



*Applied Behavioral Analysis and
Other Behavioral Therapies for the
Treatment of Autism Spectrum
Disorder*

June 2011

Center for Evidence-based Policy

Oregon Health & Science University
3455 SW US Veterans Hospital Road
Mailstop SN-4N, Portland, OR 97239-2941
Phone: 503.494.2182
Fax: 503.494.3807

<http://www.ohsu.edu/ohsuedu/research/policycenter/med/index.cfm>

Acknowledgements

This report was prepared by:

Alison Little, MD, MPH

Heidi Kriz, MPH, RD

Aasta Thielke, MPH

Center for Evidence-based Policy
Oregon Health and Science University

This report was reviewed by:

Valerie King, MD, MPH

Center for Evidence-based Policy
Oregon Health and Science University

This document was prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to support organizations and their constituent decision-making bodies to make informed decisions about the provision of health care services. The document is intended as a reference and is provided with the understanding that the Center is not engaged in rendering any clinical, legal, business or other professional advice.

The statements in this document do not represent official policy positions of the Center. Researchers and authors involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

This technology assessment report is based on research conducted by a contracted technology assessment center, with updates as contracted by the Washington State Health Care Authority. This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the investigators and authors who are responsible for the content. These findings and conclusions may not necessarily represent the views of the HCA/Agency and thus, no statement in this report shall be construed as an official position or policy of the HCA/Agency.

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

Table of Contents

Executive Summary.....	1
Background	7
Figure 1. CDC Average Rates of Autism per 1000 Children	12
Figure 2. WA State Autism Population Estimate	13
Figure 3. Projected Costs for ABA Therapy Based on \$50,000 Annual Benefit Cap.....	13
Figure 4. Related Medical Codes	14
Methods.....	15
Findings	16
Key Question 1. Among children ages 2 to 12 with ASDs, what are the effects of behavioral, treatment approaches that utilize ABA principles on core and commonly associated symptoms?....	17
Key Question 2. Among children ages 2 to 12 with ASDs, what are the modifiers of outcome for different behavioral treatments or approaches (including characteristics of the intervention, provider, child or family)?	36
Key Question 3. Are there any identifiable changes early in the treatment phase that predict treatment outcomes?.....	39
Key Question 4. What is the evidence that effects measured at the end of the treatment phase predict long-term functional outcomes?	39
Key Question 5. What is the evidence that specific intervention effects measured in the treatment context generalize to other contexts (e.g., people, places, materials)?	40
Key Question 6. What evidence supports specific components of treatment as driving outcomes, either within a single treatment or across treatments?	40
Key Question 7. What evidence supports the use of a specific treatment approach in children under the age of two who are at high risk of developing autism based upon behavioral, medical, or genetic risk factors?	41
Discussion.....	43
Guidelines	54
Policy Considerations.....	59
Summary	61
Appendix A. Summary of Guidelines	64
Appendix B. Quality of Guidelines	76
Appendix C. Summary of Medicare and Private Payor Policies.....	77
Appendix D. Summary of State Coverage Policies.....	78
Appendix E. Guideline Quality Assessment Tool	81
References	83

Executive Summary

Background

Autism Spectrum Disorder (ASD) is a group of pervasive developmental disorders (PDD) that includes Autistic Disorder, Asperger Syndrome, and Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS); it is estimated to affect 1 out of every 110 children. Autism spectrum disorder is characterized by impairments in communication, behavior, and social interaction and by repetitive behaviors coupled with obsessive interests, and is often accompanied by comorbid conditions, such as epilepsy and mental retardation.

A range of interventions are available for the treatment of ASD and the symptoms commonly associated with ASD (e.g., anxiety, sensory difficulties). Treatments for ASD focus on improving core deficits in social communication, as well as addressing challenging behaviors to improve functional engagement in developmentally appropriate activities. Common behavioral strategies used in the treatment of ASD are based on learning theory and make use of procedures such as reinforcement, prompting, and shaping techniques to increase the rate of positive behaviors and reduce the frequency of unwanted behaviors. Positive reinforcement and other principles to build communication, play, social, academic, self-care, work, and community living skills and to reduce problem behaviors in individuals with ASD have been used by behavioral therapists.

Applied behavioral analysis (ABA) is a general intervention approach for the treatment of ASD. It is a systemic application, at any time during a child's day, of behavioral principles to modify behavior. Some ABA techniques involve instruction that is directed by adults in a highly structured fashion, while others make use of the learner's natural interests and follow his or her initiations. Other techniques teach skills in the context of ongoing activities. All skills are broken down into small steps or components, and learners are provided many repeated opportunities to learn and practice skills in a variety of settings, with abundant positive reinforcement. Different applications of ABA include Positive Behavioral Interventions and Support (PBS), Pivotal Response Training (PRT), Incidental Teaching, Milieu Therapy, Verbal Behavior, and Discrete Trial Training (also known as Discrete Trial Learning), among others.

Early intensive behavioral intervention (EIBI) in contrast to ABA, is a much more prescriptive, manualized program that integrates components of ABA. Children in an EIBI program have therapy approximately 40 hours per week over the course of up to two years. Proponents of EIBI recommend starting therapy as early as possible and preferably before the age of three. Two manualized EIBI programs are the University of California, Los Angeles (UCLA)/Lovaas model and the Early Start Denver Model (ESDM). Both programs involve high intensity instruction using ABA techniques but have several differences. The UCLA/Lovaas method uses one-on-one therapy sessions and discrete trial teaching. The ESDM uses ABA principles with developmental and relationship-based approaches for young children. Other treatment approaches exist that emphasize parent training for treatment (e.g., Pivotal Response Training, Hanen More than Words) and/or use joint attention interventions, symbolic play, and play-based interventions (e.g., Stepping Stones Triple P Program, Relationship Development

Intervention (RDI), Mifne model). These therapies have not been manualized but are based on ABA principles.

Other behavioral interventions, aside from those based in ABA, are also used in the treatment of ASD. Cognitive behavioral therapy is used to teach children with ASD to monitor and manage their own behaviors through changing their perceptions, self-understanding and beliefs, based on the assumption that change is most likely to occur when a child is actively involved in their own behavior management. Neurofeedback involves the monitoring of brain activity while an individual interacts with specially designed computer programs created to promote attention or other skills. Sleep interventions train parents and children strategies to deal with difficult sleep behaviors common in children with ASD, and to establish sleep routines. All of these behavioral interventions are used in addition to the ABA, ABA-based, and EIBI interventions described above.

Currently, no Washington State agency covers ABA therapy for autism; however, other services that are commonly identified as components or alternatives to ABA are covered given they are under a treatment plan of medically necessary therapies. In comparison, an increasing number of states are considering or have laws mandating insurers to cover the diagnosis and treatment of ASD. Currently, 27 states mandate insurance coverage for treatment of autism, with a number including the coverage of ABA in their mandates. Total lifetime per capita cost of direct medical treatment for an individual with ASD is estimated to be \$305,956. Given the high cost of treatment, the large number and variety of available treatments, and constrained budgets, state policymakers need to determine which treatments are likely to improve outcomes for children with ASD, so they can better target the use of limited state resources.

Methods

At the direction of the Washington HTA program, the recent Agency for Healthcare Research and Quality (AHRQ) systematic review, *Comparative Effectiveness of Therapies for Children with Autism Spectrum Disorders* (Warren et al., 2011), was identified as the sole source of evidence for this report.

A search for relevant clinical practice guidelines was conducted using predetermined high quality sources from the Medicaid Evidence-based Decisions Project (MED). Included guidelines were limited to those published after 2005. Select private and federal payor coverage policies, as identified by the Washington HTA program, were reviewed. State coverage policies were identified through the National Conference of State Legislatures, Kaiser Family Foundation, and Autism Votes.

Included clinical practice guidelines and the Warren et al. (2011) systematic review were quality assessed using standard instruments developed and adapted by the MED Project that are modifications of systems in use by the National Institute of Clinical Excellence (NICE) and the Scottish Intercollegiate Guidelines Network (SIGN), and the Appraisal of Guidelines Research and Evaluation (AGREE) Collaboration, respectively.

Findings

The Warren et al. (2011) systematic review evaluated a wide variety of interventions, including behavioral, educational, family, medical, allied health and CAM treatment approaches. However, at the direction of the Washington HTA program, this report is limited to behavioral interventions that are not delivered in an educational setting.

Methods (Warren et al., 2011)

Methods of the Warren et al. (2011) systematic review included studies published in English from January 2000 to May 2010. The MEDLINE®, ERIC and PsycInfo® databases were searched, as well as grey literature from the US Food and Drug Administration, and clinical trial registries such as ClinicalTrials.gov. Reference lists were hand searched. All study designs were included except case reports. Medical studies with fewer than 30 participants, and behavioral, education, and allied health studies with fewer with 10 participants were excluded. Studies without a comparison group with at least 10 children with ASDs were included in the review. Single-subject design studies were not excluded on the basis of their design alone. However, the majority of single subject studies do not include at least 10 participants and were therefore not included in the Warren et al. (2011) review.

Two reviewers quality assessed each study with differences resolved through discussion. Studies were rated as good, fair, poor. The overall strength of the evidence was assessed using the *Evidence-based Practice Centers Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. The strength of evidence was presented as insufficient, low, moderate, or high.

Results (Warren et al. 2011)

Searches retrieved 4,120 citations, of which 183 articles representing 159 studies were included in the report. Of these, 78 studies pertained to behavioral interventions.

Key Questions [modified for Washington HTA to focus on behavioral interventions only]

KQ1. Among children ages 2 to 12 with ASDs, what are the effects of behavioral, treatment approaches that utilize ABA principles on core and commonly associated symptoms?

The evidence suggests that early intensive behavioral and developmental intervention (EIBDI) may improve core areas of deficit for individuals with ASDs; however, randomized controlled trials (RCTs) are few and include small numbers of participants. In addition, there are no direct comparison trials. Within this category, studies of UCLA/Lovaas-based interventions report greater improvements in cognitive performance, language skills, and adaptive behavior skills than other broadly defined treatments. However, strength of evidence is currently low. In addition, the consistency of benefit is lacking, in that not all children demonstrate rapid gains, and many children continue to display substantial impairment. Although positive results are reported for the effects of intensive interventions that use a developmental framework, such as ESDM, evidence for this type of intervention is currently insufficient because few studies have been published to date.

Less intensive interventions focusing on providing parent training for bolstering social communication skills and managing challenging behaviors have also been studied. Some

interventions have shown short-term gains in social communication and language use, but the current evidence base for such treatment remains insufficient.

Although all of the studies of social skills interventions reported some positive results, most have not included objective observations of the generalizability and the maintenance of the improvements. Strength of evidence is considered insufficient for social skills training and play- and interaction-based approaches. Several studies suggest that interventions based on cognitive behavioral therapy are effective in reducing anxiety symptoms, but replication of results is needed. Strength of evidence for these interventions is currently insufficient.

KQ2. Among children ages 2 to 12 with ASDs, what are the modifiers of outcome for different behavioral treatments or approaches (including characteristics of the intervention, provider, child or family)?

Only two studies were identified that directly addressed this question. One analyzed the initial characteristics of the subject children and found that children who were low in initial object exploration benefited more from Response Education and Prelinguistic Milieu Teaching (RPMT), while children who were relatively high in initial object exploration demonstrated more benefit from Picture Exchange Communication System (PECS). Another study examined the impact of which provider (parent vs. professional) delivered the UCLA/Lovaas protocol-based interventions. There was no significant difference in outcomes for children receiving the intervention in a clinical setting vs. at home from highly trained parents.

Other potential correlates that warrant further study because of conflicting data include pretreatment IQ and language skills, and age of initiation of treatment (with earlier age potentially associated with better outcomes). Social responsiveness and imitation skills have been suggested as skills that may correlate with improved treatment response in UCLA/Lovaas treatment, whereas “aloof” subtypes of ASDs may be associated with less robust changes in IQ. Other studies have seen specific improvement in children with PDD-NOS vs. Autistic Disorder diagnoses, which may be indicative of baseline symptom differences. However, many other studies have failed to find a relationship between autism symptoms and treatment response.

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

The literature offers very little information about characteristics or responses early in treatment that might predict long-term outcomes. Some evidence suggests that changes in IQ over the first year of either UCLA/Lovaas-based or ESDM intervention predicts, or accounts for, longer term change in IQ.

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

One study specifically addressed end-of-treatment effects to predict longer range outcomes. The feasibility of such studies was established in this language study, which reported outcomes 12 months post intervention.

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

Few studies measured generalization of effects seen in treatment conditions to either different conditions or different locations. Among behavioral studies, those of treatments for commonly associated conditions, such as anxiety, employed outcomes assessment outside the therapeutic environment, with positive results observed. However, in most cases, outcomes are parent reported and not confirmed by direct observation.

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

No studies were identified to answer this question.

KQ7. What evidence supports the use of a specific treatment approach in children under the age of two who are at high risk of developing autism based upon behavioral, medical, or genetic risk factors?

Research on very young children is preliminary, with four studies identified. One good-quality RCT suggested benefit from the use of ESDM in young children, with improvements in adaptive behavior, language, and cognitive outcomes. Diagnostic shifts within the autism spectrum were reported in close to 30 percent of children but were not associated with clinically significant improvements in ADOS severity scores or other measures.

Guidelines

Two guidelines (NZ 2010; SIGN 2007) make recommendations for ABA and interventions based on ABA principles. The SIGN (2007) guideline states that the Lovaas program should not be presented as an intervention that will lead to normal functioning, and that behavioral interventions should be considered in young people with ASD. The New Zealand (NZ) (2010) guideline states that ABA should be considered for children and young people with ASD, and that there is a lack of knowledge about the suitability of ABA for persons with Asperger Syndrome and those 15 years or older. The NZ guideline also recommends the use of EIBI in young children with ASD but states that regular monitoring for the evaluation of effectiveness is crucial. The NAC (2009) and AAP (2007) guidelines summarize the evidence and do not make specific recommendations.

Three guidelines (NAC, NZGG, and SIGN) included in this report addressed CBT. All three guidelines state that CBT can be a therapy option. The SIGN guideline (based on a systematic review of the evidence) was unable to draw conclusions about the effectiveness of CBT and recommends that professionals be aware that some of these interventions require a level of verbal and cognitive development. Other interventions addressed in this report were not covered by the included guidelines, were not supported by the evidence, or were grouped into broad categories making it difficult to draw conclusions about the individual interventions.

Policy Considerations

Federal, state and private payor policies are not consistent in mandating coverage of ABA therapy for the treatment of ASD. Of the federal and private payor policies reviewed, Aetna is the only payor to cover intensive educational interventions and explicitly mentions that there is insufficient evidence regarding the superiority of any specific intervention, such as ABA. An increasing number of states have coverage mandates for the diagnosis and treatment of ASD. Mandate components, such as included treatments, age restrictions, and maximum benefit limits vary significantly between states. With a lack of standardized educational and/or practical requirements for ABA providers, a small number of states have included ABA Licensure Boards in their state coverage mandates.

Limitations of the evidence

- There are very few well-controlled trials for ASD treatments based in ABA theory.
- Most studies report on short-term outcomes and the degree to which those outcomes translate to functional outcomes over time is largely unknown.
- The range of treatment approaches evaluated in the literature may not match those that are available in practice, and the highly controlled treatment environments may not translate to outcomes that can be achieved in the community.
- Fidelity to treatment in the community may be limited, particularly for those interventions that are not manualized.
- Of the published trials, many have small sample sizes, different treatment approaches, varying durations of treatment, different follow-up times and outcome measures, and cover a variety of treatment intensities.

Background

Clinical overview

Autism Spectrum Disorder (ASD) is a group of pervasive developmental disorders (PDD) that includes Autistic Disorder, Asperger Syndrome, and Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS) (Warren et al., 2011). The Centers for Disease Control and Prevention (CDC) estimate the national prevalence of ASD to be 9.0 per 1,000 children aged eight years, or 1 out of every 110 children (Rice, 2009). The prevalence in males is 4.5 times greater than the prevalence in females (CDC, 2010; Rice, 2009). Autism spectrum disorder is characterized by impairments in communication, behavior, and social interaction and by repetitive behaviors coupled with obsessive interests, and is often accompanied by comorbid conditions (Warren et al., 2011). About a third of individuals with ASD have epilepsy and three quarters have mental retardation (CDC, 2002; Myers & Johnson, 2007).

A range of interventions are available for the treatment of ASD and the symptoms commonly associated with ASD (e.g., anxiety, sensory difficulties). Treatments for ASD focus on improving core deficits in social communication, as well as addressing challenging behaviors to improve functional engagement in developmentally appropriate activities (Warren et al., 2011). Autism spectrum disorder lacks a cure and there is no universal consensus on which treatment interventions are most effective (Warren et al., 2011).

General description of treatments based on behavioral principles

Behavioral strategies are based on learning theory¹ and make use of procedures such as reinforcement, prompting, and shaping techniques to increase the rate of positive behaviors and reduce the frequency of unwanted behaviors. Since the early 1960's, hundreds of behavior analysts have used positive reinforcement and other principles to build communication, play, social, academic, self-care, work, and community living skills and to reduce problem behaviors in learners with autism of all ages. Behavioral therapies have often been adapted for training parents and teachers to be a part of, and sometimes the primary providers of, the therapy.

The effectiveness of behavioral interventions to improve the functioning of children with ASD and to ameliorate behavioral difficulties has been recognized since the 1960's (Bandura, 1969; Ullman & Krasner, 1965). Over the past four decades there has been a steady growth in behaviorally based programs for young children with ASDs under a number of different titles. Although many psycho-educational and behavioral interventions aim to help with specific skills or symptoms, more comprehensive intervention programs for young children with ASD aim to address elements of behavioral, developmental and educational functioning. These comprehensive intervention approaches are described in more detail below, followed by a summary of those interventions that aim to address specific skills.

¹ All psycho-educational programs have important elements in common and essential components of many are techniques developed from learning theory (Skinner, 1953). Behavioral strategies, sometimes referred to as behavior modification or operant conditioning, involve the use of consequences to modify the occurrence and form of behavior. These principles are part of any successful education program for any child, not just children with ASD.

Behavioral Interventions

Applied Behavioral Analysis (ABA) – Applied Behavior Analysis (ABA) means the systematic application of behavioral principles to modify behavior at any time during the child’s day. It was first defined as “the process of applying sometimes tentative principles of behavior to the improvement of specific behaviors and simultaneously evaluating whether or not any changes noted are indeed attributable to the process of application” (Baer, Wolf, & Risley, 1968, p. 91).

Some ABA techniques involve instruction that is directed by adults in a highly structured fashion, while others make use of the learner’s natural interests and follow his or her initiations. Other techniques teach skills in the context of ongoing activities. All skills are broken down into small steps or components, and learners are provided many repeated opportunities to learn and practice skills in a variety of settings, with abundant positive reinforcement. The goals of intervention, as well as the specific types of instructions and reinforcers used, are customized to the strengths and needs of the individual learner. Performance is measured continuously by direct observation, and the intervention is modified if the data show that the learner is not making satisfactory progress.

Applied behavior analysis is a *general* approach to intervention which is readily adaptable to many different circumstances and settings and can therefore be used in treatment of ASD, either as a technique for teaching specific skills, or to form the basis of a comprehensive treatment program in combination with a range of other psycho-educational and behavioral strategies. In comprehensive ABA, the skills and behavior of each child are assessed, and appropriate functional skills to be taught are chosen with respect to the child’s ability. The teaching environment is continually analyzed to optimize classroom structure, adapt instructional activities, and to develop meaningful curricula. Different applications of ABA commonly used for individuals with ASD include Positive Behavioral Interventions and Support (PBS), Pivotal Response Training (PRT), Incidental Teaching, Milieu Therapy, Verbal Behavior, and Discrete Trial Training (also known as Discrete Trial Learning), among others.

Early Intensive Behavioral Intervention Program (EIBI) – In contrast to ABA, early intensive behavioral intervention (EIBI) (Lovaas, 1987; McEachin, Smith, & Lovass, 1993) is a much more prescriptive, manualized program in which children have therapy approximately 40 hours per week and treatment can last at least two years. It includes components of the ABA theory listed above. Proponents of EIBI recommend starting therapy as early as possible and preferably before the age of three (Howlin, Magiati, & Charman, 2009).

Two manualized intensive programs are the University of California, Los Angeles (UCLA)/Lovaas model and the Early Start Denver Model (ESDM)². Both programs involve high intensity instruction using ABA techniques but have several differences. The UCLA/Lovaas method uses one-on-one therapy sessions and discrete trial teaching. The ESDM uses ABA principles with

² Published treatment manuals are highly detailed and are designed to guide providers in directing and monitoring treatment (Howlin et al., 2009; Warren et al., 2011).

developmental and relationship-based approaches for young children (Warren et al., 2011). Other treatment approaches exist that emphasize parent training for treatment (e.g., Pivotal Response Training, Hanen More than Words). These therapies have not been manualized but are based on ABA principles.

Social Skills Interventions – There are many different approaches that address social difficulties for children with ASD. Peer-mediated intervention is one approach that is used to both encourage specific social skills and broader interactions and relationships (Rogers, 2000; McConnell, 2002). In this type of intervention, children without ASD are taught how to initiate, elicit, prompt and reinforce social behaviors of children with ASD (Odom, Chandler, Ostrosky, McConnell, & Reaney, 1992). Parents can also be taught to train siblings to use peer-mediated approaches at home to improve child-sibling interactions (Strain, Kohler, Storey & Danko, 1994).

Play- /Interaction-based Interventions – Play- and interaction-based interventions focus on using interactions between children and adults to improve outcomes, such as the ability to engage in symbolic play, to imitate, or joint attention skills (Warren et al., 2011). Common play-based interventions include Stepping Stones Triple P Program, Relationship Development Intervention (RDI), and the Mifne model.

Cognitive Behavioral Therapy – Cognitive behavioral interventions can be used to teach children with ASD to monitor and manage their own behaviors through changing their perceptions, self-understanding and beliefs, based on the assumption that change is most likely to occur when a child is actively involved in their own behavior management. For this reason, cognitive behavioral methods are most appropriate for children with some degree of self-understanding and self-awareness and are therefore mostly used with school-age children and adolescents with High Functioning Autism and Asperger's Disorder.

Sleep Hygiene – These interventions include sleep workshops for parents and children and are directed towards establishing sleep routines and strategies for dealing with difficult sleep behaviors. Common sleep difficulties addressed by sleep hygiene programs include disordered sleep patterns, night waking, and difficulty falling asleep, all which are common in children with ASD (Warren et al., 2011).

Neurofeedback – This type of intervention uses the placement of electrodes to monitor brain activity while an individual uses computer games specially designed to promote attention or other skills. Through these exercises, individuals learn to control brain activity patterns associated with anxiety, ADHD and ASDs (Warren et al., 2011).

Single-Subject Research

Some reviewers of intervention programs for children with autism have recently been critical of the validity and generalizability of case report and case series research. More specifically, there have been discussions over the use of single subject study designs for evaluating the effectiveness of interventions. First described in the 1960s, single-subject research became a key research design in the field of special education and has grown in its use throughout other

education and psychology disciplines (Horner et al., 2005). This design was introduced into clinical research in the late 1980s as the “N-of-1” study design. It serves the purpose to document a cause and effect relationship between an intervention and outcome for a single individual (Guyatt, 1986). In single-subject or N-of-1 studies, the individual serves as his or her own control. If possible, the individual is randomly assigned to an experimental (intervention) or control condition and the outcome (dependent variable) is measured. The individual is then crossed over to the other condition and again the outcome is measured. Ideally, this cycle is repeated at least three times, and the outcomes are assessed by an evaluator blind to the experimental and control conditions (Guyatt et al., 1990; Horner et al., 2005; Yelland et al., 2009). Horner et al. (2005) and others have outlined indicators of high quality single-subject research. If done well, these studies can provide the highest standards for establishing the benefits and harms of an intervention for a particular individual (Guyatt, Sackett, and Taylor, 1986; Schuffham, et al., 2010). One key assumption is that neither the experimental nor the control condition should influence the effect of the next condition on the outcome.

The main issue for single-subject or N-of-1 trials is the external validity or generalizability of the results beyond the individual(s) in the study. Horner et al. (2005) proposed standards to enhance confidence that the results of single-subject studies can be generalized beyond the subjects in the studies. These standards involve replication of the study across different participants, settings, and materials. The replication should include at least five studies involving 20 or more subjects, and these studies should be carried out by at least three different researchers in three different locations. Moreover, techniques have been developed to quantitatively combine the results of rigorous single-subject and N-of-1 trials to estimate intervention effectiveness for a target population (Zucker et al., 1997). Unfortunately, these standards and methods that lend support to the external validity or generalizability of results from single-subject research have not been widely applied.

Policy context and cost information

An increasing number of states are considering or have laws mandating insurers to cover the diagnosis and treatment of ASD (Kaiser Family Foundation (KFF), 2011). Currently, 35 states and the District of Columbia have laws related to autism and insurance coverage. This includes 27 states that mandate insurance coverage for treatment of ASD (Autism Votes, 2011; KFF, 2011; National Conference of State Legislators, 2011). Furthermore, the total lifetime per capita cost of direct medical treatment for ASD is estimated to be \$305,956, with total lifetime societal per capita costs of autism estimated to be approximately \$3.2 million (Ganz, 2007). Given the high cost of treatment, the large number and variety of available treatments, and constrained budgets, state policymakers need to determine which treatments are likely to improve outcomes for children with ASD, so they can better target the use of limited state resources.

Washington State Agency Data

The following data is provided by the Washington State agencies on their utilization and cost information.

Washington State Agency Coverage – ABA Therapy

Currently, no Washington State agency covers ABA Therapy for Autism. However, there is information about other services covered, that are commonly identified as components or alternatives to ABA Therapy; and there is information about potentially impacted agency population, prevalence, and potential cost.

Services covered by DSHS and UMP/PEB

As noted, Washington State purchasers do not currently cover ABA Therapy for ASD specifically. However, a range of services are covered. In general, these services are covered if they are provided under a treatment plan of medically necessary therapies, designed and administered within the scope of practice for state licensed professionals (e.g., psychologists, speech language therapists, occupational therapists, physical therapists). Please note that treatment plans are developed to address the medically/psychologically presenting symptoms of each child, rather than on a specific autism diagnosis.

Uniform Medical Plan, Public Employee Benefit Plan, 2011

- Outpatient mental health and behavioral health therapies, unlimited.
- Outpatient physical, occupational, and speech therapy services up to 60 visits per calendar year.
- Inpatient/outpatient neurodevelopmental therapy, up to 60 visits per calendar year.
- Drugs on the preferred drug list, including stimulants, antidepressants, mood stabilizers, anti-anxiety and anti-psychotics.

DSHS/Medicaid, 2011

- Psychotherapy services provided by psychiatrists, psychiatric ARNPs, psychologists, and licensed mental health professionals, including insight oriented, behavior modifying/supportive, individual, family or group, up to 20 hours per year. Cognitive behavioral therapy and elements of sensory integration, verbal behavior intervention, and applied behavioral analysis may be included in treatment plans for autistic children.
- Physical therapy (PT) including therapies to develop strength, endurance, range of motion, and flexibility; re-education of movement, balance, coordination, kinesthetic sense, posture, proprioception for sitting, gait training; group therapy; and use of dynamic activities to improve functional performance.
- Occupational therapy (OT) including development of cognitive skills to improve attention, memory, problem solving, enhancement of sensory processing and adaptive responses to environmental demands, self-care/home management in activities of daily living; and use of assistive/adaptive equipment, community and work integration training.
- Speech therapy (ST) including treatment and evaluation of speech, language, voice communication and auditory processing, speech-generating devices, oral and pharyngeal swallowing function.

- PT, OT, ST are available as outpatient services. Annual coverage is not limited for clients 20 years old and younger; daily coverage is limited to one treatment unit per day.
- Pharmaceutical drugs for behavioral management.
- Beyond these services, further treatment is provided through Aging and Disability Services (ADSA), Division of Developmental Disabilities (DDD), ITEIP (Early Intervention Services, birth through age three), and local school districts.

Population, Prevalence, and Utilization Estimates for DSHS and UMP/PEB

As noted, Washington State purchasers do not currently cover ABA Therapy for ASD specifically.

Analysis References:

- Autism prevalence is estimated at 0.6 to 0.9% (1 out of 110 average in 2002 to 1 out of 150 average in 2006 (CDC, Autism Website accessed 9/1/2010 <http://www.cdc.gov/ncbddd/autism/index.html>)
- Agency population data for children aged 2 to 12 displayed for years 2006 through 2009. This age range based on the literature review.
- For demonstration of potential utilization, ABA Therapy with benefit cap of \$50,000 per year was used based on model mandated benefit language.

Figure 1. CDC Average Rates of Autism per 1000 Children

Changes in Prevalence of ASDs among Children 8 Years Old, 2002 to 2006

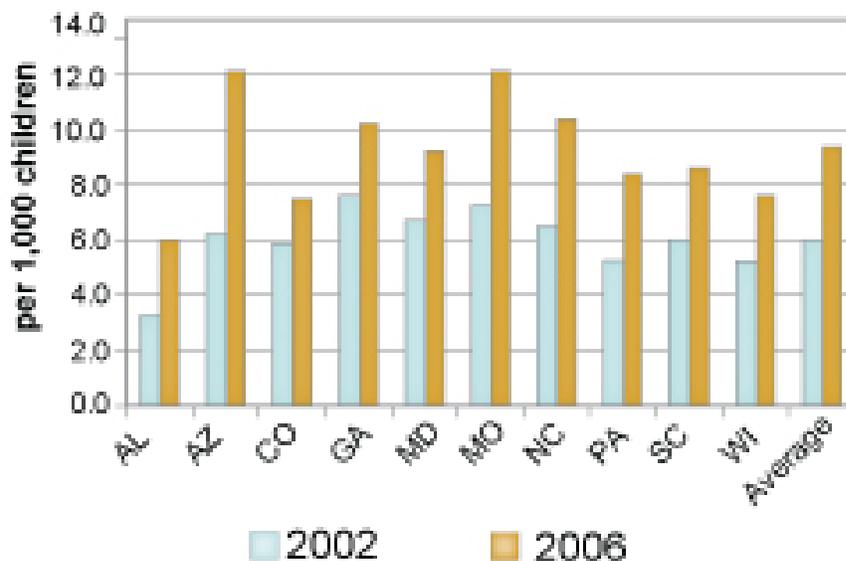


Figure 2. WA State Autism Population Estimate

	2006	2007	2008	2009
DSHS 2-12 Population	333,592	336,949	358,745	399,124
UMP/PEP 2-12 Population	16,675	17,303	21,903	22,450
Total Children 2-12 Population	350,267	354,202	380,648	421,574
Low Estimate Autism (1/150)	2,102	2,125	2,284	2,529
Hi Estimate Autism (1/110)	3,152	3,188	3,426	3,794

Figure 3. Projected Costs for ABA Therapy Based on \$50,000 Annual Benefit Cap

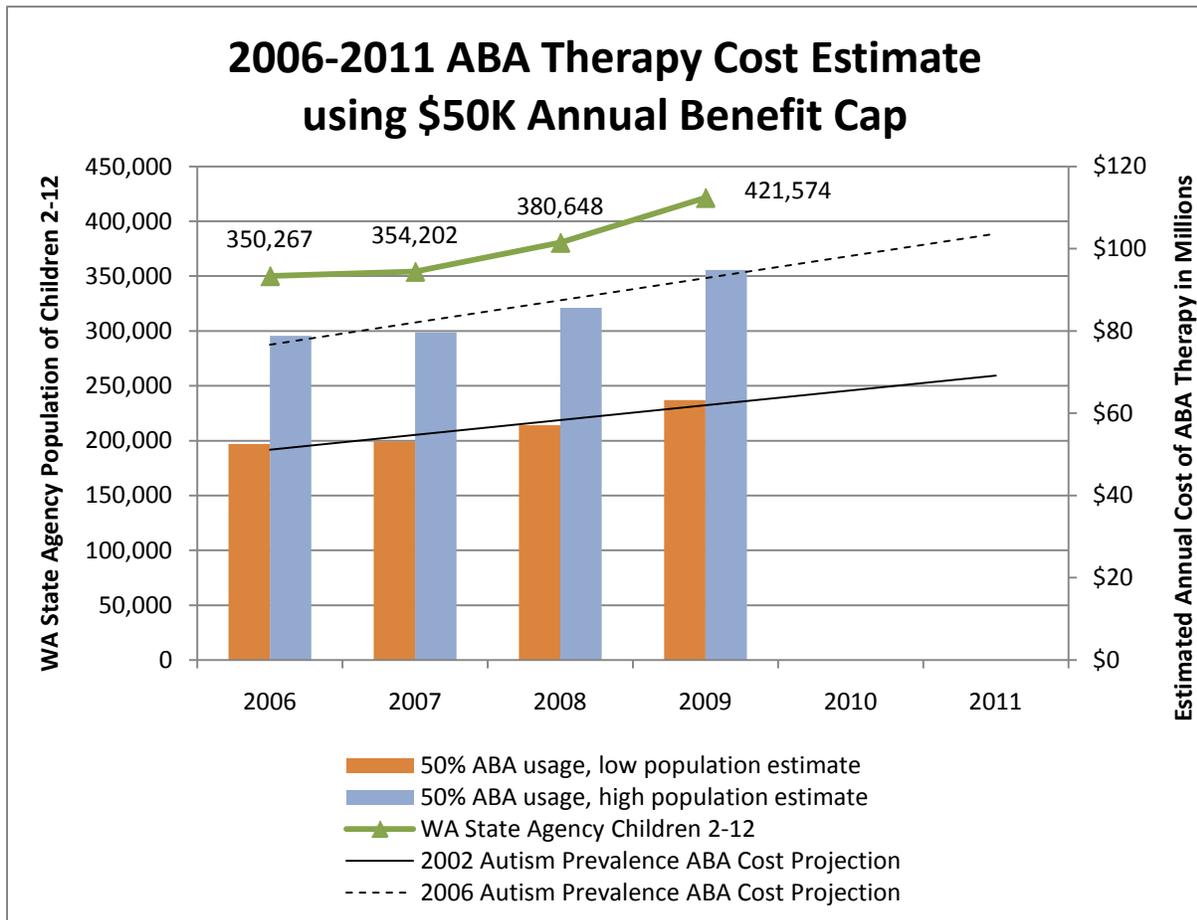


Figure 4. Related Medical Codes

Related Medical Codes		
Major CPT Codes		
Applied Behavior Analysis	96116	Neurobehavioral status exam
	90804-90807	Individual psychotherapy, insight oriented, behavior modifying and/or supportive
	90808	Fact to fact behavior modifying therapy, outpatient
	97532	ABA Therapist/Instructor Code – development of cognitive skills to improve attention, memory, problem solving
	97535	Self-care/home management training (ADL)
ICD-9 Procedure Codes	742.9	Unspecified anomaly of brain, spinal cord, and nervous system
	315.9	Unspecified delay in development or learning NOS
	299.0	Autistic disorder, Childhood autism, excluding disintegrative psychosis (299.1), Heller’s syndrome (299.1) schizophrenic syndrome of childhood (299.9)
	299.8	Other specified pervasive developmental disorders – Asperger’s disorder, Atypical childhood psychosis
	299.9	Unspecified pervasive developmental disorder, Pervasive developmental disorder NOS (also psychosis and schizophrenia)
	299.00-299.91	Pervasive developmental disorders
	V40.0-V40.9	Mental and behavioral problems
	V71.01-V71.09	Observation for suspected mental condition
Related CPTs	97003-4, 97110, 97112, 97140, 97530, 97510	Occupational therapy
	92506-8, 92597	Speech Therapy
	92510	Auditory Integration Therapy
	97001-2, 97112-3, 97116, 97110, 97530, 97150,	Physical Therapy
	90809	Individual psychotherapy, behavior modifying
	90847	Family psychotherapy with patient present
	90887	Parent education

Methods

Search strategy

At the direction of the Washington HTA program, the recent Agency for Healthcare Research and Quality (AHRQ) systematic review, *Comparative Effectiveness of Therapies for Children with Autism Spectrum Disorders*, was identified as the sole evidence source for this report (Warren et al., 2011).

A search for relevant clinical practice guidelines (CPGs) was conducted, using the following sources: the National Guidelines Clearinghouse database, the Institute for Clinical Systems Improvement (ICSI), the Scottish Intercollegiate Guidelines Network (SIGN), the National Institute for Health and Clinical Excellence (NICE), the Veterans Administration/Department of Defense (VA/DOD) guidelines, US Preventive Services Task Force (USPSTF), Australian National Health and Medical Research Council, New Zealand Guidelines Group, Center for Disease Control and Prevention (CDC), American Academy of Pediatrics (AAP), American Academy of Child and Adolescent Psychiatry (AACAP), and American Psychiatric Association (APA). Included guidelines were limited to those published after 2005.

Select private and federal payor coverage policies, as identified by the Washington HTA program, were reviewed. State coverage policies were identified through the National Conference of State Legislatures, Kaiser Family Foundation, and Autism Votes.

Quality assessment

The methodological quality of the Warren et al. (2011) systematic review was assessed using standard instruments developed and adapted by the MED Project that are modifications of the systems in use by NICE and SIGN (Guyatt, Oxman, et al., 2008; NICE, 2009; SIGN, 2009). In brief, good quality systematic reviews include a clearly focused question, a literature search that is sufficiently rigorous to identify all relevant studies, criteria used to select studies for inclusion (e.g., RCTs) and assess study quality, and assessments of heterogeneity to determine if a meta-analysis would be appropriate. Good quality systematic reviews also have low potential for bias from conflicts of interest and funding source.

The methodological quality of the guidelines was assessed using an instrument adapted from the Appraisal of Guidelines Research and Evaluation (AGREE) Collaboration (AGREE Next Steps Consortium, 2009). The guidelines were rated by two individuals. A third rater was used to obtain consensus if there were disagreements. Each guideline was assigned a rating of good, fair, poor, based on its adherence to recommended methods and potential for biases. A guideline rated as good quality fulfilled all or most of the criteria. A fair quality guideline fulfilled some of the criteria and those criteria not fulfilled were thought unlikely to alter the recommendations. If no or few of the criteria were been met, the guideline was rated as poor quality.

Findings

Warren et al. (2011). *Comparative Effectiveness of Therapies for Children with Autism Spectrum Disorders*. Rockville, MD: Agency for Healthcare Research and Quality.

At the direction of the Washington HTA program, the Warren et al. (2011) systematic review was identified as the sole source of evidence for this report. The Warren et al. (2011) systematic review evaluated a wide variety of interventions, including behavioral, educational, family, medical, allied health and CAM treatment approaches. However, this summary is limited to behavioral interventions. The key questions, methods, and findings of the report, subject to that limitation, are summarized below. The full report is available at http://effectivehealthcare.ahrq.gov/ehc/products/106/656/CER26_Autism_Report_04-14-2011.pdf. The Warren et al. (2011) systematic review was assigned a quality rating of good.

Key Questions

KQ1. Among children ages 2 to 12 with ASDs, what are the short- and long-term effects of available behavioral, medical, allied health, or CAM treatment approaches? Specifically,

KQ2. Among children ages 2 to 12, what are the modifiers of outcome for different treatments or approaches?

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 treatment as driving outcomes, either within a single treatment or across treatments?

KQ7. What evidence supports the use of a specific treatment approach in children under the age of two who are at high risk of developing autism based upon behavioral, medical, or genetic risk factors?

Warren et al. Methods

Studies published in English from January 2000 to May 2010 were included. The MEDLINE®, ERIC and PsycInfo® databases were searched, as well as grey literature from the US Food and Drug Administration, and clinical trial registries such as ClinicalTrials.gov. Reference lists were hand searched. All study designs were included except case reports. Medical studies with fewer than 30 participants, and behavioral, education, and allied health studies with fewer with 10 participants were excluded (Warren et al., 2011). Studies without a comparison group with at least 10 children with ASDs were included in the review. Single-subject design studies were not excluded on the basis of their design; however, the majority of single subject studies do not

include at least 10 participants and are therefore not represented in the AHRQ review (Warren et al., 2011).

Two reviewers quality assessed each study with differences resolved through discussion. Studies were rated as good, fair, poor. The overall strength of the evidence was assessed using the Evidence-based Practice Centers Methods Guide for Effectiveness and Comparative Effectiveness Reviews. The strength of evidence was presented as insufficient, low, moderate, or high.

Warren et al. Key Findings

Key findings of the Warren et al. (2011) review for each key question are presented below, as they pertain to behavioral interventions which are NOT delivered in an educational setting. The Warren et al. (2011) review includes other interventions, such as medical interventions, complementary and alternative treatments, as well as interventions that are delivered in educational settings. These other types of interventions are not reviewed here. The behavioral interventions included in this report include the broad categories of early intensive behavioral and developmental interventions, social skills interventions, play or interaction-based interventions, those interventions focused on associated behaviors and miscellaneous interventions.

KQ1. Among children ages 2 to 12 with ASDs, what are the effects of behavioral, treatment approaches that utilize ABA principles on core and commonly associated symptoms?

Note: The text indented below is excerpted directly from the Warren et al. systematic review (2011, p. 30-52). In the Warren et al. (2011), references can be found beginning on page 128. Additionally, table and appendix numbers referred to in this section correspond to the Tables and Appendices in the Warren et al. (2011) report.

Note: While ESDM is considered an early intensive behavioral intervention, because it applies to children under age two who have not been diagnosed with autism (but are merely at risk), it is reviewed under Key Question 7.

Early Intensive Behavioral and Developmental Interventions

Early intensive behavioral and developmental interventions include interventions based on:

- ABA-based approaches including the UCLA/Lovaas method and variants,
- Naturalistic/developmental principles (i.e., ESDM)
- Parent/family-based training (e.g., Pivotal Response Training, Hanen More Than Words, and social communication training).

We adopted a similar approach to the operationalization of this category as Rogers and Vismara¹² in their review of “comprehensive” evidence-based treatments for early ASDs. Interventions in this category all have their basis in or draw from principles of applied behavior analysis (ABA), with differences in methods and setting. 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 ASDs.

We included in this category two intensive interventions manualized (i.e., have published treatment manuals to facilitate replication) interventions: the UCLA/Lovaas model and the ESDM. These two interventions have several key differences in their theoretical framework and implementation, although they are similar in the use of high intensity (many hours per week, one-on-one) instruction utilizing ABA techniques. 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 the 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, but have not been manualized. (...) A third set of interventions included here are those using 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 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 are reviewed here.

We review the results of UCLA/Lovaas-based approaches and parent training approaches focused on pivotal behaviors below; we discuss results of the ESDM in the KQ7 section of the report given the question's focus on younger children.

Studies focusing on one specific targeted outcome area (e.g., social skills, maladaptive behavior, mental health comorbidities, play) and intervention studies delivered primarily via educational protocols or allied health providers are reviewed in other sections of this report.

Content of the literature. We identified 34 papers¹⁰⁰⁻¹³³ from 30 unique study populations that addressed early intensive behavioral and developmental interventions. A majority of the reviewed literature examined specific early intensive behavioral and developmental approaches, with most using variants of the UCLA/Lovaas model or other ABA-based approaches.^{101-107,110,111,113-115,118,121,122,124-127,129-133}

Four papers evaluated various parent trainings aimed at social communication skills,^{100,108,109,128} two papers examined Pivotal Response Training,^{117,120} two studies examined and described eclectic approaches^{112,119,123} and one study examined a parent training blending Pivotal Response Training and other behavioral approaches (Group Intensive Family Training).¹¹⁶

Summary of the literature. Of the 34 papers in this section¹⁰⁰⁻¹³⁰ comprising 30 unique studies, 11 were fair, and 19 were poor. Outcomes of RCTs and cohort studies rated fair in quality are summarized in Table 10.

Studies of UCLA/Lovaas-based approaches. The one RCT on the UCLA/Lovaas treatment that met inclusion criteria had fair quality.¹¹⁴ This study compared a clinic-based method to a parent program, and targeted children at about 36 months of age. The study¹¹⁴ was the first attempted replication of Lovaas' manualized intervention to use random assignment, a standardized assessment battery, and explicit accounting of intervention hours. It included 28 children with a mean intelligence quotient (IQ) of 51 randomized to either an intensive treatment group (UCLA/Lovaas model with an average of 25 hours per week of individual treatment per year with reduced intervention over next 1 to 2 years) or a parent-training group (3-9 months of parent training). Gains in IQ were much more tempered than that of Lovaas' original noncontrolled study.²¹ Children in the treatment group gained a mean of 15 IQ points in comparison to the relatively stable cognitive functioning of the control group, although average IQ in the treatment group remained in the impaired range. Most of the children who demonstrated large gains in IQ were within the subgroup diagnosed with Pervasive Development Disorder-Not Otherwise Specified (PDD-NOS), whereas children with classically defined Autistic Disorder demonstrated modest improvements.

Two children in the experimental group (vs. one in the control) achieved the “best outcome” or “recovery” status previously defined by Lovaas. No post-treatment group differences were seen in adaptive behavior or challenging behavior. Thus, while replicating improvements in cognitive ability for some children with ASDs within the repeated discrete trial teaching inherent to UCLA/Lovaas method, the study in fact demonstrated a less dramatic impact for the population of children for whom this approach is often recommended (i.e., children with classically defined Autistic Disorder) compared with what was previously reported.

Seven prospective cohort studies and nonrandomized trials were available on UCLA/Lovaas-based methodologies, but none made the same comparisons either in terms of interventions or populations. Hayward and colleagues^{126,132} examined the progress of children receiving either intensive clinic directed UCLA/Lovaas-based intervention (n=23; mean age=36 months; 37 hours of weekly treatment) or an intensive parent-managed model (n=23; mean age=34 months; 34 hours of weekly treatment) over the course of one year in the United Kingdom. Group assignment was based solely on geographic location. At follow up, both groups had improved significantly in IQ (16 point gain), nonverbal IQ (10 points), language use/understanding, and most areas of adaptive functioning with the exception of daily living skills but there were no differences between the groups.

Two studies compared intensive center-based treatment to community care. Howard and colleagues¹²⁹ studied preschool-aged children receiving intensive behavior analytic treatment (n=29, 1:1 treatment for 25-40 hours per week), intensive “eclectic” intervention (n =16, higher teacher-student ratio intervention for approximately 30 hours per week), and children receiving general intervention in public early intervention programs (n=16, combined methods, small groups, 15 hours per week). Groups were assigned via educational placement teams that specifically included parent input. Controlling for age at diagnosis and combined parental education, children in the intensive behavior analytic group demonstrated significant improvements in all areas assessed at followup, including an average IQ of 89 (41-point improvement over baseline) and a 24-point difference from the combined mean of the other intervention groups.

Significant differences between the eclectic and generic intervention groups were not present at followup. Findings do suggest substantial improvement via an intensive approach for young children with autism; however, important differences in group assignment at baseline, difficulties with systematic measurement overtime, the lack of reported treatment fidelity or adherence characteristics, and the small number of children in the comparison group limits the interpretation of these findings.

These results were echoed in another study¹⁰⁵ of 42 children in which those receiving the Lovaas program had significantly higher IQs (mean=87, gain of 25; mean=73, 14 points) and adaptive behavior skills at outcome, compared with children in undefined community care. Receptive language improvements were observed but were not significant, and expressive language skills and socialization scores on the Vineland Adaptive Behavior Scale (VABS) were not different for the two groups at year 3 outcome. Twelve of the 21 children in the behavioral group had IQs >85 compared with 7 of 21 in the eclectic treatment group at outcome. Likewise, more children in the Lovaas group were in typical schools subsequent to intervention (17 vs. 1); although this specific outcome is potentially attributable to a wide variety of factors including some that might correlate with differences in socioeconomic status and family constellation evident between the groups.

One study¹²⁵ of two centers compared an eclectic approach (including the Developmental, Individual-Difference, Relationship-Based/Floortime model, Treatment and Education of Autistic and Communication related handicapped Children (TEACCH) and ABA-based approaches) to UCLA/Lovaas-based intervention alone. Hours spent in the intervention were consistent at 8 hours per day, and children were assessed over one year. Significant group differences were noted in terms of both language/communication and reciprocal social interaction domain scores on the Autism Diagnostic Observation Schedule (ADOS), with both groups showing decreases in symptom tallies but more

substantial decreases in the ABA group. No significant differences in IQ change were reported. While demonstrating impact on certain ADOS symptom scores, these changes were small, and more recent approaches suggest that calculating an ASD severity score may be a more valuable and sensitive way for measuring changes in ASD symptoms in response to intervention.¹³⁴ In a subsequent study on diagnostic stability¹²⁴ with unclear sample overlap, most children receiving intervention continued to display scores in the ASDs range on the ADOS (n=53) although some children's classification did shift.

Finally, one study tried to assess the role of intensity of the intervention on outcomes. Reed and colleagues¹⁰³ studied the effectiveness of varying intensity of home-based Lovaas-based programs offering primarily one-to-one teaching. High intensity interventions (n=14) were defined as those provided for an average of 30 hours per week. Low intensity interventions (n=13) were provided for on average 13 hours per week. Assignment to the particular intervention modality was based on geographic location, and children in the high intensity group had higher ability and cognitive scores and lower autism severity scores at baseline. Children were assessed 9-10 months after initiation of intervention. Children receiving high intensity intervention demonstrated statistically significant improvements in intellectual and educational functioning from baseline. Children receiving low intensity intervention demonstrated statistically significant changes in educational functioning and nonsignificant improvement in cognitive functioning. The only significant difference between the groups was in improved educational functioning associated with high intensity interventions. No group differences were found in autism severity, cognitive functioning, or adaptive behavior functioning.

Three additional cohort studies^{101,106,130} of UCLA/Lovaas-based methodologies provided inconsistent data on the benefit of behavioral approaches, but all three had substantial risk of bias and were thereby rated as poor quality in this report. Nonetheless, they suggest that behavioral approaches may have promise for bolstering aspects of cognitive, language and adaptive functioning in preschool children with ASDs.

Case series of early intervention approaches^{104,113,118,119,131} had mixed results, likely in part due to the substantial heterogeneity of interventions examined even within individual studies, little or no control of concomitant interventions, and poor fidelity to any given approach. Outcomes in these studies were more likely to be parent-reported and not based on validated tools.

Several chart reviews and other retrospective analyses have been used to understand treatment patterns and effects.^{111,112,115,121-123} Interpretation of findings is most appropriately confined to noting that some children receiving intervention have displayed improvements during intervention in cognitive, adaptive, and autism-specific impairments, that characteristics of starting treatment and baseline abilities are correlated with improvement in some instances, and heterogeneity in terms of improvement is quite common. We do not describe these studies here, but details on all of them are available in the evidence table in Appendix C.

One chart review,¹²² however, does provide some evidence for the feasibility of providing intensive behavioral interventions on a larger scale as it reviews data on 322 children served in a large service catchment area. Given the methodological limits including lack of a clearly defined intervention characteristics/protocol, lack of a comparison group, retrospective collection, and lack of key measures for certain children at certain times, the intervention results are limited. However, the study suggests the feasibility of providing intensive intervention to a large group of children.

Studies of intensive parent training approaches. Of the seven studies^{100,108,109,116,117,120,128} on parent training, four^{100,108,109,120} included comparison groups and had fair^{100,108,109} or poor¹²⁰ quality. Three were RCTs,^{100,108,109} including one pilot study¹⁰⁸ with a report of a later implementation of the intervention including different participants.¹⁰⁰ Drew et al.¹⁰⁹ compared the effects of a home-based, parent-delivered intervention aimed at improving social communication and managing challenging behavior for 12 children with ASDs with a community-based control intervention group of 12 children (mean age 23 months at start of treatment).

Components of the interventions for social communication included developing joint attention, teaching routines, and play activities promoting interaction. Reinforcement techniques, including for alternative behaviors, were used to address challenging behaviors. Training was conducted at home visits (3 hours weekly for 6 weeks), with parents asked to engage in intervention activities for a half to 1 hour daily. One year after treatment initiation, the parent training group reported that their children used more words than the community group. There were no group differences on nonverbal intelligence quotient (NVIQ), autism symptom severity, or words/gestures observed during followup assessment. Unexpectedly, the treatment group lost IQ points during the study; whereas the control group demonstrated relatively stable cognitive abilities. This finding is further confounded by a significantly higher IQ present in the treatment group at initiation of the study.

Aldred et al.¹⁰⁸ compared a parent-based intervention focused on advancing social communication skills within interactions (n = 14, median age 51 months) to treatment as usual (n=14, median age 48 months). Parents participated in initial workshops, monthly intervention sessions where videotaped interactions were reviewed, and 6 months of maintenance visits (approximately once every 2 months). Twelve months after baseline, blinded evaluations showed improvements on ADOS scores, with substantial improvement within the social domain, increased expressive vocabulary, as well as improved communication-related behaviors coded during interactions. Language gains were most prominent in younger, lower-functioning children. A lack of standardized measures of developmental performance, including baseline cognitive skills, as well as challenges in understanding and defining “treatment as usual” limit interpretation of the findings.

In a report of a later intervention of this model, 152 children between the ages of 2 and 4 years were randomized to treatment as usual or treatment as usual plus parent training in social communication.¹⁰⁰ Time in “treatment as usual” interventions was similar across groups as were the types of interventions employed. Similar numbers of children in both groups experienced diagnostic shifts from core autism to other diagnoses on the ASDs spectrum as diagnosed on the ADOS-G. Teacher ratings of language and communication after intervention were not significantly different between groups, though ratings of parent-child interactions by independent assessors were positive for children in the social communication group. Parent ratings of language and social communication were also more positive for the social communication group.

Stahmer and Gist¹²⁰ examined the effects of an explicit parent education support group with a parent education program focusing on Pivotal Response Training, a treatment program designed to enhance core skill areas in autism using naturalistic interactions. Parents met with the intervention provider weekly for 12 weeks and were taught techniques for presenting clear instructions, following and supplementing child choice, and providing direct/naturalistic reinforcement. Involvement in the 12-week intervention was successful in changing parenting techniques and perceived language gain. However, the lack of randomization, wide variation in children served, the lack of objectively assessed changes in child behavior, and the small number of participating limit the reported results (Warren et al., 2011, p. 30-35).

Table 10. Outcomes of early intensive behavioral and developmental interventions

Author, year, country Groups, N enrollment/N final Study quality	Age, mean (months) ±SD IQ, mean ± SD	Key outcomes
UCLA/Lovaas-based approaches		
Hayward et al. ^{126,132} 2009, UK G1: Intensive clinic-based UCLA/Lovaas-based intervention, 23/20 G2: Intensive parent- managed treatment, 21/19 Quality: Fair	G1: 35.7 ± 6.2 G2: 34.4 ± 5.7 NR	<ul style="list-style-type: none"> No significant group differences at followup. Improvements in both groups in IQ, non-verbal IQ, language use/understanding, and most areas of adaptive functioning, with the exception of daily living skills.
Reed et al. ¹⁰³ 2007, UK G1: High intensity intervention, 14/14 G1a: High intensity with focus on Lovaas techniques, 4/4 G1b: High intensity with focus on verbal behavior, 5/5 G1c: High intensity with focus on CABAS methods, 5/5 G2: Low intensity intervention in home-based direct teaching sessions, 13/13 Quality: Fair	G1: 42.9 (14.8) G1a: 47.5 (13.5) G1b: 38.0 (9.9) G1c: 44.2 (20.5) G2: 40.8 (5.6) NR	<ul style="list-style-type: none"> Children in the high intensity group had higher ability and cognitive scores and lower autism severity scores at baseline. G1: statistically significant improvements in intellectual and educational functioning from baseline. G2: statistically significant changes in educational functioning. Group comparisons showed educational functioning improvements for G1 compared with G2. No group differences were found in autism severity, cognitive functioning, or adaptive behavior functioning.
Zachor et al. ¹²⁵ 2007, Israel G1: UCLA/Lovaas-based intervention, 53/53 G2: Eclectic approach, 15/15 Quality: Fair	G1: 25.1 ± 3.8 G2: 26.3 ± 4.6 NR	<ul style="list-style-type: none"> No baseline differences in terms of family characteristics or child functioning. Significant time by intervention effects noted in ADOS language/communication and reciprocal social interaction domain scores—more substantial decreases in the UCLA/Lovaas group. Following intervention both groups showed improvements in cognitive and verbal scores and adaptive behavior skills.
Cohen et al. ¹⁰⁵ 2006, US G1: UCLA/Lovaas-based intervention, 21/21 G2: Local services, 21/21 Quality: Fair	G1: 30.2 ± 6.8 G2: 33.2 ± 3.7 G1: 61.6 ± 16.4 G2: 59.4 ± 14.7	<ul style="list-style-type: none"> Significantly higher IQs and adaptive behavior skills post-treatment in G1. Receptive language improvements noted at 3 years, but expressive language skills and socialization scores were not different for the two groups. Twelve of 21 in the behavioral group had IQs >85 compared with 7 of 21 in the eclectic treatment group.
Howard et al. ¹²⁹ 2005, US G1: UCLA/Lovaas-based intervention, 37/29 G2: Intensive eclectic therapy G3: Non-intensive eclectic therapy G2+G3: 41/32 Quality: Fair	At intake: G1: 30.88 ± 5.16 G2: 37.44 ± 5.68 G3: 34.56 ± 6.53 At followup: G1: 45.68 ± 6.24 G2: 50.69 ± 5.64 G3: 49.25 ± 6.81 G1: 58.84 ± 18.15 G2: 53.69 ± 13.50 G3: 59.88 ± 14.85	<ul style="list-style-type: none"> G1: significant improvements in all areas assessed at followup, including average IQ of 89 (representing a 41 pt improvement over baseline and a 24 pt improvement over the combined mean of the other intervention groups).

Table 10. Outcomes of early intensive behavioral and developmental interventions (continued)

Author, year, country Groups, N enrollment/N final	Age, mean (months) ±SD IQ, mean ± SD	Key outcomes
Study quality		
Eikeseth et al. ^{110,133} 2002, Norway	G1: 66.31 ± 11.31 G2: 65 ± 10.95	<ul style="list-style-type: none"> • Analysis of change scores demonstrated more improvement for G1 regarding IQ and language. • G2 scores were higher at baseline across most areas of measurement compared with G1.
G1: UCLA/Lovaas-based intervention, 13/13 G2: Eclectic therapy, 12/12	G1: 61.92 ± 11.31 G2: 65.17 ± 14.97	
Quality: Fair		
Smith et al. ¹¹⁴ 2000, US	Intake: G1: 36.07 ± 6.00 G2: 35.77 ± 5.77 Followup: G1: 94.07 ± 13.07 G2: 92.23 ± 17.24	<ul style="list-style-type: none"> • G1 gained mean of 15 IQ pts compared with relatively stable cognitive functioning of controls. • Significant improvement for G1 in visual-spatial skills and expressive language. • IQ scores averaged in impaired range at outcome for G1 and PDD-NOS children appeared to account for majority of change. • No post-treatment group differences seen for adaptive or challenging behavior.
G1: UCLA/Lovaas-based intervention, 15/15 G2: Parent training from Lovaas manual, 13/13	G1: 50.53 ± 11.18 G2: 50.69 ± 13.88	
Quality: Fair		
Parent training		
Aldred et al. ¹⁰⁸ 2004, UK	G1: median 48 mo G2: median 51 mo	<ul style="list-style-type: none"> • 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.
G1: Parent training in social communication intervention plus community intervention, 14/14 G2: Community intervention, 14/14	NR	
Quality: Fair		
Drew et al. ¹⁰⁹ 2002, UK	Intake: G1: 21.4 ± 2.7 G2: 23.6 ± 3.8 Followup: G1: 33.5 ± 2.5 G2: 36.2 ± 4.5	<ul style="list-style-type: none"> • At 12 mo, G1 had more words and a trend toward understanding more words than G2. • No group differences on NVIQ, autism symptom severity, parental report of stress, or words or gestures produced during followup assessment.
G1: Parent training, 12/12 G2: Local/eclectic services, 12/12	G1: 88.1 ± 11.2 (NVIQ) G2: 23.6 ± 3.8 (NVIQ)	
Quality: Fair		

ABA=applied behavior analysis; ADI=Autism Diagnostic Interview; ADOS=Autism Diagnostic Observation Schedule; ASDs=autism spectrum disorders; G=group; IQ=intelligence quotient; mo=month; N=number; NVIQ=nonverbal intelligence quotient; PDD-NOS=Pervasive Development Disorder-Not Otherwise Specified; RBS=Repetitive Behavior Scale; SD=standard deviation; UCLA=University of California, Los Angeles; UK=United Kingdom; VABS=Vineland Adaptive Behavior Scale

(Warren et al., 2011, p. 35-37)

Social Skills Interventions

The social interventions reviewed in this section focus primarily on children at elementary-school ages and those functioning at higher cognitive/developmental levels. They use various approaches to address three primary dimensions of social competence: specific behavioral skills (e.g., greetings, initiating game play, joint attention), affective understanding (e.g., recognizing emotions in self and others), and social cognition (e.g., theory of mind, problem-solving, self-regulation).

Content of the literature. We located 16 unique papers addressing social skills interventions. This number includes two sets of papers with possibly overlapping samples evaluating a Skillstreaming intervention^{135,136} and a cognitive-behavioral-ecological social skills approach.^{137,138} The ages of children studied ranged from 4-16 years old. Twelve studies focused exclusively on higher functioning children or included language and/or cognitive requirements among their eligibility criteria.¹³⁵⁻¹⁴⁶ Three studies provided individual treatment to children,^{137,145,147} three used a combination of individual and small group formats,^{138,146,148} and nine employed a small group format only.^{135,136,139-144,149} In addition, five interventions included some form of parent training or involvement as an adjunct to child treatment.^{137,139,141,144,146} For the 14 studies with prospective designs, the total amount of training

provided ranged from 6.7 hours to 180 hours. (...) Among studies of social skills interventions, seven were fair quality and nine were poor.

Summary of the literature. Three RCTs^{139,141,146} (Table 11) evaluated social skills interventions targeting high functioning children with ASDs using a format that involved training for both children and their parents. The criteria for determining whether a child was high functioning and therefore eligible to participate varied by study, but at a minimum the child had to have a verbal IQ above 60. Different outcome measures were used across the samples, making direct comparisons difficult.

The Children's Friendship Training¹⁴¹ program involves children with and without ASDs, and uses didactic instruction on rules of social behavior; modeling, coached behavioral rehearsal, and performance feedback during treatment sessions; rehearsal at home; homework assignments; and coaching by parents during play dates with a peer. Children were randomly assigned to receive Children's Friendship Training either immediately or 12 weeks later (Delayed Treatment Control group). Treatment was conducted in 60-minute small parallel group sessions for parents and children, and lasted 12 weeks.

Immediately following treatment, the Children's Friendship Training group showed significant improvements in social behavior and social cognition compared with the Delayed Treatment Control group. Children in the treatment group also spent less time during the play date engaged in minimally socially interactive activities (such as watching television) compared with the delayed treatment group ($p < 0.001$), but did not spend significantly more time in socially interactive activities (e.g., talking). Parents of children in the Children's Friendship Training group reported that their children demonstrated increased self-control when provoked by others relative to the control group ($p < 0.05$).

Parent- and teacher-reported reductions in social withdrawal showed nonsignificant changes. Children in the treatment group self-reported decreased loneliness ($p < 0.025$) and increased popularity ($p < 0.025$) relative to the control group. Three months post-treatment significant improvements were maintained in the treatment group on parent reported hosting of play dates, conflict during play dates, time spent in minimally socially interactive activities, assertion, self-control, and social withdrawal compared with the baseline scores. After treatment, findings from the Delayed Treatment Control group largely replicated those of the Children's Friendship Training group.

Relative to Children's Friendship Training, the Social Adjustment Enhancement Curriculum has a more comprehensive curriculum targeting emotion and facial expression recognition; theory of mind, the ability to ascribe mental states to oneself and others to understand and forecast behavior; perspective taking; executive functioning, which allows for planning and abstract thinking; problem solving; and conversation skills. Eighteen boys between 8 and 12 years old met eligibility criteria.¹³⁹

Participants were matched on age and IQ and randomly assigned to an immediate intervention condition or a wait list condition. Parents and children in the treatment condition received the Social Adjustment Enhancement Curriculum at a clinic for 20 weekly 1.5 hour sessions. Children and parents met separately. Child groups of four or five were structured with a high adult-to-child ratio and followed a consistent schedule each week, using a variety of instructional strategies including in vivo teaching, visual templates, games, and role playing.

Immediately following the intervention participants in Social Adjustment Enhancement Curriculum had higher facial recognition scores post-treatment ($p < 0.05$), while the scores of the participants in the wait list control group declined (although not significantly). There was significantly improved executive function skills (covarying Verbal IQ) post-treatment ($p < 0.05$) in the intervention group, while the scores of those in the wait-list control declined. However, when the one child with a PDD-NOS diagnosis was excluded from the treatment group these results were no longer significant. Both the control and Social Adjustment Enhancement Curriculum group demonstrated significant improvements on the Faux Pas Stories Task post-treatment ($p < 0.001$) but not on the Strange Stories Task. Total social problems reported

per time reporting dropped significantly from the first eight weeks of the intervention to the last eight weeks of the intervention ($p < 0.05$).

Beaumont and Sofronoff¹⁴⁶ investigated a comprehensive social skills intervention that utilized a computer game as well as child and parent small therapy groups to teach emotion recognition and regulation, problem solving, and social interaction skills. Forty-nine children diagnosed with Asperger syndrome between the ages of 7.5 and 11 years old were randomly assigned to the Junior Detective Training Program or a wait list control. Data suggests that this computerized intervention was beneficial for improving knowledge of emotion management strategies and parent-reported social skills, but not emotion recognition, immediately after treatment over a the waitlist control.

Some of these results were also replicated when the wait-list group underwent treatment in pre-post analyses. Pre- post scores were significantly different on the parent-reported measures of social skills for the intervention group immediately, 6 weeks, and 5 months following the intervention, suggesting maintenance of these treatment effects. However this study had substantial risk of bias and was rated as poor quality in this report. Additional details on this and other studies not fully described in this section are available in the evidence table in Appendix C.

One study attempted to ascertain whether the type of feedback that children received during a social skills intervention affected the outcomes. Skillstreaming¹⁵⁰ is a comprehensive, structured social skills curriculum that employs systematic procedures for teaching specific social behaviors (e.g., listening, sharing, having a conversation, accepting a compliment, responding to teasing), as well as social cognition (using self-control), and affect (e.g., recognizing and expressing feelings, responding to anger). The Skillstreaming curriculum used in the study was adapted to focus on social skills particularly important for children with autism.

Unlike in the previous RCTs reviewed in this section, this intervention did not include a parent training component. Fifty-four children between the ages of 6 and 13 years with high functioning ASDs were randomly assigned to small-group Skillstreaming intervention that used either a response-cost condition (involving immediate performance feedback and rewards based on specific social skills and behaviors) or a noncategorical feedback condition (involving more general feedback and noncontingent rewards). The only difference found between the response cost and noncategorical feedback intervention conditions post-treatment was that interventionists reported significant improvements measures of atypicality, withdrawal, and behavior symptoms in the response cost group relative to the noncategorical feedback group ($p < 0.05$).

However, both groups combined made significant improvements after treatment on both parent and interventionist reports of social skills, withdrawal, adaptive skills, and behavior symptoms ($p < 0.001$ -- $p < 0.05$). As for facial recognition, participants in neither group made significant improvements on the Diagnostic Analysis of NonVerbal Accuracy. A previous case series to assess Skillstreaming¹³⁶ for 21 children between 6 and 13 years old diagnosed with Asperger disorder found similar results: significant improvements in parent reported social skills, adaptability, and atypicality) and on staff reported social skills.

Three RCTs^{143,145,149} and a related retrospective cohort study¹⁴⁸ evaluated social skills interventions focused on improving children's ability to socially interact with others while playing. The Quirnbach et al.¹⁴⁵ study evaluated the effectiveness of using Social Stories to teach seven to 14 year old children with ASDs social skills when playing board games. Social Stories¹⁵¹ are descriptive brief vignettes constructed according to a specific formula that are read to or by individuals with ASDs to convey appropriate behavior expected for a specific situation. Children in one of two social stories groups (standard or directive) showed significant game play skill improvements across the four trials ($p < 0.001$) while the children who received the control story did not. Children in the two experimental conditions maintained the results of the intervention a week later.

These results provide preliminary support for the effectiveness of a short, focused intervention on improving the specific targeted skills. However, further research is needed to ascertain whether these results generalize to other people (such as peers) and other settings, whether these results are maintained when the intervention is discontinued (i.e., the child stops reading the Social Story), and whether other Social Stories are successful at improving the skills that they target. Despite authors' predictions that the children who read the directive story would improve their game play skills at a faster rate than the children who read the standard story (because the directive story does not include additional information), there were no significant differences in results between participants receiving the standard vs. directive social stories (both groups showed significant improvements across trials).

In the other studies, direct teaching was associated with greater gains in initiating, responding, and interacting behaviors than an unstructured play group,¹⁴⁹ in 4 to 6 year olds. Results on LEGO therapy were conflicting, with one a retrospective cohort study¹⁴⁸ showing benefit for LEGO therapy over an unspecified "other" intervention on socialization measures, while one RCT¹⁴³ had inconsistent results on the benefit of LEGO therapy over a Social Use of Language Program and no intervention. The Lego group improved on measures of social skills when compared with the Social Use of Language Program and control groups; and pre-post scores did not significantly differ on these measures for the Lego group. Both the Lego and Social Use of Language Program groups improved on measures of maladaptive behavior over the no intervention group. The Lego group improved in the duration of social interaction on the playground from pre to post treatment. Seven additional studies used prospective case series designs to evaluate the effectiveness of social skills interventions.^{137,138,140,142,144,147,152} All studies noted improvements in some social behaviors that, depending on the study, included eye contact, emotion recognition, and interaction with peers; outcome measures were generally parent-reported. The studies also lacked control groups so it is difficult to determine whether improvements are treatment-specific (Warren et al., 2011, p. 37-41).

Table 11. Outcomes of RCTs of social skills behavioral interventions

Author, year, country Groups, N enrollment/N final	Age, mean years ± SD IQ, mean ± SD	Key outcomes
Study quality		
Quirnbach et al. ¹⁴⁵ 2009, US	G1: 9.49 ± 2.09 G2: 10.33 ± 2.53 G3: 8.85 ± 1.59	<ul style="list-style-type: none"> • G1 & G2 showed significant game play skill improvements across four trials while G3 did not (p<0.001). • Game play skills for G1 & G2 maintained a week later.
G1: Social Stories, standard condition, 15/15 G2: Social stories, directive condition, 15/15 G3: Control story unrelated to social skills, 15/15	G1: 86.2 ± 22.8 G2: 81.00 ± 20.28 G3: 79.47 ± 22.88	
Quality: Fair		
Lopata et al. ¹³⁵ 2008, US	G1: 9.60 ± 2.12 G2: 9.41 ± 2.31	<ul style="list-style-type: none"> • Both groups (as a whole) demonstrated significant improvements on parent and interventionist reported social skills post-treatment (p<0.01). Group differences were not significant on any of parent reported measures. • Interventionists reported significant improvements on BASC Atypicality and Withdrawal subscales in G1 compared with G2 (p<0.05). • Neither group improved significantly on facial expression recognition.
G1: Response-cost; receive feedback based on operationally defined behaviors), 29/29 G2: Noncategorical; receive feedback based on no predetermined categories, 25/25	G1: 100.87 ± 17.92 G2: 97.56 ± 13.62	
Quality: Fair		
Solomon et al. ¹³⁹ 2004, US	G1a: 8.58 G1b: 10.83 G2a: 8.33 G2b: 10.17	<ul style="list-style-type: none"> • Fewer social problems reported by parents of G1 (p<0.05). • G1 recognized more facial expressions post-intervention than G2 (p=0.003) (but not more than before treatment). • No group differences evident on theory of mind measures post-intervention. • G1 demonstrated improved executive function skills post-intervention, compared with G2, (p<0.05).
G1: Social Adjustment Enhancement Intervention, 9/9 G2: Waitlist group, 9/9 Ga: Younger participants with higher mean FSIQ Gb: Older participants with lower mean FSIQ	G1a: 115 G1b: 86 G2a: 119 G2b: 95	
Quality: Fair		
Frankel et al. ¹⁴¹ 2010, US	G1: 8.6 ± 1.27 G2: 8.46 ± 1.25	<ul style="list-style-type: none"> • 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.
G1: Children's Friendship Training, 35/26 G2: Delayed Treatment Control group, 33/31	G1: 106.9 ± 19.1 G2: 100.5 ± 15.7	
Quality: Fair		
BASC=Behavioral Assessment System for Children; FSIQ=full scale intelligence quotient; G=group; N=number; NR=not reported; SD=standard deviation; SULP=Social Use of Language Program; VABS=Vineland Adaptive Behavior Scale		

(Warren et al., 2011, p. 41-42)

Play-/Interaction-Based Interventions

These interventions focused on children's interactions with either their parents or experimenters and targeted skills including joint attention and play abilities. Most studies were conducted in the context of a play situation, and included children across broad age and developmental ranges.

Content of the literature. We included 15 papers addressing play- or interaction-based interventions¹⁵³⁻¹⁶⁷ comprising 13 unique populations. Seven studies were randomized controlled trials,^{153-157,161,163-165}

including a trial of the Stepping Stones Triple P program with two publications,^{153,154} and a trial comparing joint attention and symbolic play interventions with two publications.^{155,156} Two additional studies assessed joint attention and symbolic play and likely share overlapping participants with this trial.^{157,158} Three RCTs assessed comparable interventions (imitation compared with contingent responsiveness) using similar procedures;¹⁶³⁻¹⁶⁵ two of these^{163,165} may share participants.

Multiple interventions involved parent training or parent interaction components, including Parent-Child Interaction Therapy,¹⁶¹ responsive teaching,¹⁶⁶ play-based approaches based on the Floortime model,¹⁶⁰ the Mifne model,¹⁶² the Stepping Stones Triple P program,^{153,154} and the Relationship Development Intervention program.¹⁵⁹ Participants ranged in age from 12 months¹⁶⁶ to 12 years¹⁶¹ across all studies. Duration of therapy in prospective studies ranged from five weeks^{156,157} to 12 months.^{160,166} Table 10 includes additional study details. Among the 13 unique studies, three were fair quality and 10 were poor.

Summary of the literature. Among the fair quality studies was an RCT evaluating Parent-Child Interaction Therapy,¹⁶¹ in which parents of children with an ASD were trained to interact with their children using behavior management strategies (Table 12). The Parent-Child Interaction Therapy intervention group consisted of ten children and the wait-list control group included nine; children in both groups were on average 8 years old. Improvements were greater in the intervention group in challenging behavior, behavioral flexibility and atypical behaviors, and hyperactivity, inattention, challenging behaviors, and depression ratings. However changes on each scale fell short of statistical significance in comparison with the control group. A second parent-focused RCT addressed the Stepping Stones Triple P Parenting Program,^{153,154} which focuses on managing children's behavior by considering the function of the behavior and uses procedures such as descriptive praise, planned ignoring, skill acquisition, and communication.

Parents of the children in the treatment group reported statistically significant decreases in child challenging behavior on the Eyberg Child Behavior Inventory Intensity and Problem Scales. Wait-list controls eventually received the same treatment, and parents of children in this group also reported statistically significant decreases in child challenging behavior on both Eyberg Child Behavior Inventory scales. At six-month follow up, the treatment group maintained gains on both the Eyberg scales.

The additional studies in this section included three RCTs that compared the effects of imitation and contingent responsiveness.¹⁶³⁻¹⁶⁵ Contingently responsive behavior refers to the adult responding to the child's initiations by either commenting back or gesturing within the play context. In the first phase, the child entered the room with an adult present holding a neutral facial expression. During Phase 2, the adult interacted with the child by using either imitation or contingently responsive behavior in response to the child's behavior. The third phase mimicked Phase 1, and the fourth and final phase included a spontaneous play interaction. Each of these four phases was three minutes in duration.

Each of the three RCTs included 20 children randomly assigned to either the imitation group or the contingently responsive group.¹⁶³⁻¹⁶⁵ [sic] Significantly greater effects were seen in the imitation group compared with the contingent responsiveness groups in all three studies. Improvements included spending more time engaged with both objects and adults,¹⁶³ a greater reduction in motor activity,¹⁶⁵ and more social interest.¹⁶⁴

Two RCTs,¹⁵⁵⁻¹⁵⁷ one of which was fair quality,^{155,156} and two case series^{158,167} focused on the potential for interventions based on joint attention or symbolic play. Generally speaking, interventions with a joint attention focus did result in improvements in tasks based on joint attention. In the first RCT,¹⁵⁷ all groups improved in coordinated joint looks over time. No differences were found in pointing to a toy or giving a toy to an adult to share in any group. Both Joint Attention and Symbolic Play groups improved in the following areas compared with controls: showing toys to an adult, shared looks between a toy and the child's mother, and symbolic play skills.

Compared with other groups, the Joint Attention group showed more improvement in responding to joint attention over time. With respect to mother-child interactions (generalization) assessing the same

outcome areas, the Joint Attention group had significantly greater improvement than the Symbolic Play group in giving and showing a toy. Children in the Joint Attention group engaged in more child-initiated joint engagement than those in the control group. The Symbolic Play group showed significantly greater improvement on the Structured Play Assessment than did the control group for overall mastered level of play. In the second RCT,¹⁵⁷ significantly more children in the Joint Attention group engaged in coordinated looks during the final stimulus presentation (76.5 percent) than in the Symbolic Play group (38.9 percent). Children in the Joint Attention group engaged in significantly longer periods of coordinated looks between the person in the room and the stimulus presentations across the three time periods.

A second RCT^{155,156} comparing joint attention and symbolic play interventions included 58 children with autism 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. 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 fair quality case series describing an eight week, 24-session intervention designed to foster joint attention and language skills as well as joint engagement with the mother,¹⁶⁷ episodes of distress occurred in an average of 9.4 sessions (range=four to 24 sessions), with children displaying negativity for an average of 20 percent of the time (range=6-52 percent). There were no associations between negativity and children's mental or chronological age. Both mothers and children showed improvements in behavior regulation over the course of the intervention. Children engaged in behavioral strategies significantly more often during episodes of negativity than in nonnegative episodes ($p < .01$). The study also reports associations between mothers' vocal behavior regulation strategies and child-related stress as reported on the Parenting Stress Index; mothers with greater child-related stress used fewer vocal strategies such as vocal comfort and reassurance. Mothers whose children exhibited more externalizing problems (as rated on the Child Behavior Checklist) used more active behavior regulation strategies (e.g., shifting child's attention away from negative stimulus, hugging child, etc.).

None of the four additional case series that met criteria for inclusion in this section described the same intervention. They described a relationship-focused intervention teaching parents to use responsive teaching strategies to assist their children with acquiring pivotal behaviors,¹⁶⁶ the Developmental, Individual-Difference, Relationship-Based/ Floortime model,¹⁶⁰ the Relationship Development Intervention,¹⁵⁹ and the Mifne treatment model.¹⁶² All four report positive outcomes that are difficult to interpret absent a comparison group (Warren et al., 2011, p. 42-44).

Table 12. Outcomes of RCTs assessing play-/interaction-based interventions

Author, year, country Groups, N enrollment/ N final Study quality	Age, mean ± SD (range) IQ, mean ± SD	Key outcomes
Parent-focused interventions		
Solomon et al. ¹⁵¹ 2008, US G1: Parent training focused on behavior management and requesting (PCIT), 10/10 G2: Wait list, 9/9 Quality: Fair	G1: 8.2 yrs ± 1.7 G2: 8.1 yrs ± 2.2 NR	<ul style="list-style-type: none"> • Challenging behaviors decreased in both groups. • Scores declined on BASC Hyperactivity Scale for G1 but not G2. • Score on BASC Adaptability Scale increased significantly for G1. • Parents of G1 children reported significantly less atypicality on the BASC scale.
Kasari et al. ^{155,156} 2008, US G1: Joint attention intervention, 20/20 G2: Symbolic play intervention, 21/17 G3: Control group, 17/16 Quality: Fair	G1: 43.2 ± 7.05 G2: 42.67 ± 6.93 G3: 41.94 ± 4.93 NR	<ul style="list-style-type: none"> • 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.

BASC=Behavioral Assessment for Children; G=group; IQ=intelligence quotient; PCIT=Parent-Child Interaction Therapy; N=number; NR=not reported; SD=standard deviation

(Warren et al., 2011, p. 45)

Behavioral Interventions Focused on Associated Behaviors

Several behavioral interventions target symptoms commonly associated with autism, such as anxiety and anger management. Cognitive behavioral therapy-based (CBT) interventions are particularly common and involve teaching cognitive skills and relaxation strategies, promoting recognition of anxious feelings, and providing children with behavioral exposures in which to utilize their new coping skills in the face of anxiety-provoking stimuli, with an ultimate goal of reducing anxiety symptoms over time.²⁹

Parent training protocols, often implemented to help parents deal with challenging behaviors such as noncompliance, tantrums, self-injury, and aggression, attempt to teach parents strategies to curb negative behaviors. Once trained, parents can act as “co-therapists,” shaping behavior toward the goal of reducing challenging behaviors in daily life, where parents by necessity must act as the primary interventionist. Parent training interventions also often have secondary targets of improving parental feelings of self-efficacy and decreasing parental stress.

Many of the studies of behavioral methods used to treat challenging behaviors, such as functional behavior analysis and positive behavior support, included fewer than 10 participants with ASDs and thus were not included in this review.

Content of the literature. We identified 11 studies reported in 12 papers^{25,26,168-177} that addressed behavioral interventions focused on symptoms commonly associated with ASDs including anxiety and anger management. Six studies reported on CBT interventions,^{25,26,168-171,176} four used parent training techniques,^{172,174,175,177} and one used teacher training methods.¹⁷³

While the overlap among studies is somewhat unclear, sets of studies from the same authors and using the same methodology appear to include the same or overlapping samples.^{169,176;170,171;174,175} Accounting for this potential overlap, it appears that at least four independent studies of CBT interventions and three independent studies of parent training address anxiety and anger in children with ASDs. All studies examining CBT treatments included children ages seven and older, with means ranging from nine to eleven years of age. In two studies examining CBT treatments, only children with an Asperger diagnosis

were included,^{169,176} while the Wood et al. RCT enrolled children with an ASD and a comorbid anxiety disorder.^{170,171}

Parent training studies included parents of children ranging from age four to twelve with mean ages spanning seven to nine years.^{172,174,175,178} In three of four parent training studies, only parents of children with Asperger syndrome were included.^{174,175,178} In the teacher training study, children ranged in age from two to fifteen and all had diagnoses of autistic disorder.¹⁷³ Table 10 summarizes additional study details. Among all studies, six were fair quality and five were poor.

Summary of the literature. Among the studies assessing CBT approaches, one RCT examined the efficacy of a modified version of the Building Confidence CBT program for treating comorbid anxiety disorders (i.e., separation anxiety disorder, social phobia, or obsessive compulsive disorder) in seven to eleven year-old children with ASDs.^{170,171} This was the only RCT in which CBT occurred at the individual level.

The intervention program consisted of sixteen 90-minute weekly sessions conducted by clinical or educational psychologists or trainees in these programs. In the first report from the study,^{170,171} anxiety symptoms were assessed by evaluators blind to treatment condition using the Anxiety Disorders Interview Schedule, Clinical Global Impression (CGI)–Improvement Scale, and both parent and child versions of the Multidimensional Anxiety Scale for Children.

On the CGI, 92.9 percent of children in the intervention condition met criteria for positive treatment response, while only 9.1 percent of children in the waitlist control group met the same criteria; on the Anxiety Disorders Interview Schedule, 64.3 percent of children in the intervention group no longer met criteria for any anxiety disorder, whereas only 9.1 percent of children in the waitlist control group lost their anxiety disorder diagnosis at post-test.

Eight of ten children from the intervention group who returned for a three-month followup did not meet criteria for any anxiety disorder at followup. Maintenance of treatment response was also indicated by CGI and Multidimensional Anxiety Scale for Children scores at followup. The second report from the study¹⁷¹ included 58 percent of participants from the initial report (42 percent new participants), and measured effects of the intervention on autism symptoms using the Social Responsiveness Scale. Significant group differences were observed at outcome in the Social Responsiveness Scale total score as well as the social communication, social motivation, and social awareness subscales, with children in the intervention group showing fewer autism symptoms post-treatment than children in the waitlist control group.

The remainder of CBT-based interventions (Table 13) were conducted in group settings or directed toward parents. Reaven et al.²⁶ conducted a nonrandomized trial of a 12-week CBT-based group intervention for high-functioning (i.e., IQ above 70) children ages eight to fourteen years (mean = 11.83) with ASDs and comorbid anxiety disorders.

The authors created an original protocol,²⁷ and treatment involved both children and their parents. Ten children received active treatment in this pilot study, while 23 served as a wait-list control. Anxiety symptoms in children participating in the treatment group decreased over time, while symptoms in the control group did not on the parent (but not child) version of the Kiddie-Schedule for Affective Disorders and Schizophrenia or on the Screen for Child Anxiety and Related Emotional Disorders.

Chalfant et al.²⁵ examined children ages eight to thirteen years (mean = 10.8) with ASDs and one or more comorbid anxiety disorder diagnoses including separation anxiety, generalized anxiety, social phobia, specific phobia, and panic disorder confirmed by structured clinical interview using the Anxiety Disorders Interview Schedule. Children were randomly assigned to treatment and waitlist conditions. Treatment involved a 12-session CBT-based group therapy protocol, led by licensed clinical psychologists, with nine weekly two-hour sessions followed by three monthly booster sessions.

The protocol for the study was based on a manualized CBT-based anxiety intervention for children (Cool Kids) with adaptations made to account for the learning style of children with ASDs (e.g., more visual aids and structured worksheets, increased focus on relaxation and exposure, simplification and decreased emphasis on cognitive components of the treatment). Parents of children in the intervention group participated in concurrent parent groups with a manual also adapted from the Cool Kids program.

Measures were collected at baseline and at the completion of intervention (approximately five and a half months later); clinicians administering the pre- and post-intervention measures were the same clinicians who led treatment groups. No group differences were observed on any measure at baseline. However, children in the treatment group improved significantly over time while children on the waitlist did not in the number of anxiety disorder diagnoses present, as well as in the number of anxiety symptoms reported by children on the Children’s Automatic Thoughts Scale Internalising Scales, Revised Children’s Manifest Anxiety Scale, and Spence Children’s Anxiety Scale, by parents in their report on the Spence Children’s Anxiety Scale—Parent and the Strengths and Difficulties Questionnaire Emotional and Externalizing Scales, and by teachers using the Strengths and Difficulties Questionnaire Emotional and Externalizing Scales (Warren et al., 2011, p. 45-47).

Table 13. Studies assessing interventions targeting conditions commonly associated with ASDs

Author, year, country Groups, N enrollment / N final	Age, mean/yrs ± SD IQ, mean ± SD	Key outcomes
Study quality		
Reaven et al. ¹⁷⁵ 2009, US G1: Active CBT, 10/10 G2: Wait list Note: for children with comorbid anxiety, 23/21 Quality: Fair	G1+G2: 11.02 ± 1.9 G1+G2: 102.65 ± 18.22 NR	<ul style="list-style-type: none"> Anxiety symptoms in G1 decreased over time, while symptoms in G2 did not (p=0.01).
Wood et al. ^{170,171} 2009, US G1: Building confidence CBT program, 17/17 G2: Wait list control, 23/23 Quality: Fair	G1: 9.18 ± 1.42 G2: 9.22 ± 1.57 NR	<ul style="list-style-type: none"> 92.9% of children in the intervention condition met criteria for positive treatment response. 64.3% of children in G1 no longer met criteria for any anxiety disorder on the ADIS. MASC scores were significantly lower (i.e., reduction in anxiety) in G1 than in G2 post-test (p<0.0001). Maintenance of treatment response was indicated by diagnosis and CGI and MASC scores at followup. Children in the autism group had lower scores than control group children at outcome on the SRS total score as well as the social communication, social motivation, and social awareness subscales.
Sofronoff et al. ¹⁶⁸ 2007, Australia G1: CBT, 24/24 G2: Wait list control, 21/21 Note: for children with Asperger disorder and anger management difficulties Quality: Fair	G1: 10.79 ± 1.12 G2: 10.77 ± 0.87 G1: 105.24 ± 22.3 G2: 108.7 ± 21.6	<ul style="list-style-type: none"> G1 had significant improvement on parent-reported anger inventory between pre- and post-intervention (p<0.0001) and between pre-intervention and 6-wk followup (p<0.001) Significant improvement on frustration and relationships with authority subscales in G1. Parents of children in G1 reported fewer instances of anger post-intervention (and at six-wk follow up) than pre-intervention. Significant between-group differences in reports of anger incidents post-intervention (p<0.02) and at followup (p=0.005). G1 generated significantly more anger management strategies post-intervention and at six-wk follow up (p<0.01 and p<0.05, respectively) relative to baseline and relative to children in G2 at post-intervention (p<0.01).

Table 13. Studies assessing interventions targeting conditions commonly associated with ASDs (continued)

Author, year, country Groups, N enrollment / N final Study quality	Age, mean/ yrs ± SD IQ, mean ± SD	Key outcomes
Sofronoff et al. ¹⁶⁹ 2005, Australia G1: Child only CBT, 23/22 G2: Wait list, 23/20 G3: Child and Parent CBT, 25/24 Note: Children with Asperger disorder and anxiety symptoms Quality: Fair	G1: 10.56 ± 0.99 G2: 10.75 ± 1.04 G3: 10.54 ± 1.26 G1: 107.5 ± 27.3 G2: 101 ± 27.2 G3: 105.6 ± 21.2	<ul style="list-style-type: none"> Significant differences on the SCAS-P total score observed between the two intervention groups, G3 (p<0.03). Significant time by group interaction (SWQ) observed (p<0.0001), with significant improvement in scores between baseline and six-wk followup observed for both G1 and G3 (p<0.001). G1 and G3 scored better than G2 at followup on the James and the Maths test, and G3 scored better than G1 at followup (p<0.0001).
Aman et al. ¹⁷⁷ 2009, US G1: Risperidone, 49/40 G2: Risperidone + parent training, 75/55 Quality: Fair	G1: 7.5 ± 2.80 G2: 7.38 ± 2.21 NR	<ul style="list-style-type: none"> Significant group by time interaction on the HSQ (p<0.006); HSQ scores declined (i.e., decreased severity) in more children in G2. ABC irritability, stereotypic behaviors, hyperactivity subscales all showed significant group differences over time with less severe symptoms in each of the domains in G2.

ABC=Aberrent Behavior Checklist; ADIS=Anxiety Disorders Interview Schedule; CBT=cognitive behavioral therapy; CGI=Clinical Global impression; CHiAP=Children's Inventory of Anger-Parent report; ECBI=Eyberg Child Behavior Inventory; G=group; HSQ=Home Situations Questionnaire; MASC=Multidimensional Anxiety Scale for Children; NR=not reported;

SCAS-P=Spence Child Anxiety Scale-Parent version; SRS=Social Responsiveness Scale; SD=standard deviation; SWQ=Social Worries Questionnaire

(Warren et al., 2011, p. 47-49)

A series of papers examined CBT approaches delivered directly to children and via parent training. CBT provided by graduate students in psychology was assessed in high functioning children with Asperger disorder with comparisons made across two intervention conditions (child-only and parent-plus-child) and waitlist controls.^{169,176} Significant improvements in Spence Child Anxiety Scale-Parent scores were observed for both intervention groups on the total score and separation anxiety, obsessive compulsive disorder, social phobia, panic, and generalized anxiety scales; significant improvement on the personal injury scale was observed for the parent-plus-child intervention group. No significant differences were observed from baseline to six-week followup in the waitlist control group.

On the Social Worries Questionnaire, there was significant improvement in scores between baseline and six-week followup observed for both intervention groups, but not for the waitlist control group. Similarly, children in both intervention groups generated more strategies to cope with anxiety at six-week followup than at baseline, while children in the waitlist control group did not. Both intervention groups scored better than the wait-list control group at followup, and children in the parent-plus-child condition scored better than children from the child-only groups at followup. A separate study of the same intervention¹⁶⁸ to examine the impact of CBT-based treatment on anger management difficulties in high-functioning (i.e., average IQ above 100) children ages ten to fourteen years with Asperger syndrome found similarly positive results.

Parent training in using CBT approaches^{174,175} for parents of children ages six to twelve years with Asperger syndrome diagnoses includes psychoeducation, comic strip conversations and social stories introduction, and management techniques for externalizing behaviors, rigid behaviors, and anxiety. In studies of this approach, parents who attended a one-day workshop or who participated in six weekly one-hour individual sessions reported fewer challenging behaviors at both one-month post-treatment and

three-month followup relative to baseline, while there were no significant differences over time for the waiting list control group.

Parents from both intervention groups also reported significantly fewer challenging behaviors in their children, decreased challenging behavior intensity and improved social skills at both time points. At three-month followup, individual session participants reported significantly lower intensity of challenging behaviors relative to both the waiting list control group and workshop intervention group; the workshop group no longer showed differences from the control group by three-month followup in terms of parental report of child challenging behavior intensity.

The Research Units on Pediatric Psychopharmacology (RUPP) Autism Network first reported on the feasibility of a parent-training program for parents of children with autism spectrum disorders ages 4 to 13 years who were on stable medications for behavior problems.¹⁷² The parent training protocol consisted of 11 required sessions covering topics including prevention strategies, schedules, reinforcement, planned ignoring, compliance training, functional communication training, teaching techniques, and generalization. Two home visits were always conducted, four optional sessions were available, and booster sessions were provided to parents in later weeks; parent training was administered according to a structured curriculum.

Outcome measures related to child functioning included the Home Situations Questionnaire, the Aberrant Behavior Checklist (ABC), the Clinical Global Impressions – Improvement Scale (CGI-I), the VABS, and the Assessment of Basic Language and Learning Skills. Results indicated significant decrease in noncompliance on the Home Situations Questionnaire over the course of parent training intervention. Irritability and Hyperactivity/Noncompliance measured on the ABC showed improvement over time. Fifty-three percent of children were reported as very much improved on the CGI-I, and thirty percent were reported to show minimal improvement. Finally, with regard to adaptive behavior, improvement in daily living skills and increase in adaptive skills were also shown over the course of treatment. The correlation between improved compliance and improved adaptive behavior also strengthened over the course of treatment.

Following the initial feasibility study,¹⁷² Aman et al.¹⁷⁷ conducted an RCT assessing whether risperidone treatment combined with parent training in behavior management was superior to risperidone treatment alone; this study was conducted as part of the RUPP Autism Network. Parents of children ages 4 to 13 years with ASDs and significant tantrums, self-injury, and aggression who were randomly assigned to the combined treatment group received parent training with a behavior therapist according to a RUPP manual. As noted, the manual specified 11 core treatment sessions, three optional sessions, and up to three booster sessions of 60-90 minutes in length.

On average, parents in the combined condition participated in 10.82 sessions. As in the feasibility study, outcome was assessed on the Home Situations Questionnaire and ABC; the Children's Yale-Brown Obsessive Compulsive Scale–PDD version was also administered both pre- and post-intervention. After 24 weeks of treatment, HSQ scores for 71 percent of children assigned to the combined treatment group and 60 percent of children assigned to the medication-only treatment group declined (i.e., decreased severity), which represents a significant difference between groups over time. In addition, the ABC irritability, stereotypic behaviors, and hyperactivity/noncompliance subscales all showed significant group differences over time, with children of parents who received the parent training showing less severe symptoms in each of the domains.

One case series of a teacher training procedure in reducing challenging behaviors (e.g., aggression, noncompliance, off-task behavior)¹⁷³ reported a significant reduction in the rate of the target behavior following classroom instruction (45 hours) and practical application, training, and supervision (45 hours) in applied behavior analysis (Warren et al., 2011, p. 49-50).

Other Behavioral Interventions

Additional behavioral interventions include techniques such as neurofeedback and sleep hygiene education. Neurofeedback, or electroencephalogram (EEG) biofeedback, aims to remediate abnormal brainwave activity associated with disorders such as anxiety, ADHD, and ASDs through training individuals to control brain activity patterns. Neurofeedback involves the placement of electrodes to monitor brain activity while participants interact with specially designed computer games or other modalities designed to promote attention or other skills.¹⁷⁹ Behavioral treatments for sleep problems may attempt to affect the timing of sleep, sleep-wake cycle disorders, or promote efficacious sleep behaviors like bedtime routines and positive reinforcement.¹⁸⁰

Content of the literature. Three studies¹⁸¹⁻¹⁸³ of additional behavioral interventions met our inclusion criteria. Participant ages ranged from three to fourteen years across the studies, and all three occurred in a clinic setting. Jarusiewicz¹⁸¹ and Coben et al.¹⁸² used neurofeedback with children directly while the Reed et al. sleep workshops were aimed at parents using a group approach.¹⁸³ Table 10 includes additional study details. All three studies in this section were considered poor quality.

Summary of the literature. Jarusiewicz's RCT examined the efficacy of neurofeedback on autistic symptoms as assessed using the parent-rated Autism Treatment Evaluation Checklist as the primary outcome measure.¹⁸¹ Participants included 40 children ages four to 13 (mean=7) with a previous diagnosis of autism; participants were matched on gender, age, and autism severity, and individuals in each pair were randomly assigned to either neurofeedback or a wait list. Diagnostic and randomization procedures were not described.

Neurofeedback protocols varied depending on a child's autism severity as assessed by the Autism Treatment Evaluation Checklist and parental report of troubling symptoms; children typically received one to three sessions per week. Eight children in the neurofeedback group dropped out of the study due to family considerations or non-ASDs-related illness; the twelve remaining participants completed 20 to 69 neurofeedback sessions (mean=36). Scores on the Autism Treatment Evaluation Checklist improved from eight percent to 56 percent post-neurofeedback training, with an overall average reduction of 26 percent ($p < 0.001$). Scores for control participants improved by three percent overall (ns).

Coben et al.¹⁸² sought to extend Jarusiewicz's findings in a nonrandomized controlled trial of 49 children diagnosed with ASDs; diagnostic techniques were not described. Children in the experimental ($n=37$) and control ($n=12$) groups were matched on age, gender, handedness, ASDs severity, and other treatments received. Participants' ages across groups ranged from 3-14 years; the majority (75 percent) of participants in the neurofeedback group were diagnosed with PDD-NOS or autism. Four children in this group had Childhood Disintegrative Disorder. Outcome measures included the Autism Treatment Evaluation Checklist, Gilliam Autism Rating Scale, Gilliam Asperger Disorder Scale, the Personality Inventory for Children, Behavior Rating Inventory of Executive Function as well as parental ratings of the effectiveness of the treatment and a battery of neuropsychological tests to assess attention, visual-perceptual, executive function, and language skills.

Neurofeedback protocols were individualized for each child based on assessment information and initial quantitative electroencephalogram results; treatment consisted of 20 sessions, with sessions occurring twice weekly for an unspecified duration. Eighty-nine percent of parents reported improvement in the neurofeedback group; 83 percent of control group parents reported no change ($z=2.167$, $p=0.000$). Scores on all measures except the Gilliam Autism Rating Scale, improved significantly in the treatment group ($p=0.000$ to 0.006) as did scores on neuropsychological tests. The authors did not correct for multiple testing, however.

Reed et al.¹⁸³ employed sleep hygiene workshops targeted at parents and taught by a neurology sleep specialist, pediatrician with an ASDs treatment background, educational psychologist, and nurse educator. Twenty families participated and completed both baseline and followup assessments; the mean age of

children in the study was 5.8 ± 2.7 years, and the majority ($n=15$) had ADOS scores in the autism range. Workshops addressed establishing effective daytime/nighttime routines, minimizing night and early waking, and discussion of techniques to handle individual sleep concerns. Assessments, conducted prior to the initial workshop and approximately one month after the final session assessed sleep changes, repetitive behavior, and parental stress and also included a week of actigraphy measurement of sleep-wake patterns coupled with a parent-maintained sleep diary.

Significant improvements ($P < 0.05$) over baseline scores were seen in subscales of measures assessing hyperactivity, sleep disturbance, self-stimulatory, bedtime resistance, sleep onset delay, sleep duration subscales, and restricted behavior. Items related to reduction of stimulating activities before bedtime and the use of bedtime routines also improved. Actigraphy data, available for 12 children, illustrated a decrease in sleep latency in nine children with difficulty initiating sleep ($p=0.039$); among all 12 children, time in bed also significantly improved ($p=0.039$). Parental stress did not change significantly with the workshops (Warren et al., 2011, p. 50-51).

KQ2. Among children ages 2 to 12 with ASDs, what are the modifiers of outcome for different behavioral treatments or approaches (including characteristics of the intervention, provider, child or family)?

The information below addresses Key Question #2. The indented text is excerpted directly from the Warren et al. systematic review (2011, p. 87-90). References cited below can be found beginning on page 128 of Warren et al. (2011).

Understanding the degree to which child characteristics (i.e., specific ASDs 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. However, with rare exceptions,^{259,260,287} few studies are designed or powered to allow analysis of heterogeneous effects in order to identify true modifiers of treatment effect. Although we sought studies of treatment modifiers, only one study^{259,260} actually demonstrated true treatment modifiers based upon appropriate study design and statistical analysis. One other study²⁸⁷ was designed to examine the role of provider on outcomes, but showed no difference, possibly because it was underpowered to do so.

This first study²⁵⁹ included an analysis of initial characteristics of the children demonstrating that children who were low in initial object exploration benefitted more from RPMT, which explicitly teaches play with objects, while children who were relatively high in initial object exploration demonstrated more benefit from PECS. These results were maintained at 6 months. An additional analysis based on this study²⁶⁰ showed greater increases in generalized turn taking and initiating joint attention in the RPMT group than in PECS. The increased benefit for RPMT in joint attention was only seen, however, in children who began the study with at least some initiation of joint attention. Specifically, children most likely to benefit from RPMT in increasing joint attention had demonstrated at least seven acts of joint attention in the pre-intervention assessment. RPMT was also superior in this analysis in increasing object exchange turns.

One study²⁸⁷ explicitly sought to examine the impact of provider choice (parent versus professional) using similar interventions in an RCT. The study did not show a difference in outcomes for children receiving UCLA/Lovaas protocol-based intervention in a clinical setting versus at home from highly trained parents. Both clinic and parent groups received over 30 hours of intervention weekly and no group differences related to IQ, language, adaptive behavior, or other outcomes were seen. Children in both groups demonstrated substantial gains in a number of areas. Nonetheless, the results do provide further evidence of response to treatments anchored in the UCLA/Lovaas method, with some children demonstrating rapid acquisitions of new skills and change in IQ. Other studies not specifically designed to

examine modifiers have also compared parent to clinic-based interventions^{126,132,288} and demonstrated equivalent group change when delivered in the same intensity.

Other studies in this section are those in which potential correlates were identified that may act as true moderators, but not in the context of studies designed and powered to identify modifiers. These potential moderators should be assessed in properly designed and powered studies for this purpose.

Behavioral Interventions

Frequency, duration, and intensity. Apart from the study described above, a number of potential correlates of treatment effect are observed in the existing literature and should be studied further. The most commonly noted characteristics as potential correlates of effectiveness in the study of behavioral interventions are treatment intensity and approach (e.g., parent-led versus clinician-led) as well as baseline measures of child characteristics, including IQ, language and verbal skills and severity of the autistic disorder.

Vismara and colleagues¹⁷⁸ found equivalent results across training (distance vs. in person) modalities for providers of ESDM treatment. When examining characteristics of UCLA/Lovaas-based intervention, Luiselli et al. found that months of treatment was significantly related to language gain, but numbers of hours per week and total hours of treatment were not.¹²¹ Intensity of supervision within UCLA/Lovaas-based treatment has also been demonstrated to be positively correlated with change in cognitive in cognitive abilities, although not other skills domains, within one treatment study.^{126,132}

Because of the potentially increased efficiency and desirability of having parents provide intervention to their children in their own homes, several studies have reported on varying approaches to preparing parents to provide behavioral therapies. Sofronoff et al.^{174,175} conducted a parent training intervention with parents of children ages six to twelve years with Asperger syndrome diagnoses. Parents either (a) participated in a one-day workshop, (b) attended six weekly 1-hour individual sessions conducted by masters or doctoral students in psychology, or (c) were placed in a waitlist control group. Components of the intervention were the same in both treatment groups and involved psychoeducation, comic strip conversations and social stories introduction, and management techniques for externalizing behaviors, rigid behaviors, and anxiety. Parents from both intervention groups reported significantly better social skills in their children than did parents in the waitlist control group at both 1-month post-treatment and 3-month followup; at 3-month followup, parents from the individual session group reported marginally better social skills for their children than did parents from the workshop group, suggesting little modification of effect by intensity (one day vs. weekly training).

Finally, in a case series assessing an intervention intended to improve either joint attention or symbolic play skills, a teacher-led approach was compared with one in which the child took the lead and found positive effects associated with the teacher leadership.¹⁵⁸

Child characteristics. Several characteristics of the child have been assessed to determine whether there were identifiable variables associated with positive outcomes in intensive behavioral interventions.

Cognitive abilities/IQ. The most commonly reported characteristic investigated relates to pretreatment cognitive abilities/IQ. Several investigations have noted that pretreatment IQ and language predicts IQ at followup within the context of UCLA/Lovaas-based methodologies.^{101,104,115,124,287} However, other studies have suggested having a lower IQ at initiation of treatment is related to increased change in IQ over time¹²⁷ or and change in response to intervention^{102,126,132} within this same methodology. In contrast to UCLA/Lovaas-based methodologies, parent training interventions for teaching early social communication skills demonstrate that children with lower language levels and/or lower IQ at baseline may actually benefit more from this intervention.^{108,109} Some data from Pivotal Response Training studies suggest that less impaired children do better in response to offered parent training.¹¹⁷

Language/communication skills [sic]. Baseline language/communication skills may also correlate with treatment success, with studies generally suggesting a benefit for communication skills, including changes in ASDs classification associated with baseline language skills in an ABA-based approach.^{102, 124} In one RCT^{155, 156} comparing the use of targeted joint attention intervention to development of symbolic play skills, children with initially higher levels of expressive language showed greater growth in expressive language from pre-intervention to 12 months post-intervention. Among children with lower expressive language initially, those in the joint attention group showed significantly greater improvements in expressive language. In addition, joint attention initiations, responding to joint attention, the duration of child-initiated joint attention, average highest level of play, total number of symbolic play types, and initial receptive language age all predicted greater gains at 6 and 12 months post intervention.

Similarly, social skills studies have found verbal skills, either verbal comprehension (using the Verbal Comprehension Index) or expressive communication skills to be associated with social skills at outcome. Children with higher verbal comprehension scores who participated in the Social Story intervention¹⁴⁵ made larger gains in the evaluated game play skills, while children with extremely low verbal comprehension scores did not. Social Stories, an intervention program that relies heavily on the child understanding information presented in a written format, may not be as effective for children with low verbal comprehension abilities. In another study¹³⁹ pre-treatment communication skills, as measured by VABS Communication domain and Verbal IQ, were associated with social skills at outcome (VABS Socialization) in both a Lego treatment group and the treatment as usual control group (but more so in the Lego group).

Autism symptom severity. Some evidence indicates that specific constellations of symptoms related to ASDs may be important in understanding response to treatment. Social responsiveness and imitation skills have been suggested as skills that may predict improved treatment response in UCLA/Lovaas-based approaches,²⁸⁷ whereas “aloof” subtypes of ASDs have been suggested to be associated with less robust changes in IQ,¹⁰⁷ and lower baseline symptom tallies have also been demonstrated to be related to specific gains.¹⁰⁴ Other studies have seen specific improvement with UCLA/Lovaas-based intervention for children with PDD-NOS vs. Autistic Disorder diagnoses,¹¹⁴ which may be indicative of baseline symptom differences. However, many other studies have failed to find a relationship between autism symptoms and treatment response.

Two social skills studies^{139,148} looked at the diagnosis of participants (PDD-NOS vs. high functioning autism vs. Asperger syndrome for one study, autistic disorder vs. Asperger/PDD-NOS for the other) as a potential modifier of treatment effects and failed to find any significant direct effects. However in the study evaluating the social adjustment enhancement curriculum,¹³⁹ the results on a measure of theory of mind were no longer significant when the one participant with PDD-NOS was excluded.

Age at identification/initiation of treatment. Some evidence suggests that children initiating treatment at earlier ages may benefit more from UCLA/Lovaas-based intervention,^{115,129} however, other explicit comparisons have not found this same relationship for UCLA/Lovaas-based approaches¹²¹ and age at initiation of treatment may in fact be confounded by type of treatment initiated.¹²⁹

Neurobiological and genetic variation. Only one of the included and reviewed studies examined the relations between potential underlying neurobiological markers/variation and this study simply indexed head circumference as a measurement within design¹⁰² and this did not appear to be related to outcome.

Family characteristics. Although family characteristics were rarely reported in the behavioral literature, in one study of a parent-directed play interaction, change in child behavior was not significantly predicted by whether parents perceived their child having a causal role in their own behavior or the parent having a causal role in their child’s behavior,^{154,161} but parent positive affect, measured through behavioral coding was positively related to parental reports of child adaptive behavior and negatively related to parental reports of child challenging behaviors (Warren et al., 2011, p. 87-90).

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

The information below addresses Key Question #3. The indented text is excerpted directly from the Warren et al. systematic review (2011, p. 93). References cited below can be found beginning on page 128 of Warren et al. (2011).

Early Identifiable Changes Predicting Response/Outcome

Information about early response to treatment, or lack thereof, can be essential to guiding treatment selection, implementation, and modification. The reviewed literature offers almost no information about what specific changes predict long-term outcomes and response. Some evidence indicates that early response to both UCLA/Lovaas-based approaches and ESDM intervention in terms of changes in IQ over the first year of treatment predicts, or accounts for, longer-term change in IQ.^{287,290} However, findings also suggest that while gains in the cognitive domain might be accounted for primarily within the first year of treatment, changes in adaptive behavior in response to these same interventions may occur over a longer time frame^{110,133,287,290} if they occur at all¹⁰⁵.

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

The information below addresses Key Question #4. The indented text is excerpted directly from the Warren et al. systematic review (2011, p. 93-94). References cited below can be found beginning on page 128 of Warren et al. (2011).

One study meeting our criteria addressed whether outcomes measured at the end of treatment could predict longer term functional outcomes. An RCT comparing joint attention and symbolic play interventions^{155,156} included 58 children with autism 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. Children in the symbolic play and joint attention groups showed significantly greater growth expressive language over time than did participants in the control group ($p < .01$, 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 both the joint attention and symbolic play groups showed significantly more growth in initiation of joint attention and duration of child-initiated joint attention than did the control group ($p < .01$ to $< .05$). 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.

The investigators also assessed differences in the amount (total hours) of intervention services (speech and overall) children in the three groups received post-intervention, with children in the control group receiving significantly more hours of overall services than either the joint attention or symbolic play groups ($p < .05$ and $< .01$, respectively); differences in hours of speech interventions received were not significant. Only the duration of child-initiated joint attention episodes was related to hours of intervention received post-treatment, with children with fewer hours of overall services showing greater growth in child-initiated joint attention episodes.¹⁵⁵ Hours of speech interventions received did not affect growth in skills.

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

The information below addresses Key Question #5. The indented text is excerpted directly from the Warren et al. systematic review (2011, p. 94-95). References cited below can be found beginning on page 128 of Warren et al. (2011).

Parents and clinicians wish to know whether outcomes observed in the treatment setting are likely to also be found in other settings and are thus generalizable. To try to assess generalizability, we recorded the degree to which studies collected outcomes data in multiple settings when it would be appropriate. For example, we noted when studies occurring in the clinical setting also collected data in the home or school. We also noted the period of time for which studies collected data.

For some areas of intervention, outcomes are primarily measured outside of the setting in which the treatment takes place. This includes, for example, behavioral interventions for associated conditions like anxiety, in which treatment occurs in therapy sessions. For these interventions, outcomes are usually measured using parent, self, and/or teacher report at home, at school and in the community. Studies of these behavioral interventions do, in fact, report positive outcomes in children's natural settings to mirror what is seen in the treatment setting; however, these outcomes are generally identified with parent report rather than the preferred direct observation. Few behavioral interventions continue to monitor children in their studies and so maintenance of the results over time is largely unknown.

In a number of studies of social skills interventions^{154-155,162-163}, parents reported positive outcomes outside of the treatment session, but parents were not blinded to intervention status. Participants in cognitive-behavioral-ecological^{137,138} and Lego therapy¹⁴³ were shown to have improved social skills outside of the intervention settings. Although the parents of children involved in Children's Friendship Training¹⁴¹ reported significant changes in child social behavior at home immediately following the intervention (as well as 3 months later), teachers did not report any changes in the children's behavior at school. On the other hand, teachers of children involved in a social competency and social skills training program¹⁴⁰ reported improvements in student behavior at school.

One study attempted to assess the ability of children to apply new skills across changing intervention conditions. Participants in Social Stories¹⁴⁵ were able to generalize the social skills they learned while playing with one set of board games to a different set of board games. However these "generalization" trials were conducted by the same experimenter in the same room as the other assessments, so it is not clear whether the targeted social skills would generalize to more naturalistic settings with peers.

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

The information below addresses Key Question #6. The indented text is excerpted directly from the Warren et al. systematic review (2011, p. 95).

No studies were identified to answer this key question.

KQ7. What evidence supports the use of a specific treatment approach in children under the age of two who are at high risk of developing autism based upon behavioral, medical, or genetic risk factors?

The information below addresses Key Question #7. The indented text is excerpted directly from the Warren et al. systematic review (2011, p. 95-97). References cited below can be found beginning on page 128 of Warren et al, (2011).

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 autism based upon behavioral, medical, or genetic risk factors. Studies located typically included participants whose mean age exceeded 24 months; however, the studies address interventions which can be used with children under age 2. The average age for diagnosis of ASDs in the US is not until at least age 3, but a reliable diagnosis may be possible as early as age 2.²⁹¹⁻²⁹³ Research suggesting that early intervention can improve outcomes has compelled investigators to consider intervening in very young children.¹¹⁵

We identified four papers^{178,290,294,295} with unique study populations addressing treatment approaches for very young children. Three studies were conducted in the US^{178,290,294} and one in the UK.²⁹⁵ Two of the studies were prospective case series,^{178,294} one was a nonrandomized controlled trial,²⁹⁵ and one was a randomized controlled trial.²⁹⁰ Table 26 summarizes outcomes for studies considered to be fair or good quality and employing comparison groups.

The RCT²⁹⁰ and nonrandomized trial²⁹⁵ were completed in a clinic setting with instruction to continue with parents at home. All children in the RCT met DSM-IV criteria as well as criteria on ADOS and Toddler Diagnostic Interview for diagnosis confirmation; the mean age of participants in the treatment and control groups was 23 months. The nonrandomized trial²⁹⁵ employed parent training techniques to teach social communication skills and included children with a mean age of 38 months in the intervention group and 34 months in the control group.

One of the case series describes an evaluation of techniques to train personnel to provide ESDM-based therapy and included children with a mean age of 33 months.¹⁷⁸ The second case series²⁹⁴ was completed in the home and classroom and focused on social-communication and language outcomes; children assessed in the study were between 18 and 36 months. Among studies in this section, 1 was considered good quality, 1 fair quality, and 2 were considered poor.

The Dawson et al.²⁹⁰ randomized controlled trial evaluated the effectiveness of the ESDM for young children with ASDs. ESDM, a comprehensive, manualized intervention that blends ABA with developmental and relational approaches, was designed to be used with children as young as 12 months, delivered in the home, and to utilize parents as well as trained therapists.

After 2 years of intensive intervention (31 hours of intervention per week, 15 from a therapist and 16 from parents) children receiving ESDM treatment displayed significantly larger gains in IQ (when compared with a community sample receiving 18 hours of individual and group intervention). Children in the experimental group also demonstrated significantly larger gains in terms of adaptive behavior skills (i.e., all areas except socialization) than controls. The authors also reported greater diagnostic shifts (i.e., from Autistic Disorder to PDD-NOS for seven (29.2 percent) children in the ESDM group and for one (4.8 percent) child in the community services group; two (8.3 percent) children in the ESDM group and five (23.8 percent) children in the community services group experienced a diagnosis change from PDD-NOS to ASDs); however, these shifts were not matched with clinically significant improvements in terms of ADOS severity scores nor measurements of restricted and repetitive behaviors (i.e., RBS scores).

While no replication of this study has been conducted, the model had been subject to an early effectiveness trial¹⁷⁸ wherein the research team compared distance learning vs. live instruction for

community-based therapists implementing intervention and training parents. Results suggest that both modalities of learning were effective in teaching therapists to implement and train parents, with significant child gains over time and across modalities; however, results also suggested that implementation with fidelity required specific and explicit supervision. Thus, while promising in terms of treatment efficacy and extension to a younger population of children with ASDs, training demands for broad implementation appear substantial. Further, the average age for enrollment was very close to 2 years of age. As such, concerns about how this model would apply to children closer to 1 year of age remain.

In another evaluation of an early intervention approach, parents of 51 preschool-aged children suspected of ASDs (mean age, intervention group = 38 months, mean age, control group = 34 months) participated in the Hanen More than Words program, as created by the Hanen Center either immediately (n = 26) or after a delay (n = 25).²⁹⁵ The program focused on weekly group instruction in enhancing interactions and facilitating communication. In addition to 20 hours of group intervention, parents received individual in-home feedback on three occasions. Operationalization of “suspected ASDs” was identification of language delay and some aspect of concern about social behavior by a pediatrician and/or a speech and language therapist.

Ultimately, this resulted in inclusion of children within intervention and control groups without ASDs, with the authors grouping PDD-NOS and other developmental concerns under a category of “non-core autism.” After the intervention period, reported language use was substantially higher for the intervention group, with both the core autism and non-core autism children demonstrating improvements. Parent use of taught strategies was also higher in the intervention group than in the comparison group but only for the children with core autism. No group differences were found for ADOS scores or behavior issues.

Notably, more children in the intervention group had ASDs, and the intervention group also received more “substantial intervention” outside of the treatment context. Thus, while demonstrating potential benefit for parent training in social communication for young children with ASDs, the unique impact of this program for specific children remains unclear.

Wetherby and colleagues²⁹⁴ prospective case series served as a preliminary study for the Early Social Interaction Project, which emphasizes a parent-implemented individualized curriculum in a natural environment. The authors found significant within-group differences from pre- to post-test for 11 of the 13 social-communication measures on the Communication and Symbolic Behavior Scales Developmental Profile in the Early Social Interaction group (n=17). The post-Early Social Interaction group performed significantly better than the third-year contrast group (n=18) on three measures of social signals, rate of communicating, three measures of communicative functions, and understanding.

The third-year contrast group performed significantly better than the pre-Early Social Interaction group on all three measures of communicative means and on actions to others in play, but there were no significant differences on the three measures of social signals, rate of communicating, the three measures of communicative functions, understanding, and inventory of actions. The percentage of children who were verbal was 5.9 percent in the pre- Early Social Interaction group, 76.5 percent in the post- Early Social Interaction group, and 55.6 percent in the third-year contrast group.

These findings suggest that the Early Social Interaction project has a positive impact on ASDs symptoms, but because the groups were unable to be compared at pretest, we cannot conclude whether the benefits were due to Early Social Interaction or to normal maturation. Another limitation in the authors’ methodology is the lack of documentation of parental implementation in the home, given that the parents’ involvement is a significant factor in the effectiveness of Early Social Interaction treatment (Warren et al., 2011, 95-97).

Table 26. Outcomes of interventions for children at risk for diagnosis of ASDs

Author, year, country Groups, N enrollment/N final Study quality	Age, mean (mo) ± SD Diagnostic category, N (%)	Key outcomes
Dawson et al. ²⁹⁰ 2010, US G1: ESDM, 24/24 G2: Community-based interventions, 24/21 Quality: Good	G1+G2: Intake: 38 Followup: 52 Autism: 39 (75) PDD-NOS: 9 (17)	1 yr outcomes: <ul style="list-style-type: none"> • Significantly greater improvement in IQ for ESDM (154 vs. 22 pts) than community-based. • No adaptive behavior differences. 2 yr outcomes: <ul style="list-style-type: none"> • Significantly more improvement in ESDM group vs. community-based on IQ; receptive language, and expressive language. • Adaptive behavior improvements in both groups (all domains except socialization); significantly greater improvements in ESDM group. • No change in ADOS severity scores or repetitive behavior. • Diagnostic shift toward milder diagnosis (PDD-NOS) greater for ESDM group.
McConachie et al. ²⁹⁵ 2005, UK G1: More than Words (MW), 26/26 G1a: MW, participants with autism dx, 17/17 G1b: MW, participants with PDD-NOS or other childhood developmental disorder, 9/9 G2: Wait list control, 21/21 G2a: Wait list control, participants with autism dx, 12/12 G2b: Wait list control: participants with PDD-NOS or other childhood developmental disorder, 13/13 Quality: Fair	G1: 38.12 (6.54) G2: 34.96 (6.68) G1: Autism: 17 (85) NCA: 9 (35) G2: Autism: 12 (48) NCA: 13 (52)	<ul style="list-style-type: none"> • Reported language use was substantially higher for G2 with both the core autism (on average 50 words) and NCA groups demonstrating improvements. • No group differences were found for ADOS scores or behavior issues.

ADOS=Autism Diagnostic Observation Schedule, dx=diagnosis; ESDM=Early Start Denver Model, G=group; IQ=intelligence quotient; mo=months; MW=More than Words; NCA=non core autism

(Warren et al., 2011, p. 97)

Discussion

In the sections that follow, the rationale for how the report is organized, and how the strength of the evidence is evaluated are presented. Given the complex nature and broad diversity of interventions for the treatment of ASD, there are multiple options for how to organize a report. The authors present the rationale for their organizational choice, which is to provide maximal information to end users for making treatment decisions. Assessment of strength of the evidence is done in conformity with standard EPC methodology, and considers the four elements of precision, directness, consistency and risk of bias.

The information below is directly excerpted from the Warren et al. report (2011, p. 98).

The organization of interventions into categories followed in this report is one of many possible approaches, none of which is uniformly accepted in the field. In developing a comparative effectiveness review for the Effective Healthcare Program, our primary intent is to provide information to end users making treatment choices, rather than to academic researchers who might choose to organize the report differently, for example by underlying philosophy or approach. Therefore, in selecting the categories of interventions reflected here, we attempted to incorporate both treatment approach and treatment setting, as these two elements would be considered in a treatment decision. This consideration means that some categorical divisions of similar approaches are reviewed in different sections. We considered

whether alternate organizations would have changed our conclusions in any area and determined that neither our assessment of the literature nor our strength of the evidence determinations would have changed.

The information below is directly excerpted from the Warren et al. report (2011, p. 98-99).

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 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. Interventions that have shown significant benefit in a small number of studies but have not yet been replicated using rigorous study designs will have insufficient or low strength of evidence, despite potentially offering clinically important benefits. Future research may find that the intervention is either effective or ineffective.

Methods for applying strength of evidence assessments are established in the Evidence-based Practice Centers' Methods Guide for Effectiveness and Comparative Effectiveness Reviews⁹⁹ and are based on consideration of four domains: risk of bias, consistency in direction of the effect, directness in measuring intended outcomes, and precision of effect. For determining the strength of evidence for effectiveness outcomes, we only assessed the body of literature deriving from studies that included comparison groups. We required at least 3 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 risk of bias. For determining the strength of evidence related to harms, we also considered data from case series.

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. As could be expected in a field that is testing a broad array of interventions, most intervention-outcome pairs had insufficient strength of evidence to establish confidence in the stability of observed effects.

Warren et al. (2011) Summary

In the text and tables that follow, the evidence is summarized for each key question in the Findings section of the report, and for each category of intervention. In addition, the strength of the evidence for a variety of outcomes is presented.

KQ1. Among children ages 2 to 12 with ASDs, what are the effects of behavioral, educational, family, treatment approaches that utilize ABA principles on core and commonly associated symptoms?

The information below is directly excerpted from the Warren et al. report (2011, p. 100-106). References cited below can be found beginning on page 128 of Warren et al. (2011).

Early intensive behavioral and developmental interventions.

Summary. We located 38 papers^{100-133,178,290,294,295} comprising 34 unique studies addressing early intensive behavioral and developmental interventions. Individual studies using UCLA/Lovaas-based interventions or ESDM report improvements in outcomes for some preschool and early school-aged children. Improvements are most often seen in cognitive abilities and educational attainment, and less consistently

in adaptive, social, and challenging behaviors. Of note, however, even children who have meaningful improvement in specific areas (most commonly in cognitive skills) often continue to have substantial impairment in adaptive, social, and behavioral functioning. This sustained level of impairment, along with a lack of longer-term outcomes data, makes it difficult to assess whether treatment-related changes can modify long-term functional and developmentally appropriate adaptive independence.

To date, studies have failed to characterize adequately the subpopulation of children who experience positive response to intervention, although it is clear that positive outcomes are more prominent in some children but not others. One powerfully replicated finding is that not all children receiving early intensive intervention demonstrate robust gains, and many children continue to display prominent areas of impairment. Nonetheless, dramatic improvements are observed in a subset of children and even small improvements in standardized outcomes may translate into meaningful improvements in quality of life. Early intensive behavioral and developmental approaches have significant potential, yet require further research.

Unfortunately, there have been to date very few well-controlled trials and those conducted have used small samples; different treatment approaches (i.e., developmental to intensive behavioral); 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 different outcome measurements over different periods of time (weeks to years).

Observational and non-controlled studies also have reported improvement for children receiving early intensive treatments when compared with eclectic treatments. Positive outcomes have been most common when early intensive behavioral and developmental interventions are systematically delivered by expert providers, including well-supervised and trained parents, over fairly lengthy intervals of time (> 1 year). A challenge to interpreting the observational literature, however, is that although authors assert that they used early intensive behavioral and developmental interventions, many of the studies are inadequately described, fail to include fidelity and treatment adherence measurements and procedures, and may in fact be delivering very different interventions. As a result, the body of observational literature categorized in this report as “early intensive behavioral” is so disparate that conclusions cannot easily be drawn.

Few studies directly comparing the effects of different treatment approaches are available (for example, direct comparison of UCLA/Lovaas and ESDM), and few data on practical effectiveness or feasibility beyond research studies exist, so questions remain about whether reported findings would be observed on a larger scale within communities. Similarly, no studies in this category reported harms of intervention.

Less intensive interventions to provide parent training for bolstering social communication skills and managing challenging behaviors may be useful for younger children with ASDs, particularly to improve social communication, language use, and potentially symptom severity and family functioning.^{108,109,120,295} However, while parent training programs can modify parenting behaviors during interactions, data are limited about their contribution to specific child improvements in the short- and long-term beyond simple language gains for some children.

Table 27. Summary of results of studies of early intensive behavioral and developmental approaches (continued)

Intervention	Study design/Quality	Study results and overall strength of evidence
Early Start Denver Model	1 RCT/1 good ²⁹⁰ 1 Prospective case series ¹⁷⁸	<ul style="list-style-type: none"> • Improvements in cognitive, language, and adaptive behavior skills are seen over 2 years in one RCT of ESDM intervention for young children with ASDs. • ESDM findings are not yet replicated and it is unclear how core ASDs symptoms change in response to treatment. • Strength of evidence for ESDM-based intervention in affecting cognitive, language, and adaptive outcomes currently is insufficient.
Intensive parent training	3 RCTs / 3 fair ^{100,108,109} 1 Nonrandomized controlled trial / 1 poor ¹²⁰ 3 Prospective case series ^{116,117,128}	<ul style="list-style-type: none"> • Some indication of short-term improvements in language, social, and adaptive skills for children whose parents receive training in these areas but studies vary in interventions and outcomes studied. • Data do not yet demonstrate long-term functional improvements across domains for any specific form of training. • Strength of evidence for changing core ASDs deficit areas is insufficient as studies vary in interventions and outcomes reported.

ASDs=autism spectrum disorders; ESDM=Early Start Denver Model; RCT=randomized controlled trial; UCLA=University of California, Los Angeles

(Warren et al., 2011, p. 101)

Strength of evidence. In general, there are too few studies of either UCLA/Lovaas-based approaches, ESDM, or intensive parent training approaches to assert that observed estimates of effect for either approach are unlikely to change with future research. With a relatively larger (albeit still inadequate) body of literature, the UCLA/Lovaas studies report positive shifts in language, adaptive, cognitive and educational outcomes, but our confidence (strength of evidence) in that effect is low, based on the need for additional, confirmatory research (Table 27). With only one RCT, we can only judge the literature on ESDM to be insufficient; although results in this one study were positive and the study warrants replication. On balance, however, the combined research on UCLA/Lovaas and ESDM suggests a benefit of early intensive approaches for some children that should continue to be studied. The evidence for parent training interventions was insufficient; the few available studies used interventions that varied from study to study. Furthermore, outcomes assessed in these studies were frequently short-term, indirect (intermediate) measures (Warren et al., 2011, p. 102).

Social Skills Training

Summary. We located 16 papers addressing interventions targeting social skills.^{135-149,152} Although all of the studies of social skills interventions reported some encouraging results, most have not included objective observations of the extent to which social skills improvements are maintained within everyday peer interactions. In addition, the current research focuses almost exclusively on children considered high functioning based on IQ and language skills, excluding the majority of children diagnosed with an ASD. The quality of the studies was poor to fair, although some results may suggest benefit for a subgroup of particularly high functioning children. No two studies evaluated the same intervention, making it impossible to know whether observed results are likely to be consistently observed. No studies reported harms of intervention.

Strength of evidence. The strength of evidence for the effect of social skills interventions on social outcomes is insufficient (Table 28). Of 8 RCTs, four were fair in quality and none was good. All studies did demonstrate benefit on at least one outcome measure but a lack of consistency in the interventions or

outcome measures makes it impossible to assess consistency or precision. Most studies relied on report of intermediate outcomes (Warren et al., 2011, p., 102-103).

Table 28. Summary of results of social skills interventions

Intervention	Study design/Quality	Study results and overall strength of evidence
Group-format	6 RCTs / 3 fair ^{145,149,141} , 3 poor ^{143,146,148} 1 Retrospective cohort / 1 poor ¹⁴⁸ 5 Prospective case series ^{136,138,140,142,144}	<ul style="list-style-type: none"> • High functioning children with ASDs improved on various social outcomes in individual studies, however the specific social skills in which benefits were observed and reported (such as emotion recognition, theory of mind, and observed peer interactions) varied depending on the study. • Strength of evidence on social outcomes is insufficient given variations in the interventions and outcomes assessed.
Individual-format	2 RCTs / 1 fair, ¹⁴⁵ 1 poor ¹⁴² 2 Prospective case series ^{137,147}	<ul style="list-style-type: none"> • Improvements were seen in targeted social skills for treated participants but interventions and outcomes varied substantially across studies. • Strength of evidence for social outcomes is insufficient given variations in the interventions assessed.

ASDs=autism spectrum disorders; RCT=randomized controlled trial

(Warren et al., 2011, p. 103)

Play- and Interaction-Based Interventions

Summary. Fifteen papers (13 unique study populations) assessed play-/interaction-based approaches.¹⁵³⁻¹⁶⁷ Parent training in play-based interventions shows some promise for reducing challenging behavior and encouraging early social communication skills (e.g., joint attention and symbolic play). Joint attention and symbolic play interventions also promoted expressive language growth.^{155,156} No studies reported harms of intervention.

Strength of evidence. Although there were at least two RCTs available for most categories of play interventions (parent-focused, relationship-based, imitation, joint attention and symbolic play), none was of good quality and the diversity of specific interventions and outcomes prohibits drawing conclusions about specific approaches (Table 29) (Warren et al., 2011, p. 103).

Table 29. Summary of results of studies of play-/interaction-based interventions

Intervention	Study design/ Quality	Study results and overall strength of evidence
Parent-focused therapies	2 RCTs / 1 fair, ¹⁵¹ 1 poor ^{153,154}	<ul style="list-style-type: none"> • Problem behavior declined for the treated group in both studies. • Adaptive behavior skills increased for the treated group in one RCT. • Parent reports indicated that the treated group appeared more typical following intervention in one study. • Strength of evidence for effectiveness in affecting challenging behavior is insufficient.
Imitation	3 RCTs / 3 poor ^{152,155}	<ul style="list-style-type: none"> • Children in imitation treatment groups showed more interaction with adults compared with those in contingent response groups in all three studies. • Strength of evidence for the effect on social behavior is insufficient.
Joint attention and symbolic play	2 RCTs / 1 fair ^{152,156} , 1 poor ¹⁵⁷ 2 Prospective case series ^{158,167}	<ul style="list-style-type: none"> • Joint attention and symbolic play were both effective in improving responsive joint attention or expressive language in the short and long term in one RCT. • Greater improvement in outcomes predicated on increased joint attention in the joint attention groups in one RCT. • Mother-mediated joint attention intervention yielded increases in joint engagement in one study. • Strength of evidence for effectiveness of joint attention intervention in affecting joint attention outcomes is insufficient.
Relationship-focused interventions	2 Prospective case series ^{160,166} 2 Retrospective case series ^{159,162}	<ul style="list-style-type: none"> • Positive behavioral outcomes noted in all series, but no comparison groups. • Insufficient evidence to determine effectiveness.

RCT=randomized controlled trial

(Warren et al., 2011, p. 104)

Behavioral Interventions for Commonly Associated Conditions

Summary. We identified 11 studies reported in 12 papers^{25,26,168-177} that addressed behavioral interventions focused on symptoms commonly associated with ASDs. Most studies of behavioral interventions to address commonly associated conditions are limited to high-functioning children (based on IQ) with ASDs who are at least school age. These studies evaluated behavioral treatments for commonly occurring comorbid symptoms in ASDs, including anxiety, anger management difficulties, and challenging behaviors. All report promising results, with caveats concerning study quality.

Interventions included cognitive behavioral therapy in individual and group formats, parent training, and teacher training to address target symptoms. Cognitive behavioral therapy (CBT)-based treatments varied across studies and were generally adapted from existing manuals to be more amenable for use in children with ASDs. Several studies suggested that CBT-based interventions were effective in reducing anxiety symptoms.^{26,170,171}

This category of intervention also included various parent training approaches to decrease challenging behaviors. Results of two studies combining parent training with risperidone treatment suggested that adding parent training to medication increased adaptive behavior and decreased noncompliance and irritability/aggression in children with ASDs.^{172,177} Another set of parent training studies suggested that training parents improved both the frequency and intensity of a child's challenging behaviors.^{174,175}

While individual studies of CBT and parent training for decreasing comorbid anxiety, anger management, and externalizing symptoms reported positive results, results should be interpreted cautiously. The small number of studies overall use disparate intervention approaches and different outcome measures. Additionally, in some of these studies, parents were involved in delivering the interventions and completed the majority of questionnaires to assess symptoms before and after treatment. No studies reported harms of intervention.

Strength of evidence. Current strength of evidence for CBT- based, parent-training, and teacher-training interventions on comorbid symptoms is insufficient. Consistent positive findings of improvement in anxiety, anger, and challenging behavior levels are offset by variation among the interventions and outcomes assessed (Table 30) (Warren et al., 2011, p. 104-105).

Table 30. Summary of results of studies targeting behaviors commonly associated with ASDs

Intervention	Study design/ Quality	Study results and strength of evidence
CBT for anxiety	4 RCTs / 2 fair, ¹⁶²⁻¹⁷¹ 2 poor ^{25,176} 1 Nonrandomized trial / 1 fair ²⁶	<ul style="list-style-type: none"> • Decrease in anxiety symptoms in treated groups in individual studies. • Participants meeting criteria for anxiety disorders decreased in one study. • Improvement in social skills in treated children. • Strength of evidence for a positive effect on comorbid symptoms was insufficient based on variation in the interventions assessed.
CBT for anger management	1 RCT / 1 fair ¹⁶⁸	<ul style="list-style-type: none"> • Reduction in parent-reported instances of anger in the treated group of one RCT. • Strength of evidence for a positive effect on comorbid symptoms was insufficient, based on only on RCT of fair quality.
Parent and teacher training focused on commonly associated behaviors	1 RCT / 1 fair ¹⁷⁷ 2 prospective cohorts / 2 poor ^{174,175} 2 prospective case series ^{172,173}	<ul style="list-style-type: none"> • Less severe challenging behaviors were observed in children taking risperidone whose parents participated in parent training in one RCT • Parent training in individual sessions was more effective than in a workshop setting in one study. • Strength of evidence for a positive effect on comorbid symptoms was insufficient, based on variation in the interventions and outcomes assessed.

CBT=cognitive behavioral therapy; RCT=randomized controlled trial

(Warren et al., 2011, p. 105)

Additional Behavioral Interventions

Summary. Three studies¹⁸¹⁻¹⁸³ of additional behavioral interventions (neurofeedback, sleep workshops) met our inclusion criteria. These intervention studies were limited by small sample sizes, short-term followup and largely parent-reported outcomes. No studies reported harms of intervention.

Strength of evidence. With few studies of additional behavioral interventions, all of poor quality, there is insufficient evidence to evaluate the relative effect of other behavioral interventions on targeted outcomes including ASDs symptom severity, problem behaviors, and sleep concerns (Table 31) (Warren et al., 2011, p. 105).

Table 31. Summary of results of studies of other behavioral interventions

Intervention	Study design/ Quality	Study results and overall strength of evidence
Neurofeedback	2 RCTs / 2 poor ^{181,182}	• Insufficient strength of the evidence based on few, poor studies.
Sleep workshops	1 Prospective case series ¹⁸³	• Insufficient strength of the evidence.

ASDs=autism spectrum disorders; RCT=randomized controlled trial

(Warren et al., 2011, p. 106)

In the tables that follow, the authors' assessment of the strength of the evidence is presented.

Table 1 is modified from Table 36 in Warren et al. (2011, p. 113) to show only those interventions that are behavioral in nature. It presents assessments for each domain pertaining to strength of evidence for each of the major intervention-outcome combinations that received a strength of evidence rating of low, moderate or high. Risk of

bias refers to issues in study design and conduct that could result in biased estimates of effect. Consistency refers to the similarity of effect sizes seen across studies, and to the consistency of the direction of study results. Consistency can only be assessed when more than one study is available. Directness is a reflection of the relationship between the intervention and the ultimate health outcome of interest. Precision is an assessment of certainty around the effect observed.

Table 1. Intervention, strength of evidence domains, and strength of evidence for key outcomes

Intervention	Domains pertaining to Strength of Evidence (SOE):				SOE
	Risk of Bias	Consistency	Directness	Precision	
Adaptive behavior					
Behavioral, UCLA/Lovaas	Medium	Consistent	Direct	Imprecise	Low
ASDs symptom severity					
Behavioral, UCLA/Lovaas	Medium	Inconsistent	Direct	Precise	Low
IQ/cognitive					
Behavioral, UCLA/Lovaas	Medium	Consistent	Direct	Precise	Low
Language/communication					
Behavioral, UCLA/Lovaas	Medium	Consistent	Direct	Precise	Low

Table 2 is modified from Table 37 in Warren et al. (2011, p. 114-115), and presents all behavioral interventions that were assessed to have an insufficient strength of evidence for the specified outcomes.

Table 2. Interventions/outcomes with insufficient strength of evidence by outcomes assessed

Intervention	Adaptive behavior	Adverse events/ harms	Anger	Anxiety	ASDs symptom severity	Challenging behavior	Hyperactivity/ inattention	IQ/cognitive	Joint attention	Language/ communication	Motor/sensory	Repetitive behavior	Sleep	Social skills/ social behaviors
Behavioral, CBT (commonly associated conditions)			✓	✓						✓				
Behavioral, ESDM	✓				✓			✓		✓				
Behavioral, Imitation (play-/interaction-based)														✓
Behavioral, Joint attention/symbolic play (play-/interaction-based)									✓					
Behavioral, Other—Neurofeedback					✓									
Behavioral, Other—Sleep						✓						✓	✓	
Behavioral, Parent & teacher training (commonly associated conditions)			✓	✓		✓								
Behavioral, Parent training (early intensive behavioral)										✓		✓		✓
Behavioral, Parent-focused (play-/interaction-based)						✓								
Behavioral, Relationship-focused (play-/interaction-based)														✓
Behavioral, Social skills														✓

CAM=complementary and alternative medicine; CBT=cognitive behavioral therapy; ESDM=Early Start Denver Model; PECS=Picture Exchange Communication System; RPMT= Responsive Education and Prelinguistic Milieu Teaching SRI=serotonin reuptake inhibitor; TEACCH=Treatment and Education of Autistic and Communication related handicapped Children

KQ2. Among children ages 2 to 12 with ASDs, what are the modifiers of outcome for different behavioral treatments or approaches (including characteristics of the intervention, provider, child or family)?

The information below is directly excerpted from the Warren et al. report (2011, p. 115-117). References cited below can be found beginning on page 128 of Warren et al. (2011).

Understanding the degree to which child characteristics (i.e., specific ASDs 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. However, with rare exceptions,^{259,260,287} few studies are designed or powered to allow analysis of heterogeneous effects. Although we sought studies of treatment modifiers, only one included study^{259,260} actually demonstrated true treatment modifiers based upon appropriate study design and

statistical analysis. One other study²⁸⁷ was designed to examine the role of provider on outcomes, but showed no difference, possibly because it was underpowered to do so.

This first study²⁵⁹ included an analysis of initial characteristics of the children demonstrating that children who were low in initial object exploration benefitted more from RPMT, which explicitly teaches play with objects, while children who were relatively high in initial object exploration demonstrated more benefit from PECS. These results were maintained at 6 months. An additional analysis based on this study²⁶⁰ showed greater increases in generalized turn taking and initiating joint attention in the RPMT group than in PECS. The increased benefit for RPMT in joint attention was only seen, however, in children who began the study with at least some initiation of joint attention. Specifically, children most likely to benefit from RPMT in increasing joint attention had demonstrated at least seven acts of joint attention in the pre-intervention assessment. RPMT was also superior in this analysis in increasing object exchange turns.

One study²⁸⁷ explicitly sought to examine the impact of provider choice (parent versus professional) using similar interventions in an RCT. The study did not show a difference in outcomes for children receiving UCLA/Lovaas protocol-based intervention in a clinical setting versus at home from highly trained parents. Both clinic and parent groups received over 30 hours of intervention weekly and no group differences related to IQ, language, adaptive behavior, or other outcomes were seen. Children in both groups demonstrated substantial gains in a number of areas. Nonetheless, the results do provide further evidence of response to treatments anchored in the UCLA/Lovaas method, with some children demonstrating rapid acquisitions of new skills and change in IQ. Other studies not specifically designed to examine modifiers have also compared parent to clinic-based interventions^{126,132,288} and demonstrated equivalent group change when delivered in the same intensity.

Other 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.

In terms of correlates with positive outcomes, several investigations have noted that pretreatment IQ and language predicts IQ at followup in early intensive behavioral and developmental studies.^{101,104,115,124,287} However, other studies have suggested having a lower IQ at initiation of treatment is related to increased change in IQ over time¹²⁷ or failed to find a relationship between IQ and change in response to intervention.^{102,126,132} IQ and verbal ability also predict treatment outcomes in educational interventions. Baseline language/communication skills may also correlate with treatment success, with studies generally suggesting a benefit for communication skills, including changes in ASDs classification associated with baseline language skills in an UCLA/Lovaas-based approach.^{102,124} Similarly, social skills studies have found verbal skills, either verbal comprehension (using the Verbal Comprehension Index) or expressive communication skills to be associated with greater improvements in social skills.

Data on the degree to which earlier age of treatment initiation is associated with better outcomes with early intensive behavioral and developmental intervention is conflicting. Studies suggesting a preference for early intervention may be confounded by characteristics of treatment.¹²⁹

Finally, some studies suggest that specific constellations of symptoms related to ASDs may be important in understanding response to treatment. Social responsiveness and imitation skills have been suggested as skills that may predict improved treatment response in UCLA/Lovaas treatment,²⁸⁷ whereas “aloof” subtypes of ASDs have been suggested to be associated with less robust changes in IQ,¹⁰⁷ and lower baseline symptom tallies have also been related to specific gains.¹⁰⁴ Other studies have seen specific improvement in early intensive intervention for children with PDD-NOS vs. Autistic Disorder diagnoses,¹¹⁴ which may be indicative of baseline symptom differences. However, many other studies have failed to find a relationship between autism symptoms and treatment response (Warren et al., 2011, p. 115-117).

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

*The information below is directly excerpted from the Warren et al. report (2011, p. 117).
References cited below can be found beginning on page 128 of Warren et al. (2011).*

Information about early response to treatment, or lack thereof, could guide treatment selection, implementation, and modification. The reviewed literature offers almost no information about what specific observations of children might be made early in treatment to predict long-term outcome and response. Some evidence suggests that changes in IQ over the first year of treatment with UCLA/Lovaas-based approaches and ESDM predicts, or accounts for, longer-term change in IQ.^{287,290} However, findings also suggest that while gains in the cognitive domain might be accounted for primarily within the first year of treatment, changes in adaptive behavior in response to these same interventions may occur over a longer time frame^{110,133,287,290} if they occur at all¹⁰⁵.

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

*The information below is directly excerpted from the Warren et al. report (2011, p. 117).
References cited below can be found beginning on page 128 of Warren et al. (2011).*

Few studies assess end of treatment effects that may predict outcomes; however, this type of research is feasible as exemplified in one study which assessed language development and joint attention and play skills in 3 to 4 year old children with ASDs.^{155,156} Children in the symbolic play and joint attention intervention 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.

The investigators also assessed differences in the amount (total hours) of intervention services (speech and overall) children in the three groups received post-intervention, with children in the control group receiving significantly more hours of overall services than either the joint attention or symbolic play groups ($p < .05$ and $< .01$, respectively); differences in hours of speech interventions received were not significant. Only the duration of child-initiated joint attention episodes was related to hours of intervention received post-treatment, with children with fewer hours of overall services showing greater growth in child-initiated joint attention episodes.¹⁵⁵ Hours of speech interventions received did not affect growth in skills.

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

The information below is directly excerpted from the Warren et al. report (2011, p. 118).

Few studies included in this review explicitly measured generalization of effects seen in treatment conditions to either different conditions or locations. The majority of studies in the behavioral interventions targeting associated conditions did not measure outcomes in the treatment context (i.e., within therapy sessions or groups). Outcomes were primarily assessed using parent, self, and/or teacher report of targeted symptoms (e.g., anxiety, externalizing behaviors) at home, at school, and in the community, suggesting that those interventions conducted in a clinical setting for which measured outcomes were positive may generalize in the sense that they achieve outcomes in the daily context/life

of the child. On the other hand, 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. What evidence supports specific components of treatment as driving outcomes, either within a single treatment or across treatments?

The information below is directly excerpted from the Warren et al. report (2011, p. 118).

We identified no studies answering this question.

KQ7. What evidence supports the use of a specific treatment approach in children under the age of two who are at high risk of developing autism based upon behavioral, medical, or genetic risk factors?

The information below is directly excerpted from the Warren et al. report (2011, p. 118).

References cited below can be found beginning on page 128 of Warren et al. (2011).

Research on very young children is preliminary but promising, with only four studies identified in our review.^{178,290,294,295} One was a good quality RCT²⁹⁰ that suggested benefit for the use of ESDM in young children with improvements in adaptive behavior, language, and cognitive outcomes. Diagnostic shifts were also seen in close to 30 percent of children (but still on the autism spectrum). The observed diagnostic shifts, however, were not associated with clinically significant improvements in terms of ADOS severity scores or other measures. Developing interventions directed to toddlers that take into account the diagnostic uncertainty at this age is a critical need. Therefore, we considered the strength of evidence in this area currently insufficient, pending additional data.

Guidelines

The search for clinical practice guidelines identified four guidelines (American Academy of Pediatrics, 2007; National Autism Center, 2009; New Zealand Guideline Group, 2008; SIGN, 2007). The included guidelines are summarized below and described in more detail in Appendix A. The quality assessment of the included guidelines is available in Appendix B.

Summary of Guidelines and Quality Assessment

American Academy of Pediatrics

The American Academy of Pediatrics (AAP) released a guideline (poor quality) in 2007 titled *Management of Children with Autism Spectrum Disorders* (Myers, 2007). The focus of the guideline is to “assist pediatricians in educating families and guiding them toward empirically supported interventions for their children” (Myers, 2007, p. 1162). Myers and colleagues reviewed the primary educational strategies and associated therapies in the treatment of children with ASD (2007).

The AAP guideline does not provide specific recommendations for the use of ABA but it does state that “the effectiveness of ABA-based intervention in ASDs has been well documented through five decades of research by using single-subject methodology and in controlled studies of comprehensive early intensive behavioral intervention programs in university and

community settings” (Myers, 2007, p. 1154). Myers (2007) also states that “there is empirical support for the use of certain educational strategies, particularly those based on ABA, across all age groups” (p. 1166), and that children receiving EIBI have been shown to make substantial and sustained gains in IQ, language, academic performance, and adaptive behavior as well as some measures of social behavior.

The AAP guideline describes developmental models (including the Denver model) as interventions based on the use of developmental theory to organize hypotheses regarding the fundamental nature of ASDs, which can assist in designing approaches that address deficits. Improvements in cognitive, motor, play, and social skills have been demonstrated according to the several studies on the Denver model, however, controlled trials are lacking. Early intervention relationship-focused models covered in the AAP guideline include the DIR model, RDI, and the RT curriculum. The published evidence for the efficacy of the DIR model is limited and has significant methodologic flaws. The AAP guideline considers the evidence to be anecdotal for RDI and only one study without a control group reported beneficial effects of RT on young children with ASDs or other developmental disabilities.

Speech and language therapy includes a variety of approaches including naturalistic and didactic behavioral methods³. The AAP guideline states that developmental-pragmatic approaches⁴ have some empirical support (Myers, 2007, p. 1165) such as Social Communication Emotional Regulation Transactional Support, Denver Model, RDI, and Hanen model. The guideline further recommends that treatment by a speech-language pathologist is usually appropriate. Myers states that “speech-language pathologists are likely to be most effective when they train and work in close collaboration with teachers, support personnel, families, and the child’s peers to promote functional communication in the natural settings throughout the day” (2007, P. 1154). In addition, augmentative and alternative communication modalities are often effective in enhancing communication. The Picture Exchange Communication System (PECS), which incorporates ABA principles, is discussed as one widely used communication model (Myers, 2007). Although published evidence for voice-output is lacking, the AAP guideline states that some nonverbal people may benefit.

In addition to speech-language pathologists, occupational therapy may be used to promote development of self-care skills, academic skills, and play skills. However, the evidence for the efficacy of occupational therapy is currently lacking.

Finally, Myers states that “there is some objective evidence to support traditional and newer naturalistic behavioral strategies and other approaches to teaching social skills” (2007, p. 1165).

³ e.g., DTT, verbal behavior, natural language paradigm, pivotal response training, milieu teaching

⁴ e.g., Social Communication Emotional Regulation Transactional Support, Denver model, RDI, Hanen model

Specifically, “joint attention training may be especially beneficial in young, preverbal children with ASDs, because joint attention behaviors precede and predict social language development” (Myers, 2007, p. 1165). Myers notes that there is primarily descriptive and anecdotal literature for social skills curriculum, including social skills groups, social stories, visual cueing, social games, video modeling, scripts, peer-mediated techniques, and play and leisure (2007, p. 1166).

National Autism Center

The National Autism Center (NAC) released a report in 2009 titled the *National Standards Project*, and is directed towards parents, caregivers, educators, and service providers who make ASD treatment decisions (NAC, 2009). The *National Standards Project* main goals include: (1) describing the strength of evidence around educational and behavioral treatments for ASD; (2) providing the age, diagnosis, and skills/behaviors associated with treatment options; (3) identifying the limitations of the evidence for treatments of ASD; and (4) providing guidance for integrating evidence-based practice into ASD treatment (NAC, 2009). The guideline groups interventions into treatment categories. The categories represent treatments that are substantially similar or have the same core characteristics. It was difficult to know exactly which interventions were included in some of the categories. The strength of the evidence was rated by the NAC as established, emerging, unestablished, or ineffective/harmful (See Appendix A for a full definition). The NAC guideline was rated as poor quality and does not give specific recommendations for interventions or treatment categories.

The recommendations from the NAC guideline are listed below by the strength of the evidence and grouped interventions as they are presented in the National Standards Project report (NAC, 2009).

Established Treatments – NAC found 9 treatments (only including relevant interventions in this report) that are considered established and states that “there is compelling scientific evidence to show these treatments are effective; however, even among established treatments, universal improvements cannot be expected to occur for all individuals on the autism spectrum” (NAC, 2009, p. 43). The following treatments are identified as established: antecedent package, behavioral package, comprehensive behavioral treatment for young children, joint attention intervention, modeling, naturalistic teaching strategies, peer training package, PRT, and schedules. The NAC guideline (2009) states that “despite the fact that these established treatments have been shown to be effective in studies, we know that they will not be effective for all individuals on the autism spectrum.” In addition to established treatments, the NAC (2009) recommends a number of other interventions based on an emerging evidence base.

Emerging Treatments – The NAC guideline identified 10 emerging treatments (relevant to this report) which suggest that the studies may produce favorable outcomes but more high quality research is needed. The following treatments relevant to this report that are considered emerging include: augmentative and alternative communication device, CBT, DRT, imitation-based interventions, initiation training, language training (production), language training (production and understanding), picture exchange communication system, social communication intervention, and social skills package.

New Zealand Guideline Group

The *New Zealand Autism Spectrum Disorder Guideline*, published by the New Zealand Guidelines Group (NZGG) in 2008, provides a best evidence summary targeted at primary care providers, educational professionals, policy makers, funders, parents, carers, specialists, and others who make treatment decisions regarding individuals with ASD (NZGG, 2008). The NZGG guideline conducted a systematic review of the evidence. The guideline specifically discusses the evidence surrounding the identification and diagnosis of ASD, continuing assessments, and access to services and treatments for individuals with ASD, and is rated as fair quality. One of the main reasons for the fair quality rating was the lack of a direct link between the ABA-based recommendations and the evidence.

The full NZGG guideline (2008) provides a descriptive narrative of ABA therapy and the different interventions that fall under ABA. A supplementary evidence guideline on ABA therapies was published in 2010 (NZGG, 2010). The Guideline Supplementary Paper on ABA underwent additional review work after the primary ASD guideline was published. An additional search for high level secondary evidence (systematic reviews) published between December 2007 – August 2009 was undertaken. Ten systematic reviews reporting on ABA-based interventions met inclusion criteria and the methodological quality of the reviews was rated. Four of the reviews were rated as “very good” quality. Two of the “very good” quality reviews stated that there was insufficient evidence to draw any conclusions. Four more reviews were rated as “good” quality and two were rated as “fair” quality. The systematic reviews contained limited information about the included primary studies.

In addition to the evidence review, a consortium of experts was formed in addition to the NZ guidelines group. The two groups convened a two day meeting to review the evidence, make recommendations, and assign a grade to those recommendations. The Supplementary guideline recommendations do not have direct links to the evidence. However, a summary of the evidence and tables of evidence are provided in a separate document. The recommendations from the 2010 supplementary paper on ABA are listed below.

- Behavior management techniques should be used to intervene with problem behaviors following functional behavior assessment (Grade A: There are a number of studies that are valid, applicable and relevant).
- Interventions and strategies based on applied behavior analysis (ABA) principles should be considered for all children with ASD (Grade A). The guideline states that there is a lack of knowledge about the suitability of ABA for persons with an Asperger Syndrome diagnosis, and for participants aged 15 years or above.
- Early intensive behavioral intervention (EIBI) should be considered as a treatment of value for young children with ASD to improve outcomes such as cognitive ability, language skills, and adaptive behavior (Grade B: Based on studies that are mostly valid, but have concerns about volume, consistency, applicability or relevance). There is substantial individual variability in outcomes ranging from very positive improvements, through minor or minimal improvements, to no effects. Regular monitoring and evaluation of intervention effectiveness is crucial.

Cognitive behavioral therapy is also discussed in the full NZ guideline (2008). Due to the nature of ASD, the NZ guideline (2008) recommends that a counselor or therapist be carefully selected and have a general understanding of ASD and effective approaches in working with individuals of ASD. Specifically, the NZ guideline recommends (p. 139):

- Cognitive behavior therapy should be considered as a suitable treatment for many behavioral, emotional and mental health difficulties (Grade C: Expert opinion only).
- Cognitive behavioral therapist should adapt their techniques to take into account the characteristics of people with ASD (Grade C).

Scottish Intercollegiate Guidelines Network (SIGN)

The Scottish Intercollegiate Guidelines Network (SIGN) published *Assessment, Diagnosis and Clinical Interventions for Children and Young People with Autism Spectrum Disorders: A National Clinical Guideline* in 2007 to provide an evidence base and give recommendations for the assessment and clinical treatment of ASD. The guideline includes discussion on how multiple disciplines and multiple agencies and how they can work together to best meet the needs of individuals with ASD at all levels of care (SIGN, 2007). The guideline was rated as good quality.

The SIGN guideline recommends that behavioral interventions (interventions for specific behaviors was based on one systematic review, which included 251 studies on focal treatments) should be considered to address a wide range of specific behaviors in children and young people with ASD (level of recommendation: B) and states that the Lovaas program

should not be presented as an intervention that will lead to normal functioning (level of recommendation: A). Recommendations for interventions to support communication in ASD such as the use of visual augmentation are indicated (SIGN, 2007, p. 16) (level of recommendation: D) and the consideration of parent mediated intervention programs is recommended as a good practice point.

Interventions to support social communication should be considered for children and young people with ASD, and specific interventions for individuals should be assessed on an individual basis (SIGN, 2007, p. 17) (level of recommendation: D).

SIGN notes (not a specific recommendation) that cognitive behavioral therapy (CBT) “has been shown to be feasible in children with ASD who have a verbal IQ of at least 69” (2007, p.18) and recommends, as a good practice point, that professionals be aware that some interventions require a level of verbal and cognitive development. The SIGN guideline was unable to draw any reliable conclusions for CBT based on a review of the evidence.

Policy Considerations

As directed by the Washington HTA program, the policies for Medicare, Blue Cross Blue Shield, Aetna, GroupHealth and state insurance mandates were reviewed. Summaries of identified policies are provided below. Please see Appendices C and D, respectively, for more detail.

Medicare National Coverage Decision

No Medicare National Coverage Determinations for the treatment of ASD were identified.

Private Payors

Blue Cross Blue Shield (BCBS)

No national coverage policies were identified. Coverage determinations are made on a per-state basis. For example, BCBS of Michigan offers coverage for autism treatment programs that provide intensive early interventions, including ABA. Children, aged two to five years old, have coverage of up to 60 treatment sessions. Coverage of ABA is only available for purchase by consumer groups that already have outpatient mental health coverage (BCBS of Michigan, 2009).

Aetna

Aetna’s Clinical Policy Bulletin *Pervasive Developmental Disorders* includes coverage of the assessment and treatment of autism for members who meet any of the following criteria:

- Any loss of language or social skills at any age; *or*
- No 2-word spontaneous (not just echolalic) phrases by 24 months; *or*
- No babbling by 12 months; *or*
- No gesturing (e.g., pointing, waving bye-bye) by 12 months; *or*
- No single words by 16 months.

Intensive educational interventions that include a systematic plan and developmentally appropriate activities may be included in the assessment and treatment of autism. However, the policy specifically notes that “there is insufficient evidence for the superiority of any particular intensive educational intervention strategy (such as applied behavioral analysis, structured teaching, or developmental models) over other intensive educational intervention strategies” (Aetna, 2011).

GroupHealth

GroupHealth does not cover applied behavioral analysis therapy or early intensive behavioral interventions for young children with autism based on insufficient evidence (GroupHealth, 2010).

State Mandates

The majority of US states (27 states) currently mandate insurance coverage of autism, and 15 other states, as of May 9, 2011 have pending legislation that would require the coverage of autism. Current state mandates for the coverage of autism differ substantially based on age limits, maximum benefit limits, covered services, and whether coverage mandates apply to all insurers or only state regulated insurance plans. The range of coverage specifications are listed by category below.

Age limits

The age limits for state mandates of autism coverage differ significantly. Four states (FL, ME, VT, VA, TX) limit coverage to children five to six years or younger. Five states set coverage limits for children aged up to 10 through 17 years (AZ, CT, LA, SC, TX). Five states limit coverage to children aged 18 years or younger (AR, MO, MT, NV, WV). Three states restrict coverage to children at 19 years old (CO, KS, NM), and seven states set 21 years old as the limit on coverage mandates (IA, IL, KY, NH, NJ, OK, PA). Additionally, two states extend coverage to individuals aged 22 years old if they are enrolled in high school (NM, NV). Many of the age limits are further segmented into age groups as maximum benefits limits in many states are differentiated by age (see below).

Benefit limits

There are four types of benefit limits included in current state mandates: overall maximum benefit amounts per year, lifetime maximum benefit amounts, a specific to ABA maximum benefit amount per year, and a lifetime maximum benefit amount specific to ABA. Maximum overall benefit amounts in coverage mandates range from \$36,000 to \$75,000 per year with most coverage mandates explicating stating that the limits include ABA therapy. The overall maximum benefits are also commonly broken down by age, with the overall benefit maximum for older children (age 7 to 12 and older) ranging from \$12,000 to \$27,000 per year. Lifetime maximum benefit amounts range from \$125,000 to \$200,000. Coverage limits specific to ABA therapy range from \$30,000 to \$50,000 per year, with one state (FL) having a lifetime maximum benefit for ABA therapy of \$108,000. Similar to overall benefit limits, ABA specific benefit amounts are also commonly broken down by age, with the benefit maximum for older children (age nine and older) between \$12,000 and \$35,000 per year.

Included services

Almost all state coverage mandates include coverage for the diagnosis and treatment of autism for individuals with ASD. Additionally, states mandate coverage for assessment (CO), screening (OK), and ABA therapy (AR, CO, CT, FL, IA, IL, KS, KY, LA, MA, ME, MO, MT, NH, NJ, NM, NV, OK, PA, SC, TX, VA, VT, WV).

State mandate application

States have the option to limit coverage mandates to specific entities. In eight states (AR, KY, ME, MO, NH, NJ, VA, VT) coverage mandates for the diagnosis and treatment of autism only apply to state regulated insurance plans, and not self-funded insurance plans. Two states (IA, KS) only mandate state employee health care plans to cover the diagnosis and treatment of autism.

Licensure of ABA providers

Many states do not have minimum educational or practical experience requirements for providing ABA interventions. The Behavioral Analysis Certification Board (BACB) was established in 1998 to meet professional credentialing needs established by stakeholders (BACB, 2010). However, due to the increased volume of individuals practicing ABA, organizations such as the Association for Behavioral Analysis International (ABAI) are calling for states to adopt licensure for applied behavioral analyst practitioners (Weinberg, 2008). In response, a small number of states have included the creation of an ABA Licensure Board in coverage mandates, and a few states have limited reimbursement to only licensed behavioral analysts in the treatment of ASD.

Summary

General conclusions

The evidence from Warren et al. (2011) suggests that early intensive behavioral and developmental intervention (EIBDI) may improve core areas of deficit for individuals with ASDs; however, RCTs are few and include small numbers of participants. Within this category, studies of UCLA/Lovaas-based interventions report greater improvements in cognitive performance, language skills, and adaptive behavior skills than other broadly defined treatments. However, strength of evidence is currently low. In addition, the consistency of benefit is lacking, in that not all children demonstrate rapid gains, and many children continue to display substantial impairment. Although positive results are reported for the effects of intensive interventions that use a developmental framework, such as ESDM, evidence for this type of intervention is currently insufficient because few studies have been published to date.

Less intensive interventions focusing on providing parent training for bolstering social communication skills and managing challenging behaviors have also been studied. Some interventions have shown short-term gains in social communication and language use, but the current evidence base for such treatment remains insufficient.

Although all of the studies of social skills interventions reported some positive results, most have not included objective observations of the generalizability and the maintenance of the improvements. Strength of evidence is considered insufficient for social skills training and play-

and interaction-based approaches. Several studies suggest that interventions based on cognitive behavioral therapy are effective in reducing anxiety symptoms, but replication of results is needed. Strength of evidence for these interventions is currently insufficient.

Warren et al. (2011) encourages investigators to provide adequate detail as they describe their interventions to allow for replicable research. Ideally, investigators publish the treatment manuals they develop, which are then referenced in later research. However, many studies make general references to their use of an underlying approach (e.g., ABA) without specifying the ways in which they used or modified the technique. Lack of detail about the intervention makes it difficult to assess the applicability of individual studies, to synthesize groups of studies, or to replicate studies (Warren et al., 2011).

Two guidelines (NZ 2010; SIGN 2007) make recommendations on ABA and interventions based on ABA principles. The SIGN guideline states that the Lovaas program should not be presented as an intervention that will lead to normal functioning, and that behavioral interventions should be considered in young people with ASD. The NZ guideline recommends that interventions based on ABA should be considered for all children with ASD. The guideline states that there is a lack of knowledge about the suitability of ABA for persons with Asperger Syndrome and those 15 years or older. The NZ guideline also recommends the use of EIBI in young children with ASD but states that regular monitoring for the evaluation of effectiveness is crucial. The NAC (2009) and AAP (2007) guidelines summarize the evidence and do not make specific recommendations.

Three guidelines (NZGG, 2008; SIGN, 2007; NAC, 2009) addressed CBT. All three guidelines state that CBT can be a therapy option. The SIGN guideline (based on a systematic review of the evidence) was unable to draw conclusions about the effectiveness of CBT. The SIGN guideline recommends that professionals should be aware that some of these interventions require a level of verbal and cognitive development. Other interventions addressed in this report were not covered by the included guidelines, were not supported by the evidence, or were grouped into broad categories making it difficult to draw conclusions about the individual interventions.

Federal, state and private payor policies are not consistent in mandating coverage of ABA therapy for the treatment of ASD. Of the federal and private payor policies reviewed, Aetna is the only payor to cover intensive educational interventions and explicitly mentions that there is insufficient evidence regarding the superiority of any specific intervention, such as ABA. An increasing number of states have coverage mandates for the diagnosis and treatment of ASD. Mandate components, such as included treatments, age restrictions, and maximum benefit limits vary significantly between states. With a lack of standardized educational and/or practical requirements for ABA providers, a small number of states have included ABA Licensure Boards in their state coverage mandates.

Limitations of the evidence

- There are very few well-controlled trials for ASD treatments based in ABA theory.
- Most studies report on short-term outcomes and the degree to which those outcomes translate to functional outcomes over time is largely unknown.

- The range of treatment approaches evaluated in the literature may not match those that are available in practice, and the highly controlled treatment environments may not translate to outcomes that can be achieved in the community.
- Fidelity to treatment in the community may be limited, particularly for those interventions that are not manualized.
- Of the published trials, many have small sample sizes, different treatment approaches, varying durations of treatment, different follow-up times and outcome measures, and cover a variety of treatment intensities.
- It is difficult to compare data between studies and to make inferences for the general population due to the heterogeneity of study designs.
- Many observational studies and non-controlled studies lack a description of study methods and a detailed description of applied interventions.
- It difficult to identify subpopulations of children with ASD who might better respond to treatments based in ABA theory, based on current evidence.

Appendix A. Guideline Summary Table – Applied Behavioral Analysis for the Treatment of Autism Spectrum Disorder

Guideline and Quality	Guideline Text	*Guideline Grading System
Autism Spectrum Disorder		
<p>American Academy of Pediatrics (2007 – reaffirmed 2010) – Management of Children with Autism Spectrum Disorders</p> <p>Quality: Poor Evidence cited: evidence cited, but methods unclear</p>	<p>The AAP guideline states in the abstract that the guidance is to assist pediatricians in educating families and guiding them toward empirically supported interventions for their children. The AAP guideline does not provide specific recommendations for the use of ABA. A modified summary of the guidance for ABA is below.</p> <p>Applied Behavior Analysis</p> <p>The effectiveness of ABA-based intervention in ASDs has been well documented through five decades of research by using single-subject methodology and in controlled studies of comprehensive early intensive behavioral intervention programs in university and community settings. Children who receive early intensive behavioral treatment have been shown to make substantial, sustained gains in IQ, language, academic performance, and adaptive behavior as well as some measures of social behavior, and their outcomes have been significantly better than those of children in control groups.</p> <p>Highly structured comprehensive early intervention programs for children with ASDs, such as the Young Autism Project developed by Lovaas at the University of California Los Angeles, rely heavily on discrete trial training (DTT) methodology, but this is only one of many techniques used within the realm of ABA. DTT methods are useful in establishing learning readiness by teaching foundation skills such as attention, compliance, imitation, and discrimination learning, as well as a variety of other skills. However, DTT has been criticized because of problems with generalization of learned behaviors to spontaneous use in natural environments and because the highly structured teaching environment is not representative of natural adult-child interactions. Traditional ABA techniques have been modified to address these issues. Naturalistic behavioral interventions, such as incidental teaching and natural language paradigm/ pivotal response training, may enhance generalization of skills.</p> <p>Functional behavior analysis, or functional assessment, is an important aspect of behaviorally based treatment of unwanted behaviors. Functional assessment is a rigorous, empirically based method of gathering information that can be used to maximize the effectiveness and efficiency of behavioral support interventions. It includes formulating a clear description of the problem behavior (including frequency and intensity); identifying</p>	<p>None</p>

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p>the antecedents, consequences, and other environmental factors that maintain the behavior; developing hypotheses that specify the motivating function of the behavior; and collecting direct observational data to test the hypothesis. Functional analysis also is useful in identifying antecedents and consequences that are associated with increased frequency of desirable behaviors so that they can be used to evoke new adaptive behaviors. (p. 1164)</p> <p>Some model programs provide programming throughout childhood and into adulthood. More commonly, the focus of specialized programs is on early childhood, and published research evaluating comprehensive educational programs for older children and adolescents with ASDs is lacking. However, there is empirical support for the use of certain educational strategies, particularly those that are based on ABA, across all age groups to increase and maintain desirable adaptive behaviors, reduce interfering maladaptive behaviors or narrow the conditions under which they occur, teach new skills, and generalize behaviors to new environments or situations (p. 1166).</p> <p>Developmental Models</p> <p>Developmental models are based on use of developmental theory to organize hypotheses regarding the fundamental nature of ASDs and design approaches to address the deficits. Several studies have demonstrated improvements in cognitive, motor, play, and social skills beyond what would be expected on the basis of initial developmental rates in children who are treated according to the Denver model, but controlled trials are lacking.</p> <p>Relationship-focused early intervention models include Greenspan and Wieder’s developmental, individual-difference, relationship-based (DIR) model and Gutstein and Sheely’s relationship-development intervention (RDI), and responsive-teaching (RT) curriculum developed by Mahoney et al. Published evidence of the efficacy of the DIR model is limited to an unblended review of case records (with significant methodologic flaws, including inadequate documentation of the intervention, comparison to a suboptimal control group, and lack of documentation of treatment integrity and how outcomes were assessed by informal procedures) and a descriptive follow-up study of a small subset (8%) of the original group of patients. Some reviewers have praised the face validity of this model, which targets the core impairment in social reciprocity. However, the evidence of efficacy of RDI is anecdotal; published empirical scientific research is lacking at this time. One study reported beneficial effects of RT on young children with ASDs or other developmental disabilities. Parents were taught to use RT strategies to encourage their children to acquire and use pivotal developmental behaviors (attention, persistence, interest, initiation, cooperation, joint attention, and affect). Children in both groups improved significantly on</p>	

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p>nonstandardized play-based measures of cognition and communication and standardized parent ratings of socioemotional functioning. Although a control group was lacking and the potential role of concurrent educational services was unclear, the improvements were beyond what the authors expected from maturational factors alone.</p> <p>Speech and Language Therapy A variety of approaches have been reported to be effective in producing gains in communication skills in children with ASDs. Didactic and naturalistic behavioral methodologies (e.g., DTT, verbal behavior, natural language paradigm, pivotal response training, milieu teaching) have been studied most thoroughly, but there is also some empirical support for developmental-pragmatic approaches (e.g., Social Communication Emotional Regulation Transactional Support, Denver model, RDI, Hanen model).</p> <p>People with ASDs have deficits in social communication, and treatment by a speech-language pathologist usually is appropriate. Most children with ASDs can develop useful speech, and chronologic age, lack of typical prerequisite skills, failure to benefit from previous language intervention, and lack of discrepancy between language and IQ scores should not exclude a child from receiving speech-language services. However, traditional, low-intensity pull-out service delivery models often are ineffective, and speech-language pathologists are likely to be most effective when they train and work in close collaboration with teachers, support personnel, families, and the child’s peers to promote functional communication in natural settings throughout the day.</p> <p>The use of augmentative and alternative communication modalities, including gestures, sign language, and picture communication programs, often is effective in enhancing communication. (...) Some nonverbal people with ASDs may benefit from the use of voice-output communication aids, but published evidence for these aids is scant. Introduction of augmentative and alternative communication systems to nonverbal children with ASDs does not keep them from learning to talk, and there is some evidence that they may be more stimulated to learn speech if they already understand something about symbolic communication (p. 1165).</p> <p>Social Skills Instruction There is some objective evidence to support traditional and newer naturalistic behavioral strategies and other approaches to teaching social skills. Joint attention training may be especially beneficial in young, preverbal children with ASDs, because joint attention behaviors precede and predict social language development. A recent randomized,</p>	

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p>controlled trial demonstrated that joint attention and symbolic play skills can be taught and that these skills generalize to different settings and people.</p> <p>A social skills curriculum should target responding to the social overtures of other children and adults, initiating social behavior, minimizing stereotyped perseverative behavior while using a flexible and varied repertoire of responses, and self-managing new and established skills. Social skills groups, social stories, visual cueing, social games, video modeling, scripts, peer-mediated techniques, and play and leisure curricula are supported primarily by descriptive and anecdotal literature, but the quantity and quality of research is increasing number of social skills curricula and guidelines are available for use in school programs and at home.</p> <p>Occupational Therapy Occupational therapy may be used to promote development of self-care skills, academic skills, and play skills. However, the evidence for the efficacy of occupational therapy is currently lacking.</p>	
<p>National Autism Center (2009) – <i>The National Standards Project – Addressing the Need for Evidence-based Practice Guidelines for Autism Spectrum Disorders</i></p> <p>Quality: Poor Evidence cited: systematic review</p>	<p>The recommendations from the NAC guideline are listed below as they are presented in the guideline report.</p> <p><i>Comprehensive Behavioral Treatment for Young Children</i> (may also be referred to as ABA programs or behavioral inclusive programs and early intensive behavioral intervention (22 studies). Evidence level: Established.</p> <p><u>Skills increased:</u> communication, higher cognitive functions, interpersonal, motor, personal responsibility, placement, and play</p> <p><u>Behaviors decreased:</u> problem behaviors, general symptoms</p> <p><u>Ages:</u> 0-2, 3-5, 6-9</p> <p><u>Diagnostic Classifications:</u> Autistic disorder, PDD-NOS</p> <p><i>Antecedent Package</i> (includes ABA, behavioral psychology, and positive behavior supports) (99 studies) Evidence level: Established.</p> <p><u>Skills Increased:</u> communication, interpersonal, learning readiness, personal responsibility, play and self-regulation</p> <p><u>Behaviors decreased:</u> problem behaviors, sensory or emotional regulation (SER)</p> <p><u>Ages:</u> 3-5, 6-9, 10-14, and 15-18</p>	<p>Established: Sufficient evidence is available to confidently determine that a treatment produces beneficial treatment effects for individuals on the autism spectrum. That is, these treatments are established as effective.</p> <p><i>(Please see below for full grading system)</i></p>

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p><u>Diagnostic</u> classifications: autistic disorder</p> <p><i>Behavioral Package</i> (treatments in this category reflect research in the fields of ABA, behavioral psychology, and positive behavior supports) (231 studies). Evidence level: Established.</p> <p><u>Skills Increased</u>: academic, communication, interpersonal, learning readiness, personal responsibility, play and self-regulation</p> <p><u>Behaviors decreased</u>: problem behaviors, restricted, repetitive, nonfunctional patterns of behavior, interests, or activity (RRN), sensory or emotional regulation (SER)</p> <p><u>Ages</u>: 0-2, 3-5, 6-9, 10-14, 15-18, and 19-21</p> <p><u>Diagnostic</u> classifications: autistic disorder, PDD-NOS</p> <p><i>Modeling</i> (intervention rely on an adult or peer providing a demonstration of the target behavior) (50 studies). Evidence level: Established.</p> <p><u>Skills Increased</u>: communication, higher cognitive functions, interpersonal, personal responsibility, play</p> <p><u>Behaviors decreased</u>: problem behaviors, SER</p> <p><u>Ages</u>: 3-5, 6-9, 10-14, and 15-18</p> <p><u>Diagnostic</u> classifications: autistic disorder, Aspergers, PDD-NOS</p> <p><i>Naturalistic Teaching Strategies</i> (treatments involve using primarily child-directed interactions to teach functional skills in the natural environment) (32 studies). Evidence level: Established.</p> <p><u>Skills Increased</u>: communication, interpersonal, learning readiness, play</p> <p><u>Behaviors decreased</u>: none</p> <p><u>Ages</u>: 0-2, 3-5, and 6-9</p> <p><u>Diagnostic</u> classifications: autistic disorder, PDD-NOS</p> <p><i>Peer Training Package</i> (treatments in this category involve teaching children without disabilities strategies for facilitating play and social interactions with children on the autism spectrum) (33 studies). Evidence level: Established.</p> <p><u>Skills Increased</u>: communication, interpersonal, and play</p>	

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p><u>Behaviors decreased</u>: RRN <u>Ages</u>: 3-5, 6-9, and 10-14 <u>Diagnostic</u> classifications: autistic disorder, PDD-NOS</p> <p><u>Pivotal Response Treatment</u> (focuses on targeting pivotal behavioral areas) (14 studies). Evidence level: Established. <u>Skills Increased</u>: communication, interpersonal, play <u>Behaviors decreased</u>: none <u>Ages</u>: 3-5, 6-9 <u>Diagnostic</u> classifications: autistic disorder</p> <p><u>Schedules</u> (treatments in this category involve the presentation of the task list that communicates a series of activities or steps required to complete a specific activity) (12 studies). Evidence level: Established. <u>Skills Increased</u>: self-regulation <u>Behaviors decreased</u>: none <u>Ages</u>: 3-5, 6-9, and 10-14 <u>Diagnostic</u> classifications: autistic disorder</p> <p><u>Augmentative and Alternate Communication Device</u> (intervention involve the use of high or low technologically sophisticated devices to facilitate communication.) (14 studies). Evidence level: Emerging. <u>Skills Increased</u>: communication <u>Behaviors decreased</u>: none <u>Ages</u>: 3-5 and 6-9 <u>Diagnostic</u> classifications: autistic disorder</p> <p><u>Joint Attention Intervention</u> (interventions involve building foundation skills involved in regulating the behaviors of others) (6 studies). Evidence level: Established. <u>Skills Increased</u>: communication, interpersonal <u>Behaviors decreased</u>: none <u>Ages</u>: 0-2, 3-5</p>	

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p><u>Diagnostic</u> classifications: autistic disorder, PDD-NOS</p> <p><i>Cognitive Behavioral Package</i> (interventions focus on changing everyday negative or unrealistic thought patterns and behaviors) (3 studies). Evidence level: Emerging.</p> <p><u>Skills Increased</u>: interpersonal</p> <p><u>Behaviors decreased</u>: restricted, repetitive, nonfunctional patterns of behavior, interests, or activity (RRN), sensory or emotional regulation (SER)</p> <p><u>Ages</u>: 6-9, 10-14, and 15-18,</p> <p><u>Diagnostic</u> classifications: autistic disorder, Asperger’s Syndrome <i>Developmental Relationship-based Treatment</i> (treatments involve a combination of procedures that are based on developmental theory and emphasize the importance of building social relationships (e.g. DIR, Denver Model, DRI, RT).) (7 studies). Evidence level: Emerging.</p> <p><u>Skills Increased</u>: communication, higher cognitive functions, interpersonal, play and self-regulation</p> <p><u>Behaviors decreased</u>: sensory or emotional regulation (SER), general symptoms</p> <p><u>Ages</u>: 0-2 and 3-5</p> <p><u>Diagnostic</u> classifications: autistic disorder, PDD-NOS</p> <p><i>Initiation-based Interactions</i> (interventions rely on adults imitating the actions of child) (6 studies). Evidence level: Emerging.</p> <p><u>Skills Increased</u>: interpersonal, learning readiness, play</p> <p><u>Behaviors decreased</u>: none</p> <p><u>Ages</u>: 0-2, 3-5, 6-9, 10-14</p> <p><u>Diagnostic</u> classifications: autistic disorder</p> <p><i>Initiation Training</i> (interventions involve directly teaching individuals with ASD to initiate interactions with their peers) (7 studies). Evidence level: Emerging.</p> <p><u>Skills Increased</u>: higher cognitive function, interpersonal</p> <p><u>Behaviors decreased</u>: problem behaviors, sensory or emotional regulation (SER)</p> <p><u>Ages</u>: 6-9, 10-14</p> <p><u>Diagnostic</u> classifications: autistic disorder, Aspergers syndrome, PDD-NOS</p> <p><i>Language Training (Production)</i> (interventions have as their primary goal to increase both</p>	

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p>speech production and understanding of communicative acts) (7 studies). Evidence level: Emerging.</p> <p><u>Skills Increased:</u> communication <u>Behaviors decreased:</u> none <u>Ages:</u> 3-5, 6-9 <u>Diagnostic classifications:</u> autistic disorder</p> <p><i>Language Training(Production and Understanding)</i> (treatment involves the application of a specific augmentative and alternate communication system based on behavioral principles that are designed to teach functional communication to children with limited verbal and/or communication skills) (13 studies). Evidence level: Emerging.</p> <p><u>Skills Increased:</u> communication, interpersonal <u>Behaviors decreased:</u> none <u>Ages:</u> 0-2, 3-5, 6-9 <u>Diagnostic classifications:</u> autistic disorder, PDD_NOS</p> <p><i>Picture Exchange</i> (interventions have as their primary goal to increase speech production) (13 studies). Evidence level: Emerging.</p> <p><u>Skills Increased:</u> communication, interpersonal, play <u>Behaviors decreased:</u> none <u>Ages:</u> 0-2, 3-5, 6-9 <u>Diagnostic classifications:</u> autistic disorder</p> <p><i>Social Communication Interventions</i> (interventions involve targeting some combination of social communication impairments such as pragmatic communication skills, and the inability to successfully read social situations.) (5 studies). Evidence level: Emerging.</p> <p><u>Skills Increased:</u> communication, interpersonal, motor, personal responsibility <u>Behaviors decreased:</u> none <u>Ages:</u> 0-2, 3-5 <u>Diagnostic classifications:</u> autistic disorder</p> <p><i>Social Skills Package</i> (interventions designed to build social interaction skills in children with ASD by targeting basic and complex social skills) (16 studies). Evidence level: Emerging.</p>	

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p><u>Skills Increased</u>: interpersonal</p> <p><u>Behaviors decreased</u>: none</p> <p><u>Ages</u>: 3-5, 6-9, 10-14, and 15-18</p> <p><u>Diagnostic</u> classifications: autistic disorder, Asperger’s Syndrome, and PDD-NOS</p>	
<p>New Zealand (2008) – <i>New Zealand Autism Spectrum Disorder Guideline.</i></p> <p>Quality: Fair Evidence cited: Systematic review</p> <p>New Zealand (2010) – <i>New Zealand Autism Spectrum Disorder Guideline. Supplementary Evidence on Applied Behavior Analysis</i></p> <p>Quality: See full 2008 guideline Evidence cited: Systematic review</p>	<p>The full NZ guideline (2008) provides a descriptive narrative of ABA therapy and the different interventions that fall under ABA. A supplementary evidence guideline on ABA therapies was published in 2010. The recommendations from the 2010 supplementary paper on ABA are listed below. The recommendations below are from the 2010 supplementary paper on ABA.</p> <ul style="list-style-type: none"> • Behavior management techniques should be used to intervene with problem behaviors <u>following functional behavior assessment</u> (Recommendation 4.3.4) (Grade A). • Consumers of <u>applied</u> behavior analysis interventions should refer to recently published guidelines for identifying, selecting and evaluating behavior analyst services for people with ASD (Recommendation 4.3.6) (Grade C). • Interventions and strategies based on applied behavior analysis (ABA) principles should be considered for all children with ASD (Grade A). <p>Additional text: There is a lack of knowledge about the suitability of ABA for persons with an Asperger Syndrome diagnosis, and for participants aged 15 years or above.</p> <ul style="list-style-type: none"> • Early intensive behavioral intervention (EIBI) should be considered as a treatment of value for young children with ASD to improve outcomes such as cognitive ability, language skills, and adaptive behavior (Grade B). <p>Additional text: There is substantial individual variability in outcomes ranging from very positive improvements, through minor or minimal improvements, to no effects. Families need to be advised of this conditional evidence about treatment outcomes. We still cannot specify which attributes of participants, families, treatment methods etc., are critical to outcome, apart from findings that higher IQ and language competence in individuals at the pre-treatment stage are predictive to some extent of greater gains post treatment, and at longer follow up.</p> <p>Regular monitoring and evaluation of intervention effectiveness is crucial (refer to</p>	<p>Grade A: The recommendation is supported by GOOD evidence (where there is a number of studies that are valid, applicable and clinically relevant)</p> <p>Grade B: The recommendation is supported by FAIR evidence (based on studies that are mostly valid, but there are some concerns about the volume, consistency, applicability and/or clinical relevance of the evidence that may cause some uncertainty, but are not likely to be overturned by other evidence).</p> <p>Grade C: The recommendation is supported by EXPERT OPINION only (from external opinion, published or unpublished, e.g., consensus guidelines).</p> <p>Good practice point: Where a recommendation is based on the clinical and educational experiences of members of the guideline development teams, this is referred</p>

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p>recommendation 3.1.5 and 4.3.03).</p> <ul style="list-style-type: none"> • Cognitive behavior therapy should be considered as a suitable treatment for many behavioral, emotional and mental health difficulties (Recommendation 4.3.9) (Grade C). • Cognitive behavior therapists should adapt their techniques to take into account the characteristics of people with ASD (Recommendations 4.3.10) (Grade C). <p><u>Good practice points:</u></p> <ul style="list-style-type: none"> • ABA interventions and strategies should be relevant to the child's context and culture • Interventions based on the principles of ABA can be introduced before the diagnosis of ASD is confirmed in a child displaying some of the symptoms of ASD. <i>“Services should not wait for the diagnostic process to be completed but should be available as soon as a significant developmental need is identified.” (Grade C)</i> 	<p>to as a good practice point.</p>
<p>SIGN (2007) – <i>Assessment, diagnosis, and clinical interventions for children and young people with autism spectrum disorder: A national clinical guideline.</i></p> <p>Quality: Good Evidence cited: systematic review</p>	<ul style="list-style-type: none"> • The Lovaas program should not be presented as an intervention that will lead to normal functioning (Recommendation 5.3.1) (Level of recommendation: A). • Behavioral interventions should be considered to address a wide range of specific behaviors in children and young people with ASD, both to reduce symptom frequency and severity and to increase the development of adaptive skills (Recommendation 5.3.2) (Level of recommendation: B). • Parent mediated intervention programs should be considered for children and young people of all ages, who are affected by ASD, as they may help families interact with their child, promote development and increase parental satisfaction, empowerment and mental health (Section 5.1) (Good Practice Point). • Interventions to support communication in ASD are indicated, such as the use of visual augmentation, e.g., in the form of pictures of objects (Section 5.2.1) (Level of recommendation D). • Interventions to support communication in children and young people with ASD should be informed by effective assessment (Section 5.2.1) (Good Practice Point) • Interventions to support social communication should be considered for children and young people with ASD, with the most appropriate intervention being assessed 	<p>Grade A: At least one meta-analysis, systematic review, or RCT rated as 1++ (high quality MA, SR, or RCT with very low risk of bias), and directly applicable to the target population, or</p> <p>A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results</p>

Guideline and Quality	Guideline Text	*Guideline Grading System
	<p>an individual basis (Section 5.2.2) (Level of recommendation: D).</p> <ul style="list-style-type: none"> • Adapting the communicative, social and physical environments of children and young people with ASD may be of benefit (options include providing visual prompts, reducing requirements for complex social interactions, using routine, timetabling and prompting and minimizing sensory irritations) (Section 5.2.2) (Good Practice Point). • Professionals should be aware that some interventions require a level of verbal and cognitive development which precludes their employment with some groups of children and young people with ASD (Section 5.5) (Good Practice Point). Based on a systematic review of the evidence, conclusions about effectiveness and potential harms of CBT cannot be drawn. CBT has been shown to be feasible in children with ASD who have a verbal IQ of at least 69. <p><i>A comprehensive literature search, did not find any good quality evidence for other intensive behavioral interventions.</i></p>	

Note: The National Institute for Clinical Excellence (NICE) expects the publication of the following guidelines within the next year:

- Autism Spectrum disorders in Children and Young people (expected publication 9/2011) [focus on recognition, referral and diagnosis]
- Autism – Management of Autism in Children and Young People (expected publication 11/2011)
- Autistic Spectrum Conditions in Adults (expected publication 6/2012)

***Individual Guideline Rating Keys**

National Autism Center

Established: Sufficient evidence is available to confidently determine that a treatment produces beneficial treatment effects for individuals on the autism spectrum. That is, these treatments are established as effective.

Emerging: Although one or more studies suggests that a treatment produces beneficial treatment effects for individuals with ASD, additional high quality studies must consistently show this outcome before we can draw firm conclusions about treatment effectiveness.

Unestablished: There is little or no evidence to allow us to draw firm conclusions about treatment effectiveness with individuals with ASD. Additional research may show the treatment to be effective, ineffective or harmful.

Ineffective/Harmful: Sufficient evidence is available to determine that a treatment is ineffective or harmful for individuals on the autism spectrum.

New Zealand Guidelines Group

Recommendations

Grade A: The recommendation is supported by GOOD evidence (where there are a number of studies that are valid, applicable and clinically relevant).

Grade B: The recommendation is supported by FAIR evidence (based on studies that are mostly valid, but there are some concerns about the volume, consistency, applicability and/or clinical relevance of the evidence that may cause some uncertainty, but are not likely to be overturned by other evidence).

Grade C: The recommendation is supported by EXPERT OPINION only (from external opinion, published or unpublished, e.g., consensus guidelines).

Good Practice Point (GPP): Where no evidence is available, best practice recommendations are made based on the experience of the Guideline Development Team, or feedback from consultation within New Zealand.

SIGN

Levels of Evidence

1++ High quality meta-analyses, systematic reviews or RCTs, or RCTs with a very low risk of bias

1+ Well conducted meta-analyses, systematic reviews or RCTs with a low risk of bias

1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++ High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+ Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2- Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is causal

3 Non-analytic studies, e.g., case reports, case series

4 Expert opinion

Grades of Recommendations

Grade A: At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population, or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results, or Extrapolated evidence from studies rated as 1++ or 1+

Grade C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, or Extrapolated evidence from studies rated as 2++

Grade D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+.

Good Practice Points: recommended best practice based on the clinical experience of the guideline development group.

Appendix B. Quality Assessment of Selected Guidelines

Key Recommendations	Guideline Developer, Year			
	AAP, 2007 (reaffirmed 2010)	NAC, 2009	NZGG, 2008 w/ 2010 supplement on ABA	SIGN, 2007
Section 1: Primary Criteria				
Rigor of Development: Evidence	Poor	Poor	Good	Good
Rigor of Development: Recommendations	Poor	Poor	Fair	Good
Editorial Independence	Poor	Poor	Fair	Good
Section 2: Secondary Criteria				
Scope and Purpose	Fair	Fair	Good	Good
Stakeholder Involvement	Fair	Fair	Good	Good
Clarity and Presentation	Poor	Poor	Fair	Good
Applicability	Poor	Poor	Fair	Good
Section 3: Overall Assessment of the Guideline				
How well done is this guideline?	Poor	Poor	Fair	Good

Appendix C. Summary of Federal and Private Payor Policies on the Treatment of Autism Spectrum Disorder

Payor	Coverage summary
Medicare	<i>No National Coverage Determinations identified.</i>
Aetna	<p data-bbox="474 375 1335 399"><u>Aetna Clinical Policy Bulletin Number 0648: Pervasive Developmental Disorders</u></p> <ol data-bbox="527 435 1871 678" style="list-style-type: none"> 1. Aetna considers certain procedures and services medically necessary for assessment and treatment of autism and other pervasive developmental disorders (PDD) when the member meets any of the criteria listed below: <ol data-bbox="621 524 1415 678" style="list-style-type: none"> 1. Any loss of any language or social skills at any age; <i>or</i> 2. No 2-word spontaneous (not just echolalic) phrases by 24 months; <i>or</i> 3. No babbling by 12 months; <i>or</i> 4. No gesturing (e.g., pointing, waving bye-bye) by 12 months; <i>or</i> 5. No single words by 16 months. <p data-bbox="474 719 1562 743">The following services may be included in the assessment and treatment of the member’s condition:</p> <p data-bbox="621 751 716 776">[1. – 18.]</p> <ol data-bbox="621 784 1881 873" style="list-style-type: none"> 19. Intensive educational interventions in which the child is engaged in systematically planned and developmentally appropriate educational activity toward identified objectives, including services rendered by a speech-language pathologist to improve communication skills. <p data-bbox="667 914 783 938">***<u>Notes:</u></p> <p data-bbox="716 946 800 971">[1. – 2.]</p> <ol data-bbox="716 979 1881 1068" style="list-style-type: none"> 3. There is insufficient evidence for the superiority of any particular intensive educational intervention strategy (such as applied behavioral analysis, structured teaching, or developmental models) over other intensive educational intervention strategies.
Blue Cross Blue Shield	<i>No national coverage policy identified.</i>
GroupHealth	<p data-bbox="474 1149 1917 1239">“No criteria were developed at this time for Commercial Members. There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies (and/or) provides better long-term outcomes than current standard services/therapies.”</p> <p data-bbox="474 1271 1917 1328">5/4/2010 – Medical Director Clinical Review and Policy Committee Decision: “The committee decided not to recommend coverage at this time and that the evidence be evaluated again in the future.”</p>

Appendix D. State Legislative Action on Autism

State Legislative Action (adapted from National Conference of State Legislatures (2011), Kaiser Family Foundation (2010), and Autism Votes (2011))

	State	Status	Details
Mandate in place (27)	AR	Passed 3/11	HB 1315 – mandates coverage for screening, diagnosis and treatment, includes ABA (\$50,000 max), age cap at 18 yrs old. Effective 10/1/11. (Only applies to state regulated insurance plans NOT self-funded insurance plans).
	AZ	Passed 2008	SB 1263/HB 2847 “Steven’s Law” signed March 21, 2008; in effect June 30, 2009. Prohibits insurers from denying coverage for ASD; \$50,000/yr up to age 9; \$25,000/year 9-16.
	CO	Passed 6/09	SB 244 – mandates coverage for assessment, diagnosis, and treatment of ASD, includes ABA (at least \$34,000/yr 0-9 yrs; \$12,000/yr 9-19 yrs).
	CT	Passed 6/09	SB 301 - mandates coverage for diagnosis and treatment, including ABA (up to \$50,000/yr under 9 yrs; \$35,000/yr 9-12 yrs; \$25,000/yr 13-14 yrs).
	FL	Passed 5/08	SB 2654– authorizes Medicaid to seek approval for federal coverage of ABA (limited to \$36,000/yr; \$108,000 total lifetime benefits) for children 5 yrs or younger; creates a working group to develop a binding insurance mandate
	IA	Passed 4/10	HF 2531 –mandates coverage for diagnosis and treatment for individuals under 21 years of age; max benefit of \$36,000/yr, includes ABA (only applies to state employee health care plans)
	IL	Passed 11/08	SB 934– mandates coverage for individuals under 21 yrs, including ABA, up to \$36,000 per year.
	IN	Code issued 3/06	Indiana code 27-4-14.2 bars limitations on the number of ABA visits; mandates medically necessary coverage; does not cover therapies provided in public schools.
	KS	Passed 4/10	HB 2160 – mandates coverage by state employee health plan for diagnosis and treatment, max of \$36,000/yr up to age 7; \$27,000 7 to 19, includes ABA
	KY	Passed 4/10	HB 159 – mandates coverage for diagnosis and treatment, max benefits: \$50,000/yr 1-6 yrs; \$1,000/month 7-21 yrs), includes ABA. (Only applies to state regulated insurance plans NOT self-funded insurance)
	LA	Passed 2008	HB 958 (Act 648) – mandates coverage, including ABA for individuals under 17, up to \$36,00 per year/ \$144,000 lifetime
	MA	Passed 8/10	HB 4935 – mandates coverage for diagnosis and treatment, includes ABA
	ME	Passed 4/10	SB 446 – mandates coverage for diagnosis and treatment for individuals 5 yrs and younger, includes ABA (\$36,000/yr, no limits on number of visits) (Only applies to state regulated insurance plans NOT self-funded insurance)
	MO	Passed 6/10	HB 1311 – mandates insurance coverage for diagnosis and treatment for individuals up to 18 yrs, includes ABA (max \$45,000/yr) (Only applies to state regulated insurance plans NOT self-funded insurance)
	MT	Passed 5/09	SB 234 – requires coverage up to \$50,000/yr (under 8), up to \$20,000 /yr (9 to 18 yrs), includes ABA
	NH	Passed 7/10	HB 569 (Connor’s Law)– clarifies coverage mandate for diagnosis and treatment, max benefit of \$36,000 for 0 to 12 yrs; \$27,000 for 13 to 21 yrs, includes ABA (Only applies to state regulated insurance plans NOT self-funded insurance)
	NJ	Passed 8/09	Bill 2238 – mandates coverage for screening and diagnosis for individuals under 21 yrs, mandates private insurers to cover ABA as prescribed through a treatment plan) (Only applies to state regulated insurance plans NOT self-funded insurance)
	NM	Passed 4/09	SB 39 Passed – covers up to \$36,000/yr until age 19 (or 22 if still in high school), lifetime limit of \$200,000, includes ABA
	NV	Passed 5/09	AB 162 –requires up to \$36,000 for ABA up to age 18 (or 22 if still in high school)
OK	Passed 4/10	SB 2045 (Nick’s Law) – mandates coverage for screening, diagnosis, testing and treatment for individuals under 21 yrs, includes ABA (max benefit of \$75,000/yr)	

State Legislative Action (adapted from National Conference of State Legislatures (2011), Kaiser Family Foundation (2010), and Autism Votes (2011))

	State	Status	Details
	PA	Passed 7/08	HB 1150 – mandates coverage for diagnosis and treatment for individuals under 21 yrs, up to \$36,000/yr, includes ABA
	SC	Veto overridden 6/07	A65, R85, S20 - Mandates coverage of treatment for individuals diagnosed at age 8 or younger and continues to apply up to age 16, at least \$50,000/year, includes ABA
	TX	Passed 6/07	HB 1919 & HB 451- mandates coverage for individuals under 10 yrs, includes ABA
	VA	Passed 5/2011	SB 1062/HB2467 –mandates coverage for diagnosis and treatment of ASD for ages 2 to 6 yrs, with annual max benefit of \$35,000 for ABA (only applies to state-regulated insurance plans, NOT self-funded insurance plans)
	VT	Passed 5/10	SB 262 – mandates coverage for diagnosis and treatment for individuals between 18 months and 6 yrs, includes ABA (Only applies to state regulated insurance plans NOT self-funded insurance)
	WI	Passed 6/09	Act 28 – mandates coverage for diagnosis and treatment of at least \$50,000/yr (intensive-level services) for a minimum of 4 yrs; mandates coverage of at least \$25,000/yr for non-intensive-level services)
		Passed 5/10	SB 667 – coverage of behavior analysts or paraprofessionals services for ASD
	WV	Passed 4/11	HB 2693 – mandates coverage for ages 3 to 18 yrs old, includes ABA (max benefit \$30,000/yr for first three consecutive yrs from the date treatment commences; max \$2,000/month thereafter until individual reaches age 18)
Pending (15)	AK	In Rules Committee (4/11)	SB 74 – would require coverage for individuals under 21 yrs, includes ABA (only applies to state-regulated insurance plans, NOT self-funded insurance plans)
	CA*		AB 171/SB 166 – would require coverage for behavioral intervention therapy. No age, number of visits, or annual benefit dollar amount caps.
	DE	In committee	SB 22 – would mandate coverage for screening, diagnosis and treatment for individuals under 21 yrs, includes ABA (max \$36,000/yr)
	HI	In multiple committee	SB 744/HB 821 – would mandate coverage for screening, diagnosis, and treatment for individuals under 26 yrs, , max benefit of \$50,000/yr, includes ABA (only applies to state regulated insurance plans NOT self-funded insurance plans)
	MD		HB 273/SB 394 – would mandate coverage for diagnosis and treatment, including ABA (Only applies to state regulated insurance plans NOT self-funded insurance)
			SB 2268 – would require coverage for ASD, related to public employees retirement system medical benefits coverage for ASD.
	MN	In committee	HF 204 – would require coverage for diagnosis, evaluation and medically necessary care, includes ABA (only applies to state-regulated insurance plans, NOT self-funded insurance plans)
	NE		Bill 630 – Applied Behavior Analysis Practice Act
	NC	In committee	HB 826 – would mandate coverage for diagnosis and treatment, includes behavioral care (any practices for the purpose of increasing appropriate or adaptive behaviors, developing, maintaining, or restoring, to maximum extent practicable, the functioning of an individual) (max benefit \$75,000/yr) (only applies to state-regulated insurance plans, NOT self-funded insurance plans)
	NH		HB 309 – would repeal mandatory coverage for diagnosis and treatment of ASD

State Legislative Action (adapted from National Conference of State Legislatures (2011), Kaiser Family Foundation (2010), and Autism Votes (2011))

	State	Status	Details
	NY	In committee	AB 4005/AB 6305 - would require coverage for screening, tests, assessments, and treatment including any medically necessary care for treatment, includes ABA
	OH		HB 8 (2010) – would require coverage of medically necessary treatment, max benefit of \$36,000/yr, includes ABA
	OR	In committee	HB 2214/SB 555 – would mandate coverage for diagnosis and treatment, includes ABA (only applies to state-regulated insurance plans, NOT self-funded insurance plans)
	RI	Vote pending	SB 107 – would mandate coverage for screening, diagnosis and treatment, includes ABA (only applies to state-regulated insurance plans, NOT self-funded insurance plans)
	UT		SB 43: would require insurers to offer a plan that includes up to \$35,000 (up to age 9); \$17,500 up to age 17.
	WA	In committee	SB 5059 – would require coverage of screening, diagnosis, and treatment, includes ABA (Only applies to state regulated insurance plans NOT self-funded insurance)
Other action (2)	AL	Task force	HJR 3a (2008) – required to develop long term plan, identify barriers such as duplicative or fragmented policies that may require modification, development of coordinated program of services, and fiscal review and recommendations for state spending on programs and services.
	MS	Advisory committee	HB 1125 – (2011) creates Autism Advisory Committee
Mandate Introduced, Not passed (4)	GA	No vote in 2010	SB 161 – would have mandated coverage for diagnosis and treatment for individuals diagnosis by age 8, and coverage provided until age 16, includes ABA (max benefit \$36,000/yr; lifetime benefit of \$200,000) (Only applies to state regulated insurance plans NOT self-funded insurance)
	MD	No vote in 2011	HB 783/SB 759 – would have required coverage for diagnosis and treatment, includes ABA (Only applies to state regulated insurance plans NOT self-funded insurance)
	MI	No vote in 2010	HB 4476/HB 4183 – would have required coverage of diagnosis and treatment, includes ABA (up to \$50,000), HB 4476 applied only to BCBS, HB 4183 applied to other insurance companies
	TN	No vote in 2010	HB 2015 – would require coverage up to \$50,000 up to age 9, \$25,000 between 9 and 16 (Only applies to state regulated insurance plans NOT self-funded insurance)
No Action	ID	No action	
	SD	No action	
	WY	No action	

* State has mental health parity law in place.
 Legislative Analysis and Action current as of May 2011.

Appendix E. Guideline Quality Assessment Tool

[This tool is adapted from the Appraisal of Guidelines Research & Evaluation (AGREE) II tool.

The full AGREE II tool is available from <http://www.agreetrust.org/resource-centre/agree-ii/>]

MED PROJECT	Methodology Checklist: Guidelines		
Guideline citation <i>(Include name of organization, title, year of publication, journal title, pages)</i>			
MED Topic:		Key Question No.(s), if applicable:	
Checklist completed by:			Date:
SECTION 1: PRIMARY CRITERIA			
<i>To what extent is there</i>		<i>Assessment/Comments:</i>	
1.1	RIGOR OF DEVELOPMENT: Evidence <ul style="list-style-type: none"> • Systematic literature search • Study selection criteria clearly described • Quality of individual studies and overall strength of the evidence assessed • Explicit link between evidence & recommendations <i>(If any of the above are missing, rate as poor)</i>	GOOD	FAIR POOR
1.2	RIGOR OF DEVELOPMENT: Recommendations <ul style="list-style-type: none"> • Methods for developing recommendations clearly described • Strengths and limitations of evidence clearly described • Benefits/side effects/risks considered • External review 	GOOD	FAIR POOR
1.3	EDITORIAL INDEPENDENCE⁵ <ul style="list-style-type: none"> • Views of funding body have not influenced the content of the guideline • Competing interests of members have been recorded and addressed 	GOOD	FAIR POOR
<i>If any of three primary criteria are rated poor, the entire guideline should be rated poor.</i>			
SECTION 2: SECONDARY CRITERIA			
2.1	SCOPE AND PURPOSE <ul style="list-style-type: none"> • Objectives described • Health question(s) specifically described • Population (patients, public, etc.) specified 	GOOD	FAIR POOR

⁵ Editorial Independence is a critical domain. However, it is often very poorly reported in guidelines. The assessor should not rate the domain, but write “unable to assess” in the comment section. If the editorial independence is rated as “poor”, indicating a high likelihood of bias, the entire guideline should be assessed as poor.

SECTION 2: SECONDARY CRITERIA, CONT.				
2.2	STAKEHOLDER INVOLVEMENT <ul style="list-style-type: none"> • Relevant professional groups represented • Views and preferences of target population sought • Target users defined 	GOOD	FAIR	POOR
2.3	CLARITY AND PRESENTATION <ul style="list-style-type: none"> • Recommendations specific, unambiguous • Management options clearly presented • Key recommendations identifiable • Application tools available Updating procedure specified 	GOOD	FAIR	POOR
2.4	APPLICABILITY <ul style="list-style-type: none"> • Provides advice and/or tools on how the recommendation(s) can be put into practice • Description of facilitators and barriers to its application • Potential resource implications considered Monitoring/audit/review criteria presented 	GOOD	FAIR	POOR
SECTION 3: OVERALL ASSESSMENT OF THE GUIDELINE				
3.1	How well done is this guideline?	GOOD	FAIR	POOR
3.2	Other reviewer comments:			

Description of Ratings: Methodology Checklist for Guidelines

The checklist for rating guidelines is organized to emphasize the use of evidence in developing guidelines and the philosophy that “evidence is global, guidelines are local.” This philosophy recognizes the unique situations (e.g., differences in resources, populations) that different organizations may face in developing guidelines for their constituents. The second area of emphasis is transparency. Guideline developers should be clear about how they arrived at a recommendation and to what extent there was potential for bias in their recommendations. For these reasons, rating descriptions are only provided for the primary criteria in section one. There may be variation in how individuals might apply the good, fair, and poor ratings in section two based on their needs, resources, organizations, etc.

Section 1. Primary Criteria (rigor of development and editorial independence) ratings:

Good: All items listed are present, well described, and well executed (e.g., key research references are included for each recommendation).

Fair: All items are present, but may not be well described or well executed.

Poor: One or more items are absent or are poorly conducted

References

- Aetna. (2011). *Clinical policy bulletin: Pervasive Developmental Disorders*. Retrieved May 9, 2011, from http://www.aetna.com/cpb/medical/data/600_699/0648.html
- AGREE Next Steps Consortium. (2009). *Appraisal of guidelines for research and evaluation II: Instrument*. Retrieved May 12, 2011, from <http://www.agreetrust.org/?o=1397>
- Aldred, C., Green, J., & Adams, C. (2004). A new social communication intervention for children with autism: Pilot randomised controlled treatment study suggesting effectiveness. *Journal of Child Psychology & Psychiatry*, 45,1420-1430.
- Autism Votes. (2011). *Autism Speaks state autism insurance reform initiatives*. Retrieved May 6, 2011, from http://www.autismvotes.org/site/c.frKNI3PCImE/b.3909861/k.B9DF/State_Initiatives.htm
- Baer, D.M., Wolf, M.M., & Risley, T.R. (1968). Some current dimensions of applied behavioral analysis. *Journal of Applied Behavior Analysis*, 1, 91-7.
- Baird, G., Cass, H., & Slonims, V. (2003). Diagnosis of autism. *BMJ*, 327, 488-493.
- Bandura, A. (1969). *Principles of behavior modification*. New York; London: Holt, Rinehart and Winston.
- Behavioral Analysis Certification Board. (2010). *About BACB*. Retrieved May 12, 2011, from <http://www.bacb.com/index.php?page=1>
- Blue Cross Blue Shield of Michigan. (2009). Blue Cross Blue Shield of Michigan plans to offer customer groups ability to purchase coverage of autism treatment programs that provide intensive early intervention. Retrieved May 10, 2011, from http://www.bcbsm.com/pr/pr_05-11-2009_78322.shtml
- Center for Disease Control and Prevention (CDC). (2002). *Autism and developmental disabilities Monitoring (ADDM) Network*. Retrieved October 11, 2010, from <http://www.cdc.gov/ncbddd/autism/addm.html>
- Center for Disease Control and Prevention (CDC). (2010). *Autism spectrum disorders: Facts about ASD*. Retrieved September 28, 2010, from <http://www.cdc.gov/ncbddd/autism/facts.html>
- Drew, A., Baird, G., Baron-Cohen, S., Cox, A., Slonims, V.W., S., Swettenham, J., et al. (2002). A pilot randomised control trial of a parent training intervention for preschool children with autism- Preliminary findings and methodological issues. *European Child and Adolescent Psychiatry*, 11, 266-272.
- Diggle, T., McConachie, H.R., & Randle, V.R.L. (2002). Parent-mediated early intervention for young children with autism spectrum disorder. *Cochrane Database of Systematic Reviews*, Issue 2. Chichester, UK: John Wiley & Sons, Ltd.

- Ganz, M.L. (2007). The lifetime distribution of the incremental societal costs of autism. *Archives of Pediatrics & Adolescent Medicine*, 161, 343-349.
- GroupHealth. (2010). Clinical review criteria. Applied behavioral analysis therapy (ABA), early intensive behavior interventions (EIBI) for young children with autism. Retrieved May 9, 2011, from https://provider.ghc.org/all-sites/clinical/criteria/pdf/aba_autism.pdf
- Gutstein, S., & Sheeley, R. (2002). *Relationship development intervention with young children. Social and emotional development activities for Asperger Syndrome, autism, PDD and NLD*. London: Jessica Kingsley Publishers.
- Guyatt, G.H., Drummond, R., Meade, M.O., & Cook, D.J. (Eds). (2008). *User's Guides to the Medical Literature: A Manual for Evidence-based Clinical Practice (2 Ed.)*. New York: McGraw-Hill Medical.
- Guyatt, G.H., Keller, J.L., Jaeschke, R., et al. (1990). The n-of-1 randomized controlled trial: Clinical usefulness. Our three-year experience. *Annals of Internal Medicine*, 112, 293–9.
- Guyatt, G.H., Oxman, A.D., Vist, G.E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., et al. (2008). GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*, 336(7650), 924-926.
- Guyatt, G.H, Sackett, D., & Taylor, D. (1986). Determining optimal therapy. Randomized trials in individual patients. *New England Journal of Medicine*, 314(14), 889–92.
- Horner, H.H, Carr, E.G., Halle, et al. (2005). The use of single-subject research to identify evidence-based practice in special education. *Exceptional Children*, 71(2), 165-179.
- Kaiser Family Foundation. (2010). *Autism specific mandates: Individual health insurance market, 2010*. Retrieved May 5, 2011, from <http://www.statehealthfacts.org/comparetable.jsp?ind=852&cat=7&sort=a&gsa=2>
- Kaiser Family Foundation. (2010). *Autism specific mandates: Small group market, 2010*. Retrieved May 5, 2011, from <http://www.statehealthfacts.org/comparetable.jsp?ind=853&cat=10&sort=a&gsa=2>
- Kaufman, B. (1994). *Son-Rise: The miracle continues*. Tiburon, CA: H.J. Kramer.
- King, M., & P. Bearman (2009). Diagnostic change and the increased prevalence of autism. *International Journal of Epidemiology*, 38(5), 1224-1234.
- Koegel, L.K. (1995). Communication and language intervention. In R.L Koegel & L.K. Koegel (Eds.), *Teaching children with autism: Strategies for initiating positive interactions and improving learning opportunities* (pp. 17–32). Baltimore, MD: Brookes Publishing.
- Lovaas, O. (1987). Behavioural treatment and normal educational and intellectual functioning in young autistic children. *Journal of Consulting and Clinical Psychology*, 55, 3-9.

- McConachie, H., & Diggle, T. (2007). Parent implemented early intervention for young children with autism spectrum disorder: A systematic review. *Journal of Evaluation in Clinical Practice*, 13(1), 120-9.
- McConnell, S.R. (2002). Interventions to facilitate social interaction for young children with autism: Review of available research and recommendations for educational intervention and future research. *Journal of Autism and Developmental Disorders*, 32, 351-372.
- McEachin, J., Smith, T., & Lovass, O. (1993). Long term outcome for children with autism who received early intensive behavioural treatment. *American Journal on Mental Retardation*, 97, 359-372.
- Myers, S. M., & Johnson, C. P. (2007). Management of children with autism spectrum disorders. *Pediatrics*, 120(5), 1162-1182.
- National Autism Center. (2009). *National standards report*. Randolph, MA: National Autism Center. Retrieved October 11, 2010, from http://www.nationalautismcenter.org/pdf/NAC%20NSP%20Report_FIN.pdf
- National Conference of State Legislatures. (2011). *Autism legislation database*. Retrieved May 5, 2011, from <http://www.ncsl.org/default.aspx?tabid=14109>
- National Institute for Health and Clinical Excellence (NICE). (2009). *The guidelines manual*. London: National Institute for Health and Clinical Excellence. Retrieved October 4, 2010, from http://www.nice.org.uk/media/5F2/44/The_guidelines_manual_2009_-_All_chapters.pdf
- New Zealand Guidelines Group. (2010). *Guidelines supplementary paper: New Zealand autism spectrum disorder guideline, supplementary evidence on applied behavioral analysis*. Wellington: New Zealand Guidelines Group.
- New Zealand Ministry of Health. (2008). *New Zealand autism spectrum disorder guideline*. Wellington: New Zealand Ministry of Health.
- Reddy, V., Hay, D., Murry, L., & Trevarthen, C. (1997). Communication in infancy: Mutual regulation of affect and attention. In G. Bremner, A. Slater, & G. Butterworth (Eds.), *Infant development: Recent advances* (pp. 247-274). Hove, UK: Psychological Press.
- Rice, C. (2009). Prevalence of autism spectrum disorders: autism and developmental disabilities monitoring network, United States, 2006. *MMWR Surveillance Summaries*, 58(SS10), 1-20.
- Rogers, S.J. (2000). Interventions that facilitate socialization in children with autism. *Journal of Autism and Developmental Disorders*, 30, 399-409.
- Schopler, E., Mesibov, G.B., & Hearsey, K. (1995). Structured teaching in the TEACCH system. In E. Schopler & G.B. Mesibov (Eds.), *Learning and cognition in autism* (pp.243-268). New York: Plenum Press.

- Scottish Intercollegiate Guidelines Network (SIGN). (2007). *Assessment, diagnosis, and clinical interventions for children and young people with autism spectrum disorder: A national clinical guideline*. Edinburgh: Scottish Intercollegiate Guidelines Network. Retrieved October 11, 2010, from <http://www.sign.ac.uk/pdf/sign98.pdf>
- Scottish Intercollegiate Guidelines Network (SIGN). (2008). Critical appraisal: Notes and checklists. In: *SIGN 50: A guideline developer's handbook*. Retrieved August 23, 2010, from <http://www.sign.ac.uk/methodology/checklists.html>
- Scottish Intercollegiate Guidelines Network (SIGN). (2009). *Critical Appraisal: Notes and Checklists*. Retrieved November 15, 2010, from <http://www.sign.ac.uk/methodology/checklists.html>
- Scuffham, P.A., Nikles, J., Mitchell, G.K. et al. (2010). Using N-of-1 trials to improve patient management and save costs. *Journal of General Internal Medicine*, 25(9). 906-13
- Siller, M., & Sigman, M. (2002). The behaviours of parents of children with autism predict the subsequent development of their children's communication. *Journal of Autism and Developmental Disorders*, 32, 77-89.
- Skinner, B.F. (1953). *Science and human behavior*. New York: Macmillan.
- Strain, P.S., Kohler, F.W., Storey, K., & Danko, C.D. (1994). Teaching preschoolers with autism to self-monitor their social interactions: An analysis of results in home and school settings. *Journal of Emotional and Behavioral Disorders*, 2, 78-88.
- Sussman, F. (1999). *More than words: Helping parents promote communication and social skills in children with autism spectrum disorder*. Toronto.
- Ullman, L.P., & Krasner, L. (Eds.). (1965). *Case studies in behaviour modification*. New York: Holt, Rinehart and Winston.
- Warren, Z., Veenstra-VanderWeele, J., Stone, W., Bruzek, J.L., Nahmias, A.S., Foss-Feig, J.H., et al. (2011). *Therapies for children with autism spectrum disorders. Comparative effectiveness review no. 26*. (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2007-10065-I). AHRQ Publication No. 11-EHC029-EF. Rockville, MD: Agency for Healthcare Research and Quality. Retrieved May 5, 2011, from <http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=651>
- Washington State Department of Health. (2010). *Autism awareness project*. Retrieved May 17, 2011, from <http://www.doh.wa.gov/cfh/mch/autism/autism.htm>
- Weinberg, M. (2008). ABAI's commitment to licensing of applied behavior analysts. *Association of Behavior Analysis International Newsletter*, 31(3). Retrieved May 12, 2011, from <http://www.abainternational.org/ABA/newsletter/vol313/Licensure.asp>

- Yelland, M., Poulos, C., Pillans, P., et al. (2009). N-of-1 randomized trials to assess the efficacy of gabapentin for chronic neuropathic pain. *Pain Medicine, 10*(4), 754–761.
- Yoder, P.J., & Warren, S.F. (2002). Effects of prelinguistic milieu teaching and parent responsivity education on dyads involving children with intellectual disabilities. *Journal of Speech, Language and Hearing Research, 45*, 1158-1174.
- Zucker, D.R., Schmid, C.H., McIntosh, M.W., et al. (1997). Combining single patient [N-of-1] trials to estimate population treatment effects and to evaluate individual patient responses to treatment. *Journal of Clinical Epidemiology, 50*, 401–10.