 ± 3.25	**Social skills:** Social-Emotional Scale: Time x group: $p = 0.02$ **Communication/ language:** ESCS Initiating joint attention $p < 0.05$ **Elicited imitation:** **G1:** 20.64 ± 11.40 **G2:** 7.20 ± 6.65 $p < 0.05$ **Spontaneous imitation:** **G1:** 17.27 ± 11.56 **G2:** 4.70 ± 3.83 $p < 0.05$ **Harms:** NR **Modifiers:** NR

	G2: 13.2 ± 8.8 **N at enrollment:** **G1:** 15 **G2:** 14 **N at follow-up:** **G1:** 14 **G2:** 13	Maternal education, n (%): NR Household income, mean (range): NR **Diagnostic approach:** In Study & Referral Diagnostic tool/method: DSM-IV-TR criteria by psychologic & Autism Diagnostic Observation Schedule-Generic (ADOS-G) **Diagnostic category, n (%):** Autism: 29 (100) PDD-NOS: 0 Aspergers: 0 **Other characteristics, n (%):** NR

Comments: Pre- and post-treatment imitation data from 22 of these children were presented in a previous publication. The original numerical data is not presented, only conclusions.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Kaale et al. 2012[41] **Country:** Norway **Intervention setting:** clinic **Enrollment period:** October 2006 to August 2008 **Funding:** South-Eastern Norway Regional Health Authority and Center for Child and Adolescent Mental Health, Eastern and Southern Norway **Design:** RCT	**Intervention:** Joint attention intervention (modification of Kasari manual); intervention was individualized and relied on combination behavioral and developmental model. Lasted 8 week with two daily sessions (5 days/week) each session was 20 minutes—5 min of table top training and 15 min of floor play. Control group received regular preschool program **Assessments:** Mullen Scale of Early Learning (MSEL), Early Social Communication Scale (ESCS), preschool teacher-child play observed **Groups:** **G1:** Joint Attention **G2:** control **Provider:** Preschool teachers **Treatment manual followed:** Yes **Defined protocol**	**Inclusion criteria:** • chronological age 24-60 months • confirmed ICD-10 diagnosis of childhood autism • attendance in preschool **Exclusion criteria:** • central nervous system disorders (e.g epilepsy, cerebral palsy) • non Norwegian speaking parents **Age, mean/mos ± SD:** **G1:** 47.6 ± 8.30 **G2:** 50.3 ± 8.3 **Mental age, mean/mos (range):** **G1:** 25.6 ± 10.8 **G2:** 30.3 ± 12.0 **Sex:** M, n (%): **G1:** 26 (76.5) **G2:** 22 (81.5) F, n (%): **G1:** 8 (23.5) **G2:** 5 (18.5) **Race/ethnicity, n (%):** NR **SES:**	JA during ESCS **G1:** 1.3 ± 2.8 **G2:** 1.3 ± 1.8 JA during teacher-child play **G1:** 0.7 ± 1.3 **G2:** 0.4 ± 1.1 JE during teacher-child play (%) **G1:** 53.1 ± 23.1 **G2:** 58.0 ± 23.8 JA during mother-child play **G1:** 1.1 ± 1.6 **G2:** 1.4 ± 2.0 JE during mother-child play (%) **G1:** 45.1 ± 23.4 **G2:** 50.2 ± 21.7	JA during ESCS **G1:** 1.6 ± 2.6 **G2:** 1.6 ± 2.2 p=0.99 JA during teacher-child play **G1:** 1.8 ± 3.2 **G2:** 0.4 ± 0.7 p=0.036 JE during teacher-child play (%) **G1:** 56.0 ± 22.2 **G2:** 62.7 ± 20.9 p=0.53 JA during mother-child play **G1:** 2.4 ± 3.6 **G2:** 1.8 ± 3.2 p=0.09 JE during mother-child play (%) **G1:** 57.3 ± 22.8 **G2:** 49.2 ± 19.9 p=0.015 **Harms:** NR **Modifiers:** Chronological age, language age, DQ and program philosophy did NOT moderate the effect of JA intervention

	followed: Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 34 **G2:** 27 **N at follow-up:** **G1:** 34 **G2:** 27	**Mean education level (scale 1-5)** **G1:** 3.2 ± 1.3 **G2:** 3.5 ± 1.0 **Diagnostic approach:** In Study/Referral Diagnostic tool/method: Comprehensive clinical evaluation; 80% tested with ADOS and/or ADI-R **Diagnostic category, n (%):** Autism :100% **Other characteristics, n (%):** Developmental quotient mean ± SD: **G1:** 53.3 ± 19.2 **G2:** 59.9 ± 19.7 Receptive language age, mean/mos ± SD: **G1:** 21.0 ± 10.3 **G2:** 25.8 ± 11.7 Expressive language age, mean/mos ± SD: **G1:** 18.8 ± 10.5 **G2:** 24.9 ± 12.8 **Preschool placement, n (%)** Mainstream preschool **G1:** 30 (88) **G2:** 24 (89) ASD-unit in mainstream

	pre-school **G1:** 2 (6) **G2:** 2 (7) ASD preschool **G1:** 2 (6) **G2:** 1 (4) Program philosophy ABA-based program **G1:** 20 (59) **G2:** 12 (44) Eclectic program **G1:** 14 (41) **G2:** 15 (56) Hours/week in school **G1:** 36.4 ± 5.7 **G2:** 38.4 ± 3.6 1:1 training hours/week **G1:** 11.0 ± 5.2 **G2:** 10.7 ± 6.9 1:1 support in group hrs/week **G1:** 19.2 ± 7.6 **G2:** 19.0 ± 7.3 Ordinary group hr/week **G1:** 6.1 ± 7.9 **G2:** 10.0 ± 7.7

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Kasari et al., 2012 [42, 43] **Country:** US **Intervention setting:** Clinic **Enrollment period:** NR **Funding:** NIH grant **Design:** RCT *Note: see data from earlier studies[44, 45] reporting on this population in 2011 AHRQ review[9]	**Intervention:** Joint attention intervention: Goal to increase child's joint attention initiations during novel play routines. Symbolic play intervention to increase child's level and frequency of play acts according to play scale adapted from Lifter. Treatment sessions held every day for 5-6 weeks. Control group received standard treatment (ABA) **Assessments:** Early Language Communication Scale (ESCS); Mullen Scales of Early Learning; Reynell Developmental Language Scales **Groups:** **G1:** joint attention intervention **G2:** symbolic play **G3:** control **Provider:** see Kasari et al 2006 **Treatment manual followed:** Yes	**Inclusion criteria:** • Diagnosis of autism on the ADI-R and ADOS • Age < 5 years old • Accessible for follow-up **Exclusion criteria:** • Seizures • Additional medical diagnoses (e.g., genetic syndromes) • Geographically inaccessible for follow-up visits • Did not plan to stay in the early intervention program for at least 4 weeks **Age, mean/mos ± SD:** **G1:** 43.05 ± 6.863 **G2:** 41.41 ± 6.491 **G3:** 41.31 ± 4.542 **Mental age, mean/ mos ± SD:** **G1:** 26.29± 8.713 **G2:** 26.59 ± 7.550 **G3:** 22.05 ± 9.532 **Sex:** M, n (%): **G1:** 15 (75) **G2:** 11 (69) **G3:** 14 (87.5)	Joint attention and shared positive effect, mean ± SD: **G1:** 3.25± 5.37 **G2:** 3.25 ± 4.38 **G3:** 4.50 ± 6.57 Joint attention and shared positive effect and utterance (s) , mean ± SD: **G1:** 1.05± 2.44 **G2:** 1.56 ± 4.00 **G3:** 2.50 ± 4.56	At 6 month follow-up Joint attention and shared positive effect, mean ± SD: **G1:** 6.15± 5.72 **G2:** 7.91 ± 3.06 **G3:** 3.06 ± 4.39 Joint attention and shared positive effect and utterance, mean ± SD: **G1:** 4.10± 4.64 **G2:** 3.19 ± 3.58 **G3:** 1.75 ± 3.38 At 12 month follow-up Joint attention and shared positive effect, mean ± SD: **G1:** 7.65± 6.80 **G2:** 9.44 ± 3.88 **G3:** 3.88 ± 5.32 Joint attention and shared positive effect and utterance (s) , mean ± SD: **G1:** 5.30± 5.68 **G2:** 5.75 ± 7.02 **G3:** 1.56 ± 3.10 At 5 years follow-up (n=40/58): Cognitive and language ability: >30 Months:

	Defined protocol followed: Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 20 **G2:** 21 **G3:** 17 **N at follow-up:** **G1:** 20 **G2:** 16 **G3:** 16 At 5 years follow-up: **G1:**15 **G2:**14 **G3:**11	F, n (%): **G1:** 5 (25) **G2:** 5 (31) **G3:** 2 (12.5) **Race/ethnicity, n (%):** White **G1:** 16 (80) **G2:** 12 (75) **G3:** 9 (56.3) Minority **G1:** 4 (20) **G2:** 4 (25) **G3:** 7 (43.7) **SES:** Maternal education, n (%): High school **G1:** 0 **G2:** 0 **G3:** 1 Some College/technical **G1:** 2 **G2:** 3 **G3:** 4 College/professional **G1:** 18 **G2:** 13 **G3:** 11 Household income, mean (range): NR **Diagnostic approach:** In Study/Referral Diagnostic tool/method: ADOS/ADI-R		**G1:** 13 (87%) **G2:** 11 (79%) **G3:** 8 (73%) total: 32 (80%), p=0.67 DAS (standard score): **G1:**93.5 (22.32) **G2:**87.73 (17.96) **G3:**89.23 (13.13) total: 90.44 (18.51) p=0.75 EVT (standard score): **G1:**86.5 (18.9) **G2:**86.4 (19.3) G3:80.5 (22.3) total: 85.0(19.4), p=0.77 Baseline play predicting spoken language at 5 years (X^2= 18.15, p< .01, R^2 = 0.58).and cognitive scores at 8 years of age (functional play types- (F1,30=14.62, p<0.01)). For a 1-unit increase in functional play types, there was a 2.12 (SE 0.55) standard score increase on the DAS. Children gained a standard score of 1.1 (SE =0.3) in spoken vocabulary ability per month that they enter the treatment earlier and they gain a standard score of 2.1 (SE =0.9) in spoken vocabulary ability per

	Diagnostic category, n (%): Autism (100) **Other characteristics**, n (%)**:** **Expressive language age, mean/ mos ± SD:** **G1:** 20.6± 6.508 **G2:** 23.18 ± 7.418 **G3:** 19.75 ± 7.819 **Receptive language age, mean/ mos ± SD:** **G1:** 20.55± 7.272 **G2:** 23.35 ± 9.380 **G3:** 17.94 ± 8.813	one frequency increase in joint attention initiations G1 scored an average of 12.5 (SE =5.8) points higher than G3 on the language measure, and G2 scores an average of 10.6 (SE = 6.2) points higher on the language measure than G3. No group difference (p=0.61). **Harms:** NR **Modifiers** Interactions of group and time were found for both types of joint attention quality.

Comments: Used data from previous published RTC (Kasari et al 2006); Original study had 58 participants; 6 were not included in this analysis because portions of their ESCS data were missing.
Kasari et al 2012 followed 40/58 children at 5 years and 8 years after intervention

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Kasari et al. 2012[46] **Country:** US **Intervention setting:** School **Enrollment period:** August 2003 to September 2007 **Funding:** NIMH, HRSA, NCT **Design:** RCT	**Intervention**: Child-assisted approach: Children with ASD given 20 min twice weekly sessions for 6 weeks with direct instruction, to develop strategies to engage socially with their peers Peer-mediated: Three classroom peers of child with ASD taught strategies for engaging children with social challenges on the playground. Training given for 20 min twice weekly sessions for 6 weeks **Assessments:** Social Network Survey, Teacher perception of social skills (TPSS), Playground observation of peer engagement, behavioral assessment (direct observations, and peer, self and teacher reports) **Groups *:** G1: CHILD-assisted G2: PEER-mediated G3: Both PEER and CHILD Interventions	**Inclusion criteria:** • met criteria for ASD on the ADI–R and ADOS administered by blind, • independent psychologists • fully included in a • regular education classroom for at least 80% of the school day • between the ages of 6–11 years old • in grades 1–5 • IQ of 65 or higher • did not have additional • diagnoses **clusion criteria:** See inclusion **Age, mean ± SD:** 8.14 years ± 1.56 **Mental age, mean ± SD:** IQ: 90.97 ± 16.33 **Sex:** M, 90 % F, 10 % **Race/ethnicity, n (%):** Caucasian 46.6%, African American, 5%	**Mean ± SD** Social network Salience: **Assigned to CHILD:** 0.26 ± 0.22 **Not assigned to CHILD:** 0.38 ± 0.26 **Assigned to PEER:** 0.35 ± 0.29 **Not assigned to PEER:** 0.29 ± 0.19 Received friendship nominations (range 0–8) **Assigned to CHILD:** 1.23 ± 1.48 **Not assigned to CHILD:** 1.80 ± 1.83 **Assigned to PEER:** 1.80 ± 2.01 **Not assigned to PEER:** 1.23 ± 1.22 Outward nominations (range 0–15) **Assigned to CHILD:** 4.27 ± 2.89	**Mean ± SD** Social network salience **Assigned to CHILD:** 0.46 ± 0.29, 0.34 ± 0.25 **Not assigned to CHILD:** 0.37 ± 0.21, 0.37 ± 0.30 **Assigned to PEER:** 0.51 ± 0.29, 0.41 ± 0.29 **Not assigned to PEER:** 0.32 ± 0.18, 0.30 ± 0.25 children who received both the CHILD and PEER interventions had significantly higher SNS scores (M = 0.60; SD = 0.30) when compared to children who received the CHILD intervention (M = 0.31; SD = 0.21), t(28) =)2.99, p = .006, d = 1.12, as well as those who received neither CHILD nor PEER intervention (M = 0.32; SD = 0.15), t(28) = 3.23, p = .003, d = 1.18. Received friendship nominations

	G4: Neither PEER nor CHILD **Provider:** Graduate students in Educational Psychology **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR N at enrollment: **G1:** 15 **G2:** 15 **G3:** 15 **G4:** 15 **N at follow-up:** **G1:** 14 **G2:** 15 **G3**: 15 **G4:** 15	Latino,21.7% Asian: 16.7% Other: 10% **SES:** NR **Diagnostic approach:** NR Diagnostic tool/method: ADI-R, ADOS **Diagnostic category, n (%):** ASD: 100 **Other characteristics**, n**:** first grade: 15 second grade: 18 third grade: 8 fourth grade: 11 fifth grade: 8	**Not assigned to CHILD:** 3.43 ± 2.49 **Assigned to PEER:** 4.17 ± 2.93 **Not assigned to PEER:** 3.53 ± 2.47 Rejection nominations (range 0–9) **Assigned to CHILD:** 1.71 ± 2.02 **Not assigned to CHILD:** 1.69 ± 1.85 **Assigned to PEER:** 2.17 ± 2.07 **Not assigned to PEER:** 1.19 ±1.62 Reciprocal friendships (%age) (range 0–100) **Assigned to CHILD:** 6.25 ± 25.00 **Not assigned to CHILD:** 18.18 ± 40.45 **Assigned to PEER:** 13.33 ± 35.19 **Not assigned to PEER:** 8.33 ± 28.87 Teacher perceptions	(range 0–8) **Assigned to CHILD:** 2.00 ± 2.10, 1.41 ± 1.52 **Not assigned to CHILD:** 2.33 ± 1.49, 1.53 ± 1.55 **Assigned to PEER:** 2.80 ± 1.96, 1.73 ± 1.76 **Not assigned to PEER:** 1.53 ± 1.43, 1.21 ± 1.21 **Outward nominations (range 0–15)** **Assigned to CHILD:** 4.67 ± 2.20, 4.10 ± 2.43 **Not assigned to CHILD:** 4.43 ± 3.22, 3.40 ± 2.19 **Assigned to PEER:** 4.63 ± 2.28, 4.10 ± 2.54 **Not assigned to PEER:** 4.47 ± 3.17, 3.38 ± 2.04 Rejection nominations (range 0–9) **Assigned to CHILD:** 2.11 ± 2.82, 2.15 ± 2.54 **Not assigned to CHILD:** 2.03 ± 1.80, 1.93 ± 1.91 **Assigned to PEER:** 2.37 ± 2.25, 2.40 ± 2.27 **Not assigned to PEER:**

Assigned to CHILD: 23.31 ± 4.61 **Not assigned to CHILD:** 23.31 ± 3.63 **Assigned to PEER:** 23.13 ± 4.02 **Not assigned to PEER:** 23.51 ± 4.27 Solitary engagement Mean (SD): Child: 0.36 ± 0.29 Peer: 0.34 ± 0.29 Joint engagement Mean (SD): Child: 0.41 ± 0.34 Peer: 0.43 ± 0.34	1.74 ± 2.43, 1.62 ± 2.12 Reciprocal friendships (%age) (range 0–100) **Assigned to CHILD:** 15.79 ± 37.46 12.50 ± 34.16 **Not assigned to CHILD:** 13.33 ± 35.19 5.56 ± 23.57 **Assigned to PEER:** 13.64 ± 35.13 10.00 ± 30.78 **Not assigned to PEER:** 16.67 ± 38.93 7.14 ± 26.73 Teacher perceptions **Assigned to CHILD:** 24.18 ± 3.33 24.76 ± 4.05 **Not assigned to CHILD:** 24.62 ± 4.47 23.97 ± 4.20 **Assigned to PEER:** 25.19 ± 3.45 24.95 ± 3.72 **Not assigned to PEER:** 23.49 ± 4.26 23.61 ± 4.50 End of Treatment:

Solitary engagement
Mean (SD):
Child: 0.33 ± 0.27)
Peer: 0.28 ± 0.26)

Joint engagement
Mean (SD):
Child: 0.43 ± 0.27
Peer: 0.44 ± 0.31

Follow-up:
Solitary engagement
Mean (SD):
Child: 0.33 ± 0.30
Peer: 0.19 ± 0.24

Joint engagement
Mean (SD):
Child: 0.43 ± 0.35
Peer: 0.51 ± 0.34

Harms: NR

Modifiers: NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Landa et al. 2011[47, 48] **Country:** US **Intervention setting:** Classroom at autism center **Enrollment period:** NR **Funding:** National institutes of Mental Health;lHealth Resources and Services Agency **Design:** RCT	**Intervention:** Interpersonal synchrony (IS) four days per week for 2.5 hours / day for 6 months, home-based parent training (1.5 hours per month), parent education (38 hours), and instructional strategies, + supplementary social curriculum. Non-interpersonal synchrony includes everything as in the IS group except supplementary curriculum Both groups received Assessment, Evaluation, and Programming System for Infants and Children (AEPS) curriculum. **Assessments:** Communication and Symbolic Behavior Scales Developmental Profile to measure initiation of joint attention (JA) and shared positive affect (SPA). Socially engage imitation (SEI) Socially engaged imitation (SEI) coded from videotapes of structured imitation task. MSEL Expressive Language	**Inclusion criteria:** • meeting criteria on the ADOS for ASD or autism and receiving ASD diagnosis by expert clinician • chronological age between 21-33 months • non-verbal mental age at least 8 months per Mullen Scales of Early Learning Visual Reception Scale • no siblings with ASD • English primary language spoken at home • no known etiology for ASD **Exclusion criteria:** • see inclusion **Age, mean ± SD/ months (range):** Range: 21-33 months G1: 28.6 ± 2.6 G2: 28.8 ± 2.8 **Mental age:** NR **Sex, n (%):** Males: **G1:** 20 (83.3) **G2:** 20 (80)	**Primary outcomes, mean ±SD** SEI: **G1:** 0.17 ± 0.19 **G2:** 0.25 ± 0.24 IJA : **G1:** 2.29 ± 3.16 **G2:** 2.79 ± 3.62 SPA: **G1:** 2.42 ± 2.93 **G2:** 3.54 ± 3.56 **Secondary Outcomes, mean ± SD** EL T scores: **G1:** 23.92 ± 5.50 **G2:** 25.92 ± 8.12 VR T scores: **G1:** 27.50 ± 8.27 **G2:** 31.12 ± 9.86	Post-test: SEI: **G1:** 0.42 ± 0.24 **G2:** 0.35 ± 0.23 IJA: **G1:** 7.70 ± 9.33 **G2:** 5.00 ± 7.91 SPA: **G1:** 6.87 ± 7.55 **G2:** 5.33 ± 6.64 EL T: **G1:** 34.08 ± 14.59 **G2:** 31.92 ± 13.67 VR T: **G1:** 36.75 ± 14.54 **G2:** 32.24 ± 14.07 At 6 month follow-up: Group Difference effect size (p value); SEI: 0.86 (0.01) IJA: 1.56 (0.07) SPA:0.81 (0.27) EL T: 0.57 (0.24) VR T: 0.46 (0.33) Growth trends: Difference between G1 & G2: Baseline to post-test: Effect size (p value): SEI: 76 (0.04) IJA: 0.93 (0.11)

	(EL) and VR. Assessments were conducted pre-intervention, immediately post-intervention, and at six-month follow-up. **Groups:** **G1:** Interpersonal synchrony (IS) G2: Non-interpersonal synchrony (Non-IS) **Provider:** Interventionists (Master's level teacher and teaching assistants) **Treatment manual followed:** NR **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):**# hrs of Speech Language treatment (pre to post): G1:24.45 (19.38) G2:21.38 (16.20) # hrs of Speech Language treatment (post to follow-up):	Females: **G1:** 4 (16.7) **G2:** 5 (20) **Race/ethnicity, n (%):** Caucasian **G1:**19 (79.2) **G2:**19 (79.2) **SES:** Maternal education: NR Household income, Hollingshead SES score, mean ± sd G1: 54.7 ± 8.7 G2: 53.3 ± 10.3 **Diagnostic approach:** In Study Diagnostic tool/method: Expert clinician **Diagnostic category, n (%):** Autism: 100% ? **Other characteristics**, n (%)**:** NR		SPA:0.83 (0.17) EL T: 0.60 (0.13) VR T: 0.84 (0.02) Post-test to follow-up; SEI: 0.43 (0.24) IJA: 0.68 (0.25) SPA:0.41 (0.52) EL T: 0.09 (0.83) VR T: -0.10 (0.78) T1–T4 change: n, mean ± SD: IQ: N= 42, 21.4 ± 22.9, d= 1.02, p<0.001 Vineland Communication Domain standard score: N= 46, 12.7 ± 19.4 , d=0.81, p<0.001 ASD severity: N= 47, 0.1 ±2.5, d= 0.05, p=NS **Harms:** NR **Modifiers:** NR

G1:28.07 (27.01)
G2:26.26 (18.82)

N at enrollment:
G1: 25
G2: 25

N at follow-up:
G1: 24
G2: 24

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Lawton et al. 2012 [49] **Country:** US **Intervention setting:** Preschool classrooms **Enrollment period:** Fall 2008 to Fall 2009 **Funding:** NR **Design:** RCT	**Intervention:** Joint Attention and Symbolic Play/Engagement and Regulation Intervention (JASP/ER) for 6 weeks; teachers received training once/week; interventionists met with the dyads twice/week for 30 minutes **Assessments:** Class observation; Early Social Communication Scales (ESCS); taped play interaction **Groups:** **G1:** JASP/ER intervention **G2:** Delayed treatment with standard practice **Provider:** Preschool teachers **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:**	**Inclusion criteria for child:** • school district label of autism or autism spectrum disorder (ASD) • met research criteria for autism or ASD on the Autism Diagnostic Observation System-Generic • between 3-5 years of age • attended public preschool at least 4 hours a day, 3 times a week • attends a classroom with a teacher willing to participate in the study **Inclusion criteria for teacher or paraprofessional:** • able to work with one child in the classroom through the entire study • available to attend the intervention meetings **Exclusion criteria:**	**Social skills:** Engagement States Duration of engagement states in minutes: Object engagement, mean ± SD: **G1**: 4.12 ± 1.99 **G2**: 4.28 ± 1.71 Supported engagement, mean ± SD: **G1**: 4.27 ± 1.77 **G2**: 3.94 ± 1.89 **Communication/ language:** Class observation Frequency of joint attention initiations (IJAs): Total IJA, mean ± SD: **G1**: 1.67 ± 2.60 **G2**: 2.43 ± 2.51 Point, mean ± SD: **G1**: 1.33 ± 2.59 **G2**: 0.29 ± 0.49 Show, mean ± SD: **G1**: 0.33 ± 0.50 **G2**: 0.71 ±1.11 Give, mean ± SD: **G1**: 0.00 ± 0.00 **G2**: 0.71 ± 1.25 Look, mean ± SD: **G1**: 0.00 ± 0.00	**Social skills:** Engagement States Duration of engagement states in minutes: Object engagement, mean ± SD: **G1**: 2.87 ± 1.31 **G2**: 4.94 ± 1.71 p < 0.01 Supported engagement, mean ± SD: **G1**: 5.58 ± 4.11 **G2**: 4.11 ± 1.68 p < 0.05 **Communication/ language:** Class observation Frequency of joint attention initiations (IJAs): Total IJA, mean ± SD: **G1**: 7.00± 4.15 **G2**: 1.83 ± 1.00 p < 0.005 Point, mean ± SD: **G1**: 2.77 ± 1.99 **G2**: 0.14 ± 0.38 p < 0.005 Show, mean ± SD: **G1**: 1.11 ± 1.05 **G2**: 0.00 ±0.00 p < 0.01 Give, mean ± SD:

	NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 9 dyads (dyad= 1 instructor and student) **G2:** 7 dyads **N at follow-up:** **G1:** 9 dyads **G2:** 7 dyads	• children with seizures, associated physical disorders, or co-morbidity with other syndromes or diseases **Age, mean/months ± SD:** **G1:** 46.0 ± 5.00 **G2:** 43.01 ± 6.00 **Mental age, mean/months SD:** **G1:** 30.3 ± 5.01 **G2:** 33.8 ± 8.74 **Sex:** NR **Race/ethnicity, n (%):** Child: Caucasian: **G1:** 4 (44.4) **G2:** 5 (71.4) Minority: **G1:** 5 (55.6) **G2:** 2 (28.6) Instructor: Caucasian: **G1:** 7 (77.8) **G2:** 3 (42.9) Minority: **G1:** 2 (22.2) **G2:** 4 (57.1) **SES:** NR **Diagnostic approach:** Diagnostic tool/method:	**G2**: 0.71 ± 1.11 ESCS Frequency of Joint Attention Initiations (IJAs): Total IJA, mean ± SD: **G1**: 11.89 ± 10.01 **G2**: 13.29 ± 7.34 Point, mean ± SD: **G1**: 5.78 ± 5.70 **G2**: 7.57 ± 5.09 Show, mean ± SD: **G1**: 1.13 ±1.81 **G2**: 0.43 ± 0.79 Give, mean ± SD: **G1**: 0.33 ± 1.00 **G2**: 0.14 ± 0.38 Look, mean ± SD: **G1**: 4.78 ± 4.52 **G2**: 5.14 ± 3.53 Taped play interaction Frequency of joint attention initiations : Total IJA, mean ± SD: **G1**: 4.78 ± 3.05 **G2**: 7.29 ± 6.04 Point, mean ± SD: **G1**: 2.33 ± 2.29 **G2**: 2.14 ± 2.19 Show, mean ± SD: **G1**: 1.44 ± 3.25 **G2**: 0.71 ± 1.25 Give, mean ± SD: **G1**: 0.56 ± 0.73 **G2**: 0.29 ± 0.49	**G1**: 2.22 ± 2.49 **G2**: 0.14 ± 0.38 p=NS Look, mean ± SD: **G1**: 0.89 ± 1.45 **G2**: 0.71 ± 1.89 p=NS ESCS frequency of joint attention initiations (IJAs): Total IJA, mean ± SD: **G1**: 15.33 ± 10.89 **G2**: 9.00 ± 7.23 p=NS Point, mean ± SD: **G1**: 8.67 ± 9.66 **G2**: 4.29 ± 6.24 p=NS Show, mean ± SD: **G1**: 1.00 ±0.87 **G2**: 0.00 ± 0.00 p=0.025 Give, mean ± SD: **G1**: 1.44 ± 3.61 **G2**: 0.43 ± 1.13 p=NS Look, mean ± SD: **G1**: 4.22 ± 1.99 **G2**: 4.29 ± 5.02 p=NS Taped play interaction frequency of joint attention initiations (IJAs): Total IJA, mean ± SD: **G1**: 6.22 ± 5.19 **G2**: 4.00 ± 2.31

	Autism Diagnostic Observation System-Generic (ADOS-G) **Diagnostic category, n (%):** Autism: 100% PDD-NOS: 0 Aspergers: 0 **Other characteristics**, n (%)**:** Instructors Teacher: **G1:** 2 (22.2) **G2:** 2 (28.6) Paraprofessional, n: **G1:** 7 (77.8) **G2:** 5 (71.4) Instructor years of experience, mean ± SD: **G1:** 12.8 ± 12.5 **G2:** 7.33 ± 9.29 Instructor age, mean/yrs ± SD: **G1:** 42.3 ± 16.3 **G2:** 34.3 ± 16.9	Look, mean ± SD: **G1**: 0.44 ± 0.73 **G2**: 4.14 ± 5.33	p=NS Point, mean ± SD: **G1**: 1.11 ± 1.57 **G2**: 1.29 ± 1.89 p=NS Show, mean ± SD: **G1**: 1.77 ± 2.63 **G2**: 0.29 ± 0.49 p=NS Give, mean ± SD: **G1**: 1.11 ± 1.69 **G2**: 0.71 ± 1.11 p=NS Look, mean ± SD: **G1**: 2.22 ± 2.99 **G2**: 1.71 ± 2.56 p=NS **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Lerner et al. 2012[50] **Country:** US **Intervention setting:** After-school? **Enrollment period:** NR **Funding:** Jefferson Scholars' Foundation Graduate Fellowship **Design:** RCT	**Intervention:** Sociodramatic Affective Relational Intervention (SDARI) 90 minute meetings once/week for 4 weeks; each session included two 40 minute sessions using abridged versions of the curricula Skillstreaming: 90 minute meetings once/week for 4 weeks; each session included two 40 minute sessions using abridged versions of the curricula **Assessments:** parents completed standardized measures of children's social functioning before and after SSI; intervention staff completed standardized measure of social functioning after first and last session. Social Interaction observation system (SIOS) and sociometrics; Social Skill rating system – teacher (SSRS-T) Parent reported: SCQ, SRS, Social Skills Rating System- Parent (SSRS-P) And post-treatment satisfaction questionnaire	**Inclusion criteria:** • previous diagnosis of HFASD from a licensed professional • clinical cutoff scores on SCQ **Exclusion criteria:** NR **Age, mean/yrs (range):** **G1:** 10.86 ± 1.68 **G2:** 11.33 ± 1.63 **Mental age, mean/yrs (range):** NR **Sex:** M, 13 (100%): **Race/ethnicity, n (%):** White Asian **SES:** Parental education[a], mean ± SD : **G1:** 5.43 ± 0.79 **G2:** 5.33 ± 0.82 Household income, mean (range): **G1:** $70,000 ± $27,080 **G2:** $86,700 ± $19,660 **Diagnostic approach:** In Study/Referral Diagnostic tool/method:	**Social Skills** SRS, mean ± SD **G1:** 76.57 ± 10.47 **G2:** 82.17 ± 10.68 SSRS parent, mean ± SD **G1:** 77.57 ± 8.70 **G2:** 82.33 ± 17.76 Reciprocated friend nominations, mean ± SD **G1:** 0.14 ± 0.12 **G2:** 0.13 ± 0.10 Social preference, mean ± SD **G1:** 0.43 ± 0.30 **G2:** 0.00 ± 0.31 SSRS- Teacher, mean ± SD **G1:** 80.43 ± 11.87 **G2:** 73.17 ± 19.17 SIOS- Positive, mean ± SD **G1:** 0.69 ± 0.54 **G2:** 0.43 ± 0.35 SIOS- Negative, mean ± SD **G1:** 0.18 ± 0.21 **G2:** 0.05 ± 0.13 SIOS- Low level, mean ± SD **G1:** 1.63 ± 0.52 **G2:** 1.34 ± 0.81	**Social Skills** SRS, mean ± SD **G1:** 75.57 ± 13.05 **G2:** 76.17 ± 9.56 SSRS parent, mean ± SD **G1:** 79.71 ± 9.59 **G2:** 82.33 ± 15.65 Reciprocated friend nominations, mean ± SD **G1:** 0.24 ± 0.09 **G2:** 0.27 ± 0.21 Social preference, mean ± SD **G1:** 0.29 ± 0.44 **G2:** 0.43 ± 0.46 SSRS- Teacher, mean ± SD **G1:** 94.00 ± 13.92 **G2:** 88.17 ± 13.80 SIOS- Positive, mean ± SD **G1:** 0.37 ± 0.29 **G2:** 1.00 ± 0.45 SIOS- Negative, mean ± SD **G1:** 0.05 ± 0.09 **G2:** 0.28 ± 0.25 SIOS- Low level, mean ± SD **G1:** 1.41 ± 0.62

	Groups: **G1:** SDARI **G2:** Skillstreaming **Provider:** Intervention staff members, who received 3 hours training in intervention and weekly supervision in intervention administration and behavior management **Treatment manual followed:** Yes **Defined protocol followed:** NR **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 7 **G2:** 6 **N at follow-up:** **G1:** NR **G2:** NR	**Diagnostic category, n (%):** Autism **G1:** 0 **G2:** 2 (33) PDD-NOS **G1:** 1 (14) **G2:** 1 (17) Asperger syndrome **G1:** 6 (86) **G2:** 3 (50) **Other characteristics, n (%):** Grade **G1:** 5.29 ± 1.50 **G2:** 5.33 ± 2.07 SCQ, mean ± SD **G1:** 17.57 ± 3.55 **G2:** 16.83 ± 6.27	**G2:** 1.42 ± 0.36 **Harms:** NR **Modifiers:** NR

Comments: [a] Parental education scale: 1= 8th grade or less, 2= some high school, 3= some college, 4= some college, 5= college graduate and 6= graduate degree

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Reaven et al. 2012[51] **Country:** US **Intervention setting:** clinic **Enrollment period:** NR **Funding:** Cure Autism Now, Autism Speaks, USDHHS grants **Design:** RCT	**Intervention:** Facing Your Fears (FAF) 12 multifamily group sessions, 1 ½ hours, supported by manuals for facilitators, parents and youth. Duration of intervention was 4 months **Assessments:** ADOS, Anxiety Disorders Interview Schedule for Children – parent version; Clinical Global Impressions Scale-Improvement ratings **Groups:** **G1:** facing your fears **G2:** control (usual treatment) **Provider:** 13 clinicians **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** Yes, n	**Inclusion criteria:** • chronological age between 7 and 14 years • confirmed diagnosis of ASD, determined by one of three expert clinical psychologists using recent ADOS and SCQ • speaking in full complex sentences reflected in recent standardized cognitive assessment • clinically significant symptoms of anxiety (score above clinical significance cutoff on separation, social and/or generalized anxiety subscales of the SCARED **Exclusion criteria:** • see above **Age, mean ± SD months:** **G1:** 125.75 ± 21.47 **G2:** 125.00 ± 20.45 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%) **G1:** 24 (100)	**Anxiety Disorders Interview schedule for children** Separation **G1:** 2.45 ± 2.33 (0-5) **G2:** 2.22 ± 2.49 (0-6) Social **G1:** 3.85 ± 2.13 (0-6) **G2:** 3.70 ± 2.36 (0-7) Specific phobia **G1:** 3.45 ± 2.35 (0-7) **G2:** 3.09 ± 2.09 (0-6) Generalized anxiety **G1:** 4.46 ± 2.02 (0-7) **G2:** 5.09 ± 1.44 (0-7) ADIS-P principal anxiety diagnoses (SAP, SOC, GAD, SpP) **G1:** 2.90 ± 0.91 (1-4) **G2:** 2.91 ± 0.95 (1-4)	**Anxiety Disorders Interview schedule for children** Separation **G1:** 1.05 ± 1.90 (0-5) **G2:** 1.87 ± 2.70 (0-7) Social **G1:** 2.40 ± 2.30 (0-5) **G2:** 3.61 ± 2.55 (0-7) Specific phobia **G1:** 1.88 ± 1.80 (0-6) **G2:** 3.65 ± 1.70 (0-6) Generalized anxiety **G1:** 2.55 ± 2.50 (0-6) **G2:** 4.61 ± 1.70 (0-7) ADIS-P principal anxiety diagnoses (SAP, SOC, GAD, SpP) **G1:** 2.25 ± 0.91 (1-4) **G2:** 2.83 ± 0.98 (1-4) **Harms:** NR **Modifiers:** NR

G1: 23 **G2:** 23 **Concomitant therapies, n (%):** Psychiatric medication use - any **G1:** 10 **G2:** 14 SSRI **G1:** 5 **G2:** 7 Atypical antipsychotic **G1:** 4 **G2:** 3 Stimulant **G1:** 5 **G2:** 4 Anticonvulsants **G1:** 1 **G2:** 3 Alpha-blockers **G1:** 1 **G2:** 5 Mood stabilizers **G1:** 0 **G2:** 1 **N at enrollment:** **G1:** 24 **G2:** 26 **N at follow-up:** **G1:** 21 **G2:** 26	**G2:** 24 (92.3) F, n (%) **G1:** 0 **G2:** 2 (7.7) **Race/ethnicity, n (%):** White **G1:** 22 (91.7) **G2:** 20 (76.9) Asian/Pacific Islander **G1:** 0 **G2:** 1 (3.8) African-American **G1:** 1 (4.2) **G2:** 2 (7.7) Multi-racial **G1:** 1 (4.2) **G2:** 3 (11.5) **SES:** Maternal education: Graduated from college, n(%): **G1:** 15 (62.5) **G2:** 15 (57.7) **Diagnostic approach:** In Study/Referral Diagnostic tool/method: **Diagnostic category, n (%):** Autistic disorder **G1:** 16 (67.7) **G2:** 15 (58.9) PDD-NOS

	N for analysis (ITT): **G1:** 24 **G2:** 26	**G1:** 0 **G2:** 3 (11.5) Asperger syndrome **G1:** 8 (33.3) **G2:** 8 (30.8) Other characteristics: **Full scale IQ estimate, mean ± SD (range):** **G1:** 107.08 ± 16.85 (70-139) **G2:** 102.23 ± 17.33 (70-134) **Verbal IQ, mean ± SD (range):** **G1:** 107.00 ± 19.51 (65-133) **G2:** 100.73 ± 18.98 (67-134) **Nonverbal IQ, mean ± SD (range):** **G1:** 109.67 ± 16.38 (75-133) **G2:** 105.04 ± 17.86 (70-134) **# Psychiatric diagnoses other than ASD** **G1:** 1-7 **G2:** 2-8

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Reed et al. 2012[52] **Country:** UK **Intervention setting:** School/home **Enrollment period:** NR **Funding:** NR **Design:** Cohort	**Intervention:** ABA: Followed well-recognized ABA procedures of discrete trial type. Overseen by trained supervisors and conducted by trained tutors in accordance with appropriate intervention manuals. All programs were home-based and mainly 1:1 with mean intensity of 30 hours/wk. Special Nursery Placement: 7 schools in south east England. Children taught in classes of 6-8, under supervision of teacher with postgraduate qualifications and specialist training. Portage: Home based program for preschool children with special ed needs, conducted in three authorities in south-east England. Relatively low-intensity (mean 8.5 hours/week) with majority of work conducted 1:1; supervised by trained portage supervisor with graduate level qualification and followed	**Inclusion criteria:** • between 2 years 6 months and 4 years old • at the start of first intervention • no other teaching interventions • independent diagnosis of autistic disorder or PDD-NOS made by specialist pediatrician according to DSM-IV-TR criteria **Exclusion criteria:** • see above **Age, mean/mos ± SD:** **G1:** 39.0 ± 6.9 **G2:** 41.5 ± 4.0 **G3:** 39.5 ± 6.3 **G4:** 40.2 ± 6.3 **Mental age, mean/yrs (range):** NR **Sex:** **M, n:** **G1:** 13 **G2:** 18 **G3:** 16 **G4:** 12 F, n: **G1:** 1 **G2:** 3	GARS Autism Quotient, mean ± SD **G1:** 91.1 ± 14.4 **G2:** 97.1 ± 9.7 **G3:** 88.9 ± 24.4 **G4:** 99.0 ± 9.7 Psycho-Educational Profile (PEP-R) overall score, mean ± SD **G1:** 55.1 ± 17.3 **G2:** 52.2 ± 17.7 **G3:** 54.0 ± 15.4 **G4:** 51.7 ± 14.5 BAS Cognitive Ability mean ± SD **G1:** 56.1 ± 18.6 **G2:** 57.1 ± 11.8 **G3:** 52.7 ± 10.4 **G4:** 51.5 ± 8.6 VABS composite mean ± SD **G1:** 58.4 ± 10.6 **G2:** 53.3 ± 4.2 **G3:** 56.6 ± 7.0 **G4:** 54.0 ± 4.5	VABS composite change score mean ± SD **G1:** 11.9 ± 7.7 **G2:** 6.8 ± 15.7 **G3:** 2.5 ± 6.1 **G4:** 2.7 ± 8.7 **Adaptive behavior:** VABS change score mean ± SD **G1:** 2.1 ± 4.9 **G2:** 3.8 ± 5.9 **G3:** 0.2 ± 4.9 **G4:** 0.8 ± 5.1 **Educational/ cognitive/ academic attainment:** PEP-R change score mean ± SD **G1:** 14.5 ± 16.0 **G2:** 10.4 ± 28.5 **G3:** 0.6 ± 11.1 **G4:** 3.2 ± 16.4 BAS change score mean ± SD **G1:** 18.8 ± 13.6 **G2:** 6.6 ± 18.0 **G3:** 7.3 ± 8.2 **G4:** 4.2 ± 7.3 **Harms:** NR **Modifiers** Autism severity- for special nursery, portage

	a written manual. Local authority: Home based program for pre-school children. Begins with intensive 5 day training class for parents. Home based supervision and support sessions delivered by educational psychologist up to 4 sessions/wk. These are 1:1 teaching sessions based on discrete trials and reinforcement, conducted by trained teaching assistants. **Assessments:** Gilliam Autism Rating Scale (GARS), Psycho-Educational Profile (PEP-R), British Abilities Scale (BAS II), Vineland Adaptive Behavior Scale (VABS) Conducted by experienced educational psychologist, blinded to group assignment, who completed PEP-R and BAS; assisted parents in completing GARS and VABS. Post intervention measures taken by same person at nine months after initial assessment. **Groups:** **G1:** ABA	**G3:** 2 **G4:** 1 **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** In Study/Referral Diagnostic tool/method: DSM-IV-TR **Diagnostic category, n (%):** NR **Other characteristics**, n (%)**:** Intervention hours mean (range) **G1:** 30.4 (20-40) **G2:** 12.7 (3-23) **G3:** 8.5 (2-15) **G4:** 12.6 (11-22) 1:1 Intervention hours mean **G1:** 28.3 **G2:** 3.1 **G3:** 6.5 **G4:** 12.2 (2.5) Group Intervention hours mean **G1:** 2.1 **G2:** 9.6 **G3:** 2.0 **G4:** 0.5 (0.9) Tutors (family tutors) mean number		and local authority (G2, G3, G4) gains made by children inversely related to autism severity and directly related to time-input. The converse was true for ABA.

	G2: Special Nursery **G3:** Portage **G4:** Local authority **Provider:** See above **Treatment manual followed:** ABA and Potage-yes **Defined protocol followed:** NR **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** Yes – “Receiving no other teaching interventions” **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 14 **G2:** 21 **G3:** 18 **G4:** 13 **N at follow-up:** **G1:** 14 **G2:** 21 **G3:** 18 **G4:** 13	**G1:** 4.4 (1.0) **G2:** 4.0 (1.0) **G3:** 4.0 (2.0) **G4:** 3.1 (1.)	

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Rogers et al. 2012[53, 54] **Country:** US **Intervention setting:** University clinics for parent training **Enrollment period:** NR **Funding:** Autism speaks grants, NIMH, NICHD **Design:** RCT	**Intervention:** Parent delivery - Early Start Denver Model (P-ESDM) 12-week, low-intensity (1-hour/wk of therapist contact), intervention for toddlers at risk for ASD Treatment duration (hours), mean (SD): P-ESDM: 1.48 (1.94) Community treatment as usual: 3.68 (3.91) **Assessments:** Parent acquisition of ESDM intervention skills, developmental gains and core autism symptoms at baseline and 12 weeks later, immediately after the end of parent coaching sessions. Developmental Measures: Mullens Scales of Early Learning (MSEL), MacArthur-Bates Communicative Development Inventory: Words and Gestures (MCDI), VABS-II. Child Moderating variables: Imitation and Orienting to Social, Nonsocial, and Joint Attention Stimuli. Parent measures: General Family	**Inclusion criteria:** • Met risk criteria for ASD on two screeners (Early Screening of Autistic Traits Questionnaire, Infant Toddler Checklist, Modified Checklist for Autism in Toddlers) • Met criteria for ASD in a clinical assessment • Ambulatory (crawling or walking), • Had developmental quotients (DQ) of 35 or higher, • Had English as one language spoken daily in the home **Exclusion criteria:** • Parental self-reported significant mental illness or substance abuse, • Child significant medical conditions including cerebral palsy, gestational age of less than 35 weeks, genetic disorders related to developmental disabilities, • DQ below 35, • Current or previous	**Mean ± SD**: Modified ADOS social affect **G1:**29.45 ± 9.16 **G2:**34.14 ± 8.69 ADOS–Restrictive and Repetitive **G1:** 3.92 ± 2.01 **G2:**4.31 ± 1.92 Mullen DQ **G1:**64.88 ± 17.22 **G2:**63.08 ± 15.93 Mullen Verbal DQ **G1:** 47.78 ± 22.19 **G2:** 44.45 ± 20.37 Mullen Nonverbal DQ **G1:** 80.96 ± 16.68 **G2:** 80.73 ± 15.51 MCDI Part I: Phrases Understood **G1:** 8.22 ± 7.02 **G2**: 9.38 ± 7.95 MCDI Part I: Vocabulary Comprehension **G1:** 64.53 ± 65.73 **G2:** 70.31 ± 78.34 MCDI Part I: Vocabulary Production **G1:** 12.24 ± 35.6 **G2:** 12.44 ± 39.72	**Mean ± SD**: Modified ADOS social affect **G1:** 26.61 ± 10.14 **G2:** 27.33 ± 10.62 ADOS–Restrictive and Repetitive **G1:** 3.96 ± 1.86 **G2:** 3.82 ± 2.04 Mullen DQ **G1:** 69.82 ± 17.9 **G2:** 67.92 ± 17.93 Mullen Verbal DQ **G1:** 56.65 ± 23.65 **G2:** 54.35 ± 21.94 Mullen Nonverbal DQ **G1:** 81.98 ± 14.82 **G2:** 80.57 ± 18.45 MCDI Part I: Phrases Understood **G1:** 12.73 ± 9.11 **G2:** 14.77 ± 8.14 MCDI Part I: Vocabulary Comprehension **G1:** 106.51 ± 96.81 **G2:** 125.72 ± 106.39 MCDI Part I: Vocabulary Production **G1:** 42.27 ± 61.99 **G2:** 38.87 ± 73.71

	Demographic Data, Symptom Checklist-90-R (SCL-90-R), ESDM Parent Fidelity Tool, Child Intervention Hours **Groups:** **G1:** Parent-delivered ESDM **G2:** Community interventions **Provider:** Therapists provided parent training **Treatment manual followed:** Yes **Defined protocol followed:** yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 49 **G2:** 49 **N at follow-up:** **G1:** 49 **G2:** 49	enrollment in intensive 1:1 autism intervention of more than 10 hours per week. **Age, mean ± SD/months (range): 14 to 24 months** **G1:** 21.02 ± 3.51 **G2**: 20.94 ± 3.42 **Mental age, mean/yrs (range):** NR **Sex**, n (%)**:** Male **G1:** 37 (75.5) **G2:** 39 (62.5) **Race/ethnicity, n (%):** White **G1:** 34 (69.4) **G2:** 37 (75.5) **SES, n (%):** Maternal education Less than high school **G1:** 6 (12.8) **G2:** 13 (27.1) Some college **G1:** 10 (21.3) **G2:** 8 (16.7) College **G1:** 17 (36.2) **G2:** 21 (43.8) Some graduate school or graduate school **G1:** 14 (29.8) **G2:** 6 (12.5)	MCDI Part II: Total Gestures **G1:**19.89 ± 10.12 **G2:** 20.33 ± 11.15 VAB II: Communication **G1:**67.66 ± 13.19 **G2:**67.29 ± 11.05 VAB II: Daily Living Skills **G1:** 83.07 ± 12.4 **G2:** 83.21 ± 10.6 VAB II: Socialization **G1:** 76.68 ± 8.74 **G2:** 77.95 ± 8.01 VAB II: Adaptive Behavior Composite **G1:** 76.76 ± 10.3 **G2:** 78.22 ± 8.88 imitative Sequences **G1:** 3.78 ± 3.12 **G2:** 2.53 ± 2.6 Mean Social Orient l **G1:** 0.47± 0.33 **G2:** 0.41± 0.29 Mean Nonsocial Orient **G1:** 0.65 ± 0.3 **G2:** 0.62 ± 0.35 Mean Orient to Joint Attention **G1:** 0.35 ± 0.35 **G2:** 0.28 ± 0.33	MCDI Part II: Total Gestures **G1:** 28.02 ± 12.62 **G2:** 29.79 ± 13.51 VAB II: Communication **G1:** 72.55 ± 12.06 **G2:** 74.29 ± 14.55 VAB II: Daily Living Skills **G1:** 82.25 ± 13.82 **G2:** 84.04 ± 13.5 VAB II: Socialization **G1:** 77.32 ± 9.19 **G2:** 78.67 ± 10.78 VAB II: Adaptive Behavior Composite **G1:** 77.43 ± 9.59 **G2**: 80.33 ± 11.34 Imitative Sequences **G1:** 4.58 ± 3.45 **G2:** 3.76 ± 3.44 Mean Social Orient l **G1:** 0.47± 0.28 **G2:** 0.43± 0.35 Mean Nonsocial Orient **G1:** 0.74± 0.28 **G2:** 0.6 ± 0.37 Mean Orient to Joint Attention **G1:** 0.34± 0.29 **G2:** 0.34± 0.34 **Harms:** NR

	Household income: <50K **G1:** 10 (22.2) **G2:** 15 (32.6) 50K–75K **G1:** 5 (11.1) **G2:** 9 (19.6) 75K–100K **G1:** 15 (33.3) **G2:** 12 (26.1) >100K **G1:** 15 (33.3) **G2:** 10 (21.7) **Diagnostic approach:** In Study Diagnostic tool/method: ADOS-T **Diagnostic category, n (%):** ASD: 100% **Other characteristics, n (%):** NR		**Modifiers:** younger age and more intervention hours positively affect developmental rates (p=0.002), and related to the degree of improvement in children's behavior for most variables

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Strauss et al. 2012[55] **Country:** Italy **Intervention setting:** clinic and home **Enrollment period:** NR **Funding:** NR **Design:** Prospective Cohort Note see related study, Fava 2011[56]	**Intervention:** EIBI – cross-setting, staff and parent mediated. For 12 months, alternated between one week of 25 hours of therapist-led center-based intervention and 3 weeks of an average of 14 hrs/week parent-led home intervention. Comparison (eclectic): parents not actively seeking parental involvement; approximately 12 hours per week of in-home developmental intervention and cognitive behavioral treatment without active parental inclusion in therapy sessions. ** Group assignments not random. Parents were able to choose which group their children were assigned to. **Assessments:** ADOS, Griffith Mental Developmental Scales for ages 2-8 (GMDS-ER 2-8), VABS, MacArthur	**Inclusion criteria:** • diagnosis of autism or PDD-NOS • absence of major medical issues other than autism or mental retardation • completed first 6 months of treatment progress • re-evaluated by child psychiatrist after 6 mos. **Exclusion criteria:** • see above Age, mean/mos ± SD (range): **G1:** 55.67 ±17.63 (26-81) **G2:** 41.94 ± 13.07 (27-69) **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 22 (92) **G2:** 19 (95) F, n (%): **G1:** 2 (8) **G2:** 1 (5) **Race/ethnicity, n (%):** NR	Autism severity, mean ± SD Social interaction **G1:** 10.54 ±2.34 **G2:** 9.63 ± 3.24 Communication **G1:** 6.04 ±1.88 **G2:** 4.94 ± 2.23 ADOS total **G1:** 15.96 ±4.33 **G2:** 14.56 ± 5.05 GMDS-ER GQ **G1:** 55.65 ±20.06 **G2:** 74.29 ± 29.37 Early language skills CDI Comprehension **G1:** 53.83 ±28.81 **G2:** 47.17 ± 27.80 CDI production **G1:** 35.29 ±35.97 **G2:** 19.17 ± 28.12 VABS standard scores Communication **G1:** 71.00 ±39.24 **G2:** 60.78 ± 30.42 Daily living **G1:** 78.43 ±33.39 **G2:** 56.44 ± 23.81 Socialization	Outcomes at 6 months post-treatment initiation: Autism severity, mean ± SD Social interaction **G1:** 8.83 ±2.70 **G2:** 9.00± 2.97 Communication **G1:** 4.38 ±1.34 **G2:** 4.56 ± 1.97 ADOS total **G1:** 13.21 ±3.83 **G2:** 13.56 ± 4.72 **Communication/ language:** Early language skills CDI Comprehension **G1:** 70.33 ±27.04 **G2:** 61.33 ± 32.37 CDI production **G1:** 51.81 ±35.23 **G2:** 33.17 ± 42.27 **Adaptive behavior:** VABS standard scores Communication **G1:** 91.43 ±40.44 **G2:** 83.56 ± 41.32 Daily living **G1:** 100.26 ±35.60 **G2:** 88.33 ± 37.29

	Communication Developmental Inventories (CDI), video coded challenging behaviors (including amount/difficulty of behavior targets), Parental Stress Index-Short Form (PSI-SF) **Groups:** **G1:** EIBI **G2:** eclectic **Provider:** Eclectic: In-home therapists with monthly or no supervision EIBI: Program director led parent trainings; staff therapists provided child treatment in centers **Treatment manual followed:** NR **Defined protocol followed:** NR **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:**	**SES:** NR **Diagnostic approach:** Confirmed In Study Diagnostic tool/method: DSM and ADI-R **Diagnostic category, n (%):** NR	**G1:** 61.96 ±21.31 **G2:** 56.88 ± 19.21 Motor **G1:** 105.78 ±22.38 **G2:** 92.00 ± 19.97 ABC **G1:** 79.29 ±22.84 **G2:** 66.92 ± 19.25	Socialization **G1:** 67.78 ±19.93 **G2:** 70.50 ± 24.04 Motor **G1:** 112.87 ±13.30 **G2:** 106.59 ± 21.63 ABC **G1:** 93.09 ±23.61 **G2:** 84.88 ± 29.03 **Educational/ cognitive/ academic attainment:** GMDS-ER GQ **G1:** 68.75 ±19.58 **G2:** 76.00 ± 26.08 **Harms:** NR **Modifiers** EIBI group: Older children achieved better adaptive behavior outcomes; younger children made more gains in early language comprehension and production. Children who gained more language comprehension had higher adaptive behavior scores pre-treatment. Pre-treatment language comprehension predicted post-treatment language production. Eclectic group: Higher pre-treatment mental

	G1: 24 **G2:** 20 **N at follow-up:** **G1:** NR **G2:** NR	development state and early language skills predicted better outcome on adaptive behaviors. Initial higher adaptive behaviors predicted better post-treatment early language comprehension. In both groups, the predictive power of parental stress on outcome autism severity was modified by perception of difficult child, with higher perceptions of difficulty associated with lower decreases in autism severity. In both groups, child outcomes on early language skills, mental developmental state and adaptive behaviors are significantly influenced by parental stress, child ability to respond correctly to prompts, number and difficulty of treatment targets, and child problem behaviors in sessions.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Fava et al. 2011[56] **Country: Italy** **Intervention setting:** Treatment center and home **Enrollment period:** NR **Funding:** Foundation Vodafone Italy; Anima, Foundation BNL, Federalalberghi, Insurance Consulting Group, Azienda Romana Mercat, Hotel Hilton, Sky, Promusic, Ms. Adelaide Mazzeo, Mr. Mauro Paissan **Design:** Retrospective cohort Note: See related study Strauss 2011[55]	**Intervention:** **G1:** Rotated between 3 weeks of center-based EIBI and parent training (approx. 26 hours per week) followed by 3 weeks of parent-mediated home treatment (approx. 12 hours/week) and a 1-week follow-up in a clinic setting for 1 year **G2:** Eclectic mix of in-home developmental and cognitive behavioral treatment (approx 12 hours/week) **Assessments:** Independent professionals/raters: Autism Diagnostic Observation Schedule; Griffith Mental Development Scales; MacArthur Communication Developmental Inventories; Video ratings of challenging behaviors Parent reports: Vineland Adaptive Behavior Scales; Child Behavior Checklist 1.5-5;; Parenting Stress	**Inclusion criteria:** • Diagnosis of autism or PDD-NOS • Absence of major medical issues other than ASD or mental retardation • Completed 6 month evaluation **Exclusion criteria:** NR **Age, mean/months ± SD:** **G1:** 52.0 ± 19.5 **G2:** 43.7 ± 26.9 **Mental age, mean/yrs (range):** GMDS-ER GQ **G1:** 62.1 (38-103) **G2:** 69.8 (44-87) **Sex, n (%):** **G1 :** M: 10 (83) F: 2 (17) **G2:** M: 9 (90) F: 1 (10) **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:**	**Overall ratings:** **Global Rating of Severity, mean ± SD:** ADOS total: **G1**: 15.6 ± 4.0 **G2**: 12.8 ± 5.0 **Social skills, mean ± SD:** ADOS social interaction: **G1**: 10.0 ± 2.9 **G2**: 8.6 ± 2.7 VABS socialization: **G1**: 69.9 ± 24.5 **G2**: 44.9 ± 14.2 **Communication/ language, mean ± SD:** ADOS communication: **G1**: 5.8 ± 2.1 **G2**: 4.2 ± 2.7 CDI comprehension: **G1**: 48.6 ± 32.5 **G2**: 84.5 ± 4.9 CDI production: **G1**: 33.7 ± 38.6 **G2**: 29.0 ± 7.1 VABS communication: **G1**: 77.3 ± 45.2 **G2**: 49.3 ± 30.6 **Problem behavior, mean ± SD:** Parent session:	**Note: all p-values represent within-group changes vs. baseline over a six month time period. "Not all measures were available for all included children," but specific ns are not provided. **Overall ratings:** **Global Rating of Severity, mean ± SD:** ADOS total: **G1**: 12.3 ± 3.2 p=0.001 **G2**: 12.0 ± 4.5 p=NS **Social skills, mean ± SD:** ADOS social interaction: **G1**: 8.3 ± 2.1 p=0.004 **G2**: 8.1 ± 2.6 p=NS VABS socialization: **G1**: 70.8 ± 24.7 p=NS **G2**: 57.0 ± 15.5 p<0.001 **Communication/ language, mean ± SD:** ADOS communication: **G1**: 4.0 ± 1.3 p=0.011

	Inventory – Short Form Assessments made at baseline and at 6 months **Groups:** **G1**: EIBI **G2**: Eclectic Group assignment based on parental preference **Provider:** Staff and parents **Treatment manual followed:** No **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1**: 12 **G2**: 10 **N at follow-up:** **G1**: 12 **G2**: 10	Referral ("diagnosis …made independently of the study by external neuro-psychiatrists and child psychologists…") Diagnostic tool/method: DSM and ADI-R **Diagnostic category, n (%):** Autism: NR PDD-NOS: NR Aspergers: NR **Other characteristics**, n (%)**:** NR	Aggression: **G1:** 11.7 ± 6.6 **G2:** NR Stereotypes: **G1:** 17.0 ± 5.9 **G2:** NR Dysfunctional: **G1:** 14.5 ± 5.1 **G2:** NR Staff session: Aggression: **G1:** 6.5 ± 4.4 **G2:** NR Stereotypes **G1:** 12.3 ± 5.2 **G2:** NR Dysfunctional **G1:** 10.1 ± 0.8 **G2:** NR **Adaptive behavior, mean ± SD:** VABS ABC: **G1**: 63.3 ± 25.9 **G2**: 44.3 ± 16.4 VABS daily living: **G1**: 74.5 ± 36.3 **G2**: 47.4 ± 16.3 **Commonly occurring co-morbidities, mean ± SD:** CBCL affective problems **G1**: 58.0 ± 7.2 **G2**: 56.8 ± 7.1 CBCL anxiety problems: **G1**: 56.1 ± 6.8 **G2**: 59.6 ± 14.6	**G2**: 3.9 ± 2.2 p=NS CDI comprehension: **G1**: 59.4 ± 32.5 p=0.001 **G2**: 72.6 ± 41.7 p=NS CDI production: **G1**: 48.0 ± 39.7 p=0.049 **G2**: 52.5 ± 28.6 p=NS VABS communication: **G1**: 89.3 ± 48.4 p=0.010 **G2**: 66.0 ± 38.2 p<0.001 **Problem behavior, mean ± SD:** Parent session: Aggression: **G1:** 4.6 ± 3.5 p<0.0001 **G2:** NR Stereotypes: **G1:** 7.8 ± 2.9 p<0.0001 **G2:** NR Dysfunctional: **G1:** 5.9 ± 1.7 p<0.0001 **G2:** NR Staff session: Aggression: **G1:** 3.0 ± 2.2

	CBCL pervasive developmental: **G1**: 69.0 ± 8.9 **G2**: 67.7 ± 9.8 CBCL attention deficit/ hyperactivity: **G1**: 57.1 ± 5.3 **G2**: 57.2 ± 5.8 CBCL oppositional defiant: **G1**: 54.1 ± 5.5 **G2**: 55.3 ± 6.9 **Motor skills, mean ± SD:** VABS motor: **G1**: 99.7 ± 17.9 **G2**: 84.9 ± 14.2 **Educational/ cognitive/ academic attainment:** GMDS-ER GQ: **G1**: 62.1 ± 21.5 **G2**: 69.8 ± 16.6 **Parental quality of life, mean ± SD:** PSI total: **G1**: 92.0 ± 13.1 **G2**: 88.7 ± 2.3 PSI, parental distress **G1**: 29.4 ± 10.4 **G2**: 26.1 ± 10.9 PSI, parent-child difficult interaction: **G1**: 25.9 ± 5.9 **G2**: 26.1 ± 5.9 PSI, difficult child: **G1**: 37.3 ± 8.2	P=0.0003 **G2:** NR Stereotypes **G1:** 6.0 ± 2.7 p<0.0001 **G2:** NR Dysfunctional **G1:** 4.2 ± 1.6 p<0.0001 **G2:** NR **Adaptive behavior, mean ± SD:** VABS ABC: **G1**: 77.4 ± 34.4 p=0.010 **G2**: 65.0 ± 23.0 p=0.006 VABS daily living: **G1**: 101.5 ± 40.8 p<0.001 **G2**: 67.8 ± 17.8 p<0.001 **Commonly occurring co-morbidities, mean ± SD:** CBCL affective problems **G1**: 55.3 ± 6.3 p=NS **G2**: 59.9 ± 8.7 p=NS CBCL anxiety problems: **G1**: 54.6 ± 5.6 p=NS **G2**: 60.2 ± 11.7 p=NS

	G2: 39.3 ± 4.5	CBCL pervasive developmental: **G1**: 66.6 ± 7.6 p=NS **G2**: 68.9 ± 6.7 p=NS CBCL attention deficit/ hyperactivity: **G1**: 53.8 ± 3.6 p=0.030 **G2**: 56.8 ± 8.1 p=NS CBCL oppositional defiant: **G1**: 53.1 ± 3.6 p=NS **G2**: 53.8 ± 5.3 p=NS **Motor skills, mean ± SD:** VABS motor: **G1**: 109.9 ± 14.6 p=0.007 **G2**: 102.8 ± 11.2 p=0.002 **Educational/ cognitive/ academic attainment:** GMDS-ER GQ: **G1**: 76.4 ± 21.6 p=0.005 **G2**: 95.5 ± 9.7 p=NS **Parental quality of life, mean ± SD:** PSI total: **G1**: 94.3 ± 9.7

p=NS
G2: 81.0 ± 12.1
p=0.023

PSI, parental distress:
G1: 31.1 ± 9.5
p=NS
G2: 28.3 ± 19.2
p=NS

PSI, parent-child difficult interaction:
G1: 25.8 ± 5.9
p=NS
G2: 40.1 ± 25.5
p=NS

PSI, difficult child
G1: 37.5 ± 10.8
p=NS
G2: 49.6 ± 28.8
p=NS

Harms: NR

Modifiers: NR

Comments: Paper only provided significance testing results for within-group differences; no between-group differences analyzed or reported

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Thomeer et al. 2012[57] **Country:** US **Intervention setting:** Clinic **Enrollment period:** NR **Funding:** John R. Oishei Foundation **Design:** RCT	**Intervention:** Skillstreaming psychosocial intervention 5 days per week, five 70 minute treatment cycles per day for 5 weeks. Treatment groups were divided by age (7-8 year, 9-10 year, and 11-12 year olds) with 6 children and 3 staff per group. **Assessments:** Adapted Skillstreaming Checklist, Social Responsiveness Scale, BASC-2-PRS and BASC-2 Teacher Rating Scales, Skillstreaming Knowledge Assessment, Diagnostic Analysis of Nonverbal Accuracy-2, Parent, Child and Staff Satisfaction Surveys, Comprehensive Assessment of Spoken Language, WISC-IV, ADI-R **Groups:** **G1:** intervention **G2:** wait-list control **Provider:** Staff were undergraduate and graduate students. **Treatment manual**	**Inclusion criteria:** • prior clinical diagnosis of HFASD • Wechsler Intelligence Scale test for Children-4th edition short form IQ > 70 (and verbal comprehension index or perceptual reasoning index score ≥ 80) • Comprehensive Assessment of Spoken Language short form expressive or receptive language >80 • score meeting ASD criteria on ADI-R **Exclusion criteria:** • IQ a/o language score below minimum • elevated physical aggression **Age, mean/yrs (range):** **G1:** 9.24 ± 1.64 **G2:** 9.39 ± 1.91 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%) **G1:** 14 (82.4)	ASC Total Score, mean ± SD **G1:** 107.29 ± 19.85 **G2:** 102.82 ± 17.65 SRS Total Score **G1:** 83.24 ± 17.27 **G2:** 83.06 ± 12.61 BASC-2 PRS withdrawal **G1:** 72.65 ± 17.34 **G2:** 71.53 ± 16.07 BASC-2 PRS Social Skills **G1:** 36.53 ± 9.00 **G2:** 33.94 ± 4.96 SKA Total **G1:** 33.74 ± 13.00 **G2:** 36.11 ± 14.28 DANVA-2 Child Faces **G1:** 93.79 ± 12.59 **G2:** 94.67 ± 18.76 CASL Idioms **G1:** 9.94 ± 6.02 **G2:** 11.65 ± 7.66	ASC Total Score, mean ± SD **G1:** 118.65 ± 12.82 **G2:** 100.59 ± 21.63 SRS Total Score **G1:** 75.24 ± 13.54 **G2:** 84.29 ± 13.84 BASC-2 PRS **G1:** 69.76 ± 13.86 **G2:** 74.53 ± 14.50 BASC-2 PRS Social Skills **G1:** 40.94 ± 6.04 **G2:** 34.94 ± 7.16 SKA Total **G1:** 50.47 ± 17.58 **G2:** 34.11 ± 13.22 DANVA-2 Child Faces **G1:** 97.94 ± 12.36 **G2:** 94.22 ± 20.75 CASL Idioms **G1:** 12.65 ± 6.22 **G2:** 11.94 ± 7.79 **Harms:** NR **Modifiers:** NR

	followed: Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** Yes **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 17 **G2:** 18 **N at follow-up:** **G1:** NR **G2:** NR	**G2:** 16 (88.9) F, n (%) **G1:** 3 (17.6) **G2:** 2 (11.1) **Race/ethnicity, n (%):** White **G1:** 14 (82.4) **G2:** 14 (77.8) African American **G1:** 1 (5.9) **G2:** 1 (5.6) Hispanic **G1:** 1 (5.9) **G2:** 0 Asian American **G1:** 0 **G2:** 1 (5.6) Other **G1:** 1 (5.9) **G2:** 2 (11.1) **SES:** Parent education, years mean : **G1:** 15.32 ± 2.42 **G2:** 14.69 ± 1.21 **Diagnostic approach:** In Study/Referral **Diagnostic category, n (%):** HFA **G1:** 1 (5.9) **G2:** 0

PDD-NOS
G1: 3 (17.6)
G2: 6 (33.3)

Asperger syndrome
G1: 13 (76.5)
G2: 12 (66.7)

Other characteristics, n (%)**:**
WISC-IV Short form IQ, mean ± SD:
G1: 104.26 ± 14.13
G2: 103.42 ± 13.26

CASL Expressive Language
G1: 101.29 ± 13.90
G2: 99.17 ± 13.54

CASL Receptive Language
G1: 102.88 ± 15.59
G2: 109.44 ± 13.71

ADI-R Social
G1: 19.59 ± 5.50
G2: 16.22 ± 5.66

ADI-R Communication
G1: 14.00 ± 5.61
G2: 13.72 ± 4.87

ADI-R Repetitive Behavior
G1: 6.65 ± 2.06
G2: 6.11 ± 2.17

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Venker et al. 2012[58] **Country:** US **Intervention setting:** Research clinic **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** More than Words (MTW) a parent training intervention that teaches parents how to better understand children's communication and adapt their interactions to support language learning Five parent education sessions (two hours each) and two individual coaching sessions (45 min each) plus a small group component on twice weekly basis led by graduate student **Assessments:** Preschool Language Scale, Mullen Scales of Early Learning, Infant and Toddler forms of MacArthur Communicative Development Inventory (CDI) Pre-treatment and post-treatment (approximately 10 weeks) **Groups:** **G1:** MTW immediate treatment **G2:** delayed treatment **Provider:**	**Inclusion criteria:** • NR (Families recruited from an ongoing longitudinal study of language development in autism) **Exclusion criteria:** NR **Age, mean/mos ± SD (range):** **G1+G2:** 41.14 ± 10.40 (28-68) **Mental age, mean/yrs (range):** NR **Sex:** NR Race/ethnicity, n (%): NR **SES:** NR **Diagnostic approach:** Referral Diagnostic tool/method: Confirmed in study with ADOS or ADI-R **Diagnostic category, n (%):** ASD (100) **Other characteristics, mean ± SD (range):** ADOS severity score **G1+G2**: 8 ± 2.13 (4-10)	Parent Variables, mean ± SD (range): Follow-in commenting **G1:** 53.43 ± 24.35 (14-75) **G2:** 73.86 ± 25.91 (42-125) Linguistic mapping and expansions **G1:** 0.14 ± 0.38 (0-1) **G2:** 0.71 ± 0.76 (0-2) Prompts **G1:** 1.14 ± 1.46 (0-4) **G2:** 3.14 ± 3.29 (0-8) Redirects **G1:** 14.00 ± 8.58 (2-28) **G2:** 12.29 ± 10.00 (3-32) Child Variables, mean ± SD (range): Prompted communication acts **G1:** 0.29 ± 0.49 (0-1) **G2:** 2.00 ± 2.24 (0-6) Spontaneous verbal communication acts **G1:** 1.29 ± 3.40 (0-9) **G2:** 11.71 ± 13.70 (0-34) Spontaneous nonverbal communication acts **G1:** 0.57 ± 0.79 (0-2) **G2:** 0.57 ± 0.53 (0-1)	Parent Variables, mean ± SD (range): Follow-in commenting **G1:** 74.57 ± 33.51 (31-111) **G2:** 73.00 ± 19.04 (47-100) Linguistic mapping and expansions **G1:** 7.57 ± 7.37 (0-21) **G2:** 1.57 ± 1.81 (0-5) Prompts **G1:** 13.43 ± 11.91 (0-32) **G2:** 1.43 ± 2.30 (0-6) Redirects **G1:** 4.29 ± 3.35 (1-10) **G2:** 14.29 ± 15.39 (0-45) Child Variables, mean ± SD (range): Prompted communication acts **G1:** 9.71 ± 14.08 (0-40) **G2:** 1.86 ± 2.67 (0-7) Spontaneous verbal communication acts **G1:** 4.71 ± 6.13 (0-15) **G2:** 12.57 ± 19.81 (0-54) Spontaneous nonverbal communication acts **G1:** 2.43 ± 3.15 (0-9) **G2:** 2.14 ± 2.73 (0-7)

	Hanen certified speech language pathologist **Treatment manual followed:** NR **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 7 **G2:** 7 **N at follow-up:** **G1: 7** **G2: 7**	Preschool language scale-4 Auditory comprehension age equivalent months **G1+G2**: 14.79 ± 7.04 (6-32) Preschool language scale-4 Expressive communication age equivalent months **G1+G2**: 20.21 ± 7.47 (12-41) Communicative Development Inventory (CDI) words understood (infant form**)** **G1+G2**: 181 ± 143.05 (20-396) CDI Words produced infant form **G1+G2**: 108.23 ± 151.00 (0-384) CDI words produced toddler form **G1+G2**: 148.38 ± 223.87 (0-657) Mullen Visual reception age equivalent **G1+G2**: 28.79 ± 13.80 (12-60)		**Proportion of parents and children who improved, n** Follow-in commenting **G1:** 7 **G2:** 4 p=0.037 Linguistic mapping and expansions **G1:** 6 **G2:** 3 p=0.070 Prompts **G1:** 6 **G2:** 1 p=0.007 Redirects **G1: 6** **G2:** 3 p=0.070 Prompted communication acts **G1:** 5 **G2:** 1 p=0.022 Spontaneous verbal communication acts **G1:** 5 **G2:** 3 p=0.172 Spontaneous nonverbal communication acts **G1:** 5 **G2: 3** p=0.172

Group comparisons of parents and child variables, median gain score
Follow-in commenting
G1: 17
G2: 9
p=0.029

Linguistic mapping and expansions
G1: 6
G2: 0
p=0.025

Prompts
G1: 12
G2: -1
p=0.002

Redirects
G1: -7
G2: 1
p=0.004

Prompted communication acts
G1: 4
G2: -1
p=0.007

Spontaneous verbal communication acts
G1: 1
G2: 0
p=0.196

Spontaneous nonverbal communication acts
G1: 1

G2: 0
p=0.320

Harms: NR

Modifiers: NR

Comments: all reported p-values from one-tailed test

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Williams et al. 2012[59] **Country:** Australia **Intervention setting:** home **Enrollment period:** October 2009 to January 2011 **Funding:** Financial Marets Foundation for Children, Australia **Design:** RCT	**Intervention:** *Transporters* DVD has 15 five minute episodes. Watched at home for 15 minutes/day over 4 weeks Control group watched Thomas the Tank DVD-series 5 **Assessments:** WPPSI-III; Socialization Domain of Vineland-II; ADOS; emotion identification and emotion masking tasks; NEPSY-II affect recognition and Theory of Mind (TOM) tasks Baseline, post intervention and three month follow-up. **Groups:** **G1:** intervention DVD **G2:** control DVD **Provider:** Clinician conducted assessments **Treatment manual followed:** NR **Defined protocol followed:** NR **Measure of treatment**	**Inclusion criteria:** • met criteria for diagnosis of autistic disorder based on current assessments including ADOS and case review • age 4-7 at baseline • able to complete WPPSI-III cognitive assessment at baseline or within previous 12 months (cognitively ≥ 30 months) • not previously watched the *Transporters* **Exclusion criteria:** NR **Age, mean/mos ± SD (range):** **G1:** 62.83 ± 11.17 (48.20-84.24 **G2:** 61.93 ± 9.91 (48.10-83.09) **Mental age, mean ± SD (range):** WPPSI FSIQ **G1:** 77.93 ± 13.96 (54-107) **G2:** 74.56 ± 13.59 (42-96) **Sex:** M, %: **G1:** 89.3 **G2:** 85.2	**Identification of emotions, mean ± SD** Total emotions (max score 12) **G1:** 8.12 ± 2.62 **G2:** 7.00 ± 2.32 Happiness (max score 3) **G1:** 2.68 ± 0.56 **G2:** 2.42 ± 0.83 Sadness (max score 3) **G1:** 1.64 ± 1.08 **G2:** 1.17 ± 0.82 Anger (max score 3) **G1:** 1.88 ± 1.09 **G2:** 1.58 ± 1.14 Fear (max score 3) **G1:** 1.92 ± 1.15 **G2:** 1.79 ± 1.06 **Matching of emotions, mean ± SD** Total emotions (max score 16) **G1:** 10.64 ± 4.08 **G2:** 10.63 ± 3.77 Happiness (max score 4) **G1:** 3.21 ± 1.17 **G2:** 3.04 ± 1.22 Sadness (max score 4) **G1:** 2.68 ± 1.31 **G2:** 2.41 ± 1.39	**Time 3 (3 month follow-up)** **Identification of emotions, mean ± SD** Total emotions (max score 12) **G1:** 9.00 ± 2.29 **G2:** 7.36 ± 3.25 Happiness (max score 3) **G1:** 2.88 ± 0.33 **G2:** 2.52 ± 0.96 Sadness (max score 3) **G1:** 1.80 ± 1.08 **G2:** 1.40 ± 1.19 Anger (max score 3) **G1:** 2.12 ± 1.05 **G2:** 1.84 ± 1.07 Fear (max score 3) **G1:** 2.20 ± 0.87 **G2:** 1.64 ± 1.11 **Matching of emotions, mean ± SD** Total emotions (max score 16) **G1:** 11.82 ± 3.66 **G2:** 10.26 ± 4.11 Happiness (max score 4) **G1:** 3.61 ± 0.79 **G2:** 3.30 ± 1.10 Sadness (max score 4)

	fidelity reported: Yes parents completed daily diary recording DVD viewing hours **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 29 **G2:** 31 **N at follow-up:** **G1:** 28 **G2:** 27	**Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** In Study/Referral Diagnostic tool/method: ADOS **Diagnostic category, n (%):** Autism = NR PDD-NOS = NR Aspergers = NR **Other characteristics**, n (%)**:** **ADOS Severity scores, mean ± SD** **G1:** 6.79 ± 1.5 **G2:** 7.56 ± 2.29 WPPSI VIQ, mean ± SD **G1:** 73.61 ± 14.26 (48-93) **G2:** 74.33 ± 14.59 (46-107) WPPSI PIQ, mean ± SD **G1:** 87.89 ± 16.24 (59-122) **G2:** 82.22 ± 15.57 (47-112) DVD hours, mean ± SD **G1:** 11.76 ± 9.16 (3.33-47.12) **G2:** 7.41 ± 3.21 (1.58-14.67) = 0.03	Anger (max score 4) **G1:** 2.00 ± 1.54 **G2:** 2.41 ± 1.34 Fear (max score 4) **G1:** 2.75 ± 1.30 **G2:** 2.74 ± 1.26 **NEPSY-II, mean ± SD** Affect recognition (max score 25) **G1:** 12.33 ± 4.20 **G2:** 12.72 ± 3.53 TOM verbal (max score 15) **G1:** 7.60 ± 3.68 **G2:** 6.28 ± 3.10 TOM contextual (max score 6) **G1:** 3.63 ± 1.67 **G2:** 2.83 ± 1.10 **Mindreading and social skill, mean ± SD** Mindreading situational (max score 6) **G1:** 4.35 ± 1.50 **G2:** 4.55 ± 1.91 Mindreading desire based (max score 6) **G1:** 4.22 ± 1.59 **G2:** 4.00 ± 1.29 **Vineland-II socialization domain**, **mean ± SD** **G1:** 74.22 ± 13.66 **G2:** 71.93 ± 9.94	**G1:** 2.79 ± 1.34 **G2:** 2.48 ± 1.37 Anger (max score 4) **G1:** 2.54 ± 1.23 **G2:** 2.00 ± 1.44 Fear (max score 4) **G1:** 2.89 ± 1.17 **G2:** 2.48 ± 1.25 **NEPSY-II, mean ± SD** Affect recognition (max score 25) **G1:** 16.00 ± 4.66 **G2:** 13.17 ± 3.43 TOM verbal (max score 15) **G1:** 9.67 ± 3.27 **G2:** 6.94 ± 3.40 TOM contextual (max score 6) **G1:** 3.70 ± 1.49 **G2:** 3.80 ± 1.40 **Mindreading and social skill, mean ± SD** Mindreading situational (max score 6) **G1:** 5.05 ± 0.91 **G2:** 4.50 ± 1.61 Mindreading desire based (max score 6) **G1:** 4.32 ± 1.46 **G2:** 4.42 ± 1.54 **Vineland-II socialization domain**,

	SIQ , % < 69 **G1:** 25.0 **G2:** 33.3 70-79 **G1:** 32.1 **G2:** 33.3 ‘> 79 **G1:** 42.9 **G2:** 33.3	**mean ± SD** **G1:** 76.35 ± 13.11 **G2:** 73.52 ± 9.80 **Harms:** NR **Modifiers:** NR **Predictors** Age and VIQ were predictors for outcome measures

Comments: Attrition problems due to challenging behaviors interfering with intervention adherence

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Young et al. 2012[60] **Country:** Australia **Intervention setting:** Home **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** *The Transporters* DVD children's animated series designed to enhance emotion recognition and social understanding Control group watched *Thomas the Tank Engine* DVD. Both groups received user guides. Participants were asked to watch at least 3 episodes per day for 3 weeks. Parents kept log books. **Assessments:** Wechsler Scales (WPPSI-III or WISC-IV subtests) to measure non-verbal and general language abilities; Affect Recognition subset of NEPSY-II and the Faces Task; Parent SCQ **Groups:** **G1:** *The Transporters* DVD **G2:** Thomas the Tank DVD **Provider:** Parent/Caregiver **Treatment manual followed:** NR	**Inclusion criteria:** • children between 4 and 8 years old • met DSM-IV criteria for PDD • minimum score of 11 on Social Communication Questionnaire (SCQ) **Exclusion criteria:** NR **Age, mean/yrs (range):** **G1 + G2:** (4-8) **Mental age, mean/yrs (range):** NR **Sex:** NR Race/ethnicity, n (%): NR **SES:** NR **Diagnostic approach:** In Study/Referral Diagnostic tool/method: DSM-IV **Diagnostic category, n (%):** Autism =NR PDD-NOS =NR Aspergers =NR	NEPSY-II affect recognition, mean ± SD: **G1:** 6.15 ± 3.26 **G2:** 6.75 ± 3.62 Faces task, mean ± SD: **G1:** 10.62 ± 3.64 **G2:** 8.58 ± 3.92 Social behavior, mean ± SD Social peer interest **G1:** 3.15 ± 1.21 **G2:** 2.50 ± 0.81 Eye Contact **G1:** 2.92 ± 1.10 **G2:** 2.83 ± 1.03 Gaze Aversion **G1:** 3.00 ± 1.00 **G2:** 3.08 ± 1.24 Stereotyped behavior **G1:** 2.15 ± 1.07 **G2:** 2.58 ± 1.16	**Social skills** NEPSY-II affect recognition, mean ± SD: **G1:** 12.00 ± 3.71 **G2:** 6.42 ± 3.23 Faces task, mean ± SD: **G1:** 14.08 ± 3.59 **G2:** 9.33 ± 4.05 Social behavior, mean ± SD Social peer interest **G1:** 3.31 ± 1.18 **G2:** 2.92 ± 1.10 Eye Contact **G1:** 3.46 ± 0.78 **G2:** 3.42 ± 1.08 Gaze Aversion **G1:** 3.00 ± 1.21 **G2:** 2.85 ± 0.80 Stereotyped behavior **G1:** 2.15 ± 1.07 **G2:** 2.50 ± 1.09 **Harms:** NR **Modifiers:** NR

	Defined protocol followed: No **Measure of treatment fidelity reported:** No **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 13 **G2:** 12 **N at follow-up:** **G1:** 13 **G2:** 12	**Other characteristics**, n (%)**:** Autism severity scale, mean ± SD: **G1:** 18.38 ± 5.59 **G2:** 18.08 ± 4.81 Block Design, mean ± SD: **G1:** 11.31 ± 4.17 **G2:** 8.67 ± 4.05 Comprehension, mean ± SD: **G1:** 7.08 ± 5.06 **G2:** 3.67 ± 3.87 Vocabulary, mean ± SD: **G1:** 9.62 ± 4.39 **G2:** 7.83 ± 2.92

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Begeer et al., 2011[61] **Country:** Netherlands **Intervention setting:** Academic center **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** Theory of Mind training, including 16 weekly sessions of 1.5 hrs each, with parent involvement in last 15 minutes of each session **Assessments:** standardized child interviews and assessments, parent report **Groups:** **G1:** Theory of Mind intervention **G2:** wait list controls **Provider:** Certified therapists **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** No **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR	**Inclusion criteria:** • clinical diagnosis within the autism spectrum • IQ scores within the normal range ($\geq$ 70) • age 8-13 years old **Exclusion criteria:** • see inclusion criteria **Age, mean/yrs;months ± SD (range):** **G1:** 10;3 ± 1;3 (8;5 – 13;7) **G2:** 10;3 ± 1;1 (8;3 – 12;7) **Mental age, mean ± SD (range):** Full-scale IQ: **G1:** 100.1 ± 15.3 (79 - 133) **G2:** 103.3 ± 12.9 (82 – 126) Verbal IQ: **G1:** 101.3 ± 16.2 (68 – 123) **G2:** 109.1 ± 11.1 (89 – 130) Nonverbal IQ: **G1:** 98.4 ± 16.8 (73 – 132) **G2:** 96.6 ± 17.9 (67 – 125) **Sex:** M, n (%): **G1:** 18 (94.7) **G2:** 15 (88.2)	**Social skills, mean ± SD:** Theory of Mind total score: **G1:** 50.89 ± 5.31 **G2:** 54.00 ± 5.93 Theory of Mind precursors: **G1:** 18.05 ± 1.51 **G2:** 17.94 ± 1.89 Elementary Theory of Mind: **G1:** 25.10 ± 3.30 **G2:** 27.59 ± 3.12 Advanced Theory of Mind scale: **G1:** 7.44 ± 1.00 **G2:** 8.47 ± 1.91 LEAS-C total: **G1:** 32.89 ± 8.64 **G2:** 31.53 ± 5.95 LEAS-C mixed emotions: **G1:** 1.83 ± 1.72 **G2:** 2.94 ± 3.11 LEAS-C complex emotions: **G1:** 1.89 ± 2.87 **G2:** 4.52 ± 4.45 Self-reported empathy: **G1:** 3.95 ± 2.07 **G2:** 4.65 ± 2.18 CSBQ:	**Social skills, mean ± SD:** Theory of Mind total score: **G1:** 58.21 ± 4.00 **G2:** 58.00 ± 5.78 p=0.03 Theory of Mind precursors: **G1:** 19.37 ± 1.38 **G2:** 19.05 ± 1.71 p=NS Elementary Theory of Mind: **G1:** 29.84 ± 2.36 **G2:** 29.24 ± 3.70 p=0.005 Advanced Theory of Mind scale: **G1:** 9.00 ± 2.11 **G2:** 9.71 ± 1.45 p=NS LEAS-C total: **G1:** 37.72 ± 10.73 **G2:** 33.47 ± 6.40 p=NS LEAS-C mixed emotions: **G1:** 4.72 ± 5.40 **G2:** 2.24 ± 3.19 p=0.02 LEAS-C complex

	N at enrollment: **G1:** 20 **G2:** 20 **N at follow-up:** **G1:** 19 **G2:** 17	F, n (%): **G1:** 1 (5.3) **G2:** 2 (11.8) **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** In Study Diagnostic tool/method: DSM-IV-TR, SRS and/or ASQ **Diagnostic category, n (%):** Autism **G1:** 2 **G2:** 0 PDD-NOS **G1:** 14 **G2:** 10 Aspergers **G1:** 3 **G2:** 7 **Other characteristics**, n (%)**:** Autism quotient score, mean ± SD: **G1:** 125.7 ± 19.4 **G2:** 138.9 ± 19.8 Social responsiveness scale, mean ± SD: **G1:** 74.9 ± 21.6 **G2:** 80.2 ± 22.54	**G1:** 36.67 ± 14.76 **G2:** 42.94 ± 13.77 **Commonly occurring co-morbidities** ADHD: **G1:** 4 **G2:** 3 Learning disorder: **G1:** 1 **G2:** 0	emotions: **G1:** 4.16 ± 4.40 **G2:** 1.71 ± 3.06 p=0.001 Self-reported empathy: **G1:** 4.00 ± 2.62 **G2:** 4.41 ± 2.11 p=NS CSBQ: **G1:** 34.80 ± 17.60 **G2:** 40.00 ± 14.54 p=NS **Harms:** NR **Modifiers** PDD-NOS group performed similar to the overall analysis, including treatment effects on total Theory of Mind score (p<0.05), elementary Theory of Mind tasks (p<0.05), understanding of mixed emotions and complex emotions (both p<0.05). The high-functioning autism/Asperger group only showed improvement on understanding of complex emotions (p<0.01). No effect of ASD diagnostic group on self-reported empathy or parent reported social skills.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Carter et al. 2011[62] **Country:** US **Intervention setting:** Clinic and home **Enrollment period:** NR **Funding:** Autism Speaks and Marino Autism Research Institute **Design:** RCT conducted at 3 sites	**Intervention:** Hanen's "More than Words" (MTW) over 3.5 months; 8 group sessions with parents only and 3 in-home individualized parent –child sessions Time 2: 5 months (m = 5.3, sd = .47) Time 3: 9 months (m = 9.3, sd = .56) **Assessments:** Screening Tool for Autism in Two year olds (STAT), Mullen Scales of Early Learning (MSEL), Vineland Adaptive Behavior Scales – Second Edition (VABS), Autism Diagnostic Observatoin Schedule (ADOS), Parent Interview Autism-Clinical Version, Early Social Communication Scales, Parent Child Free Play procedure, Parent Interview for Autism – Clinical Version, Developmental Play Assessment, questionnaires assessing parent treatment satisfaction **Groups:**	**Inclusion criteria:** e below **Exclusion criteria:** • child > 24 months • genetic disorder failed to obtain predetermined "at risk" score on STAT and/or did not meet symptom criteria for ASD based on expert clinical impression • Fragile X diagnosis Age, mean/months ± SD (range): **G1:** 21.11 ± 2.71 **G2:** 21.51 ± 2.82 **Mental age, mean/yrs (range):** NR **Sex:** M, 51 (82%) F, 11 (18%) **Race/ethnicity, (%):** White (47.4) Asian /White (5.3) Hispanic or Latino (38.6) Black (3.5) American Indian/Alaskan Native/White (3.5) American Indian/Alaskan Native /Hispanic (1.8)	Mullen Expressive Language Age (mos), mean ± SD **G1:** 8.22 ± 6.01 **G2:** 7.33 ± 3.71 Mullen Receptive Language Age (mos), mean ± SD **G1:** 8.41 ± 5.42 **G2:** 8.17 ± 4.44 Vineland Socialization SS, mean ± SD **G1:** 73.95 ± 6.46 **G2:** 72.42 ± 6.59 Vineland Communication SS, mean ± SD **G1:** 66.61 ± 12.87 **G2:** 63.21 ± 9.13 Parent-Child Free Play (PCFP) proportion of codable intervals with parental responsivity, mean ± SD **G1:** 0.32 ± 0.06 **G2:** 0.29 ± 0.08 ESCS initiating joint attention, mean ± SD **G1:** 5.90 ± 5.41 **G2:** 5.59 ± 6.14 ESCS initiating behavior requests, mean ± SD	**Social skills:** Vineland Socialization SS, mean ± SD **G1:** 71.42 ± 7.07 **G2:** 70.70 ± 6.89 PCFP proportion of codable intervals with parental responsivity, mean ± SD **G1:** 0.34 ± 0.07 **G2:** 0.30 ± 0.10 T1 to T3 residualized gain scores, mean ± SD Effect size (95% CI) **G1:** 0.03 ± 0.08 **G2:** -0.02 ± 0.10 0.50 (-0.18, 1.18) **Communication/ language:** ADOS Social-Communication Total **G1:** 15.56 ± 4.56 **G2:** 13.60 ± 4.89 Mullen Expressive Language Age (mos), mean ± SD **G1:** 16.20 ± 7.23 **G2:** 16.68 ± 7.88 Mullen Receptive Language Age (mos), mean ± SD **G1:** 15.52 ± 6.93

	G1: intervention (MTW) **G2:** control (“business as usual”) **Provider:** Speech/language pathologist and parent **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** No **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 32 **G2:** 30 **N at follow-up:** **G1:** 29 **G2:** 26	**SES:** Maternal education, (%): High school (16) Some college, an associate’s degree or vocational/trade degree (33) College degree (35 Advanced degree (16) Household income, mean (range): **Diagnostic approach:** Referral Diagnostic tool/method: ADOS and DSM-IV-based clinical impressions of a clinical psychologist familiar with ASD in early childhood **Diagnostic category, n (%):** Autism 46/50 (92%) at Time 3 PDD-NOS - NR Aspergers - NR **Other characteristics**, n (%)**:** NR	**G1:** 11.87 ± 10.09 **G2:** 9.00 ± 6.22 PCFP weighted frequency of intentional communication, mean ± SD **G1:** 5.55 ± 6.29 **G2:** 8.20 ± 12.63 PIA-CV nonverbal communication, mean ± SD **G1:** 2.30 ± 0.64 **G2:** 2.28 ± 0.73	**G2:** 17.48 ± 8.33 Vineland Communication SS, mean ± SD **G1:** 76.14 ± 13.85 **G2:** 76.43 ± 14.05 ESCS initiating joint attention, mean ± SD **G1:** 10.33 ± 9.82 **G2:** 8.68 ± 9.26 T1 to T3 residualized gain scores, mean ± SD Effect size (95% CI) **G1:** 0.06 ± 1.21 **G2:** -0.06 ± 1.01 0.12 (-0.46, 0.70) ESCS initiating behavior requests, mean ± SD **G1:** 16.50 ± 14.33 **G2:** 15.48 ± 13.20 T1 to T3 residualized gain scores, mean ± SD Effect size (95% CI) **G1:** 0.03 ± 0.34 **G2:** -0.03 ± 0.37 0.16 (-0.42, 0.74) PCFP weighted frequency of intentional communication, mean ± SD **G1:** 18.91 ± 20.50 **G2:** 20.75 ± 21.14 T1 to T3 residualized gain scores, mean ± SD Effect size (95% CI) **G1:** 0.18 ± 1.69

G2: -0.16 ± 2.21
0.15 (-0.57, 0.88)

PIA-CV nonverbal communication, mean ± SD
G1: 2.89 ± 0.67
G2: 2.92 ± 0.65

T1 to T3 residualized gain scores, mean ± SD
Effect size (95% CI)
G1: -0.05 ± 0.63
G2: 0.06 ± 0.58
-0.19 (-0.81, 0.43)

Adaptive behavior:
Vineland Daily Living SS:
G1: 77.84 ± 7.07
G2: 72.95 ± 10.11

Motor skills:
Mullen Fine Motor Age (mos):
G1: 22.00 ± 3.50
G2: 21.92 ± 4.09

Vineland Motor SS:
G1: 83.16 ± 7.36
G2: 81.55 ± 9.26

Educational/ cognitive/ academic attainment:
Mullen Visual Reception Age (mos)
G1: 22.42 ± 5.75
G2: 21.64 ± 6.53

Mullen Early Learning Composite:
G1: 62.88 ± 18.41

G2: 64.88 ± 13.94

Harms: NR

Modifiers
Treatment effects on child communication games to Time 3 were moderated by children's Time 1 object interest. Children with lower levels of T1 object interest (playing with fewer than 3 toys) had greater facilitated growth in communication; higher levels of object interest (playing with more than 5 or 6 toys) led to growth attenuation

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Castorina et al., 2011 [63] **Country:** Australia **Intervention setting:** Clinic **Enrollment period:** NR **Funding:** NR **Design:** Partially randomized (first 15 participants randomly assigned to one of 3 groups; later recruits assigned based on whether they had an older sibling; if no sibling, randomly assigned to "no sibling" training or wait-list control group)	**Intervention:** Social skills training, adapted from training package by Spence (1995), 8 weekly 2-hour sessions **Assessments:** observed/standardized assessment by study staff; parent report; teacher report **Groups:** **G1:** social skills training with older sibling (no more than 4 years older than subject) **G2:** social skills training alone **G3:** wait-list control **Provider:** Co-therapists (Master of Psychology students) supervised by a clinical psychologist **Treatment manual followed:** NR **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** No	**Inclusion criteria:** • boys between ages of 8 and 12 years • diagnosis of Asperger syndrome **Exclusion criteria:** • female **Sex** • age younger than 9 or older than 12 **Age, mean/yrs ± SD:** 10.30 ± 1.15 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): 21 (100) F, n (%): 0 **Race/ethnicity, n (%):** White Asian **SES:** Maternal education, n (%): High school College NR Household income, mean (range): NR **Diagnostic approach:** In Study and Referral:	**Social skills:** SSRS-parents (general social skills), mean ± SD: Pre-test, mean ± SE **G1:** NR **G2:** NR **G3:** NR Overall: 33.50 ± 2.16 SSRS-teachers (general social skills), mean ± SD: NR CASP Cues (Social competence), mean ± SD: Pre-test (p=.52) **G1:** 14.00 ± 8.33 **G2:** 15.50 ± 7.69 **G3:** 10.67 ± 7.26 CASP Emotions, mean ± SD: Pre-test, mean ± SE **G1:** NR **G2:** NR **G3:** NR **Overall:** 16.15 ± 1.40	**Social skills:** SSRS-parents (general social skills), mean ± SD: Post-test, mean ± SE **G1:** NR **G2:** NR **G3:** NR **Overall:** 35.96 ± 2.32 3-month follow-up, mean ± SE **G1:** NR **G2:** NR **G3:** NR **Overall:** 40.49 ± 1.34 SSRS-teachers (general social skills), mean ± SD: Post-test NR 3-month follow-up: NR CASP Cues (Social competence), mean ± SD: Post-test **G1:** 38.00 ± 12.46 **G2:** 37.50 ± 6.59 **G3:** 15.33 ± 7.47 Between groups: p<0.001 G1+G2 vs. G3: p<0.001 3-month follow-up: **G1:** 34.43 ± 9.78 **G2:** 38.88 ± 10.56 **G3:** 13.17 ± 8.38 Between groups: p<0.001

	Co-interventions held stable during treatment: NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 7 **G2:** 8 **G3:** 6 **N at follow-up:** **G1:** 7 **G2:** 8 **G3:** 6	Referral (previous diagnosis of Asperger syndrome by a specialist diagnostic team) In study (parent questionnaire and cross-referencing tool) Diagnostic tool/method: Autism Spectrum Screening Questionnaire (ASSQ), by semi-structured interview of parents; Australian Scale for Aspberger's Syndrome (ASAS), for cross-referencing, by semi-structured interview of parents **Diagnostic category, n (%):** Autism: 0 PDD-NOS : 0 Aspergers: 21 (100) **Other characteristics**, n (%)**:** Attending mainstream primary school: 21 (100)		**G1 vs. G3:** p=0.003 **G2 vs. G3:** p<0.001 **G1 vs. G2:** p=NS CASP Emotions, mean ± SD: Post-test, mean ± SE **G1:** NR **G2:** NR **G3:** NR **Overall:** 20.84 ± 1.4 Between groups over time: p=NS G1 and G2 vs. baseline: p<0.001 G3 vs. baseline: p=NS 3-month follow-up, mean ± SE **G1:** NR **G2:** NR **G3:** NR **Overall:** 21.32 ± 1.53 **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: DeRosier et al. 2011[64] **Country:** US **Intervention setting**: Private, community based practice **Enrollment period:** NR **Funding:** NIMH **Design:** RCT	**Intervention:**Social skills intervention, Social Skills GRoup INtervention-High Functioning Autism (S.S.GRIN-HFA) Fifteen 60-minute group social skills sessions during consecutive weeks. Parents attended and participated in four of the sessions (1, 5, 10, and 15) with their child. Children in the traditional S.S.GRIN condition participated in ten 60-min group sessions during consecutive weeks **Assessments:** Parents completed: Demographic questionnaire, Social Responsiveness Scale (SRS), Achieved Learning Questionnaire (ALQ). Child completed Social Dissatisfaction Questionnaire. Parent and Child completed Social Self-efficacy. Completed 2 weeks before intervention and within two weeks after treatment. **Groups:**	**Inclusion criteria:** • between ages of 8 and 12 years • prior diagnosis of high functioning autism, Asperger's Disorder, or Pervasive Developmental Disorder-NOS (by parent report) • IQ ≥ 85 **Exclusion criteria:** • children with CBCL • Aggressive scale T score > 70 **Age, mean ± SD yrs (range): (**8-12 years) **G1:** 10.2 ± 1.3 **G2:** 9.9 ± 1.1 **Mental age, mean/yrs (range):** IQ ≥ 85 **Sex:** Male, % **G1:** 96.3 **G2:** 100 **G1+G2:** 98.2 **Race/ethnicity, %:** White **G1:** 89 **G2:** 96 Asian **G1:** 7	**Mean ± SD:** Parent report: SRS total score **G1:** 70.4 ± 6.1 **G2:** 68.0 ± 5.7 Awareness **G1:** 70.1 ± 7.2 **G2:** 69.5 ± 7.4 Cognition: **G1:** 70.9 ± 6.9) **G2:** 69.7 ± 7.6 Communication: **G1:** 69.6 ± 6.6 **G2:** 66.0 ± 5.1 p<0.05 Motivation: **G1:** 65.4 ± 7.0 **G2:** 64.6 ± 10.1 Mannerisms: **G1:** 61.0 ± 8.2 **G2:** 58.7 ± 9.7 Self-efficacy: **G1:** 2.6 ± 0.7 **G2:** 2.8 ± 0.7 ALQ: **G1:** 1.2 ± 0.3 **G2:** 1.4 ± 0.4 Child report: Self-efficacy:	**Effect size: Standardized change scores over time** Parent report: SRS, mean ± SD, Effect size (Cohen's d) Awareness **G1:** -0.33 ± 1.17 **G2:** 0.38 ± 0.86 ES=-.69 p< 0.05 Cognition: **G1:** -0.13 ± 1.22 **G2:** 0.24 ± 0.97 ES= NS p= NS Communication: **G1:** -0.38 ± 1.07 **G2:** 0.50 ± 0.78 ES=-0.94 p< 0.01 Motivation: **G1:** -0.22 ± 0.77 **G2:** 0.31 ± 0 .82 ES= -0.67 p< 0.05 Mannerisms: **G1:** -0.35 ± 1.18 **G2:** 0.35 ± 0.86 ES= -0.68 p< 0.05

	G1: S.S.GRIN-HFA **G2:** Traditional S.S.GRIN-control **Provider:** Trained group leaders with experience conducting social skills groups with children **Treatment manual followed:** yes **Defined protocol followed:** yes **Measure of treatment fidelity reported**: yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 27 **G2:** 28 **N at follow-up:** **G1:** 27 **G2:** 28	**G2:** 0 African American **G1:** 0 **G2:** 4 American Indian **G1:** 4 **G2:** 0 **SES:** Maternal education College degree or greater, % **G1:** 66.7 **G2:** 88.5 **G1+G2:** 78.2 Household income, % $25,001-$50,000 **G1:** 22.2 **G2:** 10.7 **G1+G2:** 16.4 $50,001-$75,000 **G1:** 18.5 **G2:** 10.7 **G1+G2:** 14.5 $75,001-$100,000 **G1:** 22.2 **G2:** 35.7 **G1+G2:** 29.1 >$100,00 **G1:** 37 **G2:**: 42.9 **G1+G2:** 40 **Diagnostic approach:** Referral **Diagnostic tool/method:**	**G1:** 2.8 ± 0.6 **G2:** 2.5 ± 0.8 Social Dissatisfaction: **G1:** 54.6 ± 10.3 **G2:** 55.0 ± 11.2	ALQ: **G1:** 0.33 ±(.86) **G2:** -0.31 ±(.84) ES= 0.75 p< 0.05 Self-efficacy: **G1:** 0.28 ±(1.06) **G2:** -0.25 ±(1.01) ES = 0.51 Child report Self-efficacy: **G1:** -0.05 ± 1.06 **G2:** 0.08 ± 1.00 ES = NS p= NS Social dissatisfaction: **G1:** 0.08 ± 1.23 **G2:** -0.07 ± 0.79 ES= NS p= NS **Harms:** NR **Modifiers:** NR

	SCQ, ASSQ, CAST **Diagnostic category, %:** Autism-high functioning: 42 PDD-NOS: 16 Asperger syndrome: 38 **Other characteristics**, n (%)**:** NR	

Comments: Three children in G1 dropped out of study and were excluded from analysis. Two parents in G2 were excluded from parent report analysis (mother filled out pre-assessments and father completed post-assessments).

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Drahota et al. 2011[65] **Country:** US **Intervention setting:** clinic **Enrollment period:** NR **Funding:** NIMH, Cure Autism Now Foundation, UCLA Center for Autism Research and Training **Design:** RCT Note: See earlier studies reporting on this population[66, 67] in 2011 AHRQ review[9]	**Intervention:** Cognitive behavioral therapy, 16 weekly sessions, 90 min (30 with child and 60 with parents) implementing the Building Confidence CBT program modified for use with children with ASD **Assessments:** ADIS-C/P Clinical Severity Rating scale, VABS, Parent Child Interaction Questionnaire (PCIQ); Assessments at baseline and at final day or treatment or within one week; for control group post assessments were completed after 3 months **Groups:** **G1:** intervention **G2:** waitlist **Provider:** Therapists 11 doctoral students in clinical or educational psychology and 2 doctoral level psychologists **Treatment manual followed:** Yes **Defined protocol followed:** NR	**Inclusion criteria:** • met research criteria for diagnosis of autism, Asperger syndrome or PDD-NOS • met research criteria for one of the following: separation anxiety disorder, social phobia or obsessive compulsive disorder • not taking any psychiatric medicine at baseline assessment or were taking a stable dose of psychiatric medicine (at least one month of same dosage prior to baseline) • if medication was being used, maintained same dosage during study **Exclusion criteria:** • verbal IQ < 70 (assessed in previous testing, or questions noted by independent examiner at baseline, on basis of Wechsler Intelligence Scale for Children IV • currently in psychotherapy or	VABS- total daily living skills, mean ± SD **G1:** 93.47 ± 29.91 **G2:** 97.43 ± 23.91 Mean standard score **G1:** 50.06 **G2:** 55.61 Mean age equivalency **G1:** 5.2 years **G2:** 5.4 years VABS- personal daily living skills, mean ± SD **G1:** 55.54 ± 10.85 **G2:** 57.49 ± 9.27 Mean age equivalency **G1:** 4.1 years **G2:** 4.5 years PCIQ-parental involvement Mean raw score ± SD **G1:** 13.53 ± 3.78 **G2:** 14.30 ± 3.78	**Post-treatment** VABS- total daily living skills, mean ± SE **G1:** 109.63 ± 4.07 **G2:** 98.80 ± 3.50 Mean standard score **G1:** 60.24 **G2:** 55.62 Mean age equivalency **G1:** 6.0 years **G2:** 5.7 years VABS- personal daily living skills, mean ± SE **G1:** 62.81 ± 1.54 **G2:** 58.30 ± 1.32 Mean age equivalency **G1:** 5.0 years **G2:** 4.6 years PCIQ-parental involvement Mean raw score ± SE **G1:** 11.93 ± 0.55 **G2:** 13.53 ± 0.48 **3-month follow-up (n=10 families in G1 only)** VABS- total daily living skills, mean ± SD **G1:** 114.24 ± 25.66 Mean standard score

	Measure of treatment fidelity reported: NR **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 17 **G2:** 23 **N at follow-up:** **G1:** 14 (82) **G2:** 22 (96)	social skills training or receiving behavioral interventions such as applied behavioral analysis • family currently in family therapy or parenting class • child began taking psychiatric medication or changed dosage during the intervention • child or parents appeared unable to participate in intervention program **Age, mean/yrs (range):** **G1:** 9.18 ± 1.42 **G2:** 9.22 ± 1.57 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 12 (71) **G2:** 15 (65) **Race/ethnicity, n (%):** White **G1:** 8 (47) **G2:** 11 (48) Latino/Latina **G1:** 2 (12) **G2:** 3 (13) Asian **G1:** 4 (23)	**G1:** 70.00 Mean age equivalency **G1:** 6.7 years VABS- personal daily living skills, mean ± SD **G1:** 63.65 ± 9.33 Mean age equivalency **G1:** 5.2 years PCIQ-parental involvement Mean raw score ± SD **G1:** 10.89 ± 2.93 **Harms:** NR **Modifiers:** NR

G2: 2 (9)

African American
G1: 0
G2: 1 (4)

Multiracial/other
G1: 3 (18)
G2: 6 (26)

SES:
Parental education, n (%):
Graduated College
G1: 12 (71)
G2: 13 (60)

Household income, (n=37):
< $40,000
G1+G2: 9 (24.3)

$40,001-$90,000
G1+G2: 10 (27.1)

Over $90,000
G1+G2: 18 (48.6)

Diagnostic approach:
Referral

Diagnostic tool/method:

Diagnostic category, n (%):
Autistic disorder
G1: 9 (53)
G2: 11 (48)

PDD-NOS
G1: 6 (35)
G2: 11 (48)
Asperger syndrome

	G1: 2 (12) **G2:** 1 (4) **Other characteristics**, n (%)**:** NR	

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Zachor and Itzchak, 2010 [68, 69] **Country:** Israel **Intervention setting:** Preschool **Enrollment period:** NR **Funding:** Private support (Mr. Dov Moran) **Design:** Prospective cohort	**Intervention:** Applied Behavioral Analysis (ABA) or eclectic (integration of several intervention approaches) interventions implemented in autism-specific preschool settings; 8 hours per day for 1 year **Assessments:** parent; clinician **Groups:** **G1:** ABA **G2:** eclectic **Provider:** **G1:** Program supervisors, trained therapists, speech and language pathology, occupational therapy and special education preschool teachers, and parents (for home treatment) **G2:** Clinical psychologist, special education preschool teacher, speech and language pathology, occupational therapy, cognitive trainer, music therapist, and teacher's aids. **Treatment manual followed:** NR	**Inclusion criteria:** • clinical diagnosis of autism based on DSM-IV criteria and cut-off points on the ADI-R • age 15-35 months **Exclusion criteria:** • additional major medical diagnoses • incomplete post-intervention assessments **Age, mean/months ± SD (range):** **G1:** 25.1 ± 3.9 (17-35) **G2:** 26.0 ± 4.6 (15-33) **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): 71 (91) F, n (%): 7 (8) **Race/ethnicity, n (%):** NR **SES:** Maternal education, years ± SD (range): **G1:** 14.3 ± 2.2 (11-20) **G2:** 15 ± 2.7 (11-22) Paternal education, years ±	**Overall ratings:** **Global Rating of Severity, mean ± SD (range):** ADOS new algorithm **G1:** 20.9 ± 4.3 (10-26) **G2:** 20.1 ± 4.6 (10-26) **G1+G2**: 20.5 ± 4.4 ADOS severity score **G1+G2**: 8.4 ± 2.0 **Social skills, mean ± SD:** Vineland-Socialization raw score **G1:** 25.8 ± 5.5 **G2:** 28.0 ± 6.2 Vineland-Socialization standard score **G1:** 67.8 ± 7.7 **G2:** 70.7 ±7.7 **Communication/ language, mean ± SD:** MSEL-Receptive language raw score **G1:** 20.6 ± 9.7 **G2:** 17.5 ± 8.5 MSEL-Receptive language standard score **G1:** 34.4 ± 15.2 **G2:** 29.6 ± 14.8 MSEL-Expressive language raw score	**Overall ratings:** **Global Rating of Severity mean ± SD:** ADOS new algorithm **G1:** NR **G2:** NR **G1+G2**: 17.9 ± 5.0 ADOS severity score* **G1+G2**: 7.8 ± 1.9 ADOS-improved classification **G1:** 3 (6.7) **G2:** 2 (6) **Diagnosis stability, n (%):** ADOS-autism diagnosis **G1+G2**: 71 (91) **Social skills, mean ± SD:** Vineland-Socialization Socialization raw score **G1:** 38.8 ± 10.7 **G2:** 42.4 ± 11.5 Vineland-Socialization standard score **G1:** 69.6 ± 12.4 **G2:** 77.4 ± 14.4 **Communication/ language, mean ± SD:** MSEL-Receptive language raw score **G1:** 28.7 ± 10.7

	Defined protocol followed: NR **Measure of treatment fidelity reported:** No **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 45 **G2:** 33 **N at follow-up:** **G1:** NR **G2:** NR **N for each measure:** ADOS baseline: 78 follow-up: 77 Vineland baseline: 71 follow-up: 75 MSEL baseline: 71 follow-up: 69	SD (range): **G1:** 14.4 ± 2.8 (8-20) **G2:** 14.9 ± 3.1 (10-20) Household income, mean (range): NR **Diagnostic approach:** In Study Diagnostic tool/method: Autism Diagnostic Interview-Revised (ADI-R) and Autism Diagnostic Observation Schedule (ADOS) **Diagnostic category, n (%):** Autism: 78 (100) PDD-NOS Aspergers **Other characteristics**, n (%): NR	**G1:** 17.0 ± 8.4 **G2:** 16.8 ± 7.8 MSEL-Expressive language standard score **G1:** 28.8 ± 11.3 **G2:** 31.4 ± 12.5 MSEL-Verbal **G1+G2**: 60.9 ± 24.4 Vineland-Communication raw score **G1:** 19.0 ± 9.0 **G2:** 22.8 ± 12.1 Vineland-Communication standard score **G1:** 67.0 ± 7.8 **G2:** 69.5 ± 10.7 **Adaptive behavior, mean ± SD (range):** Vineland composite score **G1:** 66.2 ± 9.6 (49-75) **G2:** 68.6 ± 6.3 (59-81) **G1+G2**: 67.4 ± 6.4 Vineland-Daily Living raw score **G1:** 17.4 ± 6.7 **G2:** 19.5 ± 6.5 Vineland-Daily Living standard score **G1:** 67.7 ± 7.0 **G2:** 69.4 ± 6.0 **Motor skills, mean ± SD:** MSEL-Fine motor raw	**G2:** 26.1 ± 8.2 MSEL-Receptive language standard score **G1:** 40.1 ± 14.2 **G2:** 37.7 ± 12.8 MSEL-Expressive language raw score **G1:** 26.8 ± 11.0 **G2:** 25.9 ± 10.0 MSEL-Expressive language standard score **G1:** 35.6 ± 15.0 **G2:** 39.0 ± 14.3 MSEL-Verbal **G1+G2**: 75.0 ± 27.0 Vineland-Communication raw score **G1:** 42.0 ± 16.3 **G2:** 44.3 ± 15.7 Vineland-Communication standard score **G1:** 72.9 ± 14.7 **G2:** 78.8 ± 16.2 **Repetitive behavior:** NR **Problem behavior:** NR **Adaptive behavior, mean ± SD (range):** Vineland composite score **G1:** NR **G2:** NR **G1+G2**: 68.9 ± 13.0

	score **G1:** 25.2 ± 4.9 **G2:** 24.2 ± 4.1 MSEL-Fine motor standard score **G1:** 33.0 ± 14.0 **G2:** 34.1 ± 12.9 Vineland-Motor skills raw score **G1:** 33.5 ± 5.8 **G2:** 35.1 ± 4.6 Vineland-Motor skills standard score **G1:** 86.2 ± 11.4 **G2:** 88.1 ± 11.0 **Sensory, mean ± SD:** MSEL-Visual raw score **G1:** 29.9 ± 5.3 **G2:** 25.6 ± 4.7 MSEL-Visual standard score **G1:** 42.3 ± 12.7 **G2:** 37.7 ± 12.1 **Educational/ cognitive/ academic attainment, mean ± SD (range):** MSEL-cognitive composite **G1:** 72.2 ± 19.2 (49-135) **G2:** 73.3 ± 22.2 (49-132) MSEL Nonverbal **G1+G2**: 73.9 ± 23.7	Vineland-Daily Living-raw score **G1:** 35.8 ± 13.5 **G2:** 36.7 ± 15.2 Vineland-Daily Living standard score **G1:** 67.8 ± 10.9 **G2:** 73.0 ± 14.6 **Commonly occurring co-morbidities:** NR **Medical:** NR **Motor skills, mean ± SD:** MSEL-Fine motor raw score **G1:** 30.7 ± 6.0 **G2:** 27.9 ± 4.6 MSEL-Fine motor standard score **G1:** 33.0 ± 14.6 **G2:** 33.7 ± 14.5 Vineland-Motor skills raw score **G1:** 43.1 ± 7.0 **G2:** 45.8 ± 6.1 Vineland-Motor skills standard score **G1:** 72.0 ± 12.9 **G2:** 84.5 ± 13.0 **Sensory, mean ± SD:** MSEL-Visual raw score **G1:** 35.9 ± 7.5 **G2:** 32.6 ± 7.4

	MSEL-Visual standard score **G1:** 42.4 ± 18.2 **G2:** 43.1 ± 17.0 **Educational/ cognitive/ academic attainment, mean ± SD:** MSEL-cognitive composite **G1:** NR **G2:** NR MSEL Nonverbal **G1+G2**: 75.5 ± 29.2 **Harms:** NR **Modifiers:** Cognitive and adaptive ability, maternal age

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Kovshoff et al. 2011[70] **Country:** UK **Intervention setting:** Home, school, clinic **Enrollment period:** NR **Funding:** Esmee Fairbairn Foundation, Research Autism, Autism and Developmental Disorders Education Research **Design:** Prospective Cohort Note: See earlier study[71] reporting on this population in 2011 AHRQ review[9]	**Intervention:** EIBI- 24 month study. Follow-up 2 years after study ended. **Assessments:** Stanford-Binet Intelligence Scale – Fourth Edition, Bayley Scales of Infant Development-Second Edition; Vineland Adaptive Behavior Scale-Survey form; Reynell Developmental Language Scales – Third Edition; Positive Social Subscale of the Nisonger Child Behavior Rating Form, Autism Diagnostic Interview-Revised, Developmental Behavior Checklist **Groups:** **G1:** EIBI intervention (mix of university-based and private providers) **G2:** treatment as usual **Provider:** University-based or privately hired behavioral intervention providers **Treatment manual followed:** NR	**Inclusion criteria:** • meet criteria for diagnosis of autism based on both ADI-R and independent clinical assessment and diagnostic procedure • no chronic medical conditions • reside in family home **Exclusion criteria:** • see above **Age, mean/yrs (range):** At follow-up: Mean of 7 years, 2 months (range: 6.5-8 years) **Mental age, mean/yrs (range):** NR **Sex:** NR Race/ethnicity, n (%): NR **SES:** Maternal education, n (%): High school College Household income, mean (range): **Diagnostic approach:** In Study/Referral	IQ, mean ± SD **G1:** 61.43 ± 16.43 **G2:** 63.83 ± 13.98 Vineland Composite **G1:** 60.22 ± 5.82 **G2:** 57.17 ± 7.05 Vineland Communication **G1:** 61.52 ± 7.56 **G2:** 58.17 ± 8.63 Vineland Daily Living **G1:** 63.26 ± 5.40 **G2:** 62.22 ± 8.14 Vineland Socialization **G1:** 63.30 ± 6.74 **G2:** 59.94 ± 7.94 Nisonger Child Behavior Rating Form: positive social behavior Mother **G1:** 10.57 ± 4.24 **G2:** 9.61 ± 3.50 Father **G1:** 8.94 ± 3.47 **G2:** 8.64 ± 3.79 DBC total Mother **G1:** 50.26 ± 22.75 **G2:** 65.61 ± 18.70 Father **G1:** 46.67 ± 22.15	Two year follow-up[a] IQ, mean ± SD **G1:** 64.65 ± 33.04 **G2:** 61.94 ± 31.09 *p*= 0.339 DBC total Mother **G1:** 53.70 ± 21.13 **G2:** 63.56 ± 26.39 *p*= 0.627 Father **G1:** 48.86 ± 26.21 **G2:** 56.14 ± 21.22 *p*= 0.719 **Social skills:** Nisonger Child Behavior Rating Form: positive social behavior Mother **G1:** 14.87 ± 5.29 **G2:** 11.33 ± 5.26 *p*= 0.059 Father **G1:** 14.73 ± 6.70 **G2:** 11.64 ± 7.31 *p*= 0.321 **Adaptive behavior:** Vineland Composite **G1:** 55.13 ± 19.40 **G2:** 49.5 ± 17.39 *p*= 0.79

	Defined protocol followed: NR **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 23 **G2:** 21 **N at follow-up:** **G1:** 23 **G2:** 18	Diagnostic tool/method: **Diagnostic category, n (%):** Autism PDD-NOS Aspergers **Other characteristics, n (%):** NR	**G2:** 57.15 ± 16.23	Vineland Communication **G1:** 62.65 ± 25.11 **G2:** 57.72 ± 24.54 *p*= 0.784 Vineland Daily Living **G1:** 52.35 ± 19.61 **G2:** 43.67 ± 18.15 *p*= 0.177 Vineland Socialization **G1:** 62.57 ± 16.93 **G2:** 59.33 ± 15.58 *p*= 0.822 **Harms:** NR **Modifiers:** NR

Comments: [a] p-values refer to ANCOVA that compared group scores at 24-month treatment termination and two year follow-up.See Remington et al. 2007 for original study data.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Murdock and Hobbs, 2011 [72] **Country:** US **Intervention setting:** Autism treatment center with preschool program **Enrollment period:** NR **Funding:** NR **Design:** Prospective cohort	**Intervention:** Picture Me Playing; consisted of four 15-minute group sessions and one 5-minute individualized session with a typically developing peer. Group sessions included 3 participants and 2 typical peers at a time. Sessions included story and role-playing opportunities. **Assessments:** observation **Groups:** **G1:** Picture Me Playing **G2:** comparison group **Provider:** Second author implemented the intervention **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:**	**Inclusion criteria:** • ages 55-75 months • diagnosis of autism or PDD-NOS • able to follow group directed instructions • able to comply and attend to group activities **Exclusion criteria:** NR **Age, mean/months ± SD:** **G1:** 69.33 ± 5.9889 **G2:** 62.17 ± 6.2102 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 5 (83.3) **G2:** 5 (83.3) F, n (%): **G1:** 1 (16.7) **G2:** 1 (16.7) **Race/ethnicity, n (%):** White: NR Asian: NR **SES:** Maternal education, n (%): NR Household income, mean	**Communication/ language:** Types of utterances, n: Total utterances: **G1:** 250 **G2:** 206 Structural: **G1:** 141 **G2:** 139 Play dialogue: **G1:** 50 **G2:** 28 Sound effects: **G1:** 38 **G2:** 28 Self-talk: **G1:** 21 **G2:** 11	**Communication/ language:** Types of utterances, n: Total utterances: **G1:** 307 **G2:** 304 p=NS Structural: **G1:** 89 **G2:** 176 p=NS Play dialogue: **G1:** 180 **G2:** 66 p=NS Sound effects: **G1:** 29 **G2:** 36 p=NS Self-talk: **G1:** 9 **G2:** 26 p=NS Types of utterances, percent change from baseline: Total utterances: **G1:** 23% **G2:** 48% p=NS Structural

	NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 6 **G2:** 6 **N at follow-up:** **G1:** 6 **G2:** 6	(range): NR **Diagnostic approach:** Referral Diagnostic tool/method: NR **Diagnostic category, n (%):** Autism or PDD-NOS: **G1:** 6 (100) **G2:** 6 (100) **Other characteristics, mean ± SD:** **PPVT-4:** **G1:** 84.5 ± 11.077 **G2:** 88.5 ± 7.6092 **K-BIT:** **G1:** 86.5 ± 5.8907 **G2:** 72.33 ± 13.456 Peers: **G1:** 105.5 ± 13.026 **G2:** 108.75 ± 7.5884 **PLS-4:** **G1:** 85.667 ± 13.064 **G2:** 86.5 ± 13.368		**G1:** -37% **G2:** 27% p=NS Play dialogue **G1:** 260% **G2:** 136% p=0.041 Sound effects **G1:** -24% **G2:** 29% p=NS Self-talk **G1:** -57% **G2:** 13.6% p=NS **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Pajareya et al. 2011[73] **Country:** Thailand **Intervention setting:** Home **Enrollment period:** NR **Funding:** NR **Design:** RCT with four groups stratified based on age (24-47 months, 48-72 months) and symptom severity: (mild autism: Childhood Autism Rating Scale score of 30-40; severe autism: CARS score of 41-60)	**Intervention:** Parent-administered DIR/Floortime for an average of 15.2 hours/wk for 3 months **Assessments:** Functional Emotional Assessment Scale, Childhood Autism Rating Scale, Functional Emotional Questionnaires **Groups:** **G1:** DIR/Floortime **G2:** treatment-as-usual **Provider:** Parents (attended one day training workshop, received 3-hour DVD lecture, and had two one-hour home visits with a trainer) **Treatment manual followed:** Individualized manual with activity suggestions based upon Greenspan's affect-based language curriculum **Defined protocol followed:** Yes **Measure of treatment**	**Inclusion criteria:** • met clinical criteria for autistic disorders according to DSM-IV criteria • age 2-6 years **Exclusion criteria:** • additional medical diagnosis (e.g. genetic syndromes, diagnosed hearing impairment, diagnosed visual impairment or seizures) • geographically inaccessible for follow-up visits • parents not literate or with known chronic psychiatric or physical illness **Age, mean/months ± SD:** **G1:** 56.6 ± 10.1 **G2:** 51.5 ± 13.9 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 15 (94) **G2:** 13 (81) F, n (%):	**CARS, mean ± SD** **G1:** 37.2 ± 6.2 **G2:** 39.7 ± 6.6 **FEAS, mean ± SD** **G1:** 24.4 ± 12.7 **G2:** 23.5 ± 12.6 **FEDQ, mean ± SD** **G1:** 44.0 ± 12.9 **G2:** 40.7 ± 15.3	**Severity** CARS, mean changes ± SD **G1:** 2.9 ± 2.0 **G2:** 0.8 ±1.2 *p*=0.002 FEAS, mean changes ± SD **G1:** 7.0 ± 6.3 **G2:** 1.9 ±6.1 *p*=0.031 FEDQ, mean changes ± SD **G1:** 7.7 ± 8.1 **G2:** 0.8 ±1.4 *p*=0.006 **Harms:** NR **Modifiers:** NR

fidelity reported: Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** On medication **G1:** 5 (31) **G2:** 5 (31) 11 children in G1 continued to receive one-on-one treatment intervention based on behavioral or discrete trial principles throughout the study period. **N at enrollment:** **G1:** 16 **G2:** 16 **N at follow-up:** **G1:** 15 **G2:** 16	**G1:** 1 (6) **G2:** 3 (19) **Race/ethnicity, n (%):** NR (Thai) **SES:** Maternal education, n (%): Bachelor degree or higher **G1:** 10 (62.5) **G2:** 14 (87.5) Household income, mean (range): NR **Diagnostic approach:** Diagnosis confirmed by developmental pediatrician Diagnostic tool/method: DSM-IV **Diagnostic category, n (%):** Autism **G1:** 13 (81) **G2:** 10 (62.5) PDD-NOS **G1:** 3 (19) **G2:** 6 (37.5) Aspergers **0** **Other characteristics**, n (%)**:** Overall status No affective engagement **G1:** 0 **G2:** 0

		Only intermittent engagement **G1:** 3 **G2:** 4 Intermittent reciprocal communication, no symbolization **G1:** 3 **G2:** 6 Islands of symbolization **G1:** 10 **G2:** 6 Associated with moderate to severe motor planning problem **G1:** 5 **G2:** 6 Participation in special education (or regular) preschool program **G1:** 11 **G2:** 11 Average hours per week of paramedical services (e.g., speech therapy), mean ± SD **G1:** 3.1 ± 1.8 **G2:** 3.3 ± 1.4	

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Roberts et al. 2011[74] **Country:** Australia **Intervention setting:** 1) home 2) center **Enrollment period:** 2006 & 2007 (two consecutive 12-month offerings of program) with recruitment in late 2005 and late 2006 **Funding:** Australian Research Council Linkage Projects grant; Autism Spectrum Australia (Aspect) **Design:** RCT	**Intervention:** Two variations of the Building Blocks® program, including an individualized home-based program (40 weeks duration, 2 h visit every 2 weeks, 20 sessions max) or a small group center-based program with parent training and support group (40 weeks duration, weekly 2 h sessions) **Assessments:** Autism Diagnostic Observation Schedule, Beach Centre Family Quality of Life Scale, Vineland Adaptive Behavior Scales-II, Reynell Developmental Language Scales III, The Pragmatics Profile of Everyday Communication, Developmental Behavior Checklist, Parenting Stress Index, Parent Perception Questionnaire, Parent interview **Groups:** **G1:** individualized home-based program **G2**: small group center-based program combined with parent training and	**Inclusion criteria:** • preschool age • diagnosis of Autistic Disorder, Asperger or PDD-NOS (DSM-IV) by referring clinician • home within reasonable distance of center-based group • child's readiness for center-based program (determined by parents and staff) **Exclusion criteria:** • see inclusion criteria **Age mean/months (range):** **G1:** 41.5 (26.5 – 59.4) **G2**: 43.1 (26.3 – 60.0) **G3**: 43.7 (27.6 – 60.3) **Mental age:** Griffiths developmental quotient, mean ± SD: **G1:** 57 ± 11.7 **G2**: 66 ± 17.7 **G3**: 63.3 ± 15.5 **Sex, n (%):** M: NR (90.5%) F: NR (9.5%) **Race/ethnicity, n (%):** NR **SES:** Maternal education, n (%),	**Social skills, mean ± SD:** VABS social **G1**: 68.7 ± 7.3 **G2**: 70.1 ± 7.3 **G3**: 70.8 ± 9.9 **Communication/ language, mean ± SD:** VABS communication **G1:** 64.4 ± 12.8 **G2**: 66.9 ± 12.5 **G3**: 68.5 ± 17.0 Reynell comprehension, standard score: **G1:** 4.2 ± 9.2 **G2**: 5.5 ± 10.6 **G3**: 7.2 ± 15.2 Reynell comprehension, raw score: **G1:** 6.9 ± 9.7 **G2**: 11.3 ± 13.8 **G3**: 12.2 ± 14.9 Reynell expression, standard score: **G1:** 3.4 ± 8.3 **G2**: 8.2 ± 16.6 **G3**: 6.0 ± 10.9 Reynell expression, raw score: **G1:** 3.2 ± 5.4 **G2**: 6.9 ± 9.9 **G3**: 5.8 ± 7.9	**Social skills, mean ± SD:** VABS social **G1:** 66.4 ± 7.7 **G2**: 72.6 ± 11.2 **G3**: 73.1 ± 10.8 **G1** vs. **G2**: p=0.02 **G1** vs. **G3**: p=0.02 **G2** vs. **G3**: p=NS 3-group comparison: p=0.03 **Communication/ language, mean ± SD:** VABS communication **G1:** 68.4 ± 15.6 **G2**: 76.1 ± 17.1 **G3**: 74.2 ± 15.5 **G1 vs. G2**: p=NS **G1 vs. G3**: p=NS **G2 vs. G3**: p=NS 3-group comparison: p=NS Reynell-comprehension, standard score: **G1:** 2.6 ± 8.4 **G2**: 10.5 ± 17.4 **G3**: 5.7 ± 12.1 **G1 vs. G2**: p=0.03 **G1 vs. G3**: p=NS **G2 vs. G3**: p=NS 3-group comparison: p=NS Reynell-comprehension, raw score

	support group **G3**: waitlist (non-randomized treatment comparison) **Provider:** Multidisciplinary teams of teachers, speech pathologists, occupational therapists and psychologists **Treatment manual followed:** **G2** only: Autism Association of NSW manual (2004) – child and parent components **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** No Concomitant therapies, mean number ± SD: ASD-specific interventions used during intervention period: **G1:** 0.22 ± 0.42 **G2**: 0.14 ± 0.35 **G3**: 0.54 ± 0.79 Educational interventions used during intervention period:	(n=73): High school: 10 (13.7) College/post-high school: 28 (38.4%) Bachelors: 23 (31.5) Postgraduate: 12 (16.4) Household income, n (%), (n=78): >$75,000: 45 (57.7) $60,000-$70,000: 10 (12.8) $50,000-$60,000: 11 (14.1) $40,000-$50,000: 4 (5.1) <$40,000: 8 (10.3) Language spoken at home. n (%): Language other than English exclusively: 2 (2.6) Language in addition to English: 12 (15.4) Family members supported by income, mean ± SD (n=78): 4.0 ± 1.2 SES (ranking within New South Wales), mean ± SD (n=80): 73.0 ± 23.0 Mother's age, mean/yrs ± SD (n=75): 36.6 ± 4.3 **Diagnostic approach:** In Study and Referral Referral of autism and ASD diagnosed by clinicians; diagnosis in-study	Pragmatics Profile, total Q range: **G1:** 50.4 ± 17.5 **G2**: 58.3 ± 16.8 **G3**: 56.7 ± 16.2 **Adaptive behavior, mean ± SD:** Developmental Behavior Checklist, total: **G1:** 44.7 ± 19.0 **G2**: 58.5 ± 20.4 **G3**: 43.9 ± 21.9	**G1:** 17.5 ± 6.3 **G2**: 23.7 ± 19.9 **G3**: 22.0 ± 17.8 **G1 vs. G2**: p=NS **G1 vs. G3**: p=NS **G2 vs. G3**: p=NS 3-group comparison: p=NS Reynell-expression, standard score: **G1:** 2.8 ± 7.5 **G2**: 7.0 ± 15.1 **G3**: 4.4 ± 8.7 **G1 vs. G2**: p=NS **G1 vs. G3**: p=NS **G2 vs. G3**: p=NS 3-group comparison: p=NS Reynell-expression, raw score: **G1:** 8.8 ± 8.9 **G2**: 11.4 ± 10.9 **G3**: 11.1 ± 9.9 **G1 vs. G2**: p=NS **G1 vs. G3**: p=NS **G2 vs. G3**: p=NS 3-group comparison: p=NS Pragmatics Profile, total Q range: **G1:** 62.8 ± 19.4 **G2**: 73.0 ± 19.0 **G3**: 72.2 ± 18.8 **G1 vs. G2**: p=NS **G1 vs. G3**: p=NS **G2 vs. G3**: p=NS 3-group comparison: p=NS

	G1: 2.37 ± 1.28 **G2**: 2.41 ± 1.50 **G3**: 3.11 ± 1.64 **N at enrollment:** **G1:** 34 **G2**: 33 **G3**: 28 **N at follow-up:** **G1:** 27 **G2**: 29 **G3**: 28	Diagnostic tool/method: DSM-IV (referral), ADOS (in-study) **Diagnostic category, n (%):** Autistic disorder: **G1:** 24 (87.5) **G2:** 20 (69.0) **G3:** 17 (60.7) ASD: **G1:** 4 (14.3) **G2:** 4 (13.8) **G3:** 5 (17.9) Non ASD: **G1:** 0 (0) **G2:** 5 (17.2) **G3:** 6 (21.4) **Other characteristics**, n (%)**:** NR		**Adaptive behavior:** Developmental Behavior Checklist, total: **G1:** 52.9 ± 29.3 **G2**: 55.7 ± 19.5 **G3**: 42.9 ± 24.3 **G1 vs. G2**: p=NS **G1 vs. G3**: p=NS **G2 vs. G3**: p=NS 3-group comparison: p=NS **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Scarpa et al. 2011[75] **Country:** US **Intervention setting:** clinic **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** CBT, one hour group meetings for 9 consecutive weeks. Intervention focused on skill-building via affective education, stress management, and understanding expression of emotions. Parent group meetings occurred simultaneously with children's sessions. **Assessments:** Child's emotion regulation ability **Groups:** **G1:** intervention **G2:** wait list control **Provider:** Therapists (3 clinical graduate students and two trained staff members) supervised by licensed clinical psychologist **Treatment manual followed:** Yes **Defined protocol followed:** No **Measure of treatment**	**Inclusion criteria:** • meet ASD criteria on ADOS • 5-7 years old at time of intervention • In kindergarten or first grade • verbal and able to understand and follow verbal directions **Exclusion criteria:** • see above **Age,/yrs (range):** (4.5-7 years) **Mental age, mean/yrs (range):** NR **Sex:** M, 9 (%) F, 2 (%) **Race/ethnicity, n (%):** White, 11 (100) **SES:** Maternal education: NR Household income, median (range): $85,000 ($14,400-$175,000) **Diagnostic approach:** In Study/Referral	Emotion Regulation Checklist Emotion Regulation Subscale **G1+ G2:** 22.82 ± 2.56 Negativity/Lability Subscale **G1+ G2:** 38.00 ± 5.33 Behavioral Monitoring Sheet Frequency of episodes per hour **G1+ G2:** 0.31 ± 0.16 Duration in minutes per episode **G1+ G2:** 7.13 ± 6.68 Ben and the Bullies and James and the Reading Group Vignettes Quantity scores **G1+ G2:** 1.36 ± 0.81 Self Confidence Rating Scale Parental self-confidence-anger **G1+ G2:** 5.60 ± 1.58 Parental self-confidence-anxiety **G1+ G2:** 4.73 ± 1.90 Confidence in child- anger **G1+ G2:** 3.73 ± 1.49	**Problem behavior:** Emotion Regulation Checklist Emotion Regulation Subscale **G1+ G2:** 24.91 ± 6.17 Negativity/Lability Subscale **G1+ G2:** 33.73 ± 5.00 Behavioral Monitoring Sheet Frequency of episodes per hour **G1+ G2:** 0.18 ± 0.09 Duration in minutes per episode **G1+ G2:** 3.32 ± 2.20 Ben and the Bullies and James and the Reading Group Vignettes Quantity scores **G1+ G2:** 3.27 ± 2.24 Self Confidence Rating Scale Parental self-confidence-anger **G1+ G2:** 7.20 ± 1.81 Parental self-confidence-anxiety **G1+ G2:** 7.36 ± 1.12

	fidelity reported: No **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 5 **G2:** 6 **N at follow-up:** **G1:** NR **G2:** NR	Diagnostic tool/method: ADOS **Diagnostic category, n (%):** Autism PDD-NOS Asperger syndrome **Other characteristics**, n (%)**:** NR	Confidence in child-anxiety **G1+ G2:** 2.82 ± 1.25	Confidence in child-anger **G1+ G2:** 5.45 ± 1.92 Confidence in child-anxiety **G1+ G2:** 5.55 ± 1.81 **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Strain et al. 2011[76] **Country:** USA **Intervention setting:** Preschool classrooms **Enrollment period:** NR **Funding:** Institute for Educational Sciences, U.S. Department of Education **Design:** RCT	**Intervention:** LEAP (Learning Experiences and Alternative Program for Preschoolers and Their Parents) manuals, videos, and training manuals with training and mentoring relationship with study staff for 2 years (average of 17 hours per week) **Assessments:** Childhood Autism Rating Scale (CARS), Preschool Languge Scale-4th Edition (PLS-4), Social Skills Rating System (SSRS) **Groups:** **G1:** Full replication: Teachers received full LEAP training/coaching **G2:** Teachers provided with intervention manuals and related written materials only **Provider:** Preschool teachers, family members **Treatment manual followed:** Yes **Defined protocol followed:** Yes	**Inclusion criteria:** • classrooms "willing and able" to be LEAP replication sites. • "Able" criteria: • intensity of services provided • enrollment of children with ASD in inclusive settings • minimum ratio of adults to children (1:5) • minimum ratio of typical peers to children with ASD (2:1) **Exclusion criteria:** NR **Age, mean/months ± SD:** **G1:** 50.1 ± 4.6 **G2:** 50.7 ± 4.2 **Mental age, mean/yrs ± SD:** NR **Sex:** NR Race/ethnicity, n (%): NR **SES:** NR **Diagnostic approach:** Based upon school district	**Overall ratings: Global Rating of Severity, mean ± SD:** CARS: **G1:** 39.0 ± 6.2 **G2:** 37.4 ± 5.9 **Social skills:** SSRS-positive, mean ± SD: **G1:** 13.5 ± 21.5 **G2:** 20.7 ± 20.2 SSRS-negative, mean ± SD: **G1:** 63.5 ± 15.2 **G2:** 53.4 ± 16.5 **Communication/ language:** PLS-4 (total language), mean ± SD: G1: 32.8 ± 7.5 G2: 34.4 ± 7.2 Mullen (receptive language), mean ± SD: **G1:** 30.8 ± 7.6 **G2:** 33.4 ± 9.0 Mullen (expressive language), mean ± SD: **G1:** 28.9 ± 7.4 **G2:** 30.3 ± 8.2 **Motor skills:** Mullen (fine motor), mean	**Note: all p-values represent G1 delta (change after 2 years of study participation) vs. G2 delta **Overall ratings: Global Rating of Severity, mean ± SD:** CARS: **G1:** 32.9 ± 3.9 **G2:** 34.6 ± 4.2 p<0.05 **Social skills:** SSRS-positive, mean ± SD: **G1:** 42.1 ± 12.6 **G2:** 32.7 ± 11.9 p<0.01 SSRS-negative, mean ± SD: **G1:** 56.5 ± 4.2 **G2:** 49.1 ± 4.1 p<0.05 **Communication/ language:** PLS-4 (total language), mean ± SD: **G1:** 51.3 ± 8.1 **G2:** 43.8 ± 7.7 p<0.01 Mullen (receptive language), mean ± SD:

	Measure of treatment fidelity reported: Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** Classrooms: **G1:** 28 **G2:** 28 **N at follow-up:** Classrooms: **G1:** 27 **G2:** 23 Teachers: **G1:** 123 **G2:** 107 Children with ASD: **G1:** 177 **G2:** 117	standards for educational diagnoses of ASD **Diagnostic category, n (%):** Autism: 100% PDD-NOS: 0 Aspergers: 0 **Other characteristics**, n (%)**:** Geographic: **G1** schools, n): Metropolitan: 14 Suburban: 10 Rural: 3 G2 schools, n: Metropolitan: 12 Suburban: 8 Rural: 3	± SD: **G1:** 31.9 ± 6.4 **G2:** 34.8 ± 6.2 **General intelligence:** Mullen (visual reception), mean ± SD: **G1:** 32.3 ± 6.6 **G2:** 34.6 ± 7.0 Mullen ELC (early learning composite), mean ± SD: **G1:** 59.6 ± 6.9 **G2:** 63.2 ± 6.6	**G1:** 49.3 ± 7.9 **G2:** 40.7 ± 7.7 p<0.01 Mullen (expressive language), mean ± SD: **G1:** 38.7 ± 6.4 **G2:** 35.9 ± 4.4 p<0.05 **Motor skills:** Mullen (fine motor), mean ± SD: **G1:** 43.3 ± 5.2 **G2:** 39.8 ± 4.9 p<0.05 **General intelligence:** Mullen (visual reception):, mean ± SD **G1:** 52.7 ± 11.5 **G2:** 46.3 ± 11.6 p<0.01 Mullen ELC (early learning composite), mean ± SD: G1: 68.5 ± 7.5 G2: 61.4 ± 9.0 p<0.01 **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Sung et al. 2011[77] **Country:** SIngapore **Intervention setting:** clinic **Enrollment period:** February 2007 to August 2008 **Funding:** National Medical Research Council grant **Design:** RCT	**Intervention:** Cognitive behavioral therapy (CBT) sixteen 90-minute weekly sessions delivered in small groups of 3-4 participants. Sessions 1-3 focused on recognition and understanding of emotions; Sessions 4-9 focused on anxiety management techniques and sessions 10-16 focused on problem-solving strategies based on the STAR strategy. The social recreational (SR) group received 16 week manualized SR program. 90 minute weekly sessions in groups of 3-4 participants. **Assessments:** observed, parent report, context Spence Child Anxiety Scale- Child (SCAS-C) administered pre and post treatment and at 3 and 6 month follow-up **Groups:** **G1:** cognitive behavioral therapy **G2:** social recreational	**Inclusion criteria:** • 9-16 years old • clinical diagnosis of autism, Asperger syndrome, PDD (NOS) or ASD by DSM-IV criteria • classification of autism or autism spectrum on ADOS • verbal comprehension ≥ 80 and perceptual reasoning skills ≥ 90 on Wechsler Intelligence Scale for Children, 4th edition • no change in medication dosage one month prior to start of study and throughout duration of study **Exclusion criteria:** -see above **Age, mean ± SD yrs:** **G1:** 11.33 ± 2.03 **G2:** 11.09 ± 1.53 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%) **G1:** 34 (94) **G2:** 32 (94)	**SCAS-C, mean ± SD:** Total score **G1:** 29.96 ± 14.91 **G2:** 35.03 ± 14.13 Panic attack **G1:** 4.00 ± 3.42 **G2:** 4.34 ± 3.90 Separation anxiety **G1:** 4.39 ± 2.99 **G2:** 5.28 ± 3.45 Physical injury **G1:** 3.50 ± 2.43 **G2:** 5.03 ± 2.65 Social phobia **G1:** 5.71 ± 3.71 **G2:** 6.31 ± 3.97 Obsessive compulsive **G1:** 6.39 ± 3.73 **G2:** 8.24 ± 3.38 Generalized anxiety **G1:** 5.96 ± 3.55 **G2:** 5.83 ± 3.10	**SCAS-C, mean ± SD:**6 month follow-up Total score **G1:** 21.54 ± 14.82 **G2:** 21.17 ± 11.97 Panic attack **G1:** 2.54 ± 3.53 **G2:** 1.97 ± 2.11 Separation anxiety **G1:** 3.21 ± 3.05 **G2:** 3.10 ± 3.28 Physical injury **G1:** 3.11 ± 2.51 **G2:** 3.28 ± 2.51 Social phobia **G1:** 4.68 ± 3.51 **G2:** 4.55 ± 3.34 Obsessive compulsive **G1:** 4.79 ± 3.65 **G2:** 5.34 ± 3.64 Generalized anxiety **G1:** 3.21 ± 1.95 **G2:** 2.93 ± 2.07 **SCAS-C, n (%)** Deterioated **G1:** 3 (10.34) **G2:** 0 No change **G1:** 13 (44.83)

	Provider: CBT and SR delivered by two trained therapists **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** **Co-interventions held stable during treatment:** Yes **Concomitant therapies, n (%):** On medication **G1:** 6 (17) **G2:** 5 (15) Not on medication **G1:** 29 (81) **G2:** 28 (82) Unknown **G1:** 1 (3) **G2:** 1 (3) **N at enrollment:** **G1:** 36 **G2:** 34 **N at follow-up:** **G1:** 30 **G2:** 29 **ITT analysis** **G1:** 36	F, n (%) **G1:** 2 (6) **G2:** 2 (6) **Race/ethnicity, n (%):** Chinese **G1:** 35 (97) **G2:** 30 (88) Malay **G1:** 1 (3) **G2:** 2 (6) Indian **G1:** 0 **G2:** 1 (3) Others **G1:** 0 **G2:** 1 (3) **SES:** NR **Diagnostic approach:** Referral Diagnostic tool/method: DSM-IV, ADOS **Diagnostic category, n (%):** Autism/PDD-NOS **G1:** 30 (83) **G2:** 28 (82) Asperger syndrome **G1:** 6 (17) **G2:** 6 (18) Other characteristics**, n (%)**:	**G2:** 13 (44.83) Improved **G1:** 13 (44.83) **G2:** 16 (55.17) **Harms:** NR **Modifiers:** NR

	G2: 34	**Cognitive functioning, mean ± SD:** Verbal Comprehension **G1:** 100.25 ± 13.97 **G2:** 93.06 ± 12.81 Perceptual reasoning **G1:** 108.00 ± 12.26 **G2:** 105.94 ± 11.07

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Kasari et al. 2010[78] **Country:** US **Intervention setting:** Laboratory **Enrollment period:** 01/2002 to 09/2005 **Funding:** Grant NIMH **Design:** RCT	**Intervention:** Joint attention intervention. !0 modules completed in 24 sessions (3 per week) for 8 weeks **Assessments:** 15 minute videotaped caregiver-child interaction observed at end of intervention (8 weeks) and 12 months later (14 month from study start) Mullen scales at baseline and at 12 month follow-up **Groups:** **G1:** Immediate treatment **G2:** Wait list **Provider:** Trained interventionists (graduate students in educational psychology experienced with children with autism. Videotapes coded by blinded reviewer **Treatment manual followed:** NR **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes	**Inclusion criteria:** • age < 36 months • met DSM-IV criteria for autism by independent clinician • no additional syndromes **Exclusion criteria:** • see above **Age, mean/mos ± SD**: **G1:** 30.35 ± 0.93 **G2:** 31.31 ± 0.90 **Mental age, mean/mos ± SD Mullen scales:** **G1:** 19.83 ± 1.80 **G2:** 18.57 ± 1.09 **Sex:** M, n (%): **G1:** 15 (79) **G2:** 14 (74) F, n (%): **G1:** 4 (21) **G2:** 5 (26) **Race/ethnicity, n (%):** White **G1:** 10 (53) **G2:** 12 (63) Minority **G1:** 9 (47) **G2:** 7 (37)	Object and joint engagement, mean ± SD Unengaged/other engagement **G1:** 20.80 ± 19.03 **G2:** 19.52 ± 14.95 Object engagement **G1:** 48.58 ± 21.87 **G2:** 54.97 ± 17.43 Joint engagement **G1:** 30.26 ± 14.91 **G2:** 24.98 ± 10.74 Frequency of joint attention initiations **G1:** 3.0 ± 2.77 **G2:** 3.62 ± 5.92 Frequency of joint attention responses **G1:** 0.42 ± 0.69 **G2:** 0.63 ± 0.23 Type of functional play acts **G1:** 3.00 ± 2.38 **G2:** 4.42 ± 3.17 Type of symbolic play acts **G1:** 0.11 ± 0.46 **G2:** 0.42 ± 0.84	Object and joint engagement, mean ± SD 8 weeks post treatment Unengaged/other engagement **G1:** 22.01 ± 18.24 **G2:** 17.31 ± 10.17 Object engagement **G1:** 34.75 ± 18.39 **G2:** 54.69 ± 18.15 Joint engagement **G1:** 42.85 ± 19.96 **G2:** 27.87 ± 14.01 Frequency of joint attention initiations **G1:** 3.11 ± 3.41 **G2:** 3.77 ± 3.76 Frequency of joint attention responses **G1:** 0.79 ± 0.23 **G2:** 0.05 ± 0.23 Type of functional play acts **G1:** 5.29 ± 2.37 **G2:** 3.29 ± 2.30 Type of symbolic play acts **G1:** 0.26 ± 0.65 **G2:** 0.53 ± 1.43 Object and joint

	Co-interventions held stable during treatment: NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 19 **G2:** 19 **N at follow-up:** **G1:** 19 **G2:** 16	**SES:** Caregiver's highest level education, n (%): Some college/vocational training **G1:** 3 (16) **G2:** 2 (11) College **G1:** 12 (63) **G2:** 11 (58) Professional/graduate **G1:** 4 (21) **G2:** 6 (31) Caregiver's employment status, n (%): Not employed **G1:** 14 (74) **G2:** 12 (63) Employed part or full time **G1:** 5 (26) **G2:** 7 (37) **Diagnostic approach:** In Study/Referral Diagnostic tool/method: DSM-IV confirmed by ADI-R **Diagnostic category, n (%):** NR **Other characteristics, n (%):** Mullen scales Developmental quotient, mean ± SD:		engagement, mean ± SD Follow-up IT group only Unengaged/other engagement **G1:** 15.87 ± 13.55 Object engagement **G1:** 28.35 ± 15.87 Joint engagement **G1:** 52.27 ± 20.56 Frequency of joint attention initiations **G1:** 4.44 ± 5.61 Frequency of joint attention responses **G1:** 0.61 ± 0.70 Type of functional play acts **G1:** 8.44 ± 4.77 Type of symbolic play acts **G1:** 1.11 ± 2.37 **Harms:** NR **Modifiers:** NR

G1: 64.80 ± 5.35
G2: 59.81 ± 3.14

Birth order, n (%)
Only child
G1: 10 (53)
G2: 7 (36)

First born
G1: 7 (36)
G2: 5 (26)

Second born
G1: 2 (11)
G2: 2 (11)

Twin
G1: 0
G2: 2 (11)

Missing
G1: 0
G2: 3 (16)

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Keen et al. 2010[79] **Country:** Australia **Intervention setting:** clinic/home **Enrollment period:** NR **Funding:** NR **Design:** Prospective cohort	**Intervention:** Parent-focused intervention- professional supported- two day parent group workshop and series of 10 home-based consultations with facilitator. Workshop provided information and parent education on the following topics: autism, social, communication, play, sensory, behavior, strategies to improve social interaction and communication, embedding strategies within daily routines, using a balanced approach, and selecting a child-focused early intervention program. Comparator: self-directed parent intervention group received an interactive instructional DVD "Being Responsive: You and Your Child with Autism" Intervention lasted for 6 weeks. Follow-up assessments conducted 3 months after completion of intervention **Assessments:** Scales of	**Inclusion criteria:** • families with child aged 2-4 with clinical diagnosis of ASD received within 6 months of study entry • not receiving more than 20 hours/week of services for child • not enrolled in an intensive behavior intervention **Exclusion criteria:** NR **Age, mean/yrs (range):** **G1:** 36.38 ± 7.54 **G2:** 35.71 ± 6.92 **Mental age, mean/yrs (range):** Mullen score (DQ) mean ± SD **G1:** 53.06 ± 9.06 **G2:** 52.86 ± 6.53 **Sex:** M, n (%): **G1:** 15 (88.2) **G2:** 16 (72.7) **Race/ethnicity, n (%):** NR **SES:** Maternal education, n (%):	PSI Mother, mean ± SD Child **G1:** 147 ± 23.3 (n=17) **G2:** 146 ± 18.6 (n=22) Parent **G1:** 141 ± 21.2 **G2:** 146 ± 18.0 PSI Father, mean ± SD Child **G1:** 140 ± 23.2 (n=16) **G2:** 145 ± 17.8 (n=21) Parent **G1:** 141 ± 29.2 **G2:** 137 ± 21.6 PSOC Mother, mean ± SD Satisfaction **G1:** 33.6 ± 5.27 (n=17) **G2:** 32.8 ± 7.22 (n=22) Efficacy **G1:** 24.8 ± 4.70 **G2:** 27.0 ± 5.86 PSOC Father, mean ± SD Satisfaction **G1:** 34.4 ± 4.89 (n=17) **G2:** 36.1 ± 6.58 (n=21) Efficacy **G1:** 24.8 ± 4.23 **G2:** 25.4 ± 4.98	PSI Mother, mean ± SD Child **G1:** 132 ± 21.3 (n=17) **G2:** 141 ± 19.1 (n=21) Parent **G1:** 133 ± 23.9 **G2:** 143 ± 16.7 PSI Father, mean ± SD Child **G1:** 137 ± 21.8 (n=16) **G2:** 145 ± 17.8 (n=17) Parent **G1:** 141 ± 20.6 **G2:** 138 ± 15.4 PSOC Mother, mean ± SD Satisfaction **G1:** 37.5 ± 5.82 (n=16) **G2:** 34.5 ± 7.53 (n=21) Efficacy **G1:** 29.6 ± 4.32 **G2:** 28.8 ± 5.21 PSOC Father, mean ± SD Satisfaction **G1:** 35.9 ± 6.10 (n=15) **G2:** 36.9 ± 5.61 (n=18) Efficacy **G1:** 29.1 ± 3.33 **G2:** 28.4 ± 4.97

	independent behavior revised- early development form (SIB-R), communication and symbolic behavior scales developmental profile (CBS-DP), Mullen scales of early learning, parenting stress index (PSI), Parenting sense of competence (PSOC) **Groups:** **G1:**Professional parent intervention **G2:** Self-directed parent intervention **Provider:** Facilitator (doctoral students experienced in working with families of young children with ASD) conducted home-based consultations **Treatment manual followed:** NR **Defined protocol followed:** NR **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR	High school (9-12 grade) **G1:** 6 (35.3) **G2:** 2 (9.1) Vocational **G1:** 4 (23.5) **G2:** 5 (22.7) College graduate **G1:** 0 **G2:** 5 (22.7) University graduate **G1:** 7 (41.2) **G2:** 10 (45.5) Paternal education, n (%): High school (9-12 grade) **G1:** 6 (35.3) **G2:** 5 (22.7) Vocational **G1:** 1 (5.9) **G2:** 6 (27.3) College graduate **G1:** 0 **G2:** 2 (9.1) University graduate **G1:** 10 (58.8) **G2:** 9 (40.9) Household income, mean (range): NR **Diagnostic approach:** Referral Diagnostic tool/method: DSM-IV. Diagnosis		**Harms:** NR **Modifiers** Fathers reported higher levels of stress than mothers in both groups.

	N at enrollment: **G1:** 17 families (17 mothers/16 fathers) **G2:** 22 families (22 mothers/21 fathers) **N at follow-up:** **G1:** NR **G2:** NR	confirmed by ADOS administered by research team. **Diagnostic category, n (%):** Autistic disorder 30(77) Autism spectrum disorder 9 (23) **Other characteristics**, n (%)**:** SIB-R standard score, mean ± SD **G1:** 52.29 ± 23.14 **G2:** 43.18 ± 20.57 CSBS-DP behavior sample mean ± SD **G1:** 56.36 ± 31.84 **G2:** 55.57 ± 38.24 Social (raw scores) **G1:** 27.34 ± 10.91 **G2:** 25.07 ± 12.10 Speech (raw scores) **G1:** 17.56 ± 14.78 **G2:** 15.95 ±16.51 Symbolic (raw scores) **G1:** 11.47 ± 10.04 **G2:** 14.55 ± 12.55	

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Koenig et al. 2010[80] **Country:** US **Intervention setting:** clinic **Enrollment period:** NR **Funding:** Organization for Autism Research, Beatrice-Renfield-Yale School of Nursing clinical Initatives fund, Research Units on Pediatric Psychopharmacology, NIMH **Design:** RTC	**Intervention:** Social skills intervention, once weekly 75 minute group intervention 75 minutes for 16 weeks. Groups had 4-5 participants plus 2 peer tutors, led by two licensed clinicians **Assessments:** Characterization of subjects: Social Communication Questionnaire (SCQ), ADOS, PDD-BI. Outcomes: Clinical Global Impressions Scale (CGI) – improvement item, Social Competency Inventory, Parent Satisfaction survey **Groups:** **G1:** intervention **G2:** control/other intervention **Provider:** Licensed clinicians (included one advanced practice RN, two social workers, four clinical psychologists) **Treatment manual followed:** Yes	**Inclusion criteria:** • age 8-11 years • full scale IQ score ≥ 70 • clinical diagnosis of PDD • met criteria for PDD on ADOS, SCQ, and Pervasive Developmental Disorders Behavior Inventory **Exclusion criteria:** • participants were screened for psychiatric problems- severe aggression, self-injury or oppositional behavior • score > 18 on irritability scale of ABC • score in clinically significant range on any CSI scale **Age, mean/yrs ± SD:** **G1:** 9.2 ± 1.2 **G2:** 9.3 ± 1.2 **Mental age, mean/yrs (range):** NR **Sex:** M, 34 (77%): F, 10 (23%):	**SCI pro social index, mean ± SD:** **G1:** 2.52 ± 0.48 **G2:** 2.67 ± 0.64 **SCI social initation index, mean ± SD:** **G1:** 2.52 ± 0.90 **G2:** 2.60 ± 0.64	**Social skills:** **SCI pro social index, mean ± SD:** **G1:** 2.83 ± 0.53 **G2:** 2.77 ± 0.56 **SCI social initation index, mean ± SD:** **G1:** 2.98 ± 0.71 **G2:** 3.00 ± 0.46 **Harms:** NR **Modifiers:** NR

	Defined protocol followed: NR **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 25 **G2:** 19 **N at follow-up:** **G1:** 23 **G2:** 18	**Race/ethnicity, n (%):** White **G1+G2:** 98% African American **G1+G2:** 2% **SES:** Maternal education, n (%): NR Household income, mean (range): NR **Diagnostic approach:** In Study/Referral Diagnostic tool/method: **Diagnostic category, n (%):** Autism **G1:** 7 **G2:** 3 PDD-NOS **G1:** 11 **G2:** 12 AD **G1:** 6 **G2:** 3 **Other characteristics, n (%):** CGI severity score, mean ± SD: **G1:** 3.67 ± 0.56 **G2:** 3.78 ± 0.55 FSIQ score, mean ± SD: **G1:** 96.4 ± 20.5		

	G2: 95.9 ± 17.3 SCQ score, mean ± SD: **G1:** 17.8 ± 7.1 **G2:** 19.6 ± 6.6 ADOS Com total, mean ± SD: **G1:** 4.5 ± 1.6 **G2:** 4.1 ± 2.1 ADOS Soc total, mean ± SD: **G1:** 7.1 ± 4.0 **G2:** 6.8 ± 3.7 ADOS Soc. And Com algorithm total, mean ± SD: **G1:** 12.0.2 ± 5.2 **G2:** 10.9 ± 5.3	

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Kouijzer et al., 2010 [81] **Country:** Netherlands **Intervention setting:** NR **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** 40 neurofeedback sessions comprising seven 3-min intervals of active neurofeedback training separated by 1-min rest intervals; during active training, criterion line placement adapted to participant ability to be rewarded 50-80% of the time; sessions conducted twice weekly **Assessments:** parent and teacher report, testing by researchers Timing: at baseline, end of Treatment and again 6 months after Treatment **Groups:** **G1:** neurofeedback **G2:** control **Provider:** Researchers **Treatment manual followed:** No **Defined protocol followed:** No **Measure of treatment fidelity reported:** No	**Inclusion criteria:** • age 8-12 years • IQ score ≥ 80 • presence of autistic disorder, Asperger disorder, or PDD-NOS **Exclusion criteria:** • use of medication • history of severe brain injury • co-morbidity (e.g. ADHD, epilepsy) **Age, mean/yrs ± SD:** **G1:** 9.43 ± 1.44 **G2:** 9.14 ± 1.34 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 9 (90) **G2:** 8 (80) F, n (%): **G1:** 1 (10) **G2:** 2 (20) **Race/ethnicity, n (%):** NR **SES:** NR	**Parent Report:** **Social skills:** SCQ total: **G1:** 14.20 ± 6.56 **G2:** 16.67 ± 3.96 SRS total: **G1:** 79.60 ± 35.90 **G2:** 89.11 ± 19.47 CCC-2 total: **G1:** 106.20 ± 16.01 **G2:** 104.22 ± 15.96 Social awareness: **G1:** 11.80 ± 5.02 **G2:** 12.77 ± 2.81 Social cognition: **G1:** 14.00 ± 7.27 **G2:** 17.55 ± 3.60 Social motivation: **G1:** 15.00 ± 7.48 **G2:** 14.55 ± 5.43 Social relations: **G1:** 13.50 ± 3.34 **G2:** 15.33 ± 1.41 Interests: **G1:** 13.00 ± 1.94 **G2:** 14.56 ± 1.66 Reciprocal social interactions: **G1:** 4.10 ± 2.46	**Parent report (end of Treatment):** **Social skills:** SCQ total: **G1:** 5.80 ± 4.16 **G2:** 15.56 ± 5.79 p=0.006 SRS total: **G1:** 52.50 ± 33.07 **G2:** 88.22 ± 41.13 p=NS CCC-2 total: **G1:** 86.80 ± 23.47 **G2:** 106.11 ± 17.98 p=0.021 Social awareness: **G1:** 8.90 ± 4.0 **G2:** 12.11 ± 5.44 p=NS Social cognition: **G1:** 8.80 ± 4.89 **G2:** 18.44 ± 8.11 p=NS Social motivation: **G1:** 10.20 ± 8.68 **G2:** 14.66 ± 7.15 p=NS Social relations: **G1:** 12.90 ± 3.31 **G2:** 14.22 ± 3.49 p=NS

	Co-interventions held stable during treatment: NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 10 **G2:** 10 **N at follow-up:** **G1:** 10 **G2:** 10 **N at 12 month follow-up (G1 only):** **G1:** NR	**Diagnostic approach:** Referral Diagnostic tool/method: Met criteria for DSM-IV diagnosis of autistic disorder, Asperger disorder, or PDD-NOS **Diagnostic category, n (%):** Autism **G1:** 6 (60) **G2:** 2 (20) PDD-NOS **G1:** 4 (40) **G2:** 4 (40) Aspergers **G1:** 0 (0) **G2:** 4 (40) **Other characteristics, n (%):** SCQ total, mean ± SD: **G1:** 14.2 ± 6.56 **G2:** 16.67 ± 3.97	**G2:** 3.78 ± 2.22 **Communication/ language:** Communication (SRS): **G1:** 25.80 ± 11.97 **G2:** 27.77 ± 8.34 Speech production: **G1:** 12.60 ± 3.89 **G2:** 10.89 ± 3.78 Syntax: **G1:** 12.70 ± 2.66 **G2:** 12.11 ± 3.37 Sematics: **G1:** 13.10 ± 1.66 **G2:** 11.33 ± 2.78 Coherence: **G1:** 13.70 ± 3.02 **G2:** 12.00 ± 4.24 Inappropriate initialization: **G1:** 12.70 ± 3.33 **G2:** 14.11 ± 1.36 Stereotyped conversation: **G1:** 13.20 ± 3.64 **G2:** 14.00 ± 2.44 Context use: **G1:** 13.70 ± 3.62 **G2:** 15.44 ± 1.67 Non-verbal communication: **G1:** 14.50 ± 1.95 **G2:** 14.33 ± 2.59 Pragmatics: **G1:** 54.10 ± 10.07	Interests: **G1:** 10.50 ± 3.10 **G2:** 13.89 ± 2.36 p=NS Reciprocal social interactions: **G1:** 1.90 ± 1.44 **G2:** 5.33 ± 2.64 P<0.05 Communication (SRS): **G1:** 17.00 ± 12.02 **G2:** 27.77 ± 14.37 p=NS Speech production: **G1:** 9.20 ± 2.82 **G2:** 10.56 ± 3.97 p=NS Syntax: **G1:** 10.70 ± 3.74 **G2:** 12.56 ± 2.74 p=NS Sematics: **G1:** 9.70 ± 3.46 **G2:** 12.33 ± 2.00 p=0.01 Coherence: **G1:** 11.20 ± 3.55 **G2:** 13.67 ± 3.39 p=0.004 Inappropriate initialization: **G1:** 10.00 ± 3.46 **G2:** 13.67 ± 3.04

	G2: 57.89 ± 6.13 Communication (SCQ): **G1:** 5.90 ± 2.92 **G2:** 6.11 ± 1.83 **Repetitive behavior:** Autistic mannerisms: **G1:** 13.00 ± 7.31 **G2:** 16.44 ± 5.17 Restricted, repetitive, and stereotyped behavior: **G1:** 3.50 ± 2.63 **G2:** 5.89 ± 1.16 **Educational/ cognitive/ academic attainment:** Auditory selective attention: **G1:** 54.30 ± 25.72 **G2:** 42.66 ± 23.01 Inhibition of verbal responses: **G1:** 97.00 ± 57.33 **G2:** 71.10 ± 38.00 Inhibition of motor responses: **G1:** 86.48 ± 12.87 **G2:** 84.05 ± 12.43 Cognitive flexibility, set shifting: **G1:** 31.20 ± 43.12 **G2:** 21.30 ± 22.652 Cognitive flexibility, concept generation: **G1:** 3.36 ± 1.52	p=0.042 Stereotyped conversation: **G1:** 11.20 ± 3.76 **G2:** 13.33 ± 3.57 p=NS Context use: **G1:** 12.00 ± 4.24 **G2:** 15.56 ± 2.29 p=NS Non-verbal communication: **G1:** 11.80 ± 3.15 **G2:** 14.67 ± 1.93 p=0.022 Pragmatics: **G1:** 45.00 ± 13.44 **G2:** 60.56 ± 16.68 p=NS Communication (SCQ): **G1:** 2.50 ± 2.12 **G2:** 5.22 ± 2.43 p=0.037 **Repetitive behavior:** Autistic mannerisms: **G1:** 7.60 ± 6.36 **G2:** 16.33 ± 10.25 p=NS Restricted, repetitive, and stereotyped behavior: **G1:** 1.20 ± 1.31 **G2:** 4.56 ± 2.96 p=NS

G2: 3.09 ± 1.32 Goal setting: **G1:** 71.09 ± 15.54 **G2:** 59.00 ± 14.51 Speed and efficiency: **G1:** 1.14 ± 0.10 **G2:** 1.05 ± 0.17	**Educational/ cognitive/ academic attainment:** Auditory selective attention: **G1:** 58.09 ± 31.08 **G2:** 55.84 ± 20.98 p=NS Inhibition of verbal responses: **G1:** 43.50 ±21.69 **G2:** 43.50 ± 22.98 p=NS Inhibition of motor responses: **G1:** 91.56 ± 9.78 **G2:** 88.68 ± 12.25 p=NS Cognitive flexibility, set-shifting: **G1:** 13.40 ± 16.74 **G2:** 35.20 ± 26.35 p=0.045 Cognitive flexibility, concept generation: **G1:** 5.55 ± 0.69 **G2:** 4.41 ± 0.81 p=NS Goal setting: **G1:** 78.41 ± 13.70 **G2:** 62.97 ± 10.73 p=NS Speed and efficiency: **G1:** 1.06 ± 0.13 **G2:** 1.00 ± 0.16

p=NS
All p-values represent time x group interactions
Harms: NR

Modifiers: NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Lopata et al. 2010[82] **Country:** US **Intervention setting:** college campus **Enrollment period:** NR **Funding:** NR **Design:** RCT	**Intervention:** Manualized social treatment program conducted over 5 weeks with five treatment cycles per day, 70 minutes each (20 min of intensive instruction and 50 minute therapeutic activity). Instruction and therapeutic activities targeting social skills, face-emotion recognition, interest expansion, and interpretation of non-literal language. **Assessments:** Adapted Skillstreaming Checklist (ASC), Social Responsiveness Scale (SRS), Skillstreaming Knowledge Assessment (SKA), Diagnositc Analysis of Nonverbal Accuracy2 (DANVA2), Parent, Child and Staff satisfaction surveys, Comprehensive Assessment of Spoken Language (CASL), Wechsler Intelligence Scale for Children, 4th edition (WISC-IV) **Groups:** **G1:** Skillstreaming	**Inclusion criteria:** • written diagnosis of HFASD • WISC-IV short form IQ > 70, WISC-IV Verbal Comprehension index (VCI) or Perceptual Reasoning Index (PR) ≥ 80 • expressive or receptive language score ≥ 80 on short form of the Comprehensive Assessment of Spoken Language (CASL) **Exclusion criteria:** • severe physical aggression **Age, mean/yrs ± SD:** **G1:** 9.39 ± 1.72 **G2:** 9.56 ± 1.54 **Mental age, mean/yrs (range):** NR **Sex:** M, n (%): **G1:** 17 (94.4) **G2:** 17 (94.4) F, n (%): **G1:** 1 (5.6) **G2:** 1 (5.6)	**Parent ratings** ASC Total score, mean ± SD: **G1:** 109.67 ± 15.76 **G2:** 101.78 ± 20.47 SRS Total score, mean ± SD: **G1:** 79.94 ± 11.02 **G2:** 81.12 ± 13.78 Withdrawal, mean ± SD: **G1:** 68.78 ± 12.14 **G2:** 74.68 ± 12.48 Social Skills, mean ± SD: **G1:** 39.22 ± 9.10 **G2:** 34.22 ± 7.84 **Direct child measures ratings** SKA Total score, mean ± SD: **G1:** 46.39 ± 17.72 **G2:** 48.64 ± 12.08 DANVA-2 Child faces score, mean ± SD: **G1:** 88.97 ± 22.45 **G2:** 91.44 ± 15.96 CASL Idioms, mean ± SD: **G1:** 8.89 ± 6.82 **G2:** 11.44 ± 7.97	**Parent ratings** ASC Total score, mean ± SD: **G1:** 119.67 ± 17.13 **G2:** 103.72 ± 17.23 SRS Total score, mean ± SD: **G1:** 73.67 ± 11.42 **G2:** 82.53 ± 13.77 Withdrawal, mean ± SD: **G1:** 63.39 ± 8.76 **G2:** 76.83 ± 10.38 Social Skills, mean ± SD: **G1:** 41.39 ± 7.27 **G2:** 35.11 ± 7.65 **Direct child measures ratings** SKA Total score, mean ± SD: **G1:** 58.83 ± 11.50 **G2:** 43.31 ± 13.86 DANVA-2 Child faces score, mean ± SD: **G1:** 99.03 ± 11.44 **G2:** 91.86 ± 19.38 CASL Idioms, mean ± SD: **G1:** 12.94 ± 7.26 **G2:** 12.50 ± 9.34 **Harms:** NR

	intervention **G2:** waitlist **Provider:** Graduate and undergraduate students from psychology and education **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment:** Yes **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 18 **G2:** 18 **N at follow-up:** **G1:** 18 **G2:** 18	**Race/ethnicity, n (%):** White **G1:** 16 (88.9) **G2:** 16 (88.9) African-American **G1:** 1 (5.6) **G2:** 1 (5.6) Other **G1:** 1 (5.6) **G2:** 1 (5.6) **SES:** Parent education, years mean ± SD: **G1:** 14.78 ± 2.50 **G2:** 15.58 ± 2.08 Household income, mean (range): NR **Diagnostic approach:** In Study/Referral Diagnostic tool/method: NR **Diagnostic category, n (%):** Asperger's **G1:** 15 (83.3) **G2:** 13 (72.2) PDD **G1:** 2 (11.1) **G2:** 5 (27.8) HFA **G1:** 1 (5.6) **G2:** 0 **Other characteristics**, n		**Modifiers:** NR

(%):
WISC-IV short form IQ, mean ± SD
G1: 101.63 ± 13.75
G2: 104.45 ± 15.46

CASL4 Expressive language
G1: 101.11 ± 13.57
G2: 104.78 ± 17.59

CASL4 Receptive language
G1: 106.17 ± 11.96
G2: 107.83 ± 16.92

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: McConkey et al. 2010[83] **Country:** Northern Ireland **Intervention setting:** Home **Enrollment period:** NR **Funding:** Grants to Autism NI from the Department of Health, Social Services and Public Safety and by special project funding from the Southern Health and Social Services Board **Design:** Prospective cohort	**Intervention:** Early intervention program (known as Keyhole), based mainly around TEACCH, Picture Exchange Communication System (PECS) and Hanen approaches; Delivered to families through 15–18 home visits over a nine-month period in 2 separate geographical areas **Assessments:** Psycho-Educational Profile – Revised (PEP-R) Gilliam Autism Rating Scale, Vineland Adaptive Behavior Scales, The General Health Questionnaire (GHQ). Independent personnel who had not been involved in delivering the intervention collected the post-intervention data **Groups:** **G1:** Early intervention program **G2:** contrast **Provider:** Early	**Inclusion criteria:** • confirmed diagnosis of ASD from a specialist clinic that served the geographical area in which the project was located. • not older than four years of age and should not be attending nursery school (attendance at a playgroup was permitted) • not in receipt of Speech and Language Therapy services provided by the Health and Social Care (HSC) Trusts in which the project was located • families had to consent to taking part in both the intervention and its evaluation, and to being interviewed at home by a university researcher **Exclusion criteria:** see inclusion criteria **Age, mean/yrs :** **G1:** 2.8 years	**PEP-R, mean (SD):** **G1:** Imitation: 4.9 ± 4.7 Perception: 7.9 ± 3.3 Fine-motor: 7.07 ± 3.5 Gross-motor: 10.8 ± 3.4 Eye–hand: 4.2 ± 2.7 Cognitive – non-verbal: 5.2 ± 4.6 Cognitive – verbal : 2.8 ± 3.7 Developmental age: mean ± sd G1: 20.1 ± 7.4 **Behavior:** % children with problems reported to be 'getting better' in each group: Problems with language **G1:** 2.8 **G2:** 32.1 Problems with play **G1:** 2.8 **G2:** 17.9 Relating to other people **G1:** 8.3 **G2:** 21.4 Unusual interest in toys/objects **G1:** 5.6 **G2:** 3.7	**PEP-R, mean (SD):** **G1:** Imitation: 8.8 ± 5.0 Perception: 10.4 ± 3.1 Fine-motor: 10.5 ± 3.8 Gross-motor: 15.0 ± 3.5 Eye–hand: 7.0 ± 3.1 Cognitive – non-verbal: 12.2 ± 6.4 Cognitive – verbal: 7.57 ± 5.8 Developmental age: mean ± sd G1: 29.7 ± 11.2 Significant improvement in all subscales at p<0.001 **Behavior:** % children with problems reported to be 'getting better' in each group; p-values are within-group change comparisons over time: Problems with language **G1:** 60 (p< .001) **G2:** 41.7 (NS) Problems with play **G1:** 54.3 (p<.001) **G2:** 37.5 (p<.005) Relating to other people **G1:** 25.7 (p<.005)

	intervention therapists (speech and language therapists with an interest in ASD) **Treatment manual followed:** NR **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 36 **G2:** 26 **N at follow-up:** **G1:** 35 **G2:** 26	**G2:** 3.4 years **Mental age, mean/yrs (SD):** NR **Sex, n (%):** M: 55 (90%) F: 6 (10%). **Race/ethnicity, n (%):** % minority status: **SES:** 44 families (73%) owned their own homes with 7 (13%) renting and 4 (7%) living with their parents. **Maternal education, n (%)**: completed third level: 22 (37%) taken GCSEs: 28 (47%) Left school: 7 (12%) **Household income:** There was a wage-earner in 36 (64%) of families but not in 20 (36.0%). Diagnostic approach: In Study Diagnostic tool/method: diagnosis at a specialist clinic **Diagnostic category, n (%):** Autism : 61 (100%) **Other characteristics, n**	Difficulty in imitating **G1:** 2.8 **G2:** 25 Adaptation to change **G1:** 5.6 **G2:** 17.9 **Vineland scores, Mean (SD):** Vineland – communication **G1:** 61.5 ± 8.2 **G2:** 62.6 ± 11.9 Vineland – socialization **G1:** 63.7 ± 8.8 **G2:** 64.2 ± 8.5 Vineland – daily living **G1:** 65.9 ± 8.9 **G2:** 68.5 ± 14.8 Vineland – motor skills **G1:** 75.7 ± 16.4 **G2:** 77.0 ± 16.6 Vineland – adaptive behaviour **G1:** 61.3 ± 8.5 **G2:** 62.3 ± 9.6 **Mean (SD):** GARS – autism quotient **G1:** 85.4 ± 15.3 **G2:** 88.6 ± 10.9 GARS – percentile scores **G1:** 24.9 ± 25.2 **G2:** 27.1 ± 18.1	**G2:** 29.2 (NS) Unusual interest in toys/objects **G1:** 22.9 (NS) **G2:** 16.7 (NS) Difficulty in imitating **G1:** 22.9 (p<.005) **G2:** 29.2 (NS) Adaptation to change **G1:** 45.7 (NS) **G2:** 25 (NS) **Vineland scores, Mean (SD):** Vineland – communication **G1:** 69.5 ± 16.2 **G2:** 60.7 ± 12.3 Vineland – socialization **G1:** 75.9 ± 20.6 **G2:** 69.5 ± 13.1 Vineland – daily living **G1:** 71.2 ± 15.5 **G2:** 66.1 ± 15.3 Vineland – motor skills **G1:** 78.1 ± 20.1 **G2:** 72.9 ± 18.5 Vineland – adaptive behavior **G1:**67.7 ± 11.8 **G2:**61.7 ± 11.8 **Mean (SD):** GARS – autism quotient

		(%): Sensory impairment: 8 (13); Epilepsy 8 (13%) Physical impairment 1 (2%)	**Mean (SD):** GHQ – overall score **G1:** 7.2 ± 4.4 **G2:** 5.7 ± 4.4 GHQ – somatic **G1:** 2.8 ± 1.4 **G2:** 1.7 ± 1.7 GHQ – anxiety **G1:** 2.7 ± 2.1 **G2:** 2.3 ± 2.2 QRS total score **G1:** 8.7 ± 7.6 **G2:** 16.6 ± 6.2	**G1:** 89.2 ± 13.2 **G2:** 99.4 ± 20.4 GARS – percentile scores **G1:** 29.7 ± 25.2 **G2:** 48.1 ± 31.4 **Mean (SD):** GHQ – overall score **G1:** 1.6 ± 2.3 **G2:** 5.3 ± 6.0 GHQ – somatic **G1:** .5 ± .8 **G2:** 1.8 ± 2.4 GHQ – anxiety **G1:** .9 ± 1.8 **G2:** 2.4 ± 2.4 QRS total score **G1:** 14.3 ± 6.5 **G2:** 16.0 ± 7.6 **Harms** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Oosterling et al. 2010[84] **Country:** Netherlands **Intervention setting:** Clinic/home **Enrollment period:** Spring/2004-spring/2007 **Funding:** Grant from Korczak Foundation and European Union **Design:** RCT	**Intervention:** 'Parent Focus Training:' Two-year home-based parent training program, focused on stimulating joint attention and language skills. Started with 4 weekly 2-hour group sessions with parents, followed by individual home visits every 6 weeks during first year. Home visits were at three month intervals in second year **Assessments:** Dutch version of MacArthur Communicative Development Inventory (NCD-I), Child Behavior Checklist 1 ½-5, Symptom Checklist-90, Nijmeegse Ouderlijk Stress Index, Infant Characteristics Questionnaire, Clinical Global Impression-Improvement Scale, Erickson scales, Autism Diagnostc Observation Schedule, Autism Diagnostic Interview-Revised, Mullen Scales of Early Learning, Psycho Educational Profile – Revised,	**Inclusion criteria[a]:** • age 12-42 months • clinical diagnosis of autism and developmental age at least 12 months • clinical diagnosis of PDD-NOS and developmental age at least 12 months and Developmental Quotient < 80 **Exclusion criteria:** • substantial other problems in family (severe parental psychopathology, financial/housing problems, marital conflicts) • insufficient parental proficiency in Dutch **Age, mean/months ± SD:** **G1:** 35.2 ± 5.5 **G2:** 33.3 ± 6.4 **Mental age, mean/yrs (range):**NR **Sex: Male %** **G1:** 75 **G2:** 80.6 **Race/ethnicity, n (%):** NR	DQ, mean ± SD **G1:** 58.4 ± 16.8 **G2:** 58.0 ± 16.9 ADOS, mean ± SD SA **G1:** 15.0 ± 4.6 **G2:** 14.8 ± 4.9 RRB **G1:** 2.8 ± 1.7 **G2:** 2.8 ± 1.9 ADI-R RSI: **G1:** 16.3 (5.1) **G2:** 14.7 (4.5) Communication: **G1:** 11.2 (2.4) **G2:** 10.3 (2.8) RRSPB: **G1:** 4.1 (2.1) **G2:** 3.0 (1.8) MacArthur N-CDI Words understood **G1:** 177.9 ± 122.5 **G2:** 181.5 ± 121.4 Words said **G1:** 106.8 ± 122.2 **G2:** 101.7 ± 109.7 Gestures produced **G1:** 29.1 ± 13.7	ADOS, change Level of non-echoed language on 6 point scale **G1:** -1.6 ± 1.1 **G2:** -1.3 ± 1.2 $p < 0.001$ Joint attention factor **G1:** -0.8 ± 2.3 **G2:** -0.9 ± 0.2 Social affect **G1:** -2.5 ± 4.0 **G2:** -2.3 ± 3.7 $p < 0.05$ **Social skills: Communication/ language, mean change ± SD:** MacArthur N-CDI Words understood **G1:** 62.0 ± 75.0 **G2:** 35.2 ± 66.1 $p < 0.01$ Words said **G1:** 75.5 ± 78.8 **G2:** 56.1 ± 97.2 $p < 0.05$ Gestures produced **G1:** 6.7 ± 10.2 **G2:** 6.3 ± 9.0 $p < 0.01$

	Groups: **G1:** nonintensive parent training + care as usual **G2:** care as usual (special nursery with music, speech, play, and motor therapy) **Provider:** Psychologists or sociotherapists worked as parent-trainers **Treatment manual followed:** NR **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Co-interventions held stable during treatment: Concomitant therapies, n (%):** Care as usual, mean ± SD Day care, average number of daily periods in child special day care of medical nursery **G1:** 5.2 ± 1.7 **G2:** 4.2 ± 2.9 Speech and language therapy, minutes per week **G1:** 16.7 ± 22.4 **G2:** 19.1 ± 22.0	**SES:** Maternal education, %: Low **G1:** 41.7 **G2:** 41.9 Middle **G1:** 33.3 **G2:** 35.5 High **G1:** 25.0 **G2:** 22.6 Paternal education, %: Low **G1:** 34.3 **G2:** 56.7 Middle **G1:** 20.0 **G2:** 26.7 High **G1:** 45.7 **G2:** 16.7 Household income, mean (range): NR **Diagnostic approach:** Referral based on screening positive on the Early Screening of Autistic Traits Questionnaire Diagnostic tool/method: Consensus diagnosis of two professionals, ADOS, ADI-R and psychometric testing of developmental	**G2:** 30.1 ± 13.6 Erikson scales, mean ± SD Non-negativity **G1:** 5.9 ± 1.8 **G2:** 6.2 ± 0.8 Non-avoidance **G1:** 3.9 ± 1.5 **G2:** 4.1 ± 1.3 Compliance **G1:** 3.8 ± 1.6 **G2:** 4.2 ± 1.3 CBCL mean ± SD Internalizing **G1:** 21.3 ± 9.4 **G2:** 16.9 ± 7.3 Externalizing **G1:** 21.2 ± 11.1 **G2:** 19.4 ± 9.0 ICQ mean ± SD Total score **G1:** 146.4 ± 27.0 **G2:** 141.0 ± 18.0	Erikson scales Non-negativity **G1:** 0.7 ± 2.1 **G2:** 0.3 ± 1.3 *p* =ns Non-avoidance **G1:** 0.7 ± 1.5 **G2:** 0.5 ± 1.4 *p* =ns Compliance **G1:** 0.9 ± 1.5 **G2:** 0.5 ± 1.5 *p* =ns **Harms:** NR **Modifiers:** NR

	Physical therapy, minutes per week **G1:** 8.3 ± 18.4 **G2:** 6.4 ± 14.9 Other individual therapy, min/week **G1:** 24.9 ± 59.5 **G2:** 22.7 ± 39.7 Parental counseling, min/week **G1:** 21.0 ± 30.9 **G2:** 28.2 ± 36.2 **N at enrollment:** **G1:** 40 **G2:** 35 **N at follow-up:** **G1:** 36 **G2:** 31	abilities **Diagnostic category, %:** Autism **G1:** 91.7 **G2:** 83.9 PDD-NOS **G1:** 8.3 **G2:** 16.1 **Other characteristics**, n (%)**:** SCL-90 Mothers (n = 57) **G1:** 126.7 (31.2) **G2:** 123 (28.0) Fathers (n = 47) **G1:** 113.2 (33.7) **G2:** 112.3 (21.9)

Comments: [a] Authors note that 8 participants who did not meet these criteria were included in the study (G1: 5 G2: 3). They were included based on clinical judgment of room for improvement. 2 of these had no endpoint data.

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Peters-Scheffer et al. 2010[85] **Country:** Netherlands **Intervention setting:** Preschool- day care centers **Enrollment period:** NR **Funding:** Stichting De Driestroom, Elst (The Netherlands) **Design:** Non-RCT pre-post	**Intervention:** Low intensity behavioral treatment (elements of TEACCH) on average 6.5 hrs / week + 5–10 (M= 6.29; SD = 1.31) hrs of one-to-one treatment / week, based on Lovaas + informal use of ABA by teachers Control group attended preschools in which no one-to-one behavioral treatment was given **Assessments:** Wechsler Preschool and Primary Scale of Intelligence-Revised, SON-2.5–7, Bayley Scales of Infant Development, VABS-composite, CBCL, PDD-MRS, BSID-II or SON-2.5-7 administered pre-treatment and after 8 months. VABS, CBCL, and PDD-MRS administered pre- and post-treatment; also at two, four, and six months of treatment. **Provider:** Trainers and teachers of the preschool; treatment supervised by special	**Inclusion criteria:** • a diagnosis of Autistic Disorder or PDD-NOS and intellectual disabilities (ID) based on DSM-IV criteria established by licensed and independent psychologist or psychiatrist; level of ID assessed by standard intelligence tests (e.g., Wechsler Preschool and Primary Scale of Intelligence- revised, SON-2.5-7, Bayley Scales of Infant Development) • chronological age below 7 years • absence of medical conditions (e.g., visual impairment; uncontrolled epilepsy) that could interfere with treatment **Exclusion criteria:** • see inclusion **Age, mean ± SD months (range):** **G1:** 53.50 ± 5.52 (42–62) **G2:** 52.95 ±11.14 (38–75**)**	Developmental age in months **G1:** 25.92 ± 7.57 **G2:**23.32 ± 6.33 Mental developmental index/IQ **G1:** 47.00 ± 10.33 **G2:** 45.73 ± 15.99 VABS-composite in months **G1:** 20.83 ± 6.69 **G2:** 19.18 ± 4.14 VABS-communication in months **G1:** 26.92 ± 12.12 **G2:** 25.00 ± 10.00 VABS-daily living in months **G1:** 23.83 ± 7.28 **G2:** 20.14 ± 4.68 VABS-socialization **G1:** 20.75 ± 4.54 **G2:** 24.64 ± 8.18 CBCL-total **G1:** 60.00 ± 8.37 **G2:** 66.91 ± 7.70 CBCL-internalizing **G1:** 60.58 ± 5.58 **G2:** 67.55 ± 6.27 CBCL-externalizing	Developmental age in months **G1:** 34.83 ± 10.89 **G2:** 25.73 ± 8.26 Mental developmental index/IQ **G1:** 55.83 ±14.94 **G2:** 43.73 ± 16.74 VABS-composite in months **G1:** 31.75 ± 10.96 **G2:** 22.05 ± 7.47 VABS-communication in months **G1:** 39.42 ± 15.39 **G2:** 29.95 ± 13.39 VABS-daily living in months **G1:** 33.25 ± 9.04 **G2:** 23.23 ± 7.70 VABS-socialization **G1:** 34.08 ± 8.14 **G2:** 25.14 ±7.21 CBCL-total **G1:** 58.25 ± 8.02 **G2:** 63.23 ± 7.98 CBCL-internalizing **G1:** 59.08 ± 7.74 **G2:** 64.41 ± 8.45

	educator with 5 years of experience in applying ABA in young children **Treatment manual followed:** Yes **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** Yes **Groups:** **G1:** Early intervention **G2:** control **Co-interventions held stable during treatment:** NR **Frequency of contact during study:** baseline, 2, 3,4 months of Treatment and end of 8 months of Treatment **Concomitant therapies, n (%):** Individual physiotherapy, speech therapy, music therapy or play therapy with a maximum of 1hr /week :100% **N at enrollment:** **G1:** 12 **G2:** 22	**Mental Developmental Index/IQ, mean ± SD (range):** **G1:** 47.00 ± 10.33 (31-64) **G2:** 45.73 ± 15.99 (21-77) **Sex:** NR **Race/ethnicity, n (%):** NR **SES:** NR **Diagnostic approach:** Referral Diagnostic tool/method: DSM-IV **Diagnostic category, n (%):** NR **Other characteristics, n (%):** NR	**G1:** 58.92 ± 10.82 **G2:** 63.59 ± 7.89 PDD-MRS raw score **G1:** 11.58 ± 4.42 **G2:** 12.91 ± 3.79	CBCL-externalizing **G1:** 54.33 ± 8.52 **G2:** 58.86 ± 6.26 PDD-MRS raw score **G1:**10.25 ± 3.14 **G2:**11.27 ± 3.84 **Harms:** NR **Modifiers:** NR

	N at follow-up: **G1:** 12 **G2:** 22

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Wong 2010[86] **Country:** Hong Kong, China **Intervention setting:** Clinic **Enrollment period:** Jan – Dec 2007 **Funding:** NR **Design:** RCT, cross-over	**Intervention:** A short 2-week Early intervention with ten 30-min sessions, with a target improving communication and Social interaction. Intervention given between baseline and Time 1 for the intervention group and between Time 1 and Time 2 for the control group. The control Group undertook the Intervention starting from Week 5 and received the same 10-session intervention. By Time 2, both groups had completed the intervention, and they were combined* to give a larger sample size for detecting intervention effects **Assessments:** ADOS, Ritvo-Freeman Real Life Rating Scale, Symbolic Play Test, and Parenting Stress Index. Done at 3 time points (baseline, time 1, time 2). **Groups:**	**Inclusion criteria:** • consecutive newly diagnosed children with autism • children with autism referred to DKCAC for developmental assessment **Exclusion criteria:** NR **Age, mean ± SD, mos:** **G1:** 25.33 ± 6 **G2:** 27.88 ± 5.57 **Mental age,** mean ± SD mos (SD): **G1:** 17.85 ± 4.16 **G2:** 17.91 ± 4.49 **Sex, n (%):** M: 16 (94) F: 1 (6) Male **G1:** 8 **G2:** 8 Female **G1:** 1 **G2:** 0 **Race/ethnicity, n (%):** % minority status: NR **SES:** NR Maternal education	**Median (Range):** **ADOS (Communication and language):** **G1** (n = 9): Total: 11.0 (7.0–13.0) Vocalization: 2.0 (1.0–3.0) Pointing: 3.0 (1.0–3.0) Gestures: 2.0 (0.0–2.0) **G2** (n = 8): Total: 10.0 (7.0–14.0) Vocalization: 2.0 (2.0–2.0) Pointing: 3.0 (1.0–3.0) Gestures: 1.0 (0.0–2.0) **ADOS (Reciprocal social interaction)** : **G1:** Total: 22.0 (11.0–28.0) Unusual eye contact: 2.0 (2.0–2.0) Integration of gaze and other behaviors during social overtures: 2.0 (1.0–3.0) Requesting: 2.0 (1.0–3.0) **G2:** Total: 18.5 (13.0–26.0) Unusual eye contact: 2.0 (0.0–2.0) Integration of gaze and other behaviors during social overtures: 1.5 (1.0–3.0) Requesting: 2.0 (1.0–3.0)	**Median (Range):** **ADOS (Communication and language) :** No significant group difference in communication (X^2 = 0.95, p = 0.331) **G1:** Total: 7.0 (4.0–9.0) Vocalization: 1.0 (1.0–2.0) Pointing: 2.0 (1.0–3.0) Gestures: 1.0 (0.0–2.0) **G2:** Total: 7.50 (6.0–11.0) Vocalization: 1.0 (1.0–3.0) Pointing: 2.0 (0.0–3.0) Gestures: 1.0 (0.0–1.0) **ADOS (Reciprocal social interaction) :** No between group differences observed (X^2 = 0.46, p = 0.497) **G1:** Total: 15.0 (7.0–22.0) Unusual eye contact: 2.0 (0.0–2.0) Integration of gaze and other behaviors during social overtures: 1.0 (0.0–2.0)

	G1: Early intervention **G2:** control **Provider:** Trainer- autism therapist **Treatment manual followed:** NR **Defined protocol followed:** yes **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** None **Concomitant therapies, n (%):** none **N at enrollment:** **G1:** 9 **G2:** 8 **N at follow-up:** **G1:** 9 **G2:** 8	NR Household income, mean (range): NR **Diagnostic approach:** In Study Diagnostic tool/method: DSM-IV, ADI-R, ADOS **Diagnostic category, n (%):** Autism : 17 (100) **Other characteristics:** CARS, mean ± SD, (range) **G1:** 35.67 ± 4.64 (29-41.5) **G2:** 36.88 ± 4.24 (30-40.5)	**SPT (Symbolic play) :** Standard score **G1:**12.0 (12.0–21.9) **G2:**13.7 (12.0–28.5)	Requesting: 0.0 (0.0–2.0) **G2:** Total: 16.0 (10.0–24.0) Unusual eye contact: 2.0 (2.0–2.0) Integration of gaze and other behaviors during social overtures: 1.0 (1.0–2.0) Requesting: 1.0 (0.0–2.0) **SPT (Symbolic play) :** Standard score **G1:** 12.7 (12.0–27.1) **G2:** 13.7 (12.0–28.5) **Commonly occurring co-morbidities:** No co-morbid neurological or psychiatric disorders **Harms:** NR **Modifiers:** NR

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures*	Outcomes
Author: Aman et al. 2009[35-38] **Country:** US **Intervention setting:** Clinic, home **Enrollment period:** NR **Funding:** NIMH **Design:** RCT Note: See earlier study[87] reporting on this population in 2011 AHRQ review[9]	**Intervention:** Risperidone (0.5 to 3.5 mg/day) or aripiprazole if risperidone was ineffective ((aripiprazole started at 2 mg and adjusted up to 15 mg) or a combination of medication plus parent training. Parents of children in combination group received an average of 11.4 parent training sessions. **Assessments:** Home Situations Questionnaire (HSQ), Aberrant Behavior Checklist-Irritability (ABC-I), Vineland Adaptive Behavior Scales (VABS), Noncompliance index. Assessed weekly for 8 weeks then every 4 weeks until week 24. Follow-up study at 1 year **Groups:** **G1:** risperidone **G2:** risperidone + parent training **Co-interventions held stable during treatment:** Yes **Frequency of contact**	**Inclusion criteria:** • age between 4 and 14 years • DSM-IV-TR diagnosis of autistic disorder, Asperger's disorder, or PDD-NOS based on clinical assessment and corroborated by the ADI-R • serious behavioral problems (e.g tantrums, aggression and self-injury) evidenced by score ≥ 18 on ABC-Irritability subscale and CGI-severity score ≥ 4 • IQ ≥ 35 or mental age of 18 months from Stanford-Binet 5, Leiter International Performance Scale or Mullen Scales of Early Learning • anticonvulsant treatment permissible if medication was stable (≥ 4 wks) and subject was seizure free (≥ 18 mos) **Exclusion criteria:** • significant medical condition by history,	**HSQ, mean ± SD:** Average severity score **G1:** 4.16 ± 1.47 **G2:** 4.31 ± 1.67 "Yes" count **G1:** 18.9 ± 3.46 **G2:** 18.6 ± 4.65 **ABC, mean ± SD:** Irritabilty **G1:** 29.7 ± 6.10 **G2:** 29.3 ± 6.97 Social withdrawal **G1:** 17.1 ± 8.37 **G2:** 15.2 ± 9.01 Stereotypic behavior **G1:** 10.6 ± 5.46 **G2:** 7.59 ± 5.20 Hyperactivity/non compliance **G1:** 36.1 ± 6.86 **G2:** 35.3 ± 9.30 Inappropriate speech **G1:** 6.37 ± 4.03 **G2:** 5.75 ± 3.43 **VABS, mean ± SD: Standard Score** Daily living skills **G1:** 41.14 ± 19.81 **G2:** 50.79 ± 18.49	**24 Week Follow-Up** **VABS, mean ± SD: Standard Score** Daily living skills **G1:** 45.34 ± 20.48 **G2:** 55.65 ± 21.86 Socialization **G1:** 56.59 ± 17.38 **G2:** 67.42 ± 18.48 Communication **G1:** 53.57 ± 20.23 **G2:** 63.90 ± 22.65 Adaptive Composite **G1:** 47.84 ± 15.81 **G2:** 57.87 ± 19.03 **Age Equivalent Score** Daily living skills **G1:** 3.49 ± 1.72 **G2:** 4.36 ± 2.25 Socialization **G1:** 2.71 ± 1.51 **G2:** 3.99 ± 2.56 Communication **G1:** 3.42 ± 2.18 **G2:** 4.58 ± 2.85 Adaptive Composite **G1:** 12.88 ± 10.83 **G2:** 8.41 ± 8.69 **One Year Follow-up****

	during study: ~weekly across groups **Concomitant therapies, n (%):** NR **N at enrollment:** **G1:** 49 **G2:** 75 **N at follow-up (1 year):** **G1:** 36 **G2:** 51	exam or lab test • lifetime diagnosis of psychosis, bipolar disorder or current diagnosis of major depression, obsessive-compulsive disorder, substance abuse, or girls with positive Beta HCG pregnancy test **Age, mean/yrs ± SD:** **G1:** 7.5 ± 2.80 **G2:** 7.38 ± 2.21 **Mental age, mean/yrs (range):** NR **Sex:** NR Race/ethnicity, n (%): White/non Hispanic **G1:** 34 (69.4) **G2:** 59 (78.7) Hispanic **G1:** 7 (14.3) **G2:** 4 (5.3) African American **G1:** 7 (14.3) **G2:** 9 (12.1) Asian American **G1:** 0 **G2:** 3 (4.0) Native American **G1:** 1 (2.0) **G2:** 0	Socialization **G1:** 53.48 ± 14.41 **G2:** 59.55 ± 15.01 Communication **G1:** 53.18 ± 19.94 **G2:** 61.15 ± 20.95 Adaptive Composite **G1:** 45.84 ± 15.5 **G2:** 53.15 ± 15.66 **Age Equivalent Score** Daily living skills **G1:** 2.85 ± 1.52 **G2:** 3.63 ± 1.94 Socialization **G1:** 2.09 ± 1.08 **G2:** 2.80 ± 1.84 Communication **G1:** 3.12 ± 2.15 **G2:** 3.99 ± 2.65 Adaptive Composite **G1:** 18.91 ± 14.18 **G2:** 16.59 ± 11.44	**HSQ-mean** **G1:** 2.12 ± 1.87 **G2:** 1.84 ± 1.46 **HSQ "yes"** **G1:** 13.67± 7.04 **G2:** 12.69 ± 5.91 **ABC, mean ± SD** Irritability **G1:**15.25 ± 3.36 **G2:** 14.10 ± 3.60 Lethargy **G1:** 7.39 ±6.83 **G2:** 4.65 ± 5.21 Stereotypy **G1:** 5.61 ± 5.31 **G2:** 4.06 ± 3.67 Hyperactivity **G1:** 18.94 ± 11.42 **G2:** 17.37 ± 11.78 Inappropriate speech **G1:** 3.22 ± 3.36 **G2:** 3.27 ± 2.77 **Predictors, F** **HSQ Total Score** Income: 0.02 Maternal education: 0.40 Child age: 4.96 IQ: 3.18 ABC-Irritability: 1.13 ABC-Hyperactivity: 0.36 CGI-S: 0.08 CASI-ADHD/Combined: 0.02 CASI-ODD: 0.06 CASI-GAD: 0.77

	SES, mean ± SD: Income (US $) <20,000 **G1:** 12 ± 25.0 **G2:** 14 ± 18.7 20,001-40,000 **G1:** 14 ± 29.2 **G2:** 21 ± 28.0 40,001-60,000 **G1:** 10 ± 20.8 **G2:** 11 ± 14.7 60,001-90,000 **G1:** 7 ± 14.6 **G2:** 16 ± 21.3 >90,000 **G1:** 5 ± 10.4 **G2:** 13 ± 17.3 Maternal education <8th grade **G1:** 1 ± 2.0 **G2:** 4 ± 5.3 Some high school **G1:** 4 ± 8.2 **G2:** 3 ± 4.0 High school graduate/GED **G1:** 15 ± 30.6 **G2:** 18 ± 24.0 Some collage **G1:** 17 ± 34.7 **G2:** 28 ± 37.3 College graduate **G1:** 10 ± 20.4	CASI-Mood disorder: 0.84 CASI-PDD: 0.11 CYBOCS: 0.42 HSQ: 7.23 (p=0.007) PSI-Parental distress: 0.20 PSI-Total stress: 0.78 VABS-daily living: 0.18 VABS-socialization: 0.34 VABS-communication: 0.58 VABS-composite: 0.60 **ABC-Hyperactivity/Non-compliance** Income: 1.02 Maternal education:0.02 Child age: 3.23 IQ: 3.43 ABC-Irritability: 0,02 ABC-Hyperactivity: 0.31 CGI-S: 0.21 CASI-ADHD/Combined: 0.30 CASI-ODD: 0.00 CASI-GAD: 0.17 CASI-Mood disorder: 0.04 CASI-PDD: 2.47 CYBOCS: 0.38 HSQ: 0.29 PSI-Parental distress: 0.54 PSI-Total stress: 0.84 VABS-daily living: 3.62 VABS-socialization: 1.45 VABS-communication: 5.04 VABS-composite: 4.56 **Moderators, F** **HSQ Total Score** Income: 0.58 Maternal education:0.08 Child age: 0.43 IQ: 0.04 ABC-Irritability: 0.08

	G2: 12 ± 16.0 Advanced degree **G1:** 2 ± 4.1 **G2:** 10 ± 13.3 **Diagnostic approach:** In Study Diagnostic tool/method: DSM-IV-TR diagnosis based on clinical assessment and corroborated by the ADI-R **Diagnostic category, n (%):** Autism **G1:** 32 (65.3) **G2:** 49 (65.3) PDD-NOS **G1:** 13 (26.5) **G2:** 22 (29.3) Aspergers **G1:** 4 (8.2) **G2:** 4 (5.3) **Other characteristics: Educational placement, n (%):** F/T, regular education **G1:** 10 (20.4) **G2:** 18 (24.0) F/T, regular education with aide **G1:** 0 **G2:** 3 (4.0)	ABC-Hyperactivity: 0.15 CGI-S: 0.32 CASI-ADHD/Combined: 0.01 CASI-ODD: 3.38 CASI-GAD: 0.43 CASI-Mood disorder: 1.14 CASI-PDD: 0.39 CYBOCS: 1.96 HSQ: 2.27 PSI-Parental distress: 0.05 PSI-Total stress: 0.11 VABS-daily living: 0.12 VABS-socialization: 0.00 VABS-communication: 0.00 VABS-composite: 0.12 **ABC-Hyperactivity/Non-compliance** Income: 0.07 Maternal education: 0.67 Child age: 0.65 IQ: 0.96 ABC-Irritability: 0.04 ABC-Hyperactivity: 0.46 CGI-S: 2.13 CASI-ADHD/Combined: 0.73 CASI-ODD: 5.70 CASI-GAD: 0.84 CASI-Mood disorder: 1.92 CASI-PDD: 0.08 CYBOCS: 1.60 HSQ: 1.02 PSI-Parental distress: 0.01 PSI-Total stress: 0.00 VABS-daily living: 0.09 VABS-socialization: 0.09 VABS-communication: 0.22 VABS-composite: 0.04 None of the predictors / moderators were significant

	Regular education, some special **G1:** 5 (10.2) **G2:** 4 (5.3) Special education classroom **G1:** 8 (10.3) **G2:** 14 (18.7) Special elementary school **G1:** 3 (6.1) **G2:** 2 (2.7) Home school **G1:** 4 (8.2) **G2:** 5 (6.7) Special preschool **G1:** 11 (22.4) **G2:** 11 (14.7) Regular preschool **G1:** 6 (12.2) **G2:** 8 (10.7) No school **G1:** 2 (24.1) **G2:** 12 (16.0)	at $p<0.01$

Table C-1. Evidence table, continued

Study Description	Intervention	Inclusion/ Exclusion Criteria/ Population	Baseline Measures	Outcomes
Author: Kouijzer et al., 2009 [88, 89] **Country:** Netherlands, France **Intervention setting:** Private practice **Enrollment period:** NR **Funding:** NR **Design**: Non-RCT	**Intervention:** Twice a week for 40 sessions of seven 3-min intervals of EEG neurofeedback separated by 1-min rest intervals **Assessments:** QEEG, executive functions skills, communicative abilities, social interaction and behaviors **Groups:** **G1:** neurofeedback **G2:** control **Provider:** Psychotherapist **Treatment manual followed:** NR **Defined protocol followed:** Yes **Measure of treatment fidelity reported:** NR **Co-interventions held stable during treatment:** NR **Concomitant therapies, n (%):** NR **N at enrollment:**	**Inclusion criteria:** • IQ-score of ≥70 • presence of ASD as diagnosed by a child psychiatrist or health care psychologist **Exclusion criteria:** • children using medication • children with a history of severe brain injury • children with co-morbidity such as ADHD and epilepsy **Age, mean/yrs ± SD (range):** **G1:** 9.63 ± 1.53 (8-12) **G2:** 10.64 ± 1.41 (9-12) p=0.220 **Mental age,:** Total IQ, mean ± SD (range) **G1**: 92.50 ± 16.05 (73-111) **G2**: 93.83 ± 13.67 (82-199) p=0.891 Mean verbal IQ: **G1:** 97.80 ± 18.38 (77-119) **G2**: 95.40 ± 18.15 (78-125) p=0.841 Mean performal IQ: **G1:** 99.60 ± 25.77 (73-134) **G2**: 93.40 ± 9.71 (81-108)	**mean ± SD:** Attentional control Visual selective attention **G1:** 4.33 ± 2.81 **G2:** 9.14 ± 14.44 Auditory selective attention **G1:** 47.87 ± 14.21 **G2:** 67.79 ± 25.61 Inhibition of verbal responses **G1:** 68.17 ± 18.87 **G2:** 65.71 ± 31.53 Inhibition of motor responses **G1:** 78.50 ± 13.16 **G2:** 89.84 ± 11.02 Cognitive flexibility -Verbal memory **G1:** 53.33 ± 3.62 **G2:** 51.29 ± 2.63 Visual memory **G1:** 46.00 ± 3.74 **G2:** 41.00 ± 5.57 Shifting **G1:** 30.00 ± 15.68 **G2:** 29.71 ± 10.50 Concept generation **G1:** 2.55 ± 1.48 **G2:** 3.50 ± 1.70	**mean ± SD:** Attentional control Visual selective attention **G1:** 4.17 ± 4.26 **G2:** 7.29 ± 8.90 Auditory selective attention **G1:** 62.40 ± 14.18 **G2:** 68.90 ± 27.30 p = .014 Inhibition of verbal responses **G1:** 30.00 ± 12.12 **G2:** 50.14 ± 26.59 p = .049 Inhibition of motor responses **G1:** 89.93 ± 9.20 **G2:** 91.47 ± 9.66 Cognitive flexibility Verbal memory **G1:** 52.17 ± 4.07 **G2:** 50.57 ± 6.604 Visual memory **G1:** 45.00 ± 4.34 **G2:** 40.29 ± 8.321 Shifting **G1:** 47.00 ± 13.27 **G2:** 34.00 ± 13.29 p= .037

	G1: 7 **G2:** 7 **N at follow-up:** **G1:** 7 **G2:** 7	p=0.628 **Sex:** M: 12 (86%) F: 2 (14%) **Race/ethnicity, n (%):** NR **SES:** NR Maternal education: NR Household income, mean (range): NR **Diagnostic approach:** In Study Diagnostic tool/method: DSM-IV confirmed by clinical psychologist and by results on the CCC questionnaire **Diagnostic category, n (%):** PDD-NOS: 14 (100%) **Other characteristics**, n (%)**:** NR	Goal setting **G1:** 55.45 ± 9.07 **G2:** 55.84 ± 18.17 Speed and efficiency **G1:** 34.33 ± 7.06 **G2:** 41.00 ±15.52 General communication **G1:** 115.14 ± 10.45 **G2:** 115.86 ± 9.42 Non-verbal communication **G1:** 15.86 (2.34 **G2:** 14.86 (2.85	Concept generation **G1:** 4.96 ±(.45) **G2:** 3.83 ±(1.42) p= .046 Goal setting **G1:** 75.85 ± 9.17 **G2:** 57.03 ± 11.89 p= .021 Speed and efficiency **G1:** 41.33 ± 5.13 **G2:** 43.86 ± 10.96 p= .542 No significant differences between post-treatment and 3-month follow-up measurements of children's executive functioning at follow-up General communication: **G1:**101.29 ± 12.09 **G2:**114.29 ± 16.45 Non-verbal communication **G1:** 13.71 ± 2.50 **G2:** 15.57 ± 2.76 p = .037 No group difference in any of the other subscales Auti-R: Social interaction **G1:**36.50 ± 3.51 **G2:**30.71 ± 0.92 p = .001

Communication
G1:29.00 ± 1.79
G2: 24.14 ± 0.64
$p = .000$

Typical behavior
G1: 48.33 ± 3.44
G2: 44.14 ± 1.06
$p = .018$

Total
G1:113.83 ± 7.17
G2: 99.00 ± 1.95

12 months:
Only data for G1 reported continuation of improvement of selective attention after 12 months
$p < .010$

Non-significant improvement was found for inhibition of verbal responses, verbal memory, concept generation, and speed and efficiency.

No significant decrease of performance was found between post-assessment and follow-up data on any aspect of executive functioning
Significant improvement maintained for general communication

Harms: NR

Modifiers: NR

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Abbreviations in Evidence Table

ABA	Applied Behavioral Analysis
ABC	Aberrant Behavior Checklist
ABC-I	Aberrant Behavior Checklist - Irritability
ACS	Autism Characteristics and Severity
ADHD	Attention Deficit Hyperactivity Disorder
ADI-R	Autism Diagnostic Interview - Revised
ADIS	Anxiety Disorders Interview Schedule
ADIS-P	Anxiety Disorders Interview Schedule – Parent Rated
ADIS-C/P	Anxiety Disorders Interview Schedule – Child and Parent Rated Versions
ADL	Activities of daily living
ADOS	Autism Diagnostic Observation Schedule
ADOS-G	Autism Diagnostic Observation Schedule - Generic
AEPS	Assessment, Evaluation, and Programming System
ALQ	Achieved Learning Questionnaire
ANCOVA	Analysis of Covariance
ASD	Autism Spectrum Disorder
ASSQ	Autism Spectrum Screening Questionnaire (High-Functioning)
BAS-II	British Abilities Scale
BASC-2	Behavior Assessment System for Children
BASC-2-PRS	Behavior Assessment System for Children – Parent Rating Scale
BSID	Bayley Scales of Infant Development
CARS	Childhood Autism Rating Scale
CASL	Comprehensive Assessment of Spoken Language
CASI	Child and Adolescent Symptom Inventory
CASP	Child and Adolescent Social Perception Measure
CAST	Childhood Asperger Syndrome Test
CBCL	Child Behavioral Checklist
CBS-DP	Communication and Symbolic Behavior Scales – Developmental Profile
CBT	Cognitive Behavioral Therapy
CCC	Children's Communication Checklist
CDI	Communication developmental Inventories
CGI	Clinical Global Impression
CHAT	Checklist for Autism
CIS-P	Columbia Impairment Scale-Parent Rated
CSBS-DP	Communication and Symbolic Behavior Scales – Developmental Profile
CSBQ	Children's Social Behavior Questionnaire
CSHQ	Children's Sleep Habits Questionnaire
CSR	Clinician Severity Rating

CTM	Comparison Comprehensive Treatment Model
CYBOCS	Children's Yale-Brown Obsessive-Compulsive Scale
DANVA	Diagnostic Analysis of Non-Verbal Accuracy
DAS	Differential Abilities Scale
DBC	Developmental Behavior Checkllist
DIR	Developmental, Individual Differences, Relationship-based
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition
EEG	Electroencephalogram
EIBI	Early and Intensive Behavioral Intervention
EL	Expressive Language
ELC	Early Learning Composite
ESAT	Early Screening for Autistic Traits
ESCS	Early Social Communications Scale
ESDM	Early Start Denver Model
EVT	Expressive Vocabulary Test
FAF	Facing Your Fears
FEAS	Functional Emotional Assessment Scale
FEDQ	Functional Emotional Development Questionnaire
FPI	Focused Playtime Intervention
FSIQ	Full Scale Intelligence Quotient
GAD	Generalized Anxiety Disorder
GARS	Gilliam Autism Rating Scale
GCSE	General Certificate of Secondary Education
GHQ	General Health Questionnaire
GMDS-ER	Griffiths Mental Development Scale – Extended Revised
HFASD	High-Functioning Autism Spectrum Disorder
HSQ	Home Situations Questionnaire
IBI	Intensive Behavioral Intervention
ICD-10	International Statistical Classification of Diseases
ICQ	Infant Characteristics Questionnaire
ID	Intellectual Disabilities
IJA	Initiating Joint Attention
IS	Interpersonal Synchrony
ITT	Intention to Treat
IQ	Intelligence Quotient
JA	Joint Attention
JASP/ER	Joint Attention and Symbolic Play/Engagement and Regulation Intervention
JE	Joint Engagement
LEAP	Learning Experiences and Alternative Program for Preschoolers

LEAS-C	The Levels of Emotional Awareness Scale for Children
MASC-P	Multidimensional Anxiety Scale for Children- Parent Rated
MCDI	MacArthur-Bates Communicative Development Inventory
MSEL	Mullen Scales of Early Learning
MTW	More Than Words
NEPSY-II	A Developmental Neuropsychological Assessment
NR	Not Reported
NRCT	Nonrandomized controlled trial
NS	Not Statistically Significant
NCD-I	MacArthur Communicative Development Inventory (Dutch Version)
OCD	Obsessive-Compulsive Disorder
ODD	Oppositional Defiant Disorder
PARS	Pediatric Anxiety Rating Scale
PCFP	Parent child free play
PCIQ	Parent-Child Interaction Questionnaire
PDD-BI	Pervasive Development Disorder - Behavior Inventory
PDD-MRS	Pervasive Development Disorder in Mentally Retarded Persons
PDD-NOS	Pervasive Developmental Disorder- Not Otherwise Specified
PECS	Picture Exchange Communication System
PEP-R	Psycho-Educational Profile – Revised
P-ESDM	Parent Delivery – Early Start Denver Model
PIA-CV	Parent Interview for Autism – Clinical Version
PIQ	Performance Intelligence Quotient
PLS-4	Preschool Language Scale
PPVT-4	Peabody Picture Vocabulary Test
PSI	Parental Stress Index
PSOC	Parenting Sense of Competence
RCMAS	Revised Children's Manifest Anxiety Scale
RCT	Randomized, Controlled Trials
RDLS	Reynell Developmental Language Scale
RSI-T	Reciprocal Social Interaction – Teacher Rated
SACA	Service Assessment for Children and Adolescents—Service Use Scale
SAD	Separation Anxiety Disorder
SCARED	Screen for Childhood Anxiety Related Emotional Disorders
SCAS	Spence Children's Interview Scale
SCAS-C	Spence Child Anxiety Scale – Child Rated
SCAS-P	Spence Children's Interview Scale – Parent Rate (?)
SCL-90-R	Symptoms Checklist – 90 – Revised
SCQ	Social Communication Questionnaire

SD	Standard Deviation
SDARI	Sociodramatic Affective Relational Intervention
SE	Standard error
SEI	Socially Engage Imitation
SES	Socioeconomic Status
SIB-R	Scales of Independent Behavior – Revised
SIOS	Social Interaction Observation System
SKA	Skillstreaming Knowledge Assessment
SOL	Sleep Onset Latency
SON-2.5-7	Snijders-Oomen Non-verbal Intelligence Test
SPA	Shared Positive Affect
SR	Social Recreational
SRB-P	Sensory and Repetitive Behaviors – Parent Rated
SRB-T	Sensory and Repetitive Behaviors – Teacher Rated
SRS	Social Responsiveness Scale
S.S. GRIN-HFA	Social Skills Group Intervention – High Functioning Autism
SSRI	Selective Serotonin Reuptake Inhibitor
SSRS-P	Social Skills Rating System – Parent Rated
SSRS-T	Social Skills Rating System – Teacher Rated
STAT	Screening Tool for Autism
TOM	Theory of Mind
TPSS	Teacher Perceptions of Social Skills
VABS	Vineland Adaptive Behavior Scales
VIQ	Verbal Intelligence Quotient
VR	Visual reception
WASI	Wechsler Abbreviated Scale of Intelligence
WASO	Wake After Sleep Onset
WISC-IV	Wechsler Intelligence Scale IV
WPPSI	Wechsler Preschool and Primary Scale of Intelligence

Appendix D. Quality of the Literature

Table D-1. Quality of the literature

First Author Year	Group Design	Random Assignment	Appropriate Comparison Group	Correct Randomization	Systematic Diagnostic Approach	Clear Sample Characterization	Clear Inclusion/ Exclusion Criteria	Attrition Reported	Drop out Characteristics Evaluated	Intervention Fully Described	Treatment Fidelity Monitored	Concomitant Interventions Held Steady/ Reported	Outcome Measures Reliable and Valid	Primary Outcomes Specified *a priori*	Outcome Data Collected From Appropriate Sources	Outcomes Coded Blindly	Appropriate Statistical Analysis	Rating
Boyd 2013[1]	+	-	+	NA	+	+	+	+	NA	+	+	-	+	+	+	-	-	F
Casenhiser 2013[2]	+	+	+	+	+	+	+	+	NA	+	+	-	+	+	+	+	+	F
Fujii 2013[3]	+	+	+	-	+	+	+	+	NA	+	+	+	+	+	+	+	-	F
Goods 2013[4]	+	+	+	+	+	+	+	+	NA	+	+	NA	+	+	+	+	+	G
Ichikawa 2013[5]	+	+	+	+	-	+	+	+	NA	+	-	-	+	+	+	-	+	P
Kasari 2013[6]	+	+	+	+	-	+	+	+	NA	+	+	-	+	+	+	-	+	F
Kenworthy 2013[7]	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	G
Malow 2013[8]	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	-	-	F
McNally-Keehn 2013[9]	+	+	+	+	+	+	+	+	NA	+	+	+	+	+	+	-	+	G

Paynter 2013[10]	+	-	+	-	+	+	-	+	NA	+	-	-	+	-	+	-	-	F
Peters-Scheffer 2013[11]	+	-	+	NA	+	+	+	+	-	+	+	-	+	-	+	-	+	G
Reed 2013[12]	+	-	+	NA	+	+	+	-	-	+	-	-	+	-	+	-	-	P
Schertz 2013[13]	+	+	+	-	+	+	+	+	NA	+	+	-	+	+	+	+	+	F
Schreibman 2013[14]	+	+	+	+	+	+	+	+	NA	+	+	+	+	+	+	-	+	G
Sharp 2013[15]	+	+	+	-	-	-	+	+	+	+	-	-	+	+	+	-	-	P
Storch 2013[16]	+	+	+	-	+	+	+	+	NA	+	+	+	+	+	+	+	-	G
Warreyn 2013[17]	+	+	+	-	+	+	+	+	-	+	-	-	+	+	+	-	-	F
Adkins 2012[18]	+	+	+	-	+	+	+	+	NA	+	-	+	+	+	+	-	+	F
Cortesi 2010[19]	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	-	F
Eikeseth 2012[20]	+	-	+	NA	-	+	-	+	-	+	-	-	+	+	+	-	-	F
Eldevik 2012[21]	+	-	+	NA	-	+	+	+	NA	+	-	-	+	-	+	-	+	F
Flanagan 2012[22-27]	+	-	+	NA	+	+	+	NA	-	+	-	-	+	+	+	-	+	F
Kaale 2012[28]	+	+	+	+	+	+	+	+	NA	+	+	+	+	+	+	+	+	F
Kasari 2012[29]	+	+	+	+	+	+	+	+	NA	+	-	-	+	+	+	-	+	F
Lawton 2012[30]	+	+	+	+	+	+	+	+	NA	+	+	+	+	+	+	+	-	F

Lerner 2012[31]	+	+	+	-	-	+	-	+	NA	+	+	-	+	+	+	+	+	F
Reaven 2012[32]	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	G
Rogers 2012[33, 34]	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	-	-	F
Strauss 2012[35, 36]	+	-	+	NA	+	+	+	+	NA	+	+	-	+	+	+	-	+	G
Thomeer 2012[37]	+	+	+	-	-	+	+	+	NA	+	+	+	+	+	+	-	+	F
Venker 2012[38]	+	+	+	-	+	+	-	-	-	+	+	-	+	+	+	-	+	F
Williams 2012[39]	+	+	+	+	+	+	+	+	NA	+	+	-	+	+	+	+	+	G
Young 2012[40]	+	+	+	-	+	+	+	+	NA	+	+	-	+	+	+	-	+	F
Begeer 2011[41]	+	+	+	+	+	+	+	+	NA	+	+	-	+	+	+	-	+	F
Carter 2011[42]	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	F
Castorina 2011[43]	+	-	+	NA	-	+	+	+	NA	+	+	-	+	+	+	-	+	F
DeRosier 2011[44]	+	+	+	-	-	+	+	+	+	+	+	-	+	+	+	-	+	F
Landa 2011[45, 46]	+	+	+	-	+	+	+	+	NA	+	+	+	+	+	+	+	+	G
Murdock 2011[47]	+	-	+	NA	-	+	+	+	NA	+	-	-	+	+	+	-	-	P
Pajareya 2011[48]	+	+	+	+	+	+	+	+	NA	+	-	+	+	+	+	-	+	F
Roberts 2011[49]	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	G

Scarpa 2011[50]	+	+	+	-	+	+	+	+	NA	+	-	-	-	+	+	-	+	F
Strain 2011[51]	+	+	+	-	-	+	+	+	NA	+	+	-	+	+	+	-	+	F
Sung 2011[52]	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	-	-	G
Wood 2011[53-55]	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	G
Ingersoll 2010[56, 57]	+	+	+	-	+	+	+	+	NA	+	+	-	+	+	+	+	+	G
Itzchak 2010[58, 59]	+	-	+	NA	+	+	+	-	-	+	-	-	+	+	+	-	-	F
Kasari 2010[60]	+	+	+	+	+	+	+	+	NA	+	+	+	+	+	+	+	+	G
Keen 2010[61]	+	-	+	NA	+	+	-	+	NA	+	+	-	+	+	+	-	+	G
Koenig 2010[62]	+	+	+	+	+	+	+	+	NA	+	+	+	+	+	+	+	-	G
Kouijzer 2010[63]	+	+	+	-	+	+	+	+	NA	+	NA	-	+	+	+	-	-	F
Lopata 2010[64]	+	+	+	+	-	+	+	+	NA	+	+	+	+	+	+	-	+	F
McConkey 2010[65]	+	-	-	NA	-	+	+	+	-	+	-	-	+	-	+	-	+	P
Oosterling 2010[66]	+	+	+	-	+	+	+	+	-	+	+	-	+	+	+	-	-	F
Peters-Sheffer 2010[67]	+	-	+	NA	+	+	+	+	NA	+	-	+	+	+	+	-	+	F
Reed 2010[68]	+	-	+	NA	+	+	+	-	-	+	-	-	+	+	+	+	-	F

Siller 2010[69]	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	F
Wong 2010[70]	+	+	+	-	+	+	+	+	NA	-	-	-	+	+	+	+	-	P
Dawson 2009[71, 72]	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	-	-	G
Kouizjer 2009[73, 74]	+	-	+	NA	-	+	+	NA	NA	+	-	-	+	-	+	-	-	P
RUPP 2009[75-78]	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	-	+	F
Remington 2007[79, 80]	+	-	+	NA	+	+	+	+	-	-	-	+	+	+	+	-	-	P
Kasari 2006[81-84]	+	+	+	-	+	+	+	+	-	+	+	-	+	+	+	+	+	F
Aldred 2004[85, 86]	+	+	+	+	+	+	+	+	NA	+	-	-	+	+	+	+	+	G

F=fair; G=good; NA=not applicable; P=poor

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Quality/Risk of Bias Assessment Approach

Study Design

1. Did the study employ a group design?

   Group designs may include randomized controlled trials, prospective or retrospective cohorts, case-control studies

   + = yes
   - = no

2. Were the groups randomly assigned?

   + = yes
   - = no

3. Was there an appropriate comparison group?

   The comparison group should accurately represent the characteristics of the intervention group in the absence of the intervention. Specifically, factors that are likely to be associated with the intervention selected and with outcomes observed should be evenly distributed between groups, if possible. These factors may include, for example, age, IQ, severity, etc.

   + = yes
   - = no or not reported (NR)

4. If an RCT, was randomization done correctly?

   + = yes
   - = no
   NR
   NA for all non-RCTs

   Considerations:
   Was the approach to randomization described? Were random techniques like computer-generated, sequentially numbered opaque envelope used?
   Were technically non-random techniques, like alternate days of the week used?
   Any studies with randomization techniques not reported (NR) will also be reviewed by the team.

Participant Ascertainment/Inclusion

1. Was a valid diagnostic approach for ASD used within the study, or were referred participants diagnosed using a valid approach?
   A. clinical DSM-IV-based diagnosis + ADI-R and/or ADOS

B. [clinical DSM-IV-based diagnosis + other] OR [ADOS + other, such as SRS, CARS, SCQ, CAST, ASSQ, OR STAT, MCHAT for under 30 months]
C. Only clinical DSM-IV-based diagnosis OR Only ADOS
D. Neither clinical DSM-IV-based diagnosis NOR ADOS

2. Was the sample clearly characterized (e.g., information provided to characterize participants in terms of impairments associated with their ASD, such as cognitive or developmental level)?

+ = yes
- = no or not reported (NR)

Considerations:
Are baseline measures of IQ, mental age, language facility, etc. reported?
How reproducible is the study in terms of the sample participants? Do the authors provide enough information that you could recreate the study population in a new study?

3. Were inclusion and exclusion criteria clearly stated?

+ = yes
- = no or not reported (NR)

Considerations:
Did the authors report this information?

4. Do the authors report attrition?

+ = yes
- = no

Considerations:
Do they report loss to follow-up and/or drop-out?
If there is no attrition (i.e., baseline and follow up Ns are the same), score as YES

5. Were characteristics of drop-out group evaluated for differences with the participant group as a whole?

+ = yes
- = no or not reported (NR)
NA or attrition was minimal

Considerations:

Were reasons for dropping out evaluated?
Does the paper describe a comparison between drop-outs and the whole group?
Score as NA if attrition was minimal.

Intervention

1. Was the intervention fully described?

    + = yes
    - = no or not reported (NR)

    Considerations:
    Is there sufficient detail to allow replication of the intervention?
    Does the study describe the dosage, formulation, timing, duration, intensity, etc. of the intervention?
    Do the authors refer to a treatment manual (score as YES if so, even is manual is unpublished)?

2. For behavioral studies, was treatment fidelity monitored in a systematic way?

    + = yes
    - = no or not reported (NR)
    NA

    Considerations:
    Was a method in place to assess whether people providing he intervention were adherent to a manual/process? We're not assessing the quality of the fidelity, just whether it was performed.

3. Did the authors measure and report adherence to the intended treatment process?

    + = yes
    - = no or not reported (NR)

    Considerations:
    Does the study report number of hours of treatment or treatment sessions or time period receiving therapy (planned vs. actually received)? Do they provide pill count data or parental medication diary, etc. for pharmacologic interventions?

4. Did the authors report differences in or hold steady all concomitant interventions?

    + = yes

- = no or not reported (NR)

Considerations:
Was an attempt made to assess/determine if other interventions were ongoing?

Outcome Measurement

1. Did outcome measures demonstrate adequate reliability and validity (including interobserver reliability for behavior observation coding)?

   + = yes
   - = no or not reported (NR)

   Considerations:
   If the study used an established measure, has validity been established previously and do the authors provide a reference?
   If the study used a new measure, was validity established?
   For interobserver coding, was reliability and /or validity tested?

2. Were the primary & secondary outcomes clearly specified a priori?

   + = yes
   - = no or not reported (NR)

   Considerations:
   Was there a “called shot?”

3. Were outcome data collected from sources appropriate to the target outcome (e.g. parent report, teacher report, direct behavior observation)?
+ = yes
- = no or not reported (NR)

Considerations:
Ex: Parent report for home-focused outcomes, teacher report for academic/school-focused, etc.

4. Were outcomes coded by individuals blinded to the intervention status of the participants?
+ = yes
- = no or not reported (NR)

Analysis

1. Was an appropriate statistical analysis used?

+ = yes
- = no

1a. For RCT’s, was there an intent-to treat analysis?
+ = yes
- = no
NA
Considerations:
Does the study report ITT analyses or last observation carried forward or note that all subjects were included in the final analyses? If ≤2 participants were lost to follow-up, consider the analysis as ITT.

1b. For negative studies, was a power calculation provided?
+ = yes
- = no
NA

1c. Did the study correct for multiple testing?
+ = yes
- = no
NA

1d. For observational studies, were potential confounders and effect measure modifiers captured?
+ = yes
- = no
NA

Considerations:
Were the groups well categorized at baseline? Were baseline differences assessed?

1e. For observational studies, were potential confounders and effect measure modifiers handled appropriately?
+ = appropriate analysis
- = inappropriate analysis
NA

Considerations:
Confounders are variables that are associated both with the intervention and the outcome and that change the relationship of the intervention to the outcome. These are variables that we would control for in analysis.

Effect measure modifiers are variables that we think of as stratifying, in that the relationship between the intervention and outcome is fundamentally different in different strata of the effect modifier. Observational research should include an assessment of potential confounders and modifiers, and if they are observed, analysis should control for or stratify on them.

Was the candidate variable selection discussed/noted?

Was the model-building approach described?

Were any variables unrelated to the studied variables that could have altered the outcome handled appropriately?

Were any variables not under study that affected the causal factors handled appropriately?

Appendix E. Excluded Studies

Exclusion reasons:

X-1 Participants not in target age range
X-2 Not original research
X-3 Study size (N<10)
X-4 Does not address Key Questions
X-5 Does not address behavioral intervention for children with ASD 0-12 years of age
X-6 Article not obtainable

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Appendix F. Characteristics and Outcomes of Studies of Early Intensive Behavioral and Developmental Interventions

Table F-1. Characteristics and outcomes of early intensive behavioral and developmental intervention studies

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months ± SD IQ, Mean ± SD	Intervention Provider Intervention Setting	Intervention Manualized?	Intervention Intensity, Duration, And Focus	Key Outcomes
ABA-Based Approaches					
Peters-Scheffer et al. 2013[1] Netherlands **G1:** Low intensity Lovaas-based intervention+specialized preschool, 20/20 **G2:** Specialized preschool, 20/20 Quality: Good	**G1+G2:** 62.52 ± 16.96 (median) **G1:** 40.66 ± 20.1 **G2:** 40.14 ± 18.3	**G1:** Master's trained special education or psychology therapists **G2:** Preschool teachers (no additional information reported) **G1+G2:** Specialized preschools	**G1:** Yes **G2:** NR	**G1:** Mean 4.98±1.45 hours/week one-to-one treatment plus standard specialized preschool for 24 months; intervention included programs focused on compliance/attention, imitation, matching, categorization, PECS, motor skills, language, memory, play, adaptive behavior, academic skills, social interaction/communication **G2:** Hours not reported; standard preschool incorporating TEACCH, PECS, individualized speech therapy, sensory integration, language, play, sensory-motor	• 9/20 participants in G1 received 1 year of treatment vs. 2 years • Developmental age in both groups improved over time, but increase was greater in G1 vs. G2 (p=.001); effect size for change=1.09 • IQ improved significantly from baseline to 12 months (mean 40.66 to 48.17, P<.001) in G1 and remained stable from 12-24 months; no significant change over time in G2 (baseline mean=40.14, 24-month mean=39.42); effect size for change=0.40 • Total Vineland and subscale scores improved in both groups with greater improvements in G1 vs. G2 (p values<.001); effect size for change in total score=1.74 • Receptive language improved at 24 months in G1 vs. G2 (p=.04); expressive language improve over time in both groups but between group differences at 24 months were not significant (effect size for change=0.40) • Both groups generally improved over time on Early Social Communication Scales domains but between group differences were not significant at 24 months

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months ± SD IQ, Mean ± SD	Intervention Provider Intervention Setting	Intervention Manualized?	Intervention Intensity, Duration, And Focus	Key Outcomes
					• Severity ratings (CARS, ADOS) decreased significantly over time for G1 but not G2; effect size for change in ADOS=1.51, CARS=1.50) • Differences between groups in measures of emotional and behavioral problems and behavioral flexibility were not significant • More G1 participants achieved clinical and reliable significant on developmental age, adaptive behavior, interpersonal relationships, play and leisure time, receptive and expressive language, ASD severity, and responding to social interaction vs. G2 • More G2 vs. G1 participants obtained clinical and reliable significance on measures of problem behavior and maternal stress; equal numbers of G1 and G2 participants obtained clinical and reliable significance on IQ, behavioral flexibility, joint attention, behavioral requests, and initiating social interaction • Diagnoses changes from autism to PDD-NOS in 45% of G1 and 20% of G2; 10% in G1 classified as non-autistic at 24 months (0 in G2); level of intellectual disability declined in 55% of G1 and 5% of G2 • Baseline hours of treatment, developmental age, IQ, level of adaptive behavior, play skills , receptive language significant predictors of progress
Dawson et al. 2012[22, 23] US	**G1:** 23.9 ± 4.0 **G2:** 23.1 ± 3.9	**G1:** Trained therapists,	**G1:** Yes **G2:** NR	**G1:** Mean 15.2 ± 1.4 therapist-delivered	1 year outcomes: • Significantly greater improvement in IQ for

Author, Year, Country **Groups, N Enrollment/N Final** **Study Quality**	**Age, Mean Months ± SD** **IQ, Mean ± SD**	**Intervention Provider** **Intervention Setting**	**Intervention Manualized?**	**Intervention Intensity, Duration, And Focus**	**Key Outcomes**
 G1: ESDM, 24/24 **G2:** Community-based interventions, 24/21 Quality: Good	 **G1:** 61.0 ± 9.2 **G2:** 59.4 ± 8.6	clinical psychologist, speech language pathologist, developmental behavioral pediatrician, parents **G2:** Community-based therapists		hours/week + mean 16.3 ± 6.2 parent-delivered hours/week for 24 months, intervention focused on interpersonal exchange, positive affect, shared engagement with real life materials/activities, communication, and adult responsiveness to child cues **G2:** Mean 9.1 hours/week of individual therapy and 9.3 of group delivered interventions, potentially including speech language and occupational therapy, developmental preschool	G1 (154 vs. 22 points) compared with G2 • No adaptive behavior differences 2 year outcomes: • Significantly more improvement in G1 vs. G2 on IQ; receptive language, and expressive language • Adaptive behavior improvements in both groups (all domains except socialization); significantly greater improvements in G1 • No change in ADOS severity scores or repetitive behavior • Diagnostic shift toward milder diagnosis (PDD-NOS) greater for ESDM group • No differences between groups in EEG measurements of perceptual face processing • EEG measures of engagement/cognitive processing comparable to those of typically developing children for G1 children with usable EEG data; 11/15 G1 participants and 4/14 G2 showed faster neural response to faces vs. objects
Peters-Scheffer et al. 2010[2] Netherlands **G1:** Specialized preschool + UCLA/Lovaas-based intervention, 12/12 **G2:** Specialized preschool, 22/22 Quality: Fair	**G1:** 53.5 ± 5.52 **G2:** 52.95 ± 11.14 **G1:** 47.00 ± 10.33 **G2:** 45.73 ± 15.99	**G1:** Psychologist, special educator, preschool teachers and parents with workshop training in ABA techniques **G2:** Psychologist,	**G1:** Yes **G2:** NR	**G1:** Mean 28.38 hours intervention/week for 8 months using elements of TEACCH, incidental and structured teaching, individualized speech, occupational, music therapy plus mean 6.29 hours/week 1:1 Lovaas-based intervention focused on developmental age and adaptive skills	• Both groups improved over time on cognitive and adaptive measures; G1 improved significantly compared with G2 on IQ/developmental age and Vineland composite, communication, daily living, and socialization domains (all p≤.02) • G2 had greater emotional and behavioral problem scores at baseline vs. G1 (p<.05), changes in scores not significant for either group over time • Decreases in symptom severity not

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months ± SD IQ, Mean ± SD	Intervention Provider Intervention Setting	Intervention Manualized?	Intervention Intensity, Duration, And Focus	Key Outcomes
		special educator, preschool teachers **G1+ G2:** Preschool for children with intellectual disabilities		**G2:** Mean 23.38 hours intervention/week using elements of TEACCH, incidental and structured teaching, individualized speech, occupational, music therapy	significant between groups
Itzchak et al. 2011[3, 4] Israel **G1:** ABA-based approach, 45/45 **G2:** Eclectic approach, 33/33 Quality: Fair	**G1:** 25.1 ± 3.9 **G2:** 26.0 ± 4.6 **G1:** 72.2 ± 19.2 **G2:** 73.3 ± 22.2	**G1:** Psychology or special education master's trained board certified behavior analysts, trained therapists, speech language pathologists, occupational therapists, preschool teachers **G2:** Clinical psychologist, special education preschool teacher, speech language pathologist, occupational	**G1:** NR **G2:** NR	**G1:** 20 hours/week for 12 months, 1:1 intervention with focus on language, play, social, emotional, academic, adaptive skills, and reducing inappropriate behavior **G2:**19 hours/week for 12 months, 1:1 intervention and parental involvement in intervention 1 day/week; overall treatment integrated developmental approaches	• Overall high level of diagnostic stability from baseline to end of 12-month intervention: 91% of children retained autism diagnosis. Classification improved for 3 G1 and 2 G2 participants and deteriorated for 2 children in G1 • Cognitive abilities (Mullen Scales) and overall Vineland raw scores improved in both groups (p<.001) over time; no significant differences between groups at followup; overall Vineland standard scores improved for both groups (p<.05) • Vineland motor skills domain decreased over time for both groups (p<.001) • Children in G1+G2 with lower severity (ADOS) improved significantly more than those with higher severity on cognitive and adaptive measures; both groups declined on measures of motor skills, with greater decline for those with higher severity • G2 participants with lower severity improved significantly on Vineland communication and socialization measures compared with G1 (p<.001)

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months ± SD IQ, Mean ± SD	Intervention Provider Intervention Setting	Intervention Manualized?	Intervention Intensity, Duration, And Focus	Key Outcomes
		therapist, cognitive trainer, music therapist, teacher's aids **G1+G2:** Autism-specific preschools			• In analyses combining G1 and G2, higher cognitive abilities at baseline, particularly verbal abilities, and older maternal age were associated with greater adaptive skills at followup (p<.05) • Among those with greater severity, greater verbal ability was associated with better adaptive skills at followup (r=.672, p<.001) • Cognitive gains were greater for those with lower severity (p<.01) and older, more educated mothers (p values <.001, .05); younger children had a better chance of cognitive improvement with intervention (p=NS)
Strain et al. 2011[5] US **G1**: LEAP program with coaching and training, 28 classrooms (27 analyzed)/177 children **G2**: LEAP intervention manuals only, 28 classrooms (23 analyzed)/117 children Quality: Fair	**G1:** 50.1 ± 4.6 **G2:** 50.7 ± 4.2 **G1:** 59.6 ± 6.9 **G2:** 63.2 ± 6.6	**G1+G2:** Preschool teachers **G1+G2:** Preschool	**G1+G2:** Yes	**G1:**2 years intervention, mean 17 hours/week (teachers received 23 full days coaching/training), peer mediated social skills, incidental teaching, pivotal response training, PECS, positive behavior support **G2:** 2 years intervention, mean 17 hours/week, intervention as above, no specific training for teachers beyond provision of LEAP manual	• Significant gains on CARS, language, cognitive, and social skills measures for G1 vs. G2 (p<.05) • G1 improved by 18.5 points compared with 9.4 for G2 on the Preschool Language Scale (effect size difference=0.92, p<.01) • G1 improved by 28.6 points compared with 12 for G2 on socials skills rating (effect size difference=1.22, p<.01) • Greater intervention fidelity associated with better outcomes on all measures
Eldevik et al. 2012[6] Norway **G1:** Preschool-based EIBI,	**G1:** 42.2 ± 9.0 **G2:** 46.2 ± 12.4 **G1:** 51.6 ± 16.9	**G1:** Board certified behavior analyst and	**G1:** Yes **G2:** NR	**G1:** Mean 13.6 hours/week over 24 months, ABA-based EIBI intervention using	• Greater gains in cognitive outcomes (p=.004) and overall adaptive behavior (p=.036) , Vineland communication (p=.034)

Author, Year, Country **Groups, N Enrollment/N Final** **Study Quality**	**Age, Mean Months ± SD** **IQ, Mean ± SD**	**Intervention Provider** **Intervention Setting**	**Intervention Manualized?**	**Intervention Intensity, Duration, And Focus**	**Key Outcomes**
31/31 **G2:** Usual care preschool, 12/12 Quality: Fair	**G2:** 51.7 ± 18.1	psychologist, bachelor's trained therapists with ABA-training **G2:** Special education teacher, trained therapists **G1+G2:** Preschool		discrete trial training, operant conditioning to promote communication, gross and fine motor skills, play and social skills, adaptive behavior **G2:** Mean 5+ hours/week over 24 months, intervention including elements of alternative communication, ABA-based approaches, sensory motor skills, TEACCH, adaptive and communication skills	and socialization (p=.008) for G1 vs. G2; no significant differences in Vineland daily living skills between groups • Effect size for change in IQ=1.03 (95% CI: .34 to 1.72) and for change in overall adaptive behavior=.73 (95% CI: .05 to 1.36) • Baseline age and PDD-NOS or Asperger diagnosis correlated with larger gains in overall adaptive behavior, communication, and daily living skills; baseline IQ positively correlated with Vineland socialization gains
Eikeseth et al. 2012 [7] Norway/Sweden **G1:** EIBI, 35/13-15 depending on outcome **G2:** Standard care, 24 / NR Quality: Fair	**G1:** 3.9 ± 0.9 years **G2:** 4.4 ± 1.2 years Vineland age equivalent: **G1:** 1.9 ± 0.9 **G2:** 2.1 ± 0.8	**G1**: Therapist, parents, Supervisor from Banyan Center, school staff **G2**: Special education teacher, teacher assistant **G1**+**G2**: Mainstream public preschools or kindergartens, and home	**G1**:Yes **G2**:NR	**G1**: One year of 15 to 37 hours-per-week, with an estimated mean of 23 hours ± 5.3 comprehensive intervention focused on adapative behavior, ASD severity **G2**: individual special education program	• G1 scored significantly higher on all Vineland scales as compared to G2 (p<0.05) with an effect size of Total (composite)=0.92, Communication=1.08, ADL=0.71, Socialization=0.75,Motor=0.70, and Learning rate=0.97 • G1: CARS scores continued to decrease significantly during the second year of treatment (from 31.8 (SD=8.5) to 27.2 (SD=6.2), p<.05), effect size of 0.59 • Children receiving G1 scored significantly higher on standard scores of adaptive behavior • Significant improvements were found in maladaptive behaviors and excess and deficit behaviors as compared to G2 • Largest gains were observed during the first year. Effect size on all measures at year one

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean Months ± SD IQ, Mean ± SD	Intervention Provider Intervention Setting	Intervention Manualized?	Intervention Intensity, Duration, And Focus	Key Outcomes
					were moderate to large
Flanangan et al. 2012[8-13] Canada **G1:** Intensive behavioral intervention, 61/61 **G2:** Wait list control (matched by age), 61/61 Quality: Fair	**G1:** 42.93 ± 11.53 **G2:** 42.79 ± 10.51 NR	**G1:** Trained instructor therapists, masters-degreed or certified behavior analyst supervisors, psychologists **G2:** Community-based interventionists **G1:** Specialized centers, preschools, home **G2:** Community-based with multiple settings	**G1:** No **G2:** NR	**G1:**Mean 25.81 ± 3.44 hours intervention/week for varied time period depending on age at enrollment, ABA-based, center- and home-based, publicly funded intervention incorporating discrete trial training and naturalistic approaches and curricula focusing on impairments of a specific child **G2:** Mean 17.9 ± 12.3 hours/week of school based services and <10 hours/week of behavioral intervention; community based interventions including low intensity ABA, speech therapy, occupational therapy, behavioral consultation	• In 2008 retrospective case series (Perry 2008) reporting on ~30% of G1 participants ASD severity (CARS), cognitive level, adaptive behavior, and rate of development improved significantly (all p<.001); outcomes varied across children: approximately 25% showed substantial improvements, 30% showed clinically significant improvement, 19% showed some/modest improvement, 25% showed no improvement or worsening of outcome. Analyses of a subset of the total participants (n=89) showed similar improvements (Freeman 2010) • Age (younger at baseline), IQ, adaptive behavior, and ASD severity were correlated with outcome; IQ was strongest predictor, accounting for 5-12% of the variance in outcomes (Perry 2011); in sub-set analysis (Shine 2010), duration of intervention also associated with better outcomes • In 151 participants with parental stress data available, higher maternal stress at baseline was correlated with lower child adaptive behavior skills at end of intervention (p<.01) (Shine 2010) • ASD severity improved for G1 vs. G2 as did Vineland composite standard and ratio scores and IQ estimates (p values ≤ .033, effect sizes ranging from 0.53 to 0.83); 19 point difference in IQ at end of intervention in favor of G1

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					• Younger age at intervention and higher adaptive skills associated with better outcomes; adaptive skills also associated with better outcomes for G2. Duration of intervention became nonsignificant after intervention type was entered into statistical models (Flanagan 2012) • In retrospective analyses (Perry 2013), higher baseline IQ predicted gains in IQ, and children starting early intervention at younger ages (2-5 yrs) gained significantly more IQ points (mean 17 points vs. mean 2 points) than children entering intervention at older ages (6-13 yrs); differences in adaptive behavior gains were not significant
Boyd et al. 2013[14] US **G1:** TEACCH preschools, 85/81 **G2:** LEAP preschools, 54/48 **G3:** Non-model specific preschools, 59/56 Quality: Fair	**G1:** 48 ± 6.84 **G2:** 47.52 ± 8.4 **G3:** 48.84 ± 7.68 NR	**G1:** Teachers in high fidelity TEACCH programs **G2:** Teachers in high fidelity LEAP programs **G3:** Teachers in inclusive or special education preschools **G1+G2+G3:** Preschools	**G1:** Yes **G2:** Yes **G3:** No	**G1:** Half or full school day for 6 months of cognitive social learning based intervention that uses visual schedules and other modifications to the environment to promote learning and engagement **G2:** Half day for 6 months of interventions blending ABA and early childhood education techniques and peer mediation and focused on reducing ASD characteristics to promote learning **G3:** Half or full day for 6	• Groups differed at baseline on autism characteristics and severity (p=.0013), communication (p<.001), parent-rated reciprocal social interaction (p=.0241) and fine motor (p=.0066) composite scores • All groups showed significant change over time on the autism characteristics and severity, fine motor, and communication composites (p values ≤.05); G1 and G2 improved on teacher-rated reciprocal social interaction (p≤.05). G1 improved on parent-rated reciprocal social interaction (p<.05) • No significant differences among groups on any measure at followup • Children with higher Mullen scores made fewer gains in G1; children with high Preschool Language Scale scores at baseline had higher communication and

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				months, inclusive or special education preschool	autism characteristics and severity composite scores in G1 • Females in G2 had smaller communication gains, although few females in study overall (n=33)
Kovshoff et al. 2011[15, 16] UK **G1:** EIBI (publicly-funded or privately purchased), 23/23 **G2:** Usual care, 21/18 Quality: Poor	**G1:** 35.7 ± 4.0 **G2:** 38.4 ± 4.4 **G1:** 61.43 ± 16.43 **G2:** 62.33 ± 16.64	**G1:** Trained behavior analysts and special educators **G2:** NR **G1:** Home **G2:** Community-based interventions	**G1:** NR **G2:** NR	**G1:** Mean 25.6 hours/week 1:1 teaching for 24 months, ABA-based intervention using discrete trial training in natural environment to improve, language, social skills, behavior **G2:** Hours of intervention over 24 months NR, intervention included speech therapy, PECS, TEACCH, medications, and other approaches as provided in the community	• Groups differed significantly on age at baseline ($p<.05$) • IQ, mental age, and language comprehension improved significantly for G1 vs. G2 after 24 months of intervention ($p \leq .05$); effect size for IQ change=0.77 • Vineland daily living and motor skills scores improved for G1 vs. G2 ($p<.05$) but composite, communication, severity, and socialization scores did not differ significantly between groups at the 24 month followup • Parents noted more positive social behavior for G1 vs. G2 at the 24 month followup • Intervention responders had higher IQ, higher mental age, higher Vineland composite, communication, and socialization scores, lower motor skills, more behavior problems, and more autistic symptoms and fewer hours of intervention in Year 2 • At followup of 41 participants 2 years after the end of the 24-month intervention, 14/23 G1 and 4/18 G2 children in mainstream education settings ($p=.013$), most receiving some 1:1 support • At 2-year followup no significant group differences in IQ, adaptive behavior, communication, socialization, or behavior; more G1 participants achieved standard

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					score on receptive language measure vs. G2 (p=.048) • In analyses of G1 participants in privately purchased vs. publicly funded EIBI programs, IQ declined for the publicly funded group compared with the control or privately purchased participants (p<.0001); privately purchased participants maintained IQ and adaptive behavior gains from end of intervention to the 2 year followup. Publicly funded group had more severe ASD symptoms, lower adaptive behavior, and received less intensive intervention than the privately purchased group
Parent Training					
Schreibman et al. 2013[17] US **G1:** Pivotal Response Training (PRT), 20/20 **G2:** PECS, 19/19 Quality: Good	**G1:** 29.5 ± 6.9 **G2:** 28.9 ± 4.2 NR	**G1+G2:** Trained therapists, parents **G1+G2:** Home	**G1:** Yes **G2:** Yes	**G1+G2:** Mean 247 hrs treatment over 23 weeks, G1 focused on motivational techniques delivered by parents to facilitate communication. G2 focused on motivational techniques to facilitate augmented communication	• Children in both G1 and G2 showed gains in language from baseline to followup 3 months after the end of treatment but no between group differences reported; effect sizes for change ranged from .001 to .486 • In the PECS group 12/19 children mastered requesting and were learning to comment using pictures • Mean number of spoken words gained across groups=80; individual progress varied widely , with 78% of children using at least 10 spoken words at final followup
Strauss et al, 2012 [18, 19] Italy **G1**: Staff and parent mediated EIBI, 24/24	**G1**: 55.67 ± 17.63 **G2**: 41.94 ± 13.07 GMDS-ER GQ **G1**: 55.65 ± 20.06	**G1+G2**: Staff and parents **G2**: Parents **G1**:	**G1**: No **G2**: No	**G1:** For 12 months, alternated between one week of 25 hours of therapist-led center-based intervention and 3	• Compared to G2, children in G1 showed significant decrease in autism symptom severity, increases in language production and mental development • Compared to G1, children in G2 had

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G2: Eclectic, 20/20 Quality: Good	**G2**: 74.29 ± 29.37	Treatment center and home **G2**: Home		weeks of an average of 14 hours/week parent-led home intervention. Focus on individual skills, problem behaviors, and facilitated play and social interaction **G2**: In-home developmental intervention and cognitive behavioral treatment for approximately 12 hours/week. Focus determined by staff expertise and preferences.	improved parent-reported socialization and motor skills • In G1, older children achieved better adaptive behavior outcomes; younger children made more gains in early language comprehension and production. Children who gained more language comprehension had higher adaptive behavior scores pre-treatment. Pre-treatment language comprehension predicted post-treatment language production • In G2, higher pre-treatment mental development state and early language skills predicted better outcome on adaptive behaviors. Initial higher adaptive behaviors predicted better post-treatment early language comprehension. • In both groups, child outcomes on early language skills, mental developmental state and adaptive behaviors were significantly influenced by parental stress, child ability to respond correctly to prompts, number and difficulty of treatment targets, and child problem behaviors in sessions. The predictive power of parental stress on outcome autism severity was modified by perception of difficult child, with higher perceptions of difficulty associated with lower decreases in autism severity • Less parent inclusion in treatment provision resulted in decreased perceptions of a difficult child and less parental stress
Landa et al. 2012[20, 21]	**G1:** 28.6 ± 2.6	**G1:** Trained	**G1:** Yes	**G1:** Mean 205.66 ±	• Greater socially engaged imitation in G1

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US **G1:** Assessment Evaluation and Programming System for Infants and Children (AEPS) curriculum+additional joint attention and social interaction opportunities, 25/24 **G2:** AEPS curriculum, 25/24 Quality: Good	**G2:** 28.8 ± 2.8 **G1+G2:** 60.1 ± 11.9	interventionist + parent **G2:** Trained interventionist + parent **G1+G2:** Specialized clinic classroom	(AEPS), NR (additional joint attention) **G2:** Yes	18.63 hours of intervention over 6 months, intervention included elements of discrete trial training, pivotal response training, routines-based interaction, augmented communication, and visual cues and structure + orchestrated opportunities for initiation of joint attention(IJA), shared positive affect (SPA), and socially engaged imitation (SEI) **G2:** Mean 196±21 hours intervention over 6 months, intervention included elements of discrete trial training, pivotal response training, routines-based interaction, augmented communication, and visual cues and structure	compared with G2 at end of intervention and at 6-month followup (effect size=0.86, p.01); growth occurred during intervention period vs. followup period • Initiations of joint attention did not differ significantly between groups at the 6-month followup, though each group improved over time • Measures of expressive language and nonverbal cognition did not differ between groups at the 6-month followup • At long-term followup of G1+G2 (n=34) at mean 37.6 months after end of intervention (mean age=72.6 ± 17.5 months), IQ and Vineland communication scores increased from baseline (mean change 21.4 ± 22.9, effect size=1.02, p<.001 and 12.7 ± 19.4, effect size=0.81, p<.001, respectively) • No change in symptom severity (ADOS) at the long-term followup
Roberts et al. 2011[24] Australia **G1**: Individualized home-based program, 34/27 **G2**: Small group center-based program combined with parent training and support group, 33/29	**Age:** **G1**: 41.5 **G2**: 43.1 **G3:** 43.7 **IQ:** **G1**: 57 ± 11.7 **G2**: 66 ± 17.7 **G3:** 63.3 ± 15.5	**G1**+**G2**+**G3**: Multidisciplinary teams of teachers, speech pathologists, occupational therapists and psychologists	**G1**: NR **G2**: Yes **G3:** NA	**G1**: 2 hour visit every 2 weeks, 20 sessions max, 40 weeks duration, focused on communication, social skills, adaptive functioning and psychopathology, parent stress **G2**: weekly 2 hour	• Significant greater improvement in Reynell comprehension standard score for G2 compared to G1 (-7.3; 95% CI: -13.9 to - 0.7, p=0.02) • Greater improvement for expression standard score of the Reynell for the G2 compared to G1 (-3.0; 95% CI: -9.0, to 2.9, p=0.31 • Reynell standard comprehension and

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G3: Waitlist, 28/28 Quality: Good		**G1**:Home **G2**:Center **G3:** home/center		sessions, 40 weeks duration, six playgroups of 4–6 children, with six concurrent parent support and training groups, focused on communication, social skills, adaptive functioning and psychopathology, parent stress **G3:** Waiting list	expression scores **G3** performed better than G1, but not significantly • For the Reynell standard comprehension and expression scores G2 performed better than **G3** but not significantly. • **G3** improved significantly more G1 on the Vineland socialization scale • There were no statistically significant differences among the three groups for other child outcomes. When analyses were limited only to children with autism spectrum diagnoses, the magnitude of the effects increased but the presence or absence of statistical significance did not. • Parent outcomes: Parenting: statistically significant differences favoring G2 vs. G1 • No significant difference between groups for stress
Aldred et al. 2011[25, 26] UK **G1:** Parent training in social communication intervention plus community intervention, 14/14 **G2:** Community intervention, 14/14 Quality: Good	**G1:** 51.4 ± 11.8 **G2:** 50.9 ± 16.3 NR	**G1:** Speech language therapists, parent **G2:** Routine care as provided in community—speech pathologists, behavior analyst **G1:** Clinic, home **G2:** Community	**G1:** Yes **G2:** NR	**G1:** Suggested 30 minutes/day parent training, parents received monthly training for 6 months followed by training ~2 months for 6 months, intervention focused on facilitating communication via parental sensitivity and responsiveness, adapted communication strategies, consolidation, elaboration + routine care **G2:** Intensity NR, routine care including speech	• G1 showed improvements in ADOS scores, social interaction, expressive language, child communication acts during interaction • No adaptive behavior differences or differences in parenting stress between groups • Language gains particularly prominent in younger, lower functioning children • Increased parental synchrony (communication which maintained vs. redirected or controlled child responses) in G1 associated with reduction in child ADOS

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				pathology, ABA-based treatment	score (decreased impairment, p=.014); reduction in synchrony for G2 and small increase in mean ADOS scores • In tests of mediation, change in parental synchrony accounted for 34% of total treatment effect on ADOS outcome
Keen et al. 2010[27] Australia **G1:** Professional parent intervention, 17 families/NR **G2:** Self-directed video based parent intervention, 22 families/NR Quality: Good	**G1:** 36.38 ± 7.54 **G2:** 35.71 ± 6.92 **G1:** 53.06 ± 9.06 **G2:** 52.86 ± 6.53	**G1**: Doctoral students (facilitator) **G2**: DVD-led curriculum **G1**: Workshop / home **G2**: Home	**G1**:NR **G2**:NR	**G1**: 2-day parent group workshop and a series of 10 home-based consultations 10 X 1 hour home-visits which occurred twice-weekly over 5–6 weeks, focused on parental stress, child communication **G2**: Self-directed parent intervention group received an interactive instructional DVD "Being Responsive: You and Your Child with Autism" lasting for 6 weeks, focused on parental stress, child communication	• G1 showed significantly greater improvement on social communication at follow-up than G2 regardless of values at baseline • Parents low in self-efficacy at baseline demonstrated relatively higher levels of self-efficacy if they received G1 vs. G2 • G1 reduced child-related stress relative to G2 for both mothers and fathers • Fathers reported higher levels of stress than mothers in both groups • Behavior sample scores at follow-up not affected by group condition • All outcomes are based on parent report
Casenhiser et al. 2013[28] **G1:** MEHRIT (developmental individualized relationship-based intervention), 25/25 **G2:** Community-based treatment, 26/26	**G1:** 42.5 ± 8.8 (mo.) **G2:** 46.4 ± 8.3 (mo.) NR	**G1:** Speech-language pathologists, occupational therapists **G2:** Varied community-based	**G1:** Yes **G2:** NR	**G1:** 2 hours/week therapist training+3 hours parent interaction for 12 months; intervention focused on social interaction, communication, parental responsiveness,	• At pretreatment, G2 had higher scores on investigator-rated "enjoyment in interaction" domain of the modified Child Behavior Rating Scale; at followup, G1 improved significantly more compared with G2 on the domains of attention to activity, involvement, initiation of joint attention, and enjoyment in

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Quality: Fair		therapists **G1:** NR **G2:** Community-based		sensory-motor skills **G2:** Mean 3.9 hours treatment/week; treatment included speech therapy, ABA-based approaches, occupational therapy, social skills training, and specialized day care	interaction (p values <.05, effect sizes 0.63-1.02); no significant difference in compliance domain • Both groups improved from baseline to followup on language developmental quotient measure but no significant between group difference • Greater baseline language skills, initiation of joint attention, and involvement were significant predictors of language change
Rogers et al. 2012[29, 30] US **G1**: Parent-delivered Early Start Denver mode (ESDM), 49/49 **G2**: Community treatment as usual, 49/49 Quality: Fair	**G1:** 21.02 ± 3.51 **G2:** 20.94 ± 3.42 **G1:** 64.88 ± 17.22 **G2:** 63.08 ± 15.93	**G1:** Credentialed therapists trained in ESDM methodology **G2:**Community-based interventionists **G1:** University clinics 60-minute session weekly for 12 weeks **G2:** Interventions available in community	**G1:** Yes **G2:** NR	**G1:** 60-minute session weekly/12 weeks, ESDM intervention using parent training in increasing child attention and motivation; sensory social routines; engagement and joint activity; nonverbal communication; imitation skills; joint attention; speech development; using antecedent-behavior-consequence relationships; prompting, shaping, and fading techniques; conducting functional assessments to develop new interventions **G2:** Community interventions as selected by parents	• At followup, G1 received mean 1.48 hours treatment/week G2 received 3.68 (p<.05) • G2 had more severe social affect symptoms at baseline, poorer imitation and nonsocial orienting scores compared with G1 (p<.05) • No significant group differences on ADOS scores or measures of development at followup • Measures of parent acquisition of parent-child interaction skills did not differ between groups at followup • Social orienting and imitation skills were not found to be moderators of outcomes; increased hours of intervention and younger child age were significantly associated with improved developmental and vocabulary scores in a pooled analysis (p≤.05). In analyses by group, age and hours of intervention associated with improvements in vocabulary for G1 (p≤.05) • Parent stress decreased in G1 compared with G2 (p<.05)

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Pajareya et al. 2011[31] Thailand **G1:** DIR/Floortime,16/15 **G2:** Usual care, 16/16 Quality: Fair	**G1:** 56.6 ± 10.1 **G2:** 51.5 ± 13.9 NR	**G1:** Clinician trained in rehabilitation medicine **G2:** NR **G1:** Parents (attended one day training workshop, received 3-hour DVD lecture, and had two one-hour home visits with a trainer) **G2:** Community-based interventions	**G1:** Yes **G2:** NR	**G1:** Parent-administered DIR/Floortime for an average of 15.2 hours/week for 3 months. Intervention focused on following child's cues related to communication and engagement **G2:** 3 months of usual care interventions	• G1 improved significantly on the Functional Emotional Assessment Scale compared with G2 (p=.045) • CARS scores decreased (improved) for G1 vs. G2 (mean change 2.9 vs. 0.8, p=.004) • G1 scores on parent-rated measure of emotional development significantly improved compared with G2 (mean change 7.7 vs. 0.8, p=.007)
Carter et al. 2011 [32] US **G1**: More than Words, 32/29 **G2**: Control, 30/26 Quality: Fair	**G1:** 21.11 ± 2.71 **G2**: 21.51 ± 2.82 **G1**& **G2**: NR	**G1**+**G2**: Speech / language therapist **G1**+**G2**: Clinic , Home	**G1**:Yes **G2**:NR	**G1**: 8 group sessions with parents only and 3 in-home individualized parent –child sessions over 3.5 months, focused on enhancing parental responsivity and child communication **G2**: No treatment /treatment as usual	• No treatment effect on parental responsivity • G1 showed differential effects on child communication depending on a baseline child factor • Children with lower levels of baseline object interest exhibited facilitated growth in communication • Children with higher levels of object interest exhibited growth attenuation

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Oosterling et al. 2010[33] **G1:** Nonintensive parent training+specialized preschool, 40/36 **G2:** Specialized preschool, 35/31 Quality: Fair	**G1:** 35.2 ± 5.5 **G2:** 33.3 ± 6.4 **G1:** 58.4 ± 16.8 **G2:** 58.0 ± 16.9	**G1:** Parents **G2:** Preschool teachers **G1:** Home **G2:** Preschool	**G1:** NR **G2:** NA	**G1:** Parents received 4 two-hour training sessions plus 3 hour home visits every 6 weeks for 12 months focusing on promoting joint attention and language skills; children also received standard preschool care as noted below (mean 5.2 periods in preschool/day, mean 70.9 ± 131.2 minutes of therapies in preschool/week) **G2:** Specialized daycare or medical nursery for children with developmental issues; both provide individualized speech, motor, music, and play therapy with variable levels of parental support (mean 4.2 periods in preschool/day, mean 76.4 ± 112.8 minutes of therapies in preschool/week)	• No between group differences on language development after 12 months of intervention, though language skills within groups improved over time • No differences in CGI-Improvement scores (G1: 57% much improved, G2: 52% much improved) • No significant effects on parenting skills in either group; engagement, early social communication precursors, parental skills not found to be mediators of effects. DQ not a significant moderator

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Reed et al. 2012[34] UK **G1:** ABA, 14 **G2:** Special nursery, 21 **G3:** Portage, 18 **G4:** Local authority-developed parent training, 13 Quality: Fair	**G1:** 39.0 ± 6.9 **G2:** 41.5 ± 4.0 **G3:** 39.5 ± 6.3 **G4:** 40.2 ± 6.3 **G1:** 55.1 ± 17.3 **G2:** 52.2 ± 17.1 **G3:** 54.0 ± 15.4 **G4:** 51.7 ± 14.5	**G1:** Board certified behavior analysts or Complete Application of Behavior Analysis to Schools-trained individuals, trained tutors **G2:** Post-graduate special education teachers, learning support assistants **G3:** Graduate level Portage supervisor **G4:** Educational psychologist, trained teaching assistants **G1:** Home **G2:** Preschool **G3:** Home **G4:** Home	**G1:** Yes **G2:** Yes **G3:** Yes **G4:** NR	**G1:** Mean 30.4 hours/week for 9 months, 1:1 discrete trial based intervention **G2:** Mean 12.7 hours/week for 9 months, group-based intervention focused on social, motor, and other skills, some TEACCH elements **G3:** Mean 8.5 hours/week for 9 months, 1:1 intervention **G4:** Mean 12.6 hours/week for 9 months, 1:1 child training plus parent-delivered intervention	• Scores on cognitive and adaptive measures were not significantly different among groups • Scores on British Abilities Scale improved for G1 vs. G2-G4 ($p<.05$) • Composite change scores (mean of change scores on cognitive, adaptive, and educational measures) were not statistically significantly different across groups, although G1 vs. G2-G4 and G2 vs. G3-G4 approached significance ($p<.06$) • Composite change scores were inversely related to initial ASD severity for G2-G4 but positively related for G1; the strength of that relationship only differed significantly between G1 and G3 ($p<.05$) • As time in intervention increased, composite scores improved for G2-G4 but worsened for G1 ($p<.05$). No differences were found in the amount of improvement between G2-G4

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Reed et al. 2011[35] UK **G1:** Barnet Early Autism Model (BEAM), 16/16 **G2:** Portage Treatment, 16/16 Quality: Poor	**G1:** 43.6 ± 5.8 **G2:** 40.1 ± 8.3 **G1:** 83.3 ± 23.7 **G2:** 72.3 ± 12.5	**G1:** Trained facilitators, speech and occupational therapists, educational psychologist **G2:** Trained Portage facilitators **G1+G2:** Home	**G1:** Yes **G2:** NR	**G1:** Mean 6.4±2.1 hours/week individualized therapy focused on social communication, emotion regulation, transactional support and including TEACCH, PECS, music and speech therapy, communication, sensory integration **G2:** 8.5±6.8 hours/week delivered by parents and focused on communication, skill building based on Floortime model	• Significant gains from baseline to followup for G1 vs. G2 in investigator-and parent-rated measures of adaptive behavior and language (p values<.05) • Greater reduction in parental stress and increase in satisfaction in G1 vs. G2 (p values <.01) • Lower parent stress at baseline correlated with gains in adaptive behavior and language (p values <.05)
Wong et al., 2010[36] China **G1**: Early intervention, 9/9 **G2**: Control, 8/8 Quality: Poor	**G1**: 25.33 ± 6 **G2**: 27.88 ± 5.57 **G1**: 17.85 ± 4.16 **G2**: 17.91 ± 4.49	**G1+G2**: Trained interventionists **G1+G2**: Clinic	**G1**: NR **G2**: NR	**G1**: Ten 30-min sessions for 2 weeks with focus on communication, social interaction, parent stress **G2**: Starting from Week 5 with the same 10-session intervention, with focus on communication, social interaction, parent stress	• No significant group difference on communication, reciprocal social interaction or symbolic play • No between group differences on parent observation on language and relationship to people • No group difference on the total parent stress scores
McConkey et al., 2010[37] UK **G1**: Keyhole EIBI program, 36/35 **G2**: Control, 26/26 Quality: Poor	**G1**: 2.8 years **G2**: 3.4 years NR	**G1+G2**: Early intervention therapists **G1+G2**: Home	**G1**: NR **G2**: NR	**G1**:15–18 home visits over a nine-month period in 2 separate geographical areas, focus on child communication, parental stress **G2**: 5 home visits (n=15) and no additional	• G1 showed significant improvements on different indices of communication than G2 • Mothers improved on measures of health G1 more than G2 but not of stress • higher percentage of parents in G2 reported the children were improving on language and imitation at Time 1 compared to G1 but the percentages were comparable at Time 2

Author, Year, Country **Groups, N Enrollment/N Final** **Study Quality**	**Age, Mean Months ± SD** **IQ, Mean ± SD**	**Intervention Provider** **Intervention Setting**	**Intervention Manualized?**	**Intervention Intensity, Duration, And Focus**	**Key Outcomes**
				services or supports (n=11), focus on child communication, parent stress	• Only parents in G1 reported significant improvements from Time 1 to Time 2 on language, imitation and relating to others • Both groups improved on ratings of improvements in play • On all the Vineland measures, the standard deviations rose markedly at Time 2 for children in G1 but not for G2

ABA-applied behavior analysis; AEPS- assessment evaluation and programming system for infants and children; ADOS- autism diagnostic observation schedule; ASD- autism spectrum disorder; CARS-Childhood Autism Rating Scale; CI-confidence interval; DIR- Developmental, Individual Difference, Relationship-based (DIR®) Model; DTT- discrete trial training; DQ- developmental quotient; EEG- electroencephalogram; EIBI- early intensive behavioral intervention; ESDM- Early Start Denver Model; Z-group; IJA- initiation of joint attention; LEAP- learning experiences and alternate program for preschoolers and their parents; N-number; NR-not reported; SD-standard deviation; SEI- socially engaged imitation; SPA- shares positive affect; PECS- picture exchange communication system; PDD-NOS-Pervasive Developmental Disorder-Not Otherwise Specified; TEACCH- treatment and education of autistic and related communication-handicapped children

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Appendix G. Applicability Tables

Table G-1. Applicability of early intensive behavioral and developmental intervention studies

Domain	Description of applicability of evidence
Population	Studies included both toddlers and preschool children (i.e., children from 2-5 years; range of mean ages: 20.94 – 55.7 months). Baseline cognitive, language, and adaptive scores typically fell within the impaired range, reflecting characteristics of young children with ASD in the community. Most participants were male. Where reported, other population demographic characteristics were mixed regarding race, ethnicity, language spoken, parental education level, and socioeconomic status.
Intervention	Interventions included early intensive behavioral intervention without (EIBI) and with (Parent training) large parent training components. Approaches ranged in terms of manualization, techniques (e.g., DIR vs. TEACCH), provider, setting (i.e., school vs. home; individual vs. group), frequency, and intensity. 14/25 studies provided at least 6 months of treatment and 11/25 provided at least a year.
Comparators	Comparators included eclectic interventions, “treatment as usual” in the community, lower levels of manualized treatments, providing manuals with no additional training/support, special education preschool curricula, DVD-based parent training, and parent support. As in the intervention groups, comparators varied by setting, provider, frequency, and intensity, all of which were inconsistently documented.
Outcomes	Studies commonly assessed IQ, language, autism severity, and adaptive behavior outcomes after anywhere from 2 weeks to 2 years of intervention. Many studies found that both groups improved in IQ, adaptive behavior, and language/communication skills. Others found differential treatment effects. Because most studies compared one treatment to another without controlling for frequency or intensity, it is not always clear whether improvement is due to receiving any treatment vs. specific treatment modalities. Some evidence emerged that baseline age, autism severity, language, and cognitive skills interacted with specific treatment types to predict differential outcomes.
Setting	Studies took place in home, clinic, and school settings in the United States, Canada, Israel, China, Sweden, Italy, Norway, the Netherlands, Australia, Thailand, and the United Kingdom. Participants were assigned to treatment groups in a variety of ways including random assignment, parental preference, educational system and governmental decisions, geographical location, and availability of services.

Table G-2. Applicability of social skills studies

Domain	Description of applicability of evidence
Population	Studies typically included school-aged children (i.e. children from 4-13), typically male, diagnosed with high-functioning autism, with baseline cognitive scores typically within the average range, even though some studies also included children and classified them as high-functioning as long as they met an IQ score cutoff of 70 or above. The populations studied generally only reflect the IQ and language characteristics of school-aged children with ASD without concomitant cognitive and/or language deficits in the community.
Intervention	Social skills interventions varied widely in terms of scope and intensity. Examples included a few studies that replicated interventions using the manualized Skillstreaming model; a few studies that incorporated peer-mediated and/or group-based approaches; and interventions that focused on emotion identification and theory of mind training. One study examined long-term follow-up of the Children's Friendship Training program and another study was a Japanese pilot study of the Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) model. The studies also varied in intensity, with the majority of the studies consisting of 1-2 hour sessions/week lasting for approximately 4-5 weeks; however, some of the group-based approaches lasted for 15-16 weeks.
Comparators	Comparators were varied but the majority of studies included a wait-list control group. Other comparative interventions included revised or updated versions of previously utilized interventions or variations of group makeup (i.e. peer group only versus peer group with a sibling; child-directed group interaction or peer-directed group interaction).
Outcomes	Studies varied widely in their assessment of outcome measures. Several studies measured learning of new skills specific to the treatment (i.e. Skillstreaming Knowledge Assessment). Several studies utilized parent-report of social skills, including scores on the Social Responsiveness Scale, the Social Skills Rating System, and the BASC-2. Other studies utilized behavioral ratings by staff and/or teachers on the child's social interactions and social network salience. Finally, some studies examined emotion identification or theory of mind measures. All of the studies were short-term in nature, with follow-up occurring approximately 2-3 months post-intervention, if follow-up was done at all. The results indicated that most studies reported short-term gains in social skills and emotion recognition as reported by parents or within study measures. However, maintenance and generalization of these skills beyond the treatment context had variable results.
Setting	Studies were conducted in the US, Australia, Japan, and Europe (The Netherlands) in primarily clinic settings, even though a few group-based interventions were utilized in the school/community setting, and the emotion-identification interventions utilizing media were implemented in the home setting.

Table G-3. Applicability of studies of interventions addressing conditions commonly associated with ASD

Domain	Description of applicability of evidence
Population	Studies included children ages 4-16 with ADOS-confirmed ASD diagnosis and often with primary anxiety diagnosis. Most studies required IQ greater than 70 with children falling in the average range. Children were recruited from a range of sources including outpatient psychiatry clinics, schools, pediatrician's offices, parent and family support groups, university medical clinics and research centers. Children were mostly male, and primarily Caucasian in studies conducted within the US.
Intervention	Interventions consisted of cognitive behavioral therapy (CBT) typically provided on a weekly basis for 60-90 minutes over a period of four months although treat although treatment times ranged from 7 to 32 weeks. Interventions were typically manualized and included both children and parents. One study did not examine CBT rather examined parent training as an augmentation to risperidone.
Comparators	Most studies compared CBT to either wait list or treatment as usual controls, and two studies compared CBT to social skills therapies The study examining parent training augmentation compared participants on risperidone with parent training to those on risperidone without parent training.
Outcomes	Studies primarily targeted anxiety symptoms therefore the outcome measures included various measures of anxiety both at end of intervention and at a follow-up interval of 3 months to one year following termination of intervention. Measures of anxiety most commonly included the Anxiety Disorders Interview Schedule, the Spence Children's Anxiety Scale, the Multidimensional Anxiety Scale for Children and the Clinical Global Impressions-Severity Scale. Several studies additionally measured improvements in adaptive behavior measured by the Vineland Adaptive Behavior Scale as an outcome, and, one study measured improvements in executive functioning and one study measured improvements in emotion regulation as the primary outcome. The study assessing utilization of parent training augmentation of risperidone examined outcomes including irritability, maladaptive behaviors, socialization and communication.
Setting	Studies were primarily conducted in the US with one study conducted in Singapore. Interventions typically occurred in outpatient treatment centers and in the participants' homes.

Table G-4. Applicability of studies evaluating play/interaction-based interventions

Domain	Description of applicability of evidence
Population	Studies included children between 21 and 75 months of age with confirmed ASD diagnoses. The majority of children were male and were generally recruited from populations of children already receiving intervention in early intervention settings, preschools, or specialty schools. Children in studies were representative of the larger population of children with ASD in early intervention programs.
Intervention	Interventions used approaches focusing on joint attention, with most joint attention interventions using elements of Kasari's 2006 model; play skills/pretend play with a typically developing peer model; imitation; and parental responsivity. On study modified the Hanen More than Words approach. Intervention was mediated by parents/caregivers, teachers, and interventionists.
Comparators	Comparators included early intervention without additional joint attention or interaction training or no specific intervention.
Outcomes	Targeted outcomes included joint attention and engagement, imitation, language, play skills, and social skills.
Setting	Studies were conducted in mainstream and ASD-specific preschools, specialty schools, mainstream public schools, and research centers in the US, Belgium, and Norway.

Table G-5. Applicability of studies evaluating other behavioral approaches

Domain	Description of applicability of evidence
Population	Studies of neurofeedback included children between the ages of 8-12 years and had IQs in the average range (>70); children were recruited from a special education school and from the community. Studies of sleep interventions included children between 2 and 10 years of age. Participants were drawn from the Autism Treatment Network and from children attending a pediatrics and psychiatry clinic. Participants were generally reflective of the larger population of children with ASD and sleep issues. One study included young children (36-104 months) who may have issues with feeding/mealtime.
Intervention	Interventions included neurofeedback training, a sleep education pamphlet, and CBT with and without melatonin, parent education in sleep hygiene and in promoting appropriate mealtime behaviors.
Comparators	Comparators included no treatment/waiting list, group vs. individual training, and in one sleep study, melatonin alone, CBT+melatonin, or placebo.
Outcomes	Outcomes in neurofeedback studies included measures of executive function and social and communication skills. Sleep studies assessed sleep parameters including night wakings, time to fall asleep, sleep duration, and sleep anxiety. The feeding study assessed mealtime behaviors such as food acceptance.
Setting	Studies were set in the home and treatment centers in the US, the Netherlands, and Italy.