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Therapies for Children With Autism Spectrum Disorder: Behavioral Interventions Update



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Introduction

Background

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

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

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

Prevalence and Burden of Disease/Illness

The prevalence of ASD in the United States is 14.7 cases per 1,000 (or 1 in 68) children living in the communities surveyed, with rate estimates varying widely by region of the country, sex, and race/ethnicity.⁷ Considerably more males (1 in 42) than females (1 in 189) are affected. For some individuals, the core symptoms of ASD (impairments in communication and social interaction and restricted/repetitive behaviors and interests) may improve with intervention and maturation⁸⁻¹⁰; however, core deficits typically translate into varying developmental presentations that remain throughout the lifespan.¹¹ Longitudinal studies indicate that adults with ASD struggle to obtain adaptive independence.¹²⁻¹⁶ The estimated costs of medical and nonmedical care (e.g., special education and daycare) for individuals with ASD are high. One study estimates that the total lifetime societal cost of caring for and treating a person with ASD in the United States is \$3.2 million, and about \$35 billion yearly for an entire birth cohort of individuals with ASD.¹⁷

Etiology and Risk Factors

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

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

Interventions/Treatment

The manifestation and severity of symptoms of ASD differs widely, and treatments pursued by families include a range of behavioral, psychosocial, educational, medical, and complementary approaches³⁵⁻³⁹ that vary by a child's age and developmental status. The goals of treatment for ASD are to improve core deficits in social communication and social interactions and minimize the impact of restricted behaviors, with an overarching goal to help children develop greater functional skills and independence.⁵ Treatment frequently is complicated by symptoms or comorbidities that may warrant targeted intervention. There is no cure for ASD and no global consensus on which intervention is most effective.^{38, 40} Individual goals for treatment vary for different children and may include combinations of behavioral therapies, educational therapies, medical and related therapies, and allied health therapies; parents may also pursue complementary and alternative medicine (CAM) therapies.

Behavioral approaches are the most common treatment approaches for ASD. In 1987, Ivar Lovaas published findings⁴¹ on a subgroup of children who demonstrated improvements in cognitive abilities and educational placement in response to intensive intervention based on the principles of applied behavior analysis (ABA). As a result, ASD was reconceptualized from a largely untreatable disorder⁴¹ to a condition characterized by plasticity and heterogeneity, where there was hope for higher functioning and better outcomes for children receiving appropriate intervention. Subsequent research focused on social communication and behavioral impairments and used both highly structured approaches and natural/developmental approaches that deliver interventions within natural/everyday contexts (Floortime and the Social Communication Emotional Regulation Transactional Support model), as well as some that integrate these different approaches (Early Start Denver Model [ESDM]). These types of early and intensive treatment programs typically target behaviors and development more broadly, instead of focusing on a specific behavior of interest.⁴² Positive effects seen with these approaches in terms of cognition and language have led to the suggestion that beginning intensive therapy at an earlier age may lead to greater improvements.^{40, 42, 43} Recent systematic reviews and meta-analyses have highlighted the potential of early intervention to promote behavioral change.^{36-39, 43-52}

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

Chronic management throughout different developmental periods is often pursued to maximize functional independence and quality of life by minimizing the core ASD features, facilitating development and learning, promoting socialization, reducing maladaptive behaviors, and educating and supporting families. For many individuals core symptoms of ASD may see improvements with intervention and over time⁸⁻¹¹; however, deficits typically remain throughout the lifespan, although developmental expression may vary.

Scope and Key Questions

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

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

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

We again adopted an approach of assessing effects on core symptoms as well as commonly associated symptoms. Changes in commonly adopted diagnostic criteria related to ASD have changed in the interim since the previous report. These changes include additions to the core symptoms of ASD (e.g., hypo/hyper-sensory reactivity now a core feature).³ Our approach to the

review encompassed both core and associated symptoms, and neither inclusion nor interpretation was affected by whether specific outcomes were considered core or associated.

Key Questions

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

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

KQ1a: What are the effects on core symptoms (e.g., social communication and interaction, restricted and repetitive behaviors), in the short term (≤ 6 months)?

KQ1b: What are the effects on commonly associated symptoms (e.g., motor, medical, mood/anxiety, irritability, and hyperactivity) in the short term (≤ 6 months)?

KQ1c: What are the longer-term effects (> 6 months) on core symptoms (e.g., social communication and interaction, restricted and repetitive behaviors)?

KQ1d: What are the longer-term effects (> 6 months) on commonly associated symptoms (e.g., motor, medical, mood/anxiety, irritability, and hyperactivity)?

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

KQ2a: Is the effectiveness of the therapies reviewed affected by the frequency, duration, and intensity of the intervention?

KQ2b: Is the effectiveness of the therapies reviewed affected by the training and/or experience of the individual providing the therapy?

KQ2c: What characteristics, if any, of the child modify the effectiveness of the therapies reviewed?

KQ2d: What characteristics, if any, of the family modify the effectiveness of the therapies reviewed?

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

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

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

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

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

Organization of This Report

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

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

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

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

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

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

Categorization of Interventions

In line with the 2011 review, we categorized behavioral interventions as follows: early intensive behavioral and developmental interventions, social skills interventions, parent training, play/interaction-focused interventions, interventions targeting symptoms commonly associated with ASD such as anxiety, and other general behavioral approaches. This categorization was largely driven by an end user perspective (i.e., taking into account how parents, clinicians, and

systems of care might attempt to access or support intervention decisions). Thus, we categorized studies based on treatment setting/context rather than outcomes examined.

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

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

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

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

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

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

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

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

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

Uses of This Report

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

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

Methods

Topic Development and Refinement

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

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

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

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

Role of the AHRQ Task Order Officer

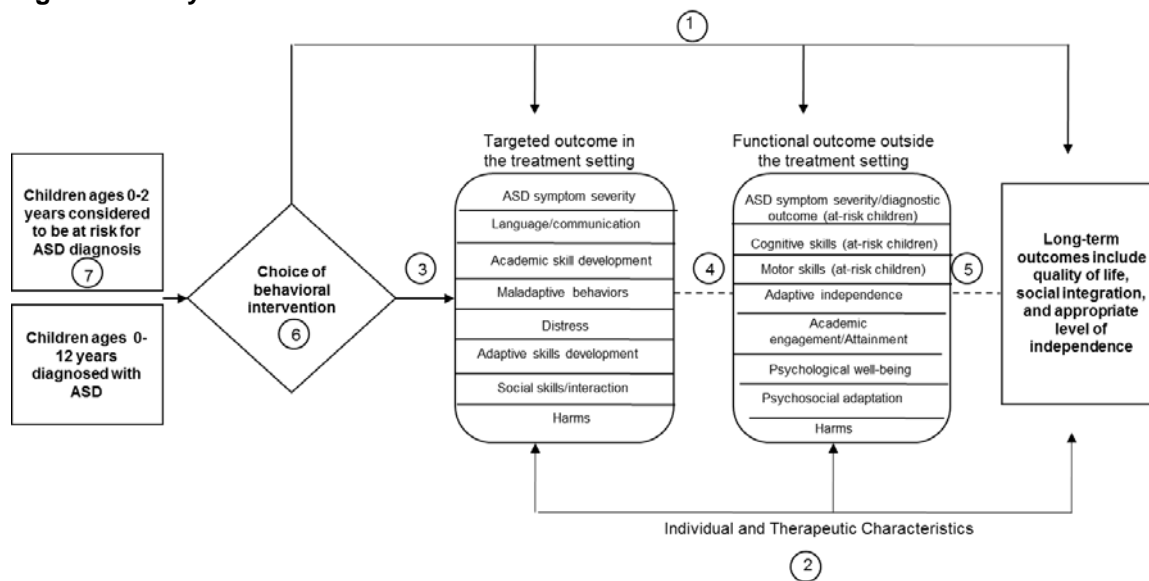
The Task Order Officer (TOO) was responsible for overseeing all aspects of this project. The TOO helped to develop a common understanding among all parties involved in the project, resolved questions and ambiguities, and addressed our queries regarding the scope and processes of the project. The TOO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

Analytic Framework

Figure 1 illustrates the placement of the review's Key Questions within the context of treatment choice, potential outcomes, and characteristics that may affect outcomes. Circled numbers indicate the KQs, and their placement indicates the points in the treatment process where they are likely to arise. This update focuses on behavioral interventions for children with ASD or considered to be at risk for ASD. The population of interest is patients 0–12 years diagnosed with ASD. A child entering treatment may be between the ages of 0 and 2 and at risk for diagnosis of ASD or ages 0 to 12 with a diagnosis of ASD. Diagnoses may occur before age 2; thus the represented age ranges overlap. Individuals engage in behavioral interventions, which may lead to specific outcomes (KQ 1). Outcomes may be modified by characteristics of the child/family or of the intervention (KQ 2). KQ 3 involves identifiable changes early in the treatment process that may affect outcomes. KQ 4 involves the relationship between targeted

outcomes in the treatment setting and functional outcomes outside the treatment setting. KQ 5 involves generalization of interventions to other contexts, and KQ 6 addresses components of treatments that may drive outcomes, the “active ingredients” of treatments. KQ 7 addresses treatments for very young children considered to be at risk for ASD. Target outcomes in the treatment setting include ASD symptom severity, language/ communication, academic skill development, maladaptive behaviors, distress, adaptive skills development, and social skills/interaction. Functional outcomes outside the treatment setting include adaptive independence, academic engagement/attainment, psychological well-being, and psychosocial adaptation; for children considered to be at risk, the outcomes include changes in ASD symptom severity or diagnostic outcome, motor skills, and cognitive skills. Long-term outcomes include quality of life, social integration, and appropriate level of independence. Harms of intervention are also considered.

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



ASD = autism spectrum disorder; KQ = Key Question

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

Literature Search Strategy

Databases

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

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

Grey Literature and Hand Searching

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

Search Terms

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