



Effective Health Care Program

Therapies for Children With Autism Spectrum Disorders *Executive Summary*

Background

Autism spectrum disorders (ASDs) have an estimated prevalence of 1 in 110 children in the United States.¹ Disorders within the spectrum include Autistic Disorder, Asperger Syndrome, and Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS).

Individuals with ASDs have impaired social interaction, behavior, and communication,² including lack of reciprocal social interaction and joint attention (i.e., the ability to use nonverbal means such as pointing to direct others' attention to something in which the child is interested); dysfunctional or absent communication and language skills; lack of spontaneous or pretend play; intense preoccupation with particular concepts or things; and repetitive behaviors or movements.³⁻⁵ Children with ASDs may also have impaired cognitive skills and sensory perception.^{1,2}

Treatment for ASDs focuses on improving core deficits in social communication, as well as addressing challenging behaviors to improve functional engagement in developmentally appropriate activities.⁴ In addition to addressing core deficits, treatments are provided for difficulties associated with the disorder (anxiety, attention difficulties, sensory difficulties, etc.). Individual goals for treatment vary for different children and may include combinations of therapies.⁴

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Objectives

Population. We focused this review on children ages 2-12 with ASDs for Key Questions (KQs) 1-6 and children under age 2 at risk of ASD for KQ7.



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Interventions. Treatments included behavioral, educational, medical, allied health, and complementary and alternative medicine (CAM) interventions (Table A).

Comparators. Comparators included no treatment, placebo, and comparative interventions or combinations of interventions.

Outcomes. Outcomes included changes in core ASD symptoms and in commonly associated symptoms (Figure A).

Table A. Description of interventions

Intervention category	Brief description
Behavioral	<ul style="list-style-type: none"> Interventions in the early intensive behavioral and developmental category have their basis in or draw from principles of applied behavior analysis (ABA), with differences in methods and setting. We included in this category two intensive interventions with published treatment manuals (manualized interventions): the University of California, Los Angeles/Lovaas model and the Early Start Denver Model (ESDM). We also included in this category interventions utilizing intensive ABA principles in a similar fashion to the UCLA/Lovaas model. Frequently these approaches included variations of the UCLA/Lovaas model, but we review this literature together because of overall similarities. An additional set of interventions included in this category use ABA principles to focus on teaching pivotal behaviors to parents rather than on directed intensive intervention. Social skills interventions focus on facilitating social interactions and may include peer training and social stories. Play- or interaction-focused interventions use interactions between children and parents or researchers to affect outcomes, including imitation, joint attention skills, or children’s ability to engage in symbolic play. Interventions focused on commonly associated behaviors attempt to ameliorate symptoms such as anxiety, often present in ASDs, using techniques including cognitive behavioral therapy (CBT) and parent training focused on challenging behaviors. Additional interventions include techniques such as sleep workshops and neurofeedback.
Educational	<ul style="list-style-type: none"> Educational interventions focus on improving educational and cognitive skills. They are intended to be administered primarily in educational settings and also include studies for which the educational arm was most clearly categorized. Some interventions in educational settings are based on principles of ABA and may be intensive, but no interventions in this category used the UCLA/Lovaas or ESDM manualized treatments.
Medical and related interventions	<ul style="list-style-type: none"> Medical and related interventions are those that include the administration of external substances to the body to treat symptoms of ASDs. Medical treatments for ASD symptoms comprise a variety of pharmacologic agents, including antipsychotics, psychostimulants, and serotonin reuptake inhibitors (SRIs), and modalities such as therapeutic diets, supplements, hormonal supplements, immunoglobulin, hyperbaric oxygen, and chelating agents.
Allied health	<ul style="list-style-type: none"> Allied health interventions include therapies typically provided by speech/language, occupational, and physical therapists, including auditory and sensory integration, music therapy, and language therapies (e.g., Picture Exchange Communication System [PECS]).
CAM	<ul style="list-style-type: none"> CAM interventions include acupuncture and massage.

Note: ABA = applied behavior analysis; ASDs = autism spectrum disorders; CAM = complementary and alternative medicine; CBT = cognitive behavioral therapy; ESDM = Early Start Denver Model; PECS = Picture Exchange Communication System; SRI = serotonin reuptake inhibitor; UCLA = University of California, Los Angeles

Key Questions

Key questions were:

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

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

KQ1b: What are the effects on commonly associated symptoms (e.g., motor, sensory, 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 deficits, communication deficits, and repetitive behaviors)?

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

KQ2: Among children ages 2-12, what are the modifiers of outcome for different 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 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 2 who are at high risk of developing autism based upon behavioral, medical, or genetic risk factors?

Analytic Framework

The analytic framework summarizes the process by which families of children with ASDs make and modify treatment choices. Treatment choices are affected by many factors that relate to the care available. Treatment effectiveness may also be affected by factors related to the child (e.g., age, IQ) or the context of care. Ideally, treatment effects are seen both in the short term in clinical changes and in longer term or functional outcomes. Eventual outcomes of interest include adaptive independence appropriate to the abilities of the specific child, psychological well-being, appropriate academic engagement, and psychosocial adaptation. The circled numbers represent the report's key questions; their placement indicates the points in the treatment process in which they are likely to arise.

Methods

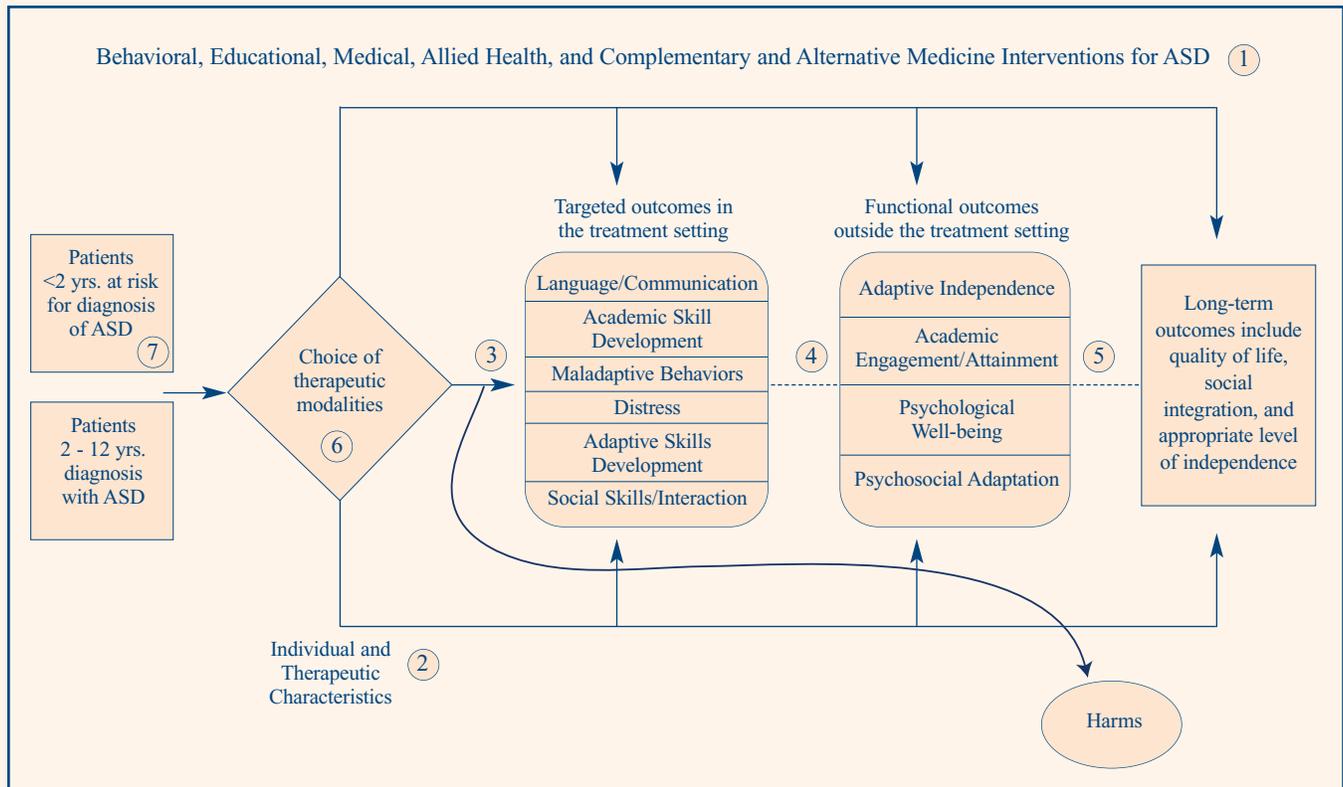
Input From Stakeholders

The topic was nominated in a public process. With key informant input, we drafted initial key questions and, after approval from the Agency for Healthcare Research and Quality (AHRQ), they were posted to a public Web site for public comment. Using public input, we drafted final key questions, which were approved by AHRQ. We convened a Technical Expert Panel to provide input during the project on issues such as setting inclusion/exclusion criteria and assessing study quality. In addition, the draft report was peer reviewed and made available for public comment.

Data Sources and Selection

We searched three databases: MEDLINE® via the PubMed interface, PsycINFO, and the Education Resources Information Center (ERIC) database. We hand-searched reference lists of included articles and recent reviews for additional studies.

Figure A. Analytic Framework for therapies for children with ASDs.



We excluded studies that

- Were not published in English.
- Did not report information pertinent to the key questions.
- Were published prior to the year 2000, the time of the revision of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)² and widespread implementation of gold standard assessment tools, including the Autism Diagnostic Observation Schedule (ADOS)⁶ and the Autism Diagnostic Interview – Revised (ADI-R).⁷
- Were not original research.
- Did not present aggregated results (i.e., only presented data for each individual participant) or presented graphical data only.

We also excluded studies with fewer than 10 total participants for studies of behavioral, educational, allied health, or CAM interventions; or fewer than 30 total participants for medical studies. We believed that, given the greater risk associated with the use of medical interventions, it was appropriate to require a larger

sample size to accrue adequate data on safety and tolerability as well as efficacy. In addition, most studies of medical interventions for ASDs with fewer than 30 subjects report preliminary results that are replaced by later, larger studies.

We accepted any study designs except individual case reports. Our approach to categorizing study designs is presented in Appendix F of the full report.

Two reviewers separately evaluated each abstract. If one reviewer concluded that the article could be eligible, we retained it. Two reviewers independently read the full text of each included article to determine eligibility, with disagreements resolved via third-party adjudication.

Data Extraction and Quality Assessment

Data extraction. All team members entered information into the evidence table. After initial data extraction, a second team member edited entries for accuracy, completeness, and consistency. In addition to outcomes for treatment effectiveness, we extracted data on harms/adverse effects.

Quality assessment. Two reviewers independently assessed quality (study design, diagnostic approach, participant ascertainment, intervention characteristics, outcomes measurement, and statistical analysis), with differences resolved through discussion, review of the publications, and consensus with the team. We rated studies as good, fair, or poor quality and retained poor studies as part of the evidence base discussed in this review. More information about our quality assessment methods is in the full report.

Data Synthesis and Analysis

Evidence synthesis. We used summary tables to synthesize studies that included comparison groups and summarized the results qualitatively.

Strength of evidence. The degree of confidence that the observed effect of an intervention is unlikely to change is presented as strength of evidence, and it can be regarded as insufficient, low, moderate, or high. Strength of evidence describes the adequacy of the current research, in quantity and quality, and the degree to which the entire body of current research provides a consistent and precise estimate of effect. We established methods for assessing the strength of evidence based on the Evidence-based Practice Centers Methods Guide for Effectiveness and Comparative Effectiveness Reviews.⁸ Details of our strength-of-evidence methods are in Chapter 2 of the full report.

Results

Our searches retrieved 4,120 nonduplicate citations. We included 183 articles, representing 159 unique studies, in the review (Figure B). The full report details reasons for exclusion.

KQ1. Outcomes of Therapies for ASDs in Children Ages 2-12

Behavioral interventions. We identified 78 unique behavioral studies.⁹⁻⁹² Early intensive behavioral and developmental intervention may improve core areas of deficit for individuals with ASDs; however, few randomized controlled trials (RCTs) of sufficient quality have been conducted, no studies directly compare effects of different treatment approaches, and little evidence of practical effectiveness or feasibility exists.

Within this category, studies of UCLA/Lovaas-based interventions report greater improvements in cognitive performance, language skills, and adaptive behavior skills than broadly defined eclectic treatments available in the community.^{11, 13, 19, 23, 35, 36, 40} However, strength of evidence is currently low. Further, not all children receiving intensive intervention demonstrate rapid gains, and many children continue to display substantial impairment.²³ Although positive results are reported for the effects of intensive interventions that use a developmental framework, such as the Early Start Denver Model (ESDM),³⁷ evidence for this type of intervention is currently insufficient because few studies have been published to date.

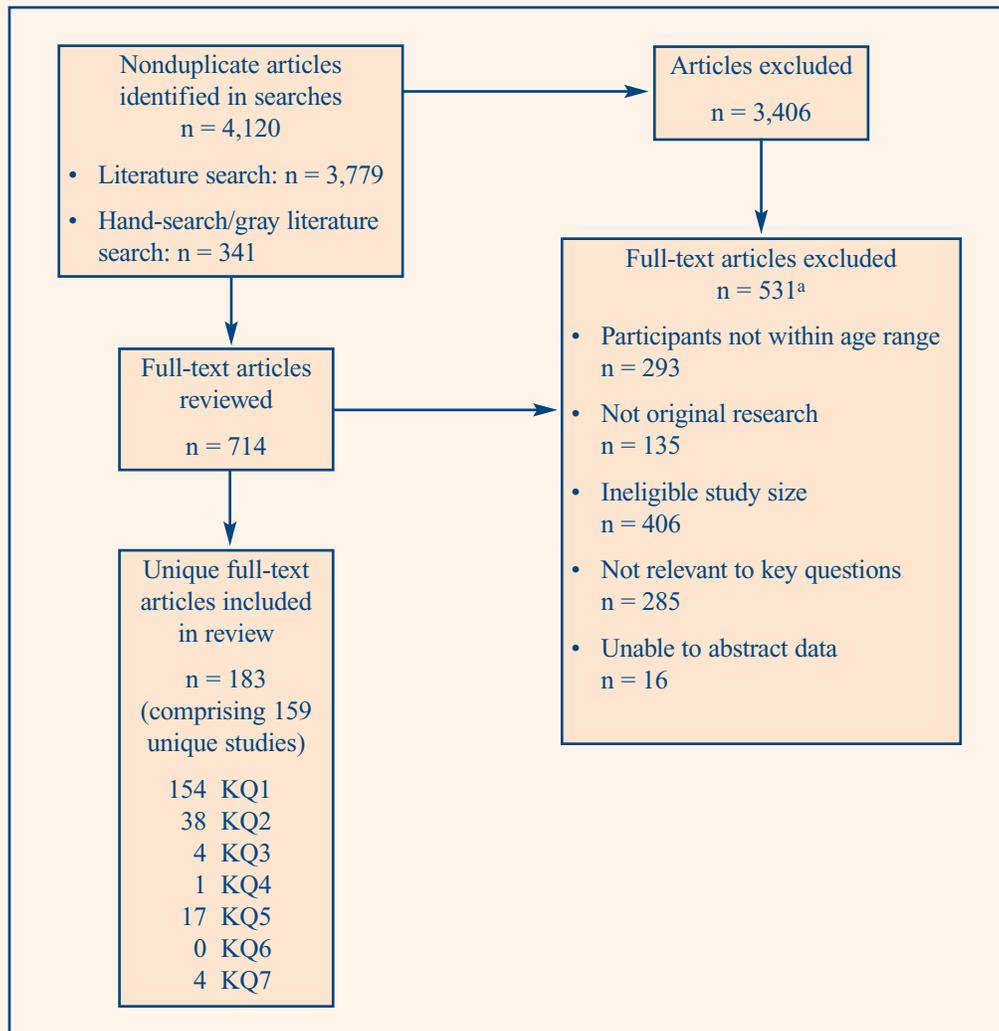
Less intensive interventions focusing on providing parent training for bolstering social communication skills and managing challenging behaviors have been associated in individual studies with short-term gains in social communication and language use.^{17, 18, 46} The current evidence base for such treatment remains insufficient, with current research lacking consistency in interventions and outcomes assessed.

Although all of the studies of social skills interventions reported some positive results,⁴⁷⁻⁶² most have not included objective observations of the extent to which improvements in social skills generalize and are maintained within everyday peer interactions. Strength of evidence is insufficient to assess effects of social skills training on core autism outcomes for older children or play- and interaction-based approaches for younger children.

Several studies suggest that interventions based on cognitive behavioral therapy are effective in reducing anxiety symptoms.⁷⁹⁻⁸² Strength of evidence for these interventions, however, is insufficient pending further replication.

Educational interventions. We identified 15 unique studies of educational interventions meeting our inclusion criteria.⁹³⁻¹⁰⁸ Most research on the Treatment and Education of Autistic and Communication related handicapped CHildren (TEACCH) program was conducted prior to the date cutoff for our review. Newer studies continue to report improvements among children in motor, eye-hand coordination, and cognitive measures.^{94, 96} The strength of evidence for TEACCH, as well as broad-based and computer-based educational

Figure B. Disposition of articles addressing therapies for children with ASDs



^a The total number of articles in the exclusion categories exceeds the number of articles excluded because most of the articles fit into multiple exclusion categories.

Note: KQ = key question.

approaches included in this category,¹⁰⁶⁻¹⁰⁸ to affect any individual outcomes is insufficient because there are too few studies and they are inconsistent in outcomes measured.

Medical and related interventions. We identified 42 unique studies in the medical literature,^{109-115, 116, 117-161} of which 27 were RCTs.^{109-120, 122-124, 126, 128, 131-133, 137-143, 145-152, 159-161} Although no current medical interventions demonstrate clear benefit for social or communication symptoms, a few medications show benefit for repetitive behaviors or associated symptoms.

The clearest evidence favors the use of medications to address challenging behaviors. The antipsychotics risperidone and aripiprazole each have at least two RCTs demonstrating improvement in a parent-reported measure of challenging behavior.^{109-120, 122, 123} A parent-reported hyperactivity and noncompliance measure also showed significant improvement. In addition, repetitive behavior showed improvement with both risperidone and aripiprazole. Both medications also cause significant side effects, however, including marked weight gain, sedation, and risk of extrapyramidal symptoms (side effects, including muscle stiffness or tremor, that occur

in individuals taking antipsychotic medications). These side effects limit use of these drugs to patients with severe impairment or risk of injury.

We rated the strength of evidence as high for the adverse effects of both medications, moderate for the ability of risperidone to affect challenging behaviors, and high for aripiprazole's effects on challenging behaviors.

Allied health. The allied health interventions reviewed here were varied and reported in 17 unique studies.¹⁶²⁻¹⁸⁴ The research provided little support for their use. Specifically, all studies of sensory integration and music therapy were of poor quality, and two fair-quality studies of auditory integration showed no improvement associated with treatment.^{173, 174} Language and communication interventions (Picture Exchange Communication System [PECS] and Responsive Education and Prelinguistic Milieu Training [RPMT]) demonstrated short-term improvement in word acquisition without effect durability, and should be studied further.¹⁶²⁻¹⁶⁵ No other allied health interventions had adequate research to assess the strength of evidence.

CAM. Evidence for CAM interventions is insufficient for assessing outcomes.¹⁸⁵⁻¹⁹¹

KQ2. Modifiers of Treatment Outcomes

With rare exceptions,^{163, 164, 192} few studies are designed or powered to identify modifiers of treatment effect. Although we sought studies of treatment modifiers, only one included study actually demonstrated true treatment modifiers based on appropriate study design and statistical analysis.^{163, 164} One other study¹⁹² was designed to examine the role of provider on outcomes but showed no difference, possibly because it was underpowered to do so.

This first study¹⁶³ included an analysis of initial characteristics of the children, demonstrating that children who were low in initial object exploration benefited more from RPMT, which explicitly teaches play with objects, while children who were relatively high in initial object exploration demonstrated more benefit from PECS. An additional analysis¹⁶⁴ showed greater increases in generalized turn-taking and initiating joint attention in the RPMT group than in PECS. The increased benefit in joint attention for RPMT was seen only in children who began the study with at least seven acts of joint attention.

One study¹⁹² explicitly sought to examine the impact of provider (parent vs. professional) using similar interventions in an RCT. The study did not show a difference in outcomes for children receiving the UCLA/Lovaas protocol-based intervention in a clinical setting vs. at home from highly trained parents.

Other studies identified potential correlates that warrant further study. Modifiers with potential for further investigation but with currently conflicting data included 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,¹⁹² whereas “aloof” subtypes of ASDs may be associated with less robust changes in IQ.¹⁶ Other studies have seen specific improvement in children with PDD-NOS vs. Autistic Disorder diagnoses,²³ 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. Early Results in the Treatment Phase That Predict Outcomes

The literature offers almost no information about specific observations of children that might be made early in treatment to 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.^{37, 192} However, findings also suggest that although gains in the cognitive domain might be identified primarily within the first year of treatment, changes in adaptive behavior in response to these same interventions may occur over a longer timeframe,^{19, 37, 45, 192} if they occur at all.¹³

KQ4. End-of-Treatment Effects That Predict 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 postintervention.^{65, 66}

KQ5. Generalization of Treatment Effects

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.

For medical studies, data across classes of medications are likely to be transferable outside of the clinic setting, primarily because the outcome measures used in these studies rely on parent report of the subjects' behavior in the home or other settings and are augmented in some studies by teacher report.

KQ6. Drivers of Treatment Effects

No studies were identified to answer this question.

KQ7. Treatment Approaches in Children Under Age 2 at Risk for ASDs

Research on very young children is preliminary, with four studies identified.^{15, 34, 37, 42} One good-quality RCT suggested benefit from the use of ESDM in young children,³⁷ 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.

Discussion

Key Findings

In the behavioral literature, some evidence supports early and intensive behavioral and developmental intervention, including intensive approaches (provided >30 hours per week) and comprehensive approaches (addressing numerous areas of functioning). These included a UCLA/Lovaas-focused approach and developmentally focused ESDM approach.^{23, 37} Both approaches were associated with greater improvements in cognitive performance, language skills, and adaptive behavior skills compared with broadly defined eclectic treatments in subgroups of children, although the strength of evidence (confidence in the estimate) is low pending replication of the available studies.

Not all children receiving such interventions demonstrate rapid gains. Some data suggest that many children continue to display prominent areas of impairment and that subgroups may account for a majority of the change within certain samples.²³ No studies directly compare effects of different treatment approaches (for example, there are no direct comparisons of UCLA/Lovaas and ESDM) and little evidence of practical effectiveness or feasibility beyond research studies exists, so questions remain about whether reported findings would be observed on a larger scale within communities. Furthermore, existing studies have used small samples, different treatment approaches and duration, and different outcome measurements. Nonetheless, improvements occur in some aspects of language, cognitive ability, adaptive behavior, challenging behaviors, and potentially, educational attainment, for some children.

Strength of evidence is insufficient for the effects of social skills training for older children and for play- and interaction-based approaches for younger children. Cognitive behavioral therapy (CBT) for associated conditions such as anxiety also has insufficient strength of evidence supporting positive outcomes.

The strength of evidence is insufficient to provide confidence in observed improvements in cognitive outcomes with educational interventions, including the TEACCH intervention, and there is insufficient evidence for broad-based educational approaches, often based on applied behavior analysis (ABA) principles and computer-based approaches.

A few medications show benefit for repetitive behaviors or associated symptoms, with the clearest evidence favoring risperidone and aripiprazole, both studied in RCTs and showing evidence of improvement in problem and repetitive behavior. Significant side effect profiles, however, make it clear that although these drugs are efficacious, caution is warranted regarding their use in patients without severe impairments or risk of injury.

A few other medical interventions show some promise for future research, including serotonin reuptake inhibitors (SRIs),¹²⁸⁻¹³⁰ methylphenidate,^{131-134, 136} omega 3 fatty acids,¹⁵⁴ and melatonin.¹⁵³ Others, including secretin,¹³⁷⁻¹⁴⁴ are clearly not efficacious and warrant no further study.

Evidence is insufficient at this time to support the use of sensory or auditory integration, insufficient for speech and language interventions, and insufficient for CAM approaches.

Applicability of Evidence

By definition, ASDs are heterogeneous. Characterizing a “typical” child with an ASD is not possible, although certain symptoms are central to the range of children within the autism spectrum. Individual therapies are developed and tested to ameliorate specific symptoms or groups of symptoms, often in a fairly circumscribed subset of children.

Behavioral interventions. Studies of early intensive behavioral and developmental interventions were conducted primarily in preschool and young children (typically children initially ages 2-7 years). Questions remain about how these approaches apply to and benefit younger children (under 2) at risk for ASD. The cognitive, language, and adaptive behavior profiles of participants included in these studies were generally in line with those typically seen in young children with ASD. Participants typically had substantial impairment or delay, but some children had less early cognitive/language impairment.

The range of approaches studied may not always match what is available in practice—that is, either the studies were often conducted in highly controlled environments (e.g., university-supported intervention trials) or the actual methodology was not well described (i.e., approaches lacking treatment manuals). Thus, individuals wishing to infer the potential results of clinical practice based on the available research need to assess carefully the degree to which the study methods matched those available and used in practice.

Most studies of social skills interventions targeted children of elementary school age (6-13 years old). Most also excluded children with IQs below 60. Therefore, evidence on social skills interventions is likely applicable only to older, higher functioning children. Similarly, CBT for commonly associated conditions was targeted toward older children who were higher functioning. The effectiveness of both of these types of interventions in other groups of children with ASDs is currently unknown.

Medical and related interventions. In the medical literature, study participants were generally recruited from non-primary-care populations. Such individuals’ parents may be seeking a higher level of care than is the case for the broader population of children with ASDs, based on more severe or acute symptoms, including aggression or other challenging behaviors. Most studies of medical interventions targeted elementary-school-age and older children with autism, with little data on the treatment of younger children. Some studies also expanded their inclusion criteria to include children with Asperger syndrome or PDD-NOS.

Gaps in the Evidence and Methodologic Concerns

Roughly 40 percent of studies in this review failed to use a comparison group. This lack of comparison groups presents substantial challenges for assessing effectiveness at a population level or for conducting comparative effectiveness research.

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 these studies do not include at least 10 participants and are therefore not represented in the review. Single-subject design studies can be helpful in assessing response to treatment in very short timeframes and under very tightly controlled circumstances, but they typically do not provide information on longer term or functional outcomes. They are useful in serving as demonstration projects, yielding initial evidence that an intervention merits further study, and in the clinical environment, they can be useful in identifying whether a particular approach to treatment is likely to be helpful for a specific child. Our goal was to identify and review the best evidence for assessing the effectiveness of therapies for children with ASDs, with an eye toward utility in the clinical setting and for the larger population of children with ASDs. By definition, “populations” in single-subject design studies are likely to be idiosyncratic and therefore unlikely to provide information that is generalizable.

Even in studies with a comparison group, sample size is frequently insufficient to draw conclusions. Larger multisite trials are needed across all treatment types. A few studies used comparison groups that were

inappropriate for observing group differences in treatment effect (e.g., comparing treatment effects in children with autism to the effects of the treatment in typically developing peers or to children with a different developmental disorder). For those studies we could use only the pre-post case series data available in the group with autism, limiting the ability to comment on effectiveness.

We encourage 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, but many studies made 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.

Characterization of the study population was often inadequate, with 125 of 159 studies failing to use or report gold standard diagnostic measures (clinical DSM-IV-based diagnosis plus ADI and/or ADOS). Because ASDs are spectrum disorders, it is difficult to assess the applicability of interventions when the population in which they were studied is poorly defined or described.

We identified more than 100 distinct outcome measures used in this literature base, not accounting for subscales of many. The use of so many and such disparate outcome measures makes it nearly impossible to synthesize the effectiveness of the interventions. We recommend a consistent set of rigorously evaluated outcome measures specific to each intended target of treatment to move comparative effectiveness research forward and to provide a sense of expected outcomes of the interventions. At the same time, the means for assessing outcomes should include increased focus on use of observers masked to the intervention status of the participant. When some outcomes are measured in a masked fashion but others not, evaluators should place more emphasis on those that are masked.

We noted a strong tendency for authors to present data on numerous outcomes without adjusting for multiple comparisons. Investigators also failed to report the outcome that was the primary outcome of a priori interest and on which, presumably, they based sample-

size calculations (when these calculations were present). This may suggest the presence of selective reporting. We attempted to identify a primary intended outcome in the papers, but in almost all cases we were unable to do so.

Duration of treatment and followup was generally short. Few studies provided data on long-term outcomes after cessation of treatment. Future studies should extend the followup period and assess the degree to which outcomes are durable. Few studies adequately accounted for concomitant interventions that might confound observed effectiveness. Accounting for concomitant interventions should be standardized in future research.

Areas for Future Research

A critical area for further research is identifying which children are likely to benefit from particular interventions. 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 than in others. One powerfully replicated finding in the available behavioral literature is that not all children receiving early intensive intervention demonstrate robust gains, and many children continue to display prominent areas of impairment. Dramatic improvements are observed in a subset of children, and mild improvements in terms of standardized outcomes are seen in others. This fact may translate into meaningful improvements in quality of life for some children and family members, suggesting that early intensive approaches have significant potential but require further research.

Behavioral interventions by their nature often employ multiple components, and data on whether specific functional components of the interventions drive effectiveness are currently unavailable. Component analyses in this field would be productive for refining intervention approaches and for assessing applicability and generalizability of the results.

Health services research on feasibility and accessibility is currently lacking, and given the growing number of children diagnosed with an autism spectrum disorder, it is needed. A few studies in this literature made preliminary strides in addressing these issues, but studies that specifically measure the role of setting,

provider, and other factors would strongly benefit our ability to inform implementation practices. In line with this need, we recommend future consideration of the ways in which the cultural context of the child and family may affect the applicability or effectiveness of specific interventions.

The medical literature lacks properly designed, appropriately powered RCTs of a number of interventions that have been inadequately studied to date. Some of the strongest studies to support the use of medical interventions have been funded by pharmaceutical companies or device manufacturers that profit from the treatment. Certainly, the NIH (National Institutes of Health) has funded some large-scale studies of a few medical interventions, but publicly funded studies of medications for ASDs are few and more are warranted.

Also lacking in the literature are comparisons of medical interventions with behavioral interventions and combinations of the two, despite the fact that most children are undergoing multiple concurrent treatments. Harms data are also typically not reported in nonmedical studies, although potential harms of behavioral and other interventions should not be discounted.

In sum, while some therapies hold promise and warrant further study, substantial needs exist for continuing improvements in methodologic rigor in the field and for larger, potentially multisite studies of existing interventions. New studies should better characterize children, both phenotypically and genotypically, to move toward personalization of treatments for improved outcomes.

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